IMPROVING WELLBEING IN PATIENTS WITH CHRONIC CONDITIONS: THEORY, EVIDENCE, AND OPPORTUNITIES

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Table of Contents

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Editorial: Improving Wellbeing in Patients With Chronic Conditions: Theory, Evidence, and Opportunities

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Editorial on the Research Topic

Improving Wellbeing in Patients With Chronic Conditions: Theory, Evidence, and Opportunities

The global epidemiological transition characterizes a shift in the nature of health and disease from acute disease to chronic conditions. Chronic conditions have now superseded acute conditions as leading burdens of morbidity, mortality, and health care expenditures (Murray and Lopez, 1997a,b; Ferrari et al., 2014). In fact, 80.45% of years lived with disability (YLDs) are attributable to chronic conditions, including back pain, depressive, and headache disorders (http://ihmeuw.org/5nrp). Furthermore, despite an increasing lifespan, we are living with more disease and infirmity (Vos et al., 2015; Kyu et al., 2018). Despite this transition our models of health care have not adapted to reflect these changes (Murray and Lopez, 1997b). Accordingly, there is an urgent need to develop more effective approaches to managing chronic conditions both to enhance care and to address the burden chronic conditions are posing on healthcare systems. It is timely then to discuss the theory, evidence, and opportunities for building wellbeing in the increasing number of people who are living with conditions. Conditions that must be managed and for which "cure" is seldom possible.

THEORETICALLY INFORMED HOLISTIC INTERVENTIONS ARE NEEDED

Despite being designed to treat acute illness and disease, "the acute medical model" has become the dominant model of healthcare. We have argued that this model of healthcare constrains opportunities to develop evidenced based holistic approaches for supporting people living with chronic conditions (Fisher et al., 2022; Kemp and Fisher, 2022). There is a pressing need for approaches that consider all domains of functioning (biological, cognitive, emotional, social) and their interactions as well as considering the influence of wider systemic factors such as our relationships, community, environment and socio-contextual factors (Wilson et al., 2009; Gracey et al., 2015; Mead et al., 2019, 2021; Wilkie et al., 2021; Fisher et al., 2022). This point is illustrated by several studies of disease burden included in our Research Topic (Belrose et al.; Barreira et al.; Biehl et al.; Huber and Havas; Bossy et al.).

For instance, Barreira et al. describe the profound impact of hepatitis C virus (HCV) on health, cognition and psychological wellbeing. The authors highlight the need for theoretically informed

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holistic interventions that address the physical, cognitive, psychological and social sequelae of the disease in order to provide more effective outcomes. Similarly, a study by Biehl et al. explored the relationship between personality, perceived stress and tinnitus related distress. The authors reported significant differences on a variety of personality indices compared to the general population, and that tinnitus-related distress is mediated by differential interactions between personal factors and perceived stress. The role of emotion-focused treatment strategies are emphasized including for example, compassion focused therapy or schema therapy. Another study by Huber and Havas points out that although cochlear implants have been shown to support language development in hearing-impaired children, speech recognition in noisy environments remains limited. This has implications for the quality of life of children and adolescents with cochlear implants highlighting a need for broader solutions including psychological support and environmental modification. Finally, the paper by Bossy et al. emphasize a need to compare different psychological treatment options for patients diagnosed with schizophrenic psychosis in an inpatient settings. The authors present a protocol for a randomized controlled trial of a novel treatment intervention to improve neuro- and social-cognition as well as emotion regulation skills.

Chronic conditions are often associated with comorbidity and "multimorbidities" (Harrison et al., 2021). Multimorbility has been identified as a priority for research (Mangin et al., 2018) and health care systems (Whitty et al., 2020) because it is highly prevalent occurring in a third of adults living in the community (Nguyen et al., 2019) and differentially affecting those from the most socioeconomically disadvantaged communities (McLean et al., 2014). By means of example, two papers in our Research Topic report on the prevalence of psychiatric comorbidity alongside other chronic conditions. In a paper by Alsaadi et al., psychiatric comorbidity in neurological disorders is reported to be as high as 39% for symptoms of depression and 34% for anxiety. A related paper by Almeida et al. reports on the prevalence of major depressive disorder in patients with variety of chronic diseases including diabetes, rheumatoid arthritis, cancer and Parkinson's disease. The authors point out that the prevalence of major depressive disorder is two- to three-fold higher in patients with chronic diseases than in the general population. Consistent with these reports, a recent meta-analysis reported a pooled prevalence of psychiatric disorders in patients with chronic physical diseases of 36.6% (95% CI 31.4–42.1) and a pooled odds ratio of 3.1 (95% CI, 1.7–5.2; Daré et al., 2019). A critical issue here is that psychological distress is associated with premature mortality in a dose response relationship (Russ et al., 2012) and that psychiatric disorders, which are themselves chronic conditions, have the potential to reduce life expectancy, with impacts that are equivalent to, and sometimes exceed, the effects of heavy smoking (Chesney et al., 2014). These findings are in keeping with many robust epidemiological studies showing that physical diseases and common mental health conditions are strongly inter-connected, highly co-morbid and share critical pathways to ill health and disease (Verhaak et al., 2005; Druss and Walker, 2011; O'Neil et al., 2015; Dai et al., 2020). This is not surprising given compelling evidence of a tight coupling between pathways subserving both physical and mental health (Thayer et al., 2009; Kemp et al., 2017b).

REDUCING ILLBEING IS NOT THE SAME AS PROMOTING WELLBEING

It has become commonplace for the construct of wellbeing to be interpreted as synonymous with the "absence of distress" rather than being associated with the presence of key determinants of wellbeing. Similarly, health has also been viewed as the absence of illness or disease. Such ideas have been enshrined in models of healthcare which are often centered around reducing impairment and distress. Again, this bias misses opportunities to promote acceptance of difficult emotions and life experiences that cannot be changed and this is the crux of the experience of those who must live with a chronic condition(s). It also neglects the growing evidence highlighting the role of promoting positive emotion to facilitate creative, flexible, and novel ways of thinking and behaving, that builds lasting physical, intellectual, psychological, and social resources (Fredrickson, 1998; Boehm and Kubzansky, 2012; Lee et al., 2019; Rozanski et al., 2019). Moreover, positive emotions and wellbeing have important implications for morbidity from a host of conditions and disease as well as premature mortality (DuBois et al., 2012; Steptoe et al., 2015). Accordingly, our Research Topic includes papers that are consistent with positive psychology and third wave CBT (e.g., mindfulness). Here the emphasis is on changing one's relationship with difficult thoughts (Robinson et al., 2019) thereby promoting acceptance and emotional balance as well as building positive emotions. For example, through connection with the present moment as well as through practicing exercises and activities that promote positive emotion (e.g., Tulip et al.; Di Giacomo et al.; Rowlands et al.; Marks et al.; Rodrigues et al.; Wigham et al.). These studies report on the potential for improvements in a range of wellbeing-related variables including connection, kindness, compassion, equanimity, quality of life, coping behaviors, self-concept, and positive mood. Taken together, this work shows the potential for promoting wellbeing in people living with chronic conditions.

THEORETICAL FOUNDATIONS

Our Research Topic includes several papers that explore the theoretical foundations for promoting wellbeing in people living with chronic conditions, shedding light on the potentially contradictory idea that people living in ill-health also have capacity for wellbeing. The unique perspective article by Hunter presents a clinician and service users' perspective on managing multiple sclerosis based on the P-P-P [Pleasure-Purpose-Practice] framework, encompassing core principles from positive psychology and behavior change science. Hunter emphasizes that it is indeed possible to experience "pleasure" despite pain or disability, highlighting that the experience of positive and negative emotions is not mutually exclusive. In another original research article, Roşca et al. report on the experiences of patients who had suffered limb amputation, observing that despite the experience of negative emotions (e.g., anxiety, guilt, and anger), social isolation and constraints on roles and routines, participants also presented with hope and determination to prevail, when supported by family, friends, and colleagues.

These insights are consistent with theory. For instance, the two continua model (Westerhof and Keyes, 2010) presents mental illness and (positive) mental health as related but distinct phenomena, reinforcing the possibility that one can experience ill-health (including mental illness) *at the same time as* a moderate level of mental health. Intriguingly, two papers in our Research Topic sought to test this hypothesis. The first, included people with DSM-5 diagnoses related to paranoid thinking (including Schizophrenia, Brief Psychotic Disorder, Delusional Disorder, or Substance/Medication-Induced Psychotic Disorder) who were without mood symptoms (Asensio-Aguerri et al.). The second included people living with an eating disorder (de Vos et al.). Reported findings were consistent with the two-continua model including the observation that positive mental health and paranoid thinking lay on two—rather than one—unipolar dimensions, and that 13% of those with eating disorders reported high levels of wellbeing (flourishing). Our own study published in this Research Topic (Tulip et al.) reports that an 8-week positive psychotherapy intervention facilitated positive emotions, empowerment, skills, and social opportunity in people living with acquired brain injury. Together, these findings defy the stereotype that "people living with chronic conditions do not have capacity for wellbeing." This work aligns closely with that of psychologist, Paul Wong, who emphasizes the important roles of meaning and purpose in life for experiencing wellbeing despite hardship and suffering, ideas that have been described as second wave positive psychology (Wong, 2019).

Other papers in our Research Topic also raise interesting considerations relating to identity (Kerr et al.), quality of life (Wigham et al.), and post-traumatic growth (Pérez-San-Gregorio et al.). For instance, the conceptual analysis by Kerr et al. describes a novel coaching-related intervention that is used to facilitate adaptive change with a focus on building skills to reconstruct narrative identity and foster hope. Often when one develops a chronic condition, the person will experience significant biopsychosocial disruption including pathology-related impact, impairments in cognition and emotions and reduced capacity to engage in activities that were previously enjoyed. This can lead to subjective sense of "threats to identity" (Gracey et al., 2019) profoundly linked to social and interpersonal contexts (Gracey et al., 2008; Gracey and Ownsworth, 2012). The Y-Shaped model of rehabilitation (Gracey et al., 2009) focuses intervention on the psychological and social discrepancies between the current and ideal "selves," and moving forwards to identify and build on continuities in identity, as realized and experienced through the lived environment. A similar point is made in the narrative approach to identity adaptation following stroke or brain injury (Ellis-Hill et al., 2009; Whiffin et al., 2021). Moving beyond identity reconstruction, the article by Pérez-San-Gregorio et al. reports on the capacity for people undergoing liver transplants to experience post-traumatic growth, an experience that is motivated by personal distress and a need to regain intra-psychic balance.

OPPORTUNITIES TO PROMOTE MENTAL AND PHYSICAL HEALTH

Our own work (Kemp and Quintana, 2013; Kemp et al., 2017a; Mead et al., 2021) as well as others have emphasized the vagus nerve as a structural link between physical and mental health. The vagus connects the central nervous system to many different organs including heart, gut, liver, and lungs. Vagal afferent fibers represent the most important function of the vagus, sending information from the viscera to the brain (Breit et al., 2018), providing a key pathway through which positive health behaviors may beneficially impact on mind. Reflecting a growing interest in the potential benefits of mind-body interventions to promote wellbeing in people living with chronic conditions, our Research Topic included papers on yoga (Telles et al.), dohsa-hou body movement relaxation tasks (Haramaki et al.; Zhu et al.). In their review article, Tarsha et al. further describe how a variety of physical interventions including massage therapy, tai-chi and dance therapy alleviate depression, anxiety, and stress while facilitating pain reduction through bidirectional pathways, which may include the vagus. In their systematic review, Edwards and Pinna examine the associations between vagal nerve function, interoception, and emotional regulation, which have important implications for wellbeing in people living with chronic conditions. Vagal nerve functioning was associated with better emotion regulation and psychological flexibility, suggesting that various interventions known to impact on vagal function may help to reduce psychological distress and promote wellbeing in people living with chronic conditions. A variety of interventions have been shown to improve vagal function including meditation, relaxation, nutrition, exercise, social connection, and spending time in nature (Kok et al., 2013; Richardson et al., 2016; Laborde et al., 2018; Young and Benton, 2018). We have sought to synthesize these findings in our GENIAL model of wellbeing, in which we define wellbeing as connection to self, others and nature, supported by functioning of the vagus nerve, which appears to provide a psychophysiological resource for connection and the subsequent experience of wellbeing (Kemp et al., 2017a; Mead et al., 2021; Kemp and Fisher, 2022).

OPPORTUNITIES TO PROMOTE SOCIAL WELLBEING

The study by Zhang et al. investigated the relationships among social support, physical comorbidity, health literacy, and depression in patients with hypertension in China, reporting that physical comorbidity is positively associated with depression, while health literacy and social support were negatively associated. The authors suggested that health education programmes combined with community-based activities may help to reduce the experience of depression.

Several other papers in this Research Topic focus on community-based interventions in order to promote wellbeing in people living with chronic conditions (Tong et al.; Faw et al.; Smith et al.). For instance, the paper by Smith et al. report on the impact of an intergenerational dementia education program, with qualitative interview revealing positive changes in children's empathy and improved community awareness. The authors further highlighted the need for support from school and community partners as key to the success of the program. Of the 12 older adults and four carers interviewed, the intergeneration program was associated with positive emotions as a result of interacting with the children and positive self-changes.

OTHER OPPORTUNITIES

Other papers in our Research Topic focused on how digital health technologies might be used to promote wellbeing in people who live with chronic conditions. The study by Wulfovich et al. for example, was an explorative mixed-method study of 200 chronically ill patients, documenting how mobile apps and wearables might be designed to better promote self-efficacy, especially in regards to activities relating to chronic disease management. These ideas are expanded on in the opinion article by Bedrov and Bulaj, who focus on opportunities to promote positive thinking, self-esteem, and empowerment using motivational quotes through digital health technologies. The authors suggest that different categories of motivational quotes may be tailored for specific causes of low self-esteem. For example, when low self-esteem arises as a function of negatively comparing oneself to others, one approach might be to design motivational quotes encouraging positive self-evaluation allowing the recognition of personal strengths and values. Another article by Gorini et al. discusses how patients might not only be empowered in disease management but also in the achievement of positive experiences and experiential growth to find innovative and personalized ways to improve care using mobile health technology. Another paper by Faw et al. explored the potential for virtual reality to be used as a salutogenic design intervention for 16 older adults including three participants with dementia and two spousal caregivers. Although in early development, the authors argue for potential application amongst those who struggle to access "in real life" events due to conditions such as dementia, highlighting opportunities to increase enjoyment and engagement.

Taken together this work touches upon the huge potential of digital technology solutions, along with other assistive technology, to have a positive impact on health and wellbeing for those living with chronic conditions. However, a meta-synthesis from our own group show that complex barriers exist to acquiring and using appropriate assistive technology for people with chronic conditions. Barriers relate to the devices themselves, the individual context, healthcare context and wider societal barriers such as stigma (Howard et al., 2020). Finding interventions to overcome such barriers, for example greater involvement of patients in the design and provision of assistive technology, will help provide more usable assistive technology solutions that assist in empowering the individual in better managing their own health, improving independence, enabling great social connections, and as such promoting wellbeing. It is important assistive technology is integrated as a tool alongside other interventions in seeking to impact on health and wellbeing and that people living with chronic conditions are involved in the design of such interventions where possible.

DISCUSSION AND CONCLUSIONS

In summary, our Research Topic encompasses a total of 31 articles that together highlight the societal burden associated with a variety of chronic conditions, while also emphasizing theory and potential interventions for facilitating wellbeing in those who must live with such conditions. There is, across this work, a clear argument for an integrated, holistic approach to wellbeing within a biopsychosocial framework that is connected to the wider sociostructural and cultural context. From this body of work there is hope for radical developments in the application of technology, traditional cultural practices such as art, music, Tai Chi, and storytelling and psychological interventions to improve wellbeing in chronic conditions. It is now incumbent on us working in academia and the healthcare sector to realize the many opportunities for promoting wellbeing in chronic conditions, especially given the increasing available evidence emphasizing the bidirectional impacts between mental and physical health that may—if not addressed—contribute to years lived with disability and lives lost. We hope that this Research Topic will inspire more researchers to further develop the emerging evidence base that explores capacity of people with a chronic condition to experience wellbeing.

AUTHOR CONTRIBUTIONS

AK and ZF wrote the first draft of the editorial, which FG and JT subsequently refined for publication. All authors were Research Topic editors. All authors contributed to the article and approved the submitted version.

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REFERENCES

Boehm, J. K., and Kubzansky, L. D. (2012). The heart's content: the association between positive psychological well-being and cardiovascular health. *Psychol. Bull.* 138, 655. doi: 10.1037/a0027448

Breit, S., Kupferberg, A., Rogler, G., and Hasler, G. (2018). Vagus nerve as modulator of the brain–gut axis in psychiatric and inflammatory disorders. *Front. Psychiatry* 9, 44. doi: 10.3389/fpsyt.2018.00044

Chesney, E., Goodwin, G. M., and Fazel, S. (2014). Risks of all-cause and suicide mortality in mental disorders: a meta-review. *World Psychiatry* 13, 153–160. doi: 10.1002/wps.20128

Dai, H., Mei, Z., An, A., and Wu, J. (2020). Epidemiology of physical and mental comorbidity in Canada and implications for health-related quality of life, suicidal ideation, and healthcare utilization: a nationwide cross-sectional study. *J. Affect. Disord.* 263, 209–215. doi: 10.1016/j.jad.2019.11.146

Daré, L. O., Bruand, P.-E., Gérard, D., Marin, B., Lameyre, V., Boumédiène, F., et al. (2019). Co-morbidities of mental disorders and chronic physical diseases in developing and emerging countries: a meta-analysis. *BMC Public Health* 19, 304. doi: 10.1186/s12889-019-6623-6

Druss, B. G., and Walker, E. R. (2011). *Mental Disorders and Medical Comorbidity. The Synthesis Project.* Research Synthesis Report, Robert Wood Johnson Foundation, 1–26.

DuBois, C. M., Beach, S. R., Kashdan, T. B., Nyer, M. B., Park, E. R., Celano, C. M., et al. (2012). Positive psychological attributes and cardiac outcomes: associations, mechanisms, and interventions. *Psychosomatics* 53, 303–318. doi: 10.1016/j.psym.2012.04.004

Ellis-Hill, C., Payne, S., and Ward, C. (2009). Using stroke to explore the Life Thread Model: an alternative approach to understanding rehabilitation following an acquired disability. *Disabil. Rehabil.* 30, 150–159. doi: 10.1080/09638280701195462

Ferrari, A. J., Norman, R. E., Freedman, G., Baxter, A. J., Pirkis, J. E., Harris, M. G., et al. (2014). The burden attributable to mental and substance use disorders as risk factors for suicide: findings from the global burden of disease study 2010. *PLoS ONE* 9, e91936. doi: 10.1371/journal.pone.0091936

Fisher, Z., Galloghly, E., Boglo, E., Gracey, F., and Kemp, AH. (2022). "Emotion, wellbeing and the neurological disorders," in *Reference Module in Neuroscience and Biobehavioral Psychology, 2nd ed.* (Amsterdam: Elsevier), 220–234. doi: 10.1016/b978-0-12-819641-0.00013-x

Fredrickson, B. L. (1998). What good are positive emotions? *Rev. Gen. Psychol.* 2, 300–319. doi: 10.1037/1089-2680.2.3.300

Gracey, F., Evans, J. J., and Malley, D. (2009). Capturing process and outcome in complex rehabilitation interventions: a "Y-shaped" model. *Neuropsychol. Rehabil.* 19, 867–890. doi: 10.1080/09602010903027763

Gracey, F., Olsen, G., Austin, L., Watson, S., and Malley, D. (2015). "Integrating psychological therapy into interdisciplinary child neuropsychological rehabilitation," in *Neuropsychological Rehabilitation of Childhood Brain Injury*, eds J. Reed, K. Byard, H. Fine (London: Palgrave Macmillan), pp. 191–214.

Gracey, F., and Ownsworth, T. L. (2012). "The experience of self in the world: The personal and social contexts of identity change after brain injury," in *The Social Cure: Identity, Health and Well-Being*, eds J. Jetten, C. Haslam and S. A. Haslam (Hove: Psychology Press), 273–295.

Gracey, F., Palmer, S., Rous, B., Psaila, K., Shaw, K., O'Dell, J., et al. (2008). "Feeling part of things": Personal construction of self after brain injury. *Neuropsychol. Rehabil.* 18, 627–650. doi: 10.1080/09602010802041238

Gracey, F., Smits, P., du Toit, P., Fish, J., and Psaila, K. (2019). "Application of the cognitive behavioural approach to enhancing emotional outcomes following acquired brain injury (ABI)," in *Psychological Therapies in Acquired Brain Injury*, eds G. N. Yeates and F. Ashworth (London: Routledge), 1–22. doi: 10.4324/9780429506796

Harrison, C., Fortin, M., Akker, M., van den, Mair, F., Calderon-Larranaga, A., Boland, F., et al. (2021). Comorbidity versus multimorbidity: why it matters. *J. Comorbid.* 11, 2633556521993993. doi: 10.1177/2633556521993993

Howard, J., Fisher, Z., Kemp, A. H., Lindsay, S., Tasker, L. H., and Tree, J. J. (2020). Exploring the barriers to using assistive technology for individuals with chronic conditions: a meta-synthesis review. *Disabil. Rehabil.* 1–19. doi: 10.1080/17483107.2020.1788181

Kemp, A. H., Arias, J. A., Fisher, Z. (2017a). "Social ties, health and wellbeing: A literature review and model," in *Neuroscience and Social Science*, eds A. Ibáñez, L. Sedeño and A. García (New York, NY: Springer International Publishing), 397–427.

Kemp, A. H., and Fisher, Z. (2022). Wellbeing, whole health and societal transformation: theoretical insights and practical applications. *Glob. Adv. Health Med.* 11, 1–16. doi: 10.1177/21649561211073077

Kemp, A. H., Koenig, J., and Thayer, J. F. (2017b). From psychological moments to mortality: a multidisciplinary synthesis on heart rate variability spanning the continuum of time. *Neurosci. Biobehav. Rev.* 83, 547–567. doi: 10.1016/j.neubiorev.2017.09.006

Kemp, A. H., and Quintana, D. S. (2013). The relationship between mental and physical health: insights from the study of heart rate variability. *Int. J. Psychophysiol.* 89, 288–296. doi: 10.1016/j.ijpsycho.2013.06.018

Kok, B., Coffey, K., Cohn, M., Catalino, L., Vacharkulksemsuk, T., Algoe, S., et al. (2013). How positive emotions build physical health: perceived positive social connections account for the upward spiral between positive emotions and vagal tone. *Psychol. Sci.* 24, 1123–1132. doi: 10.1177/0956797612470827

Kyu, H. H., Abate, D., Abate, K. H., Abay, S. M., Abbafati, C., Abbasi, N., et al. (2018). Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 392, 1859–1922. doi: 10.1016/s0140-6736(18)32335-3

Laborde, S., Mosley, E., and Ueberholz, L. (2018). Enhancing cardiac vagal activity: factors of interest for sport psychology. *Prog. Brain Res.* 240, 71–92. doi: 10.1016/bs.pbr.2018.09.002

Lee, L. O., James, P., Zevon, E. S., Kim, E. S., Trudel-Fitzgerald, C., Spiro, A., et al. (2019). Optimism is associated with exceptional longevity in 2 epidemiologic cohorts of men and women. *Proc. Nat. Acad. Sci. U.S.A.* 116, 18357–18362. doi: 10.1073/pnas.1900712116

Mangin, D., Bahat, G., Golomb, B. A., Mallery, L. H., Moorhouse, P., Onder, G., et al. (2018). International group for reducing inappropriate medication use and polypharmacy (IGRIMUP): position statement and 10 recommendations for action. *Drugs Aging* 35, 575–587. doi: 10.1007/s40266-018-0554-2

McLean, G., Gunn, J., Wyke, S., Guthrie, B., Watt, G. C., Blane, D. N., et al. (2014). The influence of socioeconomic deprivation on multimorbidity at different ages: a cross-sectional study. *Br. J. Gen. Pract.* 64, e440–e447. doi: 10.3399/bjgp14x680545

Mead, J., Fisher, Z., and Kemp, A. (2021). Moving beyond disciplinary silos towards a transdisciplinary model of wellbeing: an invited review. *Front. Psychol.* 12, 642093. doi: 10.3389/fpsyg.2021.642093

Mead, J., Fisher, Z., Wilkie, L., Gibbs, K., Pridmore, J., Tree, J., et al. (2019). Rethinking wellbeing: Toward a more ethical science of wellbeing that considers current and future generations. *Authorea. [Preprint].* doi: 10.22541/au.156649190.08734276

Murray, C. J., and Lopez, A. D. (1997a). Alternative projections of mortality and disability by cause 1990–2020: global burden of disease study. *Lancet* 349, 1498–1504. doi: 10.1016/s0140-6736(96)07492-2

Murray, C. J., and Lopez, A. D. (1997b). Global mortality, disability, and the contribution of risk factors: global burden of disease study. *Lancet* 349, 1436–1442. doi: 10.1016/s0140-6736(96)07495-8

Nguyen, H., Manolova, G., Daskalopoulou, C., Vitoratou, S., Prince, M., and Prina, A. M. (2019). Prevalence of multimorbidity in community settings: a systematic review and meta-analysis of observational studies. *J. Comorbid.* 9, 2235042X19870934. doi: 10.1177/2235042x19870934

O'Neil, A., Jacka, F. N., Quirk, S. E., Cocker, F., Taylor, C. B., Oldenburg, B., et al. (2015). A shared framework for the common mental disorders and Non-Communicable Disease: key considerations for disease prevention and control. *BMC Psychiatry* 15, 15. doi: 10.1186/s12888-015-0394-0

Richardson, M., McEwan, K., Maratos, F., and Sheffield, D. (2016). Joy and calm: how an evolutionary functional model of affect regulation informs positive emotions in nature. *Evol. Psychol. Sci.* 2, 308–320. doi: 10.1007/s40806-016-0065-5

Robinson, P. L., Russell, A., and Dysch, L. (2019). Third-wave therapies for long-term neurological conditions: a systematic review to evaluate the status and quality of evidence. *Brain Impair.* 20, 58–80. doi: 10.1017/brimp.2019.2

Rozanski, A., Bavishi, C., Kubzansky, L. D., and Cohen, R. (2019). Association of optimism with cardiovascular events and all-cause mortality. *JAMA Netw. Open* 2, e1912200. doi: 10.1001/jamanetworkopen.2019.12200

Russ, T. C., Stamatakis, E., Hamer, M., Starr, J. M., Kivimäki, M., and Batty, G. D. (2012). Association between psychological distress and mortality: individual participant pooled analysis of 10 prospective cohort studies. *BMJ* 345, e4933. doi: 10.1136/bmj.e4933

Steptoe, A., Deaton, A., and Stone, A. A. (2015). Subjective wellbeing, health, and ageing. *Lancet* 385, 640–648. doi: 10.1016/s0140-6736(13)61489-0

Thayer, J. F., Hansen, A. L., Saus-Rose, E., and Johnsen, B. H. (2009). Heart rate variability, prefrontal neural function, and cognitive performance: the neurovisceral integration perspective on self-regulation, adaptation, and health. *Ann. Behav. Med.* 37, 141–153. doi: 10.1007/s12160-009-9101-z

Verhaak, P. F. M., Heijmans, M. J. W. M., Peters, L., and Rijken, M. (2005). Chronic disease and mental disorder. *Soc. Sci. Med.* 60, 789–797. doi: 10.1016/j.socscimed.2004.06.012

Vos, T., Barber, R. M., Bell, B., Bertozzi-Villa, A., Biryukov, S., Bolliger, I., et al. (2015). Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 386, 743–800. doi: 10.1016/s0140-6736(15)60692-4

Westerhof, G. J., and Keyes, C. L. M. (2010). Mental illness and mental health: the two continua model across the lifespan. *J. Adult Dev.* 17, 110–119. doi: 10.1007/s10804-009-9082-y

Whiffin, C. J., Gracey, F., and Ellis-Hill, C. (2021). The experience of families following traumatic brain injury in adult populations: a meta-synthesis of narrative structures. *Int. J. Nurs. Stud.* 123, 104043. doi: 10.1016/j.ijnurstu.2021.104043

Whitty, C. J. M., MacEwen, C., Goddard, A., Alderson, D., Marshall, M., Calderwood, C., et al. (2020). Rising to the challenge of multimorbidity. *BMJ* 368, l6964. doi: 10.1136/bmj.l6964

Wilkie, L., Arroyo, P., Conibeer, H., Kemp, A. H., and Fisher, Z. (2021). The impact of psycho-social interventions on the wellbeing of individuals with acquired brain injury during the COVID-19 pandemic. *Front. Psychol.* 12, 648286. doi: 10.3389/fpsyg.2021.648286

Wilson, B., Gracey, F., Evans, J., and Bateman, A. (2009). *Neuropsychological Rehabilitation: Theory, Models, Therapy and Outcome*. Cambridge: Cambridge University Press. doi: 10.1017/CBO9780511581083

Wong, P. T. P. (2019). Second wave positive psychology's (PP 2.0) contribution to counselling psychology. *Counsel. Psychol. Q.* 32, 1–10. doi: 10.1080/09515070.2019.1671320

Young, H. A., and Benton, D. (2018). Heart-rate variability: a biomarker to study the influence of nutrition on physiological and psychological health? *Behav. Pharmacol.* 29, 140–151. doi: 10.1097/fbp.0000000000000383

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Spanish Adaptation and Validation of the Transplant Effects Questionnaire (TxEQ-Spanish) in Liver Transplant Recipients and Its Relationship to Posttraumatic Growth and Quality of Life

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The valid assessment of the impact of transplantation on psychological well-being is highly relevant to optimize treatment. However, to date there is no standardized instrument available in Spain. The Transplant Effects Questionnaire (TxEQ) evaluates the specific problems associated with organ transplantation, such as worry about transplant, guilt regarding the donor, disclosure of having undergone transplantation, adherence to medical treatment and responsibility toward the donor, family, friends, or medical staff. Against this backdrop the English original version of the TxEQ was translated into Spanish and validated in a sample of 240 liver transplant recipients. Participants also filled in the Posttraumatic Growth Inventory (PTGI), and the 12-Item Short Form Health Survey (SF-12v.2). Confirmatory factor analysis of the TxEQ-Spanish revealed a five-factor structure equivalent to the English original version, and satisfactory internal consistency (Cronbach's alpha: worry $\alpha = 0.82$, guilt $\alpha = 0.77$, disclosure $\alpha = 0.91$, adherence $\alpha = 0.82$, responsibility $\alpha = 0.83$). Results showed that better mental quality of life was associated with higher adherence and disclosure, as well as less worry and guilt. Higher posttraumatic growth was significantly associated with worry, guilt, and responsibility. Interestingly, the most powerful predictor of posttraumatic growth was worry. Analysis of variance showed an interaction effect of PTG and mental quality of life on adherence, with medium PTG being associated with significantly stronger adherence in participants with better mental quality of life. In conclusion our study could successfully adapt and validate the Spanish version of the TxEQ in a large sample of liver transplant recipients. Our findings show a complex relationship between emotional reactions to transplantation, mental quality of life, and posttraumatic growth, which give further insight into inner processes supporting psychological well-being and adherence after liver transplantation.

Keywords: transplant effects questionnaire, TxEQ-Spanish, posttraumatic growth, quality of life, liver transplantation

INTRODUCTION

Transplantation has a great impact on the patients' physical and psychological well-being. Standardized psychometric instruments such as the Transplant Effects Questionnaire (TxEQ) are important to be able to assess and compare these effects and may help to optimize treatment. The English original version of this questionnaire was developed and tested with kidney transplant recipients [1]. Later, it was translated to other languages. The German version (TxEQ-D) was validated in a group of heart, lung, liver, and kidney transplant recipients [2], the Dutch version (TxEQ-NL) in a group of liver transplant recipients [3], and the Polish version in a group of heart transplant recipients [4]. The factor structure of the above mentioned versions is similar to the original version consisting of the five subscales worry, guilt, disclosure, adherence, and responsibility. In the German version the five-factor structure was confirmed in Confirmatory Factor Analysis (CFA) by a scree plot [2] and in the Dutch version the Root Means Square Error of Approximation (RMSEA = 0.063) as well as the Akaike Information Criterion (AIC = 19578) confirmed good model fit [3]. For the Polish version no indices of model fit were presented [4]. Regarding reliability Cronbach's alpha varied between 0.71–0.79 in the German version [2], 0.66–0.79 in the Dutch version [3], and 0.61–0.72 in the Polish version [4] compared to 0.72–0.86 in the English original version [1].

Despite the growing importance of transplantation medicine in Spain [5] there is no Spanish translation of the TxEQ. The TxEQ has successfully been used to assess the impact of different forms of transplantation (living vs. deceased donor) [6, 7] and different organ types (heart, lung, liver, kidney) on quality of life. Thus, in a sample of 370 solid organ transplant recipients, 18.2% of liver recipients worried about the transplant compared to 14.4% of kidney recipients, 3.9% in lung recipients, and 2.4% of heart recipients [8]. Another study revealed that recipients after living donation tend to experience more guilt toward the donor compared to transplant recipients of deceased donors [7].

There is growing evidence that recipients' quality of life is closely connected to their ability to adapt to the new situation after a traumatic experience [9]. This ability has been described by Tedeschi and Calhoun [10, 11] as posttraumatic growth and several studies showed its relevance as a protective factor for psychological well-being after transplantation [12–15]. According to Tedeschi and Calhoun the experience of growth is often motivated by the experience of personal distress and worries and the inner need to find a new intra-psychic balance. The importance of worry as predictor of posttraumatic growth has been confirmed in cancer patients [16, 17]. A successful adaptation of the transplant recipient may result in a modification of coping strategies [18], a shift in priorities, and a change in family ties [19]. However, the complex relationship between specific emotional reactions to transplantation as measured by the TxEQ, posttraumatic growth and quality of life is not fully understood.

Against this backdrop our study aimed at an adaptation of the English TxEQ to Spanish and a validation of the Spanish version (TxEQ-Spanish) in a sample of liver transplant recipients. We had the following hypotheses. First, the TxEQ-Spanish has a five-factor structure similar to the original version with the subscales worry, guilt, disclosure, adherence, and responsibility. Second, posttraumatic growth is related to higher scores on worry, guilt, disclosure, adherence, and responsibility. Third, mental quality of life is related to lower scores on worry and guilt and higher scores on disclosure, adherence, and responsibility. Finally, in accordance with the theory of Tedeschi and Calhoun [10, 11] and previous studies in cancer patients [16, 17] we assumed worry to be the most powerful predictor among TxEQ scales of posttraumatic growth after transplantation.

MATERIALS AND METHODS

Participants and Procedure

This research was approved by the Ethics Committee of the Virgen del Rocío University Hospital of Seville. All patients gave their informed consent for participation. A group of 240 liver transplant recipients was selected (185 men and 55 women), with a mean age of 60.21 ± 9.30 years. 79.2% had a stable partnership and 61.7, 22.5, and 15.8% had a low, medium, and high education, respectively. The average time that had elapsed since the transplant was 87.77 ± 66.19 months. The etiology of the liver disease was as follows: alcoholic cirrhosis (32.1%), hepatocellular carcinoma (27.9%), hepatitis C-related cirrhosis (17.1%), hepatitis B-related cirrhosis (5%), and others (17.9%). The liver received by all patients was from a donor who had died from the following causes: cerebrovascular accidents (59.9%), cranioencephalic traumas (27%), and others (13.1%). For the specific patient selection procedure and inclusion criteria see Pérez-San-Gregorio et al. [9].

Instruments

Transplant Effects Questionnaire (TxEQ; [1])

The English original version consists of 23 items scored on a 5-point Likert scale ranging from "strongly agree" to "strongly disagree." It contains five subscales that assess worry about the transplant (six items, e.g., "I am worried about damaging my transplant"), guilt regarding the donor (five items, e.g., "I feel guilty about having taken advantage of the donor"), disclosure (three items; e.g., "I avoid telling other people that I have a transplant"), adherence (five items, e.g., "Sometimes I do not take my anti-rejection medicines"), and responsibility (four items, e.g., "I think that I have responsibility to the transplant team to do well"). The score of each subscale is calculated by dividing the sum score by the number of items. Higher scores show a higher degree of the dimension concerned.

The factor structure was similar in all versions derived from this questionnaire, **Table 1** presents subscales' internal consistency as measured by Cronbach's alpha.

Posttraumatic Growth Inventory (PTGI; [10])

This questionnaire consists of 21 items scored on a 6-point Likert scale (0 to 5) ranging from "no change" to "a very great degree of change," thereby evaluating the perception of personal benefits in survivors of traumatic events. Test interpretation provides a total score of posttraumatic growth and the following five subdimensions: relating to others, new possibilities, personal strength, spiritual change, and appreciation of life. We used the Spanish version by Weiss and Berger [20]. Three equal-sized groups with different levels of posttraumatic growth (low, medium, high) were formed. A higher score showed more posttraumatic growth. Cronbach's alpha was 0.94 for the sum scale and 0.74 to 0.88 for the subscales.

12-Item Short Form Health Survey (SF-12v.2; [21, 22])

This instrument is made up of 12 items scored on either 3 or 5-point Likert-scales. It evaluates the following eight dimensions of health-related quality of life covering the previous 4 weeks: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The sum score of the two components Physical Component Summary (PCS) and Mental Component Summary (MCS) was calculated by the Quality Metric Health Outcomes^{TM} Scoring Software 5.0. The sum score can range from 0 (worst state of health) to 100 (best state of health). Based on the liver transplant recipients' scores on the MCS, two groups of the same size with better or worse mental quality of life were formed. Cronbach's alpha was 0.92 for the PCS and 0.88 for the MCS [21].

Translation and Statistical Analysis

Data were analyzed and graphics were produced using the software programs, Mplus v.7 [23] and SPSS 22 (IBM Corporation, Armonk, NY, United States) for Windows PC.

TABLE 1 | Cronbach's alpha for the TxEQ-Spanish and the English, German, Dutch, and Polish versions.

	[1] (English)	[2] (German)	[3] (Dutch)	[4] (Polish)	TxEQ-Spanish
Worry	0.81	0.73	0.68	0.61	0.82
Guilt	0.76	0.74	0.66	0.63	0.77
Disclosure	0.86	0.71	0.79	0.72	0.91
Adherence	0.79	0.79	0.78	0.61	0.82
Responsibility	0.72	0.73	0.66	0.63	0.83

Translation of the Transplant Effects Questionnaire (TxEQ) Into Spanish

The translation of the English original version of the TxEQ into Spanish strictly followed the guidelines for the process of cross-cultural adaptation of self-report measures by Beaton et al. [24] as well as the guidelines to quality control by Hambleton and Zenisky [25]. After requesting permission of the original authors the questionnaire was translated into Spanish by two psychology professors with advanced levels of English (stage I). After completion of both translations, translated items were compared and checked. Non-conformities were discussed until a consensus was reached and a final version was drafted (stage II). This version was translated back into English by two professional translators (stage III). On the basis of these translations and all previous reports a final version was produced by translators as well as other research team members (stage IV). This Spanish version was pilot tested for comprehensibility in a small group of transplant recipients ($n = 10$) (stage V). All participants confirmed the comprehensibility of the TxEQ-Spanish.

Statistical Analysis

To validate the Spanish version of the TxEQ and to analyse the relationship between the TxEQ and quality of life as well as posttraumatic growth the following statistical analyses were applied.

A Confirmatory Factor Analysis (CFA) was performed to replicate the five-factor structure of the English original version of the TxEQ. In the first place, it was confirmed that the data matrix was adequate for factor analysis by measuring sample adequacy with the Kaiser-Meyer-Olkin Test ($\geq$0.08) and the Bartlett test of sphericity ($p \leq 0.0001$). To determine the best estimation method, the assumption of multivariate normality of the data was tested, checking to see whether the Mardia test [26] showed a standardized value over 5 [27]. For the fit indexes and model evaluation, the adequacy of the factorial solution was analyzed in several different ways: (a) indications of model fit: we took into account whether the Comparative Fit Index (CFI) and Non-Normed Fit Index (NNFI) or the equivalent Tucker and Lewis Index (TLI) values were near to or over 0.90, whether the Root Mean Square Error of Approximation (RMSEA) was less than 0.08 and whether the Test of Approximate Fit of RMSEA was non-significant [28, 29], and (b) significance of the parameters.

To analyze the internal consistency of the questionnaire, Cronbach's alpha coefficients were calculated for all dimensions, considering an internal consistency of at least 0.70 as adequate [30].

Pearson's chi-squared test was used to compare socio-demographic and clinical variables (gender, marital status, education, and etiology of the disease) in the patient subgroups. For the quantitative variables (age and time elapsed since transplantation), a one-way ANOVA was calculated. Before analysis of the relationship between TxEQ subscales, quality of life (SF12) and posttraumatic growth (PTGI) we checked data of the different scales for normality distribution by the Kolmogorov-Smirnov test, however scales were not normally distributed. The Levene-test for the equality of variances was not significant so that data showed homoscedasticity. According to statistical literature [31–33] ANOVA and Pearson's correlation produce reliable results under these circumstances given a large sample size of $n = 240$. A 3x2 factorial ANOVA was performed to evaluate the influence of posttraumatic growth level (low, medium, high) and MCS (worse, better) on transplantation effects. Pearson's correlation was used to analyze associations between TxEQ-Spanish dimensions, posttraumatic growth, and mental quality of life. Cohen's d (for quantitative variables) and Cohen's w (for qualitative variables) were computed as a measure of effect size. Effect sizes were interpreted as follows: for Cohen's $d < 0.20$=null effect size; $\geq 0.20 < 0.50$=small; $\geq 0.50 < 0.80$=moderate; ≥ 0.80=large. And for Cohen's $w < 0.10$=null effect size; $\geq 0.10 < 0.30$=small; $\geq 0.30 < 0.50$=moderate; ≥ 0.50=large [34].

Finally, we performed a stepwise multiple linear regression analysis to predict posttraumatic growth of liver transplant recipients (criterion or dependent variable) by means of seven predictor variables (worry, guilt, disclosure, adherence, responsibility, MCS, and PCS). Statistical requirements for the implementation of linear regression analysis (linearity, independence of residuals, homoscedasticity, no-multicollinearity) were fulfilled.

RESULTS

Spanish Adaptation and Validation of the Transplant Effects Questionnaire (TxEQ)

On an exploratory level, we confirmed that the matrix was suitable for factoring. Kaiser-Meyer-Olkin's measurement of sample adequacy was 0.80, which is considered satisfactory [35] and the Bartlett's sphericity test was not significant ($p \leq 0.0001$).

On a descriptive level, participant responses did not show any missing values or outliers. The mean scores for all 23 items varied from 1.63 ± 0.93 to 4.66 ± 0.90, with skewness (−3.11, 1.78) and kurtosis (−1.48, 9.19) which deviated from the range of −1 and 1 required to consider distribution of the items normal [36]. There was no normal distribution of data (Mardia's coefficient = 36.68; value higher than 5.00; [27]). Consequently, Robust Maximum Likelihood was employed for CFA calculation. Correlations between the TxEQ-Spanish subscales, posttraumatic growth and mental quality of life are presented in **Table 2**.

In the next step of analysis the original five-factor structure was tested. Certain adjustments had to be made for satisfactory fit and significance of all the model parameters. Specifically, three adjustments were made to the original structure: First, a new parameter was added to the model, the residual covariance of items 6 and 9, both indicators of the same responsibility dimension (**Figure 1**). Second, significant correlations were allowed between the following dimensions: worry and guilt, worry and disclosure, worry and responsibility, and guilt and disclosure. There were no other significant inter-correlations. Third, item 8 ("I do not have any feeling of guilt toward the donor") was eliminated, because it showed a saturation of < 0.2 and was negatively correlated to the corresponding dimension (guilt). The final version of the scale is shown in Appendix 1 in Supplementary Material. Moreover, in Appendix 2 in Supplementary Material we present a table comparing the TxEQ-Spanish and the English original version on an item to item basis.

After having made these adjustments, the fit indices were satisfactory: CFI = 0.90 and TLI = 0.89; RMSEA = 0.063 (H_0: RMSEA < 0.05; $p = 0.013$; 90% confidence interval = 0.053–0.072). **Figure 1** shows the diagram of the resulting model in which the standardized factor weights are given together with standard error and residuals for each item, as well as the covariance between dimensions and errors in items 6 and 9. All the estimated parameters were statistically significant ($p < 0.01$), the values were as follows: worry 0.58 to 0.75 ($M = 0.65$, $SD = 0.05$), guilt 0.42 to 0.89 ($M = 0.70$, $SD = 0.05$), disclosure 0.84 to 0.95 ($M = 0.88$, $SD = 0.04$), adherence 0.43 to 0.91 ($M = 0.68$, $SD = 0.07$), and responsibility 0.48 to 0.92 ($M = 0.70$, $SD = 0.06$). The proportion of variance explained by the predictor variables varied from 0.17 to 0.85. In the final model a correlation of $r = 0.42$ ($p < 0.001$) was observed between the factors worry and guilt, $r = -0.22$ ($p = 0.001$) between worry and disclosure, $r = 0.32$ ($p = 0.001$) between worry and responsibility, and $r = -0.43$ ($p < 0.001$) between guilt and

TABLE 2 | Correlations between the TxEQ-Spanish subscales, posttraumatic growth, and mental quality of life.

	Posttraumatic growth ***r*** **(*p*)**	**Mental quality of life** ***r*** **(*p*)**	**Worry** ***r*** **(*p*)**	**Guilt[a]** ***r*** **(*p*)**	**Disclosure** ***r*** **(*p*)**	**Adherence** ***r*** **(*p*)**
Worry	0.37 (<0.001)	−0.22 (0.001)				
Guilt[a]	0.13 (0.046)	−0.13 (0.036)	0.37 (<0.001)			
Disclosure	0.02 (0.741)	0.19 (0.002)	−0.21 (0.001)	−0.43 (<0.001)		
Adherence	0.08 (0.238)	0.16 (0.014)	−0.09 (0.164)	−0.28 (<0.001)	0.44 (<0.001)	
Responsibility	0.25 (<0.001)	0.01 (0.876)	0.33 (<0.001)	0.14 (0.030)	−0.06 (0.319)	0.10 (0.120)

[a] *TxEQ [1] item 8 ("I do not have any feeling of guilt toward the donor") was not included in the factor computation.*

disclosure. The correlation between errors on items 6 and 9 was $r = 0.64$ ($p < 0.001$).

Cronbach's alpha for internal consistency as a measure of reliability was satisfactory for all five subscales: worry 0.82, guilt 0.77, disclosure 0.91, adherence 0.82, and responsibility 0.83 (**Table 1**).

Posttraumatic Growth and Mental Quality of Life: Influence on the Effects of the Transplant

Based on patients' total score on the PTGI, three equal-sized subgroups were created: low score ($n = 80$ patients, 33.3% of the sample, 0 to 59 points), medium score ($n = 80$ patients, 33.3% of the sample, 60 to 77 points), and high score ($n = 80$ patients, 33.3% of the sample, 78 to 105 points). There were no significant differences between subgroups in age ($p = 0.506$), gender ($p = 0.639$, $w = 0.06$, null effect size), marital status ($p = 0.720$, $w = 0.05$, null effect size), education ($p = 0.187$, $w = 0.16$, small effect size), time elapsed since transplantation ($p = 0.227$), or etiology of the liver disease ($p = 0.082$, $w = 0.24$, small effect size). In a further step of analysis, another two subgroups of equal size were formed based on the SF-12 MCS: lower score or worse mental health ($n = 120$, 50% of the sample, ≤52.87 points) and higher score or better mental health ($n = 120$, 50% of the sample, >52.87 points). There were no significant differences between both subgroups regarding age ($p = 0.105$), gender ($p = 0.091$, $w = -0.11$, small effect size), marital status ($p = 0.026$, $w = -0.14$, small effect size), education ($p = 0.075$, $w = 0.15$, small effect size), time elapsed since transplantation ($p = 0.926$), or etiology of the liver disease ($p = 0.442$, $w = 0.12$, small effect size).

In the analysis of variance only the dimension adherence showed an interaction effect between the two factors posttraumatic growth and mental quality of life ($p = 0.032$) (**Table 3**). **Figure 2** demonstrates this relationship. There was only a significant difference in adherence ($p = 0.001$, $d = -0.76$) between patients with worse and better mental quality of life if they showed medium posttraumatic growth; better quality of life was associated with stronger adherence of medium effect size. This difference disappeared when posttraumatic growth was low ($p = 0.411$, $d = -0.18$, null effect size) or high ($p = 0.781$, $d = 0.06$, null effect size). Moreover, as shown in **Table 2**, adherence showed a significantly positive correlation with mental quality of life ($r = 0.16$, $p = 0.014$) and disclosure ($r = 0.44$, $p < 0.001$), and a negative correlation with guilt ($r = -0.28$, $p < 0.001$).

As shown in **Table 3**, **Figure 3**, the posttraumatic growth main effect was significant for the dimensions worry ($p < 0.001$) and responsibility ($p = 0.002$). Scores on both dimensions were significantly higher in patients with high compared to low posttraumatic growth (worry, $p < 0.001$, $d = -0.91$, large effect size;

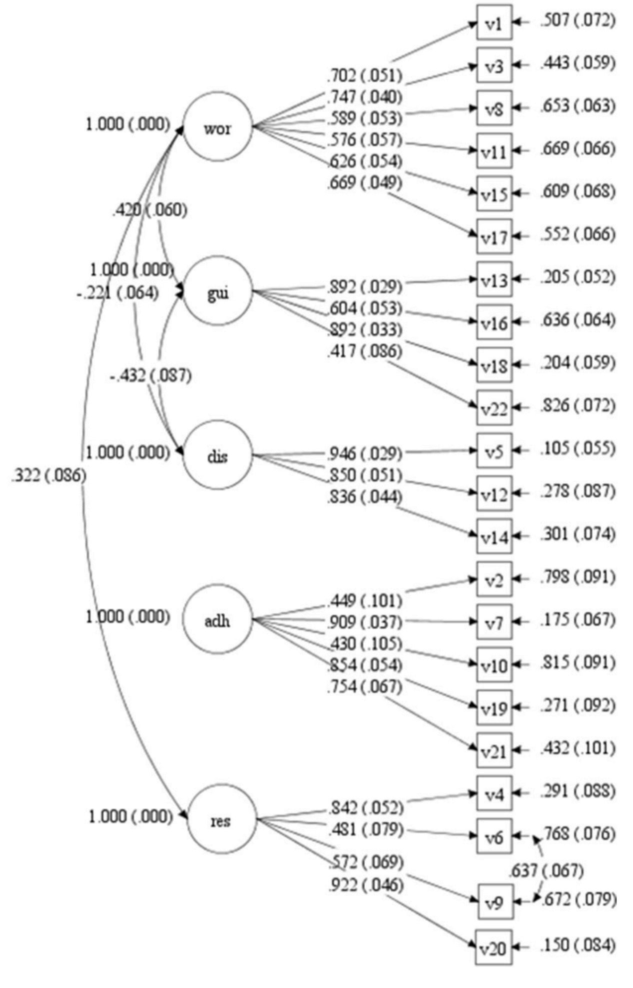
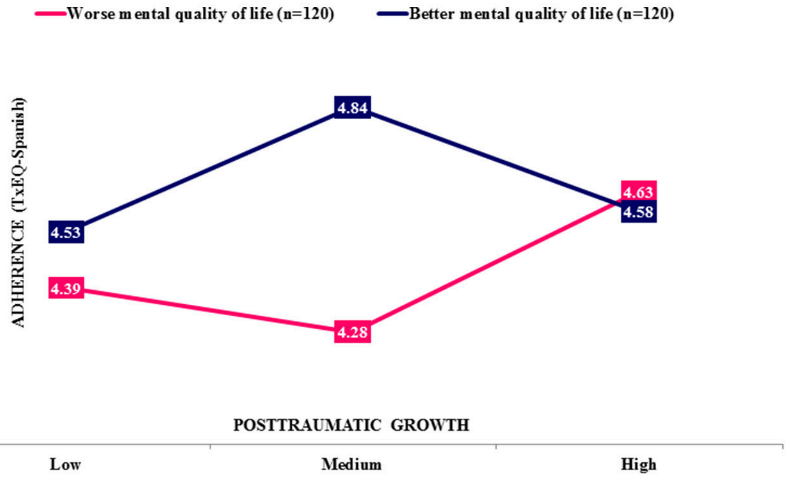


FIGURE 1 | CFA diagram. Standardized factor loadings with standard error of the items and residuals and co-variance between dimensions.

TABLE 3 | Influence of posttraumatic growth and mental quality of life on the TxEQ-Spanish subscales (3x2 factorial ANOVA).

	Main effects		**Interaction effects**
	Posttraumatic growth $F_{(2,234)}$ (p)	**Mental quality of life $F_{(1,234)}$ (p)**	**$F_{(2,234)}$ (p)**
Worry	16.68 (<0.001)	14.45 (<0.001)	1.23 (0.295)
Guilt[a]	1.64 (0.195)	5.99 (0.015)	0.30 (0.739)
Disclosure	0.17 (0.845)	4.38 (0.037)	0.71 (0.493)
Adherence	0.76 (0.468)	5.11 (0.025)	3.49 (0.032)
Responsibility	6.41 (0.002)	0.00 (0.946)	0.55 (0.576)

[a] *TxEQ [1] item 8 ("I do not have any feeling of guilt toward the donor") was not included in the factor computation.*



Posttraumatic growth	p	Cohen's d
Low		
Worse-better mental quality of life	0.411	-0.18 N
Medium		
Worse-better mental quality of life	0.001	-0.76 M
High		
Worse-better mental quality of life	0.781	0.06 N

Mental quality of life	p	Cohen's d
Worse		
Low-medium posttraumatic growth	1.000	0.16 N
Low-high posttraumatic growth	0.538	-0.31 S
Medium-high posttraumatic growth	0.108	-0.47 S
Better		
Low-medium posttraumatic growth	0.224	-0.42 S
Low-high posttraumatic growth	1.000	-0.07 N
Medium-high posttraumatic growth	0.379	0.35 S

FIGURE 2 | Simple effects on adherence. N, Null effect size; S, Small effect size; M, Medium effect size.

responsibility, $p = 0.002$, $d = -0.54$, medium effect size). Posttraumatic growth was also positively correlated with worry ($r = 0.37$, $p < 0.001$), guilt ($r = 0.13$, $p = 0.046$), and responsibility ($r = 0.25$, $p < 0.001$) (**Table 2**).

The main effect of mental quality of life was significant regarding the dimensions worry ($p < 0.001$, $d = 0.49$, small effect size), guilt ($p = 0.015$, $d = 0.32$, small effect size), disclosure ($p = 0.037$, $d = -0.27$, small effect size), and adherence ($p = 0.025$, $d = -0.29$, small effect size) (**Table 3**, **Figure 3**). Patients with better mental quality of life scored higher on disclosure and adherence, and lower on worry and guilt, which corresponded to significantly positive or negative correlations between mental quality of life and above mentioned dimensions (**Table 2**).

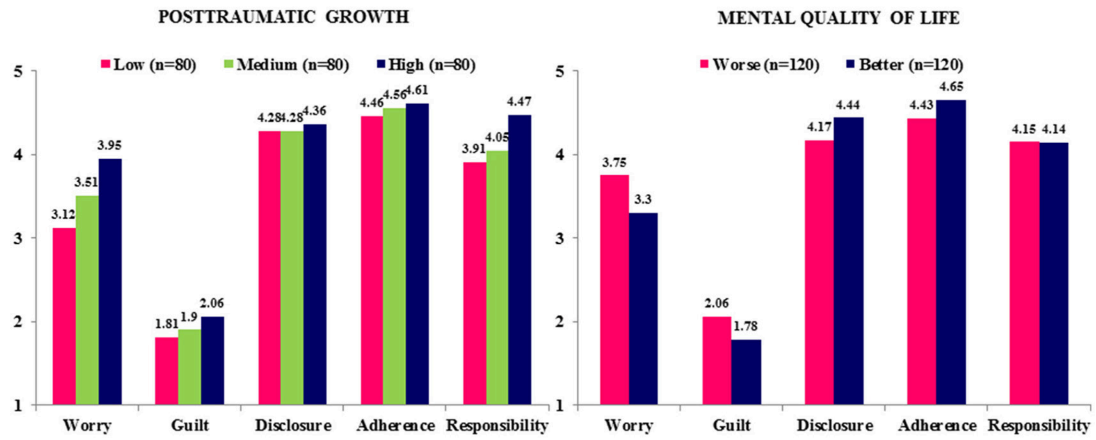
Predictors of Posttraumatic Growth

The results of the multiple linear regression analysis with posttraumatic growth as dependent variable and mental and physical quality of life, worry, guilt, disclosure, adherence, and responsibility as predictors are presented in **Table 4**. The final model [$F_{(3,\,236)} = 16.74$, $p < 0.001$] consisted of the three significant predictors worry ($p < 0.001$), PCS ($p = 0.017$) and responsibility ($p = 0.034$). This model explained 17.5% ($R^2 = 0.175$) of the variance observed in posttraumatic growth.

DISCUSSION

Spanish Adaptation and Validation of the Transplant Effects Questionnaire (TxEQ-Spanish)

To date there is no standardized instrument available in Spain to assess the impact of transplantation on psychological well-being. Against this backdrop the current study aimed at translating the English original version of the TxEQ into Spanish and validate the Spanish version in a large sample of liver transplant recipients. In our methodological approach we followed the guidelines for the process of cross-cultural adaptation of self-report measures by Beaton et al. [24]. Thus, the adaptation procedure embraced five carefully designed steps, to ensure soundness of the final version. By means of this approach we ensured semantic, idiomatic experiential, and conceptual equivalence of both questionnaires and the comparability of responses in English and Spanish speaking populations. The verification of scaling requirements by analyzing the factor structure and reliablity of the TxEQ was implemented in the next step [24] to ensure psychometric quality of the Spanish version. CFA of the TxEQ-Spanish revealed adequate fit with the original English version of the TxEQ [1] and confirmed a robust five-factor structure. After careful analysis of the internal consistency of all subscales one item (item 8: "I do not have any feelings of guilt toward the donor") showed a particularly low loading on the factor guilt and had to be excluded from the questionnaire. One possible reason for the low association of



Intergroup comparisons	Worry	Guilt	Disclosure	Adherence	Responsibility
Posttraumatic growth:					
Low-medium					
p	0.019	1.000	1.000	1.000	1.000
Cohen's *d*	-0.43 S	-0.10 N	0.00 N	-0.13 N	-0.13 N
Low-high					
p	<0.001	0.224	1.000	0.684	0.002
Cohen's *d*	-0.91 L	-0.28 S	-0.08 N	-0.19 N	-0.54 M
Medium-high					
p	0.009	0.760	1.000	1.000	0.031
Cohen's *d*	-0.47 S	-0.18 N	-0.08 N	-0.06 N	-0.41 S
Mental quality of life:					
Worse-better					
p	<0.001	0.015	0.037	0.025	0.946
Cohen's *d*	0.49 S	0.32 S	-0.27 S	-0.29 S	0.01 N

FIGURE 3 | Influence of posttraumatic growth and mental quality of life on the TxEQ-Spanish subscales. N, Null effect size; S, Small effect size; M, Medium effect size; L, Large effect size.

this item with the factor guilt might be that the translation into Spanish led to a double negative. This grammatical construction may have led to difficulties in comprehensibility, particularly in recipients with a low level of formal education, which made up 61.7% of patients in our sample. This modification of the Spanish version does not necessarily result in a relevant reduction in information provided by the subscale "guilt regarding the donor," since it contains another item (item 13: "I feel guilty about having taken advantage of the donor") with similar content. In the final version of the TxEQ-Spanish the internal consistency scores were satisfactory ranging from 0.77 to 0.91. Consistency scores were even higher than in the English original version [1] and the translated versions in German [2], Dutch [3], or Polish [4]. Therefore, our hypothesis that the TxEQ-Spanish has a factor structure (worry, guilt, disclosure, adherence, and responsibility) similar to the original version and shows satisfactory reliability has been confirmed.

TABLE 4 | Repercussions of liver transplantation (worry, guilt, disclosure, adherence, responsibility, MCS, and PCS) as predictors of posttraumatic growth.

Predictor variables	*B*	*SE*	*β*	*t* (*p*)	R^2	ΔR^2
Step 1					0.137	0.137
Worry	8.54	1.39	0.37	6.14 (<0.001)		
Step 2					0.160	0.023
Worry	9.24	1.40	0.40	6.58 (<0.001)		
PCS	0.32	0.13	0.15	2.54 (0.012)		
Step 3					0.175	0.016
Worry	8.17	1.48	0.35	5.51 (<0.001)		
PCS[a]	0.30	0.13	0.14	2.40 (0.017)		
Responsibility	2.92	1.36	0.13	2.14 (0.034)		

[a] *PCS, physical component summary.*

Mental Quality of Life, Posttraumatic Growth, and TxEQ-Spanish

Moreover, we analyzed the relationship between recipients' emotional reactions to transplantation, their mental quality of life and posttraumatic growth. In this context adherence to treatment and medication is of specific interest to optimize long-term outcome of transplantation. Analysis of variance showed an interaction effect between posttraumatic growth and mental quality of life on therapeutic adherence. Better mental quality of life was associated with more adherence merely in patients with medium posttraumatic growth. A positive association between mental health and adherence is in line with other studies [2, 6, 37–39] and confirms our hypothesis. However, it is not easy to explain, why this difference can only be seen in recipients with medium posttraumatic growth. One might argue that—taking mental health into account—there is no linear association between adherence and posttraumatic growth as **Figure 3** might suggest, but rather a u-shaped or reverse u-shaped connection as shown in **Figure 2**. This relationship could be explained by the fact that adherence to medication worsens if the patient feels cognitively overloaded [40] and improves if simplification of medication regimen lowers the cognitive load [41]. Posttraumatic growth is defined by Tedeschi and Calhoun [10, 11] as a process, which takes time and absorbs a lot of cognitive resources to be able to form cognitive schemata reconciling existential opposites. If recipients are involved in posttraumatic growth, effects may largely depend on the extent of involvement. A moderate involvement in the process of posttraumatic growth (medium PTG) may be associated with disadvantages concerning treatment in recipients with worse mental health compared to those with better mental health, as worse mental health is associated with fewer mental resources and recipients may be overwhelmed by inner conflicts ("tunnel vision"). The mental overload could be mirrored in a positive response to items from the adherence scale such as "Sometimes I forget to take my anti-rejection medicines" and "When I am too busy I may forget my anti-rejection medicines." Obviously, this explanation is highly speculative, and does not explain convincingly the lack of differences in the group with high PTG. Nevertheless, the aspect that posttraumatic growth is a resource consuming cognitive process needs to be taken into account to be able to understand the complexity of its effects. Significant predictors of PTG were the degree of physical complaints (PCS), worry, and responsibility with worry being the most important predictor. Posttraumatic growth implies a gain in self-awareness and spirituality, a re-definition of personal relationships and a greater appreciation of life with all its possibilities [10, 11]. At first sight it may be difficult to understand the relationship between worry and PTG. However, worries about the transplantation and all its implications, which are closely connected to the subjective experience of physical health (PCS), are the necessary predisposition for posttraumatic growth. The items "I am worried about damaging my transplant" or "I am hesitant to engage in certain activities because I am afraid of doing harm to my transplant" belonging to the worry-subscale demonstrate that worries affect all aspects of recipients' life. The process of posttraumatic growth is fueled by these repeated worries on the one hand and a sense of responsibility on the other, which enables the recipient to accept inner development as a personal task and not simply rely on fate. This responsibility also embraces a responsibility toward his own health and significant others. A sense of personal responsibility is closely connected to personality traits such as self-directedness and the psychological construct of self-efficacy, which both are strong predictors of psychological well-being and positive outcome after psychotherapy [42]. In summary, the prediction of posttraumatic growth by worry, physical health and responsibility gives further insight into those factors advancing positive change after liver transplantation [12, 14, 15, 19].

Regarding adherence our study confirmed a significant positive association with disclosure and a negative association with guilt [7, 43]. The difficulty of recipients to disclose their transplantation to others and a feeling of guilt toward the donor makes it difficult for recipients to exercise the adequate self-care. Thus, they may avoid taking their immunosuppressants in circumstances, where others may realize it or they may even ask themselves, whether they deserve to survive. Early identification of these problems and adequate treatment are crucial to avoid non-adherence resulting in rejection episodes and graft losses [44]. The importance of early psychological intervention can also be derived from the fact that a better mental quality of life is associated with more disclosure and less worry and guilt, which is in line with a previous study [2].

Our study shows several limitations. First, our sample consisted of liver transplant recipients, therefore our findings cannot be transferred to recipients of other organs. Second, all liver transplants were from deceased donors. Findings could be different in living donor liver transplantation [6, 7]. Third, recruitment of patients took place at a single site which may limit external validity of findings. Fourth, our cross-sectional study design does not allow for the investigation of longitudinal changes in respective questionnaires. Fifth, in our statistical analysis subgroups were created on the basis of sample distribution and not on the basis of validated cut-off values, which may restrict generalizability of study results.

Nevertheless our study successfully adapted and validated the TxEQ-Spanish in a large sample of liver transplant recipients, which allows for the future investigation of the psychological effects of transplantation by a psychometrically sound instrument in Spain.

AUTHOR CONTRIBUTIONS

MÁP-S-G: Study concept and design, data analysis and interpretation, drafting of manuscript, manuscript revisions, drafting figures, final approval of version to be published. AM-R, MS-M, MB-M and MLA-N: Study concept and design, data analysis and interpretation, manuscript revisions, final approval of version to be published. MÁG-B: Institutional support, data collection, critical revision of article, final approval of version to be published. RC: Data analysis and interpretation, drafting of manuscript, critical revision of article, final approval of version to be published.

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REFERENCES

1. Ziegelmann JP, Griva K, Hankins M, Harrison M, Davenport A, Thompson D, et al. The Transplant Effects Questionnaire (TxEQ): the development of a questionnaire for assessing the multidimensional outcome of organ transplantation - Example of end stage renal disease (ESRD). *Br J Health Psychol.* (2002) **7**:393–408. doi: 10.1348/135910702320645381
2. Klaghofer R, Sarac N, Schwegler K, Schleuniger M, Noll G, Muellhaupt B, et al. Questionnaire on emotional response after organ transplantation: german validation of the Transplant Effect Questionnaire (TxEQ-D). *Z Psychosom Med Psychother.* (2008) **54**:174–88. doi: 10.13109/zptm.2008.54.2.174
3. Annema C, Roodbol PF, Stewart RE, Ranchor AV. Validation of the Dutch version of the transplant effects questionnaire in liver transplant recipients. *Res Nurs Health* (2013) **36**:203–15. doi: 10.1002/nur.21530
4. Milaniak I, Wilczek-Ruzyczka E, Wierzbicki K, Sadowski J, Przybyłowski P. The influence of sense of coherence on emotional response in heart transplant recipients - a preliminary report. *Kardiochir Torakochirurgia Pol.* (2014) **11**:220–24. doi: 10.5114/kitp.2014.43856
5. White SL, Hirth R, Mahíllo B, Domínguez-Gil B, Delmonico FL, Noel L, et al. The global diffusion of organ transplantation: trends, drivers and policy implications. *Bull World Health Organ.* (2014) **92**:826–35. doi: 10.2471/BLT.14.137653
6. Griva K, Ziegelmann JP, Thompson D, Jayasena D, Davenport A, Harrison M, et al. Quality of life and emotional responses in cadaver and living related renal transplant recipients. *Nephrol Dial Transplant.* (2002) **17**:2204–11. doi: 10.1093/ndt/17.12.2204
7. Zimmermann T, Pabst S, Bertram A, Schiffer M, de Zwaan M. Differences in emotional responses in living and deceased donor kidney transplant patients. *Clin Kidney J.* (2016) **9**:503–9. doi: 10.1093/ckj/sfw012
8. Goetzmann L, Sarac N, Ambühl P, Boehler A, Irani S, Muellhaupt B, et al. Psychological response and quality of life after transplantation: a comparison between heart, lung, liver and kidney recipients. *Swiss Med Wkly.* (2008) **138**:477–83. doi: 10.5167/uzh-7058
9. Pérez-San-Gregorio MÁ, Martín-Rodríguez A, Borda-Mas M, Avargues-Navarro ML, Pérez-Bernal J, Conrad R, et al. Post-traumatic growth and its relationship to quality of life up to 9 years after liver transplantation: a cross-sectional study in Spain. *BMJ Open* (2017) **7**:e017455. doi: 10.1136/bmjopen-2017-017455
10. Tedeschi RG, Calhoun LG. The Posttraumatic Growth Inventory: measuring the positive legacy of trauma. *J Trauma Stress* (1996) **9**:455–71. doi: 10.1002/jts.2490090305
11. Tedeschi RG, Calhoun LG. Posttraumatic growth: conceptual foundations and empirical evidence. *Psychol Inq.* (2004) **15**:1–18. doi: 10.1207/s15327965pli1501_01
12. Fox KR, Posluszny DM, Dimartini AF, DeVito Dabbs AJ, Rosenberger EM, Zomak RA, et al. Predictors of post-traumatic psychological growth in the late years after lung transplantation. *Clin Transplant.* (2014) **28**:384–93. doi: 10.1111/ctr.12301
13. Kamran F, Ogden J. Transitions in psychological well-being and life orientation: the phenomenon of post traumatic growth after renal transplantation. *Pak J Psychol Res.* (2016) **31**:419–40.
14. Scrignaro M, Sani F, Wakefield JR, Bianchi E, Magrin ME, Gangeri L. Post-traumatic growth enhances social identification in liver transplant patients: a longitudinal study. *J Psychosom Res.* (2016) **88**:28–32. doi: 10.1016/j.jpsychores.2016.07.004
15. Zieba M, Zatorski M, Boczkowska M, Gozdowska J, Kieszek R, Laskowski W. The affective tone of narration and posttraumatic growth in organ transplant recipients. *Pol Psychol Bull.* (2015) **46**:376–83. doi: 10.1515/ppb-2015-0044
16. Balfe M, O' Brien K, Timmons A, Butow P, O'Sullivan E, Gooberman-Hill R, et al. What factors are associated with posttraumatic growth in head and neck cancer carers? *Eur J Oncol Nurs.* (2016) **21**:31–7. doi: 10.1016/j.ejon.2015.11.005
17. McDonough MH, Sabiston CM, Wrosch, C. Predicting changes in posttraumatic growth and subjective well-being among breast cancer survivors: the role of social support and stress. *Psychooncology* (2014) **23**:114–20. doi: 10.1002/pon.3380
18. Pérez-San-Gregorio MÁ, Martín-Rodríguez A, Borda-Mas M, Avargues-Navarro ML, Pérez-Bernal J, Gómez-Bravo MÁ. Coping strategies in liver transplant recipients and caregivers according to patient posttraumatic growth. *Front Psychol.* (2017) **8**:18. doi: 10.3389/fpsyg.2017.00018
19. Anand-Kumar V, Kung M, Painter L, Broadbent E. Impact of organ transplantation in heart, lung and liver recipients: assessment of positive life changes. *Psychol Health* (2014) **29**:687–97. doi: 10.1080/08870446.2014.882922
20. Weiss T, Berger, R. Reliability and validity of a Spanish version of the Posttraumatic Growth Inventory. *Res Soc Work Pract.* (2006) **16**:191–9. doi: 10.1177/1049731505281374
21. Maruish ME. *User's Manual for the SF-12v2 Health Survey.* 3rd ed. Lincoln, RI: QualityMetric Incorporated (2012).
22. Ware JE, Kosinski M, Turner-Bowker DM, Gandek B. *How to Score Version 2 of the SF-12 Health Survey (with a supplement Documenting Version 1).* Lincoln, RI: QualityMetric Incorporated (2002).
23. Muthén LK, Muthén BO. *Mplus User's Guide, 6th Edn*. Los Angeles, CA: Muthén & Muthén (2007).
24. Beaton DE, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measures. *Spine* (2000) **25**:3186–91.
25. Hambleton RK, Zenisky AL. Translating and adapting tests for cross-cultural assessments. In Matsumoto D, van de Vijver FJR, editors. *Cross-Cultural Research Methods in Psychology*. New York, NY: Cambridge University Press (2011). p. 46–70.
26. Mardia KV. Measures of multivariate skewness and kurtosis with applications. *Biometrika* (1970) **57**:519–30. doi: 10.2307/2334770
27. Bentler PM. *EQS 6 Structural Equation Program Manual*. Encino, CA: Multivariate software (2005).
28. Hooper D, Coughlan J, Mullen M. Structural equation modelling: guidelines for determining model fit. *EJBRM* (2008) **6**:53–60.
29. Hu L, Bentler PM. Cutoff criteria for fit indexes in covariance structure analysis: conventional criteria versus new alternatives. *Struct Equ Model.* (1999) **6**:1–55. doi: 10.1080/10705519909540118
30. Nunnally JC, Bernstein IH. *Psychometric Theory*. New York, NY: McGraw Hill (1994).
31. Pagano RR. *Understanding Statistics in the Behavioral Sciences*. 9th ed. Belmont, WA: Thomson Wadsworth (2010).
32. Salkind NJ. *Encyclopedia of Research Design*. Vol. 2. Los Angeles, CA: Sage (2010).
33. Wilcox RR. *Introduction to Robust Estimation and Hypothesis Testing.* 3rd ed. *Statistical Modeling and Decision Science*. Amsterdam; Boston, MA: Academic Press (2012).
34. Cohen J. *Statistical Power Analysis for the Behavioral Sciences.* 2nd ed. Hillsdale, NJ: Lawrence Erlbaum Associates (1988).
35. Costelo AB, Osborne JW. Best practices in exploratory factor analysis: four recommendations for getting the most from your analysis. *PARE* (2005) **10**:1–9.
36. Ferrando PJ, Lorenzo-Seva U. Exploratory item factor analysis: some additional considerations. *An Psicol.* (2014) **30**:1170–5. doi: 10.6018/analesps.30.3.199991
37. Kim IK, Bae SH, Son S, Kim MS, Jun SY, Ju MK. Health-related quality of life and psychologic distress in korean kidney transplant recipients. *Transplant Proc.* (2016) **48**:855–7. doi: 10.1016/j.transproceed.2015.12.084
38. Lamba S, Nagurka R, Desai KK, Chun SJ, Holland B, Koneru B. Self-reported non-adherence to immune-suppressant therapy in liver transplant recipients: demographic, interpersonal, and intrapersonal factors. *Clin Transplant.* (2012) **26**:328–35. doi: 10.1111/j.1399-0012.2011.01489.x
39. Pabst S, Bertram A, Zimmermann T, Schiffer M, de Zwaan M. Physician reported adherence to immunosuppressants in renal transplant patients: prevalence, agreement, and correlates. *J Psychosom Res.* (2015) **79**:364–71. doi: 10.1016/j.jpsychores.2015.09.001
40. Tarantino V, Cappellari G, Cardaioli C, Rumiati R, Savadori L, Barilli E, et al. Sociocognitive factors associated with nonadherence to medication after hospital discharge. *Behav Med.* (2010) **36**:100–7. doi: 10.1080/08964281003774935
41. Conn VS, Hafdahl AR, Cooper PS, Ruppar TM, Mehr DR, Russell CL. Interventions to improve medication adherence among older adults: meta-analysis of adherence outcomes among randomized controlled trials. *Gerontologist* (2009) **49**:447–62. doi: 10.1093/geront/gnp037

42. Conrad R, Wegener I, Geiser F, Kleiman A. Temperament, character and personality disorders in chronic pain. *Curr Pain Headache Rep.* (2013) **17**:318. doi: 10.1007/s11916-012-0318-3
43. Goetzmann L, Irani S, Schwegler K, Stamm M, Spindler A, Bricman R, et al. Lung function, sociodemographic characteristics, and psychological reaction to transplant associated with chronic stress among lung recipients. *Anxiety Stress Coping* (2010) **23**:213–33. doi: 10.1080/10615800903038882
44. Denhaerynck K, Dobbels F, Cleemput I, Desmyttere A, Schäfer-Keller P, Schaub S, et al. Prevalence, consequences, and determinants of nonadherence in adult renal transplant patients: a literature review. *Transpl Int.* (2005) **18**:1121–33. doi: 10.1111/j.1432-2277.2005.00176.x

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Long-Term Effects of Tai Chi Intervention on Sleep and Mental Health of Female Individuals With Dependence on Amphetamine-Type Stimulants

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Previous studies provide evidence that Tai Chi (TC) can reduce the symptoms of sleep problems and be of benefit for the rehabilitation of substance abusers. In this study, we investigated if TC practice can improve sleep quality and mood of females who are dependent on amphetamine-type stimulant (ATS). Eighty subjects were randomly assigned to TC intervention and standard care (SC) for 6 months. We applied analysis of variance on repeated-measure with the year of drug dependence as the covariate to test the changes of the self-rated Pittsburg Sleep Quality Index (PSQI), Self-Rating Depression Scale (SDS), as well as fitness after 3 and 6 months. Relapse investigation was conducted by checking the database of China's National Surveillance System on Drug Abuse and that of the Shanghai Drug Control Committee's illicit drug dependents. Our investigation focused on the relapse of participants who had undergone and completed treatment in the Shanghai Mandatory Detoxification and Rehabilitation Center in 2015. The result showed that the PSQI scores of sleep duration [$F_{(2,\,92)} = 9.86$], need for sleep medications [$F_{(2,\,92)} = 36.44$] and daytime dysfunction [$F_{(2,\,92)} = 5.15$] were found to have a significant difference by time × group interaction after 6 months. SDS showed no significant difference between the two groups; however, the score of SDS in TC decreased after 6-month intervention, and no changes were observed in SC. Pulse rate had significantly decreased in the TC group compared with the SC group after 6 months. 9.5% (4) ATS dependents in TC and 26.3% (10) ATS dependents in SC were found to have relapsed. Our result suggested that TC had positive effects on sleep quality, depression and fitness. Long-term study demonstrated that TC may be a cheap and potential supplementary treatment for ATS-dependent individuals. TC may also be considered as an alternative exercise to escalate abstinence for ATS-dependent females. Clinical trial registration: ChiCTR-IPR-14005343 chictr. org.cn

Keywords: tai chi, sleep quality, depression, fitness, amphetamine-type stimulants, relapse, women

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INTRODUCTION

Substance abuse is a major public health concern worldwide. Amphetamine-type stimulants (ATSs) are the second most prevalent drugs used globally. ATS use has been correlated with serious health consequences, such as cognitive impairment, poor physical status, high risk of mortality, and increased social burden (Chen et al., 2015). Recently, the population of ATS use in China has grown substantially (Du et al., 2014). The registered drug use identified as methamphetamine (MA) user increased from 29 to 43.8% in 2014 (Zhu et al., 2016). With East Asia regarded as a major region of concern due to its high MA production and trafficking (Rawson, 2013; Gowing et al., 2015; Kittirattanapaiboon et al., 2017), many researchers have raised an alert about ATS use/abuse around the world. The challenges of ATS use disorder have been recognized in China, and a large body of research on ATS use has emerged (Du et al., 2014).

Chronic substance use disorder (SUD) may exhibit symptoms that can include significant insomnia and mood disturbances (Bao et al., 2013). Numerous studies have shown that sleep is disrupted during active use of MA, withdrawal, and abstinence (Lipinska et al., 2015). A cross-sectional study found that the prevalence of sleep disturbance was high in drug users, which was twice the sleep latency of non-drug users. The study further indicated a link between sleep problems and duration of drug use (Tang et al., 2015). Excessive daytime sleepiness in stimulant users, which can result from poor sleep quality and/or reduced sleep time, may lead to partial sleep deprivation and deleteriously affect cognitive functioning. A study revealed that MA use disorder had elevated daytime sleepiness and a significantly higher score of Pittsburgh Sleep Quality Index (PSQI) compared with those with normal daytime sleepiness (Mahoney et al., 2014). However, a report revealed no association between sleep quality and substance use and further indicated that worse sleep was associated with worse mood (Putnins et al., 2012). Depression is another prevalent psychiatric symptom among ATS-dependent individuals. Evidence provided a result to support the consequence that more than half of the ATS dependents had depression symptoms (Du et al., 2014). Sleep quality and mood may play a role in the course of ATS use disorders and affect the outcome of treatment (Putnins et al., 2012).

Men and women abuse the same drugs, but not always in the same ways. Significant gender differences have been reported in the initiation of drug use, reasons for continuing to use drugs and the resumption of drug taking after periods of abstinence (relapse) (Fattore et al., 2014). Women affected by drug dependence and HIV are more vulnerable and more stigmatized than men. They suffer from co-occurring mental health disorders to a greater extent than men, and they are more likely to have been victims of violence and abuse. Women often also bear a heavy burden of violence and deprivation associated with the drug dependence of family members, hindering the achievement of the sustainable development target of eliminating all forms of violence against all women and girls (Greenfield et al., 2007; UNODC World Drug Report, 2016). They need help to build supportive social networks and establish a safe and predictable family environment for themselves and their children (Wiig et al., 2017). Female SUDs encounter significant systemic, structural, social, cultural, and personal barriers in accessing substance abuse treatment (United Kingdom., 2010; Guerrero et al., 2014). Although studies found that sleep duration is longer and sleep quality is higher on average in women than men (Knutson, 2013), women are diagnosed with depression and anxiety disorders roughly twice as often as men (Fattore et al., 2014). Current studies focus on specific vulnerable populations, such as sex workers and women with HIV (Rawson, 2013; Rodriguez et al., 2014; Zhang et al., 2015; Page et al., 2016; Kittirattanapaiboon et al., 2017). However, reports on the treatment of female ATS-dependent individuals are rare.

The main therapy for ATS dependence has focused on the symptomatic treatment related to ATS use complications of acute intoxication, symptoms of withdrawal such as anxiety and depression and mental disorders such as hallucinations and delusions due to chronic ATS abuse (Sun et al., 2014). Physical exercise has long been considered important in preventing and treating several medical conditions (Scully, 1998). Some evidences suggest that exercise can attenuate MA use (Miller et al., 2012) and ameliorate symptoms of depression and anxiety, which are commonly reported among MA users attempting to abstain from drug use and may be associated with drug use relapse (Dolezal et al., 2013; Segat et al., 2014). Physical exercise has been suggested to slow down the decline in cognitive function (Wayne et al., 2014; Zhang et al., 2014). Increased daytime physical activities have also been recommended to improve the quality of nighttime sleep. Exercise may effectively maintain cognitive function and improve the nighttime sleep of elderly people (Chan et al., 2016). Recent studies have focused on alternative forms of physical activity, such as tai chi (TC), which is a traditional Chinese martial art. TC has been described as a mind–body exercise regimen that benefits fitness, muscle strength, flexibility, postural control, and fall-risk reduction, as well as quality of life and well-being (Li et al., 2005; Huang et al., 2017). Several studies have evaluated the effect of TC on psychological responses, including depression, distress, well-being, life satisfaction, and perception of health (Wang et al., 2004; Taylor-Piliae et al., 2006; Garber et al., 2011).

To date, few studies focus on the effect of TC intervention on participants' sleep quality. TC can be considered a useful non-pharmacologic approach to improve sleep quality in older adults with moderate complaints and has the potential to ameliorate sleep complaints possibly before syndromal insomnia develops (Irwin et al., 2008). One study that systematically reviewed studies published between 2004 and 2014 found that TC was a common complementary exercise, which is implemented in sleep quality intervention. In the review, the most common duration of TC intervention was 60 min and the common length was 12 weeks (Wang et al., 2016). Recent studies investigated the effect of TC on heroin and ATS dependents, with reports that TC participants had better psychological and physical outcomes compared with control groups (Li et al., 2013). However, whether TC intervention works on the physical and mental effect of female ATS dependencies is not clear. As TC includes training in sustained attention focusing and multitasking (Fong et al., 2014), the meditation component may have direct benefits by enhancing attention and executive functions.

It is notable that gender differences emerged with regard to the types of exercise as well as the perceived benefits of engaging in exercise-based intervention, Yoga, stretching, and use of exercise videos are more appealing to women (Abrantes et al., 2011). As such, TC may be an effective intervention to influence female ATS dependents mentally and physically. The objective of this study is to assess the effect of TC intervention on female ATS dependents for sleep quality and fitness change at Shanghai Mandatory Detoxification and Rehabilitation Center (SMDRC). We hypothesized that TC intervention may improve sleep quality and mental health for female individuals of ATS dependent.

MATERIALS AND METHODS

Design, Setting, and Participants

This single-blind (assessors-blind), two-group randomized controlled trial was conducted between May 2014 and December 2014. In accordance with the "Narcotic Control Act", newly found drug users are sent to the drug abuse treatment hospital to assess the severity of their drug use and then back to the community to receive detoxification treatment under the supervision of social workers. If they relapse, drug users are sent to the mandatory detoxification and rehabilitation center for drug rehabilitation, where they participate in a combination of detoxification treatment, physical exercise and manual labor for 2 years (Du et al., 2014). Relapse investigation was conducted through a data check with China's National Surveillance System on Drug Abuse (NSSDA) and using the database of illicit drug dependents monitored by the Shanghai Drug Control Committee (SDCC). The target group monitored by NSSDA consisted of exposed illicit drug-dependent individuals. The monitoring coverage by this database in China is 96.3% (Cong et al., 2013). The database of SDCC lists illicit drug-dependent individuals who ever had or are receiving rehabilitation at SMDRC. Illicit drug dependents who have left from SMDRC are monitored by these systems.

The participants were all female ATS-dependent individuals. At the time of recruitment, these individuals were receiving drug withdrawal treatment at a female SMDRC. The inclusion criteria comprised voluntary individuals who were (1) aged 18 years or above, (2) level 3 illicit drug-dependent users (assessed by using the Chinese version of Addiction Severity Index and classified in accordance with the "Regulations on Prohibition against Narcotics") (Li et al., 2010) and (3) ATS dependents identified by the Guidelines of Diagnostic and Treatment on ATS Use issued by the Chinese Ministry of Health (Sun et al., 2014) and (4) had no severe medical conditions that would preclude their participation in physical activities. The exclusion criteria consisted of (1) diagnosis of Axis I psychiatric disorders in addition to SUD, (2) medical or neurological illnesses or trauma that affects the central nervous system, and (3) undergoing pharmacological treatment with psychotropic medications.

Intervention

The participants were all female and were randomly assigned by computer-generated random numbers to either the TC ($n = 40$) or standard care (SC) groups ($n = 40$). As two participants were reallocated in accordance with the duration of their stay in SMDRC, the final numbers of participants were 42 in TC and 38 in SC. The study protocol was approved by the ethical committees of the Shanghai University of Sport and SDCC. They participated in exercise sessions five times a week during the first 3 months and three times a week during the second 3 months. These interventions conducted in SMDRC are described subsequently.

TC Group

The exercise taught to the TC group was based on a simplified 24-form TC. Movements were modified in accordance with the physical capabilities and psychological characteristics of the ATS dependents, which emphasized multidirectional weight-shifting, awareness of body alignment and multisegmental (arms, legs, and trunk) movement coordination (Li et al., 2004). Each session approximately consisted of a 10 min warm-up, 40 min TC exercise and 10 min cooldown. The objective was to provide a safe exercise that illicit drug dependents in SMDRC can participate in as a supplementary treatment. TC is one of the recommended exercises by SNCC. The movements and intensity of modified TC have been described in detail by Zhu et al. in our previous study (Zhu et al., 2016). One professional TC instructor from the Shanghai University of Sport instructed and supervised the TC group.

SC Group

The exercises in the SC group had similar exercise intensity as the experimental group, which included a 5 min recreation activity (Guang Bo Ti Cao), 5 min gesture language exercises and a self-study as recommended by SNCC. The SC model is widely applied among mandatory detoxification and rehabilitation centers in Shanghai. The ninth edition of Guang Bo Ti Cao was designed by the China General Administration of Sports. This exercise is divided into eight sections and lasts for 4 min and 45 s. The gesture language exercise consists of an upper limb exercise. Qualified instructors from the SMDRC instructed the SC group. Self-education, which was performed after the exercises, included reading books related to the knowledge of health and watching TV. The duration of the SC intervention was similar to that of the TC intervention.

Procedure

The study was performed in a female SMDRC. The participants were informed of the purpose of this study and were asked to sign a consent form during the admission process. The study was performed in accordance with the Declaration of Helsinki II. TC and SC interventions were performed on a basketball field under fair weather or in an indoor self-education room during rainy weather. The intervention outcomes were assessed at the baseline and after 3 and 6 months. Experienced researchers conducted the assessment and were blinded to the two groups. A follow-up relapse investigation was conducted.

Outcome Measures

Outcome measures were obtained at the baseline and after 3 and 6 months, to verify the changes in sleep quality, depression, and physical effects among the subjects of the two groups as a result of the interventions.

Self-Rated Sleep Quality

The self-rated sleep quality was measured by using the PSQI to evaluate the quality and pattern of sleep at the baseline and after 3 and 6 months, for ATS dependents. The PSQI, with 19 items, is a widely used questionnaire to generate seven sleep component scores, including subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, need for sleep medications, and daytime dysfunction. The sum of these component scores yields a global score (range: 0–21), with a score cutoff of greater than 5 indicating a clinical sleep impairment with a high intensity and specificity in identifying insomnia (Li et al., 2004; Peles et al., 2006; Irwin et al., 2008).

Self-Rating Depression Scale (SDS)

The SDS developed by Zung was used to measure the depression level during 6 months of intervention. The advantages of this scale include ease of use in self-rating and its applicability to a wide range of people, from healthy individuals to patients (Baba et al., 2015). The SDS is a 20-item self-assessment questionnaire that measures depression. Item scores range from 1 to 4 (total score range: 20–80) (Jegede, 1976; Sashika et al., 2017). The raw scores are cataloged into four levels: 20–39 (normal range), 40–47 (mildly depressed), 48–55 (moderately depressed), and 56 and above (severely depressed) (Yang et al., 2016).

Fitness Evaluation

The fitness tests were administrated by experienced investigators. Measurements at the baseline and after 3 and 6 months were performed in the morning at the same time. Blood pressure was measured under standardized conditions prior to other tests: participants were asked to rest for 5 min and had not taken any caffeine or tobacco products within 30 min. Body composition and body mass index were measured with Omron HBF-305. Hand grip power test was assessed using a grip dynamometer, and flexibility was tested with a sit and reach test equipment. Balance test was performed with one leg stand with eyes closed. A sport watch was used to record the duration of one leg stand with eyes closed. The progressive aerobic cardiovascular endurance run (PACER) was performed to measure the aerobic capacity of ATS dependents with following standardized procedures. The participants ran from one marker to another marker set 20 m apart while keeping pace with a pre-recorded cadence. The cadence was set to music and increased every minute. Participants were instructed to keep up with the cadence for as long as possible. The test was terminated when a participant failed to reach the appropriate marker in the allotted time twice or could no longer maintain the pace. The number of laps completed was recorded (Mahar et al., 2011; Marques et al., 2015).

Relapse Investigation

NSSDA is part of law enforcement and managed administratively by judicial departments or public security bureaus. The sites monitor the prevalence of drug users (both relapsed and new) and types of drugs used and facilitate detoxification treatment for drug users. The information collected includes basic identification and demographic information, drug type, first time drug use, results of urine tests, main places of drug use and any disease comorbidity (Cong et al., 2013; Jia et al., 2015). The ATS-dependent individual relapse in this study was investigated on the basis of NSSDA data and combined with the latest records administrated by SDCC. The content of the relapse investigation was based on data including the name and exact date of relapse for participants who had taken part in this experiment. ATS participants received treatment from July 2012 to July 2013 and were discharged to the community from July 2014 to July 2015 after 2 years of mandatory treatment in this study. The relapse investigation was conducted on June 25, 2017, to examine who has relapsed after they took part in this study.

Statistics

Statistical analyses were performed using SPSS 19.0 (Chicago, USA). Pearson chi-squared test was applied for categorical variables of demography, and independent sample *t*-test was applied for continuous variables at the baseline comparison of PSQI, SDS, fitness and relapse. Pearson chi-squared test and independent sample *t*-test was used to compare the demographic and clinic characteristics differences of trial completers and non-completers at baseline.

As all variables were normally distributed and tested with Kolmogorov–Smirnov test, a two-way repeated measures analysis of variance (ANOVA) was applied to test whether the treatments were different after 6 months. Time (baseline, 3 and 6 months) was the within-group factor, groups (TC and SC) were the between-group factors and year of drug dependence was the covariate. A *post hoc* test with Bonferroni correction was used to examine which group was different if the ANOVA showed a significant interaction.

The relapse comparison was compared with independent sample *t*-test. Correlations between PSQI, SDS, and fitness at baseline were computed using Pearson's correlation analyses. Data were reported as the mean values (plus SD), and the significance level was set to $p < 0.05$.

RESULTS

The initial 1,181 female substance dependents were receiving treatment in SMDRC, in which 915 substance dependents were synthetic drug dependents. In addition, 82 female ATS-dependent individuals voluntarily took part in this study. A total of 80 eligible subjects were recruited and randomly assigned to the TC group ($n = 42$) and SC group ($n = 38$) (**Table 1**).

Data on subjects in the TC group were as follows: 33.74 ± 7.11 years old, 159.62 ± 5.10 cm height, 60.81 ± 6.66 kg weight, and 7 ± 4 years of ATS use. Data on subjects in the SC group were as follows: 37.76 ± 9.85 years old, 160.20 ± 5.21 cm height, 63.16 ± 7.79 kg weight, and 8 ± 6 years of ATS use. Five participants

TABLE 1 | Demography of ATS dependent ($N = 80$).

Content		Tai chi ($N = 42$)			Stand care ($N = 38$)		
		N	**Percent (%)**	**Valid percent (%)**	***N***	**Percent (%)**	**Valid percent (%)**
Education	College Level or higher	3	7	7	1	3	3
	High school or equivalent	13	31	31	6	16	16
	Middle school	23	55	55	27	71	71
	Elementary school	3	7	7	4	11	11
Occupation	Service	11	26	26	7	18	18
	Staff	2	5	5	1	3	3
	Owner	4	10	10	7	18	18
	Worker	2	5	5	2	5	5
	Farmer	1	2	2	1	3	3
	Unemployed	22	52	52	20	53	53
Marital status	Single	21	50	50	11	29	29
	Married	9	21	21	12	32	32
	Divorced/widow	12	29	29	15	39	39
Type of drug	Meth	42	46.7	100	34	57.6	89.5
	Ketamine	21	23.3	50	5	8.5	13.2
	Heroin	15	16.7	35.7	16	27.1	42.1
	Cocaine	3	3.3	7.1	1	1.7	2.6
	Ecstasy	4	4.4	9.5	1	1.7	2.6
	Marijuana	5	5.6	11.9	2	3.4	5.3
Treatment	Never	23	55	55	22	58	59
	Mental treatment	6	14	14	1	3	3
	Social assistant	1	2	2	2	5	5
	Medical treatment	12	29	29	12	32	32

in the TC group and 26 participants in the SC group dropped out during the intervention. The reason for dropout was leaving SMDRC to the community (**Figure 1**).

At baseline, no statistically significant differences were observed between groups in terms of sleep quality, depression, fitness, and relapse times except for sleep duration, $t = -2.15$, $p < 0.05$; need for sleep medications, $t = 7.66$, $p < 0.01$; and PACER score, $t = 2.48$, $p < 0.05$. There was no demographic and clinic characteristics differences between trial completers and non-completers (**Tables 2**, **3**).

Sleep Quality (PSQI)

Significant differences were found regarding the scores of sleep duration [$F_{(2, 92)} = 9.86$, $p < 0.001$, $\eta^2 = 0.18$] by time × group interaction after 6 months. The *post hoc* test further revealed a significantly long sleep duration in the TC group [$F_{(1, 46)} = 23.75$, $p < 0.001$]. Need for sleep medications [$F_{(2, 92)} = 36.44$, $p < 0.001$, $\eta^2 = 0.44$] and daytime dysfunction [$F_{(2, 92)} = 5.15$, $p = 0.01$, $\eta^2 = 0.10$] were found to be significantly different by time × group interaction after 6 months. Although the scores of PSQI showed no significant difference between the two groups by time × group interaction after 6 months, the *post hoc* test revealed that PSQI score [$F_{(1, 46)} = 5.19$, $p = 0.027$, $\eta^2 = 0.10$] and habitual sleep efficiency [$F_{(1, 46)} = 8.05$, $p = 0.007$, $\eta^2 = 0.15$] in the TC group significantly decreased statistically compared with those in the SC group. The PSQI score with the repeated measure by group × year of drug dependence revealed significant differences, $F_{(2, 92)} = 5.21$, $p = 0.007$.

Between-group results showed that sleep duration [$F_{(1, 46)} = 23.75$, $p < 0.001$], habitual sleep efficiency [$F_{(1, 46)} = 8.05$, $p = 0.007$], need for sleep medications [$F_{(1, 46)} = 35.4$, $p < 0.001$], and PSQI score [$F_{(1, 46)} = 5.19$, $p = 0.027$] were significantly different (**Table 4**).

SDS

Although no significant difference was observed between the two groups, the score of SDS decreased in the TC group, whereas that in the SC group was the same after 6 months (**Table 4**).

Fitness Outcome

Our findings showed that the pulse rate had significantly decreased in the TC group compared with the SC group [$F_{(2, 92)} = 3.32$, $p = 0.04$] after 6 months by time × group interaction.

Between-group test by repeated measures ANOVA revealed significant differences between groups in terms of body fat [$F_{(1, 46)} = 4.49$, $p = 0.04$] and running laps of PACER [$F_{(1, 46)} = 9.83$, $p = 0.003$]. Compared with the baseline, the results of PACER in both groups had decreased. A significant difference was observed in the between-group test by ANOVA with years of drug dependence, $F_{(1, 46)} = 9.83$, $p < 0.003$ (**Table 4**).

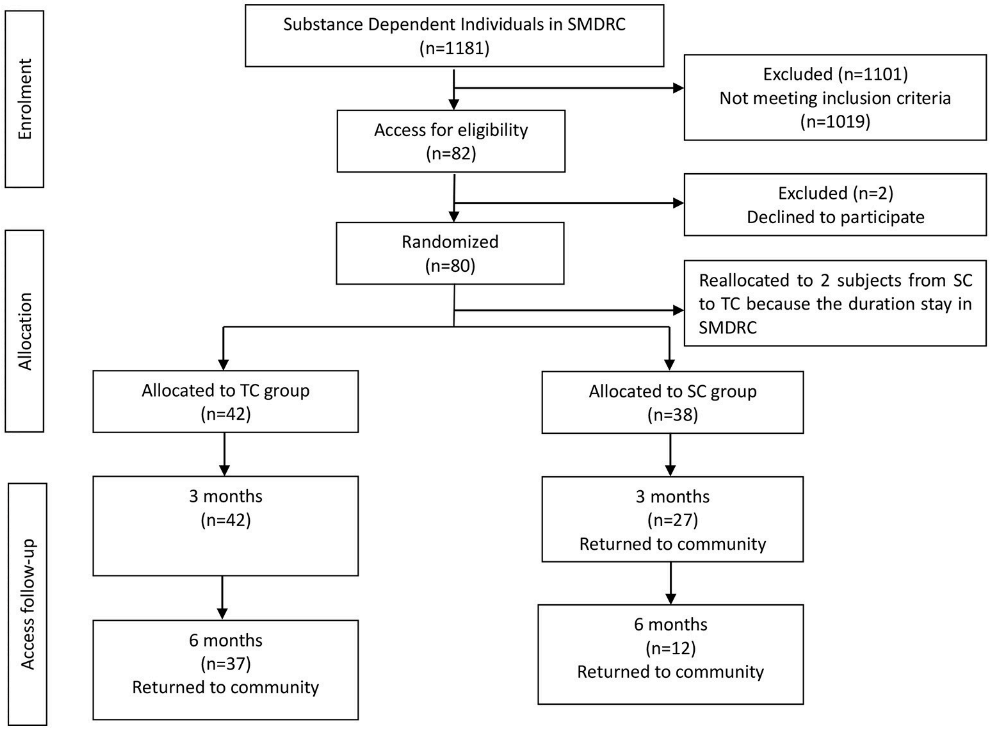

FIGURE 1 | Flow diagram of the intervention progress through the phases of the two groups.

Relapse

Independent t-test revealed a significant difference between the two groups in terms of relapse ($t = 3.37$, $p = 0.006$). The relapse in the TC group was 9.5% and that in the SC group was 26.3% because ATS-dependent individuals had left SMDRC. The relapse investigation further demonstrated that the duration of ATS cessation among relapse individuals was significantly different ($t = 4.94$, $p < 0.01$). The cessation durations of ATS-dependent individuals from the last relapse to be found this time to relapse were 1,209 and 880 days in the TC and SC groups, respectively (**Table 5**).

Associated Factors Among ATS-Dependent Individuals

The Pearson correlation test revealed that several significant results were associated with baseline outcomes. The correlation between PACER and the score of SDS was $r = 0.30$, $p = 0.008$. The correlation between PACER and the years of illicit drug use was $r = -0.33$, $p = 0.003$. The correlation between total score of PSQI and the years of illicit drug use was $r = 0.27$, $p = 0.016$.

DISCUSSION

To our knowledge, this paper is the first to discuss the effect of TC intervention on female ATS-dependent individuals. Our study found that ATS-dependent individuals in the TC group had a better score of PSQI and SDS and some positive changes in terms of fitness compared with the SC group. A follow-up relapse investigation demonstrated that participants in the TC group had less relapse.

Sleep Quality and Mood

The main outcome of PSQI showed that ATS-dependent individuals in the TC group had a better PSQI score than those in the SC group. The duration of sleep and daytime dysfunction were found to have significantly improved in the TC group. Furthermore, ATS-dependent individuals in the TC group had shorter sleep latency than that in the SC group after 6 months of treatment. At baseline, the sleep duration and need for sleep medication had significant differences as the result of the high percentage of participants in the TC group that used sleep medication. With the intervention, participants in the TC group that needed sleep medication decreased from 71.5% (30) to 2.7% (1) after 6 months.

To date, a cross-sectional study on the sleeping problem in Chinese illicit drug-dependent subjects has been conducted (Tang et al., 2015). The study investigated a total of 2,178 illicit drug users and 2,236 non-drug users in Changsha, China. The PSQI score in our study at baseline was slightly lower than that in the report (7.97 ± 4.39). The reason for this difference is that subjects were collected following a 10-day detoxification treatment in the earlier study, while in our study, all subjects had experienced detoxification and rehabilitation for at least 6 months at SMDRC. Interestingly, the PSQI score in the TC group after 6 months of intervention in our study was lower than

TABLE 2 | Baseline of PSQI, SDS, and relapse time comparison of the groups ($N = 80$).

	Tai chi	**Standard care**		
Contents	**($N = 42$)**	**($N = 38$)**	***T***	***p*-value**
Pittsburgh Sleep Quality Index				
Subjective sleep quality, M(SD)	1.02 (0.68)	1.08 (0.78)	−0.34	0.74
Sleep latency, M (SD)	1.31 (0.72)	1.37 (0.88)		
≤15 min, n,%	5,11.9%	7,18.4%		
16–30 min, n,%	20,47.6%	13,34.2%		
31–60 min,n,%	16,38.1%	15,39.5%		
>60 min, n,%	1,2.4%	3,7.9%		
Sleep duration, M(SD)	0.24 (0.43)	0.5 (0.65)	−2.15	<0.05*
>7 h, n,%	32,76.2%	22,57.9%		
6–7 h, n,%	10,23.8%	13,34.2%		
5-6 h, n,%	0	3,7.9%		
Habitual sleep efficiency, M(SD)	92.50 (6.59)	88.50 (11.45)	1.94	0.06
≥85%, n,%	35,83.4%	27,70.9%		
75–84%, n,%	7,16.7%	7,18.4%		
65–74%, n,%	0	1,2.6%		
<65%, n,%	0	3,7.8%		
Sleep disturbances, M(SD)	1.21 (0.47)	1.34 (0.58)	−1.08	0.28
Need for sleep medications, M(SD)	0.88 (0.67)	0.03 (0.16)	7.66	<0.001**
Daytime dysfunction	1.10 (0.91)	1.11 (1.09)	−0.05	0.96
PSQI score	5.07 (2.44)	5.89 (3.25)	−1.29	0.2
Self-rated Depression Scale	48.55 (8.25)	49.95 (9.29)	−0.71	0.48
History of relapse (n)	1.81 (1.04)	2.03 (1.17)	0.77	0.38

*Data presented as mean (SD); * $p < 0.05$; ** $p < 0.01$.*

TABLE 3 | Baseline of fitness comparison of the groups ($N = 80$).

	Tai chi	**Standard care**		
Contents	**($N = 42$)**	**($N = 38$)**	***T***	***p*-value**
Mass (kg)	60.81 (6.66)	63.16 (7.79)	−1.4	0.15
Body fat (%)	31.24 (2.48)	32.50 (4.28)	−1.6	0.12
Systolic (mmHg)	121.40 (14.71)	119.61 (11.69)	0.6	0.55
Diastolic (mmHg)	78.40 (10.77)	79.50 (10.50)	−0.46	0.65
Pulse (bmp)	85.45 (9.64)	80.97 (12.26)	1.83	0.07
Vital capacity (ml)	2699.07 (727.14)	2571.24 (678.81)	0.81	0.42
Hand grip (R) (kgf)	24.57 (5.30)	24.07 (5.51)	0.41	0.68
Sit-and-reach (cm)	11.60 (6.66)	8.61 (7.95)	1.83	0.07
One-leg stand with eye closed (s)	26.93 (25.55)	31.65 (30.74)	−0.75	0.46
PACER (laps)	20.93 (7.47)	16.95 (6.68)	2.48	< 0.05*

*Data presented as mean (SD); * $p < 0.05$.*

that of non-drug users reported by Tang et al., but the PSQI score in the SC group was close to what that study displayed (4.20 ± 2.468).

While practicing TC, the mind should be calm. Integrating movements and the spirit is required, and breathing shall be harmonious with movements. The breathing pattern may alter the functioning of the autonomic nervous system. Various breathing practices are believed to be beneficial to release emotion, calm the mind, or enhance physical power, all of which may be regarded as potential mediators of improved sleep quality (Payne and Crane-Godreau, 2013). Evidences indicated that TC can effectively improve sleep quality not only for normal older adults but also for older adults with cognitive impairment and elderly Chinese women with knee OA (Li et al., 2004; Chan et al., 2016; Lü et al., 2017). A systematic follow-up review reported positive effects of TC on the executive function of cognitively healthy adults compared with no intervention, other active interventions and exercise (Solloway et al., 2016). The rationale of TC ameliorating sleep and mood disturbance is that moderate rhythmic movement may increase the parasympathetic tone, whereas intense exertion causes further sympathetic activation. TC is a moderate-intensity exercise. The smooth rhythmic motions of TC are usually experienced as relatively pleasurable mood (Pa et al., 2014; Kim et al., 2016). Our study demonstrated that TC may be a potential physical activity to escalate sleep quality and fitness for female ATS dependents.

Numerous studies have shown high prevalence of sleep disturbance among illicit drug dependents (Mahfoud et al., 2009; Brower and Perron, 2010; Liao et al., 2011; Mahoney et al., 2014; Tang et al., 2015). Similarly, our findings showed that the PSQI score was associated with the duration of illicit drug use. In addition, aerobic capacity tested by PACER was associated with illicit drug use and depression.

In our study, the scores of self-reported depression had slightly decreased in the TC group, but no changes in the SC group were found. Thus, TC has therapeutic value for the sleep quality and depression of ATS dependents. Disturbed sleep is an important predictor of relapse. However, we compared the PSQI score with the non-relapse and relapse ATS-dependent individuals in our study. We found no significant differences. A noteworthy comparison between non-relapse and relapse individuals in our study was the balance outcome at the baseline. Findings showed that the re-relapse ATS-dependent individuals had shorter balance time (19 s) than ATS-dependent individuals who have not been found to relapse after they left SMDRC (they had a longer balance time: 31 s).

Fitness Changes

The fitness test results showed an improvement in the balance control but no significant differences between groups. Numerous studies have suggested that TC can efficiently improve the functional balance (Province et al., 1995; Campbell et al., 1997). The TC movements in the intervention included "golden rooster stands on one leg" (Jing Ji Du Li). The TC instructors observed that the participants in the TC group swayed their trunks while performing Jing Ji Du Li and when they were shifting their weight from one leg to another in the first 2 weeks. This outcome may be considered as a result from long-term ATS abuse, which negatively affected the proprioception of the participants, and the fact that they were unfamiliar with the TC movements before the intervention. The balance

TABLE 4 | Comparison of two groups at baseline, 3 and 6 months by ANOVA repeat measures (*N* = 49).

	Tai chi (*N* = 37)			Standard care (*N* = 12)					
	Baseline	**3 month**	**6 month**	**Baseline**	**3 month**	**6 month**	**Within-group**	**Between-group**	**Group × time**
PITTSBURGH SLEEP QUALITY INDEX									
Subjective sleep quality	1.03 (0.69)	0.73 (0.65)	0.70 (0.70)	0.92 (0.79)	0.92 (0.99)	0.67 (0.78)	0.41	0	0.91
Sleep latency	0.84 (0.69)	0.81 (0.84)	0.70 (0.62)	1.00 (0.95)	1.25 (1.14)	0.83 (0.94)	3.26*	1.33	0.85
Sleep duration	0.24 (0.44)	0.24 (0.49)	0.11 (0.31)	0.58 (0.67)	0.75 (0.75)	1.17 (0.58)	0.51	23.75**	9.86**
Habitual sleep efficiency (%)	92.5 (6.81)	91.86 (9.05)	93.16 (5.04)	87.92 (11.13)	84.17 (14.34)	86.33 (13.70)	0.51	8.05**	0.43
Sleep disturbances	1.24 (0.43)	1.11 (0.39)	1.03 (0.29)	1.42 (0.51)	1.17 (0.39)	1.08 (0.29)	2.43	0.89	0.48
Need for sleep medications	1.00 (0.62)	0.00 (0.00)	0.03 (0.16)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	3.45*	35.4**	36.43**
Daytime dysfunction	1.05 (0.91)	0.46 (0.73)	0.41 (0.60)	1.08 (0.90)	0.83 (0.72)	0.08 (0.29)	4.89*	0.01	5.15**
PSQI score	5.03 (2.55)	3.78 (2.76)	3.32 (1.92)	6.08 (3.06)	6.08 (3.42)	4.50 (2.51)	2.85	5.19*	2.11
Self-rated Depression Scale	48.19 (8.12)	48.86 (9.66)	46.14 (10.67)	48.25 (9.08)	52.00 (7.59)	49.25 (8.31)	4.10*	0.62	0.84
FITNESS OUTCOME									
Mass (kg)	61.57 (5.51)	60.27 (5.77)	61.51 (5.77)	64.33 (8.63)	62.83 (9.33)	61.51 (5.77)	2.42	1.53	0.4
Body fat (%)	31.33 (2.49)	30.86 (2.40)	32.61 (2.87)	32.93 (4.86)	31.97 (4.60)	32.97 (5.11)	6.01**	1.05	1.88
Systolic (mmHg)	121.59 (15.29)	109.14 (10.63)	110.46 (9.10)	119.67 (13.56)	111.83 (10.43)	117.75 (9.76)	6.01**	0.75	2.27
Diastolic (mmHg)	78.46 (11.13)	68.16 (8.20)	72.68 (7.24)	82.00 (12.29)	70.75 (10.76)	77.58 (10.67)	7.28**	2.07	0.23
Pulse (bmp)	85.65 (9.57)	70.84 (7.25)	72.78 (8.11)	81.17 (13.54)	72.83 (7.70)	75.33 (13.97)	14.69**	0	3.08*
Vital capacity (ml)	2641.32 (725.48)	2288.38 (580.20)	2207.32 (476.78)	2618.17 (697.63)	2169.83 (656.14)	2127.00 (399.31)	5.20**	0.24	0.09
Hand grip (R) (kgf)	24.59 (5.42)	25.76 (4.17)	33.03 (5.73)	24.27 (5.52)	24.24 (5.73)	32.92 (4.31)	84.41**	0.16	0.87
Sit-and-reach (cm)	10.86 (6.61)	13.82 (5.48)	10.65 (5.16)	8.09 (7.71)	14.35 (13.83)	8.82 (5.80)	3.48*	0.51	1.14
One-leg stand with eye closed (s)	28.75 (26.61)	36.53 (27.93)	45.36 (37.46)	29.36 (23.07)	21.30 (13.01)	27.97 (13.46)	0.7	1.96	2.02
PACER (laps)	20.51 (7.35)	14.14 (5.41)	17.41 (8.24)	16.92 (8.39)	13.33 (5.73)	12.42 (3.73)	1.95	2.97	1.49

*Data presented as mean (SD); * $p < 0.05$; ** $p < 0.01$.*

mechanism developed by the repeated positioning of the body and limb joints in specific spatial positions through TC can induce plastic changes in the cortex. The repetitive, afferent inputs from the cutaneous receptors in the skin and limb proprioceptors, including muscle and tendon spindles, can modify the cortical maps of the body over time (Tsang and Hui-Chan, 2003).

Blood pressure also decreased in the TC group but slightly changed in the SC group. The systolic pressure had decreased in the TC group by 11 mmHg, with no change in the SC group. The post-intervention changes in the systolic and diastolic pressures are consistent with the findings from earlier studies that reported a decrease in blood pressure after TC practice (Chen et al., 2012) (Wolf et al., 2003; Zhu et al., 2016). These changes were not associated with the antihypertensive use by ATS-dependent individuals. The record of antihypertensives indicated that four ATS dependents in each group used a Zheng Ju antihypertensive, which is a Chinese herb pill. Although the pulse decreased in both groups, results displayed that the ATS dependents' pulse in the TC group decreased significantly after 6 months of TC practice. Yoga, TC, meditation and other relaxation therapies have been reported to reduce sympathetic activity, decrease sympathoadrenal reactivity and enhance parasympathetic output, which may, in turn, reduce the prevalence and severity of vasomotor disturbances and sleep impairment (Innes et al., 2010).

TABLE 5 | Follow-up Investigation of Relapse (*N* = 80).

Contents	**Tai chi**	**Standard care**	***T***	***p*-value**
Relapse (N)	4 (9.5%)	10 (26.3%)	3.37	0.006**
Duration of ATS Cessation (Days)	1209 (79)	880 (121)	4.95	0.00**
Numbers of Cessation (N)	38 (90.5%)	28 (73.7%)	3.9	0.048*

*Data presented as mean (SD); * $p < 0.05$; ** $p < 0.01$.*

Notably, the PACER score, which represents the aerobic capacity of ATS dependents, decreased in both groups. However, although the aerobic capacity in the TC group decreased after 3 months, it had increased after 6 months. By contrast, the aerobic capacity in the SC group decreased rapidly. This result indicated that TC can slow down the decreasing trend of the aerobic capacity of ATS dependents. Furthermore, female ATS dependents in SMDRC are sedentary patients. Effective exercises shall be widely applied in mandatory detoxification and rehabilitation centers in China.

In accordance with other studies in China, after detoxification, the relapse rate for heroin abusers within the first month is 54.57%. The relapse rate within the first to third months is 31.76%, whereas it is 93.31% within the first 6 months and 96.68% within the first year. Drug addicts often fall into the vicious cycle of "drug-taking–detoxification–relapse–effort–quit" (Jia et al., 2015). The relapse investigation was conducted with relapse data examination instead of PSQI, SDS and fitness measurement. Our study indicated that TC has positive effects on sleep quality, depression and fitness and participants in the TC group had low relapse percentage. The long-term study demonstrates that TC may be a cheap and potential supplementary treatment for ATS-dependent individuals. TC may also be considered as an alternative exercise to escalate abstinence for female ATS-dependent individuals.

LIMITATION

This study has a number of limitations. First, although the participants were randomized into the TC and SC groups, the groups had to be slightly modified due to the reallocation of their residence in the SMDRC. Second, the number of dropouts in the SC group was higher than that in the TC group. The reason for dropout was not associated with the different interventions or the performance of instructors in the two groups. The findings must be interpreted with caution as the high attrition rate recorded in the SC group at 3 and 6 months can affect the sample's representativeness. Future study should consider participants' expected number of treatment days in mandatory and detoxification centers before setting up an intervention. Third, although the relapse assessment was from the data of NSSDA and SSDC, it is possible some relapsing individuals may not have been identified by the surveillance system. Nevertheless, this was the first study to report the longitudinal effect of TC exercise intervention. Forth, the intensity of our interventions was fixed, future studies should consider the effects of exercise duration.

ETHICS STATEMENT

This study was carried out in accordance with the recommendations of Policies and Procedures for Projects that Involved Human Subjects, Research Ethic Committee of Shanghai University of Sport with written informed consent from all subjects. All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the Research Ethic Committee of Shanghai University of Sport.

AUTHOR CONTRIBUTIONS

DZ conceived the trial, designed the exercise intervention, wrote and revised the manuscript. GD acquired partial financial support for the research project, and partially worked on the discussion part. DX coordinated the research project and collected the data of ATS dependents' relapse. XX revised the English grammar and abstract. JG conducted the exercise intervention and data collection. WZ contributed the idea of this trial and partially discussed the data. XJ contributed to the trial design and data collection. MT contributed to the trial design and revised the manuscript.

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REFERENCES

Abrantes, A. M., Battle, C. L., Strong, D. R., Ing, E., Dubreuil, M. E., Gordon, A., et al. (2011). Exercise preferences of patients in substance abuse treatment. *Ment. Health Phys. Act.* 4, 79–87. doi: 10.1016/j.mhpa.2011.08.002

Baba, M., Ohkura, M., Koga, K., Nishiuchi, K., Herrera, L. R., Matsuse, R., et al. (2015). Analysis of salivary cortisol levels to determine the association between depression level and differences in circadian rhythms of shift-working nurses. *J. Occup. Health* 57, 237–244. doi: 10.1539/joh.14-0079-OA

Bao, Y. P., Qiu, Y., Yan, S. Y., Jia, Z. J., Li, S. X., Lian, Z., et al. (2013). Pattern of drug use and depressive symptoms among amphetamine type stimulants users in Beijing and Guangdong province, China. *PLoS ONE* 8:e60544. doi: 10.1371/journal.pone.0060544

Brower, K. J., and Perron, B. E. (2010). Sleep disturbance as a universal risk factor for relapse in addictions to psychoactive substances. *Med. Hypotheses* 74, 928–933. doi: 10.1016/j.mehy.2009.10.020

Campbell, A. J., Robertson, M. C., Gardner, M. M., Norton, R. N., Tilyard, M. W., and Buchner, D. M. (1997). Randomised controlled trial of a general practice programme of home based exercise to prevent falls in elderly women. *Br. Med. J.* 315,1065–1069. doi: 10.1136/bmj.315.7115.1065

Chan, A. W., Yu, D. S., Choi, K. C., Lee, D. T., Sit, J. W., and Chan, H. Y. (2016). Tai chi qigong as a means to improve night-time sleep quality among older adults with cognitive impairment: a pilot randomized controlled trial. *Clin. Interv. Aging* 11, 1277–1286. doi: 10.2147/CIA.S111927

Chen, W., Li, X., Li, X. , Ling, L., Xia, Y., Chen, J., et al. (2012). Erectile dysfunction among male heroin addicts receiving methadone maintenance treatment in Guangdong, China. *J. Addict. Med.* 6, 212–218. doi: 10.1097/ADM.0b013e318259b2c4

Chen, Y. C., Chen, C. K., and Wang, L. J. (2015). Predictors of relapse and dropout during a 12-week relapse prevention program for methamphetamine users. *J. Psychoactive Drugs* 47, 317–324. doi: 10.1080/02791072.2015.1071447

Cong, M., Bao,Y., Lv,X., and Liu,Z. (2013). The research on the status of national drug abuse surveillance system. *Chin. J. Drug Depend.* 22, 386–393.

Dolezal, B. A., Chudzynski, J., Storer, T. W., Abrazado, M., Penate, J., Mooney, L., et al. (2013). Eight weeks of exercise training improves fitness measures in methamphetamine-dependent individuals in residential treatment. *J. Addict. Med.* 7, 122–128. doi: 10.1097/ADM.0b013e318282475e

Du, J., Sun, H., Huang, D., Jiang, H., Zhong, N., Xu, D., et al. (2014). Use trajectories of amphetamine-type stimulants (ATS) in Shanghai, China. *Drug Alcohol Depend.* 143, 44–50. doi: 10.1016/j.drugalcdep.2014.06.031

Fattore, L., Melis, M., Fadda, P., and Fratta, W. (2014). Sex differences in addictive disorders. *Front. Neuroendocrinol.* 35, 272–284. doi: 10.1016/j.yfrne.2014.04.003

Fong, D. Y., Chi, L. K., Li, F., and Chang, Y. K. (2014). The benefits of endurance exercise and Tai Chi Chuan for the task-switching aspect of executive function in older adults: an ERP study. *Front. Aging Neurosci.* 6:295. doi: 10.3389/fnagi.2014.00295

Garber, C. E., Blissmer, B., Deschenes, M. R., Franklin, B. A., Lamonte, M. J., Lee, I. M., et al. (2011). Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med. Sci. Sports Exerc.* 43, 1334–1359. doi: 10.1249/MSS.0b013e318213fefb

Gowing, L. R., Ali, R. L., Allsop, S., Marsden, J., Turf, E. E., West, R., et al. (2015). Global statistics on addictive behaviours: 2014 status report. *Addiction* 110, 904–919. doi: 10.1111/add.12899

Greenfield, S. F., Brooks, A. J., Gordon, S. M., Green, C. A., Kropp, F., McHugh, R. K., et al. (2007). Substance abuse treatment entry, retention, and outcome in women: a review of the literature. *Drug Alcohol Depend.* 86, 1–21. doi: 10.1016/j.drugalcdep.2006.05.012

Guerrero, E. G., Villatoro, J. A., Kong, Y., Fleiz, C., Vega, W. A., Strathdee, S. A., et al. (2014). Barriers to accessing substance abuse treatment in Mexico: national comparative analysis by migration status. *Subst. Abuse Treat. Prev. Policy* 9:30. doi: 10.1186/1747-597X-9-30

Huang, Z. G., Feng, Y. H., Li, Y. H., and Lv, C. S. (2017). Systematic review and meta-analysis: Tai Chi for preventing falls in older adults. *BMJ Open* 7:e013661. doi: 10.1136/bmjopen-2016-013661

Innes, K. E., Selfe, T. K., and Vishnu, A. (2010). Mind-body therapies for menopausal symptoms: a systematic review. *Maturitas* 66, 135–149. doi: 10.1016/j.maturitas.2010.01.016

Irwin, M. R., Olmstead, R., and Motivala, S. J. (2008). Improving sleep quality in older adults with moderate sleep complaints: a randomized controlled trial of Tai Chi Chih. *Sleep* 31, 1001–1008. doi: 10.5665/sleep/31.7.1001

Jegede, R. O. (1976). Psychometric properties of the Self-Rating Depression Scale (SDS). *J. Psychol.* 93, 27–30.

Jia, Z., Liu, Z., Chu, P., McGoogan, J. M., Cong, M., Shi, J., et al. (2015). Tracking the evolution of drug abuse in China, 2003-10: a retrospective, self-controlled study. *Addiction* 110 (Suppl. 1), 4–10. doi: 10.1111/add.12769

Kim, T. H., Pascual-Leone, J., Johnson, J., and Tamim, H. (2016). The mental-attention Tai Chi effect with older adults. *BMC Psychol.* 4:29. doi: 10.1186/s40359-016-0137-0

Kittirattanapaiboon, P., Srikosai, S., and Wittayanookulluk, A. (2017). Methamphetamine use and dependence in vulnerable female populations. *Curr. Opin. Psychiatry* 30, 247–252. doi: 10.1097/YCO.0000000000000335

Knutson, K. L. (2013). Sociodemographic and cultural determinants of sleep deficiency: implications for cardiometabolic disease risk. *Soc. Sci. Med.* 79, 7–15. doi: 10.1016/j.socscimed.2012.05.002

Li, D. X., Zhuang, X. Y., Zhang, Y. P., Guo, H., Wang, Z., Zhang, Q., et al. (2013). Effects of Tai Chi on the protracted abstinence syndrome: a time trial analysis. *Am. J. Chin. Med.* 41, 43–57. doi: 10.1142/S0192415X13500043

Li, F., Fisher, K. J., Harmer, P., Irbe, D., Tearse, R. G., and Weimer, C. (2004). Tai chi and self-rated quality of sleep and daytime sleepiness in older adults: a randomized controlled trial. *J. Am. Geriatr. Soc.* 52, 892–900. doi: 10.1111/j.1532-5415.2004.52255.x

Li, F., Harmer, P., Fisher, K. J., McAuley, E., Chaumeton, N., Eckstrom, E., et al. (2005). Tai Chi and fall reductions in older adults: a randomized controlled trial. *J. Gerontol. Ser. Biol. Sci. Med. Sci.* 60, 187–194. doi: 10.1093/gerona/60.2.187

Li, J., Ha, T. H., Zhang, C., and Liu, H. (2010). The Chinese government's response to drug use and HIV/AIDS: a review of policies and programs. *Harm Reduc. J.* 7:4. doi: 10.1186/1477-7517-7-4

Liao, Y., Tang, J., Liu, T., Chen, X., Luo, T., and Hao, W. (2011). Sleeping problems among Chinese heroin-dependent individuals. *Am. J. Drug Alcohol Abuse* 37, 179–183. doi: 10.3109/00952990.2010.535580

Lipinska, G., Timol, R., and Thomas, K. G. (2015). The implications of sleep disruption for cognitive and affective processing in methamphetamine abuse. *Med. Hypotheses* 85, 914–921. doi: 10.1016/j.mehy.2015.09.010

Lü, J., Huang, L., Wu, X., Fu, W., and Liu, Y. (2017). Effect of Tai Ji Quan training on self-reported sleep quality in elderly Chinese women with knee osteoarthritis: a randomized controlled trail. *Sleep Med.* 33, 70–75. doi: 10.1016/j.sleep.2016.12.024

Mahar, M. T., Guerieri, A. M., Hanna, M. S., and Kemble, C. D. (2011). Estimation of aerobic fitness from 20-m multistage shuttle run test performance. *Am. J. Prev. Med.* 41, S117–S123. doi: 10.1016/j.amepre.2011.07.008

Mahfoud, Y., Talih, F., Streem, D., and Budur, K. (2009). Sleep disorders in substance abusers: how common are they? *Psychiatry* 6, 38–42.

Mahoney, J. J., De La Garza, R., Jackson, B. J., Verrico, C. D., Ho, A., Iqbal, T., et al. (2014). The relationship between sleep and drug use characteristics in participants with cocaine or methamphetamine use disorders. *Psychiatry Res.* 219, 367–371. doi: 10.1016/j.psychres.2014.05.026

Marques, A., Santos, R., Ekelund, U., and Sardinha, L. B. (2015). Association between physical activity, sedentary time, and healthy fitness in youth. *Med. Sci. Sports Exerc.* 47, 575–580. doi: 10.1249/MSS.0000000000000426

Miller, M. L., Vaillancourt, B. D., Wright, M. J., Aarde, S. M., Vandewater, S. A., Creehan, K. M., et al. (2012). Reciprocal inhibitory effects of intravenous d-methamphetamine self-administration and wheel activity in rats. *Drug Alcohol Depend.* 121, 90–96. doi: 10.1016/j.drugalcdep.2011.08.013

Pa, J., Goodson, W., Bloch, A., King, A. C., Yaffe, K., and Barnes, D. E. (2014). Effect of exercise and cognitive activity on self-reported sleep quality in community-dwelling older adults with cognitive complaints: a randomized controlled trial. *J. Am. Geriatr. Soc.* 62, 2319–2326. doi: 10.1111/jgs.13158

Page, K., Stein, E. S., Carrico, A. W., Evans, J. L., Sokunny, M., Nil, E., et al. (2016). Protocol of a cluster randomised stepped-wedge trial of behavioural interventions targeting amphetamine-type stimulant use and sexual risk among female entertainment and sex workers in Cambodia. *BMJ Open* 6:e010854. doi: 10.1136/bmjopen-2015-010854

Payne, P., and Crane-Godreau, M. A. (2013). Meditative movement for depression and anxiety. *Front. Psychiatry* 4:71. doi: 10.3389/fpsyt.2013.00071

Peles, E., Schreiber, S., and Adelson, M. (2006). Variables associated with perceived sleep disorders in methadone maintenance treatment (MMT) patients. *Drug Alcohol Depend.* 82, 103–110. doi: 10.1016/j.drugalcdep.2005.08.011

Province, M. A., Hadley, E. C., Hornbrook, M. C., Lipsitz, L. A., Mulrow, C. D., Ory, M. G., et al. (1995). The effects of exercise on falls in elderly patients - a preplanned metaanalysis of the ficsit trials. *JAMA J. Am. Med. Assoc.* 273, 1341–1347. doi: 10.1001/jama.1995.03520410035023

Putnins, S. I., Griffin, M. L., Fitzmaurice, G. M., Dodd, D. R., and Weiss, R. D. (2012). Poor sleep at baseline predicts worse mood outcomes in patients with co-occurring bipolar disorder and substance dependence. *J. Clin. Psychiatry* 73, 703–708. doi: 10.4088/JCP.11m07007

Rawson, R. A. (2013). Current research on the epidemiology, medical and psychiatric effects, and treatment of methamphetamine use. *J. Food Drug Anal.* 21(Suppl. 4), S77–S81. doi: 10.1016/j.jfda.2013.09.039

Rodriguez, E. M., Fuentes, P., Ramos-Lira, L., Gutierrez, R., and Ruiz, E. (2014). Violence in the work environment of sex work and substance use in a group of Mexican women. *Salud Ment.* 37, 355–360.

Sashika, H., Takada, K., and Kikuchi, N. (2017). Rehabilitation needs and participation restriction in patients with cognitive disorder in the chronic phase of traumatic brain injury. *Medicine* 96:e5968. doi: 10.1097/MD.0000000000005968

Scully, D. (1998). Physical exercise and psychological well being: a critical review. *Br. J. Sports Med.* 32, 111–120. doi: 10.1136/bjsm.32.2.111

Segat, H. J., Kronbauer, M., Roversi, K., Schuster, A. J., Vey, L. T., Roversi, K., et al. (2014). Exercise modifies amphetamine relapse: behavioral and oxidative markers in rats. *Behav. Brain Res.* 262, 94–100. doi: 10.1016/j.bbr.2014.01.005

Solloway, M. R., Taylor, S. L., Shekelle, P. G., Miake-Lye, I. M., Beroes, J. M., Shanman, R. M., et al. (2016). An evidence map of the effect of Tai Chi on health outcomes. *Syst. Rev.* 5:126. doi: 10.1186/s13643-016-0300-y

Sun, H. Q., Chen, H. M., Yang, F. D., Lu, L., and Kosten, T. R. (2014). Epidemiological trends and the advances of treatments of amphetamine-type stimulants (ATS) in China. *Am. J. Addict.* 23, 313–317. doi: 10.1111/j.1521-0391.2014.12116.x

Tang, J., Liao, Y., He, H., Deng, Q., Zhang, G., Qi, C., et al. (2015). Sleeping problems in Chinese illicit drug dependent subjects. *BMC Psychiatry* 15:28. doi: 10.1186/s12888-015-0409-x

Taylor-Piliae, R. E., Haskell, W. L., Waters, C. M., and Froelicher, E. S. (2006). Change in perceived psychosocial status following a 12-week Tai Chi exercise programme. *J. Adv. Nurs.* 54, 313–329. doi: 10.1111/j.1365-2648.2006.03809.x

Tsang, W. W., and Hui-Chan, C. W. (2003). Effects of Tai Chi on joint proprioception and stability limits in elderly subjects. *Med. Sci. Sports Exerc.* 35, 1962–1971. doi: 10.1249/01.MSS.0000099110.17311.A2

United Kingdom. (2010). *Women in Drug Treatment: What the Latest Figures Reveal.* National Treatment Agency for Substance Misuse.

UNODC World Drug Report (2016). *United Nations Office on Drugs and Crime, 2016.*

Wang, C., Collet, J., and Lau, J. (2004). The effect of Tai Chi on health outcomes in patients with chronic conditions - a systematic review. *Arch. Intern. Med.* 164, 493–501. doi: 10.1001/archinte.164.5.493

Wang, F., Eun-Kyoung Lee, O., Feng, F., Vitiello, M. V., Wang, W., Benson, H., et al. (2016). The effect of meditative movement on sleep quality: a systematic review. *Sleep Med. Rev.* 30, 43–52. doi: 10.1016/j.smrv.2015.12.001

Wayne, P. M., Walsh, J. N., Taylor-Piliae, R. E., Wells, R. E., Papp, K. V., Donovan, N. J., et al. (2014). Effect of tai chi on cognitive performance in older adults: systematic review and meta-analysis. *J. Am. Geriatr. Soc.* 62, 25–39. doi: 10.1111/jgs.12611

Wiig, E. M., Haugland, B. S. M., Halsa, A., and Myhra, S. M. (2017). Substance-dependent women becoming mothers: breaking the cycle of adverse childhood experiences. *Child Fam. Soc. Work* 22, 26–35. doi: 10.1111/cfs.12190

Wolf, S. L., Sattin, R. W., Kutner, M., O'Grady, M., Greenspan, A. I., and Gregor, R. J. (2003). Intense tai chi exercise training and fall occurrences in older, transitionally frail adults: a randomized, controlled trial. *J. Am. Geriatr. Soc.* 51, 1693–1701. doi: 10.1046/j.1532-5415.2003.51552.x

Yang, J., Li, J., Xu, G., Zhang, J., Chen, Z., Lu, Z., et al. (2016). Elevated hair cortisol levels among heroin addicts on current methadone maintenance compared to controls. *PLoS ONE* 11:e0150729. doi: 10.1371/journal.pone.0150729

Zhang, X., Ni, X., and Chen, P. (2014). Study about the effects of different fitness sports on cognitive function and emotion of the aged. *Cell Biochem. Biophys.* 70, 1591–1596. doi: 10.1007/s12013-014-0100-8

Zhang, X. D., Kelly-Hanku, A., Chai, J. J., Luo, J., Temmerman, M., and Luchters, S. (2015). Sexual and reproductive health risks amongst female adolescents who use amphetamine-type stimulants and sell sex: a qualitative inquiry in Yunnan, China. *Harm Reduc. J.* 12:34. doi: 10.1186/s12954-015-0065-y

Zhu, D., Xu, D., Dai, G., Wang, F., Xu, X., and Zhou, D. (2016). Beneficial effects of Tai Chi for amphetamine-type stimulant dependence: a pilot study. *Am. J. Drug Alcohol Abuse* 42, 469–478. doi: 10.3109/00952990.2016.1153646

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A P5 Approach to m-Health: Design Suggestions for Advanced Mobile Health Technology

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In recent years, technology has been developed as an important resource for health care management, especially in regard to chronic conditions. In the broad field of eHealth, mobile technology (mHealth) is increasingly used to empower patients not only in disease management but also in the achievement of positive experiences and experiential growth. mHealth tools are considered powerful because, unlike more traditional Internet-based tools, they allow patients to be continuously monitored and followed by their own mobile devices and to have continual access to resources (e.g., mobile apps or functions) supporting health care management activities. However, the literature has shown that, in many cases, such technology not accepted and/or adopted in the long term by its users. To address this issue, this article reviews the main factors influencing mHealth technology acceptance/adoption in health care. Finally, based on the main aspects emerging from the review, we propose an innovative approach to mHealth design and implementation, namely P5 mHealth. Relying on the P5 approach to medicine and health care, this approach provides design suggestions to address mHealth adoption issues already at the initial stages of development of the technologies.

Keywords: mHealth, technology acceptance, P5, eHealth, patient empowerment, chronic diseases

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INTRODUCTION

Chronic conditions pose challenges to health systems worldwide. While acute diseases can be treated by means of *ad hoc* therapy, chronic conditions often need to be managed and contained from onset (or diagnosis) to death, with very limited possibilities of complete recovery. Such a scenario requires continuous attention and availability from the health provider as well as commitment from the patient, who must adhere to long-term therapy and change his or her lifestyle. Moreover, chronic condition management often extends the demands of care to other figures, such as patients' caregivers, organizations, and institutions. In recent years, new technologies have emerged as an extraordinary resource to help achieve these aims (Wiecha and Pollard, 2004; Castelnuovo et al., 2015a; Gorini et al., 2016).

In the health sector, new technologies for health (eHealth) are recognized as having a great impact on health promotion and management (Bert et al., 2014; Mirkovic et al., 2014; Barello et al., 2016; Hood et al., 2016; Jacobs et al., 2016). These tools make it possible to develop and implement integrated, sustainable, patient-centered services, and promote an effective exchange between patient and doctor, with the patient taking an active role in the health care process (Samoocha et al., 2010;

Barello et al., 2016). Such health technologies not only empower and facilitate the administration of continual care but also offer opportunities for maintaining patients' active engagement in the care process by promoting patients' psychological skills (e.g., health literacy, emotion regulation, adoption of healthy behaviors) and well-being outcomes. Eysenbach (2001) defined eHealth as a vehicle to enrich patients and stakeholders through the intersection of medical informatics and public health business. As such, eHealth promotes a new "state of mind" for medical professionals, marked by a global attitude and by the intention to improve health care locally, regionally, and worldwide.

In recent decades, eHealth has developed dramatically, consistent with the development of informatics and online technologies. One of these developments is mHealth, which refers to the implementation of *mobile technologies* as a tremendous tool to improve health outcomes (Free et al., 2013; Kumar et al., 2013; Lee et al., 2017) and to facilitate continuous health monitoring individually and from home (Stephens et al., 2017). Moreover, the global availability of mobile technologies and their ease of use have made them accessible to almost all of the population (Tokosi et al., 2017).

In recent years, mHealth obtained encouraging results in reinforcing healthy behaviors (Gurman et al., 2012; Hamine et al., 2015), mostly by using short message service (SMS) messages to improve treatment adherence; however, multiple systematic reviews still show mixed results on the effectiveness of mHealth interventions. Indeed, in spite of many studies identifying the notable advantages derived from the use of mHealth and demonstrating how these applications are appreciated by patients, acceptability, and adoption in the long term are still poor in many cases (Christensen et al., 2009; Tomlinson et al., 2013; Mohammadzadeh and Safdari, 2014; Castelnuovo et al., 2015b; Hamine et al., 2015; Guo et al., 2016; McKay et al., 2016). Also, health care apps often lack standard validation in terms of benefits, acceptance, costs, and risks (McKay et al., 2016).

Using the above-discussed evidence and controversy as a starting point, the aim of the present contribution is, after an analysis of the variables that influence mHealth technologies' acceptance/adoption, to promote guidelines for future mHealth resources and applications.

ISSUES IN mHEALTH ADOPTION

There are many factors that may influence the use of mobile apps to monitor patients' health. The first of these is related to age and expertise with technology. Chronic diseases that require life-long management generally affect elderly patients. For this reason, mHealth apps are often targeted at **middle-aged/elderly patients**, who usually have limited experience with technologies (Mattsson et al., 2017; Loerzel et al., 2018). Numerous studies reveal that older patients are less likely than younger ones to use computers regularly and, in a more general sense, have limited access to common-use technological devices (Børøsund et al., 2013). The literature on technology acceptance shows that perceived utility, perceived ease of use, and computer self-efficacy (e.g., the belief that one can use digital technology effectively) are the most important variables influencing the adoption of technology, as well as the persistence in use when difficulties are encountered (Mun and Hwang, 2003; Wu and Tsai, 2006; Kim and Chang, 2007; Wangpipatwong et al., 2008; Ward, 2013). This evidence may explain why elderly patients are less prone than younger ones to use mHealth to manage their health.

Another important factor, related to the previous one, is **usability**. Numerous applications are designed according to generic usability principles (Pagliari, 2007; Stellefson et al., 2011). However, it is possible that elderly and/or chronic patients present specific characteristics that may generate usage issues, which are difficult to predict if a "generic" user is considered as a model for usability evaluations. For example, age-related declines in sensory abilities and visual acuity may affect the ability to discriminate important information in a graphically challenging visual field (Agree et al., 2015). Regarding the content of an app, elderly patients appreciate and better understand information presented in multiple formats (e.g., when text is combined with images or videos making it easier to understand) (Bolle et al., 2016). For these usability-related reasons, older patients generally less accustomed to mobile technology than younger patients (Børøsund et al., 2013; Miller et al., 2017).

Other possible important factors related to the use of mHealth in health care are related to **patients' preferences and their subjective, lived experience of illness**. For examples, patients may not want to have "all" the information about their disease. Instead, they may desire to know only those indications that concern them personally. For this reason, they often prefer to interact directly with health professionals, who provide them with information regarding their specific case, instead of relying on information provided by the available app (Grimsbø et al., 2012). Moreover, the mobile tool could be perceived as a "substitute" for the relationship with the clinician; in other words, patients may believe that the technology is given to them as a surrogate for the clinician, and that this tool will thus reduce their ability to interact with their doctor (Goel et al., 2011; Kondylakis et al., 2013). Such a belief, albeit erroneous, often predicts technology refusal or abandonment in the long term (Benson and Dundis, 2003; Mohr et al., 2011).

The length of illness and **the stage of disease** are other aspects that can determine the use of health management apps. Research performed on an interactive application (WebChoice) reveals that metastatic patients are less prone to use it compared to those who have recently been diagnosed. Metastatic patients may feel that they have already enough information about the disease and how to manage it, making them feel that the applications are not very useful to them (Grimsbø et al., 2012; Ruland et al., 2013). In contrast, immediately after diagnosis, patients tend to search for a lot of information about their disease and its treatment. Indeed, information presented during the first consultation is often forgotten or very difficult to memorize because of patients' emotional state (e.g., anxiety and fear) (Bolle et al., 2016), so external support can be very useful to recover this information.

Gender is another factor that influences the use of mHealth. Men and women are equally familiar with how to use health apps through a smartphone (McKay et al., 2016); however, men are typically more confident than women regarding their ability to use technology and their experience with it (Cassidy and Eachus, 2002; Durndell and Haag, 2002). Since, as noted above, computer self-efficacy is an important variable influencing technology acceptance, gender may also indirectly affect mHealth adoption.

Finally, **psychological variables** such as cognitive representation of the disease, distress, and anxiety may significantly influence the adoption of mHealth (Ruland et al., 2013; Beiwinkel et al., 2017). For example, having low self-control and self-efficacy could reduce patients' confidence in their ability to deal with their symptoms (Gysels and Higginson, 2007). Furthermore, in some situations, interacting with mHealth apps creates a fear of "getting even more problems" (Kessel et al., 2017). Indeed, some health-related apps ask users to comply with novel requests for health management. For instance, patients may have to monitor their smartphones to respond to daily messages asking them to report information on a web-based platform (e.g., glycemic values in diabetes), or they may be asked to use various app functions frequently (e.g., playing with an educational serious game and filling in online questionnaires on their health status). If the patient is not convinced about the utility of these tools for his/her health management, such new commitments may be a source of further stress and, ultimately, of negative attitudes towards the treatment. In such situations, patients may not only abandon the mHealth tools but also lose faith in their health providers, resulting in detrimental effects on the effectiveness of the health management process as a whole. Also, patients do not always have good insight into their health conditions; as such, they may wrongly think that they do not need any kind of support from mHealth (Nijland et al., 2011), causing them to demonstrate active and voluntary resistance to any kind of proposed tools.

This review of the literature sheds some light on important demographic, user-experience-related, and psychological factors that may have an impact on mHealth acceptance by patients involved in interventions. It is certainly difficult to address all of these factors in any possible intervention involving mobile technology; however, a specific theoretical perspective, rooted in an approach to medicine and care, could be useful not only to adapt already-designed devices and applications but also to develop future mHealth tools. On the one side, these advanced resources would make good use of all the opportunities offered by mobile technologies; on the other side, they would be designed according to general principles allowing health professionals to consider in advance (and possibly avoid) the acceptance issues highlighted above.

A P5 mHEALTH APPROACH

Some years ago, a system approach called "P4 medicine" was proposed (Hood and Friend, 2011; Hood and Flores, 2012). This approach was intended as a sophisticated extension of what is usually called "personalized medicine." Specifically, the four Ps referred to the Predictive, Personalized, Preventive, and Participatory aspects of clinical medicine (Price et al., 2009; Auffray et al., 2010). A few years later, a P5 medicine approach was proposed (Gorini and Pravettoni, 2011; Pravettoni and Gorini, 2011), where the fifth P referred to the Psycho-cognitive aspects that play a significant and unique role in the way in which an individual experiences emotional events, copes with illness, and makes decisions about his/her own health. The time is ripe to use the P5 approach in combination with the most recent advances in technology in order to challenge the health care and technology industries to find innovative and personalized ways to improve the overall quality of care. In particular, a P5 mHealth approach can be developed (see **Figure 1**).

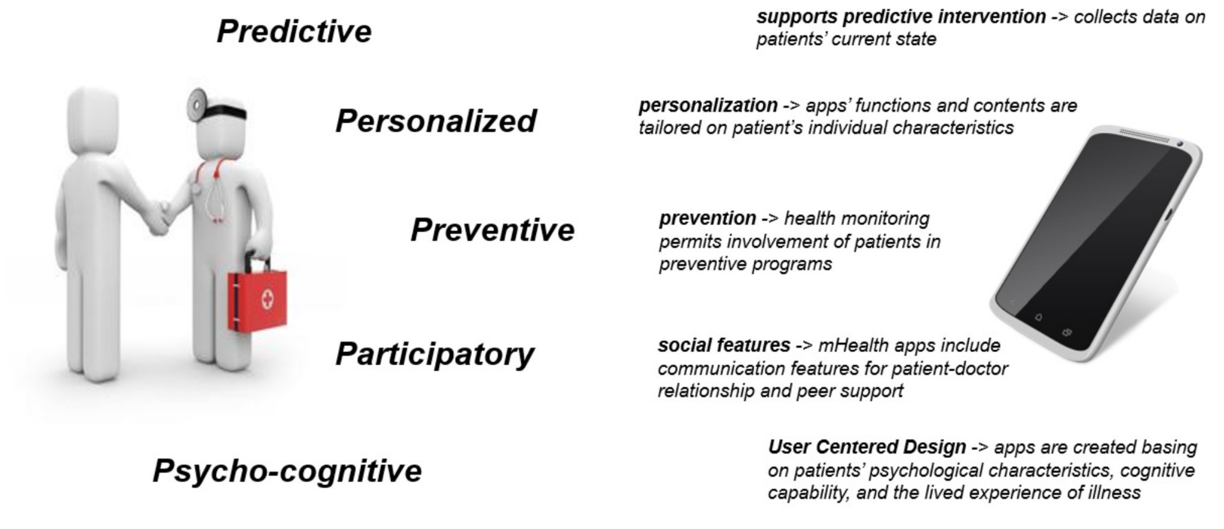

FIGURE 1 | The P5 approach to medicine (left) and its design suggestions for mHealth development.

Such an approach may lead to a new generation of mHealth apps based on the features reflecting the original P5 construct. Specifically, mHealth apps should be as follows:

Predictive

Collecting data on the patient's current health state without the need for frequent physical encounters with the health care provider (physician, psychologist, nurse, etc.) will increase the amount of available information, allowing for a more precise prediction of the patient's future health state. Specifically, mHealth apps can collect data by means of various peripherals and in-app tools. For example, they can collect physiological parameters through integration with wearable technologies (e.g., heart rate variability and skin conductance), or they can store user-generated information related to medical values (e.g., glycemic level in diabetes) (Fontecha et al., 2015; Os et al., 2017). Moreover, they can include *ad hoc* or validated questionnaires to be filled in by health providers, caregivers, and patients (e.g., data related to the patient's functional or psychological status) (Gorini et al., 2015; Renzi et al., 2017). In most cases, such data are actually used for analyses to be included in scientific publications, but their utility for therapy and health management could be further exploited. Indeed, based on predictive models, mHealth tools of the future can provide specific information from autonomous data-analysis, in order to help both the physician and the patient to foresee the patient's future health state, management issues, and possible modifications to the patient's therapy regimen and/or health management activities, as well as interventions targeted to different aspects of the patient's well-being (e.g., improving relaxation and positive emotions or promoting engagement in self-actualizing experiences).

Examples: Chih et al. (2011) used a mobile app with patients addicted to alcohol; implementing a Bayesian predictive model, they were able to predict the likelihood of relapse based on repeated self-report questionnaires investigating relapse history and psychological aspects related to the recovery progress. Wearable and mobile technology (e.g., actigraphy devices) have been used to satisfactorily predict factors relevant for quality of life, such as sleep efficiency based on physical activity during waking hours (Sathyanarayana et al., 2016).

Personalized

Apps' functions and contents (including requested information, feedback to the patients, etc.) should be tailored to the patient's individual bio-psycho-social characteristics to provide more useful, more accepted by patients, and non-redundant information (Gorini et al., 2015; Pravettoni et al., 2016). Moreover, the personalization factor also relates to the possibility for the patient to express him- or herself through the use of the application. For example, app functions and automatic communications will be not generalized to patient populations but rather will be based on individual characteristics. mHealth tools of the future should be able to adapt their functioning and interfaces to previously collected data on each person's specific features (e.g., age, sex, life cycle phase, and temporary health state, as well as attitudes, needs, and preferences). It is essential not to ask patients to perform tasks/activities that are difficult or even dangerous for them to achieve (e.g., asking patients with a cardiac illness to perform too much physical activity). Moreover, properties of applications devoted to user engagement (e.g., gamification aspects) should not be underestimated; for example, serious games have been developed with avatars designed for the user to see examples of healthy activities and be more motivated to replicate them in real life (Proteus effect) (Yee and Bailenson, 2007; Murray et al., 2013; Villani et al., 2018); such tools are also interesting resources that can be used to guarantee personalization features to users.

Examples: In the medical field, innovative approaches have been proposed to use avatars (or, better, "supermodels" as this is the term used) of the patients to include key medical components of the patient, as well as predictive analytics, so as to tailor health interventions to the individual (Brown, 2015); these could be updated with user-generated characteristics to aid in diagnosis and treatment with self-reported data (Triberti and Chirico, 2016).

Preventive

A long-term monitoring of patients' health would make it possible to provide timely preventive interventions and improved patient involvement in preventive programs. As noted previously, such technologies present remarkable opportunities in terms of data collection and analysis, which should be further exploited in terms of aid to health care management and therapy effectiveness. Collected data may be the basis for preventive interventions, in order to modify users' behavior and responses before problematic consequences arise. For example, engaging health apps may not only address existing problems but also help to positively change users' behavior, attitudes, and motivation toward health care management and treatment adherence. In this sense, mHealth should not be used as a digital assistant to treatment (i.e., "virtual medicine") but rather as an empowerment technology that directly influences patients' everyday activities in order to promote a healthier lifestyle and prevent negative consequences of illness.

Examples: mHealth apps for prevention have been found to be effective and positively accepted by patients. For example, some of these apps make use of automated texting to reinforce healthy behavior (e.g., physical activity) or boost it when the patient is reluctant to perform it (Martin et al., 2015).

Participatory

Recent approaches to medicine highlight that the most successful interventions are those that recognize patients not as passive recipients of care but rather as active decision makers who can make use of their own social support resources (McNutt, 2004; Lucchiari et al., 2010; Cutica et al., 2014). Patient–doctor communication is fundamental in any health management process; in this sense, mobile-based technologies should not be used as a substitute for this relationship, but rather specific functions intended to promote it should be envisaged by designers and policy makers. These include Instant Messaging functions and social networking features, as well as the possibility for the patient to have a personal profile that is continually updated with the patient's personal information.

Second, peer support has been recognized as a tremendous opportunity for positive and effective health management (Fisher et al., 2012; Merolli et al., 2013): patients benefit from interaction and collaboration with other patients who are living with similar experiences and could give them useful suggestions, as well as simply sharing their experiences, in order to empower one another's health management abilities. mHealth tools should include such opportunities by making use of social/interpersonal technologies embedded in mobile interfaces.

Examples: An integrative review (McColl et al., 2014) found that peer support (traditionally via telephone, then via mobile functions such as texting) increases engagement in wellness activities, reduces depressive symptoms, and improves social support-related coping. Studies show that, when mobile apps include features for communication with the clinician, patients use them to transmit not only medical information but also personal needs and feelings (Triberti et al., 2018).

Psycho-Cognitive

Using a user-centered design approach, apps are created on the basis of patients' psychological characteristics, their cognitive capabilities, and their lived experience of illness. Indeed, research on health technology shows that eHealth may systematically fail when the patient's subjective experience has not been taken into consideration from the first steps of the technology design (Triberti and Barello, 2016). These features will improve the patients' abilities to manage their emotions, to cope with their illness, and to make decisions about their health, becoming active actors in the health management process. In other words, the design and development of advanced mHealth tools not only should make use of the tremendous opportunities offered by these tools (e.g., continual monitoring, reaching the patient wherever he/she is, integration with multiple devices, and functions by means of apps) but also should be based on the application of specific research techniques in order to (1) identify users' characteristics, needs, and contexts of use; (2) develop efficient and personalized decision support tools to help patients to make the right decisions about their health; and (3) test the technology's effectiveness and adequacy at multiple steps of their implementation in the field.

Examples: An effective self-management platform could be based on research on patients' needs and cognitive style, by using multiple design-oriented methods (Pravettoni et al., 2015; Kondylakis et al., 2017). Regarding psycho-cognitive aspects to be included in implementation, Kondylakis et al. (2014) developed and validated ALGA-C, a web-based tool featuring a questionnaire for cancer patients (analyzing psycho-cognitive aspects ranging from personal needs to cognitive/decision making style) and a profiling mechanism. This tool enables the clinician to modulate language, communication style, and content of the subsequent encounters with the patient, in order to empower mutual understanding and collaboration. This tool is an example of automated data-gathering tools that could be adapted to mHealth technology in order to adapt the intervention to the

TABLE 1 | Design suggestions for mHealth applications from the P5 perspective.

5 Ps	Definition	How to achieve It in Design
Predictive	Collecting data on the patient's current health state to increase the amount of available information, allowing for a more precise prediction of the patient's future health state.	– Collect physiological parameters through integration with wearable technologies; – Store user-generated information related to medical values; – Include *ad hoc* or validated questionnaires to be filled in by health providers, caregivers and patients.
Personalized	Tailoring apps' functions and contents on the patient's individual bio-psycho-social characteristics to provide more useful and non-redundant information.	– Adapt mHealth's functioning and interfaces to previously collected data on each person's specific features; – Design application features devoted to user engagement.
Preventive	Long-term monitoring of patients' health to provide timely preventive interventions and increased involvement of the patient in preventive programs.	– Collect data in order to modify users' behavior and responses before problematic consequences actually show up; – Configure an empowerment technology that directly influences patients' everyday activities in order to promote a healthier lifestyle.
Participatory	Recognizing patients not as passive recipients of care but rather as active decision makers who can make use of their own social support resources.	– Sustain patient–doctor communication, as well as communication with designers and policy makers (Instant Messaging functions, social networking features); – Promote the possibility for the patient to have a personal profile that is continually updated with the patient's personal information; – Make use of social/interpersonal technologies embedded in mobile interfaces in order to empower health management abilities via peer support.
Psycho-cognitive	Improving the patients' ability to manage their emotions, to cope with their illness and to make decisions about their health, becoming active actors in the health management process.	– The design and development of advanced mHealth tools based on the application of specific research techniques; – Identify users' characteristics, needs and contexts of use; – Develop efficient and personalized decision support tools; – Test technology's effectiveness and adequacy at multiple steps of its implementation in the field.

uniqueness of the patient over time, taking into account not only his/her physical health status but also psychological processes influencing adoption.

CONCLUSION

Despite their increasing popularity, the literature shows that there are still significant limitations in the acceptance and long-term adoption of mHealth apps, mostly because these technologies do not take users' needs and contexts of use into account from the first steps of design and implementation. Here, we presented a "P5 mHealth approach" as a set of suggestions (and related examples) for aspects of the mobile technologies that could be exploited in the future advanced mHealth resources (see **Table 1**). Rather than relying on the intrinsic properties of technologies only, health management processes should appreciate the uniqueness of patients in order to foster mHealth abilities in terms of prediction, personalization, prevention, participatory features, and the psycho-cognitive uniqueness of the individual. Future studies in the field would implement such suggestions in design, as well as to test their utility for identifying possible improvements for the already-existing mHealth tools that are hindered by adoption issues.

AUTHOR CONTRIBUTIONS

AG conceived the ideas presented in the article and wrote the first draft. KM and ST contributed with discussion on the ideas presented in the article and edited the manuscript. VS and LS performed relevant bibliographic search and contributed to revisions. GP supervised the whole process and contributed with important intellectual content.

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REFERENCES

Agree, E. M., King, A. C., Castro, C. M., Wiley, A., and Borzekowski, D. L. (2015). "It's got to be on this page": age and cognitive style in a study of online health information seeking. *J. Med. Internet Res.* 17:e79. doi: 10.2196/jmir.3352

Auffray, C., Charron, D., and Hood, L. (2010). Predictive, preventive, personalized and participatory medicine: back to the future. *Genome Med.* 2:57. doi: 10.1186/gm178

Barello, S., Triberti, S., Graffigna, G., Libreri, C., Serino, S., Hibbard, J., et al. (2016). eHealth for patient engagement: a systematic review. *Front. Psychol.* 6:2013. doi: 10.3389/fpsyg.2015.02013

Beiwinkel, T., Hey, S., Bock, O., and Rössler, W. (2017). supportive mental health self-monitoring among smartphone users with psychological distress: protocol for a fully mobile randomized controlled trial. *Front. Public Health* 5:249. doi: 10.3389/fpubh.2017.00249

Benson, S. G., and Dundis, S. P. (2003). Understanding and motivating health care employees: integrating Maslow's hierarchy of needs, training and technology. *J. Nurs. Manag.* 11, 315–320. doi: 10.1046/j.1365-2834.2003.00409.x

Bert, F., Giacometti, M., Gualano, M. R., and Siliquini, R. (2014). Smartphones and health promotion: a review of the evidence. *J. Med. Syst.* 38:9995. doi: 10.1007/s10916-013-9995-7

Bolle, S., Romijn, G., Smets, E. M., Loos, E. F., Kunneman, M., and van Weert, J. C. (2016). Older cancer patients' user experiences with web-based health information tools: a think-aloud study. *J. Med. Internet Res.* 18:e208. doi: 10.2196/jmir.5618

Børøsund, E., Cvancarova, M., Ekstedt, M., Moore, S. M., and Ruland, C. M. (2013). How user characteristics affect use patterns in web-based illness management support for patients with breast and prostate cancer. *J. Med. Internet Res.* 15:e34. doi: 10.2196/jmir.2285

Brown, S. A. (2015). Building supermodels: emerging patient avatars for use in precision and systems medicine. *Front. Physiol.* 6:318. doi: 10.3389/fphys.2015.00318

Cassidy, S., and Eachus, P. (2002). Developing the computer user self-efficacy (CUSE) scale: investigating the relationship between computer self-efficacy, gender and experience with computers. *J. Edu. Comput. Res.* 26, 133–153. doi: 10.2190/JGJR-0KVL-HRF7-GCNV

Castelnuovo, G., Pietrabissa, G., Manzoni, G. M., Corti, S., Ceccarini, M., Borrello, M., et al. (2015a). Chronic care management of globesity: promoting healthier lifestyles in traditional and mHealth based settings. *Front. psychol.* 6:1557. doi: 10.3389/fpsyg.2015.01557

Castelnuovo, G., Zoppis, I., Santoro, E., Ceccarini, M., Pietrabissa, G., Manzoni, G. M., et al. (2015b). Managing chronic pathologies with a stepped mHealth-based approach in clinical psychology and medicine. *Front. psychol.* 6:407. doi: 10.3389/fpsyg.2015.00407

Chih, M.-Y., Patton, T., McTavish, F., Isham, A., Judkins-Fisher, C., Atwood, A., et al. (2011). Predictive modeling of addiction lapses in a mobile health application. *J. Subst. Abuse Treat.* 22, 233–245. doi: 10.1016/j.jsat.2013.08.004

Christensen, H., Griffiths, K. M., and Farrer, L. (2009). Adherence in internet interventions for anxiety and depression: systematic review. *J. Med. Internet Res.* 11:e13. doi: 10.2196/jmir.1194

Cutica, I., Mc Vie, G., and Pravettoni, G. (2014). Personalised medicine: the cognitive side of patients. *Eur. J. Intern. Med.* 25, 685–688. doi: 10.1016/j.ejim.2014.07.002

Durndell, A., and Haag, Z. (2002). Computer self efficacy, computer anxiety, attitudes towards the internet and reported experience with the Internet, by gender, in an East European sample. *Comput. Hum. Behav.* 18, 521–535. doi: 10.1016/S0747-5632(02)00006-7

Eysenbach, G. (2001). What is e-health? *J. Med. Internet. Res.* 3:e20. doi: 10.2196/jmir.3.2.e20

Fisher, E. B., Boothroyd, R. I., Coufal, M. M., Baumann, L. C., Mbanya, J. C., Rotheram-Borus, M. J., et al. (2012). Peer support for self-management of diabetes improved outcomes in international settings. *Health Aff.* 31, 130–139. doi: 10.1377/hlthaff.2011.0914

Fontecha, J., Hervás, R., and Bravo, J. (2015). "A sensorized and health aspect-based framework to improve the continuous monitoring on diseases using smartphones and smart devices," in *Ambient Intelligence for Health*, eds J. Bravo, R. Hervás, and V. Villarreal (Cham: Springer), 68–73.

Free, C., Phillips, G., Galli, L., Watson, L., Felix, L., Edwards, P., et al. (2013). The effectiveness of mobile-health technology-based health behaviour change or disease management interventions for health care consumers: a systematic review. *PLoS Med.* 10:e1001362. doi: 10.1371/journal.pmed.1001362

Goel, M. S., Brown, T. L., Williams, A., Cooper, A. J., Hasnain-Wynia, R., and Baker, D. W. (2011). Patient reported barriers to enrolling in a patient portal. *J. Am. Med. Inform. Assoc.* 18(Suppl. 1), i8–i12. doi: 10.1136/amiajnl-2011-000473

Gorini, A., Masiero, M., and Pravettoni, G. (2016). Patient decision aids for prevention and treatment of cancer diseases: are they really personalised tools? *Eur. J. Cancer Care* 25, 936–960. doi: 10.1111/ecc.12451

Gorini, A., Mazzocco, K., Gandini, S., Munzone, E., McVie, G., and Pravettoni, G. (2015). Development and psychometric testing of a breast cancer patient-profiling questionnaire. *Breast Cancer* 7:133. doi: 10.2147/BCTT.S80014

Gorini, A., and Pravettoni, G. (2011). P5 medicine: a plus for a personalized approach to oncology. *Nat. Rev. Clin. Oncol.* 8:444. doi: 10.1038/nrclinonc.2010.227-c1

Grimsbø, G. H., Engelsrud, G. H., Ruland, C. M., and Finset, A. (2012). Cancer patients' experiences of using an interactive health communication application (IHCA). *Int. J. Qual. Stud. Health Well-Being* 7:15511. doi: 10.3402/qhw.v7i0.15511

Guo, X., Zhang, X., and Sun, Y. (2016). The privacy–personalization paradox in mHealth services acceptance of different age groups. *Electron. Commer. Res. Appl.* 16, 55–65. doi: 10.1016/j.elerap.2015.11.001

Gurman, T. A., Rubin, S. E., and Roess, A. A. (2012). Effectiveness of mHealth behavior change communication interventions in developing countries: a systematic review of the literature. *J. Health Commun.* 17(Suppl. 1), 82–104. doi: 10.1080/10810730.2011.649160

Gysels, M., and Higginson, I. J. (2007). Interactive technologies and videotapes for patient education in cancer care: systematic review and meta-analysis of randomised trials. *Support. Care Cancer* 15, 7–20. doi: 10.1007/s00520-006-0112-z

Hamine, S., Gerth-Guyette, E., Faulx, D., Green, B. B., and Ginsburg, A. S. (2015). Impact of mHealth chronic disease management on treatment adherence and patient outcomes: a systematic review. *J. Med. Internet Res.* 17:e52. doi: 10.2196/jmir.3951

Hood, L., and Flores, M. (2012). A personal view on systems medicine and the emergence of proactive P4 medicine: predictive, preventive, personalized and participatory. *New biotechnol.* 29, 613–624. doi: 10.1016/j.nbt.2012.03.004

Hood, L., and Friend, S. H. (2011). Predictive, personalized, preventive, participatory (P4) cancer medicine. *Nat. Rev. Clin. Oncol.* 8:184–187. doi: 10.1038/nrclinonc.2010.227

Hood, M., Wilson, R., Corsica, J., Bradley, L., Chirinos, D., and Vivo, A. (2016). What do we know about mobile applications for diabetes self-management? A review of reviews. *J. Behav. Med.* 39, 981–994. doi: 10.1007/s10865-016-9765-3

Jacobs, R. J., Lou, J. Q., Ownby, R. L., and Caballero, J. (2016). A systematic review of eHealth interventions to improve health literacy. *Health Inform. J.* 22, 81–98. doi: 10.1177/1460458214534092

Kessel, K. A., Vogel, M. M., Kessel, C., Bier, H., Biedermann, T., Friess, H., et al. (2017). Mobile health in oncology: a patient survey about app-assisted cancer care. *JMIR Mhealth Uhealth.* 5:e81. doi: 10.2196/mhealth.7689

Kim, D., and Chang, H. (2007). Key functional characteristics in designing and operating health information websites for user satisfaction: an application of the extended technology acceptance model. *Int. J. Med. Inform.* 76, 790–800. doi: 10.1016/j.ijmedinf.2006.09.001

Kondylakis, H., Bucur, A., Dong, F., Renzi, C., Manfrinati, A., Graf, N., et al. (2017). IManagecancer: developing a platform for empowering patients and strengthening self-management in cancer diseases. *Paper presented at the IEEE 30th International Symposium on Computer-Based Medical Systems (CBMS)*, Piscataway, NJ, 755–760. doi: 10.1109/CBMS.2017.62

Kondylakis, H., Kazantzaki, E., Koumakis, L., Genitsaridi, I., Marias, K., Gorini, A., et al. (2014). Development of interactive empowerment services in support of personalised medicine. *Ecancermedicalscience* 8:400. doi: 10.3332/ecancer.2014.400

Kondylakis, H., Koumakis, L., Tsiknakis, M., Marias, K., Genitsaridi, E., Pravettoni, G., et al. (2013). "Smart recommendation services in support of patient empowerment and personalized medicine," in *Multimedia Services in Intelligent Environments*, eds G. Tsihrintzis, M. Virvou, and L. Jain (Heidelberg: Springer), 39–61.

Kumar, S., Nilsen, W. J., Abernethy, A., Atienza, A., Patrick, K., Pavel, M., et al. (2013). Mobile health technology evaluation: the mHealth evidence workshop. *Am. J. Prev. Med.* 45, 228–236. doi: 10.1016/j.amepre.2013.03.017

Lee, H., Ghebre, R., Le, C., Jang, Y. J., Sharratt, M., and Yee, D. (2017). Mobile phone multilevel and multimedia messaging intervention for breast cancer screening: pilot randomized controlled trial. *JMIR Mhealth Uhealth* 5:e154. doi: 10.2196/mhealth.7091

Loerzel, V., Clochesy, J., and Geddie, P. (2018). Using a community advisory board to develop a serious game for older adults undergoing treatment for cancer. *Appl. Nurs. Res.* 39, 207–210. doi: 10.1016/j.apnr.2017.11.030

Lucchiari, C., Botturi, A., and Pravettoni, G. (2010). The impact of decision models on self-perceived quality of life: a study on brain cancer patients. *Ecancermedicalscience* 4:187. doi: 10.3332/ecancer.2010.187

Martin, S. S., Feldman, D. I., Blumenthal, R. S., Jones, S. R., Post, W. S., McKibben, R. A., et al. (2015). mActive: a randomized clinical trial of an automated mHealth intervention for physical activity promotion. *J. Am. Heart Assoc.* 4:e002239. doi: 10.1161/JAHA.115.002239

Mattsson, S., Olsson, E. M. G., Johansson, B., and Carlsson, M. (2017). Health-related internet use in people with cancer: results from a cross-sectional study in two outpatient clinics in Sweden. *J. Med. Internet Res.* 19:e163. doi: 10.2196/jmir.6830

McColl, L. D., Rideout, P. E., Parmar, T. N., and Abba-aji, A. (2014). Peer support intervention through mobile application: an integrative literature review and future directions. *Can, Psychol.* 55, 250–257. doi: 10.1037/a0038095

McKay, F. H., Cheng, C., Wright, A., Shill, J., Stephens, H., and Uccellini, M. (2016). Evaluating mobile phone applications for health behaviour change: a systematic review. *J. Telemed. Telecare* 24, 22–30. doi: 10.1177/1357633X16673538

McNutt, R. A. (2004). Shared medical decision making: problems, process, progress. *JAMA* 292, 2516–2518. doi: 10.1001/jama.292.20.2516

Merolli, M., Gray, K., and Martin-Sanchez, F. (2013). Health outcomes and related effects of using social media in chronic disease management: a literature review and analysis of affordances. *J. Biomed. Inform.* 46, 957–969. doi: 10.1016/j.jbi.2013.04.010

Miller, D. P. Jr., Weaver, K. E., Case, L. D., Babcock, D., Lawler, D., Denizard-Thompson, N., et al. (2017). Usability of a novel mobile health iPad app by vulnerable populations. *JMIR Mhealth Uhealth* 5:e43. doi: 10.2196/mhealth.7268

Mirkovic, J., Kaufman, D. R., and Ruland, C. M. (2014). Supporting cancer patients in illness management: usability evaluation of a mobile app. *JMIR Mhealth Uhealth* 2:e33. doi: 10.2196/mhealth.3359

Mohammadzadeh, N., and Safdari, R. (2014). Patient monitoring in mobile health: opportunities and challenges. *Med. Arch.* 68:57.

Mohr, D. C., Cuijpers, P., and Lehman, K. (2011). Supportive accountability: a model for providing human support to enhance adherence to eHealth interventions. *J. Med. Internet Res.* 13:e30. doi: 10.2196/jmir.1602

Mun, Y. Y., and Hwang, Y. (2003). Predicting the use of web-based information systems: self-efficacy, enjoyment, learning goal orientation, and the technology acceptance model. *Int. J. Hum. Comput. Stud.* 59, 431–449. doi: 10.1016/S1071-5819(03)00114-9

Murray, T., Hardy, D., Spruijt-Metz, D., Hekler, E., and Raij, A. (2013). "Avatar interfaces for biobehavioral feedback," in *Proceedings of the International Conference of Design, User Experience, and Usability*, (Berlin: Springer), 424–434. doi: 10.1007/978-3-642-39241-2_47

Nijland, N., van Gemert-Pijnen, J. E., Kelders, S. M., Brandenburg, B. J., and Seydel, E. R. (2011). Factors influencing the use of a Web-based application for supporting the self-care of patients with type 2 diabetes: a longitudinal study. *J. Med. Internet Res.* 13:e71. doi: 10.2196/jmir.1603

Os, J., Verhagen, S., Marsman, A., Peeters, F., Bak, M., Marcelis, M., et al. (2017). The experience sampling method as an mHealth tool to support self-monitoring, self-insight, and personalized health care in clinical practice. *Depress. Anxiety* 34, 481–493. doi: 10.1002/da.22647

Pagliari, C. (2007). Design and evaluation in eHealth: challenges and implications for an interdisciplinary field. *J. Med. Internet Res.* 9:e15. doi: 10.2196/jmir.9.2.e15

Pravettoni, G., Folgieri, R., and Lucchiari, C. (2015). "Cognitive science in telemedicine: from psychology to artificial intelligence," in *Tele-oncology*, eds G. Gatti, G. Pravettoni, and F. Capello (Cham: Springer), 5–22.

Pravettoni, G., and Gorini, A. (2011). A P5 cancer medicine approach: why personalized medicine cannot ignore psychology. *J. Eval. Clin. Pract.* 17, 594–596. doi: 10.1111/j.1365-2753.2011.01709.x

Pravettoni, G., Mazzocco, K., Gorini, A., and Curigliano, G. (2016). Understanding cognitive processes behind acceptance or refusal of phase I trials. *Crit. Rev. Oncol. Hematol.* 100, 69–73. doi: 10.1016/j.critrevonc.2016.01.023

Price, N. D., Edelman, L. B., Lee, I., Yoo, H., Hwang, D., Carlson, G., et al. (2009). "Systems biology and systems medicine," in *Essentials of Genomic and Personalized Medicine*, eds G. S. Ginsburg and H. F. Willard (Maryland Heights: Elsevier Academic Press), 131–141.

Renzi, C., Fioretti, C., Oliveri, S., Mazzocco, K., Zerini, D., Alessandro, O., et al. (2017). A qualitative investigation on patient empowerment in prostate cancer. *Front. Psychol.* 8:1215. doi: 10.3389/fpsyg.2017.01215

Ruland, C. M., Maffei, R. M., Børøsund, E., Krahn, A., Andersen, T., and Grimsbø, G. H. (2013). Evaluation of different features of an eHealth application for personalized illness management support: cancer patients' use and appraisal of usefulness. *Int. J. Med. Inform.* 82, 593–603. doi: 10.1016/j.ijmedinf.2013.02.007

Samoocha, D., Bruinvels, D. J., Elbers, N. A., Anema, J. R., and van der Beek, A. J. (2010). Effectiveness of web-based interventions on patient empowerment: a systematic review and meta-analysis. *J. Med. Internet Res.* 12:e23. doi: 10.2196/jmir.1286

Sathyanarayana, A., Joty, S., Fernandez-Luque, L., Ofli, F., Srivastava, J., Elmagarmid, A., et al. (2016). Impact of physical activity on sleep: a deep learning based exploration. *JMIR Mhealth Uhealth* 4:e125. doi: 10.2196/mhealth.6562

Stellefson, M., Hanik, B., Chaney, B., Chaney, D., Tennant, B., and Chavarria, E. A. (2011). eHealth literacy among college students: a systematic review with implications for eHealth education. *J. Med. Internet Res.* 13:e102. doi: 10.2196/jmir.1703

Stephens, J. D., Yager, A. M., and Allen, J. (2017). Smartphone technology and text messaging for weight loss in young adults: a randomized controlled trial. *J. Cardiovasc. Nurs.* 32, 39–46. doi: 10.1097/JCN.0000000000000307

Tokosi, T. O., Fortuin, J., and Douglas, T. S. (2017). The impact of mHealth interventions on breast cancer awareness and screening: systematic review protocol. *JMIR Res. Protoc.* 6:e246. doi: 10.2196/resprot.8043

Tomlinson, M., Rotheram-Borus, M. J., Swartz, L., and Tsai, A. C. (2013). Scaling up mHealth: where is the evidence? *PLoS Med.* 10:e1001382. doi: 10.1371/journal.pmed.1001382

Triberti, S., and Barello, S. (2016). The quest for engaging AmI: patient engagement and experience design tools to promote effective assisted living. *J. Biomed. Inform.* 63, 150–156. doi: 10.1016/j.jbi.2016.08.010

Triberti, S., Bigi, S., Rossi, M. G., Caretto, A., Laurenzi, A., Dozio, N., et al. (2018). The active ageing mobile app for diabetes self-management: first adherence data and analysis of patients' in-app notes. *Paper presented at: 7th EAI International Symposium on Pervasive Computing Paradigms for Mental Health – MindCare 2018*, Boston, MA.

Triberti, S., and Chirico, A. (2016). "Healthy Avatars, Healthy People," in *Transformative Healthcare Practice through Patient Engagement*, ed. G. Graffigna (Hersey, PA: IGI Global), 247–275.

Villani, D., Carissoli, C., Triberti, S., Marchetti, A., Gilli, G., and Riva, G. (2018). Videogames for emotion regulation: a systematic review. *Games Health J.* 7, 85–99. doi: 10.1089/g4h.2017.0108

Wangpipatwong, S., Chutimaskul, W., and Papasratorn, B. (2008). Understanding citizen's continuance intention to use e-government website: a composite view of technology acceptance model and computer self-efficacy. *Electron. J. E Gov.* 6, 55–64.

Ward, R. (2013). The application of technology acceptance and diffusion of innovation models in healthcare informatics. *Health Policy Technol.* 2, 222–228. doi: 10.1177/1460458211435425

Wiecha, J., and Pollard, T. (2004). The interdisciplinary eHealth team: chronic care for the future. *J. Med. Internet Res.* 6:e22. doi: 10.2196/jmir.6.3.e22

Wu, Y. T., and Tsai, C. C. (2006). University students' internet attitudes and internet self-efficacy: a study at three universities in Taiwan. *Cyberpsychol. Behav.* 9, 441–450. doi: 10.1089/cpb.2006.9.441

Yee, N., and Bailenson, J. (2007). The Proteus effect: the effect of transformed self-representation on behavior. *Hum. Commun. Res.* 33, 271–290. doi: 10.1111/j.1468-2958.2007.00299.x

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Improving Self-Esteem With Motivational Quotes: Opportunities for Digital Health Technologies for People With Chronic Disorders

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INTRODUCTION

Living with a chronic medical condition is often accompanied by low self-esteem, a diminished sense of personal worth, and lower self-efficacy, a diminished sense of one's ability to influence behavioral outcomes. This can significantly affect health-related quality of life and wellbeing, with low self-esteem and self-efficacy contributing to poor coping, helplessness, a decrease in positive health behaviors, and increased risk of comorbidities. Thus, it becomes important to promote self-esteem and empowerment over one's condition.

Digital health technologies (also known as mobile health, mHealth, digital medicine, or digital therapeutics) have received increased recognition among chronically-ill patients and healthcare professionals as non-pharmacological treatment strategies for providing disease-specific, self-management content while also improving patient engagement. Since motivational quotes are increasingly used in various media and therapeutic programs to promote positive thinking and self-esteem, this article explores their medical applications and integration into digital health, with particular emphasis on tailoring different categories of motivational quotes to address specific causes of low self-esteem in chronically-ill adult populations.

SELF-ESTEEM AND SELF-EFFICACY IN CHRONIC CONDITIONS

Being afflicted with a chronic mental or physical condition, such as depression, diabetes, or other long-term illness, presents a myriad of difficulties that significantly impact quality of life. In addition to physical symptoms that interfere with daily activities, one faces a range of psychosocial difficulties. Common sources of distress include unmet emotional support needs, feelings of loss or alienation, and tolls on finances, work, and leisure (Vellenga and Christenson, 1994; Morasso et al., 1999; Vallis et al., 2016). Mental illness is frequently accompanied by depressed mood and anxiety, and chronic physical diseases such as asthma, arthritis, and diabetes have similarly been associated with comorbid depression (Moussavi et al., 2007; Connell et al., 2012). Another struggle for chronically-ill individuals is low self-esteem, which is both a consequence of the condition and obstacle for effective self-management and coping. Low self-esteem has been correlated with self-stigma that often accompanies mental illness, in which one internalizes negative perceptions of the condition and perceives the illness as a poor reflection of the self (Corrigan et al., 2006). It may also arise from the decreased independence and autonomy frequently associated with chronic illness, and from maladaptive coping strategies involving avoidance or blame (Felton et al., 1984; Connell et al., 2012). Low self-esteem in turn becomes a risk factor for depression, anxiety, eating disorders, aggression, and substance abuse, further compounding the negative effects of a chronic condition and introducing significant comorbidities (Mann et al., 2004; Sowislo and Orth, 2013). Thus, it becomes important to assist chronically-ill individuals with overcoming low self-esteem in order to prevent negative consequences on disease self-management and quality of life.

High self-esteem becomes even more critical given its potential impact on self-efficacy, which has been associated with reduced disease impact and more effective self-management through medication adherence, stress management, exercise, and nutrition (Clark et al., 1988; Clark and Dodge, 1999). Perceived self-efficacy has also been shown to reduce depressive symptoms and predict positive health behavior change (Strecher et al., 1986; Karademas, 2006). Several self-management programs emphasize self-efficacy for coping with illness, improving health status, and collaborating with health professionals to maximize treatment outcomes (Lorig et al., 2001; Bodenheimer et al., 2002). Self-efficacy can influence effective disease self-management by helping one persevere through difficulties, recover from setbacks, and maintain good habits (Bandura, 2004). Consequently, self-efficacy becomes essential for dealing with chronic disorders, for it is not uncommon for feelings of despair, hopelessness, or frustration to cause individuals to neglect positive health behaviors.

While self-esteem and self-efficacy are distinct constructs, high levels of both enable better coping with and recovery from physical diseases (Mann et al., 2004). Furthermore, self-esteem has been identified as an intrapersonal influence on self-efficacy, suggesting that increasing self-esteem could subsequently increase self-efficacy (Flay and Petraitis, 1994; Flay et al., 2009). According to the Theory of Triadic Influence, high self-esteem increases the value of willpower and self-determination in changing health-related behaviors, which in turn builds self-efficacy (Flay and Petraitis, 1994). Thus, improving low self-esteem could have downstream effects of increasing one's willpower to effectively manage the disease. Additionally, high self-esteem may prevent a chronically-ill individual from discounting positive feedback about his or her self-efficacy (Strecher et al., 1986). This would protect against falling into a negative, doubtful state regarding one's ability to cope with or overcome the illness. Given its relationship to self-esteem, one way to address the physical and psychosocial difficulties faced by chronically-ill individuals would be to improve self-efficacy by targeting low self-esteem.

ADDRESSING LOW SELF-ESTEEM WITH MOTIVATIONAL QUOTES

Motivational quotes have been integrated into various programs and interventions in clinical and educational settings, effectively increasing confidence, motivation, empowerment, and satisfaction in adults struggling with stress, anxiety, depression, mental illness, and substance abuse (Czuchry and Dansereau, 2005; Kendall et al., 2005; Brann and Sloop, 2006; Marchinko and Clarke, 2011; Littlechild et al., 2013; Poon, 2016). However, inspirational quotes or similar attempts to increase self-esteem are not always effective. Self-selected inspirational quotes had no effect on children's perceived autonomy, competence, or intrinsic motivation in the classroom (Collins, 2015), and inflated praise of children with low self-esteem led to decreased challenge seeking rather than increased self-esteem (Brummelman et al., 2014). Self-help literature in general has been criticized as overly simplistic and idealistic, with excessive optimism, self-affirmation, and imperative statements not always having the intended positive effects and sometimes leading to lower self-esteem or unrealistic world views (Gokhale, 2012). This suggests that some motivational quotes are more effective than others, with different types of quotes being better suited to address low self-esteem depending on its causes. **Table 1** presents several categories of motivational quotes, each of which can be tailored to address a specific source of low self-esteem. By carefully selecting motivational quote categories for particular individuals, digital health therapies and interventions may more effectively improve low self-esteem in chronically-ill individuals. This article specifically focuses on motivational quotes for adult populations, but the same approach can apply to children by using more child-friendly inspirational quotes.

Low self-esteem is multi-faceted and may arise from various factors related to chronic illness. According to sociometer theory, self-esteem reflects the extent that one feels accepted by others and is a social construct that highly values perceptions of close friends and family (Leary and Baumeister, 2000). Living with a chronic disease often makes one feel isolated or excluded, whether it be from perceived disease-related stigma or missing out on social activities due to decreased mobility or high treatment demands. In this case, the best way to address low self-esteem is to situate the individual within a social context, allowing one to relate to others or receive direct feedback indicating understanding and social acceptance. Both "Experience of Others/'I'" and "Empowerment/'You'" motivational quotes would fulfill this purpose, with the former allowing one to relate to others' firsthand experiences, and the latter providing positive feedback and clear indication of social support.

However, individuals with low self-esteem have also preferred accurate self-appraisals over self-enhancing feedback, with depressed individuals holding more accurate self-views to determine whether behavioral changes are necessary (Kirkpatrick and Ellis, 2001). In this case, attempting to convince one of the faultiness of negative self-appraisals would be less efficient. Unrealistically positive appraisals could be met with skepticism, disgust, or rejection for being overly optimistic. A more effective strategy than "Empowerment/'You'" quotes would be "Reality Check" or "General Statement" quotes that acknowledge the negative aspects of life one is experiencing, or discuss general concepts in a passive, observational manner, without presenting what could otherwise be perceived as false praise.

Low self-esteem may also arise from poor self-evaluation due to socially comparing oneself to others (Mann et al., 2004). With chronic illness, others can easily seem superior because they are not debilitated by the physical or psychological symptoms that the afflicted individual struggles with daily. This source of low self-esteem may be addressed in two ways. The first approach is to eliminate the perception of others as somehow superior. "Reality

TABLE 1 | Categories of motivational quotes for addressing low self-esteem.

Quote type	Description	Example
Choice	Presents the option of acting to change one's present state or maintaining the status quo, preserving the individual's sense of agency and control over steps taken to improve wellbeing	"The difference between misery and happiness depends on what we do with our attention."—Sharon Salzberg "Instead of begging to be picked by others, you have the choice to pick yourself and build your brand."—Bernard Kelvin Clive
Self-directed question	Poses a question to the individual that stimulates introspection and self-examination which in turn may promote insight into the self and the causes behind diminished wellbeing	"Why should we worry about what others think of us, do we have more confidence in their opinions than we do our own?"—Brigham Young "What would it be like to look in the mirror and actually accept what you see? Not loathe the reflection, or despite it, or be resigned to it? But to like it?"—Justina Chen
Cause-and-effect	Outlines the positive effects that may result from particular thoughts or actions, preserving the individual's sense of agency by only providing information rather than ordering action	"Once you start making the effort to 'wake yourself up'—that is, be more mindful in your activities—you suddenly start appreciating life a lot more."—Robert Biswas-Diener "We build confidence by daring to step outside our comfort zone in small increments."—Sam Owen
Imperative/command	Provides direction and explicit commands for the individual to follow in order to improve wellbeing, potentially limiting personal agency but also providing valuable guidance	"Look within, and seek That."—Jalaluddin Rumi "If you cannot do great things, do small things in a great way."—Napoleon Hill
Empowerment/"You"	Addresses the individual directly with positive, affirming statements meant to empower and increase self-esteem, self-worth, self-confidence, etc.	"You yourself, as much as anybody in the entire universe, deserve your love and affection."—Siddhartha Gautama "Stop trying to 'fix' yourself; you're NOT broken! You are perfectly imperfect and powerful beyond measure."—Steve Maraboli
Experience of others/"I"	Offers the opinion or first-person account of someone else, providing the individual with someone to relate to or an example of how others deal with diminished wellbeing or difficulties	"Why am I trying to be somebody? I am somebody."—Eric Christopher Jackson "I am only one, but I am one. I cannot do everything, but I can do something. And because I cannot do everything, I will not refuse to do the something that I can do."—Edward Everett Hale
Reality check	Disrupts the perception of a perfect world, highlighting life's negative aspects and showing the individual that it is natural to face pain and difficulties, emphasizing that others also share these experiences	"Even a happy life cannot be without a measure of darkness, and the word happy would lose its meaning if it were not balanced by sadness."—Carl G. Jung "No one has it all, and no one lacks it all."—Christopher Peterson
General statement	Discusses general concepts or situations in life, often in an observational manner, so as to guide cognitions, mindsets, or perspectives of the world to be more positive, thus promoting wellbeing without imposing on the individual	"Surrendering is not giving up—it is gaining strength."—Grace Sara "Every person on this earth is full of great possibilities that can be realized through imagination, effort, and perseverance."—Scott Barry Kaufman

A more extensive list of motivational quotes organized by category can be found in the supplementary material under ***Datasheet 1****.*

Check" quotes highlighting others' imperfections or difficulties would effectively disrupt the high esteem one holds others in, illustrating that they are not inherently better or flawless. The second approach is to make self-evaluations less deprecating and more affirming. "Empowerment/'You"' and "Self-Directed Question" motivational quotes would encourage positive self-evaluations by emphasizing the individual's laudable qualities and promoting self-reflection that would subsequently allow one to recognize personal strengths and value.

Another cause of low self-esteem may be confusion about one's identity, leading to maladaptive coping responses of escapism or avoidance of current issues (Mann et al., 2004). In having a chronic medical condition, one may feel lost and not know one's place in the world, unable to separate the self from the disease, treatments, or hospital settings that seem to consume everyday life. At this point, the individual is likely to accept direction from others in searching for a solution to increase confidence and self-assurance. "Cause-and-Effect" and "Imperative/Command" motivational quotes would effectively provide this guidance, allowing one to take the necessary steps toward clarity and self-discovery.

In addressing low self-esteem, two important considerations are autonomy and perceived control, for chronically-ill individuals may be highly susceptible to perceiving a lack of control over symptoms or life in general. This may arise from the unpredictable nature of symptoms or important decisions being controlled by medical professionals rather than the individual. Adolescents with serious or chronic diseases were found to have a significantly reduced sense of control over their health-related futures (Kellerman et al., 1980), and control, autonomy, and choice regarding quality of life, symptoms, and major decisions were particularly important for individuals with mental health problems (Connell et al., 2012). Experiencing personal control over life was positively correlated with quality of life in late-stage cancer patients (Lewis, 1982). Thus, for individuals particularly concerned with maintaining control over their lives, and whose low self-esteem stems from a perceived lack of control or autonomy, "Choice" and "General Statement" motivational quotes would be most effective. These categories merely present general observations or options for action, allowing one to decide whether to act or not without imposing outside control or infringing upon one's sense of agency.

As the above discussion illustrates, the multi-faceted nature of self-esteem requires motivational quotes to be specifically tailored to the cause of low self-esteem to be effective, rather than applied indiscriminately across all situations.

DIGITAL HEALTH AND MOBILE MEDICAL APPLICATIONS

Although still in its infancy, digital medicine is being embraced by patients, doctors, nurses, healthcare and pharmaceutical industries, and regulatory agencies such as the US Food and Drug Administration (FDA). Several FDA-approved mobile medical apps (for diabetes and addiction) and video games (for stroke and traumatic brain injury) illustrate how non-pharmacological interventions delivered by digital technologies can provide clinical benefits for chronically-ill patients. Positive findings in recent clinical studies of mobile health interventions for depression (Mantani et al., 2017; Ben-Zeev et al., 2018; Berger et al., 2018; Silva Almodovar et al., 2018) emphasize new opportunities to improve treatments of mental disorders.

Digital therapies can deliver behavioral interventions by mobile apps, internet (web-based apps), and video games. An apparent benefit of mobile health is its "personalized medicine" aspect that adjusts digital content to an individual's current needs through just-in-time adaptive interventions (Nahum-Shani et al., 2018). The use of wearables can further optimize digital interventions through neurobiofeedback mechanisms (Ramirez et al., 2015), with new biofeedback technologies, such as the FDA-cleared smartwatch Embrace (Empatica), being developed. The flexibility of digital content in mobile health technologies is further emphasized by adding music as an "active component" of therapy (Schriewer and Bulaj, 2016; Afra et al., 2018) or integrating exercise and educational empowerment into a video game designed for children with cancer (Bruggers et al., 2018). Integrating judiciously tailored motivational quotes into digital content as an "active ingredient" in mobile and web-based apps may offer additional means to improve patient engagement, self-esteem, and ultimately self-efficacy. Daily delivery of such motivational quotes will likely appeal to chronically-ill individuals across various disorders, for many of them live with depression or anxiety as comorbidities.

In conclusion, digital health technologies are promising for delivering self-esteem interventions to improve engagement and treatment outcomes and ultimately improve quality of life for people living with chronic disorders.

AUTHOR CONTRIBUTIONS

AB and GB conceived the study and wrote and edited the manuscript. AB reviewed the literature, compiled, and analyzed the quotes.

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SUPPLEMENTARY MATERIAL

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REFERENCES

Afra, P., Bruggers, C. S., Sweney, M., Fagatele, L., Alavi, F., Greenwald, M., et al. (2018). Mobile software as a medical device (SaMD) for the treatment of epilepsy: development of digital therapeutics comprising behavioral and music-based interventions for neurological disorders. *Front. Hum. Neurosci.* 12:171. doi: 10.3389/fnhum.2018.00171

Bandura, A. (2004). Health promotion by social cognitive means. *Health Educ. Behav.* 31, 143–164. doi: 10.1177/1090198104263660

Ben-Zeev, D., Brian, R. M., Jonathan, G., Razzano, L., Pashka, N., Carpenter-Song, E., et al. (2018). Mobile health (mHealth) versus clinic-based group intervention for people with serious mental illness: a randomized controlled trial. *Psychiatr. Serv.* 69, 978–985. doi: 10.1176/appi.ps.201800063

Berger, T., Krieger, T., Sude, K., Meyer, B., and Maercker, A. (2018). Evaluating an e-mental health program ("deprexis") as adjunctive treatment tool in psychotherapy for depression: Results of a pragmatic randomized controlled trial. *J. Affect. Disord.* 227, 455–462. doi: 10.1016/j.jad.2017.11.021

Bodenheimer, T., Lorig, K., Holman, H., and Grumbach, K. (2002). Patient self-management of chronic disease in primary care. *JAMA* 288, 2469–2475. doi: 10.1001/jama.288.19.2469

Brann, D. W., and Sloop, S. (2006). Curriculum development and technology incorporation in teaching neuroscience to graduate students in a medical school environment. *Adv. Physiol. Educ.* 30, 38–45. doi: 10.1152/advan.00068.2005

Bruggers, C. S., Baranowski, S., Beseris, M., Leonard, R., Long, D., Schulte, E., et al. (2018). A prototype exercise-empowerment mobile video game for children with cancer, and its usability assessment: developing digital empowerment interventions for pediatric diseases. *Front. Pediatr.* 6:69. doi: 10.3389/fped.2018.00069

Brummelman, E., Thomaes, S., Orobio de Castro, B., Overbeek, G., and Bushman, B. J. (2014). "That's not just beautiful – that's incredibly beautiful!": the adverse impact of inflated praise on children with low self-esteem. *Psychol. Sci.* 25, 728–735. doi: 10.1177/0956797613514251

Clark, N. M., and Dodge, J. A. (1999). Exploring self-efficacy as a predictor of disease management. *Health Educ. Behav.* 26, 72–89. doi: 10.1177/109019819902600107

Clark, N. M., Rosenstock, I. M., Hassan, H., Evans, D., Wasilewski, Y., Feldman, C., et al. (1988). The effect of health beliefs and feelings of self efficacy on self management behavior of children with a chronic disease. *Patient Educ. Couns.* 11, 131–139. doi: 10.1016/0738-3991(88)90045-6

Collins, G. (2015). Language to motivate learning: the power of inspirational quotes. *A Rising Tide.* 7, 1-22. Available online at: http://www.smcm.edu/mat/wp-content/uploads/sites/73/2015/06/Gabrielle-Collins-2015.pdf

Connell, J., Brazier, J., O'Cathain, A., Lloyd-Jones, M., and Paisley, S. (2012). Quality of life of people with mental health problems: a synthesis of qualitative research. *Health Qual. Life Outcomes.* 10:138. doi: 10.1186/1477-7525-10-138

Corrigan, P. W., Watson, A. C., and Barr, L. (2006). The self-stigma of mental illness: implications for self-esteem and self-efficacy. *J. Soc. Clin. Psychol.* 25, 875–885. doi: 10.1521/jscp.2006.25.8.875

Czuchry, M., and Dansereau, D. F. (2005). Using motivational activities to facilitate treatment involvement and reduce risk. *J. Psychoactive Drugs* 37, 7–13. doi: 10.1080/02791072.2005.10399744

Felton, B. J., Revenson, T. A., and Hinrichsen, G. A. (1984). Stress and coping in the explanation of psychological adjustment among chronically ill adults. *Soc. Sci. Med.* 18, 889–898. doi: 10.1016/0277-9536(84)90158-8

Flay, B. R., and Petraitis, J. (1994). The theory of triadic influence: a new theory of health behavior with implications for preventive interventions. *Adv. Med. Sociol.* 4, 19–44.

Flay, B. R., Snyder, F. J., and Petraitis, J. (2009). "The theory of triadic influence," in *Emerging Theories in Health Promotion Practice and Research,* eds R. J. DiClemente, R. A. Crosby, and M. C. Kegler (San Francisco, CA: Jossey-Bass), 451–510.

Gokhale, M. (2012). The implications of simplification in "inspirational literature". *International J. Soc. Sci. Hum.* 2, 400–404. doi: 10.7763/IJSSH.2012.V2.134

Karademas, E. C. (2006). Self-efficacy, social support and well-being: the mediating role of optimism. *Pers. Individ. Dif.* 40, 1281–1290. doi: 10.1016/j.paid.2005.10.019

Kellerman, J., Zeltzer, L., Ellenberg, L., Dash, J., and Rigler, D. (1980). Psychological effects of illness in adolescence. I. Anxiety, self-esteem, and perception of control. *J. Pediatr.* 97, 126–131. doi: 10.1016/S0022-3476(80)80152-1

Kendall, J., Waddington, C., and Kendall, C. (2005). The daily moment: a stress reduction program for cancer center staff. *J. Oncol. Manage.* 14, 68–71.

Kirkpatrick, L. A., and Ellis, B. J. (2001). "An evolutionary-psychological approach to self-esteem: multiple domains and multiple functions," in *Blackwell Handbook of Social Psychology: Interpersonal Processes,* eds G. J. O. Fletcher and M. S. Clark (Malden, MA: Blackwell Publishing), 411–436.

Leary, M. R., and Baumeister, R. F. (2000). The nature and function of self-esteem: sociometer theory. *Adv. Exp. Soc. Psychol.* 32, 1–62. doi: 10.1016/S0065-2601(00)80003-9

Lewis, F. M. (1982). Experienced personal control and quality of life in late-stage cancer patients. *Nurs. Res.* 31, 113–119. doi: 10.1097/00006199-198203000-00012

Littlechild, B., Smith, A. H., Meredith-Windle, G., Gale, T., Lloyd, M., and Hawley, C. (2013). Recovery approaches in mental health: a qualitative evaluation of the whole life therapy programme for persons with schizophrenia. *Health* 5, 582–587. doi: 10.4236/health.2013.53A077

Lorig, K. R., Sobel, D. S., Ritter, P. L., Laurent, D., and Hobbs, M. (2001). Effect of a self-management program on patients with chronic disease. *Effect. Clin. Pract.* 4, 256–262. Available online at: http://ecp.acponline.org/novdec01/lorig.pdf

Mann, M., Hosman, C. M., Schaalma, H. P., and De Vries, N. K. (2004). Self-esteem in a broad-spectrum approach for mental health promotion. *Health Educ. Res.* 19, 357–372. doi: 10.1093/her/cyg041

Mantani, A., Kato, T., Furukawa, T. A., Horikoshi, M., Imai, H., Hiroe, T.i., et al. (2017). Smartphone cognitive behavioral therapy as an adjunct to pharmacotherapy for refractory depression: randomized controlled trial. *J. Med. Internet Res.* 19:e373. doi: 10.2196/jmir.8602

Marchinko, S., and Clarke, D. (2011). The wellness planner: empowerment, quality of life, and continuity of care in mental illness. *Arch. Psychiatr. Nurs.* 25, 284–293. doi: 10.1016/j.apnu.2010.10.003

Morasso, G., Capelli, M., Viterbori, P., Di Leo, S., Alberisio, A., Costantini, M., et al. (1999). Psychological and symptom distress in terminal cancer patients with met and unmet needs. *J. Pain Symptom Manage.* 17, 402–409. doi: 10.1016/S0885-3924(99)00034-2

Moussavi, S., Chatterji, S., Emese, V., Tandon, A., Patel, V., and Ustun, B. (2007). Depression, chronic diseases, and decrements in health: results from the world health surveys. *Lancet* 370, 8–14. doi: 10.1016/S0140-6737(07)61415-9

Nahum-Shani, I., Smith, S. N., Spring, B. J., Collins, L. M., Witkiewitz, K., Tewari, A., et al. (2018). Just-in-time adaptive interventions (JITAIs) in mobile health: key components and design principles for ongoing health behavior support. *Ann. Behav. Med.* 52, 446–462. doi: 10.1007/s12160-016-9830-8

Poon, S. K. (2016). *Pacifica*: stressed or worried? An app to help yourself (Mobile App User Guide). *Br. J, Sports Med.* 50, 191–192. doi: 10.1136/bjsports-2015-095747

Ramirez, R., Palencia-Lefler, M., Giraldo, S., and Vamvakousis, Z. (2015). Musical neurofeedback for treating depression in elderly people. *Front. Neurosci.* 9:354. doi: 10.3389/fnins.2015.00354

Schriewer, K., and Bulaj, G. (2016). Music streaming services as adjunct therapies for depression, anxiety, and bipolar symptoms: convergence of digital technologies, mobile apps, emotions, and global mental health. *Front. Public Health* 4:217. doi: 10.3389/fpubh.2016.00217

Silva Almodovar, A., Surve, S., Axon, D. R., Cooper, D., and Nahata, M. C. (2018). Self-directed engagement with a mobile app (Sinasprite) and its effects on confidence in coping skills, depression, and anxiety: retrospective longitudinal study. *JMIR mHealth uHealth* 6:e64. doi: 10.2196/mhealth.9612

Sowislo, J. F., and Orth, U. (2013). Does low self-esteem predict depression and anxiety? A meta-analysis of longitudinal studies. *Psychol. Bull.* 139, 213–240. doi: 10.1037/a0028931

Strecher, V. J., DeVellis, B. M., Becker, M. H., and Rosenstock, I. M. (1986). The role of self-efficacy in achieving health behavior change. *Health Educ. Behav.* 13, 73–92. doi: 10.1177/109019818601300108

Vallis, M., Bruns, K. K., Hollahan, D., Ross, S., and Hahn, J. (2016). Diabetes attitudes, wishes, and needs second study (DAWN2): understanding diabetes-related psychosocial outcomes for Canadians with diabetes. *Can. J. Diab.* 40, 234–241. doi: 10.1016/j.jcjd.2015.11.002

Vellenga, B. A., and Christenson, J. (1994). Persistent and severely mentally ill clients' perceptions of their mental illness. *Issues Ment. Health Nurs.* 15, 359–371. doi: 10..3109/01612849409006914

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Having an Eating Disorder and Still Being Able to Flourish? Examination of Pathological Symptoms and Well-Being as Two Continua of Mental Health in a Clinical Sample

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Introduction: Eating Disorders (EDs) are serious psychiatric disorders, impacting physical and psychosocial functioning, often with a chronic course and high mortality rates. The two continua model of mental health states that mental health is a complete state, that is, not merely the absence of mental illness, but also the presence of mental health. This model was studied among ED patients by examining the presence and correlates of well-being and psychopathology. In addition, the levels of well-being were compared to the Dutch general population.

Method: A total of 468 female ED patients participated in this study during application and intake at a specialized ED treatment Center in the Netherlands. They filled out questionnaires about well-being (MHC-SF), general psychopathology (OQ-45), and ED psychopathology (EDE-Q). Categorical and mean well-being levels were calculated. Also, the relationships between these variables were examined with Pearson correlation and multiple hierarchical regression analysis.

Results: ED patients showed lower levels of emotional, psychological, and social well-being on average compared to the general population. About 26% of the ED patients experienced low levels of well-being (languishing). However, also 13% experienced high levels of well-being (flourishing), varying between 9% in Anorexia Nervosa to 25% in Binge Eating Disorder. ED psychopathology and general well-being showed a moderate negative correlation. For patients with Bulimia Nervosa and Binge Eating Disorder however no such correlation was found. Lower general psychopathology, not having a history of hospitalization for the ED, and adaptive personal functioning were correlated with well-being among ED patients.

Conclusion: This study shows initial support for the two continua model of mental health among ED patients. Psychopathology and well-being should be considered as related, but distinct dimensions of mental health in ED patients. Further research should

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focus on the possible reciprocal relationships between psychopathology and well-being during recovery. It is recommended to monitor well-being during treatment and to implement interventions for well-being to realize complete recovery for those patients with inadequate levels of well-being.

Keywords: eating disorders, anorexia nervosa, bulimia nervosa, binge eating disorder, well-being, psychological well-being, positive functioning

INTRODUCTION

Eating Disorders (EDs) are serious psychiatric disorders (American Psychiatric Association, 2013). They often lead to severe psychological, physical, and social impairment and chronic conditions (Lowe et al., 2001; Jenkins et al., 2011; Mitchison et al., 2012; Mond et al., 2012). Anorexia Nervosa (AN) has the highest mortality rate of all psychiatric disorders, because of the severe physical conditions and suicide (Harris and Barraclough, 1998; Hoek, 2006). The lifetime prevalence estimates for women with eating disorders are 0.9% for AN, 1.5% for Bulimia Nervosa (BN), 3.5% for Binge Eating Disorder (BED), and 0.3, 0.5, and 2.0% among men (Hudson et al., 2008).

The severity and chronicity of ED disorders might explain the main focus in research on psychopathological symptoms and the ignorance of well-being (Tomba et al., 2014). However, mental health is more than the absence of mental illness or psychopathological symptoms. Mental health is also about the presence of well-being (Jahoda, 1958; Seligman and Csikszentmihalyi, 2000; Keyes, 2002, 2012; World Health Organization, 2005; Westerhof and Keyes, 2010). Well-being consists of three components, namely emotional, psychological, and social well-being (Ryff and Keyes, 1995; Keyes, 2002; Westerhof and Keyes, 2010). Emotional well-being is about satisfaction with life and positive affect (Diener et al., 1999; Lamers et al., 2011). Psychological well-being concerns optimal psychological functioning and consists of six dimensions: positive relationships, self-acceptance, environmental mastery, autonomy, personal growth, and purpose in life (Ryff, 1989; Ryff and Keyes, 1995). Social well-being is about optimal functioning in the societal context and consists of five dimensions: social contribution, integration, actualization, acceptance, and coherence (Keyes, 1998). People with high levels of well-being have been described as flourishers, whereas those who are low on well-being languishers (Keyes, 2002, 2005).

Studies among the general and clinical populations showed the importance of well-being in mental health. Psychopathology and well-being are not two opposites of one dimension, but represent two distinct, yet negatively related dimensions of mental health, the so-called two continua model (Keyes, 2005, 2006, 2007; Keyes et al., 2008; Lamers et al., 2011; Peter et al., 2011; Magalhães and Calheiros, 2017; Perugini et al., 2017; Franken et al., 2018). This means that someone with psychopathology may still have high levels of well-being, and that someone with low levels of well-being does not necessarily also have psychopathology. Further evidence for the two continua model comes from studies that show that pathological symptoms and well-being have different correlates. For example, Westerhof and Keyes (2010) found different correlates for psychopathology (age, married, employed, number of illnesses, subjective health) compared to well-being (gender, migration, subjective health) in the general population.

The two continuum structure of mental health in clinical samples is further substantiated by results of a randomized controlled study of Acceptance and Commitment Therapy, where 64% of the participants improved either on depressive symptoms, or on well-being, but not on both (Trompetter et al., 2017).

Well-being has been considered as an important component of recovery in psychological treatments (Fava, 1996) and specific therapies for improving well-being among clinical populations have been developed (Fava et al., 1998, 2005; Fava and Ruini, 2003; Gilbert, 2009; Bolier et al., 2013; Weiss et al., 2016). Even though persons who are recovered from an ED consider several aspects of well-being as fundamental criteria for ED recovery in addition to symptom remission (de Vos et al., 2017), the important role of well-being for mental health has been widely neglected in research among ED patients (Tomba et al., 2014). Some researchers have focused on health-related components among ED patients, such as quality of life or subjective well-being (de la Rie et al., 2005, 2007; Doll et al., 2005; Jenkins et al., 2011; Mond et al., 2012; Tomba et al., 2014). Two studies examined the presence of psychological well-being (PWB) among ED outpatients (Tomba et al., 2014, 2017). In the first study it was found that ED patients had impaired PWB compared to a healthy control group (Tomba et al., 2014). Furthermore, patients with Bulimia Nervosa had greater impairment on all psychological well-being scales compared to a control group, whereas patients with Binge Eating Disorder showed greater impairment only on autonomy, environmental mastery, and self-acceptance, and patients with AN only on positive relationships with others and self-acceptance. This study also found that impaired levels of PWB were independent from the presence of psychopathology, indicating that the presence of PWB does not simply correspond to the absence of psychopathology (Tomba et al., 2014). In the other study, change in PWB among ED patients during outpatient cognitive-behavioral-based treatment was examined. It was found that patients improved on the PWB dimensions during treatment (Tomba et al., 2017). However, after treatment, ED patients still showed impaired positive relationships with others and self-acceptance compared to controls (Tomba et al., 2017). Whereas, previous studies addressed several aspects of well-being, no study has examined all levels of well-being or the two continua model among ED patients.

Psychopathology and well-being might have different correlates among ED patients. Correlates related to the severity of ED psychopathology are, among others, personality traits, emotion regulation difficulties, psychiatric pathology such as depression and anxiety, traumatic past, and body mass index (BMI) (Johnson et al., 2002; Jacobi et al., 2004; Cassin and Von Ranson, 2005; Costa et al., 2008; Haynos et al., 2015). Correlates with well-being have not been examined yet, while this may provide information on which ED patients might be vulnerable to inadequate well-being, which would give guidance in the treatment of eating disorders.

In summary, there is growing support that well-being is an important dimension of mental health, while no studies have been conducted on all three levels of well-being. This study aimed to answer the question whether the two continua model for mental health can be confirmed among a clinical sample of ED patients by addressing the following research questions:

1. What are the levels of well-being and the proportions of ED patients who are languishing and flourishing, and does this differ from the general population?
2. To what extend are psychopathology and well-being related in ED patients?
3. What are the correlates of psychopathology and well-being in ED patients?

Question *one* and two are also examined per eating disorder type in addition to the overall sample of ED patients. For research question *one* we expect that ED patients will have lower levels of well-being and are less likely to flourish compared to the general population. However, we also expect substantial variation in well-being between ED patients, with a substantial part showing moderate to high well-being, as an indicator that well-being functions as a distinct continuum of mental health. Regarding the specific ED types, based on the study of Tomba et al. (2014), we expect more patients with BN languishing compared to other ED types and more patients with AN flourishing compared to other ED types. For research question *two* we expect a low to moderate negative correlation between (a) general psychopathology and well-being, and (b) eating disorder psychopathology and well-being as additional indicators for the two continua model. We expect no differences between ED types. For research question *three* we expect, based on the two-continua model, that different correlates will be associated with ED pathology and well-being. The analysis of correlates is however explorative since this is the first study to examine correlates for well-being in eating disorder patients. Overall, we expect that the two-continua model of complete mental health can be replicated among ED patients, and we consider the results of all three research questions as potential support for the two-continua model.

METHODS

Participants And Procedure

A cross-sectional research design with a control group was used. Participants were patients who applied for outpatient treatment and followed the intake procedure at the Human Concern Foundation, a specialized treatment center for eating disorders in the Netherlands. Data collection took place between March 2015 and January 2017. Inclusion criteria for this study were participants with (a) a minimum age of 16 years, which was the minimum age to apply for treatment at the treatment center, (b) a DSM 5 (American Psychiatric Association, 2013) ED diagnosis at intake, and (c) a signed informed consent. In total, 472 patients were diagnosed with an ED during the period of data collection and initially included in the study. However, after examining sex status, only four men were present in the study and excluded because of the very low sample size. In total 468 participants, all women were included in the final study. Patients were diagnosed by a psychiatrist in collaboration with an intake team consisting of a dietician, psychiatrist, or clinical psychologist, and a clinician with an eating disorder history who has been trained to use this experiential knowledge in treatment (de Vos et al., 2016). All patients filled in the questionnaires as part of the intake procedure and for the measurement baseline of Routine Outcome Monitoring (ROM). ROM is used during the treatment to monitor treatment progress. The following characteristics were collected during the intake interview and used in this study; presence of psychiatric history among family members in the first line (parents, brothers, sisters, medical classification), using psychotropic medication, having followed earlier treatments, being hospitalized earlier for the ED, duration, and start year of the ED, complex trauma, daily activities such as work or study and the financial situation (whether there were financial worries or actual financial problems). The intake interview consists of a semi-structured interview and is conducted by a licensed psychologist. Also, the answers which the patients have given are discussed during a meeting with the psychiatrist. Patients were asked whether they had experienced any life-events or trauma in the past. All answers which confirmed life-events or trauma were noted by the psychologist and/or psychiatrist. During the study the data was labeled by the researchers as life-events, trauma, or complex trauma (sexual abuse, verbal/physical abuse, severe instability in the family, or multiple negative life events). Only the label complex trauma was used in the study. The financial situation was explored with the following questions: are there any current financial problems, and, are there any current financial worries. All answers which confirmed financial problems or worries were noted and used by the researchers as an indication for a poor financial situation. Educational level and living situation were collected according to the instructions of Stichting Benchmark GGZ (SBG), a nationwide benchmark for treatment outcomes of mental health providers in the Netherlands (Stichting Benchmark GGZ., 2013). SBG was established in 2010 as an independent party to facilitate benchmarking among mental health providers in the Netherlands (Blijd-Hoogewys et al., 2012). All mental health institutions were obliged by mental health insurers to deliver data about their treatment outcomes and background variables of their patients, such as educational level and living situation. The results are used to compare outcomes (benchmarking) between treatment centers (Blijd-Hoogewys et al., 2012).

Patients were informed about the aims of the study and signed an informed consent stating that they could terminate the possibility to include their data for scientific research. Patients were consecutively selected based on application. This study required no additional data collection directly from patients apart from the regular intake procedure. Data was anonymized before data analysis. Only two patients declared that they did not want to have their data used in the study and were excluded. This study protocol was approved by the BMS Ethics Committee of the University of Twente.

To compare the well-being scores of ED patients with the general population, a control group of the LISS-panel (Longitudinal Internet Study in the Social Science) of CentERdata was used with a sample of 835 Dutch speaking non-institutionalized women from households in the Netherlands (Lamers et al., 2013). Data of the LISS-panel was collected between 2007 and 2008.

Measures

Eating Disorder Psychopathology (EDE-Q)

Eating disorder psychopathology was measured with the original 36-item Eating Disorder Examination (EDE-Q), a widely used questionnaire for measuring ED psychopathology (Fairburn and Beglin, 1994). The scale consists of 22 items measuring the core attitudinal ED psychopathology. The global score is considered as a valid index of the general level of ED psychopathology (Aardoom et al., 2012). Patients rated the frequency of symptoms in the last 28 days using a 7-point Likert scale (0 = *not 1 day*; 6 = *every day*). The internal consistency of the global score in this sample was 0.92. Lower scores are indicative for lower ED psychopathology.

General Psychopathology (OQ-45 Symptomatic Distress Scale)

The scale symptomatic distress (SD scale) of the OQ-45 (Jong et al., 2008) was used as a measure for general psychopathology, in accordance with the Dutch benchmark for mental healthcare (Warmerdam et al., 2017). The OQ-45 SD scale has 25 items and shows good psychometric properties (Jong et al., 2008). Items are scored on a 5-point Likert scale, ranging from 0 "never" to 4 "always." The internal consistency in this sample was 0.91. Higher scores are indicative of higher psychopathology.

Well-Being (MHC-SF)

Well-being was measured with the Mental Health Continuum Short Form (MHC-SF). The Dutch MHC-SF was developed by Lamers et al. (2011) and includes emotional, psychological and social well-being. It consists of 14 items, rated on a six-point Likert scale ranging from 0 "never" to 5 "always," and gives an overall impression of well-being. To examine whether the MHC-SF measures the same three dimensions of well-being in ED patients, as found in the general population (Lamers et al., 2011), confirmatory factor analysis (CFA) was tested prior to the main analysis in R statistics (R Core Team, 2013) with the Lavaan package version 0.5–23.1097 (Rosseel, 2012). The following fit indices were used: Root Mean Squared Error of Approximation (RMSEA), Comparative Fit Index (CFI), and Tucker-Lewis Index (TLI). CFA showed that a three-factor model, with the dimensions emotional, social, and psychological well-being, showed the best fit in our data, compared to a one or two factor model (RMSEA = 0.075, CFI = 0.93, and TLI = 0.92). The internal consistency in this sample was 0.90 for the total scale, 0.86 for the scale emotional well-being, 0.73 for the scale social well-being, and 0.83 for the scale psychological well-being. Higher scores are indicative of higher well-being.

The percentages of ED patients languishing, and flourishing were calculated according to Keyes (2002, 2012) and Lamers et al. (2011) instructions. For the category languishing, participants had to score low ("never" or "once or twice" during the past month) on at least one of the three emotional well-being dimensions and at least six of the eleven (combined) psychological and social well-being dimensions. For the category flourishing, participants had to score high ("almost every day," or "every day" during the past month) on the same dimensions.

Severity Indices of Personality Problems (SIPP-SF)

The SIPP-SF measures the core components of (mal)adaptive personality functioning in clinical samples using 60 items and is a shortened version of the SIPP-118 (Verheul et al., 2008). The SIPP measures the following components: self-control, identity integration, responsibility, relational capacities, and social concordance. Only the first three components were relevant for this study because the last two show a high overlap in construct and meaning with the social and psychological well-being dimensions. Self-control relates to the capacity to tolerate, use and control emotions and impulses. Identity integration relates to experiencing a coherence of self or identity and the capacity to see oneself and one's own life as stable, integrated, and purposive. Responsibility is related to taking responsibility for one's own life and the capacity to set realistic goals, and to achieve these goals (Verheul et al., 2008). The scales self-control, identity integration and responsibility all consist of 12 items and were rated from 1 "fully disagree" to 4 "fully agree." Higher scores are indicative for lower levels of personality problems. The scales of the SIPP-SF show good construct validity and can be used to screen for (mal)adaptive personality functioning in adults (Verheul et al., 2008; Rossi et al., 2016). The internal consistency in this sample was 0.89 for the self-control/emotion regulation scale, 0.91 for the identity integration scale, and 0.86 for the responsibility scale. There was a lower response on the SIPP-SF ($N = 269$) because it was not administered in the first year of the data collection.

Analysis

Analyses were performed in Statistical Package of the Social Sciences (SPSS) 24. Differences in mean levels of well-being between ED patients and the general population, and between AN, BN, BED, Other Specified Feeding and Eating Disorders (OSFED) and the general population were examined using one-way analysis of variance (ANOVA) with the groups as fixed factor. Partial eta-squared values (η^2) were reported as measures for the effect size. Eta-squared values were interpreted as follows; low, ranging from 0.01 to 0.05, medium between 0.06 and 0.13, and large when 0.14 and higher (Field, 2005). Tukey's test was used for *post-hoc* analysis when homogeneity of variances was met. Welch's ANOVA and Games-Howell *post-hoc* tests were used when homogeneity of variances was not met.

Chi-square tests were used with *post-hoc* analysis using a Bonferroni correction to analyze differences in proportions flourishers and languishers between ED patients and the general population, and between the ED types. For correlation analysis Pearson coefficient was used. Correlations were interpreted as follows (Santrock, 2007): very low: 0 to 0.20 low: 21 to 0.40; moderate: 0.41–0.60; high moderate: 0.61–0.80; high: 0.81–0.90, and very high: 0.91–1.0. In addition, partial correlation analysis was run to determine whether possible confounders would lead to different results compared to Pearson correlation coefficient. The following control variables were used: age, living situation, educational level, duration of illness, start-age of the illness, financial situation, BMI, and whether patients had work or were following a study during the intake procedure. Although there were small changes when controlling for these variables (minimum difference 0.00, maximum difference 0.08), none led to changes in significance levels compared to Pearson correlation coefficient. For reasons of comparability with other research on the relationship between psychopathology and well-being, Pearson coefficient was used.

For the analysis of correlates that are expected to be associated with mental health, a multiple hierarchical regression analysis was used with the ED psychopathology and the well-being dimensions as dependent variables. Hierarchical regression was chosen because we used a broad set of potential correlates which could be classified into four main categories (1. demographics, 2. illness history related correlates, 3. current illness related correlates, and 4. (mal)adaptive personality functioning). Separate analyses were run on the following dependent variables; emotional well-being, psychological well-being, social well-being, and eating disorder psychopathology. Analysis of the three separate dimensions of well-being instead of only general well-being was done, because the dimensions are both theoretical and psychometrically different concepts of well-being (Deci and Ryan, 2008; Joshanloo and Lamers, 2016). The following predictor variables were used: demographic determinants: age, educational level, living situation, having a job or studying, and financial situation; illness history related determinants: ED duration, start age of ED, earlier hospitalization for the ED without remission, psychiatric history of a family member (1st degree), history with complex trauma; current illness-related determinants: eating disorder type, using psychotropic medication, general psychopathology, having frequent suicidal thoughts, Body Mass Index (BMI kg/m^2) and personality related determinants: self-control/emotion-regulation, identity integration, and responsibility. Given the substantial number of independent variables in the regression analysis ($N = 18$), only p-values of <0.01 were considered as significant determinants in the models.

Four hierarchical Models were used to test the stability of the associated correlates (independent variables) across the Models. In Model 1 the demographic variables were tested, in Model 2 the addition of illness-history-related variables to demographic variables were tested. In Model 3 and 4, respectively, the addition of current illness-related variables and (mal-)adaptive personality functioning were tested. The assessments of the Q-Q plots, partial regression plots, plots of studentized residuals, and the tolerance values below 0.1, indicated that the assumptions for linearity, homoscedasticity and normality were met, and that there was no multicollinearity.

RESULTS

Background Characteristics

In total 468 female patients with an average age of 28.4 years ($SD = 9.9$) participated in the study. Thirty-five patients (7.8%) had low education, 71 participants (15.8%) had intermediate education, and 343 (76.4%) had high education. The average start age of the ED was 16.0 years ($SD = 5.0$) and the average duration of the ED was 10.9 years ($SD = 9.6$). Hundred-sixty-one patients (34.4%) were diagnosed with Anorexia Nervosa (AN), 96 patients (20.5%) with Bulimia Nervosa (BN), 61 patients (13.0%) with Binge Eating Disorder (BED), and 150 patients (32.1%) with Other Specified Feeding or Eating Disorders (OSFED). The average start age and duration for AN was, respectively; 16.6 years ($SD = 4.2$) and 7.7 years ($SD = 7.8$), for BN; 15.5 years ($SD = 4.9$), and 11.6 years ($SD = 8.6$), for BED; 16.3 years ($SD = 7.3$) and 16.1 years ($SD = 10.2$) and for OSFED; 15.7 years ($SD = 4.9$) and 11.9 years ($SD = 10.8$). Eighty-five percent of the patients have received earlier psychiatric treatment. Mean scores on the EDE-Q global scale were 4.00 ($SD = 1.19$) for the overall ED sample, and 3.75 ($SD = 1.25$) for AN, 4.45 ($SD = 0.92$) for BN, 4.17 ($SD = 1.01$) for BED, and 3.93 ($SD = 1.27$) for OSFED. See the online **Supplementary Material** for an overview of the other background characteristics of the sample.

Levels of Well-Being And Percentages of Flourishers And Languishers

The first research question concerned the levels of well-being and the proportions of ED patients languishing and flourishing (categorical scores) compared to the general population. There were statistically significant differences between ED patients and the general population for overall well-being, *Welch's* $F_{(1,884.14)} = 188.55$, $p < 0.001$, emotional well-being, *Welch's* $F_{(1,800.779)} = 464.89$, $p < 0.001$, psychological well-being, $F_{(1,1301)} = 199.78$, $p < 0.001$, and social well-being $F_{(1,1301)} = 13.83$, $p < 0.001$. ED patients had lower average scores compared to the general population on all well-being scales with medium effect sizes for overall ($\eta^2 = 0.13$) and psychological well-being ($\eta^2 = 0.13$), a low effect size for social well-being ($\eta^2 = 0.01$) and a large effect size for emotional well-being ($\eta^2 = 0.29$). See **Table 1** for an overview of the results. *Post-hoc* analysis showed statistically significant lower well-being scores for all ED types compared to the general population on overall ($p < 0.001$), emotional ($p < 0.001$), and psychological well-being ($p < 0.001$). Social well-being was only statistically significant lower for AN ($p < 0.05$), and BN ($p < 0.05$) compared to the general population. Differences between the ED types were only found between AN and BED for emotional ($p < 0.01$) and psychological well-being ($p < 0.05$).

Sixty-one patients in this sample were flourishing (13.0%), 285 patients had moderate well-being (60.9%), and 122 patients (26.1%) were languishing. Compared to the general population, there were statistically significant differences in the proportions

TABLE 1 | Categorical and mean scores of well-being for the general population and ED patients.

	Groups							**ED Types**									
	General population (N = 835, women)		**ED patients (N = 468)**		**Statistics**			**AN (N = 161)**		**BN (N = 96)**		**BED (N = 61)**		**OSFED (N = 150)**		**Statistics**	
	N	**%**	***N***	**%**	χ^2	***p***		***N***	**%**	***N***	**%**	***N***	**%**	***N***	**%**	χ^2	***p***
MENTAL HEALTH CATEGORIES					169.327	.000										17.204	.009
Languishing	40	4.8%	122	26.1%**				54	33.5%*	27	28.1%	12	19.7%	29	19.3%		
Moderate	488	58.4%	285	60.9%				92	57.1%	59	61.5%	34	55.7%	100	66.7%		
Flourishing	307	36.8%	61	13.0%**				15	9.3%	10	10.4%	15	24.6%*	21	14%		
	M	***SD***	***M***	***SD***	***F***	***p***	η^2	***M***	***SD***	***M***	***SD***	***M***	***SD***	***M***	***SD***	***F***	***p***
WELL-BEING																	
Total	3.00	0.84	2.29	0.94	188.555	0.000	.13	2.17	0.94	2.21	0.92	2.52	1.02	2.36	0.89	52.632	0.000
Emotional	3.70	0.92	2.36	1.16	464.899	0.000	.29	2.16	1.25	2.34	1.04	2.79	1.12	2.40	1.10	119.922	0.000
Psychological	3.22	0.98	2.40	1.04	199.780	0.000	.13	2.25	1.04	2.32	1.03	2.68	1.12	2.50	0.99	52.803	0.000
Social	2.32	1.02	2.10	1.00	13.836	0.000	.01	2.07	0.93	2.00	1.06	2.18	1.12	2.17	0.99	4.018	0.003

*Statistically significant different at post-hoc comparisons at the p < 0.01 level with Bonferroni correction, **Statistically significant different at post-hoc comparisons at the p < 0.001 level, with Bonferroni correction, percentages are rounded to the nearest tenth.*

of ED patients who were languishing, had moderate well-being and were flourishing, $\chi^2_{(2)} = 169.327$, $p < 0.001$. *Post hoc* comparisons of categorical scores showed that statistically significantly more patients with AN were languishing (33.5%, $p < 0.001$) and more patients with BED were flourishing (24.6%, $p < 0.001$), compared to the other ED types.

These results confirm our hypothesis that ED patients show lower levels of well-being and have a higher change to languish compared to the general population. Substantial variation was found in ED patients' well-being, while all were diagnosed with severe psychopathology. These results suggest that psychopathology and well-being are two related but distinct continua of mental health.

Relationship of Psychopathology With Well-Being

The second research question concerned the correlation between psychopathology and well-being. **Table 2** shows the correlations (Pearson's r) between psychopathology and well-being for ED patients overall and the specific ED types.

General psychopathology showed a *high moderate negative* correlation with overall ($r = -0.73$, $p < 0.001$), and emotional well-being ($r = -0.71$, $p < 0.001$), and a *moderate negative* correlation for psychological ($r = -0.69$, $p < 0.001$) and social well-being ($r = -0.55$, $p < 0.001$).

ED psychopathology showed a *low negative* correlation with overall ($r = -0.35$, $p < 0.001$), emotional ($r = -0.33$, $p < 0.001$), psychological ($r = -0.33$, $p < 0.001$), and social well-being ($r = -0.29$, $p < 0.001$).

Analysis per ED type showed *moderate* to *high moderate negative* correlations of general psychopathology with all well-being dimensions for AN, BN, BED, and OSFED ($p < 0.001$). For ED psychopathology however, only significant *low to moderate negative* correlations with well-being dimensions were found for AN and OSFED ($p < 0.001$), while for BN and BED no significant correlation was found with any well-being dimension.

TABLE 2 | Pearson correlation between psychopathology and well-being per eating disorder type.

ED type	**Psychopathology**		**Well-being**			
		General path	**Total**	**Emotional**	**Psychological**	**Social**
Total	ED path	0.43*	−0.35*	−0.33*	−0.33*	−0.29*
	General path	–	−0.73*	−0.71*	−0.69*	−0.55*
AN	ED path	0.52*	−0.53*	−0.48*	−0.54*	−0.41*
	General path	–	−0.75*	−0.74*	−0.72*	−0.58*
BN	ED path	0.48*	−0.20	−0.20	−0.15	−0.18
	General path	–	−0.69*	−0.62*	−0.64*	−0.57*
BED	ED path	0.22	−0.07	−0.08	−0.00	−0.14
	General path	–	−0.72*	−0.72*	−0.69*	−0.56*
OSFED	ED path	0.42*	−0.39*	−0.38*	−0.37*	−0.29*
	General path		−0.72*	−0.72*	−0.68*	−0.51*

**correlation is significant at the 0.001 level (2 sided), ED path = Eating Disorder psychopathology; General path = General psychopathology.*

The results suggest that ED psychopathology and well-being are two related but distinct continua, whereas general psychopathology and well-being are two separate but stronger related continua. Overall, our hypothesis was confirmed.

Correlates With Mental Health

The third question concerned correlates for psychopathology and well-being. See **Table 3** for each regression model, and **Table 4** for the tested variables in the hierarchical multiple regression.

TABLE 3 | Hierarchical Multiple Regression with four models consisting of variables with: 1. Demographics, 2. Illness history, 3. Current illness, and 4. Personality traits.

Model	R^2	F	Sig	R^2 change	F change	Sig change
ED PSYCHOPATHOLOGY						
Model 1	0.032	1.216	0.295	–	–	–
Model 2	0.045	0.976	0.472	0.013	0.653	0.659
Model 3	0.271	5.276	0.000	0.226	10.700	0.000
Model 4	0.281	4.724	0.000	0.010	1.103	0.348
EMOTIONAL WB						
Model 1	0.053	2.023	0.053	–	–	–
Model 2	0.066	1.476	0.133	0.014	0.726	0.604
Model 3	0.522	13.887	0.000	0.455	32.894	0.000
Model 4	0.596	16.051	0.000	0.075	14.757	0.000
PSYCHOLOGICAL WB						
Model 1	0.056	2.169	0.037	–	–	–
Model 2	0.076	1.703	0.067	0.019	1.047	0.390
Model 3	0.497	12.609	0.000	0.422	29.009	0.000
Model 4	0.642	19.460	0.000	0.144	32.080	0.000
SOCIAL WB						
Model 1	0.061	2.374	0.023	–	–	–
Model 2	0.069	1.544	0.109	0.008	0.419	0.835
Model 3	0.342	6.580	0.000	0.272	14.299	0.000
Model 4	0.444	8.685	0.000	0.103	14.720	0.000

Model 1: Demographics: age, educational level, living situation, having a job or study, and financial situation, Model 2: model 1 + Illness history: ED duration, start age of ED, earlier inpatient treatment(s) without remission, psychiatric history of a family member (1st degree), having complex trauma, Model 3: model 2 + Current Illness variables: eating disorder type, using psychotropic medication, general psychopathology, having frequent suicidal thoughts, Body Mass Index (BMI kg/m^2), Model 4: model 3 + Personality traits: self-control/emotion-regulation, identity integration, responsibility.

Correlates Associated With ED Psychopathology

The explained variance of the baseline Model (1) with demographic variables related to ED psychopathology was not statistically significant [$R^2 = 0.032$, $F_{(7,254)} = 1.21$, $p > 0.01$]. The addition of illness-history-related variables correlated to ED psychopathology (Model 2) above the standard demographic variables (Model 1) did not lead to a statistically significant increase in $R^2 = 0.013$, $F_{(7,254)} = 0.653$, $p > 0.01$. Explained variance increased significantly with the addition of current illness-related variables relating to ED psychopathology (Model 3): $R^2 = 0.226$, $F_{(19,242)} = 10.70$, $p < 0.001$. The addition of personality-related variables relating to ED psychopathology (Model 4) did not lead to a statistically significant increase in $R^2 = 0.010$, $F_{(22,239)} = 1.10$, $p > 0.01$. Model 3 showed the best fit determining ED psychopathology [$R^2 = 0.281$, $F_{(19,242)} = 4.238$, $p < 0.001$]. AN ($\beta = -0.332$, $p < 0.01$) and general psychopathology ($\beta = 0.413$, $p < 0.001$) was significantly associated with ED psychopathology.

Correlates Associated With Emotional Well-Being (EWB)

The explained variance of the baseline Model (1) with demographic variables relating to EWB was not statistically significant [$R^2 = 0.053$, $F_{(7,254)} = 2.023$, $p > 0.01$]. The addition of illness-history-related variables relating to EWB (Model 2) above the standard demographic variables (Model 1) did not lead to a statistically significant increase in $R^2 = -0.014$, $F_{(7,254)} = 0.726$, $p > 0.01$. Explained variance increased significantly with the addition of current illness related variables relating to EWB (Model 3): $R^2 = 0.455$, $F_{(19,242)} = 32.894$, $p < 0.001$. The addition of personality related variables relating to EWB (Model 4) showed a statistically significant increase in $R^2 = 0.075$, $F_{(22,239)} = 14.757$, $p < 0.001$. The final model (4) showed the best fit to determine EWB [$R^2 = 0.596$, $F_{(22,239)} = 16.051$, $p < 0.001$]. General psychopathology ($\beta = -0.236$, $P < 0.01$), and identity integration ($\beta = 0.575$, $p < 0.001$) were significantly associated with EWB.

Correlates Associated With Psychological Well-Being (PWB)

The explained variance of the baseline Model (1) with demographic variables relating to PWB was statistically significant [$R^2 = 0.056$, $F_{(7,254)} = 2.16$, $p < 0.05$]. The addition of illness-history-related variables relating to PWB (Model 2) above the standard demographic variables (Model 1), did not lead to a significant increase in R^2 of 0.019, $F_{(7,254)} = 1.05$, $p > 0.05$. The addition of current illness-related variables relating to PWB (Model 3) led to a statistically significant increase in R^2 of 0.422, $F_{(19,242)} = 29.01$, $p < 0.001$. The addition of personality-related variables relating to PWB (Model 4) led to a statistically significant increase in R^2 of 0.144, $F_{(22,239)} = 33.08$, $p < 0.001$. The final Model (4) showed the best fit to determine PWB [$R^2 = 0.642$, $F_{(22,239)} = 19.46$, $p < 0.001$]. Specific correlates for PWB were, an Earlier hospitalization ($\beta = 0.150$, $p < 0.001$), and the personality traits identity integration ($\beta = 0.711$, $p < 0.001$), and responsibility ($\beta = 0.195$, $p < 0.001$).

Correlates Associated With Social Well-Being (SWB)

The baseline Model (1) with demographic variables relating to SWB was not statistically significant [$R^2 = 0.061$, $F_{(7,254)} = 2.37$ $p > 0.05$]. The addition of illness history related variables relating to SWB (model 2) above the standard demographic variables (Model 1), led not to a statistically significant increase in R^2 of 0.008, $F_{(7,254)} = 0.419$, $p > 0.05$. The addition of current illness-related variables relating to SWB (Model 3) showed a statistically significant increase in R^2 of 0.272, $F_{(19,242)} = 14.23$, $p < 0.001$. The addition of personality-related variables relating to SWB (Model 4) led to a statistically significant increase in R^2 of 0.103, $F_{(22,239)} = 14.72$, $p < 0.001$. The final Model (4) showed the best fit to determine SWB [$R^2 = 0.444$, $F_{(22,239)} = 8.69$, $p < 0.001$]. The personality trait identity integration ($\beta = 0.600$, $p < 0.001$) was significantly associated with SWB.

Our hypothesis can be partly confirmed, as there were different correlates associated with ED psychopathology (having AN) and well-being (earlier hospitalization for the ED, identity integration, and responsibility). However, general psychopathology was associated with both ED psychopathology and emotional well-being.

TABLE 4 | Hierarchical multiple regression: correlates associated with ED psychopathology and well-being.

Variable	Psychopathology			Well-being								
	Eating disorder			Emotional			Social			Psychological		
	B (CI 95%)	*SE*	β	B (CI 95%)	*SE*	β	B (CI 95%)	*SE*	β	B (CI 95%)	*SE*	β
BLOCK 1 DEMOGRAPHICS												
Age	−0.018 (−0.047–0.011)	0.015	−0.151	0.002 (−0.019–0.023)	0.011	0.021	−0.002 (−0.023–0.020)	0.011	−0.015	−0.014 (−0.032–0.004)	0.009	−0.135
Low education	0.312 (−0.504–1.127)	0.414	0.069	−0.084 (−0.678–0.511)	0.302	−0.019	−0.135 (−0.737–0.466)	0.306	−0.036	−0.342 (−0.845–0.160)	0.255	−0.087
Intermediate education	0.173 (−0.565–0.911)	0.375	0.052	−0.225 (−0.763–0.312)	0.273	−0.070	−0.428 (−0.972–0.118)	0.277	−0.153	−0.477 (−0.932–−0.022)	0.231	−0.165
High education	0.068 (−0.607–0.743)	0.343	0.025	−0.231 (−723–0.260)	0.250	−0.089	−0.248 (−0.746–0.250)	0.253	−0.110	−0.325 (−0.741–0.091)	0.211	−0.138
Living situation	−0.104 (−0.385–0.177)	0.143	−0.042	0.018 (−0.187–0.225)	0.104	0.007	0.097(−0.111–0.304)	0.105	0.047	0.068 (−0.105–0.241)	0.088	0.032
Main activity	−0.110 (−0.441–0.221)	0.168	−0.039	0.017 (−0.224–0.258)	0.122	0.006^{a,b}	−0.082 (−0.326–0.162)	0.124	−0.035^{a,b}	0.078 (−0.126–282)	0.104	0.032^{a,b}
Financial situation	0.083 (−0.382–0.548)	0.236	0.020	−0.008 (−0.347–0.331)	0.172	−0.002	−0.061 (−0.404–0.282)	0.174	−0.018	0.004 (−0.283–0.291)	0.146	0.001
BLOCK 2 ILLNESS HISTORY												
ED duration	0.002 (−0.028–0.032)	0.015	0.015	−0.004 (−0.025–0.018)	0.011	−0.029	−0.002 (−0.024–0.020)	0.011	−0.017	0.005 (−0.013–0.024)	0.009	0.050
Start age ED	0.007 (−0.029–0.042)	0.018	0.028	−0.004 (−0.030–0.021)	0.013	−0.018	−0.006 (−0.032–0.020)	0.013	−0.031	−0.004 (−0.025–0.018)	0.011	−0.017
Earlier hospitalized	0.145 (−0.197–0.488)	0.174	0.050	−0.189 (−0.438–0.061)	0.127	−0.067	−0.245 (−0.497–0.008)	0.128	−0.101	**−0.380 (−0.591–−0.169)**	**0.107**	**0.150*****
Psychiatric family	−0.067 (−0.348–0.214)	0.143	−0.028	0.006 (−0.211–0.199)	0.104	0.003	0.031 (−0.177–0.339)^{c}	0.105	0.015	−0.067 (−0.240–0.107)	0.088	−0.032
Complex trauma	0.198 (−0.247–0.644)	0.226	0.051	−0.216 (−0.514–0.109)	0.165	−0.057	−0.062 (−0.391–0.267)	0.167	−0.019	−0.004 (−0.279–0.271)	0.139	−0.001
BLOCK 3 CURRENT ILLNESS												
AN	**−0.832 (−1.378–−0.286)**	**0.277**	**−0.332****	−0.114 (−0.511–0.265)	0.201	−0.047	0.037 (−0.366–0.440)	0.205	0.018	0.033 (−0.304–0.369)	0.171	0.015
BN	−0.012 (−0.502–0.478)	0.249	−0.004	−0.192 (−0.549–0.165)	0.181	−0.067	−0.134 (−0.495–0.228)	0.184	−0.054	−0.126 (−0.428–0.177)	0.153	−049
BED	−0.448 (−0.913–0.016)	0.236	−0.176	−0.243 (−0.581–0.096)	0.172	−0.098	−0.068 (−0.411–0.274)	0.174	−0.032	−0.119 (−0.405–168)	0.145	−0.053
BMI	0.004 (−0.019–0.027)	0.0011	0.026	−0.004 (−0.020–0.013)	0.008	−0.025	−0.015 (−0.032–002)	0.008	−0.114^{c}	0.003 (−0.011–0.017)	0.007	0.020
Psychotropic medication	0.156 (−0.179–0.492)	0.170	0.054	−0.071 (−0.315–0.174)	0.124	−0.025	0.069 (−0.178–0.317)	0.126	0.019	0.117 (−0.089–0.324)	0.105	0.046

(Continued)

TABLE 4 | Continued

Variable	**Psychopathology**			**Well-being**								
	Eating disorder			**Emotional**			**Social**			**Psychological**		
	B (CI 95%)	***SE***	**β**	**B (CI 95%)**	***SE***	**β**	**B (CI 95%)**	***SE***	**β**	**B (CI 95%)**	***SE***	**β**
General psychopathology	**0.035 (0.016–0.054)**	**0.010**	**0.413*****	**−0.020 (−0.034–−0.006)**	**0.007**	**−0.236***	0.000 (−0.015–0.014)	0.007	-0.007^{C}	0.002 (−0.012–0.016)	0.007	-0.015^{C}
Frequent suicidal thoughts	−0.010 (−0.495–0.476)	0.246	−0.002	−0.079 (−0.432–0.275)	0.180	−0.020	0.217 (−0.141–0.575)	0.182	0.063	0.262 (−0.037–0.562)	0.152	0.074
BLOCK 4 PERSONALITY TRAITS												
Self–control/emotion regulation	0.004 (−0.022–0.029)	0.013	0.021	−0.006 (−0.024–0.013)	0.009	−0.034	0.002 (−0.017–021)	0.013	0.017	−0.006 (−0.022–0.010)	0.008	−0.041
Identity integration	−0.010 (−0.042–0.022)	0.016	−0.071	**0.079 (0.056–0.103)**	**0.012**	**0.575*****	**0.071 (0.047 −0.095)**	**0.012**	**0.600*****	**0.088 (0.068–0.108)**	**0.010**	**0.711*****
Responsibility	0.019 (−0.007–0.046)	0.013	0.105	−0.008 (−0.027–0.012)	0.010	−0.043	0.021 (0.002–0.041)	0.010	0.137	**0.031 (0.015–0.048)**	**0.008**	**0.195*****

*Significant correlates in the final model are highlighted in bold, *p = <0.001 *p = <0.01, **p = <0.001, ***P < 0.0001. [a]Significant predictor in model 1; [b]Significant predictor in model 2; [c]Significant predictor in model 3. Model 1 Demographics: age, educational level, living situation, having a job or study and financial situation, Model 2: model 1 + Illness history: ED duration, start age of ED, earlier inpatient treatment(s) without remission, psychiatric history of a family member (1st degree), having complex trauma. Model 3: model 2 + Current Illness variables: eating disorder type, using psychotropic medication, general psychopathology, having frequent suicidal thoughts, Body Mass Index (BMI kg/m^2). Model 4: model 3 + Personality traits: self-control/emotion-regulation, identity integration, responsibility.*

DISCUSSION

This is one of the first studies to examine all dimensions of well-being (emotional, psychological, and social) in female eating disorder patients. The levels of well-being as well as the derived percentages of languishing and flourishing were compared to the general population. Also, the relationship of well-being with psychopathology and correlates for both were examined. Overall, results indicate a two-continuum structure of mental health where psychopathology and well-being are negatively related. As expected, ED patients in this sample had lower levels of well-being compared to the general population. There was also substantial variation in the levels of well-being among ED patients, despite the high levels of psychopathology, indicating that well-being should be considered as a distinct mental health continuum. The two continua model is further supported by the fact that there were no high correlations between ED psychopathology and well-being and that different correlates were associated with ED psychopathology and well-being.

The Presence of Well-Being in ED Patients

In this study we found overall lower mean levels of emotional, psychological, and social well-being among female ED patients compared to the general female population. In particular, a large difference was found for emotional well-being, with ED patients scoring the lowest levels compared to controls. The percentage of ED patients languishing (26.1%) was substantially higher and the percentage of flourishing substantially lower (13.0%) compared to the general population (respectively, 4.8 and 36.8%). These results correspond with earlier work of Tomba et al. (2014), who found lower levels of psychological well-being among ED patients at the start of outpatient treatment compared to general controls. The two continua model of mental health suggests that clinical populations on average will have lower levels of well-being and higher levels of psychopathology compared to the general population, but that a part may still have moderate or high levels of well-being. Although the patients in this study have been diagnosed with a severe psychiatric disorder, are seeking specialized ED treatment and show on average a long duration (10.9 years) of the ED, a substantial part of them still functions moderately well on well-being (60.9%), and a small part (13%) even shows high well-being (flourishing). It is important to further examine why some patients are still able to experience adequate levels of well-being despite having an ED.

Our research showed interesting differences between ED types. We found that languishing was most prevalent in patients with AN (33.5%) and that flourishing was most prevalent in patients with BED (about 24.6%). This seems contrary to the results of Tomba et al. (2014), who found that patients with AN were the most similar to "healthy" controls on the dimensions of psychological well-being, while patients with BN showed the most impairment compared to controls. They related the relative good outcomes of AN patients to possible ego syntonic aspects of the disease, a lack of insight, their ability of controlling weight, socio-cultural values, such as thinness desirability and personality traits (Tomba et al., 2014). This study suggests that patients with AN are vulnerable to lower overall well-being. It is possible that our sample of patients with AN was more severe in terms of lower BMI (16.1 kg/m^2 compared to 17.5 kg/m^2 in Tomba et al., 2014), a longer illness duration, or higher ED psychopathology. A recent review on the ego syntonic nature of anorexia nervosa showed that in the initial phases of the disease patients may experience a sense of mastery and self-control for being able to manage food and to reach weight-related goals, and in addition they may attain confidence and self-worth as a result of positive feedback from family and friends (Gregertsen et al., 2017). These advantages are primarily related to the dimensions of psychological well-being and reinforce the ego syntonic nature of the disease. However, as the disease progresses and begins to take over their thoughts and behavior, these patients begin to lose control, rather than be in control (Gregertsen et al., 2017). The consequences of the disease, such as physical health issues, negative changes in brain functioning, negative instead of positive feedback from family and friends, social isolation, and psychological problems, become more apparent and are beginning to outweigh the advantages (Gregertsen et al., 2017). It is plausible that patients with AN who are longer in the process of the disease and are beginning to outweigh these disadvantages above the advantages will perceive lower levels of well-being, while patients in the initial phases of the disease on the other hand will experience higher levels of well-being. Therefore, the levels of well-being in patients with AN might be determined by the duration of the ED, ego syntonic aspects, and physical consequences, which should be a topic for further study.

Patients with BED, on the other hand, showed higher well-being compared to the other ED types, but also a long average duration of the ED (16.1 years). It has been suggested that binge eating should be considered as a coping mechanism for perceived daily stress (Freeman and Gil, 2004). A possible explanation for BED patients is that using binges, without extreme compensating behaviors, could be considered as a relatively effective coping mechanism for internal and external stressors. Therefore, BED patients would be able to maintain positive functioning in their life and maintain higher levels of well-being, despite a long-term ED. Another reason might be that in general, the brain of patients with BED receives enough nutrition to be able to experience forms of well-being. For patients with AN the severe implications of prolonged malnutrition alters brain functioning and mental health (Fuglset et al., 2016), which might also contribute to the presence of lower well-being later in the illness process.

The Relationship of Well-Being With Psychopathology

General psychopathology had negative moderate to high moderate correlations, and ED psychopathology had low correlations with the well-being dimensions. Moderate correlations between general psychopathology and well-being were also found in other clinical populations (Schotanus-Dijkstra et al., 2015; Franken et al., 2018). Contrary to our expectations, the correlations between ED psychopathology and well-being were substantially lower compared to the correlations between general psychopathology and well-being. It seems that ED psychopathology functions relatively independent from the well-being levels. This may have important implications for treatment and suggests that a focus only on alleviating ED psychopathology in treatment does not necessarily adequately improve well-being among ED patients and contrariwise. Alleviating general psychopathology however, might both improve emotional well-being and alleviate ED psychopathology. While there were no differences between the correlations of general psychopathology and well-being between ED types, for ED psychopathology there were low to moderate correlations for patients with AN, OSFED and overall ED's, and no correlations with the well-being dimensions for patients with BN and BED. This was also unexpected, and we have no clear explanation for these results. It is suggested to perform qualitative research to further explore these relationships among ED patients and examine this complex relationship between psychopathology and well-being and possible reciprocal relationships in a longitudinal study design to make more reliable conclusions on correlates between ED psychopathology and well-being.

Correlates Associated With ED Psychopathology And Well-Being

Our research showed that different correlates were associated with well-being and psychopathology. Having AN and lower general psychopathology were associated with lower ED psychopathology. This probably has to do with how ED psychopathology is measured, namely with the EDE-Q. It is found that outpatients with AN score significantly lower on the global score compared to patients with BN (Dahlgren et al., 2017). In this study patients with AN scored also substantially lower on the EDE-Q global score compared to the other ED types in this study. The association of higher general psychopathology with higher ED psychopathology is well supported by other research (Jacobi et al., 2004; Spindler and Milos, 2007).

There were several associated correlates for emotional, psychological, and social well-being. Patients with higher general psychopathology and a lower identity integration had a higher change on poorer emotional well-being. Patients with a history of hospitalization for the ED and a lower score on the personality traits, responsibility, and identity integration had a higher change of poorer psychological well-being. Finally, lower identity integration was also associated with lower levels of social well-being. The importance of personality traits, more specific conscientiousness and extraversion as predictors for adequate well-being was also found in the general population (Schotanus-Dijkstra et al., 2015). Responsibility is related to conscientiousness and is related to setting goals and maintaining the discipline necessary to achieve those goals. This may suggest that patients who have learnt to take responsibility for their own recovery process, for instance, by doing the homework provided in treatment, will have a higher change to improve on well-being dimensions during treatment. Previous research shows that disturbances in overall identity development are a core vulnerability for ED pathology (Farchaus Stein and Corte, 2007), and it is suggested that the development of a positive self may be an important factor in ED recovery. Further research is needed to examine the complex relationship between identity impairment, well-being, and ED pathology. Also, these correlates should be examined in a longitudinal design to draw conclusions on whether they might predict changes in ED psychopathology and well-being later in treatment.

It is notable that being hospitalized earlier in life for an ED was associated with lower psychological well-being, while it was not associated with more severe ED psychopathology. Patients who have been admitted once for ED symptoms, often need at least one readmission, which enhances the risk of later psychosocial functioning (Steinhausen and Grigoroiu-serbanescu, 2008). In a longitudinal study, readmission showed no effect on ED symptoms at 8 years follow-up, however, there was clear evidence that patients with readmissions functioned less well in terms of psychosocial adaptation (Steinhausen and Grigoroiu-serbanescu, 2008). Hospitalization for an ED is possibly a specific negative life event, even when it was not compulsory, impacting a patient's psychological well-being. It is therefore warranted, to further study the best way to deliver these treatments, and to carefully consider and monitor the possible impact afterwards on the psychological well-being of patients.

Strengths And Limitations

The strengths of this study are the large sample of ED outpatients and the large control group. The limitations of this study are its design, having only an adult female sample, the lack of registration of specific co-morbidity and other possible confounders, the use of self-report instruments, the sample size of patients with BED, and the arbitrary criteria for categorizing levels of well-being. A cross-sectional design was used, meaning that no causal inferences can be made and that longitudinal study designs are necessary for more conclusive results. No adolescents younger than 16 and no males were included in this sample and results are therefore not generalizable to these populations. Self-report instruments were used, making it susceptible to biases, such as social desirability bias (Atkinson et al., 1997; van de Mortel, 2008). However, to date no other valid, generally recognized methods for examining well-being were available. The relatively low sample size of patients with BED, compared to patients with AN, BN, and OSFED is a limitation. Also, while in this study the severity of general psychopathology was reported, specific co-morbidity was not reported, as well as possible other confounders, such as physical activity and body image distortion.

The criteria for flourishing and languishing used in this study should be considered arbitrary, and there are other approaches, based on other questionnaires and categorical scorings to examine flourishing, which are not necessarily comparable (Schotanus-Dijkstra et al., 2015). Keyes (2005) operationalized the clusters of components for well-being (i.e., emotional, psychological, social) in the same way as the clusters of symptoms for mental disorders in the Diagnostic and Statistical Manual of Mental Disorders (DSM) (American Psychiatric Association, 2000). Just as the diagnosis of depression requires symptoms of anhedonia, well-being requires "symptoms" of emotional vitality and positive feelings toward one's life (Keyes, 2005). Keyes (2005) also proposed to use a categorical scoring, based on the DSM approach. Where depression is diagnosed when at least one symptom from the anhedonia cluster and four or more symptoms of malfunctioning are present, well-being is diagnosed when at least one "symptom" of emotional well-being and six "symptoms" of psychological and social well-being are present. However, the criteria and categorical scoring of the DSM mental disorders are based on consensus by expert workgroups, there is no such procedure orconsensus yet for establishing (cut-off) criteria for adequate well-being. It is advised to form expert workgroups to seekconsensus on the categories and cut-off criteria for determining languishing and flourishing. At last, in this study no separate analysis was done on patients between 16 and 18, compared to adolescents.

CONCLUSIONS AND CLINICAL IMPLICATIONS

Overall the results of this study have some important implications. This study shows initial support for the two continua model for mental health among ED patients. ED patients have lower levels of well-being compared to the general population, however a small part is also flourishing. Examining the levels of well-being at the start of treatment is therefore advised. A broader vision on mental health, such as the two continua model among clinical samples, may open up pathways to reduce mental health stigma. The model could support a broader focus in psychological treatments on relevant dimensions of mental health such as well-being, instead of an almost exclusive focus on the diagnostic label and underlying psychopathology. For instance, study results show that health professionals were often described by patients and their family as the source of stigma, frequently focusing on the illness and ignoring other aspects of the patient (Corrigan et al., 2014).

A focus in treatment on well-being should be considered for those patients with inadequate well-being. A focus *only* on alleviating ED psychopathology in treatment might inadequately improve well-being, given the overall low to moderate strengths of the correlations. This might be even more important to consider in specific ED subtypes such as BN and BED, where no significant correlations between both were found. Several correlates were found to be associated with ED psychopathology and well-being. A focus on alleviating general psychopathology is advised and might decrease ED psychopathology and increase emotional well-being. Treatments should aim at increasing personality functioning on identity integration and responsibility and prevent hospitalization for ED if possible, because this will have a positive effect on well-being among ED patients.

ETHICS STATEMENT

This study was carried out in accordance with the recommendations of the code of ethics for research in the social and behavioral sciences involving human participants in the Netherlands (WMO, 2016). The protocol was approved by the Ethics Committee of the University of Twente, Behavioral, Management and Social Sciences. All subjects gave written informed consent in accordance with the Declaration of Helsinki.

AUTHOR CONTRIBUTIONS

JdV wrote on all parts of the manuscript (introduction, methods, results, discussion), did the data collection and analysis. MR wrote on all parts of the manuscript and tested and supervised the analysis. EB and GW wrote on most parts of the manuscript, validated the analysis, and supervised the complete study.

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SUPPLEMENTARY MATERIAL

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REFERENCES

Aardoom, J. J., Dingemans, A. E., Slof Op't Landt, M. C. T., and Van Furth, E. F. (2012). Norms and discriminative validity of the Eating Disorder Examination Questionnaire (EDE-Q). *Eating Behav.* 13, 305–309. doi: 10.1016/j.eatbeh.2012.09.002

American Psychiatric Association (2000). *Diagnostic and Statistical Manual of Mental Disorders, 4th, Edn*. Washington, DC: American Psychiatric Association.

American Psychiatric Association (2013). *Diagnostic and Statistical Manual Of Mental Disorders (DSM-5®)*.

Atkinson, M., Zibin, S., and Chuang, H. (1997). Characterizing quality of life among patients with chronic mental illness : a critical examination of the self-report methodology. *American J. Psychiatry* 154, 99–105. doi: 10.1176/ajp.154.1.99

Blijd-Hoogewys, E., Van Dyck, R., Emmelkamp, P., Mulder, N., Oude Voshaar, R., Schippers, G., et al. (2012). Benchmarken is 'werk-in-uitvoering' [Benchmarking is work in progress. *Tijdschr. Psychiatr.* 54, 1031–1038.

Bolier, L., Haverman, M., Westerhof, G. J., Riper, H., Smit, F., and Bohlmeijer, E. (2013). Positive psychology interventions: a meta-analysis of randomized controlled studies. *BioMed Central Public Health* 13:119. doi: 10.1186/1471-2458-13-119

Cassin, S. E., and Von Ranson, K. M. (2005). Personality and eating disorders: a decade in review. *Clin. Psychol. Rev.* 25, 895–916. doi: 10.1016/j.cpr.2005.04.012

Corrigan, P. W., Druss, B. G., and Perlick, D. A. (2014). The impact of mental illness stigma on seeking and participating in mental health care. *Psychol. Sci. Public Interest* 15, 37–70. doi: 10.1177/1529100614531398

Costa, C., Ramos, E., Severo, M., Barros, H., and Lopes, C. (2008). Determinants of eating disorders symptomatology in Portuguese adolescents. *Arch. Pediatr. Adolesc. Med.* 162, 1126–1132. doi: 10.1001/archpedi.162.12.1126

Dahlgren, C. L., Stedal, K., and Rø, Ø. (2017). Eating Disorder Examination Questionnaire (EDE-Q) and Clinical Impairment Assessment (CIA): clinical norms and functional impairment in male and female adults with eating disorders. *Nordic J. Psychiatry* 71, 256–261. doi: 10.1080/08039488.2016.1271452

de la Rie, S. M., Noordenbos, G., Donker, M., and van Furth, E. (2007). The patient's view on quality of life and eating disorders. *Int. J. Eat. Disord.* 40, 13–20. doi: 10.1002/eat.20338

de la Rie, S. M., Noordenbos, G., and van Furth, E. F. (2005). Quality of life and eating disorders. *Qual Life Res*. 14, 1511–1522. doi: 10.1007/s11136-005-0585-0

de Vos, J. A., Lamarre, A., Radstaak, M., Bijkerk, C. A., Bohlmeijer, E. T., and Westerhof, G. J. (2017). Identifying fundamental criteria for eating disorder recovery: a systematic review and qualitative meta-analysis. *J. Eat. Disord.* 5, 1–14. doi: 10.1186/s40337-017-0164-0

de Vos, J. A., Netten, C., Noordenbos, G., de Vos, J. A., Netten, C., and Noordenbos, G. (2016). Recovered eating disorder therapists using their experiential knowledge in therapy: a qualitative examination of the therapists and the patients view. *Eat. Disord.* 24, 1–17. doi: 10.1080/10640266.2015.1090869

Deci, E. L., and Ryan, R. M. (2008). Hedonia, eudaimonia, and well-being: an introduction. *J. Happiness Stud.* 9, 1–11. doi: 10.1007/s10902-006-9018-1

Diener, E., Suh, E. M., Lucas, R. E., and Smith, H. L. (1999). Subjective well-being : three decades of progress. *Psychol. Bull.* 125, 276–302. doi: 10.1037/0033-2909.125.2.276

Doll, H. A., Petersen, S. E., and Stewart-brown, S. L. (2005). Eating disorders and emotional and physical well-being: associations between student self-reports of eating disorders and quality of life as measured by the SF-36. *Qual. Life Res.* 14, 705–717. doi: 10.1007/s11136-004-0792-0

Fairburn, C. G., and Beglin, S. J. (1994). Assessment of eating disorders: interview or self-report questionnaire? *Int. J. Eat. Disord.* 16, 363–370.

Farchaus Stein, K., and Corte, C. (2007). Identity impairment and the eating disorders: content and organization of the self-concept in women with anorexia nervosa and bulimia nervosa. *Eur. Eat. Disord. Rev.* 15, 58–69. doi: 10.1002/erv.726

Fava, G. A. (1996). The concept of recovery in affective disorders. *Psychother. Psychosom.* 65, 2–13. doi: 10.1159/000289025

Fava, G. A., Rafanelli, C., Cazzaro, M., Conti, S., and Grandi, S. (1998). Well-being therapy. A novel psychotherapeutic approach for residual symptoms of affective disorders. *Psychol. Med.* 28, 475–480. doi: 10.1017/S0033291797006363

Fava, G. A., and Ruini, C. (2003). Development and characteristics of a well-being enhancing psychotherapeutic strategy: Well-being therapy. *J. Behav. Ther. Exp. Psychiatry* 34, 45–63. doi: 10.1016/S0005-7916(03)00019-3

Fava, G. A., Ruini, C., Rafanelli, C., Finos, L., Salmaso, L., Mangelli, L., et al. (2005). Well-being therapy of generalized anxiety disorder. *Psychother. Psychosom.* 74, 26–30. doi: 10.1159/000082023

Field, A. (2005). *Discovering Statistics Using SPSS, 2nd Edn*. London: Sage.

Franken, K., Lamers, S. M. A., Ten Klooster, P. M., Bohlmeijer, E. T., and Westerhof, G. J. (2018). Validation of the Mental Health Continuum-Short Form and the dual continua model of well-being and psychopathology in an adult mental health setting. *J. Clin. Psychol.* doi: 10.1002/jclp.22659. [Epubh ahead of print].

Freeman, L. M. Y., and Gil, K. M. (2004). Daily stress, coping, and dietary restraint in binge eating. *Int. J. Eat. Disord*. 36, 204–212. doi: 10.1002/eat.20012

Fuglset, T. S., Landrø, N. I., Reas, D. L., and, Rø, Ø. (2016). Functional brain alterations in anorexia nervosa: a scoping review. *J. Eat. Disord.* 4:32. doi: 10.1186/s40337-016-0118-y

Gilbert, P. (2009). Introducing compassion-focused therapy. *Adv. Psychiatr. Treat.* 15, 199–208. doi: 10.1192/apt.bp.107.005264

Gregertsen, E. C., Mandy, W., and Serpell, L. (2017). The egosyntonic nature of anorexia: an impediment to recovery in anorexia nervosa treatment. *Front. Psychol.* 8, 1–9. doi: 10.3389/fpsyg.2017.02273

Harris, E. C., and Barraclough, B. (1998). Excess mortality of mental disorder. *Br. J. Psychiatry* 173, 11–53. doi: 10.1192/bjp.173.1.11

Haynos, A. F., Roberto, C. A., and Attia, E. (2015). Examining the associations between emotion regulation difficulties, anxiety, and eating disorder severity among inpatients with anorexia nervosa. *Comprehens. Psychiatry* 60, 93–98. doi: 10.1016/j.comppsych.2015.03.004

Hoek, H. W. (2006). Incidence, prevalence and mortality of anorexia nervosa and other eating disorders. *Curr. Opin. Psychiatry* 19, 389–394. doi: 10.1097/01.yco.0000228759.95237.78

Hudson, J. I., Hiripi, E., Pope, H., and Kessler, R. C. (2008). The prevalence and correlates of eating disorders in the national comorbitity survey replication. *Biol. Psychiatry* 61, 348–358. doi: 10.1016/j.biopsych.2006.03.040

Jacobi, C., Hayward, C., de Zwaan, M., Kraemer, H. C., and Agras, W. S. (2004). Coming to terms with risk factors for eating disorders: application of risk terminology and suggestions for a general taxonomy. *Psychol. Bull.* 130, 19–65. doi: 10.1037/0033-2909.130.1.19

Jahoda, M. (1958). *Current Concepts of Positive Mental Health. Joint Commission on Mental Health and Illness Monograph Series. Vol 1.* New York, NY: Basic Books.

Jenkins, P. E., Hoste, R. R., Meyer, C., and Blissett, J. M. (2011). Eating disorders and quality of life: a review of the literature. *Clin. Psychol. Rev.* 31, 113–121. doi: 10.1016/j.cpr.2010.08.003

Johnson, J. G., Cohen, P., Kasen, S., and Brook, J. S. (2002). Childhood adversities associated with risk for eating disorders or weight problems during adolescence or early adulthood. *Am. J. Psychiatry* 159, 394–400. doi: 10.1176/appi.ajp.159.3.394

Jong, K., De Nugter, M., Lambert, M., and Burlingame, G. (2008). *Handleiding voor Afname en Scoring van de Outcome Questionnaire (OQ– 45.2) [Manual for Administering and Scoring of the Outcome Questionnaire]*. Salt Lake City, UT: OQ.

Joshanloo, M., and Lamers, S. M. A. (2016). Reinvestigation of the factor structure of the MHC-SF in the Netherlands: contributions of exploratory structural equation modeling. *Pers. Individ. Dif.* 97, 8–12. doi: 10.1016/j.paid.2016.02.089

Keyes, C. L. M. (1998). Social well-being. *Soc. Psychol. Q.* 61, 121–140. doi: 10.2307/2787065

Keyes, C. L. M. (2002). The mental health continuum: from languishing to flourishing in life. *J. Health Soc. Behav.* 43, 207–222. doi: 10.2307/3090197

Keyes, C. L. M. (2005). Mental illness and/or mental health? Investigating axioms of the complete state model of health. *J. Consult. Clin. Psychol.* 73, 539–548. doi: 10.1037/0022-006X.73.3.539

Keyes, C. L. M. (2006). Mental health in adolescence: is america's youth flourishing? *Am. J. Orthopsychiatry* 76, 395–402. doi: 10.1037/0002-9432.76.3.395

Keyes, C. L. M. (2007). Promoting and protecting mental health as flourishing. A complementary strategy for improving national mental health. *Am. Psychol.* 62, 95–108. doi: 10.1037/0003-066X.62.2.95

Keyes, C. L. M. (2012). *Toward a Science of Mental Health. The Oxford Handbook of Positive Psychology, 2nd Edn.* Oxford, UK: Oxford university press.

Keyes, C. L. M., Wissing, M., Potgieter, J. P., Temane, M., Kruger, A., and van Rooy, S. (2008). Evaluation of the mental health continuum- short form (MHC-SF) in Setswana-speaking South Africans. *Clin. Psychol. Psychother.* 15, 181–192. doi: 10.1002/cpp.572

Lamers, S. M. A., Westerhof, G. J., Bohlmeijer, E. T., and Keyes, C. L. M. (2013). *Mental Health and Illness In Relation to Physical Health Across the Lifespan*. Positive Psychology. New York, NY: Springer.

Lamers, S. M. A., Westerhof, G. J., Bohlmeijer, E. T., Ten Klooster, P. P. M., and Keyes, C. L. M. (2011). Evaluating the psychometric properties of the mental health Continuum-Short Form (MHC-SF). *J. Clin. Psychol.* 67, 99–110. doi: 10.1002/jclp.20741

Lowe, B., Zipfel, S., Buchholz, C., Dupont, Y., Löwe, B., Zipfel, S., et al. Herzog, W. (2001). Long-term outcome of anorexia nervosa in a prospective 21-year follow-up study. *Psychol. Med.* 31, 881–890. doi: 10.1017/S003329170100407X

Magalhães, E., and Calheiros, M. M. (2017). A dual-factor model of mental health and social support: evidence with adolescents in residential care. *Child. Youth Serv. Rev.* 79, 442–449. doi: 10.1016/j.childyouth.2017.06.041

Mitchison, D., Hay, P. J., Slewa-Younan, S., and Mond, J. (2012). Time trends in population prevalence of eating disorder behaviors and their relationship to quality of life. *PLoS ONE* 7:e48450. doi: 10.1371/journal.pone.0048450

Mond, J., Hay, P. J., Rodgers, B., and Owen, C. (2012). Quality of life impairment in a community sample of women with eating disorders. *Aust. N. Z. J. Psychiatry* 46, 561–568. doi: 10.1177/0004867411433967

Perugini, M. L. L., de la Iglesia, G., Castro Solano, A., and Keyes, C. L. M. (2017). The mental health continuum–short form (MHC–SF) in the Argentinean context: confirmatory factor analysis and measurement invariance. *Eur. J. Psychol.* 13, 93–108. doi: 10.5964/ejop.v13i1.1163

Peter, T., Roberts, L. W., and Dengate, J. (2011). Flourishing in life: an empirical test of the dual continua model of mental health and mental illness among Canadian university students. *Int. J. Mental Health Promot.* 13, 13–22. doi: 10.1080/14623730.2011.9715646

R Core Team (2013). *A Language and Environment for Statistical Computing.* Vienna: R Foundation for Statistical Computing. Available online at: http://www.r-project.org

Rosseel, Y. (2012). Lavaan: An R package for structural equation modeling. *J. Stat. Softw.* 48, 1–36. doi: 10.18637/jss.v048.i02

Rossi, G., Debast, I., and van Alphen, S. P. J. (2016). Measuring personality functioning in older adults: construct validity of the Severity Indices of Personality Functioning – Short Form (SIPP-SF). *Aging Mental Health*. 21, 703–711. doi: 10.1080/13607863.2016.1154012

Ryff, C. D. (1989). Happiness is everything, or is it? Explorations on the meaning of psychological well-being. *J. Pers. Soc. Psychol*. 57, 1069–1081. doi: 10.1037/0022-3514.57.6.1069

Ryff, C. D., and Keyes, C. L. M. (1995). The Structure of psychological well-being revisited. *J. Pers. Soc. Psychol.* 69, 719–727. doi: 10.1037/0022-3514.69.4.719

Santrock, J. W. (2007). *Educational Psychology, 3rd Edn*. Columbus, OH: McGraw-Hill.

Schotanus-Dijkstra, M., Pieterse, M. E., Drossaert, C. H. C., Westerhof, G. J., de Graaf, R., ten Have, M., et al. (2015). What factors are associated with flourishing? Results from a large representative national sample. *J. Happiness Stud*. 17, 1351–1370. doi: 10.1007/s10902-015-9647-3

Seligman, M., and Csikszentmihalyi, M. (2000). Positive psychology: an introduction. *Am. Psychol.* 55, 5–14. doi: 10.1037/0003-066X.55.1.5

Spindler, A., and Milos, G. (2007). Links between eating disorder symptom severity and psychiatric comorbidity. *Eat. Behav.* 8, 364–373. doi: 10.1016/j.eatbeh.2006.11.012

Steinhausen, H., and Grigoroiu-serbanescu, M. (2008). Course and predictors of rehospitalization in adolescent anorexia nervosa in a multisite study. *Int. J. Eat. Disord*. 41, 29–36. doi: 10.1002/eat.20414

Stichting Benchmark GGZ. (2013). *SBG Dataprotocol 20130101 Bijlage A Minimale Dataset*. Bilthoven: Stichting Benchmark GGZ.

Tomba, E., Offidani, E., Tecuta, L., Schumann, R., and Ballardini, D. (2014). Psychological well-being in out-patients with eating disorders: a controlled study. *Int. J. Eat. Disord.* 47, 252–258. doi: 10.1002/eat.22197

Tomba, E., Tecuta, L., Schumann, R., and Ballardini, D. (2017). Does psychological well-being change following treatment? An exploratory study on outpatients with eating disorders. *Comprehens. Psychiatry* 74, 61–69. doi: 10.1016/j.comppsych.2017.01.001

Trompetter, H. R., Lamers, S. M. A., Westerhof, G. J., Fledderus, M., and Bohlmeijer, E. T. (2017). Both positive mental health and psychopathology should be monitored in psychotherapy: confirmation for the dual-factor model in acceptance and commitment therapy. *Behav. Res. Ther.* 91, 58–63. doi: 10.1016/j.brat.2017.01.008

van de Mortel, T. F. (2008). Faking it: social desirability response bias in self- report research. *Austr. J. Adv. Nurs.* 25, 40–48.

Verheul, R., Andrea, H., Berghout, C. C., Dolan, C., Busschbach, J. J. V., van der Kroft, P. J. A., et al. (2008). Severity Indices of Personality Problems (SIPP-118): development, factor structure, reliability, and validity. *Psychol. Assess.* 20, 23–34. doi: 10.1037/1040-3590.20.1.23

Warmerdam, L., Barendregt, M., and de Beurs, E. (2017). Risk adjustment of self-reported clinical outcomes in Dutch mental health care. *J. Public Health* 25, 311–319. doi: 10.1007/s10389-017-0785-4

Weiss, L. A., Westerhof, G. J., and Bohlmeijer, E. T. (2016). Can we increase psychological well-being? The effects of interventions on psychological well-being: A meta-analysis of randomized controlled trials. *PLoS ONE* 11:e158092. doi: 10.1371/journal.pone.0158092

Westerhof, G. J., and Keyes, C. L. M. (2010). Mental illness and mental health: the two continua model across the lifespan. *J. Adult Dev.* 17, 110–119. doi: 10.1007/s10804-009-9082-y

World Health Organization (2005). *Promoting Mental Health: Concepts, Emerging Evidence, Practice*. Geneva: WHO.

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ORIGINAL RESEARCH
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Emotional "Patient-Oriented" Support in Young Patients With I–II Stage Breast Cancer: Pilot Study

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Objective: The recent increased survival rate after breast cancer (BC) diagnosis and treatment is mostly related to early screening in younger age. Evidence gained from newly detected assessed psychological needs as well as certain emotional regulatory patterns in younger survivors has been related in the literature to an extremely low rate of adherence to the psychological therapies offered. Tailored psychological support is necessary. The aim of the present study was to verify the preliminary efficacy of supportive psychological intervention with an innovative orientation: the Early BC Psychological Intervention (EBC-Psy).

Methods: A controlled study design was used to investigate the efficacy of EBC-Psy intervention. Preliminary data involved twenty-four patients in the age range of 35–50 years, diagnosed with cancer at the early stage (I–II), who were exposed to the EBC-Psy intervention. To address the effect of intervention, emotional variables were tested before the treatment (Time 1) and then again after 6 months of the treatment (Time 2); evaluated emotional dimensions were anxiety, anger, depression, and psychological distress.

Results: EBC-Psy intervention appears to be effective on both depression ($p = 0.02$) and psychological distress ($p = 0.01$), even in a short time, highlighting the strength of a reinforced positive psychological conceptual approach to deal with the "disease condition" in younger patients; on the contrary, the control group evidenced an increase in the same emotional variables in timing.

Conclusion: Our findings, even if limited by this small-scale protocol, seemed to confirm the role of positive psychotherapy after BC diagnosis and treatment through the impact of cognitive processes, coping strategies, and psychological resilience. Future theoretical framework could boost the intervention to design an innovative survivorship model.

Keywords: breast cancer diagnosis, psychological distress, anger, emotional impact of BC diagnosis, psychological treatment

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INTRODUCTION

Breast cancer (BC) diagnosis is a traumatic event in a woman's life with a sudden, strong impact on her quality of life. Several studies have detected and debated the negative effects of the diagnosis: decreasing the quality of affective relations, life expectation, long-term planning, productivity, and sociality. Signs of psychological difficulty such as depression, anxiety, anger, poor mood, social retraction, isolation, and aggression have been well documented (Burgess et al., 2005; Linley, 2006; Costanzo et al., 2007; Bennet et al., 2012; Lester et al., 2015; Ng et al., 2015; Conley et al., 2016; Gibbons et al., 2016). The primary negative impact is on quality of life as a woman; the secondary effect is simultaneously on her family and her social and working environments. Most studies that detected significant emotional suffering were conducted on aged populations (55-year-olds and older) as the incidence of BC increases with age (World Cancer Research Fund International[1]). In recent decades, the characteristics of the population involved in BC clinical settings have changed. Early screening increased the chances of early detection of cancer diagnosis, improving early surgical and/or pharmacological interventions (less invasive, more conservative, and more positive survivorship outcomes), and involving patients at the ages younger than 55 (> 35-year-olds). These new protocols significantly increased the survival rate in patients with BC. The increased awareness in the research and clinical communities about the cancer experience can have positive outcomes, but it has also created new challenges: physical and mental impacts, and socioeconomic and cultural implications for patients (International Agency for Research on Cancer[2]).

Moreover, clinical practice has demonstrated that changing the psychological needs of women increases their life expectations by longer survivorship: psychological resilience is the key to dealing with and overcoming oncological disease and self-perception as a patient with a chronic illness (Min et al., 2013; Molina et al., 2014; Quattropani et al., 2017). Di Giacomo et al. (2016) investigated the impact of psychological resilience in younger patients, analyzing their emotional distress. Findings showed that younger women felt powerless but not depressed and were well motivated to deal with their own clinical treatment protocols with good compliance, and they obtained fast, positive outcomes. Lately, some authors have extended such findings to the posttraumatic growth model of Tedeschi and Calhoun (2004): the posttraumatic growth is a construct whereby positive behavioral changes can be identified in dealing with and negotiating traumatic experiences (Giuliani et al., 2014). Moreover, Kolokotroni et al. (2014) analyzed the impact of psychosocial factors on posttraumatic growth after BC diagnosis. The authors highlighted the positive influence of the cognitive process and found that coping strategies are key factors for personal growth and for dealing positively with the cancer experience. Koutrouli et al. (2016) demonstrated the influence of social constraints on disclosure (deprivation of the opportunity to express feelings and thoughts regarding the trauma). In addition, the authors noted that the related cognitive processing of one's own disease condition seems to play an important role in the development of posttraumatic growth, becoming more significant for younger patients toward reducing intrusions and reflective rumination. However, Parikh et al. (2015) maintained that patients with BC tend to experience posttraumatic growth but that psychological interventions should be implemented. In fact, only younger patients showed higher rates of dropout from psychological treatments. Brebach et al. (2016) conducted a meta-analysis investigating the uptake and adherence of cancer patients to psychological support. The adherence of patients with BC is quite low; half of all patients do not accept psychological support even though individual treatments of such services are offered. The factors influencing the uptake of intervention are distress measures, unmet needs, and the timing of the support. Research has found that patients with higher distress levels show lower rates of uptake and adherence, and an unmet need for psychological support despite declining it. Brebach et al. (2016) noticed that telephone interventions are more accepted than face-to-face interventions, and patients tend to agree more often to an intervention when it is offered by a nurse. Finally, the timing of access to the service is influential; the rate of adherence is higher when proposed close to the diagnosis.

Our study aimed to develop a tailored psychological intervention for younger patients with BC (age range 35–50) just after early medical treatment (surgical and/or pharmacological) using a cognitive approach tailored to their psychological needs after screened distress. We proceeded to plan a smart and innovative non-pharmacological treatment fitted to emotional weakness in young patients with BC: the Early BC Psychological

TABLE 1 | Demographic data of the sample.

	EBC-Psy group	Control group
Education		
Did not graduate	8.3%	8.3%
Graduated high school	66.7%	66.7%
Bachelor's degree	25.0%	25.0%
Relationship status		
Married/living with partner	75.0%	75.0%
Single	8.3%	0.0%
Divorced/Separated	16.7%	25.0%
Maternity		
No children	16.7%	0.0%
One child	33.3%	25.0%
More than one child	50.0%	75.0%
Occupation		
Housewife	16.7%	16.7%
Employed	58.3%	58.3%
Self-employed	25.0%	25.0%
Cancer stage		
0	0.0%	0.0%
I	58.3%	50.0%
II	41.7%	50.0%
III	0.0%	0.0%
Treatments*		
Mastectomy	50.0%	50.0%
Lumpectomy	50.0%	50.0%
Chemotherapy	8.3%**	0.0%
Radiation therapy	0.0%	0.0%
Hormonal therapy	83.3%	100.0%
No treatment	8.3%	0.0%

*Treatments are not mutually exclusive. **Last session of chemotherapy at the moment of enrolment.*

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[1] www.wcrf.org

[2] www.iarc.fr

Intervention (EBC-Psy). This psychological intervention has been oriented to a positive psychotherapy approach in order to develop an outcome of well-being in younger patients trying to win their life back. We conducted a controlled clinical study to verify the impact of the EBC-Psy in women in terms of efficacy after early and strong clinical treatments (scheduled medical protocols). The promising preliminary data are outlined below.

MATERIALS AND METHODS

Ethics Statement

This study received Institutional Review Board (IRB) approval from University of L'Aquila, Italy (Prot. N° 15855/2015) and San Salvatore Hospital, L'Aquila, where participants were enrolled.

Participants

Eligible participants were women who were 35 years old or older (< 50) living in Italy (the Abruzzo region, referring to L'Aquila's healthcare). Participants had been enrolled in the medical oncology department of San Salvatore Hospital in L'Aquila, Italy. Inclusion criteria were as follows: (a) diagnosed with BC in stage I or II; (b) aged between 35 and 50; (c) just completed surgical treatment (mastectomy or lumpectomy); (d) underwent chemotherapy treatment; (e) not enrolled in another study; and (f) signed the informed consent statement.

The following exclusion criteria were used: (a) cancer recurrence; (b) metastasis; (c) preview mood/personality disorders; (d) signs of psychiatric disease; (e) psycho-pharmacological treatment; (f) age > 50; (g) abuse of alcohol or substance; and (h) being involved in ongoing psychological therapy in private/public services (**Table 1**).

Study Design

Using these eligibility criteria, thirty-three patients with BC were approached for study enrolment during their last clinical visit. Of these, thirty (90%) agreed to participate and were enrolled. Patients who declined to participate cited external variables such as the facilities being too far away, the patient being unable to drive, and various family issues. Medical staff identified the eligible patients, who were then enrolled during check-up sessions, distributing them randomly into two groups; the medical staff was blinded as to which group had been exposed to the treatment. Participation in the study was voluntary. Information about patients was twofold: demographic data were compiled from self-reporting by patients, and we selected independent variables for inclusion in analysis if they were characterized according to age/life stage (e.g., having children, being employed, their marital status) and the variables were related to the cancer. Clinical data regarding the stage of BC (the TNM classification of malignant tumors), treatments, and therapies were collected from medical records.

A controlled clinical study was conducted by comparing treated and untreated groups to measure the psychological influence of the EBC-Psy.

Figure 1 shows the study design representation, distinguishing phases and timing.

Figure 2 represents the enrollment process.

The research design was divided into three phases: (1) baseline measurement, (2) grouping, and (3) final measurement.

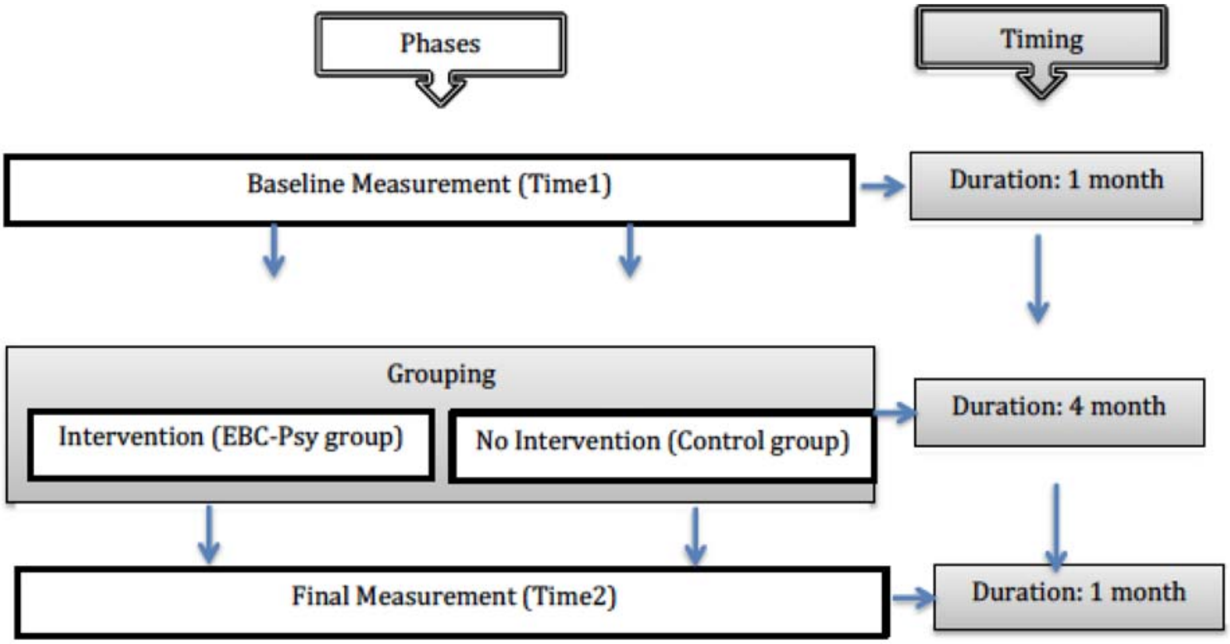


FIGURE 1 | Study design representation.

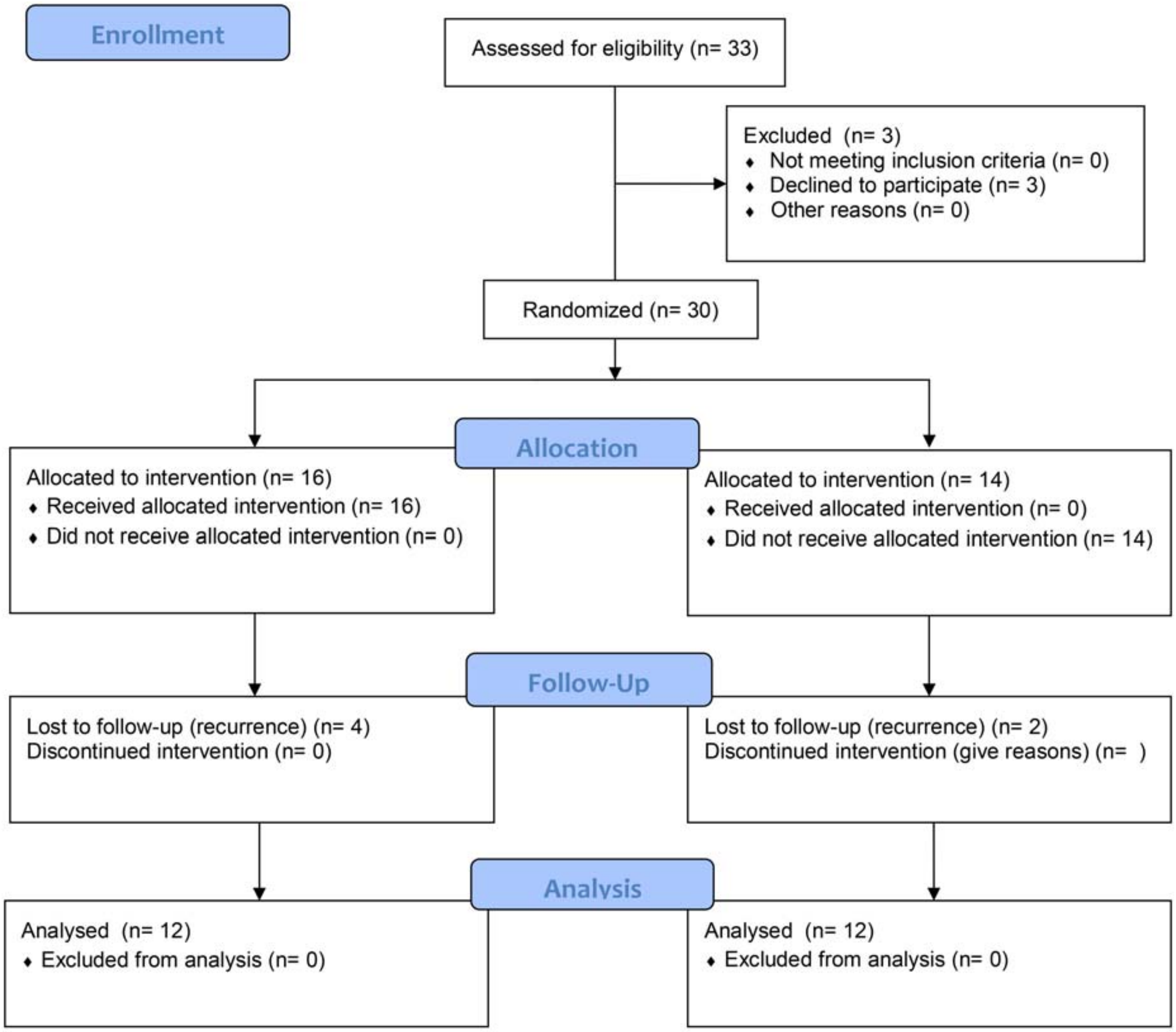


FIGURE 2 | Representation of enrolment process by CONSORT Flow diagram.

Eligible patients were approached to propose they take part in the experimental protocol (with or without psychological support), and, after acceptance, they were enrolled and distributed randomly in two groups: EBC-Psy group and Control group. The EBC-Psy group was composed of patients who took part in the whole experimental protocol (measurement and intervention phases), and the group was exposed to the EBC-Psy protocol for 4 months. The control group was composed of patients who only took part in the measurement phase of the research but not the intervention phase; it was considered the comparison group. Patients were measured by psychological testing at Time 1 and Time 2 over a 6-month period. All patients were enrolled after surgical and chemotherapy treatments (after 6–8 months from the diagnosis). The methods are consistent with CONSORT 2010 guidelines (Moher et al., 2001).

No payments were requested or given to take part in the experimental protocol.

Training, Supervision, and Quality Control

The EBC-Psy was applied by a clinical psychologist with a cognitive-behavioral psychotherapeutic orientation who had been trained over a 2-week period; the training program was based on endpoints of the EBC-Psy intervention. The psychological measurement was administered by an experienced psychologist. Both psychologists were blinded as to the aim of the study. The scoring of the testing protocol was conducted by external blind judges. All EBC-Psy intervention sessions were recorded by digital camera; seven random sessions were used for internal quality control review and clinical supervision by a clinical team.

Medical staff members were involved in the enrolment of the sample and were in charge of managing the clinical path and check-up.

Psychological Testing

The psychological measurement was conducted by self-reported testing to evaluate four emotional variables: anxiety, angry, psychological distress, and depression.

The following psychological tests were used: the State-Trait Anger Expression Inventory (STAXI) to measure the anger state, the State Trait Anxiety Inventory form Y (STAI-Y) to evaluate anxiety, the Psychological Distress Inventory (PDI) to assess distress, and the Beck Depression Inventory version 2 (BDI-II) to detect signs of depression.

State-Trait Anger Expression Inventory-2 (STAXI-2; Spielberger, 2004)

This is a self-administered questionnaire that aims to measure emotional states and personality traits; in particular, the evaluated traits are experience, expression, and control of anger. STAXI-II items are categorized into six scales—five subscales and an expression index. The experience of anger is conceptualized as having two components: State Anger (S-Ang) and Trait Anger (T-Ang). S-Ang is considered to be situational and refers to the level of anger that the respondent experiences during the assessment. T-Ang is defined as predisposition toward experiencing anger. The expression and control of anger are conceptualized as having four components: Anger Expression-Out (AX-O), Anger Expression-In (AX-I), Anger Control-Out (AC-O), and the Anger Expression Index (AX Index); the index provides an overall estimation of the anger expression and control scales. The scoring aims to reveal different personality traits related to anger risk. The internal reliability was $\alpha = 0.83$ for the patient group and $\alpha = 0.61$ for the control group.

State-Trait Anxiety Inventory-Form Y (Spielberger and Sydeman, 1994)

This is a self-reported test to measure state and trait anxiety. It is composed of forty items. The scoring is based on standard procedure. The internal reliability was $\alpha = 0.62$ for the patient group and $\alpha = 0.73$ for the control group.

Psychological Distress Inventory (Morasso et al., 1996)

This is a five-point self-administrated questionnaire that measures the impact of the disease and therapies in terms of psychological distress. It is composed of thirteen questions. The standard score indicates the presence/absence of psychological distress to measure global distress. This test was performed only in the patient group. The internal reliability was good ($\alpha = 0.86$).

Beck Depression Inventory Version II (Beck et al., 1996)

This is a self-administered test. The BDI–II consists of twenty-one items to assess the intensity of depression in clinical and normal patients. Each item is a list of four statements arranged in order of increasing severity about a particular symptom of depression. The scoring indicates the presence/absence of depression and its relative degrees (from minimal to severe signs of depression). The internal reliability was good for both patient ($\alpha = 0.81$) and control ($\alpha = 0.76$) groups.

Cancer Staging System

The method applied to classify the stage of cancer of the patients was the TNM, a cancer staging system developed by the American Joint Committee on Cancer (2010) and the Union for International Cancer Control. The TNM system is based on four main factors: (a) location of the primary tumor, (b) tumor size and extent, (c) lymph node involvement, and (d) presence or absence of distant metastasis. Basic data involved in staging the cancer are physical examinations, imaging tests, laboratory tests, pathology reports, and surgical reports. TNM staging is composed of the following stages: X (primary tumor cannot be evaluated), 0 (no evidence of primary tumor), IS (carcinoma in situ, that is, early cancer that has not spread to nearby tissue), and 1–4 (size and/or extent of the primary tumor). This cancer staging system was applied by clinical staff, and data were detected from recording files.

Early Breast Cancer Psychological Intervention (EBC-Psy)

The EBC-Psy is a brief psychological intervention applied after the diagnosis of BC for young patients (35–50 age range) following primary clinical intervention in the healthcare system. It is aimed at the wellbeing of the young woman dealing with BC diagnosis and related medical treatments. The aim of the EBC-Psy is to enhance their emotional balance, overcoming the self-perception of "patient condition" after primary care and positive clinical outcomes. The innovation of the EBC-Psy intervention is to point out the experience of responding to adversity as an opportunity to experience positive change. In particular, the EBC-Psy is focused on one's own emotional experience of the cancer and is based on the cognitive exploration of thoughts and feelings experienced as a result of cancer diagnosis and treatment. The EBC-Psy works to model in the patient an adjustment to a new perspective on life by taking care of one's own affective and emotional priorities; through this cognitive exploration and focusing on thoughts related to specific psychological indicators (outlined below), the patient actively models her vision of life, boosting her positive perspectives and feelings.

The EBC-Psy is a supportive intervention to be applied just at the end of surgical and pharmacological treatments to provide the patient with psychological strategies to deal with being back in daily life through her cognitive analysis of negative feelings as a result of the cancer diagnosis. The scheduled protocol is based on individual sessions (60 min in duration) per week for 4 months (sixteen sessions in total). The cognitive approach shapes the EBC-Psy and is based on five indicators: overcoming the mental condition; recovering one's personal perspective and expectations; changing one's life vision and renewing oneself; body adaptation; and positive assertiveness. The psychological strategies are distinguished for each indicator. The indicator “overcoming the mental condition” is based on (a) reinforcing the individual opportunities, (b) readdressing the negative distorted cognitions, and (c) compensating for a dysfunctional underlying belief—each of which is respectively addressed by sharing and elaborating on one’s own experience, highlighting success in one’s own cancer illness experience, remembering the stress experienced related to the cancer diagnosis to manage the stress that was felt, and being aware of the feeling and emotional distress experienced by personalized strategies to improve the quality of mood. The indicator “recovering one’s personal perspective and expectations” is related to rediscovering personal characteristics and life priorities by a cognitive restructuring of the reaction after diagnosis and the processing of modified priorities in life, each based on the activation of a psychosocial context, particularly with family trained by the treatment team. The indicator “changing one’s life vision and renewing oneself” is related to an enhanced positive self-perception and a high compliance with a healthy lifestyle. The indicator “body adaptation” consists of strengthening the acceptance of body image through a cognitive and positive view of the modified body (body satisfaction, self-image, sexual issues). Finally, the “positive assertiveness” indicator works to modulate the fear reduction, balancing the positive and negative effects of one’s own experience, and an acceptance of the traumatic experience of BC by adjusting to the new reality; both tend to improve awareness of management strategies and provide opportunities to carry on with daily life.

Each session features four phases. The first phase is anamnesis and detection data: detection and collection of the information about the patient, her life, her experience, and her health condition. The second phase is the pre-clinical arrangement: the choice of psychological strategies based on the relevant and urgent needs of the patient. The third phase is a clinical-cognitive elaboration: adaptive processing by the exploration of negative feelings in order to boost self-awareness. The fourth phase is the closure of the clinical session, addressing the weaknesses and strengths of one’s own disease experience.

Statistical Analyses

Descriptive statistics for baseline characteristics and the final measurement at each time point were calculated. A repeated measures MANOVA was used to detect the statistical significance of overall differences across the psychological variables when comparing emotional conditions of groups. A Kruskal-Wallis ANOVA test analyzed the effect of independent variables (the severity of cancer and typology of surgical interventions). The data were analyzed using the SPSS program with a fixed value $\alpha = 0.05$.

RESULTS

There were 33 patients eligible for the present controlled study; the uptake rate was 90% ($n = 30$), and 9% of the patients declined at baseline measurement even though they had signed the informed consent. At final measurement, the dropout rate was 20% ($n = 6$); the reason was the modification of disease conditions (evidence for the recurrence of cancer). The adherence to the psychological path was high (90%).

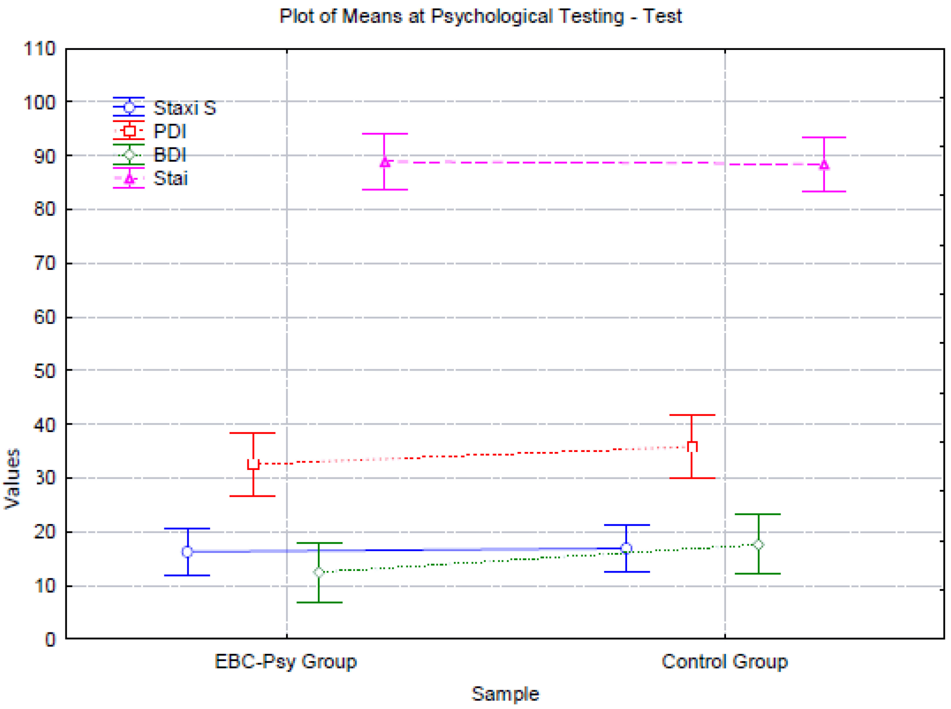
Table 2 reports the raw scores (means and standard deviations) of psychological testing in Time 1 and Time 2.

First, we conducted a one-way ANOVA (2 groups × 8 measures), comparing the emotions of the EBC-Psy and control groups at the beginning of the treatment by assessing anxiety (STAI test), anger (STAXI test, composed of five sub-measures), depression (BDI), and psychological distress (PDI) variables. The statistical analysis showed no significant difference between groups. Looking at data and **Graphic 1**, both groups tended to experience the same emotions.

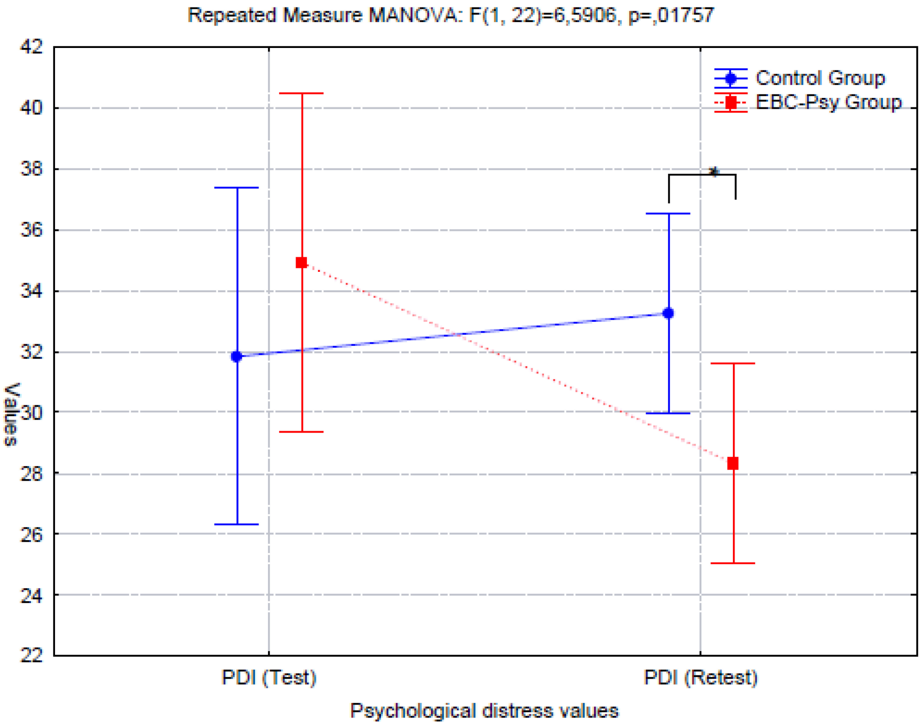
We then conducted a MANOVA for repeated measures to verify the change over time after exposure to the experimental treatment in each group. We operated a MANOVA (2 × 2 × 2) for anxiety, depression, and psychological distress measures; then, a MANOVA (2 × 5 × 5) was conducted to analyze all variables of the anger measure. The statistical analysis evidenced

TABLE 2 | Raw scores (mean and standard deviations) of EBC-Psy and Control group performances on psychological test–retest evaluation (Time 1 and Time 2).

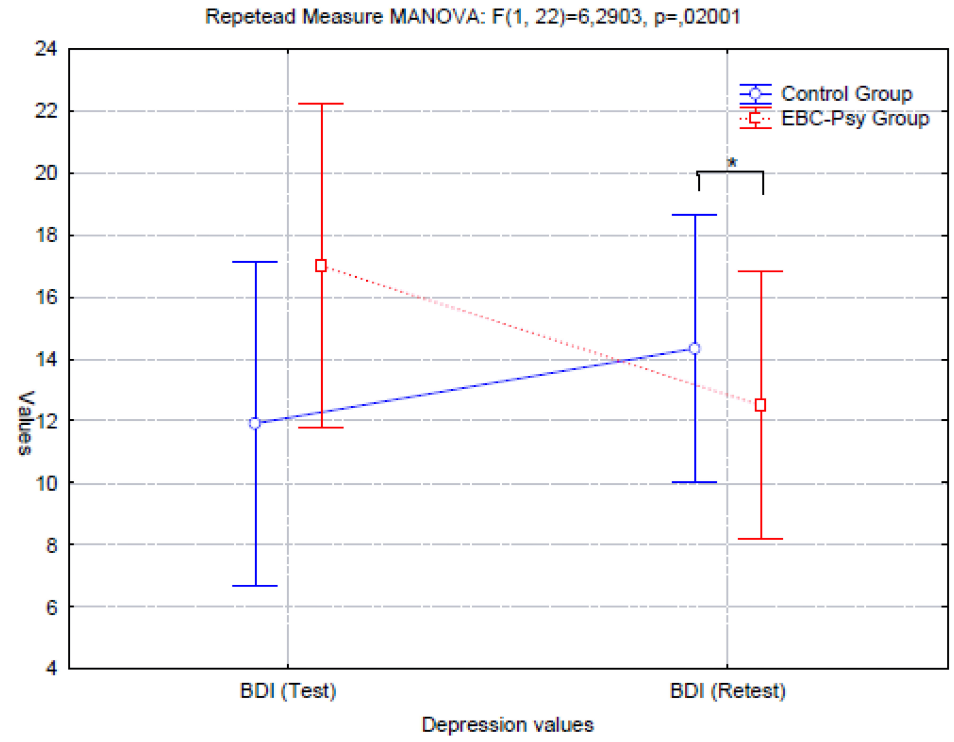
Variables	EBC-Psy group				Control group			
	Time 1		Time 2		Time 1		Time 2	
	X	*SD*	*X*	*SD*	*X*	*SD*	*X*	*SD*
STAXI								
State Anger	16.8	± 6.8	15.4	± 6.9	16.2	± 6.1	13.0	± 2.7
Trait Anger	21.3	± 4.8	19.8	± 4.9	20.9	4.9	19.3	±5.9
Ax/out	20.1	± 3.7	20.4	± 5.2	20.5	4.7	19.5	±4.7
Ax/Con	21.8	± 2.9	21.2	± 4.7	20.5	5.1	18.3	±4.2
Ax/Ex	30.2	± 6.5	29.5	± 10.8	30.1	7.1	30.7	±9.1
STAI								
Total score	88.4	± 10.7	83.1	± 5.9	88.4	± 10.7	89.0	± 3.1
BDI								
Total score	17.0	± 9.9	12.5	± 6.4	11.9	± 7.2	14.3	± 7.8
PDI								
Total score	34.9	± 11.0	28.3	± 5.3	31.8	± 7.0	33.2	± 5.5



GRAPHIC 1 | Representation of emotional condition of the participants at baseline measurement (Time 1).



GRAPHIC 2 | Representation of psychological distress conditions.



GRAPHIC 3 | Representation of depression conditions (means and standard deviations).

significant differences in BDI ($d = 0.8$; $p = 0.02$) and PDI ($d = 0.8$; $p = 0.018$) measures.

In **Graphics 2**, **3**, we report the representation of BDI and PDI performance.

Next, we conducted non-parametric analysis to verify the influence of cancer severity (TNM stage II and III) and surgical interventions (lumpectomy and mastectomy) on the decrease in psychological distress and depression at Time 2 in the EBC-Psy group. The Kruskal-Wallis ANOVA tests by variable TNM on PDI [H(1, N = 12) = 0.10 p = 0.74; X^2 = 0.34 p = 0.55] and BDI [H(1, N = 12) = 2.41 p = 0.12; X^2 = 3.08 p = 0.07] were not significant, nor was surgical intervention on PDI [H(1, N = 12) = 0.10 p = 0.70; X^2 = 0.00 p = 1.00] and BDI [H(1, N = 12) = 0.78 p = 0.30; X^2 = 1.33 p = 0.24].

DISCUSSION AND CONCLUSION

The study investigated the impact of a new psychological intervention tailored for young patients with BC experience. A controlled clinical study design was used to propose an innovative psychological intervention to be applied after urgent surgical/pharmacological treatments. The EBC-Psy is a brief treatment based on emerging scientific findings about a new pattern of psychological needs from a population involved in intensive medical settings. Preliminary data demonstrated encouraging outcomes in this vulnerable population, highlighting the positive impact of the EBC-Psy. However, the study is still ongoing with a larger number of participants to finalize the results. At the same time, the participants who adhered to the clinical protocols have reduced their distress and depression in their daily activities. The keys of the EBC-Psy intervention on emerging psychological needs for new BC targets (younger patients) are the screening of psychological distress, well-timed intervention after diagnosis, and the shaping of coping strategies. The main goals of the intervention were to reduce distress and enhance treatment benefits. The positive outcome of the EBC-Psy intervention has been based on the reduction of signs of depression and psychological distress. Findings showed that the EBC-Psy favored patients overcoming self-perception as "long-term patients" just after the end of the clinical protocol of primary care. The women in the EBC-Psy group evidenced more positive perspectives to win back their lives thanks to a more efficient management of their own emotive balancing. On the contrary, the women in the control group showed increased distress and depression signs, and consequently experienced delayed and unbalanced wellness, likely related to a lower quality of life. In Di Giacomo's studies (Di Giacomo et al., 2015, 2016; Di Giacomo, 2018), and confirmed in this research, two variables seemed to act as risk factors: (a) the reduction of the intensity and frequency of clinical sessions in the hospital (end of clinical treatments) and (b) positive responsiveness to the pharmacological protocols. Both factors fit with an increased level of distress in the patient due to the lower level of hospital stress and more negative thoughts about her own perspective on life (such as the possibility of recurrence and the risk of death). Against these risk factors, we focused on the experience of life, the changing events, and the awareness of psychological distress; they appear to be efficient counterpoints.

It will be interesting to evaluate the sustainability of the EBC-Psy intervention: actually, we are conducting follow-up evaluations 6 months from the end of the intervention and more around the 18th month after diagnosis.

Generally, our findings, even if limited by this small-scale protocol, seemed to confirm the positive psychotherapy role after BC diagnosis and treatment through the impact of the cognitive processes, coping strategies, and psychological resilience (Kolokotroni et al., 2014; Parikh et al., 2015; Di Giacomo et al., 2015, 2016; Koutrouli et al., 2016; Mattei et al., 2017a,b). In fact, they are considered key factors in personal change, in dealing positively with, and overcoming, the cancer experience. The cognitive process seems to play a preeminent role: in our EBC-Psy protocol, it worked efficiently to significantly reduce depression symptoms and psychological distress levels. Adjustment to life seemed to be the cognitive pathway to root the turning of positive behavior. The practical approach of the EBC-Psy could be in line with Tedeschi and Calhoun's (2004) suggestion: "The frightening and confusing aftermath of trauma, where fundamental assumptions are severely challenged, can be fertile ground for unexpected outcomes that can be observed in survivors: posttraumatic growth" (p. 4). Our young women showed themselves to be powerful actors in their own lives, choosing to be anchored to real life and making their daily activity their strength. At this stage of the study, we had not yet tested the EBC-Psy as directly correlated to the posttraumatic growth model, but it could be considered an important and interesting future development of the framework.

The current study has some limitations that should be addressed in future research. First, the small sample size limits the generalization of the findings. Second, missing follow-up data limits our ability to examine the clinical relevance of the effects of intervention. Although our data are preliminary, we decided to discuss them because of their encouraging outcomes; the study is ongoing, and the sample size is increasing and will be larger over a longer period of time. In future works, we will address these points and analyze the relationship between intervention-induced positive growth and psychological response patterns by follow-up data. Moreover, it will be interesting to analyze the application of the posttraumatic growth model in the EBC-Psy framework.

FUTURE DEVELOPMENTS

This study is a pilot study designed to address a specific psychological treatment for women to deal with the end of the clinical protocol of BC diagnosis and treatment. To evaluate the efficacy of the intervention, we must still conduct a randomized controlled trial in which we compare the EBC-Psy intervention to the counseling interventions that are currently applied in clinical protocols to verify the usability and specificity of the EBC-Psy. Moreover, our preliminary data are encouraging in terms of compliance and psychological strengthening, but we need other measures, controls, and data to detect its efficacy and then release the final version of the EBC-Psy; in other words, we are working to complete the validation process. However, sharing our research with the scientific community represents a valuable method to model and design better research planning, taking care to address the contributions (criticism and suggestions) of clinical professionals, and implementing the original study design.

AUTHOR CONTRIBUTIONS

DDG developed the study concept. All authors contributed to the study design. Testing and data collection were performed by JR. JR and ED performed the data analysis and interpretation under the supervision of EP. DP, KC, and DDG drafted the paper. All authors approved the final version of the paper for submission.

REFERENCES

American Joint Committee on Cancer (2010). *American International Cancer Control, AJCC Cancer Staging Manual*, 7th Edn. New York, NY: Springer. doi: 10.1007/978-0-387-88441-7

Beck, A. T., Steer, R., and Brown, G. (1996). *Bdi-Ii, Beck Depression Inventory: Manual*. Boston: Psycholoigcal Corp.

Bennet, B., Lloyd, A., Webber, K., and Friedlander, M. (2012). Predictors of resilience in women treated for breast cancer: a prospective study. *J. Clin. Oncol.* 30:15.

Brebach, R., Sharpe, L., Rhodes, P., and Butow, P. (2016). Psychological intervention targeting distress for cancer patients: a meta-analysis study investigating uptake and adherence. *Psychoncology* 25, 882–890. doi: 10.1002/pon.4099

Burgess, C., Cornelius, V., Love, S., Graham, J., Richards, M., and Ramirez, A. (2005). Depression and anxiety in women with early breast cancer: five year observational cohort study. *BMJ* 330:702. doi: 10.1136/bmj.38343.670868.D3

Conley, C., Bishop, B., and Andersen, B. (2016). Emotions and emotion regulation in breast cancer survivorship. *Healthcare* 4:E56. doi: 10.3390/helthcare4030046

Costanzo, E. S., Lutgendorf, S. K., Mattes, M. L., Trehan, S., Robinson, C. B., Tewfik, F., et al. (2007). Adjiusting to life after treatment: distress and quality of life following treatment for breast cancer. *Br. J. Cancer* 97, 1625–1631. doi: 10.1038/sj.bjc.6604091

Di Giacomo, D. (2018). Psychological resilience in early breast cancer young patients: experience in real life. *J. Psychosom. Res.* 109:99. doi: 10.1016/j.jpsychores.2018.03.047

Di Giacomo, D., Cannita, K., Ranieri, J., Aloisio, F., Cocciolone, V., and Ficorella, C. (2015). Predictive features of resilience in early breast cancer young patient: real life. *Ann. Oncol.* 26, 1–6. doi: 10.1093/annonc/mdv347.10

Di Giacomo, D., Cannita, K., Ranieri, J., Cocciolone, V., Pssafiume, D., and Ficorella, C. (2016). Breast cancer survivors and psycholoigcal resilience among young women. *J. psychopathol.* 22, 191–195.

Gibbons, A., Groarke, A. M., and Sweeney, K. (2016). Predicting general and cancer-related distress in women with newly diagnosed breast cancer. *BMC Cancer* 16, 935–943. doi: 10.1186/s12885-016-2964-z

Giuliani, A. R., Mattei, A., Santilli, F., Clori, G., Scatigna, M., and Fabiani, L. (2014). Well-being and perceived quality of life in elderly people displaced after the eatherquake in L'Aquila, Italy. *J Community Health* 39, 531–537. doi: 10.1007/s10900-013-9793-7

Kolokotroni, P., Anagnostopoulos, F., and Tsikkinis, A. (2014). Psychosocial factors related to posttraumatic growth in breast cancer survivors: a review. *Women Health* 54, 569–592. doi: 10.1080/03630242.2014.899543

Koutrouli, N., Anagnostopoulos, F., Griva, F., Gourounti, P., Kolokotroni, F., and Efstasia, V. (2016). Exploring the relationship growth, cognitive processing, psychological distress, and social constraints in a sample of breast cancer patients. *Women Health* 56, 650–667. doi: 10.1080/03630242.2015.1118725

Lester, J., Crosthwaite, K., Stout, R., Jones, R., Holloman, C., Shapiro, C., et al. (2015). Women with breast cancer: self-reported distress in early survivorship. *Oncol. Nurs. Forum* 42, E17–E23. doi: 10.1188/15.ONF.E17-E23

Linley, P. A. (2006). Counseling psychology's positive psychological agenda: a model for integration and inspiration. *Couns. Psychol.* 34, 313–322. doi: 10.1177/0011000005284393

Mattei, A., Fiasca, F., Mazzei, M., Abbossida, V. and Bianchini, V. (2017a). Burnout among healthcare workers at L'Aquila: its prevalence and associated factors. *Psychol. Health Med.* 22, 1262–1270. doi: 10.1080/13548506.2017.1327667

Mattei, A., Fiasca, F., Mazzei, M., Necozione, S., and Bianchini, V. (2017b). Stress and Burnout in Health Care Workers After the 2009 L'Aquila Earthquake: A Cross-Sectional Observational Study. *Front. Psychiatry* 8:98. doi: 10.3389/fpsyt.2017.00098

Min, J. A., Yonn, S., Lee, C. U., Chae, H. J., Lee, C., Song, K. Y., et al. (2013). Psychological resilience contributes to low emoitonal distress in cancer patients. *Support. Care Cancer* 21, 2469–2476. doi: 10.1007/s00520-013-1807-6

Moher, D., Schulz, K. F., and Altman, D. G. (2001). The consort statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. *Ann. Intern. Med.* 134, 657–662. doi: 10.7326/0003-4819-134-8-200104170-00011

Molina, Y., Martinez-Gutierrez, J., Reding, K., Yi-Frazier, J., and Rosenberg, M. (2014). Resilience among patients across the cancer continuum: diverse perspectives. *Clin. J. Oncol. Nurs.* 10, 93–101. doi: 10.1188/14.CJON.93-101

Morasso, G., Costantini, M., Baracco, G., Borreani, C., and Capelli, M. (1996). Assessing psychological distress in cancer patients: validation of a self-administered questionnaire. *Oncology* 53, 295–302. doi: 10.1159/000227576

Ng, C. G., Mohamed, S., See, M. H., Harun, F., Dahlui, M., Sulaiman, A. H., et al. (2015). Anxiety, depression, perceived social support and quality of life in malaysian breast cancer patients: a 1-year perspective study. *Health Qual. Life Outcomes.* 13, 205–213. doi: 10.1186/s12955-015-0401-7

Parikh, D., De Ieso, P., Garvey, G., Thachil, T., Ramamoorthi, R., Penniment, M., et al. (2015). Post-traumatic stress disorders and post-traumatic growth in breast cancer patients – a systematic review. *Asian Pac. J. Cancer Prev.* 16, 641–646. doi: 10.7314/APJCP.2015.16.2.641

Quattropani, M. C., Lenzo, V., and Filastro, A. (2017). Predictive factor of anxiety and depression symptoms in patients with breast cancer undergoing chemotherapy. an explorative study based on metacognitions. *J. Psychopathol.* 2, 67–73.

Spielberger, C. D. (2004). *State-Trait Anger Expression Inventory-2 (STAXI-2). Professional Manual*. Tampa, FL: Psychological Assessment Resources.

Spielberger, C. D., and Sydeman, S. J. (1994). "State-trait anxiety inventory and state-trait anger expression inventory," in *The use of psychological tests for treatment planning and outcome assessment*, ed. M. E. Maurish (Hillsdale, NJ: Erlbaum), 292–321.

Tedeschi, R. G., and Calhoun, L. G. (2004). The foundations of posttraumatic growth: new considerations. *Psychol. Inquiry* 15, 93–102. doi: 10.1207/s15327965pli1501_03

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MINI REVIEW
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Psychosocial and Neurocognitive Factors Associated With Hepatitis C – Implications for Future Health and Wellbeing

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Background: Hepatitis C virus (HCV) infection involves changes not only from the point of view of physical health, but also emotional, and social that have a significant impact on the quality of life of these patients. According to the literature review, it seems that there is an important association between psychosocial factors, in particular on a cognitive level and disease progression. The aim of this mini-review is to summarize recent literature looking at the associations between psychosocial and neurocognitive factors and HCV.

Methods: PubMed/Medline was systematically searched for psychosocial and neurocognitive factors associated with hepatitis C, treatment adherence, and patient wellbeing.

Results: Patients present with a range of extrahepatic symptoms including fatigue, anxiety, depression, and neurocognitive dysfunction. HCV's impact on quality of life and wellbeing has serious clinical and social implications.

Conclusion: Hepatitis C and its management continue to have a profound impact on health and psychologic wellbeing. Considering the serious extrahepatic implications for individuals, it is imperative that healthcare professionals pay close attention to psychosocial and neurocognitive factors. The focus on combined clinical approaches could enhance understanding about the health and social impacts of hepatitis C along the life course.

Keywords: hepatitis C, neurocognition, adherence, wellbeing, psychosocial factors

INTRODUCTION

The World Health Organization (WHO) estimates that about 3% of the world population (170 million people) is infected with the hepatitis C virus (HCV) (WHO, 1999). The disease's potential for evolution toward chronicity, hepatic cirrhosis, and hepatocellular carcinoma makes this the main indicator for a liver transplant (Marinho and Barreira, 2013) before effective therapies arise. Treatment for HCV changed in the last years from an interferon and ribavirin-based therapy to being interferon-free. These are simpler oral regimens, shorter to administer with very high efficacy rates and better side effect profiles (Smith et al., 2015). However, as advances in the treatment of HCV occur, it is imperative to evaluate clinical outcomes, assessing and quantifying the efficacy and impact of these regimens.

The identification of neuropsychiatric and neurocognitive symptoms is important during and before treatment; however, they still have little recognition or impact in clinical evaluation. Further, these symptoms (depression, cognitive disorders) are eventually associated to direct HCV neurotoxicity (Adinolfi et al., 2015), negatively affecting the individual's perceived Quality of Life (QoL), daily functioning, work, and productivity. These factors can lead to reduced involvement in medical care and life projects as well as increased morbidity and mortality, decreasing overall wellbeing, QoL, as well as treatment adherence (Younossi et al., 2007; Schaefer et al., 2012; Adinolfi et al., 2015; Monaco et al., 2015; Younossi and Henry, 2015; Chasser et al., 2017).

In a biopsychosocial model of the disease and the treatment, it is essential to understand HCV's clinical and social impact on a broader life perspective and how individuals experience it. The basic principles of this model, which uses a holistic approach regarding illness, includes the biological, psychological, and social dimensions of the person's life and the perception that the person suffers as a whole. The personality and the emotional reserves of the patient as well as the particular environmental conditions in which the person lives should be taken into account (Papadimitriou, 2017). On the other hand, positive psychology and focusing on wellbeing have inspired research into the aspect of the relation between emotion and health; namely, the relationship between subjective wellbeing and health outcomes (Okely and Gale, 2015). Wellbeing, in the context of a chronic condition such as HCV infection, must follow the WHO's inclusive definition of health and states of wellbeing (Misselbrook, 2014). The literature explains this construct as a combination of three different dimensions, each capturing a different aspect: life evaluation (quality or goodness of ones' life and overall life satisfaction), hedonic wellbeing, and eudemonic wellbeing. The hedonic dimension refers to the experience of positive and negative affect (e.g., sadness or happiness) and not to a unique positive affective valence, while the eudemonic dimension captures meaning and purpose in life (Steptoe et al., 2015). Thus, the aim of this article is to determine what is currently known about neurocognitive and psychosocial factors associated with HCV as well as to try to value disease adjustment and the implications for health and wellbeing.

METHODS

The aim of this mini-review is to summarize the more recent literature investigating the relationship between psychosocial and neurocognitive factors associated with HCV and their impact on patient wellbeing. We searched the Medline/PubMed databases. No time period limits were placed, and the key terms included "psychosocial," "neurocognitive," "hepatitis C," and "wellbeing." In addition to this selection, some research gathered outside this search was reported as evidence, if considered appropriate by all authors.

PSYCHOSOCIAL FACTORS AND HEPATITIS C

The chronic nature and individual experience of the disease are conditioning factors on QoL, with clinical and social implications, due not only to the diagnostic but also to its evolution (Negro et al., 2015; Chasser et al., 2017; Iriana et al., 2017). Several studies have stated that chronic hepatitis C may lead to several complications anddespite the fact that most of the patients with HCV are asymptomatic, they consistently report a significant reduction in health-related QoL, when compared with the general population (Baune and Air, 2016; Adinolfi et al., 2017).

Psychosocial chronic stressors are well documented as determinants of poor mental and physical health, leading to an important burden in health systems, mortality, morbidity, and psychological wellbeing, predominantly in developed societies (Yarlott et al., 2017). The relationship between physical mental and social health as well as the uncertainties about treatment and HCV have been well documented, both in the past and in recent literature (Hong et al., 2011; Kleinman et al., 2012; Armstrong et al., 2016). Emotional distress and depressive disorders have been reported in untreated HCV patients, pointing to a possible role of the virus itself in their occurrence (Alavi et al., 2012; El Khoury et al., 2012). Furthermore, studies suggest that a deficiency of social relationships is a significant risk factor for broad-based morbidity and mortality as well as negative implications for health (Cacioppo and Cacioppo, 2014; Valtorta et al., 2016). Whether these disorders are due to the uncertainty of living with a chronic disease with potentially life-threatening complications or to other psychosocial factors, remains under discussion.

Another relevant factor is the stigma associated with HCV, which may increase anxiety levels and the fear of transmitting the virus. This fear may be the main cause for social isolation and decreased intimacy in relationships (Younossi et al., 2007; Armstrong et al., 2016). Stigma may be defined as a cluster of attitudes expressed by a dominant group, which sees other individuals' behaviors as being socially unacceptable. The notion of stigma, related to shameful relationships, and deviations from what is considered to be the "norm," has a long history in the context of infectious diseases, as in the case of HCV (Bogart et al., 2008). These norms, behaviors, and beliefs may lead to alienation of family and social relationships as well as (real or perceived) to discrimination at health settings or the workplace.

Stigmatization affects not only patients but also health care professionals who are not immune to stereotypes and judgments that may influence treatment. These issues can promote an increase in patients' isolation, in therapeutic continuity, and a decrease in the search for medical help (Butt, 2008). Furthermore, several studies have suggested that stigma is associated with low treatment adherence (Kamaradova et al., 2016), including in HCV patients (Treloar et al., 2013). Implementing psychological strategies and intervention models (e.g., psychoeducation; information-motivation-behavioral skills) should be a major concern.

A recent systematic review has shown that non-adherence to the HCV treatment regimen is associated with virologic response failure (Lieveld et al., 2013), supporting that optimal adherence is needed to achieve treatment success in this area (Mathes et al., 2014). This also becomes a public health issue, since non-adherence favors the development and spread of resistant HCV mutations, highlighting adherence's crucial role in treatment success (Weiss et al., 2009).

Investigations about medication adherence indicate the need to analyze interconnected factors related to the complexity of therapeutic regimes (treatment of HCV and comorbidities), relevance of side effects (nausea, pruritus, insomnia, diarrhea, and asthenia) (Feld et al., 2014), but also patient-related variables. Research points to a steady correlation between individual characteristics, illness behaviors, health literacy, and low adherence to treatment. Among sociodemographic and clinical factors, gender, depression, psychiatric diagnosis in general, illicit drug use, HIV co-infection, treatment regimen, and hemoglobin level were identified as being significantly and consistently associated with adherence/non-adherence. Age, race, unemployment, being unmarried, genotype, treatment experience, disease severity, and HCV-related costs were classified as inconsistent predictors of non-adherence (Lieveld et al., 2013; Mathes et al., 2014).

From a psychological point of view, factors such as information, personal beliefs, personality traits, social context and the way they interact toward health-promoting behaviors, allow a better understanding of adherence bases, helping to implement individualized adaptive strategies. Further, the general physical symptomatology related to HCV can vary from musculoskeletal discomfort to chronic fatigue (Armstrong et al., 2016). In a recent study, Boscarino et al. (2015) reported that poor physical health in patients with HCV was associated with demographic factors, including income, health insurance status, marital status, and also connected with stressful life events, social support or having a liver transplant. Despite the needed level of adherence (95% or higher), non-adherence should not be a factor of exclusion to initiate antiviral treatment, but rather a factor that induces a careful evaluation in the stage of pre-prescription, as well as the implementation of strategies designed to promote adherence in the context of a multi-disciplinary team. Thus, we argue that an integrated medical and psychological approach is fundamental, being associated with a higher adherence and to a better therapeutic response.

The following steps have proven to be crucial for the success of the treatment: to evaluate the patient's preparation to start and adhere to the therapeutic regime, to choose a therapeutic regime that may improve adherence, and to select and to apply interventions during the therapeutic regime.

Hepatitis C virus diagnosis is reported by individuals as having a profound impact on their social functioning and wellbeing. Psychosocial factors (social support, coping mechanisms) not only interfere in the way the subject interprets and experiences symptoms, but they also influence the medical treatment and modify behaviors (Bielski and Chan, 1976).

NEUROCOGNITION AND HEPATITIS C

The involvement of the central nervous system (CNS), found in recent studies, supports a pathogenic role for HCV in neuropsychiatric and neurocognitive disorders (Monaco et al., 2015). In a recent review, Yarlott et al. (2017) called this association between HCV, cognitive impairment, fatigue and depression the "Hepatitis C Virus Brain Syndrome." This syndrome is probably generated by peripheral immune responses affecting the CNS, neuroinflammation associated with CNS HCV infection, as well as to negative life events and other psychogenic stressors (Yarlott et al., 2017).

Forton et al. (2001) showed evidence that HCV can cross the blood-brain barrier and replicate in the CNS, emerging through infected monocytes and infecting microglial cells. Using proton magnetic resonance spectroscopy in patients and controls, they found an increase in basal ganglia and white matter choline/creatine ratios in patients, suggesting an altered metabolism in patients with chronic HCV; these results were not explained by hepatic encephalopathy or history of drug use (Forton et al., 2001).

Neurocognitive impairment, one of the most common extrahepatic manifestations of HCV, can lead to subtle changes in processing speed, memory, attention, fatigue, and cognitive performance. Up to 50% of HCV-infected patients may develop clinical or subclinical manifestations of this dysfunction, and these cognitive deficits are independent of the stage of the liver disease (Lowry et al., 2010; Ferri et al., 2016; Iriana et al., 2017). Hilsabeck et al. (2002) found that HCV patients experience cognitive deficits, especially in attention, learning, psychomotor speed, and mental flexibility. This study shows that maintaining attention and concentration while performing accurately was the most difficult task for non-cirrhotic patients, with 50% taking an abnormally long time to complete the task, 28.9% making a significant number of omission errors, and about 20% of non-cirrhotic patients performing in the impaired range involving attention/concentration, visual scanning and tracking, psychomotor speed, and mental flexibility (Hilsabeck et al., 2002). The authors suggest that this cognitive impairment is similar to that reported in patients with a neurocognitive disorder associated to other chronic illness, such as HIV and AIDS-related dementia, and that these deficits affect QoL and functional capacity in patients (Hilsabeck et al., 2002).

Regarding cognitive and psychiatric dysfunctions, several studies were performed to assess the impact of HCV in patients, namely depression, anxiety, fatigue, attention, executive function, and visuospatial function deficits (Monaco et al., 2015; Thames et al., 2015). Cognitive impairments were previously thought to be associated with the development of hepatic encephalopathy (Gaeta et al., 2013). However, their presence was demonstrated in the absence of advanced liver disease as well as in the absence of HIV co-infection, depression, or substance abuse (Cherner et al., 2005; Kuhn et al., 2017; Yarlott et al., 2017). Despite the absence of those comorbidities, deficits in attention, concentration, psychomotor speed, and verbal fluency have been reported in HCV patients (Weissenborn et al., 2004; Clifford et al., 2009). Findings remain controversial and it is unclear if HCV eradication improves HCV-associated neurological compromise (Kuhn et al., 2017). Bladowska et al. (2013) in a follow-up study over 48 weeks after the cessation of treatment, found significant improvement in attention and working memory in patients who successfully cleared the virus. This finding suggests that over time, the benefits of HCV clearance can be more marked. However, in other research protocols sustained virologic response (SVR) was not related to any improvement in neurocognitive performance (Huckans et al., 2015; Lowry et al., 2016).

Therefore, the neurocognitive profile of these patients before treatment needs to be addressed due to the possible implications on the treatment course (e.g., non-adherence-like behavior due to cognitive abnormalities). Additionally, it is important to address other risk factors that can have a negative impact on cognition. The high rate of substance abuse and the prevalence of psychiatric disorders among HCV-infected patients are important factors associated with cognitive impairment that trigger poor adherence and treatment efficacy (Wiêdłocha et al., 2017).

Several studies have suggested that earlier treatment is associated with improvement of the QoL in chronic HCV patients (Marinho and Barreira, 2013; Boscarino et al., 2015; Lucaciu and Dumitrascu, 2015; Negro et al., 2015; Chasser et al., 2017; Iriana et al., 2017), highlighting the importance of HCV treatment. In order to optimize treatment outcomes, a pretreatment profile helps to identify risk factors that can be modifiable before and during treatment, such as treatment disruption, non-adherence, the risk of (re)infection and risk of emergence of depressive disorders (Basseri et al., 2010).

The pre-vs.-post treatment neurocognitive changes that may occur among SVR patients require further research to understand the impact of neuroanatomical and functional changes in HCV patients before, over the course of treatment, and after successful clearance of the virus.

DISCUSSION AND CONCLUSION

This mini-review shows that patients with HCV often feel stigmatized and unsupported in their care, relationships, and work environments, while simultaneously coping with physical and psychological symptoms. This synthesis points to areas where greater education, compassion, and patient-centered healthcare could improve the experience of people living with HCV.

In a broader perspective, and trying to close the loop, neurocognitive impairment can be responsible for therapy non-adherence in several diseases (Rohde et al., 2017; Smith et al., 2017) and for losing internal resources to deal with a chronic disease (Boehmer et al., 2016). Adaptive behavior is therefore impaired, social networks are disrupted and patients' deficits in instrumental daily life abilities are increased. These are factors known to be associated to a worse QoL (Vilhena et al., 2014), potential complications in disease evolution (Vere, 2009), and overall a worse prognosis. Whether, mediating variables in this process include individual psychological traits, negative or positive affective states, cognitive impairment, biological responses associated to more pathogenic viral stripes, or to the combination of multiple disease-factors, is yet an open debate. However, the relevance of those psychosocial variables in chronic diseases is nowadays unquestionable (Fava et al., 2016; Kemp, 2017; McLachlan and Gale, 2018). In what concerns wellbeing, all the described dimensions may be affected by psychosocial factors and they can be managed through an integrated intervention. Actions on preventing, identifying and treating hepatitis C should be a priority and need to be included in local health and wellbeing strategies in order to promote better health outcomes.

The association between neurocognitive functions, psychological wellbeing, and activities of daily living among patients with hepatitis C has had little attention. Understanding factors, which can impact physical functioning and psychological wellbeing, may have an important clinical relation to improving outcomes for patients with this disease.

Treatment of HCV requires education efforts of a wide base, with the goal of improving knowledge, and attitudes about this disease. These efforts must include patients and their families, policy decisions, health care professionals, and society as a whole. A thorough study of HCV-associated stigma, clinical, and social implications is essential for helping patients to cope with the disease.

Investigation supports that HCV experience and treatment adjustment may be facilitated through the use of theoretical informed psychological interventions. Considering the impact of HCV infection in patients' mental health and wellbeing, before, and during treatment, an interdisciplinary approach should be followed and encouraged. Besides HCV-associated depression, more studies are needed to characterize the eventual neurocognitive side effects of the new interferon-free regimes and their impact on mood comorbidities.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

REFERENCES

Adinolfi, L. E., Nevola, R., Lus, G., Restivo, L., Guerrera, B., Romano, C., et al. (2015). Chronic hepatitis C virus infection and neurological and psychiatric disorders: an overview. *World J. Gastroenterol.* 21, 2269–2280. doi: 10.3748/wjg.v21.i8.2269

Adinolfi, L. E., Nevola, R., Rinaldi, L., Romano, C., and Giordano, M. (2017). Chronic hepatitis C virus infection and depression. *Clin. Liver Dis.* 21, 517–534. doi: 10.1016/j.cld.2017.03.007

Alavi, M., Grebely, J., Matthews, G. V., Petoumenos, K., Yeung, B., Day, C., et al. (2012). Effect of pegylated interferon-α-2a treatment on mental health during recent hepatitis C virus infection. *J. Gastroenterol. Hepatol.* 27, 957–965. doi: 10.1111/j.1440-1746.2011.07035.x

Armstrong, A. R., Herrmann, S. E., Chassany, O., Lalanne, C., Da Silva, M. H., Galano, E., et al. (2016). The International development of PROQOL-HCV: an instrument to assess the health-related quality of life of patients treated for hepatitis C virus. *BMC Infect. Dis.* 16:443. doi: 10.1186/s12879-016-1771-0

Basseri, B., Yamini, D., Chee, G., Enayati, P. D. P., Tran, T., and Poordad, F. (2010). Comorbidities associated with the increasing burden of hepatitis C infection. *Liver Int.* 30, 1012–1018. doi: 10.1111/j.1478-3231.2010.02235.x

Baune, B. T., and Air, T. (2016). Clinical, functional, and biological correlates of cognitive dimensions in major depressive disorder – Rationale, design, and characteristics of the cognitive function and mood study (CoFaM-Study). *Front. Psychiatry* 7:150. doi: 10.3389/fpsyt.2016.00150

Bielski, B. H. J., and Chan, P. C. (1976). Reevaluation of the kinetics of lactate dehydrogenase catalyzed chain oxidation of nicotinamide adenine dinucleotide by superoxide radicals in the presence of ethylenediaminetetraacetate. *J. Biol. Chem.* 251, 3841–3844. doi: 10.5812/hepatmon.8340

Bladowska, J., Zimny, A., Kołtowska, A., Szewczyk, P., Knysz, B., Gñsiorowski, J., et al. (2013). Evaluation of metabolic changes within the normal appearing gray and white matters in neurologically asymptomatic HIV-1-positive and HCV-positive patients: magnetic resonance spectroscopy and immunologic correlation. *Eur. J. Radiol.* 82, 686–692. doi: 10.1016/j.ejrad.2012.11.029

Boehmer, K. R., Gionfriddo, M. R., Rodriguez-Gutierrez, R., Dabrh, A. M. A., Leppin, A. L., Hargraves, I., et al. (2016). Patient capacity and constraints in the experience of chronic disease: a qualitative systematic review and thematic synthesis. *BMC Fam. Pract.* 17:127. doi: 10.1186/s12875-016-0525-9

Bogart, L. M., Cowgill, B. O., Kennedy, D., Ryan, G., Murphy, D. A., Elijah, J., et al. (2008). HIV-related stigma among people with HIV and their families: a qualitative analysis. *AIDS Behav.* 12, 244–254. doi: 10.1007/s10461-007-9231-x

Boscarino, J. A., Lu, M., Moorman, A. C., Gordon, S. C., Rupp, L. B., Spradling, P. R., et al. (2015). Predictors of poor mental and physical health status among patients with chronic hepatitis C infection: the Chronic Hepatitis Cohort Study (CHeCS). *Hepatology* 61, 802–811. doi: 10.1002/hep.27422

Butt, G. (2008). Stigma in the context of hepatitis C: concept analysis. *J. Adv. Nurs.* 62, 712–724. doi: 10.1111/j.1365-2648.2008.04641.x

Cacioppo, J. T., and Cacioppo, S. (2014). Social relationships and health: the toxic effects of perceived social isolation. *Soc. Pers. Psychol. Compass* 8, 58–72. doi: 10.1111/spc3.12087

Chasser, Y., Kim, A. Y., and Freudenreich, O. (2017). Hepatitis C treatment: clinical issues for psychiatrists in the post-interferon Era. *Psychosomatics* 58, 1–10. doi: 10.1016/j.psym.2016.09.004

Cherner, M., Letendre, S., Heaton, R. K., Durelle, J., Marquie-Beck, J., Gragg, B., et al. (2005). Hepatitis C augments cognitive deficits associated with HIV infection and methamphetamine. *Neurology* 64, 1343–1347. doi: 10.1212/01.WNL.0000158328.26897.0D

Clifford, D. B., Smurzynski, M., Park, L. S., Yeh, T. M., Zhao, Y., Blair, L., et al. (2009). Effects of active HCV replication on neurologic status in HIV RNA virally suppressed patients. *Neurology* 73, 309–314. doi: 10.1212/WNL.0b013e3181af7a10

doi, Thames, A. D., Castellon, S. A., Singer, E. J., Nagarajan, R., Sarma, M. K., et al. (2015). Neuroimaging abnormalities, neurocognitive function, and fatigue in patients with hepatitis C. *Neurol. Neuroimmunol. Neuroinflammation* 2:e59. doi: 10.1212/NXI.0000000000000059

El Khoury, A. C., Vietri, J., and Prajapati, G. (2012). The burden of untreated hepatitis c virus infection: a US patients' perspective. *Dig. Dis. Sci.* 57, 2995–3003. doi: 10.1007/s10620-012-2233-1

Fava, G. A., Cosci, F., and Sonino, N. (2016). Current psychosomatic practice. *Psychother. Psychosom.* 86, 13–30. doi: 10.1159/000448856

Feld, J. J., Kowdley, K. V., Coakley, E., Sigal, S., Nelson, D. R., Crawford, D., et al. (2014). Treatment of HCV with ABT-450/r-ombitasvir and dasabuvir with ribavirin. *N. Engl. J. Med.* 370, 1594–1603. doi: 10.1056/NEJMoa1315722

Ferri, C., Ramos-Casals, M., Zignego, A. L., Arcaini, L., Roccatello, D., Antonelli, A., et al. (2016). International diagnostic guidelines for patients with HCV-related extrahepatic manifestations. A multidisciplinary expert statement. *Autoimmun. Rev.* 15, 1145–1160. doi: 10.1016/j.autrev.2016.09.006

Forton, D. M., Allsop, J. M., Main, J., Foster, G. R., Thomas, H. C., and Taylor-Robinson, S. D. (2001). Evidence for a cerebral effect of the hepatitis C virus. *Lancet* 358, 38–39. doi: 10.1016/S0140-6736(00)05270-3

Gaeta, L., Di Palo, M., Fasanaro, A. M., and Loguercio, C. (2013). Cognitive dysfunctions in hepatitis C virus (HCV) infection. A mini review. *Curr. Neurobiol.* 4, 43–46.

Hilsabeck, R. C., Perry, W., and Hassanein, T. I. (2002). Neuropsychological impairment in patients with chronic hepatitis C. *Hepatology* 35, 440–446. doi: 10.1053/jhep.2002.31257

Hong, B. A., North, C. S., Pollio, D. E., Abbacchi, A., Debold, C., Adewuyi, S. A., et al. (2011). The use of psychoeducation for a patient with hepatitis C and psychiatric illness in preparation for antiviral therapy: a case report and discussion. *J. Clin. Psychol. Med. Settings* 18, 99–107. doi: 10.1007/s10880-011-9227-6

Huckans, M., Fuller, B., Wheaton, V., Jaehnert, S., Ellis, C., Kolessar, M., et al. (2015). A longitudinal study evaluating the effects of interferon-alpha therapy on cognitive and psychiatric function in adults with chronic hepatitis C. *J. Psychosom. Res.* 78, 184–192. doi: 10.1016/j.jpsychores.2014.07.020

Iriana, S., Curry, M. P., and Afdhal, N. H. (2017). Neurologic manifestations of hepatitis C virus infection. *Clin. Liver Dis.* 21, 535–542. doi: 10.1016/j.cld.2017.03.008

Kamaradova, D., Latalova, K., Prasko, J., Kubinek, R., Vrbova, K., Mainerova, B., et al. (2016). Connection between self-stigma, adherence to treatment, and discontinuation of medication. *Patient Prefer. Adherence* 10, 1289–1298. doi: 10.2147/PPA.S99136

Kemp, A. H. (2017). Editorial: mechanisms underpinning the link between emotion. Physical Health, and Longevity. *Front. Psychol.* 8:1338. doi: 10.3389/fpsyg.2017.01338

Kleinman, L., Mannix, S., Yuan, Y., Kummer, S., L'Italien, G., and Revicki, D. (2012). Review of patient-reported outcome measures in chronic hepatitis C. *Health Qual. Life Outcomes* 10:92. doi: 10.1186/1477-7525-10-92

Kuhn, T., Sayegh, P., Jones, J. D., Smith, J., Sarma, M. K., Ragin, A., et al. (2017). Improvements in brain and behavior following eradication of hepatitis C. *J. Neurovirol.* 23, 593–602. doi: 10.1007/s13365-017-0533-0

Lieveld, F. I., van Vlerken, L. G., Siersema, P. D., and van Erpecum, K. J. (2013). Patient adherence to antiviral treatment for chronic hepatitis B and C: a systematic review. *Ann. Hepatol.* 12, 380–391.

Lowry, D., Burke, T., Galvin, Z., Ryan, J. D., Russell, J., Murphy, A., et al. (2016). Is psychosocial and cognitive dysfunction misattributed to the virus in hepatitis C infection? Select psychosocial contributors identified. *J. Viral Hepat.* 23, 584–595. doi: 10.1111/jvh.12544

Lowry, D., Coughlan, B., McCarthy, O., and Crowe, J. (2010). Investigating health-related quality of life, mood and neuropsychological test performance in a homogeneous cohort of Irish female hepatitis C patients. *J. Viral Hepat.* 17, 352–359. doi: 10.1111/j.1365-2893.2009.01188.x

Lucaciu, L. A., and Dumitrascu, D. L. (2015). Depression and suicide ideation in chronic hepatitis C patients untreated and treated with interferon: prevalence, prevention, and treatment. *Ann. Gastroenterol.* 28, 440–447.

Marinho, R. T., and Barreira, D. P. (2013). Hepatitis C, stigma and cure. *World J. Gastroenterol.* 19, 6703–6709. doi: 10.3748/wjg.v19.i40.6703

Mathes, T., Antoine, S.-L., and Pieper, D. (2014). Factors influencing adherence in Hepatitis-C infected patients: a systematic review. *BMC Infect. Dis.* 14:203. doi: 10.1186/1471-2334-14-203

McLachlan, K. J. J., and Gale, C. R. (2018). The effects of psychological distress and its interaction with socioeconomic position on risk of developing four chronic diseases. *J. Psychosom. Res.* 109, 79–85. doi: 10.1016/j.jpsychores.2018.04.004

Misselbrook, D. (2014). W is for wellbeing and the WHO definition of health. *Br. J. Gen. Pract.* 64, 582–582. doi: 10.3399/bjgp14X682381

Monaco, S., Mariotto, S., Ferrari, S., Calabrese, M., Zanusso, G., Gajofatto, A., et al. (2015). Hepatitis C virus-associated neurocognitive and neuropsychiatric disorders: advances in 2015. *World J. Gastroenterol.* 21, 11974–11983. doi: 10.3748/wjg.v21.i42.11974

Negro, F., Forton, D., Craxì, A., Sulkowski, M. S., Feld, J. J., and Manns, M. P. (2015). Extrahepatic morbidity and mortality of chronic hepatitis C. *Gastroenterology* 149, 1345–1360. doi: 10.1053/j.gastro.2015.08.035

Okely, J. A., and Gale, C. R. (2015). Well-being and chronic disease incidence: the english longitudinal study of ageing. *Psychosom. Med.* 78, 335–344. doi: 10.1097/PSY.0000000000000279

Papadimitriou, G. N. (2017). The "Biopsychosocial Model": 40 years of application in Psychiatry. *Psychiatriki* 28, 107–110. doi: 10.22365/jpsych.2017.282.107

Rohde, D., Merriman, N. A., Doyle, F., Bennett, K., Williams, D., and Hickey, A. (2017). Does cognitive impairment impact adherence? A systematic review and meta-analysis of the association between cognitive impairment and medication non-adherence in stroke. *PLoS One* 12:e0189339. doi: 10.1371/journal.pone.0189339

Schaefer, M., Capuron, L., Friebe, A., Diez-Quevedo, C., Robaeys, G., Neri, S., et al. (2012). Hepatitis C infection, antiviral treatment and mental health: a European expert consensus statement. *J. Hepatol.* 57, 1379–1390. doi: 10.1016/j.jhep.2012.07.037

Smith, D., Lovell, J., Weller, C., Kennedy, B., Winbolt, M., Young, C., et al. (2017). A systematic review of medication nonadherence in persons with dementia or cognitive impairment. *PLoS One* 12:0170651. doi: 10.1371/journal.pone.0170651

Smith, M. A., Chan, J., and Mohammad, R. A. (2015). Ledipasvir-Sofosbuvir: interferon-/Ribavirin-free regimen for chronic hepatitis c virus infection. *Ann. Pharmacother.* 49, 343–350. doi: 10.1177/1060028014563952

Steptoe, A., Deaton, A., and Stone, A. A. (2015). Psychological wellbeing, health and ageing. *Lancet* 385, 640–648. doi: 10.1016/S0140-6736(13)61489-0

Treloar, C., Rance, J., and Backmund, M. (2013). Understanding barriers to hepatitis c virus care and stigmatization from a social perspective. *Clin. Infect. Dis.* 57(Suppl. 2), S51–S55. doi: 10.1093/cid/cit263

Valtorta, N. K., Kanaan, M., Gilbody, S., and Hanratty, B. (2016). Loneliness, social isolation and social relationships: what are we measuring? A novel framework for classifying and comparing tools. *BMJ Open* 6:e010799. doi: 10.1136/bmjopen-2015-010799

Vere, C.-C. (2009). Psychosocial stress and liver disease status. *World J. Gastroenterol.* 15:2980. doi: 10.3748/wjg.15.2980

Vilhena, E., Pais-Ribeiro, J., Silva, I., Pedro, L., Meneses, R. F., Cardoso, H., et al. (2014). Psychosocial factors as predictors of quality of life in chronic portuguese patients. *Health Qual. Life Outcomes* 12:3. doi: 10.1186/1477-7525-12-3

Weiss, J. J., Bräu, N., Stivala, A., Swan, T., and Fishbein, D. (2009). Review article: adherence to medication for chronic hepatitis C-Building on the model of human immunodeficiency virus antiretroviral adherence research. *Aliment Pharmacol. Ther.* 30, 14–27. doi: 10.1111/j.1365-2036.2009.04004.x

Weissenborn, K., Krause, J., Bokemeyer, M., Hecker, H., Schüler, A., Ennen, J. C., et al. (2004). Hepatitis C virus infection affects the brain-evidence from psychometric studies and magnetic resonance spectroscopy. *J. Hepatol.* 41, 845–851. doi: 10.1016/j.jhep.2004.07.022

WHO (1999). Report of a WHO consultation organized in collaboration with the viral hepatitis prevention. *J. Viral Hepat.* 6, 35–47. doi: 10.1046/j.1365-2893.1999.6120139.x

Więdłocha, M., Marcinowicz, P., Sokalla, D., and Stañczykiewicz, B. (2017). The neuropsychiatric aspect of the HCV infection. *Adv. Clin. Exp. Med.* 26, 167–175. doi: 10.17219/acem/37787

Yarlott, L., Heald, E., and Forton, D. (2017). Hepatitis C virus infection, and neurological and psychiatric disorders – A review. *J. Adv. Res.* 8, 139–148. doi: 10.1016/j.jare.2016.09.005

Younossi, Z., and Henry, L. (2015). Systematic review: patient-reported outcomes in chronic hepatitis C – the impact of liver disease and new treatment regimens. *Aliment Pharmacol. Ther.* 41, 497–520. doi: 10.1111/apt.13090

Younossi, Z., Kallman, J., and Kincaid, J. (2007). The effects of HCV infection and management on health-related quality of life. *Hepatology* 45, 806–816. doi: 10.1002/hep.21565

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BRIEF RESEARCH REPORT
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Patients' Comprehension of Mindfulness-Based Cognitive Behavioral Therapy in an Outpatient Clinic for Resistant Depression: A Cross-Sectional Study

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The current study investigated the comprehension of mindfulness-based cognitive behavioral therapy (MBCT) by patients with resistant depression at the Psychiatry Institute of the Federal University of Rio de Janeiro, Brazil. This was the first time the model was used in the institution to treat these patients. In this study, 45 patients were invited to participate in a baseline session of MBCT that consisted in the explanation of the model and experimental exercises conducted by two experienced therapists. Twenty eight patients accepted to participate. At the end of the intervention, the patients completed a self-administered questionnaire designed by our ambulatory to assess their understanding of the method's goals. Patients with anxiety disorder was also accessed for group comparison. More than 75% of the patients rated the intervention as comprehensible and workable. Compared to patients with depression, patients with anxiety had a better understanding of the mindfulness framework (6.5%) and the meaning of cognitive behavioral therapy (17.6%). Patients that completed the intervention described the baseline session of MBCT as comprehensive and acceptable. These results may allow possible future developments in the practice of mindfulness as a treatment applicable in many condition and settings even in the Brazilian context.

Keywords: comprehension, mindfulness, cognitive therapy, depression, baseline

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INTRODUCTION

Studies have shown that the collaborative alliance is a key factor in treatment outcome (Horvath and Symonds, 1991). The collaborative alliance changes the therapeutic process, improving patient-therapist dynamics (Bordin, 1979), including several key elements: confident collaboration, bonding, idealized relationship, dedicated patient, help received, and goals and tasks. This brief study addresses patients' feelings about "goals and tasks" during a session of psychoeducation with MBCT for resistant depression (Hatcher and Barends, 1996; Segal et al., 2002).

The collaborative alliance is particularly important in mindfulness-based cognitive behavioral therapy (MBCT). MBCT is a special kind of CBT that emphasizes the importance of understanding the processes underlying the improvements in patients' thoughts, feelings, and behaviors.

The identification of negative thoughts and cognitive restructuring are taught since the beginning of the treatment (Jarrett et al., 2011).

Mindfulness-based cognitive behavioral therapy has been developed specifically to prevent relapse in patients with a history of recurrent major depressive episodes (Segal et al., 2002). According to the MBCT model, individuals with previous episodes of major depression differ from those without such a history in the patterns of negative thinking, in which small downward mood shifts are more likely to produce recurrence, because they activate patterns of self-deprecating depressogenic thinking similar to those that prevailed in preceding episodes (Williams et al., 2008). MBCT integrates aspects of CBT for depression into mindfulness-based stress reduction (MBSR). By teaching patients to become more aware of their thoughts, feelings, and bodily sensations, MBCT can mitigate depressive symptoms (Beck, 1979; Kabat-Zinn and Hanh, 2013). It is in indeed widely described in the literature how the dimensions of physical and mental health/disease elude patients awareness and are difficult to be integrated as co-occurrent (Grossman et al., 2004; Mannarini and Boffo, 2014). Hence, the MBCT can have a pivotal role in psychopathologies such as depression, in which the psychosomatic component is fundamental and co-occur with mental symptoms.

Various studies have assessed the factors associated with the impact of patients' understanding of the rationale and techniques related to the type of psychotherapy they are enrolled in. In general, the presence of basic psychological processes such as learning, perception, and social interaction are identified as common factors related to successful psychotherapies (Ablon and Jones, 1999).

Until now, no study has investigated the factors of treatment adherence and change regarding the theoretical and practical approach of MBCT in the baseline session focusing on these data. In Brazil, the adoption of this model is still limited, so little is known about patients' understanding and acceptance of the model, especially in resistant depression, where oftentimes patients have already tried different treatment modalities. Furthermore, because their cognitive impairment frequently impacts the expected evolution, it is difficult to assume that any treatment model will be fully understood.

Understanding the psychotherapy approach can impact the therapeutic adherence and change. The present study is aimed at investigating the impact of patients' understanding of MBCT and its applicability to the Brazilian population. We thus conducted an educational session including practical exercises with patients seeking psychiatric treatment, who completed a self-administered questionnaire regarding their understanding of the model and belief in its efficacy.

By teaching patients to become more aware of their thoughts, feelings, and bodily sensations, MBCT can mitigate depressive symptoms (Beck, 1979; Kabat-Zinn and Hanh, 2013). It is in indeed widely described in the literature how the dimensions of physical and mental health/disease elude patients awareness and are difficult to be integrated as co-occurrent (Grossman et al., 2004; Mannarini and Boffo, 2014). Hence, the MBCT can have a pivotal role in psychopathologies such as depression, in which the psychosomatic component is fundamental and co-occur with mental symptoms.

METHODS

Study Design

It was performed a cross-sectional analysis of the data related to the understanding of MBCT protocol by patients with depression and another group of anxiety's patients. Both groups were compared and evaluated in parallel.

Participants

A total of 45 patients referred to the Psychiatry Institute of the Federal University of Rio de Janeiro, Brazil, were invited to participate in the baseline MBCT session in the study after having their psychiatric consultation, and 28 agreed to participate. All patients were evaluated using the Mini International Neuropsychiatric Interview (MINI 5.0.0/DSM IV, 2000) applied by trained health professionals who were independent from the study for diagnostic assessment. Inclusion criteria for all patients were age between 18 and 60 years and diagnosed with depression and anxiety disorder. The sample excluded patients with schizophrenia or difficulties in reading and writing, evaluated when they were submitting their data in a form. All volunteers signed a free and informed consent form and followed instructions regarding the study's procedures. The study was approved by the Institutional Ethics Committee of IPUB/UFRJ.

Procedure

After the MINI interview, patients were invited to participate in a small group or alone in a baseline session of MBCT. Two psychologists with recognized specialization in cognitive-behavioral therapy, frequently users of meditation extensively studied the MBCT protocol (Teasdale et al., 2016) explained the model and conducted experimental exercises. All the stages were conducted in the same room. The first part consisted of the explanation of the cognitive, lasting 10 min. The points considered were: brief psychoeducation regarding the link between triggering situations, automatic thoughts, and dysfunctional attitudes (Beck and Beck, 2011).

Secondly, after confirming the patient's understanding of the cognitive model, we explained the concepts of mindfulness and guided the patients through a short meditation exercise ("mindfully eating a raisin"), providing a mindful awareness experience by paying attention to the details and being present in the moment (body scan) (Segal et al., 2012), lasting 10 to 15 min. At the end of these interventions, patients completed a self-administered questionnaire on their understanding of the goals. A quiet room from the Depression Resistant Ambulatory was separated in advance to accommodate the patients in order not to be disturbed, in comfortable chairs and air conditioning.

Instruments

We developed an instrument based on the specific rationale and strategies of the MBCT therapy (Teasdale et al., 2016), consisting of a 27-item self-report on acceptability, comprehension, and specific benefits of the model (**Table 1**). This table consisted of items adapted from a previous feasibility study (Campos et al., 2015; Kvillemo et al., 2016).

Mini International Neuropsychiatric Interview-Brazilian Version 5.0.0 – International Neuropsychiatric Interview: an instrument with a standard model of a brief structured interview (approximately 25 min) for the evaluation of the existence of Axis I psychiatric disorders according to the DSM-IV (Amorim, 2000).

All data were entered and analyzed using the software IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, United States).

RESULTS

Sociodemographic Data

The sample included patients (n = 28) with a mean age of 40.7 years (SD = 14.66), 18 of whom were men; 53.5% had completed undergraduate education. Fifty percent of the patients had depressive disorder and 50% had anxiety disorder.

Acceptability and Specific Benefits

According to the study, 60.7% of patients expressed interest in participating in this type of treatment and willingness to devote time and effort to home exercises and completion of questionnaires; 42.9% would be willing to undergo this treatment on a once-weekly basis.

Over 75% of the patients rated the intervention as understandable and feasible. Patients also stated that they would recommend this type of treatment to someone with depression (82.1%; **Table 1**).

Intervention Characteristics

As for the intervention's characteristics, 67.9% of patients felt more comfortable with meditation rather than writing their thoughts on paper (21.4%). Furthermore, 67.9% of patients reported owning a cell phone or other device to listen to the audio

TABLE 1 | Intervention acceptability questionnaire.

Intervention acceptability and comprehension		**Yes**	**Maybe**	**No**
I was able to understand the mindfulness framework	Depression	14 (82.4%)	3 (17.6%)	0 (0%)
	Anxiety	8 (88.9%)	0 (0%)	1 (11.1%)
I found the raisin exercise helpful to the purpose of the section	Depression	15 (88.2%)	2 (11.8%)	0 (0%)
	Anxiety	8 (88.9%)	1 (11.1%)	0 (0%)
I felt comfortable to perform the mindfulness exercise	Depression	15 (88.2%)	1 (5.9%)	1 (5.9%)
	Anxiety	8 (88.9%)	0 (0%)	1 (11.1%)
I would be capable of performing mindfulness exercise at home	Depression	13 (76.5%)	3 (17.6%)	1 (5.9%)
	Anxiety	8 (88.9%)	1 (11.1%)	0 (0%)
I was able to understand the meaning of cognitive behavior therapy	Depression	14 (82.4%)	3 (17.6%)	0 (0%)
	Anxiety	9 (100%)	0 (0%)	0 (0%)
I would be capable of performing this type of writing exercise at home	Depression	15 (88.2%)	2 (11.8%)	0 (0%)
	Anxiety	8 (88.9%)	1 (11.1%)	0 (0%)
I found this type of treatment complicated	Depression	2 (11.8%)	3 (17.6%)	12 (70.6%)
	Anxiety	0 (0%)	3 (33.3%)	6 (66.7%)
I would recommend this type of treatment to someone with depression	Depression	13 (76.5%)	4 (23.5%)	0 (0%)
	Anxiety	8 (88.9%)	1 (11.1%)	0 (0%)
I would like to take part in this type of treatments	Depression	11 (64.6%)	6 (45.3%)	0 (0%)
	Anxiety	5 (55.6%)	4 (44.4%)	0 (0%)
I would be available to make this treatment once weekly	Depression	7 (41.2%)	8 (47.1%)	2 (11.8%)
	Anxiety	*3 (33.3%)*	6 (66.7%)	0 (0%)
Would you commit yourself to put time and effort into home practices and fill out questionnaires?	Depression	9 (52.9%)	7 (41.2%)	1 (5.9%)
	Anxiety	*3 (33.3%)*	6 (66.7%)	0 (0%)
Intervention specific benefits				
I found that treatment would be useful to me	Depression	12 (70.6%)	5 (29.4%)	0 (0%)
	Anxiety	8 (88.9%)	1 (11.1%)	0 (0%)
This treatment would help me handle with my negative thoughts	Depression	14 (82.4%)	3 (17.6%)	0 (0%)
	Anxiety	8 (88.9%)	1 (11.1%)	0 (0%)
Would this type of treatment reduce my anxiety?	Depression	11 (64.7%)	6 (35.3%)	0 (0%)
	Anxiety	8 (88.9%)	1 (11.1%)	0 (0%)
	Anxiety	7 (77.8%)	1 (11.1%)	1 (11.1%)
This type of treatment would improve my well-being	Depression	10 (58.8%)	6 (35.3%)	1 (5.9%)
	Anxiety	8 (88.9%)	1 (11.1%)	0 (0%)

content, and 50% of patients preferred individual treatment, while 14.3% preferred group therapy.

Depression and Anxiety Outcomes

We also divided patients according to primary diagnosis between depression and anxiety disorder. The two groups of patients had similar and positive answers in the acceptability and comprehension questionnaire (>70%). Meanwhile, the questions on commitment showed a lower response, where patients with depression expressed less commitment than patients with anxiety disorder (with a difference of some 20% in their commitment to invest time and effort in home exercises and completion of questionnaires).

Regarding the answers on specific benefits, there was wide variation between patients with depression and anxiety. Patients with anxiety disorder were more likely to consider the treatment useful, compared to patients with depression (18% difference), thus emphasizing that patients with anxiety disorder were more aware of their wellbeing than patients with depression (30%). Comparing overall and specific benefits, patients with depression were 25% more likely than patients with anxiety to consider the treatment beneficial overall. Meanwhile, patients with anxiety disorder were 24.2% more likely to acknowledge specific benefits in their symptoms (**Table 1**).

Concerning the intervention's characteristics, patients with anxiety disorder had more devices like smartphones than patients with depression. Patients with anxiety disorder also had more difficulty with schedules than patients with depression (36.6% difference).

DISCUSSION

The aim of this brief study was to explore the impact of patients' understanding of MBCT and its applicability to the Brazilian population. Patients who completed the intervention described it as comprehensible and acceptable. Prior studies on MBCT have found that most patients describe MBCT as acceptable, beneficial (Finucane and Mercer, 2006), and easy to understand (Phang et al., 2015).

One study of MBCT in a heterogeneous group of adult psychiatric outpatients applied the Credibility/Expectancy Questionnaire (Devilly and Borkovec, 2000) to 26 participants at the end of session two. This credibility questionnaire assesses patients' willingness to recommend the treatment to others. The results indicated high confidence in recommending MBCT (Ree and Craigie, 2007); 82.1% of patients in the study reported that they would recommend the treatment to persons with depression.

In a previous study (Stafford et al., 2015), 95% of women completing the MBCT program reported high likelihood of continuing their mindfulness practice. We found that most patients approved the intervention and expressed their desire to commit to the treatment.

With regard to specific benefits, 75% of patients stated that "the treatment would be useful to me," compared to a pilot study by Stafford in which 93% of patients found MBCT helpful (2014). Another interesting finding was that more than half of the patients reported discomfort in writing their thoughts on paper, which should be taken into consideration when developing the protocol. In fact, there is an informal consensus between cognitive therapists brought many times in meetings and congresses regarding a tendency of the Brazilian people to dislike and do less homework from therapy due to its cultural aspects. Brazilian population overall presents flexible rules, like tolerating delays and preferring spontaneity. Perhaps to some populations, the demand for homework should be revised.

Our results also identified differences between patients with anxiety versus depression, where patients with anxiety disorder were more likely to believe in specific benefits in their symptoms. These results are in accordance with the psychopathology of the depression, in which negative thoughts related to self-efficacy and a catastrophic perspective about the future are core features (Sugiura and Sugiura, 2016).

Although mindfulness-based treatment has always been typically the prerogative of the third wave of cognitivism, this can also be conjugated from a psychodynamic perspective (Bianco et al., 2016), thus allowing to argue some possible future developments in the practice of mindfulness as a treatment applicable in many condition and settings even in the Brazilian context.

A significant limitation to conclusions drawn from the study is the small sample size and a simple statistical analysis in the baseline MBCT session. Our group future research will focus on the results of psychotherapy in association with the results of this "baseline session," enabling us to predict factors associated with success in this treatment modality. Furthermore, it is a goal of our group to amplify the use of meditation techniques to a wide broad population, and not to stay strict to diagnostic sample.

AUTHOR CONTRIBUTIONS

MR designed the study. MR, CC, LP, and IB collected, analyzed, and interpreted the data. AN, JA, and ML drafted and revisioned the manuscript. SM, AN, JA, and ML approved the final version of the manuscript.

REFERENCES

Ablon, J. S., and Jones, E. E. (1999). Psychotherapy process in the national institute of mental health treatment of depression collaborative research program. *J. Consult. Clin. Psychol.* 67, 64–75. doi: 10.1037/0022-006X.67.1.64

Amorim, P. (2000). Mini International Neuropsychiatric Interview (MINI): validação de entrevista breve para diagnóstico de transtornos mentais. *Revista Brasileira de Psiquiatria* 22, 106–115. doi: 10.1590/S1516-44462000000300003

Beck, A. T. (1979). *Cognitive Therapy of Depression*. New York, NY: Guilford Publications.

Beck, J. S., and Beck, A. T. (2011). *Cognitive Behavior Therapy, Second Edition: Basics and Beyond.* New York, NY: Guilford Publications.

Bianco, S., Barilaro, P., and Palmieri, A. (2016). Traditional meditation, mindfulness and psychodynamic approach: an integrative perspective. *Front. Psychol.* 7:552. doi: 10.3389/fpsyg.2016.00552

Bordin, E. S. (1979). The generalizability of the psychoanalytic concept of the working alliance. *Psychother. Theory Res. Pract.* 16:3. doi: 10.1037/h0085885

Campos, C., Mesquita, F., Marques, A., Trigueiro, M., Orvalho, V., and Rocha, N. B. (2015). Feasibility and acceptability of an exergame intervention for schizophrenia. *Psychol. Sport Exerc.* 19, 50–58. doi: 10.1016/j.psychsport.2015.02.005

Devilly, G. J., and Borkovec, T. D. (2000). Psychometric properties of the credibility/expectancy questionnaire. *J. Behav. Ther. Exp. Psychiatry* 31, 73–86. doi: 10.1016/S0005-7916(00)00012-4

Finucane, A., and Mercer, S. W. (2006). An exploratory mixed methods study of the acceptability and effectiveness of mindfulness-based cognitive therapy for patients with active depression and anxiety in primary care. *BMC Psychiatry* 6:14. doi: 10.1186/1471-244x-6-14

Grossman, P., Niemann, L., Schmidt, S., and Walach, H. (2004). Mindfulness-based stress reduction and health benefits: a meta-analysis. *J. Psychosom. Res.* 57, 35–43. doi: 10.1016/S0022-3999(03)00573-7

Hatcher, R. L., and Barends, A. W. (1996). Patients' view of the alliance of psychotherapy: exploratory factor analysis of three alliance measures. *J. Consult. Clin. Psychol.* 64, 1326–1336. doi: 10.1037/0022-006X.64.6.1326

Horvath, A. O., and Symonds, B. D. (1991). Relation between working alliance and outcome in psychotherapy: a meta-analysis. *J. Couns. Psychol.* 38, 139–149. doi: 10.1037/0022-0167.38.2.139

Jarrett, R. B., Vittengl, J. R., Clark, L. A., and Thase, M. E. (2011). Skills of Cognitive Therapy (SoCT): a new measure of patients' comprehension and use. *Psychol. Assess.* 23, 578–586. doi: 10.1037/a0022485

Kabat-Zinn, J., and Hanh, T. N. (2013). *Full Catastrophe Living (Revised Edition): Using the Wisdom of Your Body and Mind to Face Stress, Pain, and Illness*. New York, NY: Random House Publishing Group.

Kvillemo, P., Brandberg, Y., and Branstrom, R. (2016). Feasibility and outcomes of an internet-based mindfulness training program: a pilot randomized controlled trial. *JMIR Ment. Health.* 3:e33. doi: 10.2196/mental.5457

Mannarini, S., and Boffo, M. (2014). An implicit measure of associations with mental illness versus physical illness: response latency decomposition and stimuli differential functioning in relation to IAT order of associative conditions and accuracy. *PLoS One* 9:e101911. doi: 10.1371/journal.pone.0101911

Phang, C. K., Mukhtar, F., Ibrahim, N., Keng, S.-L., and Mohd Sidik, S. (2015). Effects of a brief mindfulness-based intervention program for stress management among medical students: the mindful-gym randomized controlled study. *Adv. Health Sci. Educ.* 20, 1115–1134. doi: 10.1007/s10459-015-9591-3

Ree, M. J., and Craigie, M. A. (2007). Outcomes following mindfulness-based cognitive therapy in a heterogeneous sample of adult outpatients. *Behav. Change* 24, 70–86. doi: 10.1375/bech.24.2.70

Segal, Z. V., Williams, J. M. G., and Teasdale, J. D. (2002). *Mindfulness-Based Cognitive Therapy for Depression, First Edition: A New Approach to Preventing Relapse*. New York, NY: Guilford Publications.

Segal, Z. V., Williams, J. M. G., Teasdale, J. D., and Kabat-Zinn, J. (2012). *Mindfulness-Based Cognitive Therapy for Depression*. New York, NY: Guilford Publications.

Stafford, L., Thomas, N., Foley, E., Judd, F., Gibson, P., Komiti, A., et al. (2015). Comparison of the acceptability and benefits of two mindfulness-based interventions in women with breast or gynecologic cancer: a pilot study. *Support Care Cancer* 23, 1063–1071. doi: 10.1007/s00520-014-2442-6

Sugiura, T., and Sugiura, Y. (2016). Relationships between refraining from catastrophic thinking, repetitive negative thinking, and psychological distress. *Psychol. Rep.* 119, 374–394. doi: 10.1177/0033294116663511

Teasdale, J. D., Williams, J. M. G., and Segal, Z. V. (2016). *Manual Prático de Mindfulness: (meditação da atenção plena): Um Programa de oito Semanas Para Libertar Você da Depressão, da Ansiedade e do Estresse Emocional. Pensamento*.

Williams, J. M., Russell, I., and Russell, D. (2008). Mindfulness-based cognitive therapy: further issues in current evidence and future research. *J. Consult. Clin. Psychol.* 76, 524–529. doi: 10.1037/0022-006x.76.3.524

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OPINION
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Yoga as a Holistic Treatment for Chronic Illnesses: Minimizing Adverse Events and Safety Concerns

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INTRODUCTION

Yoga is widely practiced for its health benefits (Alter, 2004; Singleton, 2010), especially for chronic non-communicable diseases (Holte and Millis, 2013). The Consortium of Academic Health Centers for Integrative Medicine located at Michigan, U.S. teaches yoga in most of its branches (Holte and Millis, 2013; https://imconsortium.org/)[1]. Yoga is one of the top ten complementary health practices used by adults in the U.S. where 45 percent of this population have at least one chronic illness (Wu and Green, 2000). Two meta-analyses were carried out to examine yoga in the context of stroke (Lawrence et al., 2017; Thayabaranathan et al., 2017). The authors of the meta-analyses concluded that yoga is effective but did not report any adverse event associated with yoga practice (Lawrence et al., 2017; Thayabaranathan et al., 2017). Despite this, safety is important during stroke rehabilitation, especially for practices which involve maintaining balance. Similarly, we found that in meta-analyses of yoga used for multiple sclerosis or cardiac disease there was a lack of information related to the safety of yoga interventions as adverse events related to yoga practice were not usually mentioned (Cramer et al., 2014, 2015a). Apart from this, when safety related data were reported there were no adverse events (Cramer et al., 2014, 2015b). Safety issues in yoga practice apply to all chronic illnesses.

The Need for Safety in Yoga Practice

An ancient *Hatha* yoga text gives importance to the method of practice, stating "….by the proper practice of *pranayama* (voluntarily regulated yoga breathing), all diseases are eradicated, whereas through the improper practice all diseases can arise" (*Hatha Yoga Pradipika*, *Circa* 1500 A.D., Chapter II Verse 16; Muktibodhananda, 1998).

William Broad (2012) attempted to highlight the adverse events which could occur with yoga practice in his book "*The Science of Yoga: The Risks and Rewards*" (Broad, 2012). This evoked a wide range of responses, especially from those who have benefitted from yoga practice. However the adverse events related to yoga cannot be discounted.

Hence this opinion article has two aims. (i) The first aim is to cite published examples of adverse events occurring from yoga practice due to: (a) an unusually long duration of yoga practice, (b) practice of a yoga technique more frequently than is recommended, (c) excess strain on a specific joint during yoga practice, or (d) ignoring any health condition which would be a contraindication for yoga practice. (ii) The second aim is to suggest recommendations to improve safety and reduce adverse events related to yoga practice as therapy.

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[1] Academic Consortium for Integrative Medicine and Health [Internet]. *Academic Consortium for Integrative Medicine and Health* [cited 2019 Feb 15]. Available online at: https://imconsortium.org/

Search Strategy for Published Reports on Adverse Events Related to Yoga Practice

The search strategy was carried out in two stages. (i) The authors identified common reasons which could lead to an adverse event due to yoga practice, based on (a) the authors' experience with yoga practitioners and (b) their awareness of adverse events resulting from yoga reported by conventionally trained medical practitioners. This information was in the form of oral reports from 1997 to 2018. The most common reasons for adverse events were (a) practicing yoga for an extra duration, (b) practicing yoga more frequently than is recommended, (c) excess strain on a specific joint during yoga practice and (d) adverse event related to a prior health condition. (ii) Two researchers independently searched PubMed abstracts from 1970 to 2018 for examples to demonstrate the four points mentioned above. Four examples were selected as the most appropriate and are described in the manuscript.

Published Reports on Examples of the Four Causes of Adverse Events Following Yoga Practice

An Example of Practicing Yoga for an Extra Duration

A 22 year old male, healthy college student who practiced the diamond pose (*vajrasana,* in Sanskrit) for 6 h a day for 2 months reported an abnormal gait due to foot drop (Chusid, 1971). The student had 18 months of experience in yoga. The subject recovered from foot drop after 9 weeks of discontinuing the posture. Practicing a yoga posture for 6 h a day is unusual; the recommended duration is 5–10 min for a beginner and not more than 30 min for an experienced practitioner (The divine life society[2], http://yogaindepth.blogspot.com/p/detailed-description-of-yoga-asanas.html)[3]. In this case foot drop could be considered a consequence of practicing a yoga posture for a longer duration than is recommended.

An Example of Practicing Yoga More Frequently Than Is Recommended

In certain cases it may not be the duration but the frequency of the practice which was excessive. Regurgitative cleansing (*kunjal-kriya* in Sanskrit) involves voluntarily induced vomiting after drinking saline water on an "empty stomach" upto a point where the practitioner feels the urge to vomit (Saraswati, 2012). This yoga cleansing technique resulted in dental erosion in a 38 year old male who had practiced the technique every morning for 12 years (Meshramkar et al., 2007). While an ancient *Hatha* Yoga text describes *kunjal kriya* as useful to reduce digestive disorders, it is stated that the practice should be done once a week under the supervision of an experienced yoga teacher (Saraswati, 2012). Endogenous gastric acid enters the oral cavity during vomiting (José et al., 2008). The pH of gastric acid is approximately 1.2, which is below the critical value for demineralization of the teeth (José et al., 2008). This may explain the dental erosion in the 38 year old male in the study cited above, where a yoga technique was practiced more frequently than is recommended.

An Example of Excess Strain on a Specific Joint During Yoga Practice

Another factor which could be responsible for the adverse events following yoga practice include techniques which could either strain a joint or makes it unstable (Nagura et al., 2002). A cross-sectional study conducted in southern Thailand included 576 persons (276 females; 40 years or older) without any rheumatic diseases (Tangtrakulwanich et al., 2007). The aim was to correlate radiographic knee osteoarthritis with the habit of sitting on the floor for various activities, in sitting postures which resembled yoga postures as mentioned below. Those participants who reported squatting (similar to the chair pose or *uttakatasana*), side-knee bending (similar to the hero pose or *veerasana*), the lotus pose (*padmasana*) and total life time floor activities in highest tertile, showed a two time increased risk of osteoarthritis of the knee compared to those in the lowest tertile of exposure to floor seated activities (Tangtrakulwanich et al., 2007). These postures involve extreme flexion of the knee which causes excessively large contact stress on the knee joint (Dahlkvist et al., 1982; Nagura et al., 2002), which in turn causes cartilage damage and also acts as a precursor for degenerative diseases of the joint. Whether squatting is indeed harmful definitely needs thorough investigation, however the report cited above suggests the necessity for such studies and for precautions during yoga practice.

An Example of an Adverse Event Related to a Prior Health Condition

Another factor which could result in ill effects of yoga practice is an existing condition which may predispose the practitioner to deformity or illness (Cramer et al., 2013). A case study reported that sitting in the lotus pose during a meditation session resulted in a spontaneous supracondylar femoral fracture in a 58 year old Buddhist monk who was human immunodeficiency virus (HIV) positive (Pinto Neto et al., 2011). Patients with the HIV virus have compromised bone density due to the use of antiretroviral therapies which are associated with bone loss and fractures (Puthanakit et al., 2012). The lotus pose exerts stress on the supracondylar femur through upward force from the ankles and downward force from the knees. Stress on the compromised femur of the patient who was HIV positive could have caused the supracondylar fracture. This case report shows the importance of knowing if a person practicing yoga has any health condition which could make it dangerous for them to practice specific yoga techniques.

Reporting of Adverse Events in Existing Trials

In contrast to the above mentioned reports on the adverse events associated with specific yoga practices there are a large number of studies on the benefits of yoga practice to improve physical and mental health (Hagen and Nayar, 2014; Jeter et al., 2015).

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[2] Compression Design [Internet]. *How Long to Hold a Yoga Pose* [cited 2019 Mar 19]. Available online at: https://www.compressiondesign.com/how-long-to-hold-a-yoga-pose/

[3] Yoga Asanas in Depth [Internet]. *Detailed Description of Yoga Asanas Vajrasana* [cited 2018 Aug 27]. Available online at: http://yogaindepth.blogspot.com/p/detailed-description-of-yoga-asanas.html

TABLE 1 | Recommendations for safe use of yoga at different levels.

Persons involved	Recommendations
YOGA PRACTITIONER	
a. Yoga practitioner (a person with normal health who learns and practices yoga for his/her own physical, psychological, cognitive, social and spiritual wellbeing)	1. The person should be motivated to learn yoga. 2. Yoga practice should be under the supervision of a reliable and trained yoga instructor. 3. The yoga practitioner should view yoga instructors with respect, but should not be confused by concepts of a "*guru*" or the "need to surrender" which could lead to weakness, a dissolution of boundaries and hence exploitation (Khouri, 2018, https://www.yogitimes.com/article/yoga-business-teacher-student-boundaries-relationships-friendship). 4. Any earlier accident/injury or surgery should be mentioned to the yoga instructor. 5. The person should approach yoga for self-improvement without a sense of competiveness which could lead to going beyond his/her physical ability and hence resulting in injury.
b. Yoga practitioner (a person with a diagnosed health condition who learns and practices yoga primarily for the management of his/her health condition as well as his/her own physical, psychological, cognitive and spiritual wellbeing)	1. The person should give a detailed description of their medical condition to their yoga therapist. 2. The person should be clear about the objectives to practice yoga i.e., the practice of yoga to alleviate symptoms of a chronic illness and possibly to help manage the cause of the condition. 3. Yoga practitioner should have realistic expectations and not expect miraculous cures. 4. There should not be any attempt to modify the practice given to the person. For example if a person misses the yoga session on 1 day increasing the practice the next day may not be appropriate. 5. If the yoga practitioner notices any changes in their symptoms or their medication is altered by the physician, this should be reported to yoga therapist.
Yoga instructor (a person who has undergone training to teach yoga to healthy persons)	1. The person should be motivated to teach yoga. 2. The yoga instructor should be experienced in yoga practice and theory especially with an understanding about the exact way in which a yoga technique should be practiced as well as the duration, frequency and contraindications of the practice. This should be based on knowledge of traditional yoga texts (please see the footnote below)[a] and the commentaries written on them. 3. A yoga instructor should be aware about the contraindications of yoga practices. 4. The yoga instructor should communicate with complete clarity about the method of practice and the contraindications of the practice. 5. All yoga instructors should have basic knowledge of physiology, functional anatomy and biomechanics. 6. The person should know the basics of first aid (e.g., treating minor injuries such as sprain). 7. A yoga instructor should be able to report an adverse event with sufficient accuracy (even with a diagram if necessary) to a relative of a yoga practitioner or even to a medical practitioner (if necessary).
Yoga therapist (a person who has undergone training to teach yoga for therapeutic benefits to patients)	1. A yoga therapist should have detailed case histories and knowledge of their patients. 2. A yoga therapist should be cautious attempting to treat patients who are weak, liable to fall, have poor balance or are otherwise "high risk cases." 3. Yoga therapists require additional training compared to a yoga instructor. They need to know therapeutic yoga. in theory and practice and additional information about basic diagnostic methods and the disorders they may treat. 4. A yoga therapist should be able to record the pulse, blood pressure and body temperature accurately at the very least. 5. A yoga therapist needs knowledge of first aid and on-the-spot emergency treatments (e.g., cardiopulmonary resuscitation, managing choking, bleeding and fractures) as well as the contact details of a properly equipped hospital nearby. 6. If a person experiences any injury or harm during yoga, the yoga therapist should be able to report it to a doctor with details about the patient's medical history, the yoga practice (with a diagram if necessary) and the injury.
A doctor (a conventional medical practitioner)	A doctor who treats a patient with an injury or other discomfort believed to be arising from yoga should ask for clear details about the yoga practice performed, its duration, method and frequency. This information may be supplemented with diagrams or source material. Yoga practitioners should be clear that they are not being disloyal to their yoga teacher/school when giving this information.

[a] *Hatha Yoga Pradeepika (Circa 1500 A.D.; Muktibodhananda, 1998), Gheranda Samhita (Circa 1700 A.D.; Saraswati, 2012), Patanjali's Yogasutras (Circa 900 B.C.; Ramdev, 2008) and Bhagwad Gita (Circa 400–600 B.C., Prabhupada, 2015).*

Most of the studies which were conducted to assess the efficacy of yoga practice did not identify or report adverse events in the trials (Cramer et al., 2015b) In the meta-analyses of yoga used for stroke, multiple sclerosis and cardiac disease there was a lack of information about the safety of yoga practice, as adverse events were not usually mentioned (Cramer et al., 2014, 2015a; Lawrence et al., 2017; Thayabaranathan et al., 2017). This may be due to the fact that in such studies the yoga interventions were designed and delivered under the supervision of experienced yoga teachers (Cramer et al., 2015b) whereas in the four studies mentioned above on the adverse effects associated with yoga practice the subjects were either (i) practicing the yoga technique incorrectly, (ii) having precondition(s) related to the reported adverse effect, or (iii) were not aware that the particular yoga technique they were performing could worsen the precondition that they had. It could also be that adverse events were not reported or noted by the yoga teachers as they were not trained to do so.

Precautions for Safe Yoga Practice

Descriptions From the Traditional Yoga Texts

Ancient *Hatha* yoga texts emphasize that yoga practices should be performed under the supervision of an able teacher stating "one should practice yoga as instructed by his guru" (*gurupadiūha-mārgheṇa yoghameva samabhyaset,* in Sanskrit; *Hatha Yoga Pradipika*, *Circa* 1500 A.D., Chapter I, Verse 14; Muktibodhananda, 1998). Hence though there is an increase in the number of studies reporting the efficacy of yoga to improve physical and mental health, the practice should be done with caution and under the supervision of an experienced yoga teacher.

Organizations Related to Providing Guidelines for Yoga Practice in India, the U.S. and Australia

There are known organizations to train yoga teachers and give them guidelines in different parts of the world. Examples are cited here from India, the U.S. and Australia. This is not all-inclusive as (i) there may be other organizations in India, U.S. and Australia and (ii) other countries also have similar organizations. Hence this is a non-representative description.

In India there are three main institutions which give guidelines for yoga practice. These are (i) the Morarji Desai National Institute of Yoga[4] started in 1976 as the Central Research Institute of Yoga which continued as MDNIY from 1988, (ii) the Central Council for Research in Yoga and Naturopathy (Central Council for Research in Yoga & Naturopathy, www.ccryn.gov.in)[5] and (iii) the Indian Yoga Association (Indian Yoga Association, http://www.yogaiya.in/about/)[6]. The CCRYN and the IYA were established in 1978 and 2008, respectively. The MDNIY and CCRYN are non-profit organizations funded by the Ministry of AYUSH, Government of India while the IYA is a non-profit, self-regulatory body approved by the Ministry of AYUSH and the Ministry of Health and Family Welfare, Government of India. The three organizations have no specific guidelines for reporting adverse events which occur during yoga practice.

In the U.S. there are the International Association of Yoga Therapists (IAYT, https://yogatherapy.health/about-iayt/)[7] and Yoga Alliance (www.yogaalliance.org)[8] which provide guidelines about teaching yoga. IAYT was established in 1989 while Yoga Alliance was started in 1997. The institutions are not-for-profit organizations which prepare national standards for training of yoga teachers in the United States and support research and education related to yoga as a therapy. These organizations do not have guidelines for adverse event reporting related to yoga practice. Also the National Center for Complementary and Integrative Health (Briggs, 2013) has mentioned safety concerns in yoga practice but there are no suggestions about reporting of adverse events due to yoga.

In Australia, the Australasian Association of Yoga Therapists (www. yogatherapy.org.au/)[9] and Yoga Australia (www. yogaaustralia.org.au)[10] are two associations which provide guidelines for yoga teachers and those who use yoga therapy. The associations were established in 1991 and 1999 respectively. They are not-for-profit organizations which were founded to bring yoga teachers from different traditions together and establish yoga therapy as a recognized, professional mode of treatment. Both these associations have no specific guidelines for reporting adverse events due to yoga practice.

Recommendations for Safe Use of Yoga at Different Levels

It is recommended that (a) the duration and frequency of yoga practice, (b) the amount of strain on a specific joint during yoga practice, and (c) prior health conditions should be taken into account before starting yoga, to minimize adverse events associated with yoga practice. At various levels care should be taken to ensure that yoga practice is safe and to reduce the chance of adverse events. The recommendations for the safe use of yoga at different levels have been summarized in **Table 1**.

There appears to be no organization responsible to record adverse events related to yoga. Hence an existing organization should take the initiative by having a centralized mechanism to report and track adverse events in a standard way. Organizations within a country and in different countries should come to a consensus so that this information is reported uniformly. This would be useful for yoga practitioners, yoga instructors and yoga therapists. It would also act as a resource for teaching and even to form policies.

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ST compiled the manuscript. SS and NK assisted in compilation of the manuscript. AB assisted in compilation of the manuscript and provided the infrastructure.

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[4] Morarji Desai National Institute of Yoga [Internet]. *Morarji Desai National Institute of Yoga: An Autonomous Organization Under Ministry of AYUSH Government of India*. Available online at: http://www.yogamdniy.nic.in/ (accessed February 15, 2019).

[5] Central Council for Research in Yoga and Naturopathy [internet]. *Central Council for Research in Yoga and Naturopathy: An Autonomous Body Under Ministry of AYUSH* [cited 2019 Feb 15]. Available online at: http://ccryn.gov.in/

[6] Indian Yoga Association [internet]. *About – Indian Yoga Association* [cited 2019 Feb 15]. Available online at: http://www.yogaiya.in/about/

[7] The International Association of Yoga Therapists [Internet]. *About IAYT* [cited 2019 Feb 15]. Available online at: https://www.iayt.org/page/AboutLanding

[8] Yoga Alliance [Internet]. *Yoga Alliance* [cited 2019 Feb 15]. Available online at: https://www.yogaalliance.org/

[9] The Australasian Association of Yoga Therapists [internet]. *The Australasian Association of Yoga Therapists* [cited 2019 Feb 15]. Available online at: http://yogatherapy.org.au/

[10] Yoga Australia [Internet]. *Yoga Australia* [cited 2019 Feb 15]. Available online at: https://www.yogaaustralia.org.au/

REFERENCES

Alter, J. (2004). *Yoga in Modern India: The Body Between Science and Philosophy*. Princeton, NJ: Oxford University Press.

Briggs, J. (2013). *The Safety of Yoga*. Available online at: https://nccih.nih.gov/research/blog/safeyoga (accessed March 19, 2019).

Broad, W. J. (2012). *The Science of Yoga: The Risks and the Rewards*. New York, NY: Simon and Schuster.

Chusid, J. (1971). Yoga foot drop. *JAMA* 217, 827–828. doi: 10.1001/jama.1971.03190060065025

Cramer, H., Krucoff, C., and Dobos, G. (2013). Adverse events associated with yoga: a systematic review of published case reports and case series. *PLoS ONE* 8:e75515. doi: 10.1371/journal.pone.0075515

Cramer, H., Lauche, R., Azizi, H., Dobos, G., and Langhorst, J. (2014). Yoga for multiple sclerosis: a systematic review and meta-analysis. *PLoS ONE* 9:e112414. doi: 10.1371/journal.pone.0112414

Cramer, H., Lauche, R., Haller, H., Dobos, G., and Michalsen, A. (2015a). A systematic review of yoga for heart disease. *Eur. J. Prev. Cardiol.* 22, 284–295. doi: 10.1177/2047487314523132

Cramer, H., Ward, L., Saper, R., Fishbein, D., Dobos, G., and Lauche, R. (2015b). The safety of yoga: a systematic review and meta-analysis of randomized controlled trials. *Am. J. Epidemiol.* 82, 281–293. doi: 10.1093/aje/kwv071

Dahlkvist, N. J., Mayo, P., and Seedhom, B. B. (1982). Force during squatting and rising from a deep flexion. *N. Engl. J. Med.* 11, 69–76.

Hagen, I., and Nayar, U. S. (2014). Yoga for children and young people's mental health and well-being: research review and reflections on the mental health potentials of yoga. *Front. Psychiatry*. 5:35. doi: 10.3389/fpsyt.2014.00035

Holte, A., and Millis, P. J. (2013). "Yoga and chronic illness," in *Chronic Illness, Spirituality, and Healing*, eds M. J. Stoltzfus, R. Green, and D. Schumn (New York, NY: Palgrave Macmillan), 141–163.

Jeter, P. E., Slutsky, J., Singh, N., and Khalsa, S. B. S. (2015). Yoga as a therapeutic intervention: a bibliometric analysis of published research studies from 1967 to 2013. *J. Altern. Complement. Med.* 21, 586–592. doi: 10.1089/acm.2015.0057

José, V., Gaëtan, V., and Paul, M. (2008). Dental lesions associated with exogenous and endogenous acids. *Acta Endoscopica* 38, 263–281. doi: 10.1007/s101900800005

Khouri, H., (2018). *Setting Boundaries Between Yoga Teachers and Students*. Available online at: https://www.yogitimes.com/article/yoga-business-teacher-student-boundaries-relationships-friendship (accessed August 27, 2018).

Lawrence, M., Celestino, J. F. T., Matozinho, H. H. S., Govan, L., Booth, J., and Beecher, J. (2017). Yoga for stroke rehabilitation (review). *Cochrane Database Syst. Rev.* 12:CD011483. doi: 10.1002/14651858.CD011483.pub2

Meshramkar, R., Patil, S. B., and Patil, N. P. (2007). A case report of patient practising yoga leading to dental erosion. *Int. Dent. J.* 57, 184–186. doi: 10.1111/j.1875-595X.2007.tb00123.x

Muktibodhananda, S. (1998). *Hatha Yoga Pradipika, 3rd Edn*. Munger: Yoga Publications Trust.

Nagura, T., Dyrby, C. O., Alexander, E. J., and Andriacchi, T. P. (2002). Mechanical loads at the knee joint during deep flexion. *J. Orthop. Res.* 20, 881–886. doi: 10.1016/S0736-0266(01)00178-4

Pinto Neto, L. F. S., Eis, S. R., and Miranda, A. E. (2011). Spontaneous supracondylar femoral fracture in an HIV patient in lotus position. *J. Clin. Densitom*. 14, 74–76. doi: 10.1016/j.jocd.2010.11.002

Prabhupada, A. C. B. S. (2015). *Bhagvad Gita As it Is*. Mumbai: Bhaktivedanta Book Trust.

Puthanakit, T., Saksawad, R., Bunupuradah, T., Wittawatmongkol, O., Chuanjaroen, T., Ubolyam, S., et al. (2012). Prevalence and risk factors of low bone mineral density among perinatally HIV-infected Thai adolescents receiving antiretroviral therapy. *J. Acquir. Immune Defic. Syndr*. 61, 477–483. doi: 10.1097/QAI.0b013e31826ea89b

Ramdev, S. (2008). *Maharshi Patanjali's Yogadarshana (The Yoga Philosophy)*. Haridwar: Divya Prakashan.

Saraswati, S. N. (2012). *Gheranda Samhita, 1st Edn*. Munger: Yoga Publications Trust.

Singleton, M. (2010). *Yoga Body: The Origins of Modern Postural Practice*. New York, NY: Oxford University Press. doi: 10.1093/acprof:oso/9780195395358.001.0001

Tangtrakulwanich, B., Chongsuvivatwong, V., and Geater, A.,F. (2007). Habitual floor activities increase risk of knee osteoarthritis. *Clin. Orthop. Relat. Res*. 454, 147–154. doi: 10.1097/01.blo.0000238808.72164.1d

Thayabaranathan, T., Andrew, N. E., Immink, M. A., Hillier, S., Stevens, P., and Stolwyk, R. (2017). Determining the potential benefits of yoga in chronic stroke care: a systematic review and meta-analysis. *Top. Stroke Rehabil.* 24, 279–287. doi: 10.1080/10749357.2016.1277481

Wu, S. Y., and Green, A. (2000). *Projection of Chronic Illness Prevalance and Cost Inflation*. Santa Monica, CA: RAND Health.

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Psychiatric Comorbidity in Neurological Disorders: Towards a Multidisciplinary Approach to Illness Management in the United Arab Emirates

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Aim: To determine the prevalence of mood and anxiety disorders in undiagnosed patients attending neurological services, and detect rates of referral to and attendance of psychiatric services.

Methods: Depressive symptoms and anxiety were assessed in 395 adult patients with primary diagnoses of neurological disorders. The Patient Health Questionnaire nine-item depression scale (PHQ-9), and Generalized Anxiety Disorder seven-item scale (GAD-7) were administered. Demographic details of the patients were recorded. Referral to and attendance of psychiatric services were recorded for patients scoring within the clinical range of depression and anxiety disorders (scores > 10).

Results: There was a 39% prevalence rate of depressive symptoms, 34% rate of anxiety, and 35.4% concurrent rate of both disorders in this cohort. The referral rate to psychiatric services was 33.6%, and attendance rate was 47.8%. There was significant association between severity of psychiatric symptoms and referral to psychiatric services, as well as significant association between comorbid psychiatric symptoms and attendance to psychiatric services.

Conclusion: Our results indicate similar prevalence rates of comorbid psychiatric symptoms to studies carried out in the Middle East and North Africa (MENA) region and relatively high attendance and referral rates to psychiatric services.

Implications: The results shed light on the clinical profile of patients in this region and support the need for integrated collaborative medical services. Moreover, findings have important implications for health care policies pertaining to resource distribution and funding.

Keywords: psychiatric comorbidity, neurological disorders, illness management, multidisciplinary approach, integrated collaborative medical services, United Arab Emirates

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INTRODUCTION

Medical care has traditionally been dominated by a separation between disciplines catering to physiological symptoms versus those catering to psychological symptoms (1). Emerging research points to psychiatric comorbidity in the primary care setting and in specialized services, especially with chronic conditions like cardiovascular disease and diabetes. Among psychiatric comorbidities, depression and anxiety disorders are the most prevalent and have been found to hinder treatment response, increasing disability and reducing functional outcome (2–6). Given the shared etiological processes between neurological disorders and psychiatric disorders, reports of 50% prevalence rates of depression and anxiety among neurology patients are not surprising (7). Despite ample evidence on comorbidity, the provision of psychiatric intervention for such patients remains lacking.

Several epidemiological studies have attempted to quantify psychiatric comorbidity in primary care and specialized services. In a Hungarian large-scale national community survey, Purebl et al. (8) reported that 52% of those with cardiovascular disease displayed symptoms of depression and anxiety, with 30% meeting the diagnostic criteria for depression. Similarly, a Belgian cross-sectional survey of primary care practices in the country revealed that although 5.4% of the 2,316 patients surveyed reported psychiatric complaints, 42.5% had an unreported psychiatric comorbidity (2). Mood and anxiety disorders were the most prevalent. Complications from diabetes are most prevalent in the presence of psychiatric disorders (6), and mortality rates increase in individuals with myocardial infarction if they also suffer from anxiety (7). Among 300 neurology patients surveyed in the UK, 47% met the criteria for a *Diagnostic and Statistical Manual of Disorders, Fourth Edition* (DSM-IV) diagnosis of depression and anxiety (4). In a Canadian community sample, individuals diagnosed with epilepsy were more likely to experience anxiety symptoms and had higher rates of suicidal ideation (9), and those with migraine were more likely to experience major depressive disorder, bipolar disorder, panic disorder, and social phobia (10). Moreover, it is often found that the patients with psychiatric symptoms are also those with the most disability and the least response to treatment, and are the most difficult to manage. They are also often the most frequent attendants in primary care services (5).

A multidisciplinary approach to disease management and education in primary care has been instrumental in managing the epidemic of psychiatric comorbidity in physical illnesses (11). While efforts are being seen in other parts of the world highlighting the need, such data is lacking in the United Arab Emirates (UAE). In recent years, studies have been carried out in the Arab Gulf region looking at prevalence and correlates of psychiatric disorders in patients attending primary care. Among those, one study found that 30% of patients with epilepsy showed clinically significant symptoms of depression and anxiety (12). Similarly, a study looking at psychiatric comorbidity in patients with type 2 diabetes in the UAE found a 12.5% prevalence rate of mental health concerns and a significant correlation between patients' mental health status and their primary diagnosis (13). Two independent studies looking at the impact of depression and anxiety on health-related quality of life among patients with a) epilepsy and b) multiple sclerosis found that depression and anxiety, along with the use of antidepressants, were among the highest predictors of patients' health-related quality of life (14, 15). A study that looked at the prevalence of psychiatric comorbidity in 1,046 primary health clinic attendees in Kuwait found a comorbidity rate of 20.4% between depressive symptoms, anxiety, and somatization (16); 42.7% of patients suffered from at least one type of disorder, while 11% had two, and 10.4% had symptoms of all three psychiatric disorders. Al-Otaibi and colleagues (17) found a 37.1% rate of depression in patients attending primary care in Kuwait, while Al-Qadhi et al. (18) found a 49.9% rate of depression in a similar cohort in Saudi Arabia.

While such studies are a promising start for the wider Gulf region, high prevalence rates of psychiatric disorders indicate the need for a multidisciplinary approach to disease management and provision of integrated health services. According to the Mental Health Atlas (19), there is inadequate provision and high stigmatization of mental health services in the Middle East. In the UAE, limited research in this area accounts for why medical practice remains behind in the implementation of a multidisciplinary approach. As such, the current study aims to bridge this gap by investigating the prevalence of concurrent depression and anxiety symptoms among patients attending only neurology services at a local outpatient center offering both psychiatric and neurological services. The current study capitalizes on the availability of these conjoint services to determine the prevalence of mood and anxiety disorders in patients seeking only neurological services at the center. Moreover, the study looks at whether concurrent depressive and anxiety symptoms are detected by the attending neurologist based on patient self-report, the severity threshold at which referral to psychiatric services does occur, and whether referred patients attend these services.

METHODS

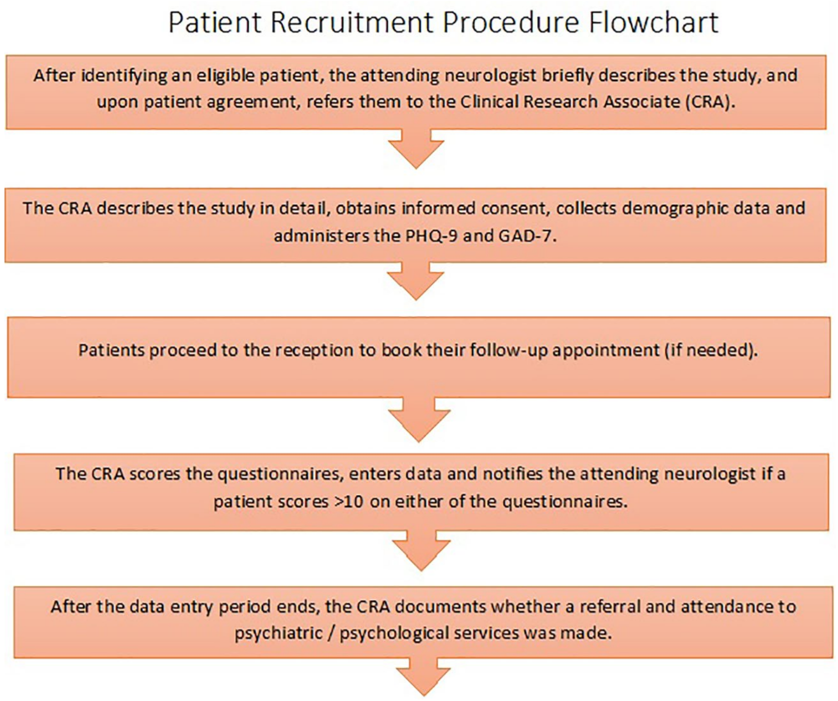
The study was granted ethics approval by the institutional review board at the American Center for Psychiatry and Neurology, Abu Dhabi, UAE. Patients were recruited between September 2016 and November 2017 and signed a written informed consent form to participate in the study. A chart displaying the patient recruitment procedure is shown in **Figure 1**.

Patients

A total of 395 Arabic- and English-speaking patients between the ages of 18 and 65 with a current diagnosable neurological disorder were included in this study. Patients who had a diagnosis of, or were being treated for, one or more psychiatric disorders were excluded from the study. Between September 2016 and November 2017, a total of 424 patients were approached to participate in the study. Only 395 agreed to participate and were included in the study.

Instruments

The Patient Health Questionnaire nine-item depression scale (PHQ-9) is a brief, self-administered tool for the screening and diagnosis of depression (20). It is based on the nine



After identifying an eligible patient, the attending neurologist briefly describes the study, and upon patient agreement, refers them to the Clinical Research Associate (CRA).

The CRA describes the study in detail, obtains informed consent, collects demographic data and administers the PHQ-9 and GAD-7.

Patients proceed to the reception to book their follow-up appointment (if needed).

The CRA scores the questionnaires, enters data and notifies the attending neurologist if a patient scores >10 on either of the questionnaires.

After the data entry period ends, the CRA documents whether a referral and attendance to psychiatric / psychological services was made.

FIGURE 1 | Patient recruitment procedure.

DSM-IV criteria for depression and can detect depression outcome and changes over time (21). The total score can range from zero to 27, and a score of >10 is indicative of the presence of depression. The PHQ-9 depression scale has been validated in the general population (22). Both the English and the validated Arabic (23) versions of the questionnaire were used in the study.

The Generalized Anxiety Disorder 7-item scale (GAD-7) (24) was used to screen for general anxiety disorder. It consists of a brief, seven-item questionnaire, and a score of >10 is indicative of the presence of generalized anxiety disorder. It has been validated for use in the general population (25). Both the English and the validated Arabic (26) versions were used in the study.

Data Collection and Safety Considerations

Patients were invited to complete the questionnaires at the end of their visit to the neurology clinic. To ensure patient safety, the clinical research associate routinely notified the attending neurologist if a patient scored >10 on either of the questionnaires; the attending neurologist then offered the patient referral to psychiatric services. Referral to psychiatry/psychology services by the neurologist and patient attendance were then recorded.

Statistical Analysis

Statistical Package for Social Sciences (SPSS), Version 22 (27), was used to analyze collected data. Descriptive statistics were used to determine a) the proportion of patients scoring in the clinically significant range, b) the proportion of those patients referred to psychiatric services, and c) the proportion of those referred who attended psychiatric services. Additionally, further analysis was done to determine the relationship between comorbid psychiatric symptoms and referral to psychiatric services, and again between comorbid psychiatric symptoms and attendance to psychiatry/psychology services.

RESULTS

A total of 395 (F: 55.2%, M: 44.8%) patients ranging between ages 18 and 64 (M = 36.14, SD = 9.71) visiting the neurology clinic at the American Center for Psychiatry and Neurology were enrolled in the study between September 2016 and November 2017. Sociodemographic characteristics of the sample are displayed in **Table 1**. Descriptive analysis was carried out for the following variables: sex, nationality, ethnicity, patient status, primary diagnosis, severity of psychiatric symptoms, referrals to psychiatric services, and psychiatric treatment. Emirati patients made up 36.7% of those enrolled, while non-Emiratis accounted for 63.3%. Of those enrolled, 319 (80.8%) were of Arab ethnicity, while the rest 76 (19.2%) were of various ethnic backgrounds, including African, Caucasian, South Asian, and Southeast Asian. There were a total of 219 (55.4%) new patients visiting the center for the first time, while the remaining 176 (44.6%) were returning patients. Of those enrolled, 102 (25.8%) had a primary diagnosis of headache (73.5% migraine with and without aura and 26.5% tension-type headache), 91 (23.1%) had epilepsy, 19 (4.8%) had multiple sclerosis, and the rest 184 (46.3%) had a variety of conditions classified under "other neurological disorders." These

TABLE 1 | Sociodemographic characteristics of the sample (n = 395).

Age (years)	**Mean: 36.14 ± 9.71**
	Range: 18–64
Sex	F: 218 (55.2%) M: 177 (44.8%)
Employment status	
Employed	216 (54.7%)
Unemployed	73 (18.5%)
Student	24 (6.1%)
Other	82 (20.8%)
Marital status	
Single	129 (32.7%)
Married	253 (64.1%)
Divorced	12 (3.0%)
Widowed	1 (.3%)
Nationality	
Emirati	145 (36.7%)
Non-Emirati	250 (63.3%)
Ethnicity	
African	4 (1.0%)
Arab	319 (80.8%)
South Asian	13 (3.3%)
Southeast Asian	11 (2.8%)
Caucasian	47 (11.9%)
Other	1 (.3%)
Primary diagnosis	
Epilepsy	91 (23.0%)
Headache	102 (25.8%)
Multiple sclerosis	19 (4.8%)
Other neurological disorders	183 (46.3%)
Psychiatric comorbidity	
Yes	140 (35.4%)
No	255 (64.6%)

included Parkinson's disease, diabetes mellitus with neurological manifestations, unspecified musculoskeletal disorders, malignant neoplasm of the brain, traumatic spondylopathy, cervical disk displacement, type 2 diabetes mellitus with polyneuropathy, myalgia, transient alteration of awareness, nondiabetic proliferative retinopathy, essential tremor, syncope and collapse, spasmodic torticollis, Bell's palsy, cerebrovascular disease, cerebral aneurysm, and benign paroxysmal vertigo.

Of the total 395 patients, 140 (35.4%) scored positively for concurrent symptoms of depression and anxiety (i.e., PHQ-9 and GAD-7 scores of >10). Seen individually, 154 (39%) patients showed symptoms of clinical depression, while 137 (34%) patients showed symptoms of generalized anxiety disorder within the clinical range. Of the 140 patients with concurrent symptoms of both disorders, 47 (33.6%) were referred to psychiatric services available at the center. There were a total of 67 (47.8%) patients receiving psychiatric treatment at the time of data analysis, 41 (61.2%) with and 26 (38.8%) without a referral from their attending neurologists.

Pearson's chi-square tests were carried out to investigate the relationship between comorbid psychiatric symptoms and referrals to psychiatric services, as well as the relationship between comorbid psychiatric symptoms and attendance to psychiatric services. The same was done for primary diagnoses and comorbid psychiatric symptoms, as well as referrals/attendance to psychiatric services. There was a very significant association between severity of psychiatric symptoms and referral to psychiatric services ($\mathcal{X}^2$ (1) = 24.96, $p < .001$). Seen separately, there was also a significant association between depressive symptoms and referral to psychiatric services ($\mathcal{X}^2$ (4) = 10.86, $p < .05$), as well as a very significant association between symptoms of generalized anxiety disorder and referral to psychiatric services ($\mathcal{X}^2$ (4) = 18.77, $p < .001$). There was also a very significant association between comorbid psychiatric symptoms and attendance to psychiatric services ($\mathcal{X}^2$ (1) = 46.21, $p < .001$).

There was no significant relationship between primary diagnosis of neurological disorders and comorbid psychiatric symptoms. Nevertheless, 31.6% of the patients with a primary diagnosis of multiple sclerosis showed comorbid psychiatric symptoms. The same observation was made for 30.8% of patients with a primary diagnosis of epilepsy, 37.3% of patients with headache, and 34.1% of patients with diagnoses of a variety of other neurological disorders. Of the 102 patients with a primary diagnosis of headache, 75 (73.5%) were categorized under migraine and 27 (26.5%) were categorized under tension-type headache. Thirty (40%) of the patients in the migraine category showed comorbid psychiatric symptoms, while seven (25.9%) of those in the tension-type category showed similar symptoms.

DISCUSSION

This study was the first step toward cross-sectional epidemiological research looking at psychiatric disorders in neurology outpatients in the UAE. It looked at prevalence rates of psychiatric comorbidity and referral rates in patients attending dedicated neurology clinics. The current study's findings of a 35.4% prevalence rate are not much different from similar, albeit larger, epidemiological studies (16–18) in the Arab Gulf region that looked at the prevalence of psychiatric disorders in patients attending primary care services. They found rates ranging between 37.1% and 49.9%, but two of these studies only measured depression. The 30.8% prevalence among patients with epilepsy supports the findings of Alsaadi et al. (12), who found the same rate of psychiatric comorbidity in a different UAE cohort. It must be said that these findings are slightly lower than those of similarly designed studies, which had prevalence rates between 47% and 55.1% (4, 28). A study that looked at neurology inpatients found a 51.3% prevalence rate of psychiatric disorders (29), while another study (30) looking at neurology outpatients found that 30% of patients referred to a neurologist had symptoms not explained by organic disease. There is a possible explanation for the slightly lower prevalence rate and high referral/attendance rates of psychiatric disorders in the current cohort. Data was collected from a center that caters to patients with psychiatry and neurology disorders. It can be argued that in medical facilities where specialized services are not available, prevalence rates would be higher and referral/attendance rates much lower than what was found in a facility that is geared toward providing integrated mental health care services. In the absence of proper screening for and diagnosis of psychiatric disorders, patients presenting with psychiatric symptoms may report them using somatic terms, leading to poor prognosis, frequent attendance to primary care services, increased resource utilization, and increased health care costs (5). Alkhadhari et al. (16) reported somatization as the most common psychiatric illness among their cohorts in a primary care setting, possibly due to the patients' tendency to report their symptoms using physical terms. They also argued that due to the cultural stigma attached to psychiatric illnesses in the region, patients prefer attending primary clinics rather than secondary or tertiary mental health care facilities. Findings from the current cohort support the need for a multidisciplinary approach to managing neurological disorders. It can be argued that access to a multi-/interdisciplinary clinical team will lead to the timely and accurate diagnosis of psychiatric illnesses, which may otherwise present as somatization. It can also lead to infrequent use of primary care services and the lowering of health care costs and resource utilization. Evidently, there is a link between patient cost-sharing patterns and usage of psychiatric services in the UAE, where 36% of the total costs of ambulatory neuropsychiatric services are paid directly by patients (31). Policies toward the regulation of health insurance plans can be adapted to include neuropsychiatric services in all basic and enhanced insurance plans.

Another important finding of this study is the 35.4% concurrence of depressive symptoms and anxiety. Studies have shown that comorbidity between psychiatric disorders has been found to cause greater disability levels when compared to patients with a single psychiatric diagnosis (32). In a review by Hirschfeld (33), patients with concurrent depression and anxiety disorders took longer to respond to treatment, had slower recovery, utilized more medical resources, and had higher rates of recurrence and psychological disability than patients presenting with either disorder alone. In this cohort, a 39% prevalence rate of depressive symptoms and 34% anxiety disorders was found, while 35.4% had concurrent occurrence of both disorders. Symptoms are found to overlap in many cases, and this necessitates careful discrimination between differences for a proper diagnosis and treatment plan. The current study highlights the need for proper and timely screening of psychiatric disorders.

Lastly, the current cohort had 25.8% of patients with a primary diagnosis of headache—the second largest group after patients classified under "other neurological disorders." Migraine sufferers made up 73.5% of that group and showed higher rates of psychiatric comorbidity than those who suffered from tension-type headache. In the past, clinical studies that compared these two types of headache patients did not observe significant differences in psychiatric comorbidity (34–36). More clinical studies with a larger sample size are needed to corroborate these findings.

Limitations

This study has only looked at two types of psychiatric disorders, which could have limited the chances of screening for other psychiatric illnesses such as somatization and posttraumatic disorder (37, 38). Moreover, confounding factors such as smoking and substance abuse that could have shed more light on the characteristics of this cohort, were not documented. Although the sample size is not insignificant, multicenter studies with a much larger sample size are needed in order to create an epidemiological database in the UAE.

CONCLUSION

This study investigated the prevalence of depressive and anxiety symptoms across neurological complaints in patients of this specialized service in the UAE. The results indicate slightly lower rates of prevalence of psychiatric comorbidity with neurological disorders and high rates of attendance and referral rates to psychiatric services. Based on the findings, the 33.6% referral rate and 47% attendance rate are promising, but more needs to be done in delivering integrated care to patients and the timely screening for psychiatric illnesses. The results shed light on the clinical profile of patients in this region and support the need for integrated collaborative medical services. Moreover, findings have important implications for health care policies pertaining to resource distribution and funding.

ETHICS STATEMENT

This study was carried out in accordance with the recommendations of the institutional review board at the American Center for Psychiatry and Neurology. The protocol was approved by the ACPN IRB.

AUTHOR CONTRIBUTIONS

All authors have made a substantial contribution to the design, data collection, and analysis of the research and the drafting of the manuscript and have reviewed and accepted the contents of the manuscript prior to its submission. TA contributed in recruiting patients for participation and reviewing the manuscript. SK collected, entered, and analyzed data and contributed in preparing the manuscript. OM contributed in designing the study, prepared the study protocol for IRB approval, and reviewed the manuscript. KM contributed in recruiting patients for participation and reviewing the manuscript. SA collected data. AA contributed in designing the study and reviewed the manuscript.

REFERENCES

1. Feinstein AR. The pre-therapeutic classification of co-morbidity in chronic disease. *J Chronic Dis* (1970) 23(7):455–68. doi: 10.1016/0021-9681(70)90054-8
2. Ansseau M, Dierick M, Buntinkx F, Cnockaert P, De Smedt J, Van Den Haute M, et al. High prevalence of mental disorders in primary care. *J Affective Disord* (2004) 78(1):49–55. doi: 10.1016/S0165-0327(02)00219-7
3. Banks SM, Kerns RD. Explaining high rates of depression in chronic pain: a diathesis–stress framework. *Psychol Bull* (1996) 119(1):95–110. doi: 10.1037/0033-2909.119.1.95
4. Carson AJ, Ringbauer B, MacKenzie L, Warlow C, Sharpe M. Neurological disease, emotional disorder, and disability: they are related: a study of 300 consecutive new referrals to a neurology outpatient department. *J Neurol Neurosurg Psychiatry* (2000) 68(2):202–6. doi: 10.1136/jnnp.68.2.202

5. Ferrari S, Galeazzi GM, Mackinnon A, Rigatelli M. Frequent attenders in primary care: impact of medical, psychiatric and psychosomatic diagnoses. *Psychother Psychosom* (2008) 77(5):306–14. doi: 10.1159/000142523
6. Katon W, Maj M, Sartorius N. *Depression and diabetes*. West Sussex, UK: John Wiley & Sons (2018). Available online at https://books.google.com/books?hl=en&lr=&id=hBnmzG1QP5YC&pgis=1. Accessed on August 9.
7. Sartorius N. Comorbidity of mental and physical disorders: a main challenge to medicine in the 21st century. *Psychiatr Danub* (2013) 1(1):4–5. doi: 10.1016/j.eurpsy.2017.01.079
8. Purebl G, Birkas E, Csoboth C, Szumska I, Kopp MS. The relationship of biological and psychological risk factors of cardiovascular disorders in a large-scale national representative community survey. *Behav Med* (2006) 31(4):133–9. doi: 10.3200/BMED.31.4.133-139
9. Tellez-Zenteno JF, Patten SB, Jette N, Williams J, Wiebe S. Psychiatric comorbidity in epilepsy: a population-based analysis. *Epilepsia* (2007) 48(12):2336–44. doi: 10.1111/j.1528-1167.2007.01222.x
10. Jette N, Patten S, Williams J, Becker W, Wiebe S. Comorbidity of migraine and psychiatric disorders—a national population-based study. *Headache* (2008) 48(4):501–16. doi: 10.1111/j.1526-4610.2007.00993.x
11. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: scientific advances and future directions. *Psychol Bull* (2007) 133(4):581–624. doi: 10.1037/0033-2909.133.4.581
12. Alsaadi T, El Hammasi K, Shahrour TM, Shakra M, Turkawi L, Almaskari B, et al. Prevalence of depression and anxiety among patients with epilepsy attending the epilepsy clinic at Sheikh Khalifa Medical City, UAE: a cross-sectional study. *Epilepsy Behav* (2015) 52:194–9. doi: 10.1016/j.yebeh.2015.09.008
13. Sulaiman N, Hamdan A, Tamim H, Mahmood DA, Young D. The prevalence and correlates of depression and anxiety in a sample of diabetic patients in Sharjah, United Arab Emirates. *BMC Fam Pract* (2010) 11:80. doi: 10.1186/1471-2296-11-80
14. Alsaadi T, Kassie S, El Hammasi K, Shahrour TM, Shakra M, Turkawi L, et al. Potential factors impacting health-related quality of life among patients with epilepsy: results from the United Arab Emirates. *Seizure* (2017) 53:13–17. doi: 10.1016/j.seizure.2017.10.017
15. Alsaadi T, El Hammasi K, Shahrour TM, Shakra M, Turkawi L, Nasreddine W, et al. Depression and anxiety as determinants of quality of life in patients with multiple sclerosis—United Arab Emirates. *Neurol Int* (2017) 9:75–8. doi: 10.4081/ni.2017.7343
16. Alkhadhari S, Alsabbrri AO, Mohammad, IHA, Atwan AA, Alqudaihi F, Zahid MA. Prevalence of psychiatric morbidity in primary health clinic attendees in Kuwait. *J Affective Disord* (2016) 195:15–20. doi: 10.1016/j.jad.2016.01.037
17. Al-Otaibi B, Al-Weqayyan A, Taher H, Sarkhou A, Gloom A, Aseeri F, et al. Depressive symptoms among Kuwaiti population attending primary health care settings: prevalence and influence of sociodemographic factors. *Med Princ Pract* (2007) 16:384–8. doi: 10.1159/000104813
18. Al-Qadhi W, Urrehman S, Ferwana MS, Abdulmajeed IA. Adult depression screening in Saudi primary care: prevalence, instrument and cost. *BMC Psychiatry* (2014) 14:190. doi: 10.1186/1471-244X-14-190
19. Department of Mental Health and Substance Abuse. *Mental health atlas*. Geneva: World Health Organization (2011).
20. Spitzer R, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary care evaluation of mental disorders. Patient Health Questionnaire. *JAMA* (1999) 282:1737–44. doi: 10.1001/jama.282.18.1737
21. Lowe B, Kroenke K, Herzog W, Grafe K. Measuring depression outcome with a brief self-report instrument: sensitivity to change of the Patient Health Questionnaire (PHQ-9). *J Affective Disord* (2004) 81:61–6. doi: 10.1016/S0165-0327(03)00198-8
22. Martin A, Winfried R, Klaiberg A, Braehler E. Validity of the brief Patient Health Questionnaire mood scale (PHQ-9) in the general population. *Gen Hosp Psychiatry* (2006) 28:71–7. doi: 10.1016/j.genhosppsych.2005.07.003
23. Becker S, Al Zaid K, Al Faris E. Screening for somatization and depression in Saudi Arabia: a validation study of the PHQ in primary care. *Int J Psychiatry Med* (2002) 3:271–83. doi: 10.2190/XTDD-8L18-P9E0-JYRV
24. Spitzer RL, Kroenke K, Williams JBW, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med* (2006) 166(10):1092–7. doi: 10.1001/archinte.166.10.1092
25. Lowe B, Decker O, Muller S, Braehler E, Schellberg D, Herzog W, et al. Validation and standardization of the Generalized Anxiety Disorder screener (GAD-7) in the general population. *Med Care* (2008) 46:266–74. doi: 10.1097/MLR.0b013e318160d093
26. Sawaya H, Atoui M, Hamadeh A, Zeinoun P, Nahas Z. Adaptation and initial validation of the Patient Health Questionnaire-9 (PHQ-9) and the Generalized Anxiety Disorder-7 questionnaire (GAD-7) in an Arabic speaking Lebanese psychiatric outpatient sample. *Psychiatry Res* (2016) 239:245–52. doi: 10.1016/j.psychres.2016.03.030
27. IBM Corp. *IBM SPSS Statistics for Windows, Version 22.0*. Armonk, NY: IBM Corp (2013). Released.
28. Fink P, Hansen M, Sondergaard L, Frydenberg M. Mental illness in new neurological patients. *J Neurol Neurosurg Psychiatry* (2003) 74:817–9. doi: 10.1136/jnnp.74.6.817
29. Jefferies K, Owino A, Rickards H, Agrawal N. Psychiatric disorders in inpatients on a neurology ward: estimate of prevalence and usefulness of screening questionnaires. *J Neurol Neurosurg Psychiatry* (2007) 78:414–6. doi: 10.1136/jnnp.2006.103044
30. Carson A, Ringbauer B, Stone J, McKenzie L, Warlow C, Sharpe M. Do medically unexplained symptoms matter? A prospective cohort study of 300 new referrals to neurology outpatient clinics. *J Neurol Neurosurg Psychiatry* (2000) 68:207–10. doi: 10.1136/jnnp.68.2.207
31. Hamidi S, Abouallaban, Y, Alhamad S, Meirambayeva A. Patient cost-sharing for ambulatory neuropsychiatric services in Abu Dhabi, UAE. *Int J Ment Health Syst* (2016) 10:34. doi: 10.1186/s13033-016-0066-6
32. Roy-Byrne PP, Strang P, Wittchen HU, Ustun B, Walters EE, Kessler RC. Lifetime panic–depression comorbidity in the National Comorbidity Survey. Association with symptoms, impairment, course, and help-seeking. *Br J Psychiatry* (2000) 176:229–35. doi: 10.1192/bjp.176.3.229
33. Hirschfeld RMA. The comorbidity of major depression and anxiety disorders: recognition and management in primary care. *J Clin Psychiatry* (2001) 3(6):244–54.
34. Marazziti D, Toni C, Pedri S, Bonuccelli U, Pavese N, Nutti A, et al. Headache, panic disorder and depression: comorbidity or a spectrum? *Neuropsychobiology* (1995) 31: 125–9. doi: 10.1159/000119182
35. Mitsikostas DD, Thomas AM. Comorbidity of headache and depressive disorders. *Cephalalgia* (1999) 19:211–7. doi: 10.1046/j.1468-2982.1999.019004211.x
36. Vasconcelos LP, Costa Silva M, Coelho Costa EA, da Silva Junior AA, Gomez RS, Teixeira AL. Obsessive–compulsive disorder and migraine: case report, diagnosis and therapeutic approach. *J Headache Pain* (2008) 9:397–400. doi: 10.1007/s10194-008-0069-z
37. Morasco BJ, Lovejoy TI, Lu M, Turk DC, Lewis L, Dobscha SK. The relationship between PTSD and chronic pain: mediating role of coping strategies and depression. *Pain* (2013) 154(4):609–16. doi: 10.1016/j.pain.2013.01.001
38. Sciolli-Salter ER, Forman DE, Otis JD, Gregor K, Valvoski I, Rasmusson AM. The shared neuroanatomy and neurobiology of comorbid chronic pain and PTSD. *Clin J Pain* (2014) 31:363–74. doi: 10.1097/AJP.0000000000000115

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Narrative Identity Reconstruction as Adaptive Growth During Mental Health Recovery: A Narrative Coaching Boardgame Approach

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Objective: The purpose of this paper is to construct a conceptual framework for investigating the reconstruction of narrative identity in mental health recovery from a complexity perspective. This conceptual framework provides the foundation for developing a health boardgame to facilitate narrative identity reconstruction.

Methods: A selective integrative review of the theoretical and empirical literature relevant to narrative identity reconstruction in recovery was conducted. Sources included books, dissertations, internet resources, and professional journals.

Findings: The reviewed material provides a conceptual framework that offers an enriched understanding of narrative identity reconstruction in recovery as a process of adaptive growth. It identifies the Hero's Journey, the life story model of identity (LSMI), and intentional change theory (ITC) as particularly relevant in informing strategies for narrative identity reconstruction. The conceptual framework can be operationalized in a narrative coaching treatment approach using a boardgame.

Conclusion and Implications for Practice: In practice, mental health professionals could use the narrative coaching boardgame to facilitate people's adaptive change with a focus on building skills to reconstruct their preferred narrative identity and foster hope. Future research should explore what aspects of narrative identity and non-linear dynamic processes of change are most important in people's recovery narratives and in particular these processes can be assessed in response to the use of the boardgame.

Keywords: mental health recovery, complex adaptive system, narrative identity, narrative coaching, serious game (boardgame)

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INTRODUCTION

Mental health recovery refers to the idea that people with severe and persistent mental illness can pursue psychological wellbeing beyond the limitations of chronic illness (Anthony, 1993; Rogers et al., 2005; Slade and Longden, 2015). Recovery is comprised of various components and processes such as building hope, taking responsibility, gaining a sense of control in life, and building a positive identity (Andresen et al., 2006). Reconstructing narrative identity, to address the loss of sense-of-self and identity that often occurs in mental illness, is a key task for people in recovery (Wisdom et al., 2008). Narrative identity refers to the internal, evolving life story that individuals construct by integrating stories related to their past, present, and future to provide their lives with unity, meaning, and purpose (Bauer et al., 2008). Narrative identity reconstruction entails the formation of an agentic identity where illness is redefined as only one aspect of a complex, multi-dimensional, evolving self that can intentionally choose to pursue wellbeing in recovery. It is a process of change characterized by personal transformation and adaptive growth (Davidson et al., 2005).

Recovery and the key task of narrative identity reconstruction can be understood from a narrative constructivist perspective. In this view, the individual is a self-in-process, ever-changing and adapting to internal and external environmental demands and storytelling is a fundamental process of human functioning (Bruner, 1987, 1991; Mahoney, 1991). As people evolve, so their stories may evolve and thus their narrative identity is open to change (McAdams, 1985; Ricoeur, 1991). The individual can be viewed as a complex adaptive system (Butz, 1997; Rickles et al., 2007; Pincus et al., 2018). This term refers to the complex non-linear nature of the individual, the adaptive evolutionary manner of personal change, and the interconnectedness of the various parts that comprise the individual as a system (Guastello and Liebovitch, 2009). Recovery processes are by nature non-linear as part of human adaptive growth (Deegan, 2001; Onken et al., 2007; Slade, 2010) and are thus highly amenable to being considered from a complex adaptive system perspective.

Non-linear change in recovery is poorly understood and is a difficult concept to apply in recovery-oriented healthcare. A need exists for novel approaches that focus on investigating those processes (Sturmberg, 2016; Graci et al., 2018). Linking narrative identity reconstruction to the complex processes of adaptation and adaptive growth may be a fruitful approach (Rudnick, 2012). A complexity approach considers the often unpredictable and erratic nature of non-linear change processes in life transitions as normal and natural. It can assist people to understand and harness those processes as part of making transitions, leading to adaptive growth and wellbeing in recovery (Bussolari and Goodell, 2009).

Narrative identity reconstruction as a process of adaptive growth can be understood and facilitated by treatment approaches that are strengths-based and target factors involved in non-linear dynamic functioning (Mobus and Kalton, 2015). One such approach is narrative coaching. Narrative coaching is a person-centered, transformational intervention approach that is often focused on identity. It is practical in orientation and commonly utilizes literary metaphors, models, and tools as means to facilitate personal change (Drake, 2010, 2018). A coaching tool in the form of a serious game (boardgame) may have particular salience for narrative identity reconstruction. The term "serious game" refers to games that, while entertaining, model real-life situations and/or have a useful outcome. They aim to promote learning objectives in an engaging and enjoyable manner (Abt, 2002; Fitzgerald and Kirk, 2013). Boardgames are often narrative in design, use a metaphorical approach (Lelardeux et al., 2013), focus on identity, and allow players to experiment with new ways of responding to challenges and explore possible identities (Treher, 2011). They also have the capacity to operationalize complex concepts in a simple manner (Salen and Zimmerman, 2004; Fullerton, 2018).

The main focus of this paper is narrative identity reconstruction during recovery from severe and persistent mental illness. It outlines a conceptual framework in which theories and models related to recovery as a complex process of adaptive growth are integrated in a narrative coaching treatment approach, using a boardgame as a coaching tool. The conceptual framework is underpinned by the common theme of non-linear phenomena, with close alignment between the theories and models outlined (see **Table 1**). Theoretical integration is operationalized in the boardgame (see **Table 2**). Narrative coaching to facilitate narrative identity reconstruction is a novel treatment approach in recovery and is aligned with improving wellbeing in patients with chronic conditions. The narrative coaching approach outlined is transdiagnostic and intended for use across common mental disorders. It is transdiagnostic as it targets people's style of narrative processing (i.e., narrating and interpreting life experiences) that underlies their personal agency. The treatment aim is to facilitate agentic narrative identity reconstruction aligned with mental health and psychological wellbeing in recovery. This approach is aligned with a key advance in the area of treatment for mental disorders, where transdiagnostic dimensions can be understood and targeted in interventions (Krueger and Eaton, 2015; Eaton, 2017; McGorry et al., 2018).

The significance of the paper is that it provides a way of integrating concepts and theories with the common theme of adaptive growth (non-linear phenomena) in narrative identity reconstruction during mental health recovery and, further, creates a framework for practically assisting clients to author their preferred narrative identity. This is important as narrative identity reconstruction is a key task in recovery. It is part of attaining psychological wellbeing, which is linked to improved recovery rates and positive outcomes across a wide range of life domains (e.g., education, employment, relationships, health) (Friedli, 2009). The paper is original in that, first, recovery concepts and theories with the common theme of non-linear phenomena do not appear to have been previously integrated in a conceptual framework, and, second, the use of narrative coaching (with a boardgame coaching tool) to facilitate narrative identity reconstruction is a novel treatment approach to promote wellbeing in recovery. The paper will be of interest to mental health professionals, people in recovery, and researchers. For practice it offers a way for mental health professionals to facilitate their clients' narrative identity reconstruction in recovery. Future research could focus on further clarifying the most important elements of narrative identity reconstruction and non-linear dynamic processes involved in people's recovery narratives.

MENTAL HEALTH RECOVERY: A JOURNEY OF ADAPTIVE GROWTH AND TRANSFORMATION

Mental health recovery as the pursuit of wellbeing despite chronic illness is a personal journey of healing and transformation in

TABLE 1 | Alignment between theories and models in an integrative conceptual framework for narrative identity reconstruction in mental health recovery.

Hero's journey (mental health recovery metaphorical journey)	Life story model of identity (LSMI) (narrative identity)	Intentional change theory (ICT) (personal change model)
Conceptualization of self		
Narrative constructivist complex adaptive system	Narrative constructivist complex adaptive system	Narrative constructivist complex adaptive system
Structure of narrative identity		
Story stages and plot-points	Storytelling elements	Sequence of change tasks
Goal underlying personal change		
Attain a valued outcome	Attain purpose and meaning	Attain a personal life vision
Personal change characteristics		
Internal/external challenges	Competing selves/stories	Internal/external barriers
Personal change mechanism		
Using inner attributes	Narrative processing	Mindfulness
Personal change process		
Non-linear dynamical	Non-linear dynamical	Non-linear dynamical
Nature of narrative identity reconstruction		
Emergence of heroic self	Evolving life story	Emergence of ideal self
Identity change outcome		
Transformation of identity	Preferred narrative identity	Realization of ideal self

which the focus is on wellness and the fulfillment of people's potential rather than the treatment of illness. Recovery can be a journey of self-discovery and personal growth (Slade, 2009; Substance Abuse and Mental Health Services Administration [SAMHSA], 2012). By nature, the journey is multidimensional and non-linear with diverse trajectories and an interplay of complex characteristics as part of human adaptive growth (Deegan, 2001; Slade, 2010). It is an intentional, self-directed, sustained endeavor that builds on hope, personal strengths, and valued goals and is characterized by a growing sense of agency where the individual accepts the limitations of illness and discovers a new world of possibility (Deegan, 1996; Drake and Whitley, 2014). In transformational personal change, the individual shifts from a passive to active sense of self. This often entails a rediscovery of self where the individual develops an enhanced ability to reflect on life experiences, learn from them, and take novel action. This is an adaptive process and is considered the essence of recovery (Glover, 2012). Recovery is aligned with a constructivist epistemological perspective. This approach prioritizes subjectivity, the non-linear dynamic processes inherent in personal change, transformation of the self, and the fulfillment of personal potential (Mahoney, 1991; Mahoney and Granvold, 2005; Slade, 2012).

Recovery is narrative in character. Creating individual recovery stories aligned with wellbeing and positive identity is central to mental health recovery (Nurser et al., 2018). Authoring a personal recovery story tends to be an empowering and healing experience for the narrator. People in recovery have the power to tell new stories that will help them overcome adversity and move forward in their recovery (Brown and Kandirikirira, 2007). Their stories are often inspirational and serve to inculcate hope and possibility in others for successful recovery (Kirkpatrick, 2008; Shepherd et al., 2008). A common core narrative in people's recovery stories is the "quest," which reframes the experience of illness as an opportunity to undergo personal transformation and attain wellbeing through overcoming difficulties and finding renewed purpose and meaning in life (Frank, 1995). This is an ongoing, redemptive journey in which the individual's life story shifts from one of chronic disability and stagnancy to a much more complex and dynamic life story (Ridgway, 2001; McAdams and McLean, 2013).

The core "quest" narrative is encapsulated in the hero's journey (Campbell, 1968) literary metaphorical framework often used in recovery (Lamprell and Braithwaite, 2016; Scottish Recovery and Network, 2016; Foundations Recovery Network, 2018). The hero's journey is an archetypal quest story referring to both males and females in which the individual as story protagonist undertakes a journey to address a pressing life issue, overcomes internal and external challenges along the way, and in doing so potentially undergoes personal transformation including a changed identity from being a victim to that of a hero (Booker, 2006; Williams, 2017). The hero is an ordinary individual, often an underdog, who finds the courage, resilience, and strength to persevere and endure despite obstacles and setbacks (Allison and Goethals, 2014). The hero's journey epitomizes the idea that challenges routinely arise in people's lives and the way that they process and respond to those challenges can mean the difference between poorer or better mental health (Robertson and Lawrence, 2015). The person as protagonist on the hero's journey gains an understanding that challenges in life are to be embraced rather than avoided and that positivity may be found in moments and experiences perceived as negative (Allison and Goethals, 2017). The hero's journey is a compelling metaphor for recovery as it encapsulates the challenges and tests of fortitude

TABLE 2 | An overview of the coaching boardgame designed to facilitate narrative identity reconstruction.

Steps in the game (Hero's journey storyline)	**Challenges at each step** (Life story model of identity)	**Coaching process** (Intentional change theory)
1 The Call Protagonist recognizes a pressing life issue that must be faced and decides to embark on a journey to address it.	**Preferred identity** *Narrative identity challenge:* Clarify your journey direction and practice the skills you will use along the way.	**Game preparation** Psychoeducation. Coaching goal chosen. Values clarification. Ideal self conceptualization. Mindfulness skills training.
2 Threshold Protagonist leaves his/her comfort zone and engages in the recovery journey.	**Underlying beliefs** *Narrative identity challenge:* Choose beliefs that could best support you on your journey.	**Game play** The game-playing mechanism is a five-step reflexive question sequence protocol used at all narrative identity challenges:
3. Road of trials Protagonist is fully engaged in the journey and is tested in the process.	**Dominant attitude/s** *Narrative identity challenge:* Choose what attitude/s could best support you on your journey.	• How would your ideal self address this challenge?
4. Setback Protagonist is faced with a significant obstacle that must be overcome to make progress.	**Story turning points** *Narrative identity challenge:* Identify a possible main setback on your journey and consider how you could overcome it.	• How is that different from the way you would currently address this challenge?
5. Rising action Protagonist is immersed in the journey and faces many competing demands.	**Managing aspects of self** *Narrative identity challenge:* Identify your life roles and consider how to manage them on your journey.	• What qualities/strengths that you have, could you draw upon to address this challenge?
6. Climax Protagonist must overcome his/her main personal limitation to succeed.	**Story high point** *Narrative identity challenge:* Identify your main personal limitation on the journey and consider how to address it.	• What archetypes and qualities/strengths could you draw upon to address this challenge?
7. The return Protagonist is changed as a person, and shares his/her learnings with others.	**Personal growth** *Narrative identity challenge:* Reflect on your journey learnings and consider how to use them beyond the game.	• Pause and reflect. Based on the above discussion, what action/s can you take to address the challenge? (i.e., support those beliefs; support those attitudes; overcome that setback; manage your life roles; overcome your personal limitation; use your learnings).

experienced by people on their recovery journey (Watkins, 2007). It places consumers as the leading protagonist in their recovery journey, enabling them to become active agents in their lives and establish new identities (O'Hagan, 2012). The hero's journey can be used as a narrative coaching or therapy tool that can be easily learnt and may be used as a scaffold for recovery (Hartley, 2010; Robinson, 2010).

The hero's journey is aligned with the strengths model of mental health care whereby people take personal responsibility for their recovery and draw on their inner resources to effect positive change in their lives (Rapp and Goscha, 2012). It is also aligned with a posttraumatic growth approach whereby people who encounter psychological difficulties following adversity often find inner strengths and abilities previously unknown and experience a positive change in self-concept (Niemeyer, 2004; Tedeschi and Calhoun, 2004).

NARRATIVE IDENTITY RECONSTRUCTION: MULTIPLE SELVES, STORIES, AND POSSIBILITIES

Mental illness often results in people experiencing a sense of loss of self that must be addressed for recovery to become possible (Wisdom et al., 2008; Yanos et al., 2010). The task is for individuals to redefine themselves, to reconstruct a preferred identity aligned with mental health and wellbeing (Slade, 2010). In the transformative process of identity reconstruction, the person gradually sheds the old self and embraces an emergent new sense of self characterized by a more stable and positive identity (Deegan, 2001; Wisdom et al., 2008).

Given that recovery and identity might be seen as narrative, the focus is frequently on narrative identity reconstruction (Bianco, 2011; Nurser et al., 2018). Severe mental illness often drastically diminishes people's ability to narrate their life story (Gallagher, 2003). Crises of identity, experienced as trauma and personal loss, can undermine the sense-of-self by disrupting the patterns of narrative coherence that are central to a person's self-concept (Mackenzie, 2008). Constructing a meaningful narrative of self and disorder that promotes recovery is a crucial aspect of identity reconstruction. The challenge for people is to tell stories about their lives in which they are a protagonist characterized by empowerment and agency (Lysaker et al., 2001). Narrative identity reconstruction is based on a view of stories as dynamic, ever-changing, and evolving processes. People's stories are continually being constructed in interaction with others and the world and are thus provisional and open to change and revision (Mackenzie, 2008). This is important because it allows people to intentionally change and evolve their stories in the pursuit of mental health and wellbeing. People's stories about their lives are a predictor of psychological wellbeing. Narrative identity has incremental validity in research where it has a stronger relationship with mental health than other common predictors (e.g., gender, personality traits, income) (Adler et al., 2016).

One of the most widely used theories of narrative identity is the life story model of identity (LSMI) (McAdams, 1985, 1993, 2001, 2013, 2018). The LSMI views narrative identity as a person's internalized and evolving life story that is comprised of smaller stories of a person's experiences in various life domains (e.g., work, health, relationships). These stories intersect and, in turn, are filled with micro-stories of specific events. The individual's life story is a cognitive script arranged in a temporal sequence complete with setting, characters, plots, scenes, and themes. Thus, it is complex and dynamic, comprised of multiple stories of the self. Narrative identity can be viewed as a personal myth, in which people make sense of themselves and their lives by creating an imaginary heroic story of self. This includes the use of archetypes (e.g., Warrior, Sage), which are universal story characters with attributes (e.g., courage, wisdom) that can be expressed outwardly in a person's life. The individual can intentionally call upon archetypal inner resources to facilitate the construction of preferred narrative identity.

Higher levels of personal agency (the feeling of being in control of one's life) in narrative identity are strongly associated with better mental health and psychological wellbeing (Brown, 2008; Adler et al., 2016). For example, Adler (2012) conducted a longitudinal study of 47 adults undergoing therapy in which participants wrote personal narratives and completed mental health assessments over the course of 12 therapy sessions. It was found that the themes of agency in participants' stories increased over time, that mental health increased, and that agency and mental health were related. Increased agency appeared in participants' stories before their mental health improved, and this was likened to participants putting put out a new version of themselves and living their way into it. Davidson and Strauss (1992) conducted interviews over 3 years with 66 persons struggling to recover from prolonged psychiatric disorders. It was found that the reconstruction of an enduring sense of self as an active, dynamical, and responsible agent provides an important aspect of improvement. Identity reconstruction was seen as a process involving (a) awareness of a more agentic sense of self, (b) taking stock of one's strengths and limitations, (c) putting aspects of the self into action, and (d) using this enhanced sense of self as a resource in recovery. Cochran and Laub (1994) conducted an in-depth small-n qualitative study with people who had undergone psychological trauma resulting from injury. Participants' initially assumed a victimic identity, but during treatment regained an agentic identity. Participants developed an understanding of themselves as active agents in charge of their lives, able to choose goals and actively direct their activities to achieve them. Identity reconstruction was held to be a correlated movement of the progressive construction of a new agentic life story and detachment from the victim story.

Agency enables people to play a part in their own adaptive growth (Bandura, 2001; Little et al., 2006). Agency is linked to the way that people reflect on their actions in their evolving life story and the sense of choice they experience when considering how to respond to life demands (Adler, 2012). This leads to a sense of control in life in which they are more likely to pursue valued goals and outcomes. There is often dramatic insight into the meaning of life and identity, with the person experiencing a transformation in self-awareness and self-understanding (McAdams, 1985).

Agentic narrative identity is comprised of a narrative agentic self within an agentic plot. The narrative agentic self is a protagonist who intentionally sets goals, strives to achieve those goals, overcomes obstacles, and actualizes ideals. The narrative agentic plot is an ongoing composition that shapes the individual's evolving life-story (Polkinghorne, 1991, 1996; Cochran and Laub, 1994). It is constantly updated as the individual makes decisions and takes actions in response to life demands (Little et al., 2006). Agentic narrative identity can be taught and learned by the use of models focused on adaptive growth. Models provide inspiration and motivation, portraying a path from the confines of what is to the possibilities of what might be. Cochran and Laub (1994) provide a guide for enhancing personal agency in narrative identity, as follows: (i) study an agentic model with which one can identify; (ii) use storytelling, to imaginatively explore and rehearse the possibilities of the model; (iii) learn skills to move from imagination to enactment in real life.

Agentic narrative identity is aligned with the notion of possible selves, a useful approach in recovery where the individual explores alternative future identities and outcomes in life (Markus and Nurius, 1986; Slade, 2009). Desired possible selves (Tse and Zhu, 2013; Bak, 2015) and desired future narratives (MacLeod and Conway, 2007; Sools et al., 2015) are linked to better outcomes in mental health. The possible self is an imaginary conception of the individual's future self that encompasses cognitive representations of the person's hopes, fears, and fantasies (Hoyle and Sherrill, 2006; Erikson, 2007; Slade, 2009). A desired possible self is a behavioral blueprint that motivates the individual, guides behavior in relation to desired outcomes in life, and promotes integrated narrative identity (Cross and Markus, 1991; Singer, 2004; Frazier and Hooker, 2006). An agentic possible self is one that intentionally pursues a preferred identity aligned with valued goals and outcomes (Cochran and Laub, 1994). In a narrative constructivist approach to mental health recovery, the possible self is one of a person's multiple selves and stories (e.g., current, ideal), any of which may be dominant at a given time in a given context (Mahoney, 1991; Mahoney and Granvold, 2005; Bianco, 2011). The possible self must compete with co-existing identities that are mutually reinforcing, in tension, contradictory, and incompatible (Davidson et al., 2005). Multiplicity of selves can reinforce mental health difficulties or contribute to a healthy sense-of-self aligned with mental health and psychological wellbeing (Koch and Shepperd, 2004). Mental health presupposes an integrated narrative identity with a diversity of selves and stories existing in relative harmony and co-operation (McAdams, 1985; Singer, 2004).

Constructing narrative identity as an active process involves the use of narrative processing. This refers to the filtering of life experiences through a template where people perceive, select, and plot their lives using narrative devices such as imagery, characters, plot, goals, and underlying morals or themes (Sarbin, 1986; Singer and Bluck, 2001; Singer, 2004; Riessman, 2008). Autobiographical reasoning is also used and refers to the meaning that people make of their created narratives (Habermas, 2011). The person's point of view (e.g., agent, victim) in narrative processing is critically important. How the person makes sense of a life experience and acts on it will emerge from that point of view (Park and George, 2013). Optimal mental health and psychological wellbeing are associated with transformational narrative processing where the person openly explores difficult life experiences, finds a positive ending to these challenges, and grows from the experience (Pals and McAdams, 2004). Transformational processing is contrasted with ruminative processing, in which the person is unable to let go of old selves and goals (King, 2001; Pals and McAdams, 2004; Pals, 2006a,b; Whitehead and Bates, 2016).

THE NARRATIVE CONSTRUCTIVIST SELF IN RECOVERY: COMPLEX CHANGE AND ADAPTIVE GROWTH

The narrative constructivist self in recovery as a complex adaptive system is an open system, intelligent, meaning-making, intentional, proactive, ever-changing, adaptive, and ever-evolving. It is a self-in-process, in a constant state of flux and becoming, underpinned by non-linear dynamical processes of human functioning. The self is inherently growth-seeking and is teleonomic (self-driven) rather than teleological (goal-driven) (Mahoney, 1991; Niemeyer, 1993; Perna and Masterpasqua, 1997; Chamberlain, 1998). Personal growth, development, and transformation are inherent in the change processes of the narrative constructivist self and individuals are viewed as active participants in their own lives (Mahoney and Granvold, 2005). This perspective is a helpful model of self when applied to mental illness since it opens up the possibility of adaptive growth in relation to the challenges inherent in the recovery journey (Slade, 2009).

Adaptive growth as part of personal change in recovery involves both first-order, developmental (gradual) growth and second-order, transformational (abrupt) change (Gelo and Salvatore, 2016). Adaptive growth is constrained or facilitated by people's potential to respond adequately to internal and/or external challenges (Mahoney and Marquis, 2002). From a complex adaptive systems perspective humans have inherently high levels of adaptive capacity, which allows them to proactively shape their life-course rather than just respond in a reactive manner to challenges. This affords them a sense of personal agency and identity (Little et al., 2006). People can enhance their adaptive capacity by engaging in personal growth exercises such as developing creative flexibility in decision-making and problem-solving (Mahoney and Granvold, 2005; Mobus and Kalton, 2015).

In relation to mental health recovery, psychopathology is a dynamical system state of equilibrium where people's habitual patterns of functioning interfere with their everyday functioning and undermine wellbeing (Mahoney and Marquis, 2002). System destabilization is a requisite for adaptive growth as the person's functional pattern will continue unless challenged. For system reorganization to take place, old functional patterns must be altered or replaced. Optimal functioning and better mental health entail a turbulent balance between stability and instability as well as order and disorder in which the person is stable yet flexible and agile, trying novel responses to find the most adaptive system state to meet internal and/or external environmental demands (Salvatore et al., 2015; Gelo and Salvatore, 2016). The main characteristic of adaptive growth in complex adaptive systems is multiplicity of possible outcomes, where an individual can explore and choose behavior in response to demand (Plsek and Greenhalgh, 2001).

Intentional change theory (ICT) (Boyatzis, 2006; Boyatzis and McKee, 2006) is a model for sustainable personal change aligned with the concept of adaptive growth that may also be used to facilitate narrative identity reconstruction. ICT is a self-directed learning framework that uses the lexicon of complex adaptive systems to describe personal change. The goal is for the individual to attain a desired ideal self (e.g., preferred narrative identity) in the context of pursuing an affectively compelling personal life outcome. The ICT change process entails movement through a sequence of five challenge steps in which the person answers a series of questions that, when successfully addressed, facilitates construction of the ideal self. Movement is from a current, undesired state-of-being (current self) which functions as a *negative emotional attractor* (i.e., habitual pattern of functioning) to a desired state-of-being (ideal self) which is a *positive emotional attractor* (i.e., novel pattern of functioning). This is a transformative shift in the individual that may be viewed as second-order change (Gelo and Salvatore, 2016). Mindfulness is viewed as a central change mechanism with the aim of raising a person's awareness in order to intentionally engage in desired personal change. It is theorized that by increasing people's understanding of the complex nature of personal change, they learn to harness the processes rather than fear or misunderstand them (Boyatzis and McKee, 2006).

NARRATIVE COACHING: AGENTIC IDENTITY IN THE MAKING

The shift from a pathology orientation of illness and disability in recovery to a focus on mental health and psychological wellbeing has resulted in the use of positive, strengths-oriented interventions such as narrative coaching (Bora, 2010; Bora et al., 2010; Slade, 2010; Cavanagh and Buckley, 2014). Narrative coaching is aligned with identity reconstruction in that it is an experiential approach that assists people to revise their personal narratives to gain fresh perspectives, pursue novel possibilities, and attain desired outcomes in life. Narrative coaching helps people become more aware of their choices in life which in turn provides an opportunity for them to intentionally author the multiple stories that comprise their narrative identity and help transform their illness narratives into healing ones (Drake, 2010, 2017, 2018).

Transformational identity change in narrative coaching can be facilitated by the use of reflexive questioning which facilitates the person's ability to think about his or her own belief systems and make new connections. This process focuses on getting a person to investigate their interactions via introspection as they happen (differentiated from reflective thinking, which refers to thinking following action). Reflexivity encourages people to question their attitudes, thought processes, values, assumptions, prejudices and habitual actions, strive to understand their life roles, and appreciate how they influence their actions (Oliver, 2005). Reflexive coaching questions are an essential tool to facilitate self-awareness and assist individuals to reframe difficulties in a novel manner and find solutions to their problems (Hawkins and Smith, 2014).

Narrative coaching often involves the use of coaching tools to facilitate personal transformation (Biswas-Diener, 2010; Boniwell et al., 2014). Serious games are increasingly used in coaching, and this includes the use of boardgames. Their focus on identity and exploring possible identities makes them highly relevant for narrative identity reconstruction in recovery. Agency is a critical factor in boardgames, where players experience choice of response and a sense of control over the game's outcome (Fullerton, 2018). This allows them to develop new concepts of self and the world and learn new, adaptive skills that they can use in real life (Mitgutsch, 2011). This is part of game-based learning in which the person develops a mental model that matches the game system which, in turn, models a real-world system (Wasserman and Banks, 2017).

HERO'S RECOVERY JOURNEY BOARDGAME: A CRUCIBLE FOR ADAPTIVE GROWTH

Based on the theoretical and practical models outlined above we have developed a boardgame designed to facilitate people's narrative identity reconstruction in recovery. The boardgame is designed to be used as a tool as part of narrative coaching. The boardgame (titled, *"Heroes and heroines: The recovery journey boardgame")* is an immersive role-play experience designed to be a crucible for people's adaptive growth in recovery. The boardgame integrates game elements that represent the key components of mental health recovery, narrative identity reconstruction, and complex adaptive systems. This encompasses simple rules, board, avatar, game-playing guide, and playing cards that are carefully selected, operationalised, and integrated. ICT is used as the narrative coaching framework, the LSMI (McAdams, 1985) is used to represent narrative identity challenges within the hero's recovery journey storyline, and a reflexive coaching style (Oliver, 2005) embedded with applied mindfulness skills (Langer, 2000) is used as the game-playing mechanism (method used by player and coach to interact with the game world). The boardgame is based on established principles of game design that includes detailed conceptualization and iterative play-testing (i.e., test, analyze, refine, repeat) followed by a pilot program to ensure the game achieves its intended aim (Salen and Zimmerman, 2004; Adams, 2014; Schell, 2014; Fullerton, 2018).

The boardgame simulates the hero's journey (Campbell, 1968). It is a model-representation of the hero archetype (agentic self) within a hero's journey storyline (agentic plot) in which the player as protagonist engages in his or her own hero's recovery journey in pursuit of a valued real-life goal (personal life vision). The purpose of the game is for the person to shift from an undesired current self narrative identity (ICT *negative emotional attractor*) (i.e., habitual pattern of functioning) to a preferred ideal self narrative identity (ICT *positive emotional attractor*) in relation to the chosen goal. Players traverse a sequential agentic storyline consisting of hero's journey steps (e.g., Threshold; Road of Trials) by completing narrative identity challenges (e.g., choosing helpful beliefs and attitudes that support goal attainment) that represent important components of narrative identity. Once players complete a narrative identity challenge, they move on to the next storyline step until all the steps in the game are completed. In completing the journey, players construct a preferred narrative identity and potentially experience personal transformation. Players also learn about the complex processes of adaptive change and how they might be harnessed in recovery. Simple metaphors are used to explain the complex non-linear processes involved in personal change. For example, attractors are explained as habitual behavioral routines and are referred to metaphorically as "life-magnets" where the person is "pulled" repeatedly in a given direction, and the aim is to create a new desired ideal self attractor "life-magnet" to replace the current self attractor.

The game-playing mechanism, used iteratively at the narrative identity challenges, is a critical component of the game. Players engage in a coaching question sequence at each step in the game where they consider (1) how they as their ideal self might address the challenge, (2) how that differs from their current self response, (3) what known personal strengths/qualities they could draw upon to meet the challenge, (4) what agentic archetypal inner attributes they can draw upon, and (5) what action they could take to meet the challenge. Players use applied mindfulness skills in the question sequence in which they engage in an adaptive process of experimentation, engaging in novel ways of thinking (i.e., agentic ideal self perspective) to search for the best solutions to address the challenge. Players refer to a set of agentic archetype cards (i.e., Warrior, Sage, Adventurer) to consider which archetypal strengths/qualities they could draw upon to meet the challenge. For example, the player might choose the Warrior to meet a given challenge and must consider which of the related attributes of skill, courage, discipline, and determination might be used. The iterative, reflexive coaching process promotes in-depth consideration of agentic attributes and how they might be used. In considering agentic attributes and experimenting with related agentic responses to the challenges, players engage in transformational narrative processing where they can shift from a victim identity to an agentic identity. Moving from step to step in the game, as narrative identity challenges are completed, players learn an agentic cognitive schema (hero's journey) and script (personal change process) which is potentially internalized in their narrative identity reconstruction. This is the mindset and cognitive skills of the everyday hero who, above all, has the adaptive capacity to overcome difficulties and attain success on his or her journey. In line with game-based learning, it is envisaged that the transformative nature of the coaching intervention will translate into real-life skills for use beyond the boardgame.

CONCLUSION

Using a narrative coaching treatment approach aligned with complex change processes inherent in adaptive growth provides an integrated framework (see **Table 1**) that may be of value in understanding and facilitating narrative identity reconstruction as part of psychological wellbeing in recovery. The development of a boardgame to facilitate narrative identity reconstruction has several research and practical implications. Future research should explore what aspects of narrative identity and non-linear dynamical processes of change are most important in people's recovery narratives, with a view to assisting them to strengthen and leverage those aspects of self in constructing a preferred narrative identity. In practice, mental health professionals could use the game to engage their clients in recovery, offer a model of adaptive change that normalizes the often irregular and uncertain journey of recovery, assist clients to build skills to reconstruct their preferred narrative identity, and foster their hope for a journey toward wellbeing and the fulfillment of their potential.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

REFERENCES

Abt, C. C. (2002). *Serious Games*. Lanham, MD. University Press of America.

Adams, E. (2014). *Fundamentals of Game Design*, 3rd Edn. Berkeley, CA: New Riders.

Adler, J., Lodi-Smith, J., Philippe, F. L., and Houle, I. (2016). The incremental validity of narrative identity in predicting well-being: a review of the field and recommendations for the future. *Personal. Soc. Psychol. Rev.* 20, 142–175. doi: 10.1177/1088868315585068

Adler, J. M. (2012). Living into the story: agency and coherence in a longitudinal study of narrative identity development and mental health over the course of psychotherapy. *J. Personal. Soc. Psychol.* 102, 367–389. doi: 10.1037/a0025289

Allison, S. T., and Goethals, G. R. (2014). "Now he belongs to the ages: the heroic leadership dynamic and deep narratives of greatness," in *Conceptions of Leadership: Enduring Ideas and Emerging Insights*, eds G. R. Goethals, S. T. Allison, R. M. Kramer, and D. M. Mesnick (New York, NY: Palgrave Macmiillan), 167–183.

Allison, S. T., and Goethals, G. R. (2017). "The hero's transformation," in *Handbook of Heroism and Heroic Leadership*, eds S. T. Allison, G. R. Goethals, and R. M. Kramer (New York, NY: Routledge), 379–400.

Andresen, R., Caputi, P., and Oades, L. G. (2006). Stages of recovery instrument: development of a measure of recovery from serious mental illness. *Aust. N. Z. J. Psychiatry* 40, 972–980. doi: 10.1111/j.1440-1614.2006.01921.x

Anthony, W. A. (1993). Recovery from mental illness: the guiding vision of the mental health service system in the 1990s. *Psychos. Rehabil. J.* 16, 11–23. doi: 10.1037/h0095655

Bak, W. (2015). Possible selves: implications for psychotherapy. *Int. J. Mental Health Addict.* 13, 650–658. doi: 10.1007/s11469-015-9553-2

Bandura, A. (2001). Social cognitive theory: an agentic perspective. *Ann. Rev. Psychol.* 52, 1–26. doi: 10.1146/annurev.psych.52.1.1

Bauer, J. J., McAdams, D. P., and Pals, J. L. (2008). Narrative identity and eudaimonic well-being. *J. Happiness Stud.* 9, 81–104. doi: 10.1007/s10902-006-9021-6

Bianco, J. A. (2011). Narrative empowerment and the talking cure. *Health Commun.* 26, 297–301. doi: 10.1080/10410236.2010.550023

Biswas-Diener, R. (2010). *Practicing Positive Psychology Coaching: Assessment, Diagnosis and Intervention*. Hoboken, NJ: John Wiley & Sons.

Boniwell, I., Kauffman, C., and Silberman, J. (2014). "The positive psychology approach to coaching," in *The Complete Handbook of Coaching*, 2nd Edn, eds T. Bachkirova, E. Duncan, and D. Clutterbuck (London: Sage), 157–169.

Booker, C. (2006). *The Seven Basic Plots: Why We Tell Stories*. London: Continuum, 69–86.

Bora, R. (2010). *Empowering People: Coaching for Mental Health Recovery*. London: Rethink Mental Illness.

Bora, R., Leaning, L., Moores, A., and Roberts, G. (2010). Life coaching for mental health recovery: the emerging practice of recovery coaching. *Adv. Psychiatr. Treat.* 16, 459–467. doi: 10.1192/apt.bp.108.006536

Boyatzis, R. E. (2006). An overview of intentional change from a complexity perspective. *J. Manage. Dev.* 25, 607–623. doi: 10.1108/02621710610678445

Boyatzis, R. E., and McKee, A. (2006). Intentional change. *J. Organ. Excell.* 25, 49–60. doi: 10.1002/joe.20100

Brown, W. (2008). Narratives of mental health recovery. *Soc. Alternat.* 27, 42–48.

Brown, W., and Kandirikirira, N. (2007). *Recovering Mental Health in Scotland. Report on Narrative Investigation of Mental Health Recovery*. Glasgow: Scottish Recovery Network.

Bruner, J. (1987). Life as narrative. *Soc. Res.* 54, 11–32.

Bruner, J. (1991). The narrative construction of reality. *Crit. Inq.* 18, 1–21. doi: 10.1086/448619

Bussolari, C. J., and Goodell, J. A. (2009). Chaos theory as a model for life transitions counseling: nonlinear dynamics and life's changes. *J. Counsel. Dev.* 87, 98–107. doi: 10.1002/j.1556-6678.2009.tb00555.x

Butz, M. R. (1997). *Chaos and Complexity: Implications for Psychological Theory and Practice*. Washington, DC: Taylor & Francis.

Campbell, J. (1968). *The Hero with a Thousand Faces*. Princeton, NJ: Princeton University Press.

Cavanagh, M., and Buckley, A. (2014). "Coaching and mental health," in *The Complete Handbook of Coaching*, 2nd Edn, eds E. Cox, T. Bachkirova, and D. Clutterbuck (London: Sage), 405–415.

Chamberlain, L. (1998). "An introduction to chaos and nonlinear dynamics," in *Clinical Chaos: A Therapist's Guide to Nonlinear Dynamics and Therapeutic Change*, eds L. L. Chamberlain and M. Butz (Philadelphia, PA: Brunner/Mazel), 3–14.

Cochran, L., and Laub, J. (1994). *Becoming an Agent: Patterns and Dynamics for Shaping Your Life.* (Albany: State University of New York Press).

Cross, S., and Markus, H. (1991). Possible selves across the life span. *Hum. Dev.* 34, 230–255. doi: 10.1159/000277058

Davidson, L., O'Connell, M. J., Tondora, J., Lawless, M., and Evans, A. C. (2005). Recovery in serious mental illness: a new wine or just a new bottle? *Prof. Psychol. Res. Pract.* 36, 480–487. doi: 10.1037/0735-7028.36.5.480

Davidson, L., and Strauss, J. (1992). Sense of self in recovery from mental illness. *Br. J. Med. Psychol.* 65, 131–145. doi: 10.1111/j.2044-8341.1992.tb01693.x

Deegan, P. (1996). Recovery as a journey of the heart. *Psychiatr. Rehabil. J.* 19, 91–97. doi: 10.1037/h0101301

Deegan, P. (2001). "Recovery as a self-directed process of healing and transformation," in *Recovery and Wellness: Models of Hope and Transformation for People with Mental Illness*, ed. C. Brown (Binghamton, NY: The Haworth Press), 5–22.

Drake, D. B. (2010). "Narrative coaching," in *The Complete Handbook of Coaching*, eds E. Cox, T. Bachkirova, and D. Clutterbuck (London: Sage), 120–131.

Drake, D. B. (2017). "Working with narratives in coaching," in *The SAGE Handbook of Coaching*, eds T. Bachkirova, G. Spence, and D. Drake (London: Sage), 291–309.

Drake, D. B. (2018). *Coaching: The Definitive Guide to Bringing Our New Stories to Life*. Petaluma, CA: CNC Press.

Drake, R. E., and Whitley, R. (2014). Recovery and severe mental illness: description and analysis. *Can. J. Psychiatry* 59, 236–242. doi: 10.1177/070674371405900502

Eaton, N. (ed.) (2017). Advances (in)transdiagnostic psychopathology research: introduction to the special issue. *Comprehen. Psychiatry* 79, 1–3. doi: 10.1016/j.comppsych.2017.09.006

Erikson, M. G. (2007). The meaning of the future: toward a more specific definition of possible selves. *Rev. Gen. Psychol.* 11, 348–358. doi: 10.1037/1089-2680.11.4.348

Fitzgerald, M., and Kirk, G. (2013). Serious games: an intervention in low-secure settings. *Ment. Health Pract.* 16, 14–19. doi: 10.7748/mhp2013.11.17.3.14.e813

Foundations Recovery Network (2018). *Heroes in Recovery*. Available at:https://heroesinrecovery.com/ (accessed November 1, 2018).

Frank, A. W. (1995). *The Wounded Storyteller: Body, Illness, and Ethics*. Chicago, IL: University of Chicago Press.

Frazier, L. D., and Hooker, K. (2006). "Possible selves in adult development: Linking theory and research," in *Possible Selves: Theory, Research and Applications*, eds C. Dunkel and J. Kerpelman (Hauppauge, NY: Nova Science Publishers), 41–59.

Friedli, L. (2009). *Mental Health, Resilience and Inequalities*. Copenhagen: World Health Organisation.

Fullerton, T. (2018). *Game Design Workshop: A Playcentric Approach to Creating Innovative Games*, 4th Edn. Boca Raton, FL: CRC Press/Taylor & Francis.

Gallagher, S. (2003). "Self-narrative in Schizophrenia," in *The Self in Neuroscience and Psychiatry*, eds T. Kircher and A. David (New York, NY: Cambridge University Press), 336–357. doi: 10.1017/CBO9780511543708.017

Gelo, O. C. G., and Salvatore, S. (2016). A dynamic systems approach to psychotherapy: a meta-theoretical framework for explaining psychotherapy change processes. *J. Counsel. Psychol.* 63, 379–395. doi: 10.1037/cou0000150

Glover, H. (2012). "Recovery, lifelong learning, social inclusion and empowerment: is a new paradigm emerging?," in *Empowerment, Lifelong Learning and Recovery in Mental Health: Towards a New Paradigm*, eds P. Ryan, S. Ramon, and T. Greacen (Basingstoke: Palgrave Macmillan), 15–35.

Graci, M. E., Watts, A. L., and Fivush, R. (2018). Examining the factor structure of meaning-making for stressful events and relations with psychological distress. *Memory* 26, 1220–1232. doi: 10.1080/09658211.2018.1441422

Guastello, S. J., and Liebovitch, L. S. (2009). "Introduction to nonlinear dynamics and complexity," in *Chaos and Complexity in Psychology: The Theory of Nonlinear Dynamical Systems*, eds S. J. Guastello, M. Koopmans, and D. Pincus (New York, NY: Cambridge University Press), 1–40.

Habermas, T. (2011). Autobiographical reasoning: arguing and narrating from a biographical perspective. *New Direct. Child Adolesc. Dev.* 131, 1–17. doi: 10.1002/cd.285

Hartley, J. (2010). "Mapping our journey: the hero's journey as a therapeutic approach," in *Psychosis and Spirituality: Consolidating the New Paradigm*, ed. I. Clarke (West Sussex: John Wiley), 227–238.

Hawkins, P., and Smith, N. (2014). "Transformational coaching," in *The Complete Handbook of Coaching*, eds E. Cox, T. Bachkirova, and D. Clutterbuck (London: Sage), 231–244.

Hoyle, R. H., and Sherrill, M. R. (2006). Future orientation in the self-system: possible selves, self-regulation, and behaviour. *J. Personal.* 74, 1673–1696. doi: 10.1111/j.1467-6494.2006.00424.x

King, L. A. (2001). The hard road to the good life: the happy, mature person. *J. Humanistic Psychol.* 41, 51–72. doi: 0.1177/0022167801411005

Kirkpatrick, H. (2008). A narrative framework for understanding experiences of people with severe mental illnesses. *Arch. Psychiatr. Nurs.* 22, 61–68. doi: 10.1016/j.apnu.2007.12.002

Koch, E. J., and Shepperd, J. A. (2004). Is self-complexity linked to better coping? A review of the literature. *J. Personal.* 72, 727–760. doi: 10.1111/j.0022-3506.2004.00278.x

Krueger, R. F., and Eaton, N. R. (2015). Transdiagnostic factors of mental disorders. *World Psychiatry* 14, 27–29. doi: 10.1002/wps.20175

Lamprell, K., and Braithwaite, J. (2016). Patients as story-tellers of healthcare journeys. *Med. Humanities* 42, 207–209. doi: 10.1136/medhum-2016-010885

Langer, E. J. (2000). Mindful learning. *Curr. Direct. Psychol. Sci.* 9, 220–223.

Lelardeux, C., Alvarez, J., Montaut, T., Galaup, M., and Lagarrigue, P. (2013). "Health-care games and the metaphoric approach," in *Serious Games for Healthcare: Applications and Implications*, eds S. Arnab, I. Dunwell, and K. Debattista (Hershey, PA: IGI Global), 24–49. doi: 10.4018/978-1-4666-1903-6

Little, D. L., Snyder, C. R., and Wehmeyer, M. (2006). "The agentic self: on the nature and origins of personal agency across the lifespan," in *The Handbook of Personality Development*, eds D. Mroczek and T. D. Little (Mahwah, NJ: Lawrence Erlbaum and Associates), 61–80.

Lysaker, P. H., Lysaker, J. T., and Lysaker, J. T. (2001). Schizophrenia and the collapse of the dialogical self: recovery, narrative and psychotherapy. *Psychother. Theory Res. Pract. Train.* 38, 252–261. doi: 10.1037/0033-3204.38.3.252

Mackenzie, C. (2008). "Introduction: practical identity and narrative agency," in *Practical Identity and Narrative Agency* Routledge Studies in Contemporary Philosophy, Vol. 14, eds C. Mackenzie and K. Atkins (New York, NY: Routledge), 1–28.

MacLeod, A. K., and Conway, C. (2007). Well-being and positive future thinking for the self versus others. *Cognit. Emot.* 21, 1114–1124. doi: 10.1080/02699930601109507

Mahoney, M. J. (1991). *Human Change Processes: The Scientific Foundations of Psychotherapy*. New York, NY: Basic Books.

Mahoney, M. J., and Granvold, D. K. (2005). Constructivism and psychotherapy. *World Psychiatry* 4, 74–77.

Mahoney, M. J., and Marquis, A. (2002). Integral constructivism and dynamic systems in psychotherapy processes. *Psychoanal. Inq.* 22, 794–813. doi: 10.1080/07351692209349018

Markus, H., and Nurius, P. (1986). Possible selves. *Am. Psychol.* 41, 954–969. doi: 10.1037/0003-066X.41.9.954

McAdams, D. P. (1985). *Power, Intimacy, and the Life Story: Personological Inquiries Into Identity*. Homewood, IL: Dorsey Press.

McAdams, D. P. (1993). *The Stories We Live by: Myths and the Making of the Self*. New York, NY: Guilford Press.

McAdams, D. P. (2001). The psychology of life stories. *Rev. Gen. Psychol.* 5, 100–122. doi: 10.1037/1089-2680.5.2.100

McAdams, D. P. (2013). The psychological self as actor, agent, and author. *Perspect. Psychol. Sci.* 8, 272–295. doi: 10.1177/1745691612464657

McAdams, D. P. (2018). Narrative identity: what is it? What does it do? How do you measure it? *Imagin. Cognit. Personal.* 37, 359–372. doi: 10.1177/0276236618756704

McAdams, D. P., and McLean, K. (2013). Narrative identity. *Curr. Direct. Psychol. Sci.* 22, 233–238. doi: 10.1177/0963721413475622

McGorry, P. D., Hartmann, J. A., Spooner, R., and Nelson, B. (2018). Beyond the "at risk mental state" concept: transitioning to transdiagnostic psychiatry. *World Psychiatry* 17, 133–142. doi: 10.1002/wps.20514

Mitgutsch, K. (2011). "Serious learning in serious games," in *Serious Games and Edutainment Applications*, eds M. Minhua, A. Oikonomou, and L. C. Jain (London: Springer-Verlag), 45–58. doi: 10.1007/978-1-4471-2161-9

Mobus, G. E., and Kalton, M. C. (2015). *Principles of Systems Science*. New York, NY: Springer, 289–296. doi: 10.1007/978-1-4939-1920-8

Niemeyer, R. A. (1993). An appraisal of constructivist psychotherapies. *J. Consul. Clin. Psychol.* 61, 221–234. doi: 10.1037//0022-006x.61.2.221

Niemeyer, R. A. (2004). Fostering posttraumatic growth: a narrative elaboration. *Psychol. Inq.* 15, 53–59.

Nurser, K., Rushworth, I., Shakespeare, T., and Williams, D. (2018). Personal storytelling in mental health recovery. *Ment. Health Rev. J.* 23, 25–36. doi: 10.1108/MHRJ-08-2017-0034

O'Hagan, M. (2012). A new story for a new leadership. *Austr. J. Psychos. Rehabil. Autumn* 8–10.

Oliver, C. (2005). *Reflexive Inquiry: A Framework for Consultative Practice*. London: Karnac.

Onken, S. J., Craig, C. M., Ridgway, P., Ralph, R. O., and Cook, J. A. (2007). An analysis of the definitions and elements of recovery: a review of the literature. *Psychiatr. Rehabil. J.* 31, 9–22. doi: 10.2975/31.1.2007.9.22

Pals, J. L. (2006a). Authoring a second chance in life: emotion and transformational processing within narrative identity. *Res. Hum. Dev.* 3, 101–120. doi: 10.1080/15427609.2006.9683364

Pals, J. L. (2006b). Narrative identity processing of difficult life experiences: pathways of personality development and positive self transformation in adulthood. *J. Personal.* 74, 1079–1110. doi: 10.1111/j.1467-6494.2006.00403.x

Pals, J. L., and McAdams, D. P. (2004). The transformed self: a narrative understanding of posttraumatic growth. *Psychol. Inq.* 15, 65–69.

Park, C. L., and George, L. S. (2013). Assessing meaning and meaning making in the context of stressful life events: measurement tools and approaches. *J. Positive Psychol.* 8, 483–504. doi: 10.1080/17439760.2013.830762

Perna, P. A., and Masterpasqua, F. (1997). "Introduction: the history, meaning, and implications of chaos and complexity," in *The Psychological Meaning of Chaos: Translating Theory Into Practice*, eds F. Masterpasqua and P. A. Perna (Washington, DC: American Psychological Association), 10–28. doi: 10.1037/10240-012

Pincus, D., Kiefer, A. W., and Beyer, J. I. (2018). Nonlinear dynamical systems and humanistic psychology. *J. Humanistic Psychol.* 58, 343–366. doi: 10.1177/0022167817741784

Plsek, P. E., and Greenhalgh, T. (2001). Complexity science: the challenge of complexity in health care. *Br. Med. J.* 323, 625–628. doi: 10.1136/bmj.323.7313.625

Polkinghorne, D. E. (1991). Narrative and self-concept. *J. Narrat. Life History* 1, 135–153. doi: 10.1075/jnlh.1.2-3.04nar

Polkinghorne, D. E. (1996). Transformative narratives: from victimic to agentic life plots. *Am. J. Occup. Ther.* 50, 299–305. doi: 10.5014/ajot.50.4.299

Rapp, C. A., and Goscha, R. J. (2012). *The Strengths Model: A Recovery-Oriented Approach to Mental Health Services*, 3rd Edn. New York, NY: Oxford University Press.

Rickles, D., Hawe, P., and Shiell, A. (2007). A simple guide to chaos and complexity. *J. Epidemiol. Commun. Health* 61, 933–937. doi: 10.1136/jech.2006.054254

Ricoeur, P. (1991). Narrative identity. *Philos. Today* 35, 73–81.

Ridgway, P. (2001). Restorying psychiatric disability: learning from first person recovery narratives. *Psychiatr. Rehabil. J.* 24, 335–343. doi: 10.1037/h0095071

Riessman, C. K. (2008). *Narrative Methods for the Human Sciences*. Thousand Oaks, CA: Sage Publications.

Robertson, D. L., and Lawrence, C. (2015). Heroes and mentors: a consideration of relational-cultural theory and "The Hero's Journey". *J. Creat. Ment. Health* 10, 264–277. doi: 10.1080/15401383.2014.968700

Robinson, E. (2010). The use of literary techniques in coaching. *J. Manage. Dev.* 29, 902–913. doi: 10.1108/02621711011084222

Rogers, E. S., Farkas, M., and Anthony, W. A. (2005). "Recovery from severe mental illnesses and evidence-based practice research," in *The Evidence-Based Practice: Methods, Models, and Tools for Mental Health Professionals*, eds C. E. Stout and R. A. Hayes (Hoboken, NJ: John Wiley & Sons), 199–219.

Rudnick, A. (2012). "Introduction," in *Recovery of People with Mental Illness: Philosophical and Related Perspectives*, ed. A. Rudnick (New York, NY: Oxford University Press), 3–12. doi: 10.1093/med/9780199691319.003.0001

Salen, K., and Zimmerman, E. (2004). *Rules of Play: Game Design Fundamentals*. Cambridge, MA: MIT Press.

Salvatore, S., Tschacher, W., Gelo, O. C. G., and Koch, S. (2015). Editorial: dynamic systems theory and embodiment in psychotherapy research. A new look at process and outcome. *Front. Psychol.* 6:914. doi: 10.3389/fpsyg.2015.00914

Sarbin, T. R. (1986). "The narrative as a root metaphor for psychology," in *Narrative Psychology: The Storied Nature of Human Conduct*, ed. T. R. Sarbin (Westport, CT: Praeger Publishers), 3–21.

Schell, J. (2014). *The Art of Game Design: A Book of Lenses*, 2nd Edn. Boca Raton, FL: CRC Press.

Scottish Recovery and Network (2016). *The Hero's Journey to Recovery*. Available at:https://www.scottishrecovery.net/resource/the-heros-journey-to-recovery/ (accessed October 30, 2018).

Shepherd, G., Boardman, J., and Slade, M. (2008). *Making Recovery a Reality*. London: Sainsbury Centre for Mental Health.

Singer, J. A. (2004). Narrative identity and meaning making across the adult lifespan: an introduction. *J. Personal.* 72, 437–459. doi: 10.1111/j.0022-3506.2004.00268.x

Singer, J. A., and Bluck, S. (2001). New perspectives on autobiographical memory: the integration of narrative processing and autobiographical reasoning. *Rev. Gen. Psychol.* 5, 91–99. doi: 10.1037/1089-2680.5.2.91

Slade, M. (2009). *Personal Recovery and Mental Illness: A Guide for Mental Health Professionals (Values-Based Practice)*. Cambridge: Cambridge University Press, 1–7. doi: 10.1017/CBO9780511581649

Slade, M. (2010). Mental illness and well-being: the central importance of positive psychology and recovery approaches. *BMC Health Ser. Res.* 10:26. doi: 10.1186/1472-6963-10-26

Slade, M. (2012). "The epistemological basis of personal recovery," in *Recovery of People with Mental Illness: Philosophical and Related Perspective*, ed. A. Rudnick (Oxford: Oxford University Press), 78–94. doi: 10.1093/med/9780199691319.003.0006

Slade, M., and Longden, E. (2015). Empirical evidence about recovery and mental health. *BMC Psychiatry* 15:285. doi: 10.1186/s12888-015-0678-4

Sools, A. M., Tromp, T., and Mooren, J. H. (2015). Mapping letters from the future: exploring narrative processes of imagining the future. *J. Health Psychol.* 20, 350–364. doi: 10.1177/1359105314566607

Sturmberg, J. (2016). "Returning to holism: an imperative for the twenty-first century," in *The Value of Systems and Complexity Sciences for Healthcare,* ed. J. P. Sturmberg (Cham: Springer International Publishing), 3–20.

Substance Abuse and Mental Health Services Administration [SAMHSA] (2012). *SAMHSA's Working Definition of Recovery [Brochure]*. Rockville, MD: Author.

Tedeschi, R. G., and Calhoun, C. G. (2004). Posttraumatic growth: conceptual foundations and empirical evidence. *Psychol. Inq.* 15, 1–18. doi: 10.1207/s15327965pli1501_01

Treher, E. N. (2011). *Learning with Board Games*. Belton, TX: The Learning Key Inc.

Tse, S., and Zhu, S. (2013). "Possible selves": concept and applications for individuals in recovery from mental health problems. *Asian Health Care J.* 3, 16–19.

Wasserman, J. A., and Banks, J. (2017). Details and dynamics: mental models of complex systems in game-based learning. *Simul. Gam.* 48, 603–624. doi: 10.1177/1046878117715056

Watkins, P. (2007). *Recovery: A Guide for Mental Health Practitioners*. London: Churchill Livingstone Elsevier, 27–79.

Whitehead, R., and Bates, G. (2016). The transformational processing of peak and nadir experiences and their relationship to eudaimonic and hedonic well-being. *J. Happiness Stud.* 17, 1577–1598. doi: 10.1007/s10902-015-9660-6

Williams, C. (2017). The hero's journey: a mudmap for change. *J. Humanistic Psychol.* 57, 1–18. doi: 10.1177/0022167817705499

Wisdom, J. P., Bruce, K., Saedi, G. A., Weis, T., and Green, C. A. (2008). 'Stealing me from myself': identity and recovery in personal accounts of mental illness. *Aust. N. Z. J. Psychiatry* 42, 489–495. doi: 10.1080/00048670802050579

Yanos, P. T., Roe, D., and Lysaker, P. H. (2010). The impact of illness identity on recovery from severe mental illness. *Am. J. Psychiatr. Rehabil.* 13, 73–93. doi: 10.1080/15487761003756860

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Promoting Self-Regulatory Management of Chronic Pain Through Dohsa-hou: Single-Case Series of Low-Functioning Hemodialysis Patients

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Hemodialysis patients suffer from long-term pain that drains their energy and contributes to behavioral interference and other negative effects on their daily lives that result in or exacerbate functional limitations. In addition, they deal with dietary restrictions, symptoms such as itching, lack of energy, and psychological stressors like the loss of self-concept and self-esteem. Self-regulation involves the capacity to notice, inform, and modulate responses and behavior, and research indicates that it promotes rehabilitation in chronic pain patients. Research on the aspects of self-regulation afforded by the Japanese psychotherapy Dohsa-hou correspond to psychological processes tied to the sense of self-control that clients realize over their body movements. This study pilot tested a hospital-integrated implementation of Dohsa-hou relaxation tasks as a chronic pain management behavioral intervention for five female hemodialysis patients between the ages of 59–62 years. We conducted an ABABABA single-case design to compare baseline A-phases (treatment-as-usual: TAU) taken at recurring 1 week intervals (three sessions per week for a total of 4 weeks, 12 total recordings) with an intervention of Dohsa-hou B-phases every 4 weeks (three sessions per week for 12 weeks, 36 total recordings) over the span of 4 months to compare effectiveness. Visual Analogue Scale (VAS) pain scores between phases were taken and self-regulatory progress was tracked and summarized from a series of semi-structured interviews. Visual analysis of scores for each participant as single cases indicated decreases for the Dohsa-hou phase compared to baseline treatment-as-usual. As a result, participants reported using Dohsa-hou to reduce pain and experienced improvements in quality of life associated with greater self-regulatory capacity to attend to personal care and domestic activities. These preliminary findings suggest that Dohsa-hou body movement relaxation tasks were feasible as a coping skill in a hospital-integrated setting and at home and show promise for promoting quality of life vis-a-vis the management of severe and chronic bodily pain associated with end-stage renal disease and its treatment, particularly by improving aspects of pain-mediated self-regulatory fatigue.

Keywords: chronic conditions, chronic pain, self-regulation, Dohsa-hou, hemodialysis patients, pain management, quality of life, single-case design

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INTRODUCTION

Patients with chronic conditions are faced with the challenging prospect of comprehensively managing their disease and its symptoms. The discomfort of pain is a source of exacerbating demand under these circumstances. Pain becomes especially troublesome as patients are already making negotiations about the quality of their lives in the form of adjusting to the changes that are required to adhere to the treatment regimen of their disease. Psychologically, regaining control in the face of the adversity posed by the life event of chronic disease diagnosis, the onset of symptoms, and their treatment is a priority. While chronic conditions each have their own subset of challenges, the treatment of end-stage renal disease (ESRD) is characterized by not only the management of its symptoms, but also by the requisite difficulties imposed by its treatment, often in the form of chronic bodily pain. The primary aim of the current study was to develop a program to provide psychological support through relief from the bodily pain that patients experience under the duress of prolonged treatment for ESRD, and to pilot test and qualitatively evaluate its proof-of-concept for indications of changes in quality of life.

ESRD patients are treated with various modalities such as hemodialysis (HD), peritoneal dialysis (PD), and kidney transplantation. In an overview of the status of treatment for ESRD globally, Grassmann et al. (2005) reported comprehensive accounts of patient numbers, treatment modalities, and associated trends. Global ESRD patient numbers were estimated as encompassing 1,783,000 individuals, and among these 76.89% (1,371,000) received dialysis treatment (HD and PD) and 23.10% (412,000) received transplants. In the case of national statistics for Japan whose population was around 127 million at the time of the study, an estimated 261,000 individuals were ESRD patients, 95.02% (248,000) of which were dialysis patients and 4.98% (13,000) received transplants (Grassmann et al., 2005). In more recent accounts, ESRD patient numbers were estimated at 334,505 individuals for Japan in a survey by the Japanese Society for Dialysis Therapy at the end of 2017 (Nitta et al., 2018). Showing a similar pattern, 97.3% (325,415) of these individuals were HD patients and 2.7% (9,090) were continuous ambulatory peritoneal dialysis patients. Efforts to document the cumulative evidence of kidney transplant recipients by the Japan Academic Consortium of Kidney Transplantation cohort study estimated that 1,614 individuals received kidney transplants from 1990 to 2014 (Okumi et al., 2018). The Japan Organ Transplant Network (JOTNW) had registered 12,449 prospective recipients of kidney transplants in 2017 (Japan Organ Transplant Network (JOTNW)., 2019). Patients diagnosed with end stage renal failure are registered for kidneys, and JOTNW reported 182 kidney transplants had been conducted (Japan Organ Transplant Network (JOTNW)., 2019). In Japan, a major contingent of ESRD patients have received HD therapy for a prolonged period, and a majority of them have tended to be elderly. In fact, there were patients who have undergone HD for over 50 years in some cases. Due to clinical features from the relatively limited treatment options for ESRD, it is clear that long-term hemodialysis patients should be a focus for managed care in the context of Japan.

Psychosocial elements play a role in the adaptation to ESRD because undergoing dialysis treatment requires being physically connected to the HD machine three times a week over the course of a year, incurring a host of major stressors (Kaptein et al., 2010). Notably, patients are faced with lifestyle changes in the form of limitations to their food and fluid intake, symptoms such as itchiness and a lack of energy, and psychological components such as the loss of self-concept and self-esteem, feelings of uncertainty about the future, feelings of guilt toward family members, and other social consequences (Kaptein et al., 2010). Seen under the lens of chronic pain management and the integrative model of the biopsychosocial approach (Engel, 1977), HD patients often suffer from long-term pain that leaves them with little energy and negatively affects their quality of life. ESRD patients have poor quality of life (Feng et al., 2013) and the prevalence of acute and chronic pain in HD patients has been systematically reported to be up to 82 and 92%, respectively (Brkovic et al., 2016). In a previous study from Japan, hemodialysis patients suffering from chronic pain were shown to have pain-related constraints to the activities of daily living as a matter of disability, particularly in the realm of personal care and domestic activities (Haramaki and Nishi, 2012). Brkovic et al. (2016) concluded that improving quality of life and pain-related disability should represent a clinical and research priority and encouraged the nephrology community to promote pain management for HD patients.

Sauer et al. (2010) suggested that self-regulation theory (Carver and Sheier, 1982, 1998) is a useful integrative framework for understanding and treating chronic pain disorders. Behavioral and physiological measures indicate that individuals with chronic pain have lower self-regulatory capacity than those without it (Solberg Nes et al., 2009, 2010). Synthesizing clinical observations and experimental advances, Solberg Nes et al. (2009) proposed relationships between self-regulatory demands, executive functions, and self-regulatory fatigue. In their model, self-regulation demands require control to be exerted over emotions, thoughts, social relations, and behaviors. These relationships indicate that pain increases self-regulatory demands which in turn reduce executive functions. Case studies from Japan utilizing the body movement technique, *Dohsa-hou*, during HD therapy showed that HD patients with chronic pain reported reductions in psychological distress amenable to the experience of physical self-regulation (e.g., relaxation) gained from executing body movements with a sense of agency (Haramaki, 2011; Haramaki and Nishi, 2012). In the follow-up period, all patients reported maintaining their self-management by performing the body movements as an adaptive skill and experiencing improvements in daily life activities, such as housekeeping (Haramaki and Nishi, 2012). Together, observations gleaned from clinical settings indicated that Dohsa-hou might activate or otherwise influence an inherent motivation for patients to self-regulate, monitor, and maintain their health or activities tied to well-being.

In Japan, Dohsa-hou has been used for psychotherapy in various developmental and psychological conditions, including schizophrenia, depression, anxiety, and others (Naruse, 1997; Imura et al., 2016; Chervenkova, 2017; Fujino, 2017). Dohsa-hou facilitates behavioral change through body movements, feeling states of the body, and the experience of relaxation and embodied change as a means of therapeutic intervention and communication (Naruse, 1995; Fujino, 2012, 2017). Dohsa-hou was originally developed in Japan in 1966 by Gosaku Naruse from studies on the use of hypnosis to improve motor difficulties in children with cerebral palsy (Naruse, 1973). Naruse formulated the clinical observations of change into an underlying theory for Dohsa-hou, in which a coherence between the psychological and physiological process of movement is achieved when the client intends to move a body part, strives toward that goal, and realizes the movement they intended (Naruse, 1988, 1997; Kabir et al., 2018). Similar to other contemplative and bodymind approaches that target improvements in body movements, self-consciousness, mood, and decentering, Dohsa-hou increases awareness about the body through attention to bodily sensations and processes thought to confer motor resonance (Konno and Ohno, 1987; Dadkhah, 1998; Shirouzu and Koshikawa, 2011; Chervenkova, 2017; Kabir et al., 2018). The "Dohsa process" is designed to enhance a sense of agency over the body and is stipulated as a psychological activity. Comparably, self-regulation involves the capacity to exercise control and guide reactions, which are abilities essential to managing health outcomes and facilitating adaptive behavior. In this manner, the theory and practice of Dohsa-hou body movements and self-regulation overlap in the domain of motor control over body movements and health-related constructs for managing bodily signals and internal states (Chervenkova, 2017; Kabir et al., 2018).

A particularly salient subset of patients with chronic pain from a chronic condition are those who have undergone HD treatment for an extensive period and experience difficulties in their everyday life because of their pain. Such patients can become isolated in their social and familial roles as a result of the adaptive necessity to undergo HD therapy and deal with their chronic condition. Notably, patients have been learning adaptation skills for a long time. They often identify or make sense of their circumstances by finding roles and activities that they are able to do by themselves (e.g., housekeeping, do-it-yourself projects, volunteer activities, etc.) (Haramaki and Nishi, 2012). Patients who experience severe pain, long periods of inactivity, and more severe disabilities and symptoms in general are defined as lower-functioning patients (Friedberg et al., 2012), and might not be able to participate in group interventions. The variable nature of pain occurrence, intensity, and relief across time settings and limitations in their measurement precision makes the nomothetic approach to understanding clinical significance and determining therapeutic gain challenging (Morley and Williams, 2015). In turn, Morley and Williams (2015) proposed that greater attention should be paid to understanding *processes* within individuals in addition to the presence or absence of symptoms aggregated into descriptive categories designed for diagnosis. This approach prioritizes the individual and allows the therapist to recognize that the anxiety and distress associated with pain are not merely accounts of comorbidity but common outcomes of worry, frustration, losses of roles and pleasures, and fears about the future. Morley and Williams (2015) stipulated that, to improve outcomes for patients, distress and psychological disturbance should be interpreted under the context and the meaning of pain for the individual. Williams and Morley (2018) also put forth the notion that treatment for chronic pain may be gainfully tailored to fit patients toward increases in treatment efficiency, cost savings, expected improvement in treatment outcome, and patient satisfaction. Toward this end, effectiveness research is required to determine whether treatments are both feasible (e.g., exhibit procedural fidelity) and have clinical and social benefits that extend to other environments, especially in clinical practice (Williams and Morley, 2018). Therefore, leveraging the idiographic strengths of single-case designs would be especially suitable for understanding the processes of physical and psychological change, if any, that could occur from a pilot implementation under such circumstances (Tate et al., 2016; Williams and Morley, 2018) to determine degrees of applicability.

Pain elicits a response of increased muscle tension, which itself produces more pain, and contributes directly to secondary problems such as sleep disturbance and immobilization (Williams and Morley, 2018). Dohsa-hou contains some elements similar to the highly specific form of graded exposure *in vivo* to pain-related movements in the work by Vlaeyen et al. (2012), while also incorporating some elements attributed to third wave treatments (Morley and Williams, 2015; Chervenkova, 2017; Kabir et al., 2018). Dohsa-hou might endow sufferers of chronic pain with the opportunity to experience physical self-regulation and break the pain-tension cycle to handle self-regulatory demands or improve self-regulatory deficits (Solberg Nes et al., 2009).

Brkovic et al. (2016) noted that one of the most important parameters for evaluating patients' quality of life is through their degree of bodily pain, and that improving quality of life means improving quality of care by understanding and relieving bodily pain in HD patients. Therefore, the aim of this study is to investigate the effectiveness of a program targeting quality of life and self-regulation experiences by providing bodily pain relief and improvement from pain-related life interference as a way to augment the treatment regimen. This study designed and implemented a hospital-integrated program of body movement relaxation tasks to a sample of HD patients and investigated questions of effectiveness with single-case design and reporting. The study proposes that hemodialysis patients learn to manage their chronic pain on their own through the deliberate practice of movement tasks aimed at changing feeling states that can be applied upon the onset of pain and at home on an as-needed basis.

METHODS

Impetus for the Study

Over a period of 3 years (2009–2011), the clinical staff members at the hemodialysis unit of a regional hospital in southern Japan participated in a stress-management program using Dohsa-hou relaxation tasks given by a psychotherapist with a supervisory license from the Japanese Association of Rehabilitation Psychology. The clinical psychologist demonstrated Dohsa-hou techniques for 5–10 min during staff meetings twice a month. The chief of staff requested that the clinical psychologist teach the clinical staff how they could apply Dohsa-hou to hemodialysis patients with chronic pain. All the staff agreed with this procedure: 7–10 patients had severe chronic pain, and the staff members were encouraged to give the patients the best care they could. In Japan, a HD patient normally receives dialysis treatment three times a week, with each session lasting 4 h. The staff at HD units provided patients with assistance not only in health matters but also with regard to matters of their daily activities. This facilitated the establishment of a cooperative relationship. It was observed that when patients suffer severe pain during dialysis treatment, analgesics are unable to provide sufficient relief. Thus, as recognized by the staff, the need to provide full treatment by alleviating pain for such patients served as an impetus for this study.

Procedure and Setting of Dohsa Tasks

HD patients typically suffer severe chronic pain at the shoulder, and in the neck and blood vessels, especially on the punctured side. In Dohsa-hou, there are two general types of tasks: relaxation and motor-action tasks. We selected relaxation tasks to be used on the patients in this study because they function to release excess muscle tension. The following Dohsa relaxation tasks were carried out by the patients in the supine position on a bed: (1) opening and closing the hand to achieve flexibility; (2) bending and stretching the wrist in a smooth movement; and (3) moving the arms and shoulders to relax stiffness in the shoulder and neck. The Dohsa-tasks performed and their effectiveness determined by phase are shown in **Figures 1**, **2**.

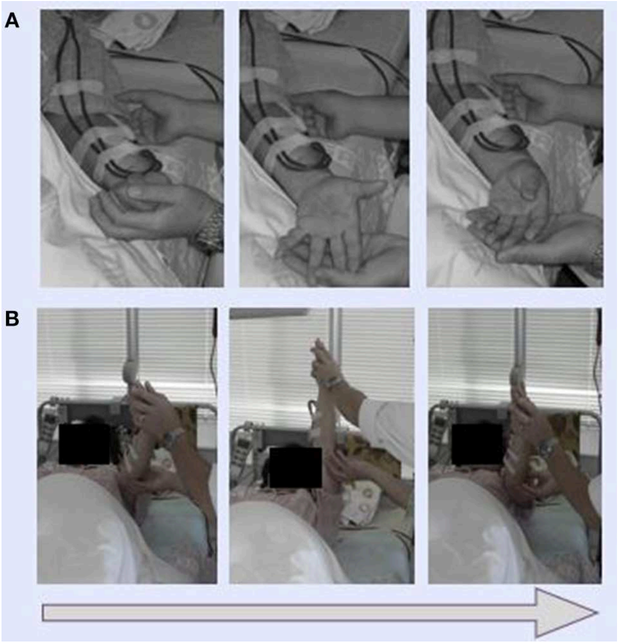

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FIGURE 1 | Demonstration of Dohsa movement tasks. **(A)** Dohsa tasks involved the clenching and opening of fists for the hands and bending back and forth for wrists. **(B)** Dohsa tasks also involved repeatedly raising and lowering the arms and shoulders along the body axis. All tasks were planned, and staff were given supervision for the psychological intervention by a licensed clinical psychologist certified by the Japanese Association of Rehabilitation Psychology.

The various steps in the Dohsa tasks were explained by means of diagrams for expanding participants' normal movement range. The Dohsa tasks were shown to be learned and replicable by the clinical staff (e.g., nurses). The staff was instructed to focus on the patient's body movement and the muscle tension they were undergoing; the staff members were also told to provide the patients with positive rather than negative feedback (e.g., "Very good, it's going smoothly. You're doing well, very well. OK. You can release your muscle tension"). Studies of Dohsa-hou in Japan have indicated that it is important to provide patients with positive feedback in regard to the awareness of their physical condition so as to improve their mental situation (Konno and Ohno, 1987; Dadkhah, 1998; Shirouzu and Koshikawa, 2011). When further questions were necessary, either the supervising clinical psychologist or the onsite clinical psychologist with a trainer license in Dohsa-hou who worked full time at the hospital visited the dialysis unit and supported or supervised the staff accordingly.

Study Design

We employed an ABABABA single-case design. All baselines were 1 week treatment-as-usual (TAU) (12 recordings) A-phases and all intervention measurements were B-phases lasting for 4 weeks (36 recordings). The Dohsa-hou intervention was applied three times a week during HD therapy. To evaluate the effect of Dohsa-hou, VAS was used to measure pain intensity before and after the Dohsa-hou intervention. Drawing from time-based pacing used in cognitive behavioral therapy, a relatively brief

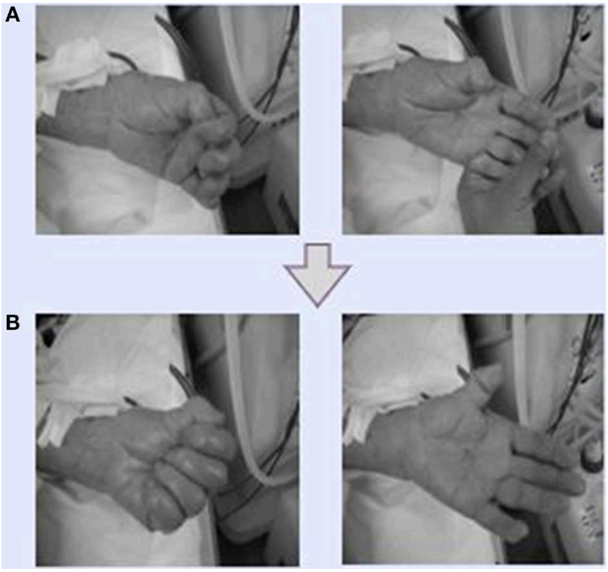

FIGURE 2 | Effectiveness of Dohsa-hou hand movements. **(A)** Dohsa tasks conducted by a participant and supervised by medical staff during HD therapy. The staff clenched and opened their fists and bent their wrists back and forth repeatedly. **(B)** After the Dohsa-hou implementation, participants could move their hands and wrists by themselves. As a result, patients reported being able to bring and wash dishes in the kitchen and proactively perform housekeeping and daily activities at home.

restful pause is known to indicate that the patient is recovering to a predetermined safe amount of activity (Friedberg et al., 2012). This was the rationale for setting the TAU baseline A-phases as withdrawal periods. In addition, the general guideline for 4 weeks observations of treatment effects in studies of chronic pain was implemented (Gewandter et al., 2015). The total period of study was 16 weeks (16 weeks of study-sessions and 1 month for follow-up). All participants rested on their beds during HD therapy. The study schedule is depicted in **Figure 3**.

Participants

Selection Criteria

The recruitment procedure was standardized along explicit inclusion criteria to target patients with chronic pain. We interviewed 69 patients (41 females) about their complaints of prolonged chronic pain. Nine patients (seven females) complained of chronic pain and seven patients (five females) gave their informed consent to participate in the study. Two male patients (71 and 69 years old) who underwent HD for a shorter period (0.3 and 0.8 years) and expressed apparent anxiety about HD from evaluation of the study, were excluded to maintain a focus on the effects of the intervention for long-term patients of severe pain and pain-related life interference associated with long-term hemodialysis treatment. This resulted in five patients who suffered from chronic bodily pain, all of whom had been recipients of hemodialysis treatment for over 10 years.

Participant Characteristics

Five women between the ages of 59 and 62 years (*M* age = 61 years old) who reported chronic pain that was particularly long-lasting and severe remained as the target participants for the present study. The patients underwent hemodialysis treatment over a long period (minimum = 16 years; maximum = 34 years; mean = 28 years). The patients were unable to do any work, having been inactive and housebound for approximately 5 years or more because of their condition. They complained of chronic pain (shoulder stiffness and pain in the vein that was punctured by the needle) during dialysis and often had to halt the treatment because of the severity (shoulder stiffness or vein pain), and this also caused difficulties in their daily lives. They took analgesics, but the effectiveness was variable (**Table 1**; treatment as usual). It should be noted that the ability of more severely ill patients (e.g., those with disabilities and largely homebound) to perform therapeutic tasks such as undergoing 30 min of additional exercise or attending counseling sessions once a week may be limited due to debilitating post-exertional pain (Nijs et al., 2008). Recent clinical studies into the condition of chronic pain patients have often used pain-related questionnaires (McCracken and Velleman, 2010; Solberg Nes et al., 2010; Wetherell et al., 2011; Wicksell et al., 2011; Hayes et al., 2013). In order to investigate an improvement in quality of life from changes in pain experiences, the patients were interviewed about their subjective experiences of pain and its interfering effects on their daily life. None of the patients had diagnoses of psychiatric illness (e.g., schizophrenia and depression).

Ethical Approval

Hemodialysis nursing staff and clinical psychologists set the study protocol. The head of hospital, vice-head of hospital, and nursing supervisor of the hospital approved the study protocol instead of an institutional review board. All the participants gave their written informed consent and voluntarily took part in the study. The study was retrospectively reviewed for compliance and approved in line with protocols from the ethical research committee of the Graduate School of Education, Hiroshima University. This review was necessary for reasons of institutional and affiliation change on the part of the principal investigator since the time of the study, and not due to ethical issues in the protocol that occurred before, during, or after the study implementation.

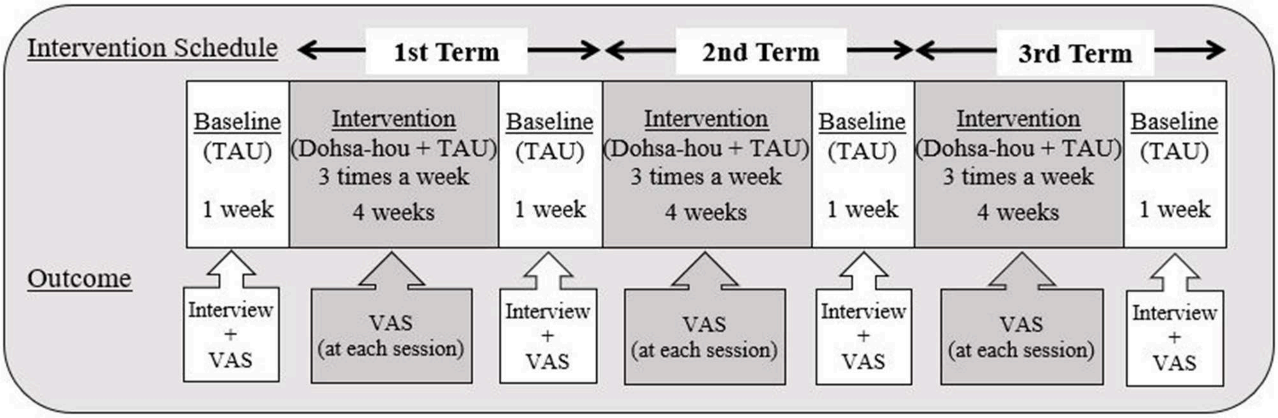

FIGURE 3 | Implementation procedure and interview schedule. This figure displays the schedule of interviews and flow of data collection points for outcome measures. There were three total terms, and each term included 1 week of baseline TAU and 3 weeks of Dohsa-hou intervention, totaling 4 weeks per term. All participants received Dohsa-hou from medical staff when they complained about their pain at its peak. All participants reported their pain intensity along the Visual Analog Scale of pain (0–10) before dialysis treatment, pre-intervention, post-intervention (1 h after Dohsa-hou intervention) and at follow-up (1 month after research period). TAU, Treatment as usual; VAS, Visual Analogue Scale (for pain).

TABLE 1 | Baseline characteristics and treatment-as-usual (TAU) for the study participants.

ID	Age (year)	Sex	Dialysis period (year)	Chronic pain	Analgesic(s)	Physical therapy	Complaint(s)
A	60	Female	16.8	Shoulder, knee	Compresses	Xenon	Difficulty with housekeeping
B	62	Female	27.8	Shoulder, knee	Loxoprofen compresses	Xenon	Difficulty with housekeeping Difficulty and disability with home activity
C	59	Female	28	Shoulder, back, chest	Loxoprofen compresses	Xenon	Difficulty with housekeeping Difficulty and disability with home activity Disability of body movement
D	62	Female	34.3	Shoulder, knee, back, hip joint	Loxoprofen compresses	Xenon Hot pack Exercise therapy	Difficulty with housekeeping Disability of home activity
E	62	Female	34.8	Shoulder, knee, back	Loxoprofen compresses	Xenon Hot pack Exercise therapy	Difficulty with housekeeping Disability of home activity Difficulty with sleeping during dialysis

All participants received their usual care for existing pain, although its effectiveness was uncertain. All staff agreed that patients needed pain care additional to their usual treatment. Xenon light refers to permeable, near-infrared wavelengths used for light therapy for living organisms. The use of photodynamic therapy relieves pain by improving blood flow.

Outcome Measures

Avoiding additional sources of physical or psychological burden for the participants was a priority in the design of the implementation. Therefore, in lieu of other invasive evaluation techniques, this study focused on two outcome measures to prioritize idiographic assessment: VAS pain scores and reports from semi-structured interviews.

The VAS pain scores included pain intensity levels, physical activity, quality of life, and life activity (or life interference). The VAS used response scales for a single item with a horizontal form: a 100 mm line anchored upward by "pain as bad as it could be" (10) and anchored downward by "no pain" (0); the patient was instructed to mark any point on the VAS continuum corresponding to their present pain intensity (Jane et al., 2011; Morley, 2018). VAS pain scores were evaluated analogically by all the participants before dialysis treatment, at 1, 2, 3, and 4 h after starting HD therapy, and after treatment. When staff conducted the Dohsa-hou intervention, VAS pain scores were measured pre and post-intervention.

The interview schedule is depicted in **Figure 3**. All participants completed the reporting at each TAU A-phase (1–3, 16–18, 31–33, and 46–48 sessions) and at follow-up (1 month after the study). All of the participants were given a semi-structured interview. The interview consisted of three main questions about the persistence of pain, the effects of Dohsa-hou, and daily life activities (especially including using the relaxation tasks in their normal daily lives). In line with the priorities of idiographic assessment that frame patient reporting of problems as the target of therapeutic change (Morley, 2018), we decided to consider patient-generated complaints and issues for regulating personal care and domestic activities (housekeeping and daily activities) as outcomes for examination.

Intervention

During the course of the study, all participants continued receiving their usual health care (TAU), including treatment for pain and other medical conditions, such as hypertension. The Dohsa-hou intervention was conducted on an individual basis and consisted of 36 sessions for each patient. The Dohsa-hou intervention schedule consisted of three terms. Complaints of pain from the five participants usually occurred around 2 h after starting HD. We conducted the Dohsa-hou tasks when participants complained of their pain. If participants did not complain of pain, we implemented Dohsa-hou at around the 2 h mark. Each intervention term lasted a total of 5 weeks, comprising 4 weeks of Dohsa-hou intervention and 1 week of TAU (see **Figure 3**).

DATA PREPARATION

VAS Scores

The VAS pain scores were averaged at 2, 3, and 4 h, and compared between intervention and TAU. The VAS pain scores were divided into two groups: one group consisted of pre-intervention values; the other consisted of post-intervention values. Participants received intervention at peak times of pain. Pre-intervention VAS pain scores were averaged from pre-dialysis treatment to before intervention. Post-intervention VAS pain scores were averaged from after intervention to 4 h after dialysis treatment. The VAS pain scores were analyzed for differences between pre-intervention and post-intervention. Visual analysis of the scores was adopted to clarify the effectiveness of the Dohsa-hou B-phases compared to the TAU baseline A-phases within the single-case design. Data plots for the series of sessions of each case are depicted in **Figure 4**. In addition, percentage-below-the-median analysis was performed as single case estimates of effect

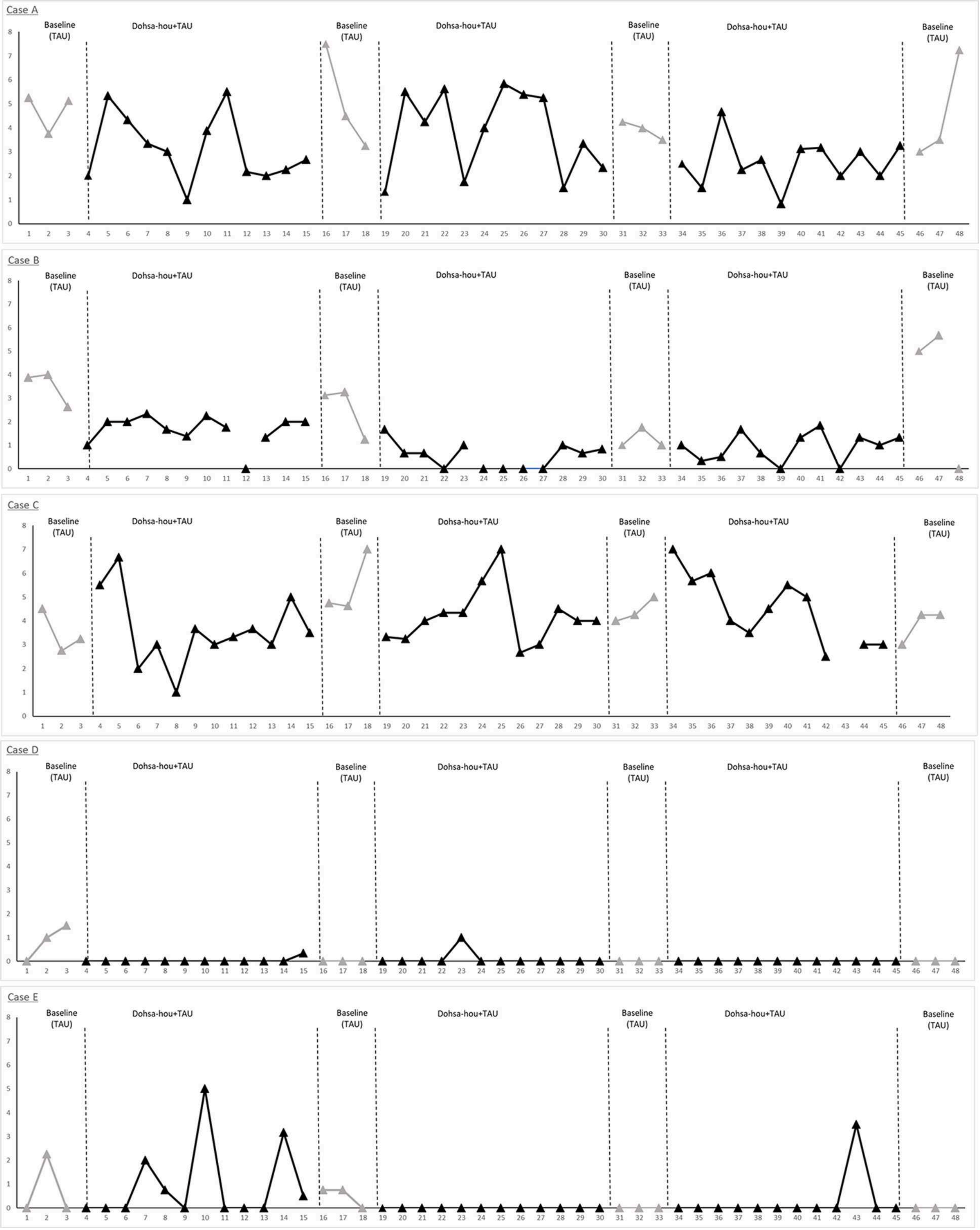

FIGURE 4 | Single-case data plots of the ABABABA design for each participant. VAS pain scores, measured five times during HD therapy, were averaged from hourly scores obtained at TAU and intervention phases. The VAS pain scores ranged from 0 to 10. Case A and C reported higher scores indicating severe pain which remained throughout the study period. Pain intensity for Case B, D, and E gradually reduced after 19 sessions. Case A and B had shunt occlusion issues at session 46 that kept them from receiving sufficient HD therapy for the final two sessions.

TABLE 2 | Ratings for categorical inclusion of interview data indicating qualitative effectiveness of Dohsa-hou for self-regulation under chronic pain from hemodialysis.

Participants	**A**					**B**					**C**					**D**					**E**				
	BL	**1st**	**2nd**	**3rd**	**FU**	**BL**	**1st**	**2nd**	**3rd**	**FU**	**BL**	**1st**	**2nd**	**3rd**	**FU**	**BL**	**1st**	**2nd**	**3rd**	**FU**	**BL**	**1st**	**2nd**	**3rd**	**FU**
EFFECTIVENESS																									
Pain reduction or experiences of pain relief																									
Pain reduction	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Reducing analgesics	No	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	No	No	No	–	–	–	–
Relaxation experience	No	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Positive feelings toward or within the body	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Bringing a sense of security	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	Yes
Total present	0	2	3	4	5	0	2	4	4	4	0	3	4	4	4	0	4	4	3	3	0	3	3	4	4
Pain management																									
Analgesics	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Physical therapy	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Engaging with Dohsa-hou by myself	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Self-management for pain through Dohsa-hou	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Using both analgesics and Dohsa-hou	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Total present	2	5	5	5	5	2	2	5	5	5	2	5	5	5	5	2	5	5	5	5	2	3	5	5	5
Behavioral regulation (deficits)																									
Regulating and controlling daily activities and behavior	Yes	No	No	No	No	Yes	–	No	No	No	Yes	No	No	No	No	Yes	Yes	No	No	No	Yes	Yes	Yes	No	No
Staying involved in treatment and appointments	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Act in socially accepted and appreciated manners	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

(Continued)

TABLE 2 | Continued

Participants	A					B					C					D					E				
	BL	1st	2nd	3rd	FU	BL	1st	2nd	3rd	FU	BL	1st	2nd	3rd	FU	BL	1st	2nd	3rd	FU	BL	1st	2nd	3rd	FU
Deficits in planning and decision making	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	Yes	No	No	No	No	Yes	Yes	Yes	No	No
Difficulties overriding automatic processes	Yes	No	No	No	No	Yes	No	No	No	No	Yes	No	No	No	No	Yes	Yes	No	No	No	Yes	Yes	Yes	No	No
Passive coping, avoidance, disengagement	Yes	–	–	–	–	Yes	–	–	–	–	–	–	–	–	–	–	–	–	–	–	Yes	Yes	Yes	No	No
Avoidance of physical exercise	Yes	–	–	–	–	Yes	–	No	–	–	–	–	–	–	–	Yes	–	–	–	–	Yes	Yes	Yes	–	–
Difficulties overriding urges, inactivity, fatigue	Yes	No	No	No	No	Yes	No	No	No	No	Yes	No	No	No	No	Yes	Yes	No	No	No	Yes	Yes	Yes	No	No
Total present	5	0	0	0	0	5	0	0	0	0	3	0	0	0	0	5	3	0	0	0	6	6	6	0	0

Effectiveness is conceptualized in terms of pain relief or reduction and pain management. Criteria for behavioral regulation as a self-regulatory domain was interpreted in accordance with the framework of chronic pain from self-regulatory demands and deficits conceptualized by Solberg Nes et al. (2009). Semi-structured interview data were evaluated under these categories.

size by comparing median VAS scores from baseline TAU and Dohsa intervention phases, as demonstrated in **Table 3** (Bulté and Onghena, 2013; Morley, 2018).

Interview Data

All participants were interviewed at the end of the first, second and third terms within the baseline TAU A-phases. The interview questions were structured to determine applied effectiveness of pain management (Haramaki and Nishi, 2012; Williams and Morley, 2018). Each case was qualitatively assessed for categories of pain management effectiveness (pain reduction or relief experiences) and indicators of behavioral regulation as theorized by Solberg Nes et al. (2009). Two clinical psychologists familiar with the cognitive, emotional and behavioral aspects of self-regulation in clinical and laboratory settings determined the fit of the interview content for each of the categories and subcategories by rating affinity and inclusion with a "Yes" or "No." The fit of correspondence between the interview content to the domains of interest are depicted in **Table 2**.

RESULTS

Background Case Characteristics

The patients had been making an effort to adapt to their severe illness (end-stage renal failure) over a long period. The participants reported having experienced severe pain during dialysis and at home for the previous 1–3 years. All the participants complained of difficulty performing everyday activities (e.g., housekeeping and cooking at home) because of their pain. Previous studies found that HD patients with chronic pain held their role as a member of their family with meaningful contributions to domestic activities as an important aspect of their self-concept under the circumstances of dealing with their chronic condition and its treatment (Haramaki, 2011; Haramaki and Nishi, 2012). All the participants received pain medicine and physical therapy: five participants used compresses that included analgesics; four were treated with loxoprofen; five were treated with xenon (physical therapy given by orthopedics) and hot-pack treatments; and two received exercise therapy (**Table 1**). It was determined that the patients were already experiencing high levels of self-regulatory fatigue, and hence it was expected that they would soon have even less capacity to do housekeeping.

Indicators of Effectiveness From Integration With the Hospital Setting

Dohsa-hou was applied by the staff to the patients on their beds when they complained of severe pain during dialysis treatment. It was observed that when the patients suffered intense pain, they had difficulty expressing themselves and were unable to describe their condition. However, if the staff gave the patients their full attention, the patients became better able to compose themselves and explain how they felt. However, because of the great demands on their time, staff members were formerly unable to devote too much time to each individual patient. In addition, many of the staff had no experience developing pain-related communication skills. In this study, both the staff and patients had the opportunity to acquire such skills through the process of

TABLE 3 | Single-case percent below the median analysis for VAS scores between treatment-as-usual baseline A-phases and Dohsa-hou intervention B-phases.

ID	A-1	B-1	No. sessions below median	Percent below median (%)	A-2	B-2	No. sessions below median	Percent below median (%)	A-3	B-3	No. sessions below median	Percent below median (%)	A-4
A	5.13	2.835	10/12	83.3	4.5	4.125	7/12	58.3	4	2.585	11/12	91.6	3.15
B	3.875	2	11/11	100	3.125	0.667	10/10	100	1	1	5/12	41.6	5.33
C	3.25	3.416	6/12	50	4.75	4	10/12	83.3	4.25	4.5	5/11	45.5	4.25
D	1	0	12/12	100	0	0	11/12	91.6	0	0	12/12	N/A	0
E	1.125	0	8/11	72.7	0.75	0	12/12	100	0	0	11/12	91.6	0

The median refers to the median of averaged VAS scores from each session in all phases. The scores can be cross-referenced with the VAS changes depicted in ***Figure 4****.*

giving and obtaining VAS pain scores, the application of Dohsa-hou tasks, and participating in the associated interviews. As a result of carrying out the Dohsa tasks with the help of clinical staff, the patients were able to release excessive muscle tension in the wrist, upper arm, shoulder, and neck by themselves.

Pain Reduction Effectiveness of Dohsa-hou Across Chronic Pain Patients

Pain management effectiveness was demonstrated from visual analysis inspection (**Figure 4**). Single-case data plots of VAS pain scores are provided in **Figure 4**, and percentage-below-the-median analysis was performed for single case estimates of effect size by comparing baseline TAU and Dohsa intervention phases (**Table 3**). These results suggest that the Dohsa-hou relaxation task intervention phase contributed to pain alleviation among the participants. These effects of pain reduction continued for 16 weeks (∼4 months) and were thus not temporary. VAS pain scores for the third pre-intervention were higher than for the other pre-intervention scores, but not considerably so.

Case-By-Case Effectiveness of Dohsa-hou From VAS Scores and Interview Data Including Follow-Up

After each Dohsa-hou session in the intervention periods, all participants reported freely about their pain and Dohsa-hou, as well as in the semi-structured interviews taken during TAU periods (TAU: analgesics and physical therapy). In terms of sequences completed, all five participants were able to complete almost all of the sessions to undergo the Dohsa tasks except at four data collection points (Case B, one missing session in the first term; Case C, one missing session in the first and third term; Case E, one missing session in the first term; for details, see **Figure 4** and **Table 3**), indicating low attrition of task implementation and a degree of procedural fidelity throughout the period of study.

Ratings for categorical inclusion of interview data indicating qualitative effectiveness of Dohsa-hou for self-regulation under chronic pain from hemodialysis are depicted in **Table 2**. The first two sections of **Table 2** show the effectiveness of each participant's pain reduction and relief experiences and pain management behaviors. Across participants, qualitative change indicating pain reduction or relief change occurred after first term of Dohsa-hou session and that criterion of effectiveness was maintained until follow-up. In terms of pain reduction and relief experiences, all participants reported experiencing pain reduction from the first term to follow-up, and points of change for experiencing relaxation and positive feelings toward the body occurred from the first term for three participants and the second term for two participants.

The bottom section of **Table 2** depicts the effectiveness of promoting self-management according to itemized aspects of behavioral regulation from the interview content. The onset of effectiveness of the intervention in this domain was more variable and required more detailed case-by-case considerations which are provided in the following section.

Case A

As can be seen in **Figure 4**, Case A indicated elevated pain scores and unstable pain conditions during the study period, but also demonstrated incremental reporting of pain relief and pain management experiences. Along the column of **Table 2**, Case A mentioned experiencing pain reduction and positive feelings toward their own body beginning in the first term and lasting throughout the study. Also, Case A reported experiencing relaxation and reducing analgesics at the second and third term. At follow-up, Case A reported a sense of security. For pain management, Case A mentioned engaging in not only the use of analgesics and physical therapy but conducting Dohsa-hou by themselves as a means of self-management for pain and using both analgesics and Dohsa-hou from the first term until the follow-up term. In terms of indicators for behavioral regulation, all of the self-regulatory deficits Case A reported at baseline session (e.g., deficits in regulating and controlling daily activities and behavior, inactivity, and fatigue) were not mentioned from the first term until the follow-up term. In summary of the results of visual analysis depicted in **Table 3**, 83.3% of the VAS scores from Case A for the Dohsa-hou sessions were below the median baseline for the first term, 58.3% under the baseline median for the second term, and 91.6% for the third term. From inspection of the VAS score medians for the baseline to follow-up A-phases, Case A exhibited a general trend of decreasing reports of pain intensity over the period of study, with a pattern of smaller median VAS pain scores in the B-phases than A-phases.

Case B

For VAS pain scores, Case B showed trends toward alleviating their pain from the first term (**Table 3**). However, at the follow-up term, the pain score increased. As can be seen in **Table 2**, Case B reported pain reduction, reducing analgesics from first term, and the experience of relaxation and positive feelings toward their own body from second term. However, a sense of security was not reported during intervention. For pain management, Case B mentioned engaging in not only analgesics and physical therapy, but also that they conducted Dohsa-hou by themselves as self-management for pain and used both analgesics and Dohsa-hou from second term until the follow-up term. For behavioral regulation, most of the deficits Case B reported at the baseline session were not mentioned from the second term until the follow-up term. In summary of the results of visual analysis depicted in **Table 3**, 100% of the VAS scores from Case B for the Dohsa-hou sessions were below the median baseline for the first term, 100% for the second term, and 41.6% for the third term. From inspection of the VAS score medians across phases, Case B exhibited longitudinally variable differences in reports of pain intensity.

Case C

Referring to **Figure 4**, Case C indicated elevated pain scores and unstable pain conditions during the research period. Case C reported pain reduction, relaxation experience, positive feelings on own body from first term, and reported reducing analgesics from second term. However, a sense of security was not reported during intervention (**Table 2**). For pain management, Case C also mentioned engaging in not only analgesics and physical therapy but using Dohsa-hou by themselves for self-management of pain and using both analgesics and Dohsa-hou from the first term until the follow-up term. Also, for behavioral regulation, all of the deficits Case C reported at the baseline session were not mentioned from the first term until the follow-up term. In summary of the results of visual analysis depicted in **Table 3**, 50% of the VAS scores from Case C for the Dohsa-hou sessions were below the median baseline for the first term, 83.3% under the baseline median for the second term, and 45.5% for the third term. From inspection of the VAS score medians for the baseline to follow-up A-phases, Case C exhibited variable reports in pain intensity over the period of study.

Case D

Case D showed trends toward alleviating their pain from the first term (**Figure 4**). Shown in **Table 2**, Case D reported pain reduction, reducing analgesics, experiencing relaxation, and having positive feelings toward their body from the first term. However, reducing analgesics was not reported from third term and a sense of security was not reported during the intervention. For pain management, Case D engaged in not only analgesics and physical therapy, but self-management for pain through Dohsa-hou, as well as using both analgesics and Dohsa-hou from the first term until the follow-up term. In terms of behavioral regulation, most of the deficits Case D reported at the baseline session were not mentioned from the second term until the follow-up term. In summary of the results of visual analysis depicted in **Table 3**, 100% of the VAS scores from Case D for the Dohsa-hou sessions were below the median baseline for the first term, 100% under the baseline median for the second term, and no reports of pain intensity at all for the sessions of the third term in either of the phases. From inspection of the VAS score medians for the baseline to follow-up A-phases, Case D exhibited a general trend of decreasing reports in pain intensity over the period of study.

Case E

Case E showed trends toward alleviating their pain from the first term onward (**Figure 4**). Depicted in **Table 2**, Case E mentioned experiencing pain reduction, relaxation, and positive feelings toward their body from the first term. Also, Case E reported a sense of security from third term. For pain management, Case E mentioned engaging in not only analgesics and physical therapy, but also Dohsa-hou as self-management for pain conducted by themselves and using both analgesics and Dohsa-hou from the second term until the follow-up term. For changes in behavioral regulation, most of deficits Case E reported at baseline session were not mentioned from the third term until the follow-up term. In summary of the results of visual analysis depicted in **Table 3**, 72.7% of the VAS scores from Case E for the Dohsa-hou sessions were below the median baseline for the first term, 100% under the baseline median for the second term, and 91.6% for the third term. From inspection of the VAS score medians for the baseline to follow-up A-phases, Case E exhibited a general trend of decreasing reports pain in intensity over the period of study.

DISCUSSION

The aim of this study was to investigate the proof-of-concept and effectiveness of a hospital-integrated program of Dohsa-hou movements for indicators of bodily pain relief, improvement of pain-related life interference as indicators of quality of life and self-regulatory change among low-functioning patients undergoing long-term hemodialysis treatment.

Reduction in Chronic Pain During Dialysis Treatment

With regard to our first research question that Dohsa-hou will contribute to a reduction in persistent chronic pain during dialysis treatment, the patients reported decreased pain intensity levels in terms of VAS scores and qualitative changes in behavioral regulation, although with varied effects by term. The results of visual analysis depicted in **Figure 4** tentatively suggest that the Dohsa-hou phase was effective in promoting pain reduction, as Case B, D, and E exhibited decreases in their pain levels during the course of the study. Case A and C demonstrated more unstable VAS scores in keeping with the nature of their pain conditions; notably, these cases had severe pain associated with multiorgan failure. After the 46th session, Case A and B were diagnosed with shunt vessel occlusion (**Figure 4**, see Case A and B). Owing to the precariousness of the symptom, they could not receive HD therapy sufficiently at that time. After diagnosis, the two participants were able to receive adequate treatment for the shunt trouble. In spite of this, comparing the intervention and TAU phases, the results of single-case series reports of qualitative interviews taken during the intervention and at follow-up (**Tables 2**, **3**) together with VAS score change comparisons suggest that the Dohsa-hou intervention phase appeared to contribute to chronic pain reduction and self-management behavior for particularly three out of the five cases.

Improvements in Pain-Related Interference

With respect to our second research question, Dohsa-hou was associated with improvements from pain-related life interference via reports of decreased emotional distress and improved activity levels, self-management ability, and quality of life for the low-functioning HD patients with chronic pain conditions. **Table 2** shows qualitative points of change as improvements in pain experience, pain-related activities, regulatory behavior, and lessened interference with personal care and domestic activities. Notably, many of these indicators of effectiveness often had an early onset across cases and were maintained from the first term to follow-up. These results indicate that Dohsa-hou was associated with improvements in pain-related life interference in terms of increases in activity levels, self-management ability (coping with Dohsa-hou), and daily life improvements. In this manner, Dohsa-hou established a proof-of-concept for application and promoted aspects of self-regulation, mainly in the realm of behavioral regulation, for improving pain-related life interference.

Promoting Quality of Life Through Self-Regulation via Dohsa-hou

In addition to lessening pain-related interference, it is important to offer coping strategies that increase self-regulatory capacity as psychological flexibility (Davey, 2016). Self-regulation theory (Carver and Sheier, 1982, 1998) underlies these self-care and coping skills as a framework for understanding and treating chronic pain conditions (Sauer et al., 2010). Self-regulation theory is based on behavioral theory where the focus is on the self and self-regulatory resources. Solberg Nes et al. (2009, 2010) found that chronic pain patients were more vulnerable to self-regulatory fatigue than matched controls. In other studies, the impact of chronic pain conditions on self-regulatory efforts was found to be mediated by pain, not by any other factors (Solberg Nes et al., 2010). Since physical self-regulation aims to redirect self-regulatory efforts toward regulation of the autonomic nervous system and emotional responses, it is useful in managing chronic disorders, and observed benefits may be easily extended to other chronic pain conditions (Carlson et al., 2001).

Dohsa-hou is a method that leverages the physiological functions of body movement to exert a direct effect on a person's psychological activity. The sense of body control in this paradigm arises from finding, feeling, and witnessing a coherence between an intended movement and a synchronous result (Chervenkova, 2017; Kabir et al., 2018). When a client acquires new body movement skills, the therapist can reasonably infer that efforts are being volitionally applied toward facing real-life psychological problems (Naruse, 1988; Haramaki, 2011; Haramaki and Nishi, 2012). Many aspects of the mechanism responsible for the clinical effects are still unclear, but some studies have indicated that the act of accomplishing Dohsa tasks contributes to body awareness that facilitates an enhanced sense of self-control (Konno and Ohno, 1987; Dadkhah, 1998; Hoshikawa, 1998; Shirouzu and Koshikawa, 2011; Fujino, 2017; Kabir et al., 2018). All participants were receiving intensive HD treatment and experienced limitations in their daily lives due to chronic pain for long periods. They were adapting to these chronic conditions characterized by low-functional status, and restricting their activity in accordance with their symptoms, pain, and other factors. Dohsa-hou encouraged all participants to engage or re-engage with personal care and domestic activities (**Tables 2**, **3**) while staying at home in the form of washing dishes, hanging up washed-clothes to dry, and decreasing the use of analgesics. While two of the cases exhibited instances of unstable VAS reporting, turning points in the analysis of the data from semi-structured interviews especially suggested that rehabilitated ability to commit to desired activities were reflected in the time course of the intervention. In this way, the results suggest that the Dohsa-hou phases conferred some effectiveness toward pain reduction (Williams and Morley, 2018) by incrementally and continuously promoting behavioral aspects of self-regulation (**Tables 2**, **3**).

In terms of the significance of these findings to research on Dohsa-hou, they add to the evidence base that suggests the psychotherapy overlaps or interfaces with mechanisms of physical self-regulation (Sauer et al., 2010), especially in the narrative sense. Descriptive comparison between clinical Dohsa-hou and the narrowed repertory of movements explicitly targeting and augmenting "self-activeness" known as Self-Active Relaxation Therapy supports this notion (Kabir et al., 2018). The focus on activity management, relaxation, and behavioral adjustment (Davey, 2016) in terms of personal care and domestic activities framed the goals of therapy under their terms and allowed for a more fine-grained evaluation of expected benefit or change. Similar to its roots in developmental conditions and movement disorders, physical regulation via Dohsa-hou might be especially equipped to target issues in functional status because the frame for goals is anchored in the simple performance of movements, in witnessing the self as the agent of change, in redirecting attention to the body, and in viscerally perceiving the accompanied experience of relaxation. In this manner, it might also be reasonable to assume that patients undergoing dialysis exhibit distress or fear of movement associated with their treatment, as body tension and movement restriction might be expected while being attached to the HD machine.

The present study did show some inconsistencies in the points of change between terms for two of the cases. Cases A and B seemed to acquire self-regulation abilities during the Dohsa-hou session compared with TAU (**Table 2** and **Figure 4**), but Cases A and B were less conclusive about the treatment effect due to fluctuations in VAS pain scores. This indicates a discrepancy between the comments from interviews indicating positive psychological change from self-regulation and VAS score results. One reason might be traced to the aforementioned experiences of severe pain between the weeks of 46 and 48 weeks that were documented to be due to issues with shunt occlusion (**Figure 4**). However, this could also be due to limitations in the study design or interview methodology to pinpoint points of change or account for treatment expectancy (see Limitations section). While this study employed these methods to keep the study burden as low as possible in an effort to facilitate high-fidelity implementation, this limitation underscores the need for future studies to extend beyond a proof-of-concept and address the treatment effect against a randomized control group. These points notwithstanding, it can reasonably be inferred as a preliminary finding that the Dohsa-hou phases were attributed with the promotion of self-regulation and a degree of quality of life improvement in the place of severe pain and fatigue, otherwise the results from the interview questions would have been chiefly comprised of continuous reports of severe pain and patterned idiographic indications of incremental VAS pain score reduction over the course of the study would not have been observed. While more clearly evident in the other three cases, these findings remain tentative as despite the use of longitudinal clinical observation, our results chiefly represent a proof-of-concept that should be carefully interpreted until the implementation is compared with stronger designs that can address possible risks of bias.

While further examination is necessary to parse the treatment effect more precisely, we surmise that one element in the mechanism of psychological change or direct contribution from physical movements in the Dohsa-hou framework to pain reduction might be similar to aspects of graded exposure *in vivo* for movements that patients might find threatening due to being recipients of intensive treatment (de Jong et al., 2005; Morley and Williams, 2015). In contrast, or in conjunction with this theoretical assertion, the relaxation element of Dohsa-hou might function as a response modulator under the umbrella of stress coping or emotion regulation (Gross and Thompson, 2007), or recruit awareness or changes in interoceptive attention tendencies (Kabir et al., 2018) that extend to pain regulation, but further research is necessary. The constructs of pain vulnerability antecedents and their consequences might provide the necessary theoretical framework or otherwise usefully clarify the contribution of Dohsa-hou to pain-related emotion regulation (Koechlin et al., 2018). Nevertheless, the approach of Dohsa-hou, like many others, appears to raise awareness about the body, and in this study, patients were able to overcome elements of their pain-related interference and functional limitations by recognizing and demonstrating some especially behaviorally-oriented regulatory capacity changes on the spectrum of adaptive behavior.

Feasibility of Dohsa-hou Implementation for Pain Management

The strength of this study lies in its ability able to provide a new and accessible pain management skill for HD patients with chronic pain. To the best of our knowledge, this is the first program of its kind for hemodialysis patients in Japan. Participants demonstrated indications that they were able to acquire self-regulation skills over the period of 16 weeks until follow-up (1 month after third term: **Tables 2**, **3**). All participants could notice a reduction in pain (changes in VAS pain score; **Figure 4**) and improvements in daily-life interferences as indicators of quality of life change through self-regulation activities that were associated with the Dohsa-hou phases (**Tables 2**, **3**). This seems to indicate that as the patients underwent Dohsa-hou, they adopted the relaxation process as a new way of coping with their chronic pain. In this way, efforts to achieve relaxation allowed the participants to break the pain-tension cycle (Williams and Morley, 2018) and vicious cycle of self-regulatory fatigue, specifically by acquiring the concrete relaxation tasks as new pain management skills to supplement their day-to-day lives.

In the present study, all of the participants demonstrated an ability to monitor and attend to their body more effectively by performing the Dohsa tasks and taking part in the semi-structured interviews (**Table 3**). Training in communication skills can be conducted with patients and staff in a general setting in terms of bedside psychotherapy (Griffith and Gaby, 2005) during dialysis treatment. In CBT, ACT, self-regulation, and Dohsa-hou, it is necessary to focus on one's own experiences of direct control (Friedberg et al., 2012), development (Hayes et al., 2013), feedback control process (Carver and Sheier, 1998), and body movement processes (Naruse, 1988). In the setting of the present study, the participants had to engage in body awareness through Dohsa-hou techniques and define their self-awareness by means of the interview in terms of their physical conditions, particularly with regard to pain. In future research, it would be useful to investigate the interaction between chronic patients' self-awareness and various clinical effects of Dohsa-hou.

The present study used a collaborative management of chronic illness approach for low-functional HD patients with chronic pain that coordinated with other health care providers to enhance feasibility and adherence (Von Korff et al., 1997). Relaxation training is one of the most widely used and effective pain coping skills (Keefe et al., 2018). Dohsa-hou focuses on body movements that anyone can perform, with no particular emphasis on disorder, dysfunctions, or disabilities. It is a simple and versatile psychological treatment technique for health providers and could usefully be integrated through future research into other settings such as nursing care plans that incorporate range of motion exercises for treatment toolkits (Tseng et al., 2007; Gordon and Bloxham, 2016). The target of the body, relative ease of use, and straightforward psychoeducation associated with Dohsa-hou may serve as distinct advantages for holistically tackling cases of severe chronic pain, especially if it can be utilized as another relaxation-based skill available to buffer simultaneous treatment modalities (Barlow et al., 2002). Toward this end, and as a direct result of the current study, the health care staff under supervision successfully integrated and longitudinally implemented the Dohsa tasks throughout a 4 months period, completing and providing data for almost all of the 48 sessions. Along with the indicators of effectiveness from the pilot implementation, this record of completion with low attrition indicates strengths for the program in terms of procedural fidelity, applicability, and feasible transfer to more rigorous designs for future research.

LIMITATIONS

It is important to note that the strength of these findings is tempered by the fact that it was a pilot implementation in a small number of cases with key representativeness and design limitations. Only 9 (13%) patients reported chronic pain when we interviewed possible patients for recruitment to this study. This differs from Brkovic et al. (2016) who reported that the general prevalence of chronic pain of HD patients ranged from 33 to 92%. As noted as a point of consideration in systematic guidelines such as the SCRIBE Checklist (Tate et al., 2016) and the Risk of Bis in *N*-of-1 Trials (RoBiNT) Scale (Tate et al., 2014), it should be emphasized that this study is a preliminary observation from one hospital and this discrepancy might limit the generalizability of these findings.

In addition, we cannot ignore the fact that positive outcomes could be explained by non-specific factors, such as the treatment expectancy effects of being in a clinical study and receiving extra attention from treatment staff. An especially notable limitation in our study is that our data cannot tease apart the effects of positive feedback itself. Improving communication skills (Ricka et al., 2002; Redondo et al., 2004), minimizing the burden for patients (Griffith and Gaby, 2005; Peterson, 2010), and engaging in voluntary activities by moderate requests could have played a role (Friedberg et al., 2012). These strategies have often been used to elicit effective cooperation from patients toward better pain relief outcomes and self-management. In addition, this study depended on the patients' self-evaluation of their own pain level and there was a lack of medical diagnostic evaluation explicitly incorporated into the dataset to account for confounders, a control group, or measurement of pain-related mediators (e.g., pain inventory, pain impairment belief, and psychological flexibility). In future research, the use of more detailed semi-structured interviews incorporating questionnaires such as the Brief Pain Inventory or Health-Related Quality of Life Measures is suggested to clarify or monitor the roles of pain intensity and or quality of life with greater specificity.

As this was a chiefly idiographic assessment of single-case series with a simple phase design using participants as their own control, the RoBiNT Scale as a resource indicates a number of other possible risks of bias that will need to be carefully addressed in future studies (Tate et al., 2014). While the length of the period of study provided a sufficient number of data points for inter-subject replication, it was still difficult to secure baseline data that could statistically verify stable pain conditions, as seen in the emergence of higher VAS pain scores for two of the cases. However, consistency of data patterns across the similar phases for the other three cases appears to be supported by visual inspection (**Figure 4** and **Table 3**) and from the interview reports of continued use of the tasks at home (**Table 2**). The data collection was scheduled and did not commence at randomly assigned start points under blind conditions. While coping skill acquisition and psychoeducation are cumulative in ways that can make it challenging to organize certain manipulations, future studies with randomized single-participant designs perhaps utilizing alternating treatments or changing criterions could be used to build on the proof-of-concept and offer more to the credible evidence base for interventions for chronic pain in hemodialysis patients using Dohsa-hou (Tate et al., 2014; Morley, 2018).

In sum, although limited, in light of the feasibility indicators of procedural fidelity and proof-of-concept in a cohort of a longitudinally applied clinical context for five participants of a known group, some degrees of effectiveness of the intervention for the clinical end points were observed to allow for the stratification of future patient groups (Lillie et al., 2011). Future studies should build on this proof-of-concept trial by monitoring other factors that affect the condition of patients in terms of physical health status as well as individual differences in pain-related constructs. While meta-analyses have indicated that psychological interventions demonstrate efficacy for chronic pain, randomized controlled trials remain the level of rigor necessary to establish their efficacy (Veehof et al., 2011). Therefore, randomized controlled trials and studies with larger samples and a comparison with other psychotherapies are needed to confirm the validity of the present findings.

CONCLUSION

The findings indicated areas of support in the domain of the promotion of self-regulation through Dohsa-hou as an adaptive pain coping skill. Specifically, this study suggested that applying body movement relaxation tasks shows promise as a psychotherapeutic approach for managing severe chronic pain, especially in a sample of individuals affected by renal disease. Dohsa-hou provided indicators of effectiveness by reducing pain during dialysis as well as improving quality of life through reports of recouped control over patient-driven desired commitments to personal care and domestic activities. Overall, this study suggested that hemodialysis patients are capable of learning to manage their chronic pain on their own through the deliberate practice of movement tasks aimed at changing feeling states and that a collaborative program to facilitate the care of chronic pain can be provided by clinical staff using Dohsa-hou. Although more research is needed, this study indicated that one way to facilitate quality of life change in low-functioning patients undergoing dialysis is to relieve the burden of chronic bodily pain by promoting self-management with body movement-based relaxation.

ETHICS STATEMENT

This study was carried out in accordance with the recommendations of the Ethical Committee of the Graduate School of Education, Hiroshima University. The protocol was approved by the Ethical Committee of the Graduate School of Education, Hiroshima University. All subjects gave written informed consent in accordance with the Declaration of Helsinki.

AUTHOR CONTRIBUTIONS

YH conducted the research, supervised the progress of the patients, and served as the primary author of the manuscript. RK provided manuscript preparation, analysis, revisions, summary, and literature review. KA provided ratings for the self-regulation categories, analytical insights, and revisions. TY contributed to confirmation of the research protocol, analysis, and manuscript preparation.

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REFERENCES

Barlow, J., Wright, C., Sheasby, J., Turner, A., and Hainsworth, J. (2002). Self-management approaches for people with chronic conditions: a review. *Patient Educ. Couns.* 48, 177–187. doi: 10.1016/S0738-3991(02)00032-0

Brkovic, T., Burilovic, E., and Puljak, L. (2016). Prevalence and severity of pain in adult end-stage renal disease patients on chronic intermittent hemodialysis: a systematic review. *Patient Prefer. Adherence* 10, 1131–1150. doi: 10.2147/PPA.S103927

Bulté, I., and Onghena, P. (2013). The single-case data analysis package: analysing single-case experiments with R software. *J. Modern Appl. Stat. Methods* 12:28. doi: 10.22237/jmasm/1383280020

Carlson, C. R., Bertrand, P., Ehrlich, A., Maxwell, A., and Burton, R. (2001). Physical self-regulation training for management of temporomandibular disorders. *J. Orofac. Pain* 15, 47–55.

Carver, C. S., and Sheier, M. F. (1982). Control theory: a useful conceptual framework for personality- social, clinical, and health psychology. *Psychol. Bull.* 92, 111–135. doi: 10.1037/0033-2909.92.1.111

Carver, C. S., and Sheier, M. F. (1998). *On the Self-Regulation of Behavior.* New York, NY: Cambridge University Press.

Chervenkova, V. (2017). *Japanese Psychotherapies: Silence and Body-Mind Interconnectedness in Morita, Naikan and Dohsa-hou*. Singapore: Springer.

Dadkhah, A. (1998). Body consciousness in Dohsa-hou, a Japanese psychorehabilitative program. *Percept. Mot. Skills* 86, 411–417. doi: 10.2466/pms.1998.86.2.411

Davey, E. S. (2016). Psychology and chronic pain. *Anaesth. Intensive Care Med.* 17, 568–570. doi: 10.1016/j.mpaic.2016.08.004

de Jong, J. R., Vlaeyen, J. W., Onghena, P., Cuypers, C., den Hollander, M., and Ruijgrok, J. (2005). Reduction of pain-related fear in complex regional pain syndrome type I: the application of graded exposure *in vivo*. *Pain* 116, 264–275. doi: 10.1016/j.pain.2005.04.019

Engel, G. L. (1977). The need for a new medical model: a challenge for biomedicine. *Science* 196, 129–136. doi: 10.1126/science.847460

Feng, L., Yap, K. B., and Ng, T. P. (2013). Depressive symptoms in older adults with chronic kidney disease: mortality, quality of life outcomes, and correlates. *Am. J. Geriatr. Psychiatry* 21, 570–579. doi: 10.1016/j.jagp.2012.12.020

Friedberg, F., Williams, D. A., and Collinge, W. (2012). Lifestyle-oriented non-pharmacological treatments for fibromyalgia: a clinical overview and applications with home-based technologies. *J. Pain Res.* 5, 425–435. doi: 10.2147/JPR.S35199

Fujino, H. (2012). Effects of Dohsa-hou relaxation on body awareness and psychological distress. *Jpn. Psychol. Res.* 54, 388–399. doi: 10.1111/j.1468-5884.2012.00517.x

Fujino, H. (2017). Psychological support for young adults with down syndrome: Dohsa-hou program for maladaptive behaviors and internalizing problems. *Front. Psychol.* 8:1504. doi: 10.3389/fpsyg.2017.01504

Gewandter, J. S., Dworkin, R. H., Turk, D. C., Farrar, J. T., Fillingim, R. B., Gilron, I., et al. (2015). Research design considerations for chronic pain prevention clinical trials: IMMPACT recommendations. *Pain* 156:1184. doi: 10.1097/j.pain.0000000000000191

Gordon, R., and Bloxham, S. (2016). A systematic review of the effects of exercise and physical activity on non-specific chronic low back pain. *Healthcare* 4:22. doi: 10.3390/healthcare4020022

Grassmann, A., Gioberge, S., Moeller, S., and Brown, G. (2005). ESRD patients in 2004: global overview of patient numbers, treatment modalities and associated trends. *Nephrol. Dial. Transplant.* 20, 2587–2593. doi: 10.1093/ndt/gfi159

Griffith, J. L., and Gaby, L. (2005). Brief psychotherapy at the bedside: countering demoralization from medical illness. *Psychosomatics* 46, 109–116. doi: 10.1176/appi.psy.46.2.109

Gross, J. J., and Thompson, R. A. (2007). "Emotion regulation: conceptual foundations," in *Handbook of Emotion Regulation*, ed J. J. Gross (New York, NY: Guilford Press), 3–24.

Haramaki, Y. (2011). Psychological support for a long period dialysis patient suffering from whole body pain. *J. Jpn. Clin. Psychol.* 29, 27–38. [In Japanese]

Haramaki, Y., and Nishi, Y. (2012). The application of Dohsa-hou for long-period dialysis patients with chronic pain. *Jpn. J. Rehabil. Psychol*. 38, 47–58. [In Japanese]

Hayes, S. C., Levin, M. E., Plumb-Vilardaga, J., Villatte, J. L., and Pistorello, J. (2013). Acceptance and commitment therapy and contextual behavioral science: examining the progress of a distinctive model of behavioral and cognitive therapy. *Behav. Ther.* 44, 180–198. doi: 10.1016/j.beth.2009.08.002

Hoshikawa, T. (1998). Effect of body control and attention on body sway induced by a tilting room. *Shinrigaku Kenkyu* 69, 310–316. doi: 10.4992/jjpsy.69.310

Imura, O., Furukawa, T., Fujino, H., Sugano, S., Chervenkova, V., Teruta, E., et al. (2016). *Introduction to Dohsa-hou: An Integrated Japanese Body-Mind Therapy*. Available online at: www.hus.osaka-u.ac.jp/en/book/911

Jane, S. W., Chen, S. L., Wilkie, D. J., Lin, Y. C., Foreman, S. W., Beaton, R. D., et al. (2011). Effects of massage on pain, mood status, relaxation, and sleep in Taiwanese patients with metastatic bone pain: a randomized clinical trial. *Pain* 152, 2432–2442. doi: 10.1016/j.pain.2011.06.021

Japan Organ Transplant Network (JOTNW). (2019). *Donors and Transplants Data* (1 January – 31 December, 2017). Available online at: https://www.jotnw.or.jp/english/index.html

Kabir, R. S., Haramaki, Y., Ki, H., and Ohno, H. (2018). Self-active relaxation therapy (SART) and self-regulation: a comprehensive review and comparison of the Japanese body movement approach. *Front. Hum. Neurosci.* 12:21. doi: 10.3389/fnhum.2018.00021

Kaptein, A. A., Dijk, S., Broadbent, E., Falzon, L., Thong, M., and Dekker, F. W. (2010). Behavioural research in patients with end-stage renal disease: a review and research agenda. *Patient Educ. Couns.* 81, 23–29. doi: 10.1016/j.pec.2009.10.031

Keefe, F. J., Beaupre, P. M., Rumble, M. E., Kelleher, S. A., and Van Denburg, A. N. (2018). "Group therapy for patients with chronic pain," in *Psychological Approaches to Pain Management-A Practitioner's Handbook, 3rd Edn.,* eds D. C. Turk and R. J. Gatchel (New York and London: The Guilford Press), 205–229.

Koechlin, H., Coakley, R., Schechter, N., Werner, C., and Kossowsky, J. (2018). The role of emotion regulation in chronic pain: a systematic literature review. *J. Psychosom. Res.* 107, 38–45. doi: 10.1016/j.jpsychores.2018.02.002

Konno, Y., and Ohno, K. (1987). A factor analytic study of the acceptance of relaxation through Dohsa Training (psychological rehabilitation training). *Shinrigaku Kenkyu* 58, 57–61. doi: 10.4992/jjpsy.58.57

Lillie, E. O., Patay, B., Diamant, J., Issell, B., Topol, E. J., and Schork, N. J. (2011). The n-of-1 clinical trial: the ultimate strategy for individualizing medicine? *Per. Med.* 8, 161–173. doi: 10.2217/pme.11.7

McCracken, L. M., and Velleman, S. C. (2010). Psychological flexibility in adults with chronic pain: a study of acceptance, mindfulness, and values-based action in primary care. *Pain* 148, 141–147. doi: 10.1016/j.pain.2009.10.034

Morley, S. (2018). *Single-Case Methods in Clinical Psychology-A Practical Guide*. London and New York: Routledge.

Morley, S., and Williams, A. (2015). New developments in the psychological management of chronic pain. *Can. J. Psychiatry* 60, 168–175. doi: 10.1177/070674371506000403

Naruse, G. (1973). *Shinri Rehabilitation [Psychological Rehabilitation]*. Tokyo: Seishin-Shobo.

Naruse, G. (1988). *JIKO-Control hou [Self-Control Method]*. Tokyo: Seishin-Shobo.

Naruse, G. (1995). *Rinsho Dohsa Gaku Kiso [Foundation of Dohsa-hou]*. Tokyo: Gakuensha.

Naruse, G. (1997). The clinical Dohsa-hou as psychotherapy. *Jpn. J. Rehabil. Psychol.* 25, 9–16. [In Japanese]

Nijs, J., Almond, F., De Becker, P., Truijen, S., and Paul, L. (2008). Can exercise limits prevent post-exertional malaise in chronic fatigue syndrome? An uncontrolled clinical trial. *Clin. Rehabil.* 22, 426–435. doi: 10.1177/0269215507084410

Nitta, K., Masakane, S., Hanafusa, N., Taniguchi, M., Hasegawa, T., Nakai, S., et al. (2018). Current situation for dialysis therapy in Japan – 1 January-31 December 2017. *J. Jpn. Soc. Dial. Ther.* 51, 699–766. doi: 10.4009/jsdt.51.699

Okumi, M., Kakuta, Y., Unagami, K., Maenosono, R., Miyake, K., Iizuka, J., et al. (2018). Cardiovascular disease in kidney transplant recipients: Japan Academic Consortium of Kidney Transplantation (JACK) cohort study. *Clin. Exp. Nephrol.* 22, 702–709. doi: 10.1007/s10157-017-1500-z

Peterson, R. A. (2010). Improving hemodialysis in patient care: critical areas. *Patient Educ. Couns.* 81, 3–4. doi: 10.1016/j.pec.2010.07.023

Redondo, J. R., Justo, C. M., Moraleda, F. V., Velayos, Y. G., Puche, J. J., Zubero, J. R., et al. (2004). Long-term efficacy of therapy in patients with fibromyalgia: a physical exercise-based program and a cognitive-behavioral approach. *Arth. Rheumatol.* 51, 184–192. doi: 10.1002/art.20252

Ricka, R., Vanrenterghem, Y., and Evers, G. C. M. (2002). Adequate self-care of dialysed patients: a review of the literature. *Int. J. Nurs. Stud.* 39, 329–339. doi: 10.1016/S0020-7489(01)00024-4

Sauer, S. E., Burris, J. L., and Carlson, C. R. (2010). New directions in the management of chronic pain: self-regulation theory as a model for integrative clinical psychology practice. *Clin. Psychol. Rev.* 30, 805–814. doi: 10.1016/j.cpr.2010.06.008

Shirouzu, T., and Koshikawa, F. (2011). The effects of attention to body sensations and muscular relaxation on mood and decentering. *Shinrigaku Kenkyu* 82, 115–122. doi: 10.4992/jjpsy.82.115

Solberg Nes, L. S., Carlson, C. R., Crofford, I. J., de Leeuw, R., and Segerstrom, S. C. (2010). Self-regulatory deficits in fibromyalgia and temporomandibular disorders. *Pain* 151, 37–44. doi: 10.1016/j.pain.2010.05.009

Solberg Nes, L. S., Roach, A. R., and Segerstrom, S. C. (2009). Executive functions, self-regulation, and chronic pain: a review. *Ann. Behav. Med.* 37, 173–183. doi: 10.1007/s12160-009-9096-5

Tate, R. L., Perdices, M., McDonald, S., Togher, L., and Rosenkoetter, U. (2014). The design, conduct and report of single-case research: resources to improve the quality of the neurorehabilitation literature. *Neuropsychol. Rehabil.* 24, 315–331. doi: 10.1080/09602011.2013.875043

Tate, R. L., Perdices, M., Rosenkoetter, U., McDonald, S., Togher, L., Shadish, W., et al. (2016). The single-case reporting guideline in behavioural interventions (SCRIBE) 2016: explanation and elaboration. *Arch. Sci. Psychol.* 4:10. doi: 10.1037/arc0000027

Tseng, C. N., Chen, C. C. H., Wu, S. C., and Lin, L. C. (2007). Effects of a range-of-motion exercise programme. *J. Adv. Nurs.* 57, 181–191. doi: 10.1111/j.1365-2648.2006.04078.x

Veehof, M. M., Oskam, M. J., Schreurs, K. M., and Bohlmeijer, E. T. (2011). Acceptance-based interventions for the treatment of chronic pain: a systematic review and meta-analysis. *Pain* 152, 533–542. doi: 10.1016/j.pain.2010.11.002

Vlaeyen, J. W. S., Morley, S. J., Linton, S. J., Boersma, K., and de Jong, J. (2012). *Pain-Related Fear: Exposure-Based Treatment for Chronic Pain.* Seattle, WA: IASP Press.

Von Korff, M., Gruman, J., Schaefer, J., Curry, S. J., and Wagner, E. H. (1997). Collaborative management of chronic illness. *Ann. Intern. Med.* 127, 1097–1102. doi: 10.7326/0003-4819-127-12-199712150-00008

Wetherell, J. L., Afari, N., Rutledge, T., Sorrell, J. T., Stoddard, J. A., Petkus, A. J., et al. (2011). A randomized, controlled trial of acceptance and commitment therapy and cognitive-behavioral therapy for chronic pain. *Pain* 152, 2098–2107. doi: 10.1016/j.pain.2011.05.016

Wicksell, R. K., Olsson, G. L., and Hayes, S. C. (2011). Mediators of change in Acceptance and Commitment Therapy for pediatric chronic pain. *Pain* 152, 2792–2801. doi: 10.1016/j.pain.2011.09.003

Williams, A., and Morley, S. (2018). "Conducting and evaluating treatment outcome studies," in *Psychological Approaches to Pain Management-A Practitioner's Handbook, 3rd Edn.,* eds D. C. Turk and R. J. Gatchel (New York and London: The Guilford Press), 51–67.

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Paranoid Thinking and Wellbeing. The Role of Doubt in Pharmacological and Metacognitive Therapies

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Introduction: Pathological confidence in one's thoughts is a key mechanism of chronic paranoid thinking. For this reason, many of the current therapies focus on trying to reduce it. In fact, the way some antipsychotics (e.g., haloperidol) work seems to be through the induction of doubt. Because of the impact of these pathological thoughts on positive health, studying the well-being of people who experience paranoid thoughts is fundamental. The first objective of this research is to apply the Complete State Model of Health (CSMH) to a sample of patients characterized by the presence of paranoid thinking. Our second objective is to evaluate the impact of therapies based on reducing pathological confidence on patients' well-being.

Methods:. Sixty participants with SCID-5 confirmed DSM-5 diagnosis related with paranoid thinking and without mood symptoms were recruited. In order to test the existence of a two continua model of mental health (CSMH), we conducted a parallel analysis and an exploratory factor analysis. To test our hypothesis regarding the partially mediating role of doubt between paranoid thinking and patients' well-being, we conducted a biased corrected bootstrapping procedure.

Results: As expected, two different unipolar dimensions emerged from the measures used to assess paranoid thinking and positive health (two continua model of mental health). When patients received metacognitive and pharmacological treatment, more paranoid thinking led to more doubt in all thoughts, which in turn affected well-being. The analyses carried out confirmed the partial mediating role of doubt.

Conclusion: Despite the efficacy shown by both metacognitive therapies and antipsychotics, it seems that they not only reduce pathological confidence, but can also affect other thoughts not linked to delirium. This effect of generalization of doubt in all thoughts negatively affected patients' well-being and quality of life.

Keywords: well-being, quality of life, paranoid thinking, doubt, Complete State Model of Health

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Abbreviations: CBT, cognitive-behavioral therapy; CI, confidence interval; CSMH, Complete State Model of Health; DSM, Diagnostic and Statistical Manual of Mental Disorders; EFA, exploratory factor analysis; HGUCR, Hospital General Universitario de Ciudad Real; GAD, generalized anxiety disorder; MCT and MyMCT, metacognitive training; PA, parallel analysis; PADS, Persecution and Deservedness Scale; PCA, principal component analysis; PIQ, Persecutory Ideation Questionnaire; SCID-5, Structured Clinical Interview for DSM-5.

INTRODUCTION

Paranoid delusional thinking is one of the central symptoms of psychosis. It can appear in a wide spectrum of disorders from individuals who do not have pathologies (Penn et al., 1997), to people with delusional disorder, brief psychotic disorder, schizophreniform disorder, schizophrenia, schizoaffective disorder, psychotic disorder induced by substances or drugs or personality disorders (e.g., paranoid personality disorder), among others (Garety et al., 1999). These delusional thoughts have traditionally been considered as false beliefs that are hard to modify, expressed with absolute conviction and not amenable to reason (Freeman et al., 2013). Therefore, in the study of paranoid thoughts, primary cognition must be considered, since irrational beliefs may be the result of a negative evaluation of situations, relationships with others and their interpretations (Freeman and Garety, 1999; Freeman et al., 2002; Morrison et al., 2015). Metacognition should also been taken into account, since delusional thinking is linked to second-order cognition (thoughts about one's thoughts) (Moritz et al., 2016). That is, delusions are also related to the pathological confidence linked to incorrigibility, and to the collection of less information before making a decision or "jumping to conclusions" (Garety et al., 1999; Freeman et al., 2002; Moritz and Woodward, 2005). This confidence in thoughts is especially important, given that, regardless of the content of what we think, trust (or doubt) guides the use of this content (Self-Validation Theory) (Briñol and Petty, 2003).

Since pathological confidence in one's thoughts is a key mechanism of delusional thinking, many of the current therapies focus on trying to reduce it. One of the most recent therapies is developed by Moritz and Woodward (2007) and Moritz et al. (2013), called MyMCT (previously MCT). This therapy is based on making patients aware of the cognitive distortions linked to delusional thinking (e.g., "jump to conclusions" or "overconfidence" in errors). Subsequently, they are taught alternative coping strategies and information processing. Therefore, one of the objectives of this therapy is to reduce confidence in pathological thoughts, in order to alter delusional beliefs (Moritz et al., 2014a; Eichner and Berna, 2016). However, not only metacognitive therapies influence the processes of secondary cognition linked to paranoid thinking. From a cognitive point of view, the induction of doubt is one of the central cognitive effects of antipsychotics (e.g., Haloperidol) (Freeman et al., 2002). The antipsychotics also cause patients to detach from their thoughts, which allow them to treat thoughts as objects and diminish confidence in them (Kapur et al., 2005).

Therefore, generating doubt to reduce pathological confidence seems to be a good option in the treatment of chronic paranoid thinking. This reduction in confidence can occur through affective or cognitive (in)validation. Affective validation occurs when people use their thoughts because they feel good about them or like them (e.g., Briñol et al., 2007; Huntsinger et al., 2014). Therefore, dampening positive emotions reduces thought reliance. Cognitive validation takes place when people use their thoughts because they believe they are valid or correct (see Briñol et al., 2018 for a description of both types of validation).

The fundamental problem is that the doubt generated (both by metacognitive therapies and by antipsychotics) could not only be limited to delusional thoughts (reducing pathological confidence), it could also be extended to cognition in general (generating an extreme doubt). This would be especially relevant given that trust in thoughts is a fundamental variable for people's positive psychological functioning and well-being (Taylor and Brown, 1988). In addition, paranoid thinking greatly affects patients' quality of life (Karow and Pajonk, 2006).

For these reasons, studying the well-being of people who experience chronic paranoid thoughts is fundamental, regardless of their psychopathological evaluation (Chan et al., 2018). In fact, the presence of health not only requires absence of disease, but also having a state of complete physical, mental and social well-being (World Health Organization, 1946). To evaluate this state Corey Keyes developed the Complete State Model of Health (CSMH) (Keyes, 2005). According to this model, health is not a state characterized solely by the absence of disease, but also by the presence of indicators of hedonic well-being (hedonia) and eudaimonic well-being (positive functioning). The application of this model for the evaluation of patients with paranoid thinking has interesting consequences given that the CSMH defends that health and disease are not two poles of a single dimension, but two unipolar dimensions correlated with each other (two continua model of mental health). Therefore, the presence of pathology does not imply the absence of positive health. Although the CSMH has been widely applied and tested in different populations (Keyes, 2006, 2009; Bariola et al., 2017; de Vos et al., 2018), the existence of two different axes (positive mental health and mental illness) should be examined for each disorder or psychopathological process (e.g., McGaffin et al., 2015; Díaz et al., 2018) since there are cases where the existence of two axes is not met (e.g., Díaz et al., 2007).

Although it is especially interesting to apply the CSMH in the study of disorders related to paranoid thinking, to the best of our knowledge there are no studies that have proven the existence of two axes in these disorders. There is just one study in which the CSMH has been applied in the study of schizophrenia spectrum disorders (Chan et al., 2018), but in that study the existence of two-dimensions related to mental illness and positive mental health was not examined. For these reasons, the first objective of the present research is to apply the CSMH to a sample of patients with paranoid thinking to explore the two different unipolar dimensions: paranoid thinking and positive mental health (i.e., well-being indicators). In addition, we expect that paranoid thinking and positive mental health will be correlated.

Finally, our second objective is to study how metacognitive and pharmacological therapies influence confidence in thoughts of people with paranoid thinking. Based on previous research (Moritz et al., 2014a; Eichner and Berna, 2016) our next hypothesis is that therapies will reduce pathological confidence. However, we also expect that these therapies will generate extreme doubt in all thoughts, and not only the ones associated with delirium. Given that confidence is a key element of positive functioning, this adverse metacognitive effect of generalization of doubt would affect patients' positive health (i.e., well-being). As a consequence, we expect doubt to partially mediate the effect of paranoid thinking on patients' well-being.

MATERIALS AND METHODS

Participants

Sixty participants (25 females and 35 males) with SCID-5 confirmed DSM-5 diagnosis related with paranoid thinking and without mood symptoms (i.e., Schizophrenia, Brief Psychotic Disorder, Delusional Disorder or Substance/Medication-Induced Psychotic Disorder) were recruited in the HGUCR. Recruitment was carried out between September 2016 and August 2017. Patients were hospitalized and were in a post-acute or stable phase of their disorders. Patients with a comorbid diagnosis of other mental disorders at the time the study was conducted were excluded (e.g., Major Depressive Disorder). In addition, participants were excluded if they could not complete questionnaires written in Spanish. Participants were recruited via letter of invitation explaining the project and the voluntary nature of participation. They were 25 women (42%) and 35 men (58%) between 18 and 76 years old. The mean age was 41.12 years (SD = 14.78). The maximum educational level reached to 57% of primary education, 20% higher no university education, 20% hold a university degree and 3% a PhD. Twenty patients had Schizophrenia, twenty Brief Psychotic Disorder, fifteen Delusional Disorder, and five Substance/Medication-Induced Psychotic Disorder. All participants were already prescribed atypical antipsychotic medication at baseline. Participants received a metacognitive therapy focused in overconfidence based on Well's metacognitive therapy, which assumes that the cause of disorder is located at the metacognitive level not at the level of cognitive content (Wells and Matthews, 1996). The adaptation of the Wells' metacognitive model of GAD (Wells, 1995) proposed by Morrison et al. (Morrison et al., 2014) was used. The exact duration of sessions varied, as a flexible use of the manuals is advocated, based on the individual case formulation (e.g., Normann et al., 2014; see Hutton et al., 2014, for a complete description of the therapy). On average, patients received 562 min of metacognitive therapy (SD = 51 min).

Procedure

The study was approved by the ethics committee of the "Universidad de Castilla – La Mancha" (UCLM) and the HGUCR (Comité Ético de Investigación Clínica HGUCR-UCLM). All participants were informed that all collected information was confidential and anonymous, and signed an informed consent. To avoid possible order effects of the two sets of scales, half of the participants first completed the PIQ, and the PADS, and then the Satisfaction with Life Scale, the Positive Affect Scale and the Psychological Well-being Scales. The other half first completed the well-being scales and, then, proceeded to complete the PIQ and PADS.

Measures

Paranoid Thinking

Participants filled the Spanish version (Fonseca-Pedrero et al., 2009) of the PIQ (McKay et al., 2006), a 10-item tool that was constructed according to comprehensive definitional considerations and criteria set out by Freeman and Garety (2000). The original PIQ and the Spanish version of the questionnaire have previously used with clinical and non-clinical samples, showing in both cases excellent reliability and validity as a brief measurement of paranoid thinking (i.e., persecutory ideation; Fonseca-Pedrero et al., 2009). Participants answered using a 5-point Likert scale response format ranging from 0 (very untrue) to 4 (very true). In addition, the Spanish version (Valiente et al., 2011) of the PADS (Melo et al., 2009); was used. This scale is a brief measure to assess both the severity of paranoid thinking (PADS-P) and the perceived deservedness of persecution (PADS-D) and is suitable for both clinical and non-clinical populations. The two subscales possess good internal consistency and factorial validity (e.g., Valiente et al., 2011). Participants were asked to rate each item on a 5-point scale ranging from 0 (certainly false) to 4 (certainly true).

Positive Health

According to the CSMH, to measure hedonia indicators, participants responded to the Satisfaction With Life Scale (Diener et al., 1985) and Positive Affect Scale. The Satisfaction With Life Scale (Spanish version; Cabañero et al., 2004) includes five items with adequate psychometric properties (e.g., Rodríguez-Carvajal et al., 2010). Participants responded to the items using a Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). Moreover, they completed the Positive Affect Scale (Spanish version; Díaz et al., 2007) indicating how frequently, during the last month, they have felt: calm and peaceful, extremely happy, in good spirits, cheerful, satisfied, and full of life. Participants answered the items using a response format ranging from 1 (never) to 5 (all the time). We also measured positive function indicators using the Psychological Well-being Scales (Ryff, 1989; Díaz et al., 2006). This instrument includes six dimensions of positive functioning (i.e., autonomy, self-acceptance, positive relations, environmental mastery, purpose in life and personal growth). Participants responded using a 6-point Likert scale anchored with 1 = strongly disagree and 6 = strongly agree. The structure of six dimensions (with or without a general factor) has been demonstrated through confirmatory factor analysis in previous research (Díaz et al., 2006, 2015; Van Dierendonck et al., 2008). Following Keyes (2005) and Díaz et al. (2018), to obtain a categorical measure of the presence (flourishing) or absence (languishing) of positive mental health, we considered the presence of each indicator when participant's score in the scale was equal to or greater than the mean of the general Spanish population according to an aggregate data set composed by three samples (Blanco and Díaz, 2005; Díaz et al., 2006, 2007). The cut-off points for the categorical mental health indicators were: satisfaction with life = 3.28; positive affect = 3.36; autonomy = 4.24; self-acceptance = 4.31; positive relations = 4.58; environmental mastery = 4.32, purpose in life = 4.48; personal growth = 4.56. The presence of positive mental health required both criteria of hedonia and positive functioning. Moreover, each patient took part in a semi-structured interview based on the indicators proposed by Keyes (2005). The professionals who interviewed the patients codified the presence or absence of each indicator. Next, the presence or absence of positive health was tested based on the same criteria (CSMH categorical diagnosis; see **Supplementary Table S1**). The evaluations of well-being scales and semi-structured interviews converged for 58 patients (96.7%). In the two divergences found, we used the result of the semi-structured interview.

Doubt in General Thoughts

To assess participants' subjective feeling of doubt in general thoughts two items anchored at not at all (1) and extremely (9) asking how much doubt they had in their general thoughts and how invalid they considered their general thoughts, were administered. Ratings were highly intercorrelated (r = 0.87), so they were averaged to create a composite doubt index. Higher values on this index indicated more doubt in general thoughts.

Data Analysis

To test the two continua model of mental health (two different dimensions emerge from the measures used to assess positive mental health and paranoid thinking), we conducted an EFA. A critical methodological decision concerning EFA is the number of factors to retain. According to previous literature, we employed PA, which is one of the most accurate factor retention methods (e.g., Glorfeld, 1995; Hayton et al., 2004). Specifically, we calculated the mean and the 95th percentile for each of the eigenvalues of 100 randomly generated data sets using a SPSS syntax (O'connor, 2000). Next, we compared these random data eigenvalues to real data eigenvalues obtained from a PCA. In the PCA we extracted a number of factors equal to the number of scales entered into the analysis. Finally, we conducted an EFA based on the criterion established by the PA regarding the number of factors to be extracted. We employed *principal axis* as factor extraction method (Fabrigar et al., 1999) and *direct oblimin* as rotation method, since the emerged dimensions were expected to be correlated. We computed factor scores following the procedure proposed by Grice (2001). To study the relationship between paranoid thinking and well-being indicators, we used Pearson's correlations, a contingency table, and a Fisher's exact test. Finally, to test our hypothesis regarding the mediating role of doubt between paranoid thinking and patients wellbeing, we conducted a biased corrected bootstrapping procedure with 10,000 bootstrap re-samples using Hayes PROCESS macro (model 4; see **Figure 2**). PROCESS is a computational procedure for SPSS and SAS that implements moderation or mediation analysis as well as their combination in an integrated conditional process model (Shrout and Bolger, 2002; Preacher and Hayes, 2004; Hayes, 2013; Bajo et al., 2018). Some factors can produce spurious associations, particularly in a non-experimental study such as the present one. Therefore, demographic data, including sex, age, and education level, and DSM-5 diagnosis were introduced as covariates in mediation analysis.

RESULTS

Descriptive statistics (means and standard deviations) and Cronbach alpha coefficients (α) of paranoid thinking, well-being scales and doubt index are displayed in **Table 1**. As we can see in **Table 2**, the results of PA indicate that only the first and second eigenvalues of the real dataset exceeded random values. Scree Plot (**Figure 1**) confirms these results. Based on these findings, an EFA was conducted. As shown in **Table 3**, all the well-being scales essentially loaded on the first factor, explaining 46% of variance. On the other hand, all paranoid thinking scales loaded on the second factor, explaining 14% of the variance. These results support the two continua model of mental health. That is, mental health has two different unipolar dimensions: Positive mental health (i.e., Satisfaction With Life Scale, Positive Affect Scale and Psychological Well-being Scales; factor 1) and paranoid thinking (i.e., PIQ, PADS-P and PADS-D; factor 2). Correlation between the two factors was -0.46, which is an indicator of the strong existing relationship between paranoid thinking and positive health. To explore in more detail this relationship, we calculated the Pearson's correlations of well-being scales and paranoid thinking scales (**Table 4**). The psychological well-being scales were all significantly correlated with PIQ, PADS-P and PADS-D (with the exception of the correlation between Personal Growth and PIQ). Precisely, the autonomy scale showed stronger relation to paranoid thinking than the rest of the scales. However,

TABLE 1 | Means (M), standard deviations (SD), and Cronbach alpha coefficients (α) of paranoid thinking, well-being measures, and doubt index.

	M	*SD*	α
Paranoid thinking			
PIQ	7.97	8.32	0.94
PADS-P	1.68	0.97	0.87
PADS-D	0.91	0.75	0.87
Subjective well-being	3.21	0.64	0.75
Life satisfaction	3.06	0.95	0.83
Positive affect	3.31	0.75	0.74
Psychological well-being	4.18	0.77	0.89
Autonomy	4.03	0.90	0.70
Self-acceptance	4.21	1.11	0.69
Positive relations	3.83	1.14	0.71
Enviromental mastery	4.15	0.90	0.68
Purpose in life	4.33	0.99	0.74
Personal growth	4.62	0.86	0.71
Doubt index	5.23	2.37	0.93

TABLE 2 | Parallel analysis.

Eigenvalues	Random means	Real data
1	1.77	5.04
2	1.52	1.62
3	1.35	0.90
4	1.20	0.81
5	1.06	0.61
6	0.95	0.52

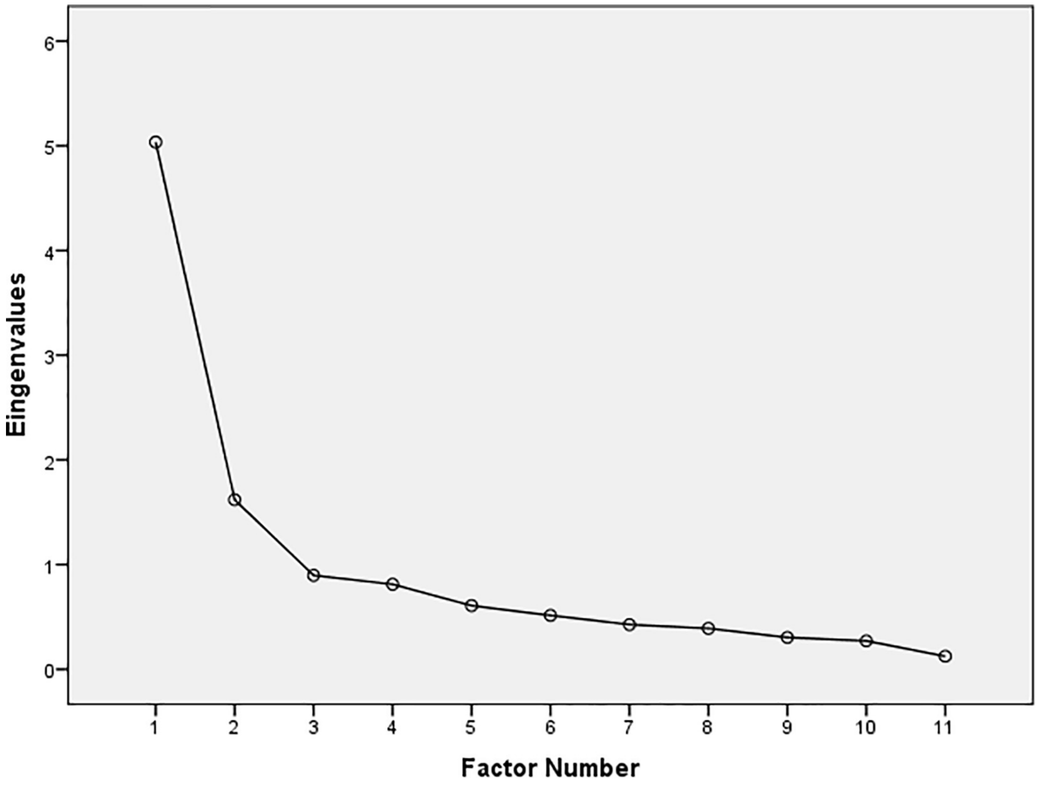

FIGURE 1 | Scree plot.

TABLE 3 | Exploratory factor analysis of paranoid thinking scales and well-being measures.

	1	2
PIQ		0.69
PADS-P	−0.44	0.91
PADS-D	−0.43	0.75
Satisfaction	0.42	
Positive affect	0.49	
Autonomy	0.63	−0.65
Self-acceptance	0.92	−0.44
Positive relations	0.50	−0.46
Enviromental mastery	0.73	−0.45
Purpose in life	0.75	
Personal growth	0.85	−0.41
Factors correlation		−0.46
% Variance	46	60

Presented is the structure matrix of a principal axis extraction with direct oblimin rotation. The table only presents loadings above 0.40. N:p ratio = 5.5. All communalities >0.50 with the exception of PIQ (0.45), Satisfaction (0.30), Positive affect (0.35), and Positive relations (0.35).

the subjective well-being scales showed a weak relationship with paranoid thinking. Only the relationship between life satisfaction and PIQ was significant.

Having the existence of the two-dimensionality hypothesis confirmed, we expected that some patients with paranoid thinking could be assessed as healthy by meeting the criteria for the presence of positive health (categorical diagnostic approach). The categorical diagnosis requires the criteria of hedonia (a high level on positive affect and/or informed life satisfaction) and positive function (a high level on three or more of the psychological well-being indicators) to be met. To test this idea, we computed a contingency table of positive mental health (presence-absence) X disorder (Schizophrenia, Brief Psychotic Disorder, Delusional Disorder and Substance/Medication-Induced Psychotic Disorder) (**Table 5**). Notably, 19 patients (31.7%) were mentally healthy.

Finally, applying the two continua model of mental health and according to our hypothesis (cognitive and pharmacological therapies reduce pathological confidence in all kind of thoughts, not only in pathological ones), we predicted that: (1) more paranoid thinking implies more external doubt (induced by longer metacognitive therapy sessions or more antipsychotics doses) in general thoughts; (2) more paranoid thinking implies less well-being; (3) more doubt implies less well-being; (4) doubt partially mediates the relationship between paranoid thinking and well-being. First, to check that metacognitive therapy was related to participants' doubt in their own thoughts we correlated the total duration of therapy with the doubt index. Pearson correlation was significant ($r = 0.58$, $p < 0.01$), therefore longer duration implied greater doubt. Next, to test our hypothesis we conducted a biased corrected bootstrapping procedure using Hayes PROCESS macro (model 4) (Shrout and Bolger, 2002;

TABLE 4 | Pearson's correlations and 95% confidence intervals of paranoid thinking scales and well-being measures.

	PIQ	PADS-P	PADS-D
Subjective well-being	−0.29* [−0.58 −0.05]	−0.25 [−0.50 0.03]	−0.20 [−0.42 −0.04]
Life satisfaction	−0.27* [−0.48 −0.03]	−0.13 [−0.41 0.19]	−0.12 [−0.38 0.15]
Positive affect	−0.18 [−0.53 0.20]	−0.26 [−0.52 0.03]	−0.25 [−0.52 0.08]
Psychological well-being	−0.42** [−0.60 − 0.21]	−0.56** [−0.71 −0.38]	−0.58** [−0.72 −0.44]
Autonomy	−0.47** [−0.66 −0.24]	−0.57** [−0.71 −0.40]	−0.54** [−0.69 − 0.40]
Self-acceptance	−0.41** [−0.63 −0.19]	−0.51** [−0.67 −0.31]	−0.44** [−0.61 −0.27]
Positive relations	−0.30* [−0.54 −0.07]	−0.40** [−0.60 −0.16]	−0.44** [−0.63 −0.23]
Enviromental mastery	−0.30* [−0.51 −0.11]	−0.45** [−0.65 −0.23]	−0.50** [−0.67 −0.28]
Purpose in life	−0.30* [−0.53 −0.05]	−0.39* [−0.60 −0.12]	−0.46** [−0.64 −0.24]
Personal growth	−0.17 [−0.48 0.11]	−0.32* [−0.54 −0.05]	−0.38** [−0.57 −0.18]

$^{*}p < 0.05$; $^{**}p < 0.01$.

TABLE 5 | Contingency table of mental disorder diagnosis and positive health.

		Disorder				
		Schizophrenia	Delusional	Brief Psychotic	Substance	Total
Positive health	Presence	6	5	6	2	19
	Absence	14	10	14	3	41
Total		20	15	20	5	

Pearson's $\chi^2 = 0.23$, $p = 0.97$. Fisher's exact test $p = 0.97$.

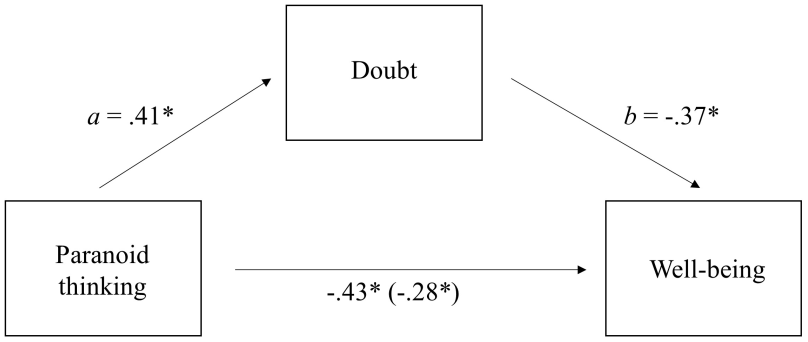

FIGURE 2 | Doubt in one's thoughts as a mediator between Paranoid Thinking and Well-being. Figure in the parenthesis (i.e., –0.28) is the direct effect of Paranoid Thinking on Well-being while accounting for the effect through the indirect path (*$p < 0.05$).

Preacher and Hayes, 2004). This approach includes procedures that compute a 95% CI around the indirect effect and mediation is supported if this CI does not include zero. Paranoid thinking was the independent variable, well-being was the dependent variable, and doubt was the mediating variable (see **Figure 2**). As predicted, the data revealed that the 95% CI of the indirect effect (i.e., the path through the mediator) did not include zero (Indirect Effect a x b = 0.15, CI 95% = from -0.34 to -0.05), thus mediation by doubt is supported (Bajo et al., 2018).

DISCUSSION

Primary social cognition (e.g., the content or direction of thoughts) has been widely studied in paranoid thinking. In fact, there are different theories that have tried to explain the importance of social cognition in the origin and maintenance of this type of thinking (Penn et al., 1997; Freeman et al., 2013). However, the study of secondary cognition or metacognition has received less attention, although research in this concept has grown exponentially in the last decade. The interest in the study of metacognitive processes linked to paranoid thinking is basically related to pathological confidence that characterizes this type of thinking. This confidence is essential to understand paranoid delusions given that, regardless of the content of what we think, trust (or doubt) directs the use we make of this content (Self-Validation Theory) (Briñol and Petty, 2003). Therefore, increased confidence in a thought leads to more use of this though. In addition, pathological confidence causes thoughts to be rigid, and makes it very difficult to modify them (e.g., through the use of cognitive therapies, CBT) (Moritz et al., 2014a). As a result, different metacognitive interventions have been developed in recent years (e.g., Moritz et al., 2014a; Morrison et al., 2014). Despite the controversy over whether these therapies act at a cognitive or metacognitive level (e.g., Andreou et al., 2018; Capobianco and Wells, 2018), they focus on the generation of doubt in thoughts related to paranoid delirium (Moritz and Lysaker, 2018). Moreover, the induction of doubt is also one of the effects of antipsychotic drugs. For this reason, the main objective of this research was to analyze the effect of doubt (vs. confidence) caused by this type of therapies (i.e., metacognitive and pharmacological based on antipsychotics) on patients' well-being and quality of life.

In order to analyze patients' well-being, we applied the CSMH to the study of paranoid thinking. First, and according to our hypothesis, we verified one of the main axioms of the CSMH, the existence of two different axes: mental illness (paranoid thinking) and positive mental health (well-being indicators). Both Horn PA and EFA indicated the presence of two oblique factors. Although previous research applied CSMH in the study of schizophrenia spectrum disorders (Taylor and Brown, 1988), the existence of two-dimensions related to mental illness and positive mental health has not been proven. To the best of our knowledge, this is the first time that the existence of this axiom is confirmed. Despite this bi-dimensionality (mental illness – positive mental health), both factors were highly correlated. In this sense, the strongest relations were between psychological well-being and paranoid thinking (PADSP, PADSD, and PIQ). In particular, autonomy showed the greatest association with paranoid thinking. Furthermore, this indicator of psychological well-being showed a high factorial load (>0.60) in factor 2 (Paranoid Thinking). These results are consistent with previous research that indicates the strong impact of schizophrenia spectrum disorders on patients' autonomy and quality of life (Prouteau et al., 2005; Carrión et al., 2013).

The existence of two different axes (mental illness – positive mental health) has interesting consequences. The first is related to the idea that the absence (or decrease) of paranoid thinking is not equivalent to the presence of health. Therefore, it is important to continue working to improve well-being and quality of life of patients with paranoid thinking, independently of the reduction of symptoms (Collins et al., 1991; Norman et al., 2000). From another perspective, a second consequence is that the presence of paranoid thinking does not necessarily imply the absence of positive health (i.e., subjective well-being and psychological well-being). In fact, according to our results, 19 out of 60 patients showed presence of positive health (flourishing) despite being diagnosed with disorders related to paranoid thinking. Therefore, patients with clinical symptoms of paranoid thinking may inform satisfactory levels of well-being and quality of life. A possible explanation of the high number of patients with presence of positive mental health is related to our sample, given that all patients were in a post-acute or stable phase of the disorders. Even so, other research has also found similar results (Chan et al., 2018).

Once the main axiom of the CSMH was verified, our main purpose was to evaluate the impact that metacognitive and pharmacological therapies based on antipsychotics have on patients' well-being. Our results suggest that when patients received metacognitive and pharmacological treatment, more paranoid thinking implied more doubt in general thoughts. This relationship probably appeared because patients with more paranoid thinking required longer sessions of metacognitive therapy and higher doses of prescribed antipsychotic. These results seem to suggest that although the main metacognitive therapies focus on reducing pathological confidence, they could be affecting thoughts regardless of whether they were related to delirium or not. The same might happen with antipsychotics, that is, their effect on generating doubt may not be specific to pathological content. Consequently, the generalization of doubt in all thoughts could negatively affect patients' well-being. This result should not be surprising because confidence in thoughts is a fundamental variable of positive functioning (Huppert and So, 2013). Indeed, doubt that patients reported in their thoughts (generated by the metacognitive and pharmacological treatment) partially mediated the effect of paranoid thinking on well-being. Therefore, despite the efficacy shown by antipsychotics (first or second generation; Leucht et al., 2009) and metacognitive therapies (Moritz et al., 2014a), they can produce a generalization of doubt which in turn can negatively affect patients' well-being and quality of life, at least in the beginning of the treatment. Previous research (Moritz et al., 2014b) indicated that in the long term there could be a "sleeper" effect of metacognitive therapy that would increase patients' self-esteem and quality of life. Future studies could explore if this "sleeper" effect is related to the recovery of confidence in thoughts not related to delirium. In this sense, to improve patients' well-being and quality of life, it seems interesting to design interventions to increase confidence in thoughts not related to delirium.

Despite the contribution described above, the present work has several limitations. The first one is related to the sample size. We determined the sample size taking into account the difficulty to access hospitalized patients with paranoid thinking who would agree to collaborate and fill out the informed consent. In fact, most studies related to paranoid thinking and schizophrenia tend to have relatively small samples (Kay et al., 1987; Briggs et al., 2008; Dias et al., 2013; Eisenacher and Zink, 2017). Although sample size may have affected some of our analyses, it did not compromise the obtained conclusions. Regarding the factorial analyses carried out, although the ratio N:p is relatively low (5.5), the communalities are greater than 0.50 (with the exceptions of PIQ = 0.45, Satisfaction = 0.30, Positive Affection = 0.35, and Positive Relationships = 0.35). These results indicate an acceptable factor recovery (MacCallum et al., 1999; Hogarty et al., 2005). In addition, with respect to external validity, different studies have found similar results showing the emergence of two different but related factors of positive health measures (i.e., well-being) and pathology (Keyes, 2005; Bajo et al., 2018). Concerning the contingency table between diagnosis of mental disorders and positive health, we used a Fisher's exact test precisely because we expected low values in the cells of the contingency table. Regarding the correlation analyses, we have included CIs to measure the impact of the sample size on the results (Altman and Gardner, 1988). Finally, in relation to the mediation analysis, the smaller the sample size, the lower are the probabilities of finding a statistically significant mediation (Shrout and Bolger, 2002). Since our research reveal the expected mediation effect, this suggests that it is unlikely our study lacked sufficient power to support the null hypothesis. Another limitation of our study is that we did not use social well-being measures to evaluate positive mental health. Given the special characteristics of our sample, we decided not to evaluate this aspect, since we did not want cognitive fatigue to affect the results. Lastly, a final limitation of our study is that patients received simultaneously pharmacological treatment and metacognitive therapy. As a consequence, we could not study the effect of the generalization of doubt in isolation for each treatment. Probably, the effect of generalization of doubt is produced in both treatments in an isolated way since the cognitive effect of the antipsychotics' confidence reduction does not seem to be specific for the paranoid thoughts, and there is a high probability that metacognitive therapy also affects thoughts unrelated to delusions (Moritz et al., 2014a, 2016). In fact, we found a significant relationship between the duration of metacognitive treatment and doubt in general thoughts. Future investigations should further explore this question.

CONCLUSION

In this study we verified, for the first time, one of the main axioms of the CSMH: positive mental health and paranoid thinking are not two poles of a single dimension, but two unipolar dimensions correlated with each other. Therefore, the absence (or reduction) of paranoid thinking does not imply the presence of health. As a consequence, it is important to continue working to improve the well-being and quality of life of patients with paranoid thinking, independently of the reduction of symptoms. In addition, the presence of paranoid thinking does not necessarily imply the absence of positive health. That is, people with paranoid thinking can experience satisfactory levels of well-being. Once the main axiom of CSMH was verified, our main purpose was to evaluate the impact that metacognitive and pharmacological therapies based on antipsychotics have on patients' well-being. Despite the efficacy shown by metacognitive therapies (Moritz et al., 2014a) and antipsychotics (first or second generation; Leucht et al., 2009), it seems that they not only reduce pathological confidence, but can also affect other thoughts not linked to delirium. This effect of generalization of doubt in all thoughts must be controlled, given that it negatively affects patient's well-being and quality of life.

DATA AVAILABILITY

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

ETHICS STATEMENT

This study was part of a research project funded by the Spanish Ministry of Education and Science, and was approved by the ethics committee of the "Universidad de Castilla – La Mancha" (UCLM) and the HGUCR ("Comité Ético de Investigación Clínica, HGUCR – UCLM"). All participants completed an informed consent form, assuring them that all information they provided would remain confidential and anonymous.

AUTHOR CONTRIBUTIONS

DD and LA-A conceived the study design. LA-A collected the data. DD, LA-A, and LB-F drafted the manuscript. MB, MS, and LA-A performed the data analysis. MS, MB, and TR-C contributed to the critical revisions of the manuscript. All authors discussed the results, implications, and literature, and approved the final version of the manuscript for submission.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2019.02099/full#supplementary-material

REFERENCES

Altman, D. G., and Gardner, M. J. (1988). Calculating confidence intervals for regression and correlation. *Br. Med. J.* 296, 1238–1242. doi: 10.1136/bmj.296.6631.1238

Andreou, C., Balzan, R. P., Jelinek, L., and Moritz, S. (2018). Letter to the editor: metacognitive training and metacognitive therapy. A reply to Lora Capobianco and Adrian Wells. *J. Behav. Ther. Exp. Psychiatry* 59, 162–163. doi: 10.1016/j.jbtep.2018.01.006

Bajo, M., Blanco, A., Stavraki, M., Gandarillas, B., Cancela, A., Requero, B., et al. (2018). Post-traumatic cognitions and quality of life in terrorism victims: the role of well-being in indirect versus direct exposure. *Health Qual. Life Outcomes* 16:96. doi: 10.1186/s12955-018-0923-x

Bariola, E., Lyons, A., and Lucke, J. (2017). Flourishing among sexual minority individuals: application of the dual continuum model of mental health in a sample of lesbians and gay men. *Psychol. Sex. Orientat. Gend. Divers.* 4, 43–53. doi: 10.1037/sgd0000210

Blanco, A., and Díaz, D. (2005). Social well-being: theoretical structure and measurement. *Psicotherma* 17, 582–589.

Briggs, A., Wild, D., Lees, M., Reaney, M., Dursun, S., Parry, D., et al. (2008). Impact of schizophrenia and schizophrenia treatment-related adverse events on quality of life: direct utility elicitation. *Health Qual. Life Outcomes* 6:105. doi: 10.1186/1477-7525-6-105

Briñol, P., Petty, R., and Barden, J. (2007). Happiness versus sadness as a determinant of thought confidence in persuasion: a self-validation analysis. *J. Pers. Soc. Psychol.* 93, 711–727. doi: 10.1037/0022-3514.93.5.711

Briñol, P., and Petty, R. E. (2003). Over head movements and persuasion: a self-validation analysis. *J. Pers. Soc. Psychol.* 84, 1123–1139. doi: 10.1037/0022-3514.84.6.1123

Briñol, P., Petty, R. E., Stavraki, M., Lamprinakos, G., Wagner, B., and Díaz, D. (2018). Affective and cognitive validation of thoughts: an appraisal perspective on anger, disgust, surprise, and awe. *J. Pers. Soc. Psychol.* 114, 693–718. doi: 10.1037/pspa0000118

Cabañero, M. J., Richard, M., Cabrero, J., Orts, M. I., Reig, A., and Tosal, B. (2004). Fiabilidad y validez de una Escala de Satisfacción con la Vida de Diener en una muestra de mujeres embarazadas y puérperas. *Psicothema* 16, 448–455.

Capobianco, L., and Wells, A. (2018). Letter to the editor: metacognitive therapy or metacognitive training: what's in a name? *J. Behav. Ther. Exp. Psychiatry* 59:161. doi: 10.1016/j.jbtep.2017.12.003

Carrión, R. E., McLaughlin, D., Goldberg, T. E., Auther, A. M., Olsen, R. H., Olvet, D. M., et al. (2013). Prediction of functional outcome in individuals at clinical high risk for psychosis. *JAMA Psychiatry* 70, 1133–1142. doi: 10.1001/jamapsychiatry.2013.1909

Chan, R., Mak, W., Chio, F., and Tong, A. (2018). Flourishing with psychosis: a prospective examination on the interactions between clinical, functional, and personal recovery processes on well-being among individuals with schizophrenia spectrum disorders. *Schizophr. Bull.* 44, 778–786. doi: 10.1093/schbul/sbx120

Collins, E. J., Hogan, T. P., and Desai, H. (1991). Measurement of therapeutic response in schizophrenia. A critical survey. *Schizophr. Res.* 5, 249–253. doi: 10.1016/0920-9964(91)90083-4

de Vos, J. A., Radstaak, M., Bohlmeijer, E. T., and Westerhof, G. J. (2018). Having an eating disorder and still being able to flourish? Examination of pathological symptoms and well-being as two continua of mental health in a clinical sample. *Front. Psychol.* 9:2145. doi: 10.3389/fpsyg.2018.02145

Dias, E. C., Bickel, S., Epstein, M. L., Sehatpour, P., and Javitt, D. C. (2013). Abnormal task modulation of oscillatory neural activity in schizophrenia. *Front. Psychol.* 4:540. doi: 10.3389/fpsyg.2013.00540

Díaz, D., Blanco, A., Horcajo, J., and Valle, C. (2007). Depression and the complete state model of health. *Psicothema* 19, 286–294.

Díaz, D., Rodríguez-Carvajal, R., Blanco, A., Moreno-Jiménez, B., Gallardo, I., Valle, C., et al. (2006). Spanish adaptation of the psychological well-being scales (PWBS). *Psicothema* 18, 572–577.

Díaz, D., Stavraki, M., Blanco, A., and Bajo, M. (2018). 11-M victims 3 years after madrid terrorist attacks: looking for health beyond Trauma. *J. Happiness Stud.* 19, 663–675. doi: 10.1007/s10902-016-9842-x

Díaz, D., Stavraki, M., Blanco, A., and Gandarillas, B. (2015). The eudaimonic component of satisfaction with life and psychological well-being in Spanish cultures. *Psicothema* 27, 247–253. doi: 10.7334/psicothema 2015.5

Diener, E., Emmons, R., Larsen, R., and Griffin, S. (1985). The satisfaction with life scale. *J. Pers. Assess.* 49, 71–75.

Eichner, C., and Berna, F. (2016). Acceptance and efficacy of metacognitive training (MCT) on positive symptoms and delusions in patients with schizophrenia: a meta-analysis taking into account important moderators. *Schizophr. Bull.* 42, 952–962. doi: 10.1093/schbul/sbv225

Eisenacher, S., and Zink, M. (2017). The importance of metamemory functioning to the pathogenesis of psychosis. *Front. Psychol.* 8:304. doi: 10.3389/fpsyg.2017.00304

Fabrigar, L., Maccallum, R., Wegener, D., and Haggard, P. (1999). Evaluating the use of exploratory factor analysis in psychological research. *Psychol. Methods* 4, 272–299. doi: 10.1037//1082-989x.4.3.272

Fonseca-Pedrero, E., Paíno-Piñeiro, M., Lemos-Giráldez, S., Villazón-García, U., and Muñiz, J. (2009). Validation of the schizotypal personality questionnaire—brief form in adolescents. *Schizophr. Res.* 111, 53–60. doi: 10.1016/j.schres.2009.03.006

Freeman, D., Dunn, G., Fowler, D., Bebbington, P., Kuipers, E., Emsley, R., et al. (2013). Current paranoid thinking in patients with delusions: the presence of cognitive-affective biases. *Schizophr. Bull.* 39, 1281–1287. doi: 10.1093/schbul/sbs145

Freeman, D., and Garety, P. A. (1999). Worry, worry processes and dimensions of delusions: an exploratory investigation of a role for anxiety processes in the maintenance of delusional distress. *Behav. Cogn. Psychother.* 27, 47–62.

Freeman, D., and Garety, P. A. (2000). Comments on the content of persecutory delusions: does the definition need clarification? *Br. J. Clin. Psychol.* 39, 407–414. doi: 10.1348/014466500163400

Freeman, D., Garety, P. A., Kuipers, E., Fowler, D., and Bebbington, P. E. (2002). A cognitive model of persecutory delusions. *Br. J. Clin. Psychol.* 41, 331–347.

Garety, P., Philippa, A., and Freeman, D. (1999). Cognitive approaches to delusions: a critical review of theories and evidence. *Br. J. Clin. Psychol.* 38, 113–154. doi: 10.1348/014466599162700

Glorfeld, L. (1995). An improvement on Horn's parallel analysis methodology for selecting the correct number of factors to retain. *Educ. Psychol. Meas.* 55, 377–393. doi: 10.1177/0013164495055003002

Grice, J. (2001). Computing and evaluating factor scores. *Psychol. Methods* 6, 430–450. doi: 10.1037//1082-989x.6.4.430-450

Hayes, A. F. (2013). *Introduction to Mediation, Moderation, and Conditional Process Analysis*. New York, NY: Guilford Press.

Hayton, J., Allen, D., and Scarpello, V. (2004). Factor retention decisions in exploratory factor analysis: a tutorial on parallel analysis. *Organ Res. Methods* 7, 191–205. doi: 10.1177/1094428104263675

Hogarty, K. Y., Hines, C. V., Kromrey, J. D., Ferron, J. M., and Mumford, K. R. (2005). The quality of factor solutions in exploratory factor analysis: the influence of sample size, communality, and overdetermination. *Educ. Psychol. Meas.* 65, 202–226. doi: 10.3758/s13428-014-0486-7

Huntsinger, J., Isbell, L., and Clore, G. L. (2014). The affective control of thought: malleable, not fixed. *Psychol. Rev.* 121, 600–618. doi: 10.1037/a0037669

Huppert, F., and So, T. (2013). Flourishing across Europe: application of a new conceptual framework for defining well-being. *Soc. Indic. Res.* 110, 837–861. doi: 10.1007/s11205-011-9966-7

Hutton, P., Morrison, A., Wardle, M., and Wells, A. (2014). Metacognitive therapy in treatment-resistant psychosis: a multiple-baseline study. *Behav. Cogn. Psychother.* 42, 166–185. doi: 10.1017/S1352465812001026

Kapur, S., Mizrahi, R., and Li, M. (2005). From dopamine to salience to psychosis—linking biology, pharmacology and phenomenology of psychosis. *Schizophr. Res.* 79, 59–68. doi: 10.1016/j.schres.2005.01.003

Karow, A., and Pajonk, F. (2006). Insight and quality of life in schizophrenia: recent findings and treatment implications. *Curr. Opin. Psychiatry* 19, 637–641. doi: 10.1097/01.yco.0000245754.21621.c9

Kay, S. R., Fiszbein, A., and Opler, L. A. (1987). The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr. Bull.* 13, 261–276. doi: 10.1093/schbul/13.2.261

Keyes, C. (2005). Mental illness and/or mental health? Investigating anxioms of the complete state model of health. *J. Consult. Clin. Psychol.* 73, 539–548. doi: 10.1037/0022-006x.73.3.539

Keyes, C. (2006). Mental health in adolescence: is America's youth flourishing? *Am. J. Orthopsychiatry* 76, 395–402. doi: 10.1037/0002-9432.76.3.395

Keyes, C. (2009). The Black-White paradox in health: flourishing in the face of social inequality and discrimination. *J. Pers.* 77, 1677–1706. doi: 10.1111/j.1467-6494.2009.00597.x

Leucht, S., Corves, C., Arbter, D., Engel, R. R., Li, C., and Davis, J. M. (2009). Second-generation versus first-generation antipsychotic drugs for schizophrenia: a meta-analysis. *Lancet* 373, 31–41. doi: 10.1016/S0140-6736(08)61764-X

MacCallum, R. C., Widaman, K. F., Zhang, S., and Hong, S. (1999). Sample size in factor analysis. *Psychol. Methods* 4, 84–99. doi: 10.1037/1082-989x.4.1.84

McGaffin, B., Deane, F., Kelly, P., and Ciarrochi, J. (2015). Flourishing, languishing and moderate mental health: prevalence and change in mental health during recovery from drug and alcohol problems. *Addict. Res. Theory* 23, 351–360. doi: 10.3109/16066359.2015.1019346

McKay, R., Langdon, R., and Coltheart, M. (2006). The persecutory ideation questionnaire. *J. Nerv. Ment. Dis.* 194, 628–631. doi: 10.1097/01.nmd.0000231441.48007.a5

Melo, S., Corcoran, R., Shryane, N., and Bentall, R. P. (2009). The persecution and deservedness scale. *Psychol. Psychother. Theory Res. Pract.* 82, 247–260. doi: 10.1348/147608308x398337

Moritz, S., Andreou, C., Schneider, B. C., Wittekind, C. E., Menon, M., Balzan, R. P., et al. (2014a). Sowing the seeds of doubt: a narrative review on metacognitive training in schizophrenia. *Clin. Psychol. Rev.* 34, 358–366. doi: 10.1016/j.cpr.2014.04.004

Moritz, S., Veckenstedt, R., Andreou, C., Bohn, F., Hottenrott, B., Leighton, L., et al. (2014b). Sustained and "Sleeper" effects of group metacognitive training for schizophrenia. *JAMA Psychiatry* 71, 1103–1111.

Moritz, S., Kolbeck, K., and Andreou, C. (2016). Antipsychotics decrease response confidence. *J. Psychopharmacol.* 30, 831–833. doi: 10.1177/0269881116650404

Moritz, S., and Lysaker, P. H. (2018). Metacognition – what did James H. Flavell really say and the implications for the conceptualization and design of metacognitive interventions. *Schizophr. Res.* 201, 20–26. doi: 10.1016/j.schres.2018.06.001

Moritz, S., Veckenstedt, R., Bohn, F., Hottenrott, B., Scheu, F., Randjbar, S., et al. (2013). Complementary group metacognitive training (MCT) reduces delusional ideation in schizophrenia. *Schizophr. Res.* 151, 61–69. doi: 10.1016/j.schres.2013.10.007

Moritz, S., and Woodward, T. (2007). Metacognitive training in schizophrenia: from basic research to knowledge translation and intervention. *Curr. Opin. Psychiatry* 20, 619–625. doi: 10.1097/yco.0b013e3282f0b8ed

Moritz, S., and Woodward, T. S. (2005). Jumping to conclusions in delusional and non-delusional schizophrenic patients. *Br. J. Clin. Psychol.* 44, 193–207. doi: 10.1348/014466505x35678

Morrison, A., Pyle, M., Chapman, N., French, P., Parker, S., and Wells, A. (2014). Metacognitive therapy in people with a schizophrenia spectrum diagnosis and medication resistant symptoms: a feasibility study. *J. Behav. Ther. Exp. Psychiatry* 45, 280–284. doi: 10.1016/j.jbtep.2013.11.003

Morrison, A. P., Shryane, N., Fowler, D., Birchwood, M., Gumley, A. I., Taylor, H. E., et al. (2015). Negative cognition, affect, metacognition and dimensions of paranoia in people at ultra-high risk of psychosis: a multi-level modelling analysis. *Psychol. Med.* 45, 2675–2678.

Norman, R. M., Malla, A. K., McLean, T., Voruganti, L. P., Cortese, L., McIntosh, E., et al. (2000). The relationship of symptoms and level of functioning in schizophrenia to general wellbeing and the quality of life scale. *Acta Psychiatr. Scand.* 102, 303–309. doi: 10.1034/j.1600-0447.2000.102004303.x

Normann, N., van Emmerik, A., and Morina, N. (2014). The efficacy of metacognitive therapy for anxiety and depression: a meta-analytic review. *Depress. Anxiety* 31, 402–411. doi: 10.1002/da.22273

O'connor, B. P. (2000). SPSS and SAS programs for determining the number of components using parallel analysis and Velicer's MAP test. *Behav. Res. Methods Instrum. Comput.* 32, 396–402. doi: 10.3758/bf03200807

Penn, D., Corrigan, P., Bentall, R., Racenstein, J., and Newman, L. (1997). Social cognition in schizophrenia. *Psychol. Bull.* 121, 114–132.

Preacher, K. J., and Hayes, A. F. (2004). SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behav. Res. Methods Instrum. Comput.* 36, 717–731. doi: 10.3758/bf03206553

Prouteau, A., Verdoux, H., Briand, C., Lesage, A., Lalonde, P., Nicole, L., et al. (2005). Cognitive predictors of psychosocial functioning outcome in schizophrenia: a follow-up study of subjects participating in a rehabilitation program. *Schizophr. Res.* 77, 343–353. doi: 10.1016/j.schres.2005.03.001

Rodríguez-Carvajal, R., Díaz, D., Moreno-Jiménez, B., Blanco, A., and van Dierendonck, D. (2010). Vitality and inner resources as relevant components of psychological well-being. *Psicothema* 22, 63–70.

Ryff, C. D. (1989). Happiness is everything, or is it? Explorations on the meaning of psychological wellbeing. *J. Pers. Soc. Psychol.* 57, 1069–1081. doi: 10.3109/09638288.2010.503835

Shrout, P., and Bolger, N. (2002). Mediation in experimental and nonexperimental studies: new procedures and recommendations. *Psychol. Methods* 7, 422–445. doi: 10.1037//1082-989x.7.4.422

Taylor, S., and Brown, J. (1988). Illusion and well-being: a social psychological perspective on mental healt. *Psychol. Bull.* 103, 193–210. doi: 10.1037/0033-2909.103.2.193

Valiente, C., Cantero, D., Vázquez, C., Sanchez, Á, Provencio, M., and Espinosa, R. (2011). Implicit and explicit self-esteem discrepancies in paranoia and depression. *J. Abnorm. Psychol.* 120, 691–699. doi: 10.1037/a0022856

Van Dierendonck, D., Díaz, D., Rodríguez-Carvajal, R., Blanco, A., and Moreno-Jiménez, B. (2008). Ryff's six-factor model of psychological well-being, a Spanish exploration. *Soc. Indic. Res.* 87, 473–479. doi: 10.1007/s11205-007-9174-7

Wells, A. (1995). Meta-cognition and worry: a cognitive model of generalised anxiety disorder. *Behav. Cogn. Psychother.* 23, 301–320. doi: 10.1017/s1352465800015897

Wells, A., and Matthews, G. (1996). Modelling cognition in emotional disorder: the S-REF model. *Behav. Res. Ther.* 34, 881–888. doi: 10.1016/s0005-7967(96)00050-2

World Health Organization (1946). *Official Records of the World Health Organization*, Vol. 2. Geneva: World Health Organization, 100.

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Restricted Speech Recognition in Noise and Quality of Life of Hearing-Impaired Children and Adolescents With Cochlear Implants – Need for Studies Addressing This Topic With Valid Pediatric Quality of Life Instruments

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Cochlear implants (CI) support the development of oral language in hearing-impaired children. However, even with CI, speech recognition in noise (SRiN) is limited. This raised the question, whether these restrictions are related to the quality of life (QoL) of children and adolescents with CI and how SRiN and QoL are related to each other. As a result of a systematic literature research only three studies were found, indicating positive moderating effects between SRiN and QoL of young CI users. Thirty studies addressed the quality of life of children and adolescents with CI. Following the criteria of the World Health Organization (WHO) for pediatric health related quality of life HRQoL (1994) only a minority used validated child centered and age appropriate QoL instruments. Moreover, despite the consensus that usually children and adolescents are the most prominent informants of their own QoL (parent-reports complement the information of the children) only a minority of investigators used self-reports. Restricted SRiN may be a burden for the QoL of children and adolescents with CI. Up to now the CI community does not seem to have focused on a possible impairment of QoL in young CI users. Further studies addressing this topic are urgently needed, which is also relevant for parents, clinicians, therapists, teachers, and policy makers. Additionally investigators should use valid pediatric QoL instruments. Most of the young CI users are able to inform about their quality of life themselves.

Keywords: QoL, hearing loss, pediatric cochlear implantation, speech recognition in noise, valid instruments

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INTRODUCTION

A cochlear implant (CI) is a prosthesis for the hair cells in the inner ear for individuals with severe to profound hearing loss. CIs support the development of oral language in hearing-impaired children (e.g., Geers et al., 2016; Cupples et al., 2018; Ruben, 2018), so that children with bilateral CIs perform better than children with unilateral CI (Lovett et al., 2010; Geers et al., 2016; Moberly et al., 2016;

Health Quality Ontario, 2019). However, there are limits to CI. Not all children with CI develop language at an average level (e.g., Sarant, 2012; Geers et al., 2016; Lund, 2016; Cupples et al., 2018). Geers et al. (2016) found a persistent language delay in 32% of 10.5 year old children with CI. Furthermore, children with CI are more restricted in speech recognition in noise (SRiN) compared to their normal hearing peers (Caldwell and Nittrouer, 2013; Chen et al., 2014; Taitelbaum-Swead and Fostick, 2017). SRiN depends on the language abilities of young CI users (Ching et al., 2017), duration of CI use, education of the mother, use of hearing aids before CI, pre-implant auditory threshold (Chen et al., 2014) and bilateral CI (vs. unilateral CI, Lovett et al., 2010; Sparreboom et al., 2012; Jacobs et al., 2016). Additionally, in the case of normal hearing children SRiN depends on their cognitive abilities (Roman et al., 2017).

In our noisy world, the ability to recognize and to understand speech in noise is of tremendous importance. Overall noise pollution may have more profound effects on children than on adults, because their cognitive functions are "less automatized and thus more prone to disruption" (Klatte et al., 2013). Furthermore, children have fewer options to influence their environment. Nevertheless, it seems that children are often exposed to substantial noise. Indoor noise levels in playschools and schools are often higher than the recommended maximum noise levels (Sarantopoulos et al., 2014; Chan et al., 2015). For example, the indoor noise level in occupied classrooms was on average 69 LAeq dB[1] and in unoccupied classrooms 47 LAeq dB (Sarantopoulos et al., 2014). The level of speech was estimated to be only 12 dB higher than the level of background noise (speech-to-noise ratio) during teaching and even less discernible during break time and outdoor activities (Sarantopoulos et al., 2014). Noise has a negative impact on school performance of normal hearing children. The performance on working memory tasks and comprehension tasks is impaired during lessons with indoor noise (Klatte et al., 2013; Sullivan et al., 2015).

Studies about hearing-impaired children indicate that restricted SRiN compromises not only the hearing health and functioning (listening and understanding), but also other areas of physical, mental and social health [see the health concept of the World Health Organization [WHO], 1948]. The effort in SRiN for hearing-impaired students is shown in longer reaction times in verbal tasks (*impeded physical health*) compared to normal hearing peers (McGarrigle et al., 2019). FM systems (Frequency Modulation radio waves send speech and other auditory signals to hearing aids or CI) support hearing-impaired students during lessons. However, not all students are using them continuously during lessons (Keilmann and Reutter, 2014). Restricted SRiN is also associated with physical stress (*physical health*), as indicated by elevated cortisol levels (Bess et al., 2016) and by fatigue (Hornsby et al., 2017). Parents seem to underestimate the fatigue of their children with CI, which may be disappointing and frustrating for the children and might lead to feelings of isolation (*impeded social health*, Werfel and Hendricks, 2016; Hornsby et al., 2017). Furthermore, restricted SRiN correlated positively with internalizing and externalizing problems of adolescent CI users (*impeded mental health*, Huber et al., 2015) and may be one of the reasons, why young CI users have more peer problems (*impeded social health*, Huber et al., 2015; Warner-Czyz et al., 2018). Accordingly, the question arises, if restricted SRiN impedes the subjective wellbeing of hearing-impaired children and adolescents, growing up with cochlear implants.

Subjective wellbeing (SWB) can be understood as a "summary measure of quality of life" (Wilson and Cleary, 1998) and is usually characterized by three domains: (i) positive affect, (ii) life satisfaction and (iii) meaning and purpose of life (Ravens-Sieberer et al., 2014a; Wallander and Koot, 2016). Quality of life (QoL) concerns different life areas like the individual‘s economic status, rights, culture and health (Fayed et al., 2012). Health related quality of life or HRQoL is commonly "considered to be a subdomain of the more global construct of QoL" (Davis et al., 2006). Based on the health concept of the World Health Organization [WHO] (1948) HRQoL spans the domains *physical health*, *mental health*, and *social health*. However, there is a lack of a common definition of pediatric QoL (HRQoL and SWB), see e.g., Drotar (2004), Davis et al. (2006), Fayed et al. (2012), Ravens-Sieberer et al. (2014a,b), and Wallander and Koot (2016).

For the assessment of pediatric QoL, child specific instruments are needed. According to the World Health Organization (WHO) valid pediatric QoL measures should be (i) *child-centered*, i.e., specifically developed for children, (ii) *age-appropriate*, taking into account the developmental status of different age groups, (iii) *validated* cross-culturally, and (iv) include *self-reports* (World Health Organization [WHO], 1994). Regarding (i) and (ii) recent studies demonstrate a downturn of SWB (Wallander and Koot, 2016) and HRQoL in adolescence (Warner-Czyz et al., 2011; Rajmil et al., 2013; Barkmann et al., 2016; Raj et al., 2017). Therefore, specific self- and parent reports for different age groups should be available. Regarding (iii) a consensus exists that children and adolescents are the most prominent informants of their own QoL (Riley, 2004; Davis et al., 2006; Upton et al., 2008; Ellert et al., 2011; Ravens-Sieberer et al., 2014a,b).

Children at the age of 5 years are able to inform about their health states, health functioning (Riley, 2004) and SWB (Ravens-Sieberer et al., 2014a). From the age of eight on, children are able to report reliably "on all aspects of their health experiences and can use a five-point response format" (Rebok et al., 2001). However, reports are only possible with "child friendly questionnaires" (Coghill et al., 2009). This implicates, that the questions of the self-report correspond to the language level, speech style, reading skills and cognitive status of the respective age-group (Rebok et al., 2001; Riley, 2004; Davis et al., 2006; Coghill et al., 2009; Ravens-Sieberer et al., 2014b). Parent reports should complement the reports of the children, completing "the picture of a child's QoL" (Coghill et al., 2009). Children can be too young or unable to understand the questions, for example because they have additional special needs. In this case parent reports are not only required, but essential. Most studies showed only a poor to moderate agreement between parent reports and children's reports about the child's QoL (Eiser and Varni, 2013; Rajmil et al., 2013; Silva et al., 2015; Lee et al., 2019. See however Quitmann et al., 2016). Accordingly, the question arises, whether

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[1] LAeq A – weighted equivalent continuous sound level.

QoL outcomes in CI users vary, depending on whether parent or self-ratings are considered.

Validated SWB and HRQoL instruments for children and adolescents correspoding the criteria of the WHO are listed in Davis et al. (2006), Fayed et al. (2012), Ravens-Sieberer et al. (2014a,b), and in Wallander and Koot (2016).

The model of Wilson and Cleary (1998) is one of the most prominent and best validated models of HRQoL in adults (Bakas et al., 2012; Ojelabi et al., 2017). According to this model, biological/physiological variables ("cells, organs, and organ systems") influence the symptom status, e.g., fever. The symptoms in turn influence the functional status, e.g., some gross motor activities ("Measures of function assess the ability of the individual to perform particular defined tasks."). This again has an impact on the (subjective) general health perceptions (a "subjective rating" of one's own health), and finally the "overall quality of life" (QoL), e.g., worry because of a disease. Additionally, there are individual influences (personality, motivation, preferences, and values) and environmental influences (social, economic and psychological support of the environment). **Figure 1** shows an adaptation of this model illustrating an example of the HRQoL of a young CIs user with a congenital hearing loss. In this example, restricted SRiN may cause attention problems (functioning) and listlessness (health perception). Possible consequences may be impeded physical wellbeing and aggrieved wellbeing at school, see **Figure 1**.

There may be other situations causing reduced QoL in young CI users with cascading effects: Communication problems with peers, caused by restricted SRiN may provide the perception of isolation and impede the social wellbeing. If parents do not notice the problems of their child, this may impede the wellbeing of the child in the family. If restricted SRiN is associated with more internalizing and externalizing problems, these problems may impede the mental wellbeing. Problems to follow instructions at school or at training, caused by restricted SRiN may worsen the appraisal of the teacher. This is possibly perceived as failing by the CI user and may impede the wellbeing at school or at the vocational place. In all these situations, there may be mediating effects between SRiN and QoL. There can also be direct effects: A young CI user perceives problems to follow the conversation because of the background noise at a party and is impeded in his social wellbeing. Studies in normal hearing children showed correlations between HRQoL and fatigue of children with cancer (Nunes et al., 2017), internalizing and externalizing problems (Dey et al., 2012; Ravens-Sieberer et al., 2012) and academic performance (Degoy and Berra, 2018).

To address the question, whether SRiN impedes HRQoL in children and adolescents a systematic review was intended strictly following the PRISMA criteria (Liberati et al., 2009). However, the systematic literature research resulted in only three papers. Therefore, we did not carry out a meta-analysis, and present the findings of our research in the format of a perspective article. In a first step, we identified all papers reporting about the HRQoL in young CI-users and summarize the outcomes, to address whether QoL was impaired in young CI-users. In a second step, we summarize the three papers reporting a relationship between SRiN and HRQoL in young CI-users, which are the main focus of this article.

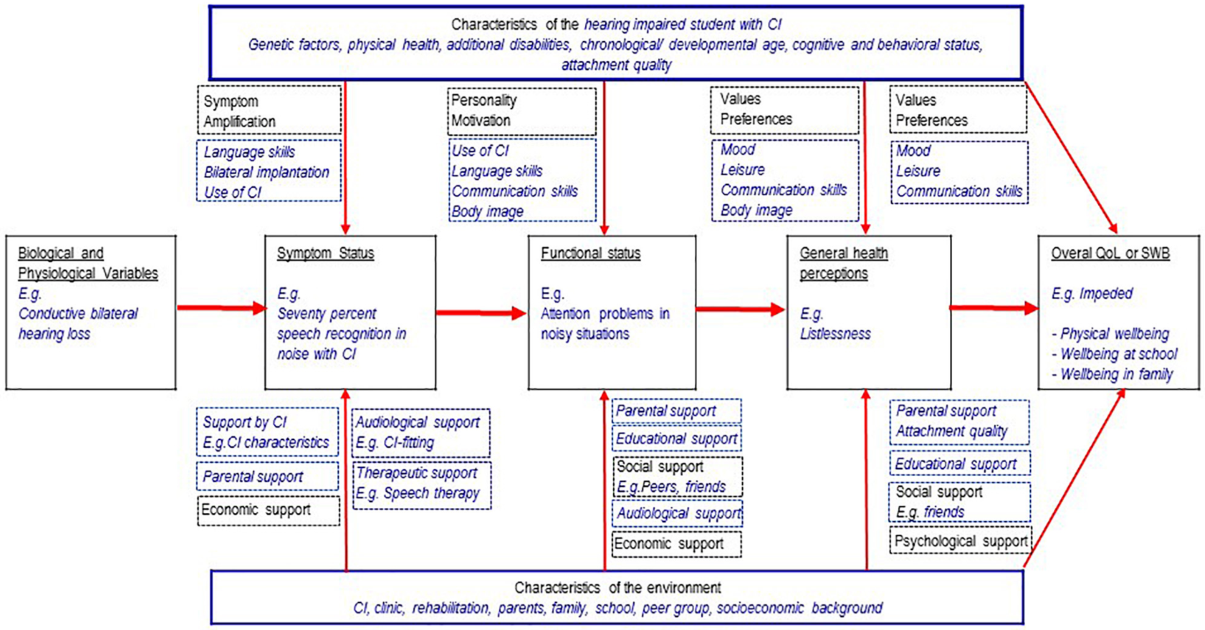

FIGURE 1 | Wilson and Cleary theoretical framework (1998, doi: 10.1371/journal.pone.0113166.g001) adapted to young CI users, with permission of the authors and the copyright holder (4/10/19, 4565201160405).

TABLE 1 | Studies addressing quality of life of children and adolescents with CI.

Author	Year	Topic	Study design	Chron. age (years)	N CI	N control NH, HA, DD	Scale	Child-centred	Age appropriate	Self version	Self-report provided	Validated	Result
Percy-Smith et al., 2008	2008	SWB	Cross-sectional	2–17	144	216 NH	No name	No	No	No	No	No	+
Chmiel et al., 2000	2000	QoL	Cross-sectional	3–20	21		No name	Yes	No	No	Yes	No	+
Stacey et al., 2006	2006	QoL	Cross-sectional	?	527		No name	Yes	No	No	No	No	+
Huttunen et al., 2009	2009	QoL	Cross-sectional	2–12	35		CCIPP	Yes	No	No	No	Yes	+
Schorr et al., 2009	2009	QoL	Cross-sectional	5–14	37		Chmiel 2000	Yes	No	No	Yes	?	+
Hashemi and Monshizadeh, 2011	2011	QoL	Cross-sectional	?	24		No name	No	No	No	No	No	+
Edwards et al., 2012	2012	QoL	Cross-sectional	3–18	89	117?	PAQL	Yes	No	No	No	Yes	+
Fortunato-Tavares et al., 2012	2012	QoL	Cross-sectional	6	10		CCIPP	Yes	No	No	No	Yes	+
Sparreboom et al., 2012	2012	QoL	Longitudinal	4–9	30 uni/9 bi		GCBI, NCIQ, HUI 3, SSQ	Yes[1]/No	No	No	No	Yes	+
							PEDsQL	Yes	Yes	Yes	No	Yes	=
Almeida et al., 2015	2015	QoL	Cross-sectional	2–12	12		CCIPP	Yes	No	No	No	Yes	+
Kumar et al., 2015	2015	QoL	Cross-sectional	10	33		CCIPP	Yes	No	No	No	Yes	+
Yorgun et al., 2015	2015	QoL	Cross-sectional	2–18	161		CCIPP	Yes	No	No	No	Yes	+
Samuel et al., 2016	2016	QoL	Cross-sectional	<5	410		BAPP	Yes	No	No	No	Yes	+
Razafimahefa-Raoelina et al., 2016	2016	QoL	Cross-sectional	6–17	32		KIDSCREEN	Yes	Yes	Yes	Yes	Yes	=
Noble et al., 2016	2016	QoL	Longitudinal	5–17	18		PEDsQL	Yes	Yes	Yes	Yes	Yes	+
Speaker et al., 2018	2018	QoL	Cross-sectional	?	16		GCBI	Yes	No	No	No	Yes	+
Sach and Barton, 2007	2007	HRQoL	Cross-sectional	9	178		EQ-5D	No	No	No	No	Yes	=
Lovett, 2010	2010	HRQoL	Cross-sectional	4–7	20 uni, 30 bi	56 NH	HUI 3, VAS, SSQ	No	No	No	No	Yes	=
Clark et al., 2012	2012	HRQoL	Longitudinal	<3	188	97 NH	VAS	?	No	No	No	Yes	+
Liu et al., 2016	2016	HRQoL	Cross-sectional	4–11	213		NCIQ, HUI 3	No	No	No	No	Yes	+
Looi et al., 2016a	2016	HRQoL	Cross-sectional	2–18	12	22 HA	CuHDQOL	?	No	No	No	Yes	–
Zhao et al., 2018	2018	HRQoL	Longitudinal	3	123		CCIPP	Yes	No	No	No	Yes	+
Huber, 2005	2005	HRQoL	Cross-sectional	8–16	29	1501 NH	KINDL R	Yes	Yes	Yes	Yes	Yes	–/=
Loy et al., 2010	2010	HRQoL	Cross-sectional	8–16	84	1501 NH	KINDL R	Yes	Yes	Yes	Yes	Yes	–
Warner-Czyz et al., 2011	2011	HRQoL	Cross-sectional	4–16[2]	134	1501NH	KINDL R	Yes	Yes	Yes	Yes	Yes	–
Meserole et al., 2014	2014	HRQoL	Cross-sectional	8	129	185 NH	CHIP-CE	Yes	Yes	Yes	Yes	Yes	=

(Continued)

TABLE 1 | Continued

Author	Year	Topic	Study design	Chron. age (years)	N CI	N control NH, HA, DD	Scale	Child-centred	Age appropriate	Self version	Self-report provided	Validated	Result
Duarte et al., 2014	2014	HRQoL	Cross-sectional	8–18	20	24HA/17NH	KIDSCREEN	Yes	Yes	Yes	Yes	Yes	=
Looi et al., 2016b	2016	HRQoL	Cross-sectional	2–18	12	22HA/44NH	PEDsQL, CuHDQOL	Yes	Yes	Yes	Yes	Yes	–
Zaidman-Zait et al., 2017	2017	HRQoL	Cross-sectional	3–7	43 CI+ DD	49 CI + no DD	KINDL R	Yes	Yes	Yes	No	Yes	–
Haukedal et al., 2018	2018	HRQoL	Cross-sectional	5–13	106	80 NH	PEDsQL	Yes	Yes	Yes	No	Yes	–

QoL, Quality of life; HRQoL, Health Related Quality of Life; SWB, Subjective Well Being; mo, months; c, children; p, parents; t, teachers; CI, CI users; NH, normal hearing; uni, unilateral; bilat, bilateral; HA, hearing aid; DD, developmental disability; Self version, Instrument with specific self versions; Self-report provided, young CI users were asked; EQ-5D, EuroQoL; CCIP, Children with cochlear implants parental perspectives; HUI, Health Utility Index; VAS, Visual Analog Scale; PAQL, Paediatric Audiology Quality of Life; NCIQ, Nijmegen Cochlear Implantation Questionnaire; GCBI, Glasgow Children Benefit Inventory; SSQ, Speech, Spatial, and Qualities of Hearing Scale; BAPP, Brief Assessment of Parental Perception; CuHDQOL, Children Using Hearing Devices Quality of Life Questionnaire (?); KINDL R, KINDL revised https://www.kindl.org/; CHIP-CE, Child Health and Illness Profile-Child Edition, https://www.ideaconnection.com/patents/5679-Child-Health-Illness-Profile-Child-Edition-CHIP-CE-Ch.html; KIDSCREEN, Health Related Quality of Life Questionnaire for Children and Young People and their Parents; https://www.kidscreen.org/; PEDsQl, Pediatric Quality of Life Inventory, http://www.pedsql.org/.(?) not clear; (+) Improved QoL in CI-group after CI, positive Qol after CI, improved QoL after remapping, satisfaction of parents with QoL of children with CI, Children with Equal or better scores of children with CI compared to normal-hearing peers (=) No Difference between pre and post CI (evaluation of status pre CI retrospectively post CI), No difference between unilateral and bilateral CI, No change in QoL after use of CI, No difference between unilateral and bilateral CI, No difference between adolescents with CI and normal hearing peers, No difference between CI group and Normal Hearing group, No difference between CI group and norm group of normal hearing peers. (–) Lower Qol of CI users, compared to HA users, Lower QoL of CI users (at least in some domais), compared to normal hearing peers, Lower Qol with growing age, Lower QoL of CI users with developmental delay compared to CI users without delay.

Yellow background: Paper with validated child centered, and age appropriate QoL, instrument (SWB, HRQoL).

Green background: Papers addressing the association between QoL measured with a child-specific self-rating scale and SRiN as examined with audiological speech recognition tests.

Blue background: Papers using self-reports. [1]GCBI. [2]Samples of Loy et al. (2010) and Warner-Czyz et al. (2011) may be partially identical.

MATERIALS AND METHODS

The procedure strictly followed the PRISMA statements. Included were papers addressing SRiN measured with speech recognition tests and QoL, HRQoL, or SWB of children and adolescents with CI, as primary or secondary outcome. HRQoL or SWB was measured with validated child-centered and age-appropriate QoL instruments (see **Supplementary Material** for inclusion criteria). Papers about CI users with single sided deafness were not included. We considered publications until January 2019 (see **Supplementary Material** for the search terms and review procedure). Primary outcomes were the correlation between SRiN performance and QoL of children and adolescents with CI and the improvement of QoL after an improvement of SRiN, respectively. The risk for biases was estimated with a short checklist (orientation to the Cochrane risk of bias tool, Cochrane Deutschland, 2016, see also **Supplementary Material**).

RESULTS

In step 1 of our review, we removed 1851 citations, all papers that were not in English or not original research articles. In step 2 191 citations were removed, which reported studies in adults, very young children, cost utility analyses or represented a double citation. The remaining 32 papers were reviewed. Two papers were removed, because no original data about QoL, HRQoL, or SWB of young CI users were reported, or the data were already reported elsewhere (see the flow diagram in the **Supplementary Material**). Only eleven out of the remaining 30 studies, i.e., one third, used validated child-centered and age appropriate QoL instruments, see **Table 1** and **Supplementary Material**. 19 studies did not use valid pediatric QoL instruments[2]. Additionally, as summarized in **Table 1**, 20 out of 30 studies relied exclusively on parent or teacher reports with a trend toward more positive QoL results, compared to the 10 studies relying additionally on self-reports, see **Table 1**.

In a small retrospective study, Huber (2005) addressed the HRQoL of 18 children with CI (at average 10.7 years old) and 12 adolescents with CI (at average 14.4 years old). There was a moderate correlation between the SRiN performance and the HRQoL total score, but only in the self-rating of the children (Spearman's $r = 0.45$, $p = 0.03$). Noble et al. (2016) performed a cohort study with 18 young CI users at average 10.7 years old. The authors investigated, if significant improvements in speech recognition in quiet and in noise (result of a remapping[3]) after 4 weeks were accompanied by an improvement in HRQoL. As the hearing performance in quiet and in noise of the CI

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[2] Two thirds (19 papers) used adult QoL questionnaires, e.g., Nijmegen Cochlear Implantation Questionnaire, homemade questionnaires (e.g., Chmiel et al., 2000), and other PROMS for children (e.g., Children with cochlear implants parental perspectives), and adults (Speech, Spatial, and Qualities of Hearing Scale), see **Table 1**.

[3] "Mapping (or MAPping) is the term for programming a cochlear implant to the specifications and needs of its use" (http://cochlearimplantonline.com/site/mapping-a-cochlear-implant/).

users improved ($p < 0.05$), the HRQoL total score improved also ($p < 0.05$), but only in the self-rating. Haukedal et al. (2018) retrospectively compared the HRQoL parent rating of 106 CI users (mean age 9.2 years) with 80 normal hearing children and adolescents (mean age 9.3 years). CI group and NH group did not differ significantly in age; however, the IQ was significantly higher in the NH group. The authors found small correlations between scores on SRiN and the HRQoL total score ($r = -0.28$, $p = 0.024$), and the school functioning ($r = -0.244$, $p = 0.048$). However, the correlations did not survive controlling for age.

In summary, all three studies point to SRiN as a possible moderator of HRQoL in children and adolescents with CI. However, the correlations were only low, and none of these studies has examined the possible moderating relationship directly in a longitudinal design. Furthermore, two of the studies were underpowered and the third one had problems with the matching criteria between study and control group (higher IQ). One study was performed without self-reports. In all three studies the risk for biases (orientation to the Cochrane risk of bias tool, Cochrane Deutschland, 2016) was low to medium (compare **Supplementary Material**).

CONCLUSION AND VIEWPOINTS

In a systematic literature research, we identified only three papers indicating positive moderating effects between SRiN and QoL of young CI users. This is astonishing, because numerous studies on adults with CI are dealing with this topic. In a systematic review and meta-analysis McRackan et al. (2018) listed 27 papers informing about 1394 adult CI users and found small, but significant associations ($r = 0.24$–0.26) between SRiN and HRQoL in adults. However, the results about hearing-impaired adults are not valid for hearing-impaired children and adolescents. First, because there is a difference in the onset of hearing loss: Most adults become hearing-impaired in adulthood, whereas most children and adolescents are hearing-impaired since birth. Second, because there is a difference in the living conditions of children and adults. For example, children must attend schools (in noisy schools, see above) whereas adults have more options to influence their environment and work place. Accordingly, there is an urgent need for further studies addressing possible associations between SRiN and QoL of young CI users.

Restricted SRiN may be a burden for the QoL of children and adolescents with CI. Information about this topic may also be relevant for parents, clinicians, and therapists who are usually not aware of a possible load of young CI users. Additionally, these studies are relevant for teachers and for policy makers, who are handling possible additional special needs, for example classes with fewer students or an additional support for trainees with CI in a noisy work place.

One of the reasons for this lack of studies may be a limited awareness of parents and clinicians for possible quality of life problems of hearing impaired children and adolescents with CI. Papers relying exclusively on parent/teacher ratings indicate a tendency toward more positive conclusions than the papers relying additionally on self-reports and may overestimate the QoL in young CI users. However, it remains to be clarified whether parents actually overestimate the QoL of their children with CI [see Huber (2005, 2007) and Loy et al. (2010) on one side and the Haukedal et al. (2018) on the other side]. Parents of non-clinical samples report higher child QoL than the children themselves (Upton et al., 2008).

Given these results, it was striking, that only a minority of studies on QoL in young CI users provided children's self-reports. One problem that may arise with children's self-reports are the language comprehension skills of children with CI. One should concede, that until school age many children with CI have a language delay (Sarant, 2012; Geers et al., 2016; Lund, 2016), but that the majority of older children and adolescents with CI have normal (age appropriate) language skills (Geers et al., 2016). Therefore, following the concepts of QoL (see section "Introduction"), we strongly recommend the inclusion of self-reports for school-aged children with CI. Additionally, speech tests examining lexicon and syntax can help to identify patients with insufficient language comprehension. If needed, written and oral support can be provided during the survey, which does not replace the questionnaire. However, these adaptions are only possible with the permission of the authors of the QoL instrument[4].

Furthermore, it was striking, that the majority of investigators used non-valid instruments for the assessment of pediatric quality of life, which may bias the results. Some authors argued that the use of adult questionnaires or homemade questionnaires was justified for children and adolescents with cochlear implants, because there are no disease (problem) specific QoL instruments[5] available. However, we think, that this no longer applies. The child HEAR-QL (Hearing Environments and Reflection on Quality of Life, 7–12 years, Umansky et al., 2011) and the adolescent HEAR-QL questionnaire, 12–18 years (Rachakonda et al., 2014) are validated problem specific HRQoL instruments. To our best knowledge these instruments are still waiting for a study addressing the HRQoL of young hearing impaired CI users. Using age-appropriate instruments is particularly important when obtaining self-reports.

Final Conclusion

The question whether restricted SRiN impairs QoL of young CI users has been understudied, possibly due to an under-estimation of QoL problems in children and adolescents with CI. In order to adequately assess QoL in young CI-users, both parent- and self-reports need to be considered and valid pediatric QoL

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[4] Support is provided by short standard sentences, which are presented both orally and written. Theses sentences are strictly following a written guideline. Paraphrase the questions of the survey, however, does not replace them. Please note, that permission of the authors of QoL instrument may be needed for this adapted format. In some cases the use of a sign language interpreter may be required.

[5] In contrast to generic instruments.

instruments should be used. Subjective well-being is an important component of QoL and the majority of young CI users are able to provide self-reports.

AUTHOR CONTRIBUTIONS

MH developed the proposal for the review, performed the review together with CH, wrote the draft version of the manuscript, and agreed to be primarily accountable for all aspects of the work. CH reviewed abstracts and articles for this review and adapted the draft version of this manuscript together with MH.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2019.02085/full#supplementary-material

REFERENCES

Almeida, R. P., Matas, C. G., Couto, M. I., and Carvalho, A. C. (2015). Quality of life evaluation in children with cochlear implants. *Codas* 27, 29–36. doi: 10.1590/2317-1782/20152014129

Bakas, T., McLennon, S. M., Carpenter, J. S., Buelow, J. M., Otte, J. L., Hanna, K. M., et al. (2012). Systematic review of health-related quality of life models. *Health Qual. Life Outcomes.* 16:134. doi: 10.1186/1477-7525-10-134

Barkmann, C., Petermann, F., Schlack, R., Bullinger, M., Schulte-Markwort, M., Klasen, F., et al. (2016). Verlauf gesundheitsbezogener lebensqualität. *Kindheit und Entwicklung* 25, 50–59. doi: 10.1026/0942-5403/a000188

Bess, F. H., Gustafson, S. J., Corbett, B. A., Lambert, E. W., Camarata, S. M., and Hornsby, B. W. (2016). Salivary cortisol profiles of children with hearing loss. *Ear Hear.* 37, 334–344. doi: 10.1097/AUD.0000000000000256

Caldwell, A., and Nittrouer, S. (2013). Speech perception in noise by children with cochlear implants. *J. Speech Lang. Hear. Res.* 56, 13–30. doi: 10.1044/1092-4388(2012/11-0338)

Chan, K. M., Li, C. M., Ma, E. P., Yiu, E. M., and McPherson, B. (2015). Noise levels in an urban Asian school environment. *Noise Health* 17, 48–55. doi: 10.4103/1463-1741.149580

Chen, Y., Wong, L. L., Chen, F., and Xi, X. (2014). Tone and sentence perception in young mandarin-speaking children with cochlear implants. *Int. J. Pediatr. Otorhinolaryngol.* 78, 1923–1930. doi: 10.1016/j.ijporl.2014.08.025

Ching, T. Y., Zhang, V. W., Flynn, C., Burns, L., Button, L., Hou, S., et al. (2017). Factors influencing speech perception in noise for 5-year-old children using hearing aids or cochlear implants. *Int. J. Audiol.* 7, 1–11. doi: 10.1080/14992027.2017.1346307

Chmiel, R., Sutton, L., and Jenkins, H. (2000). Quality of life in children with cochlear implants. *Ann. Otol. Rhinol. Laryngol. Suppl.* 185, 103–105.

Clark, J. H., Wang, N. Y., Riley, A. W., Carson, C. M., Meserole, R. L., Lin, F. R., et al. (2012). Timing of cochlear implantation and parents' global ratings of children's health and development. *Otol. Neurotol.* 33, 545–552. doi: 10.1097/MAO.0b013e3182522906

Cochrane Deutschland (2016). *Bewertung Des Biasrisikos (Risiko systematischer Fehler) in Klinischen Studien: Ein Manual Für Die Leitlinienerstellung*, 1st Edn. London: Cochrane Deutschland.

Coghill, D., Danckaerts, M., Sonuga-Barke, E., Sergeant, J., and Adhd European Guidelines Group, (2009). Practitioner review: quality of life in child mental health–conceptual challenges and practical choices. *J. Child Psychol. Psychiatr.* 50, 544–561. doi: 10.1111/j.1469-7610.2009.02008.x

Cupples, L., Ching, T. Y., Button, L., Seeto, M., Zhang, V., Whitfield, J., et al. (2018). Spoken language and everyday functioning in 5-year-old children using hearing aids or cochlear implants. *Int. J. Audiol.* 57, S55–S69. doi: 10.1080/14992027.2017.1370140

Davis, E., Waters, E., Mackinnon, A., Reddihough, D., Graham, H. K., Mehmet-Radji, O., et al. (2006). Paediatric quality of life instruments: a review of the impact of the conceptual framework on outcomes. *Dev. Med. Child Neurol.* 48, 311–318.

Degoy, E., and Berra, S. (2018). Differences in health-related quality of life by academic performance in children of the city of cordoba-argentina. *Qual. Life Res. J.* 27, 1463–1471. doi: 10.1007/s11136-018-1849-49

Dey, M., Mohler-Kuo, M., and Landolt, M. A. (2012). Health-related quality of life among children with mental health problems: a population-based approach. *Health Qual. Life Outcomes* 10:73. doi: 10.1186/1477-7525-10-73

Drotar, D. (2004). Validating measures of pediatric health status, functional status, and health-related quality of life: key methodological challenges and strategies. *Ambul. Pediatr.* 4(Suppl.), 358–364. doi: 10.1367/a03-101r.1

Duarte, I., Santos, C. C., Rego, G., and Nunes, R. (2014). Health-related quality of life in children and adolescents with cochlear implants: self and proxy reports. *Acta Otolaryngol.* 134, 881–889. doi: 10.3109/00016489.2014.930968

Edwards, L., Hill, T., and Mahon, M. (2012). Quality of life in children and adolescents with cochlear implants and additional needs. *Int. J. Pediatr. Otorhinolaryngol.* 76, 851–857. doi: 10.1016/j.ijporl.2012.02.057

Eiser, C., and Varni, J. W. (2013). Health-related quality of life and symptom reporting: similarities and differences between children and their parents. *Eur. J. Pediatr.* 172, 1299–1304. doi: 10.1007/s00431-013-2049-9

Ellert, U., Ravens-Sieberer, U., Erhart, M., and Kurth, B. M. (2011). Determinants of agreement between self-reported and parent-assessed quality of life fo children in Germany-results of the German Health Interview and Examination Survey for Children and Adolescents (KiGGS). *Health Qual. Life Outcomes* 9:102. doi: 10.1186/1477-7525-9-102

Fayed, N., de Camargo, O. K., Kerr, E., Rosenbaum, P., Dubey, A., Bostan, C., et al. (2012). Generic patient-reported outcomes in child health research: a review of conceptual content using World Health Organization definitions. *Dev. Med. Child Neurol.* 54, 1085–1095. doi: 10.1111/j.1469-8749.2012.04393.x

Fortunato-Tavares, T., Befi-Lopes, D., Bento, R. F., and Andrade, C. R. (2012). Children with cochlear implants: communication skills and quality of life. *Braz. J. Otorhinolaryngol.* 78, 15–25. doi: 10.1590/s1808-86942012000100003

Geers, A. E., Nicholas, J., Tobey, E., and Davidson, L. (2016). Persistent language delay versus late language emergence in children with early cochlear implantation. *J. Speech Lang. Hear. Res.* 59, 155–170. doi: 10.1044/2015-JSLHR-H-14-0173

Hashemi, S. B., and Monshizadeh, L. (2011). The quality of life from the point of view of parents in pre-lingual deaf children after 1.5 years of cochlear implantation in shiraz, southern Iran. *Iran. Red Crescent Med. J.* 13, 431–433.

Haukedal, C. L., von Koss Torkildsen, J., Lyxell, B., and Wie, O. B. (2018). Parents' perception of health-related quality of life in children with cochlear implants: the impact of language skills and hearing. *J. Speech Lang. Hear. Res.* 8, 2084–2098. doi: 10.1044/2018-JSLHR-H-17-0278

Health Quality Ontario, (2019). Bilateral cochlear implantation: a health technology assessment. *Ont. Health Technol. Assess. Ser.* 19, 1–139.

Hornsby, B. W. Y., Gustafson, S. J., Lancaster, H., Cho, S. J., Camarata, S., and Bess, F. H. (2017). Subjective fatigue in children with hearing loss assessed using self- and parent-proxy report. *Am. J. Audiol.* 12, 393–407. doi: 10.1044/2017_aja-17-0007

Huber, M. (2005). Health-related quality of life of Austrian children and adolescents with cochlear implants. *Int. J. Pediatr. Otorhinolaryngol.* 69, 1089–1101. doi: 10.1016/j.ijporl.2005.02.018

Huber, M. (2007). Comment on Measuring health-related quality of life after pediatric cochlear implantation: a systematic review by lin and niparko. *Int. J. Pediatr. Otorhinolaryngol.* 70, 1695–1706. doi: 10.1016/j.ijporl.2006.05.009

Huber, M., Burger, T., Illg, A., Kunze, S., Giourgas, A., Braun, L., et al. (2015). Mental health problems in adolescents with cochlear implants: peer problems persist after controlling for additional handicaps. *Front. Psychol.* 6:953. doi: 10.3389/fpsyg.2015.00953

Huttunen, K., Rimmanen, S., Vikman, S., Virokannas, N., Sorri, M., Archbold, S., et al. (2009). Parents' views on the quality of life of their children 2-3 years after cochlear implantation. *Int. J. Pediatr. Otorhinolaryngol.* 73, 1786–1794. doi: 10.1016/j.ijporl.2009.09.038

Jacobs, E., Langereis, M. C., Frijns, J. H., Free, R. H., Goedegebure, A., Smits, C., et al. (2016). Benefits of simultaneous bilateral cochlear implantation on verbal reasoning skills in prelingually deaf children. *Res. Dev. Disabil.* 58, 104–113. doi: 10.1016/j.ridd.2016.08.016

Keilmann, A., and Reutter, C. A. (2014). Nutzung von FM-Anlagen durch hörgeschädigte schülerinnen und schüler an regelschulen in rheinland-pfalz. *Hörgeschädigtenpädagogik* 68, 62–68.

Klatte, M., Bergström, K., and Lachmann, T. (2013). Does noise affect learning? A short review on noise effects on cognitive performance in children. *Front. Psychol.* 30:578. doi: 10.3389/fpsyg.2013.00578

Kumar, R., Warner-Czyz, A., Silver, C. H., Loy, B., and Tobey, E. (2015). American parent perspectives on quality of life in pediatric cochlear implant recipients. *Ear Hear.* 36, 269–278. doi: 10.1097/AUD.0000000000000108

Lee, Y.-C., Yang, H.-J., Lee, W.-T., and Teng, M.-J. (2019). Do parents and children agree on rating a child's HRQOL? A systematic review and metaanalysis of comparisons between children with attention deficit hyperactivity disorder and children with typical development using the PedsQLTM. *Disabil. Rehabil.* 41, 265–275. doi: 10.1080/09638288.2017.1391338

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Joannidis, J. P. A., et al. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *PLoS Med.* 6:e1000100. doi: 10.1371/journal.pmed.1000100

Liu, H., Liu, H. X., Kang, H. Y., Gu, Z., and Hong, S. L. (2016). Evaluation on health-related quality of life in deaf children with cochlear implant in China. *Int. J. Pediatr. Otorhinolaryngol.* 88, 136–141. doi: 10.1016/j.ijporl.2016.06.027

Looi, V., Lee, Z. Z., and Loo, J. H. (2016a). Hearing-related quality of life outcomes for Singaporean children using hearing aids or cochlear implants. *Eur. Ann. Otorhinolaryngol. Head Neck Dis.* 133, S25–S30. doi: 10.1016/j.anorl.2016.01.011

Looi, V., Lee, Z. Z., and Loo, J. H. (2016b). Quality of life outcomes for children with hearing impairment in Singapore. *Int. J. Pediatr. Otorhinolaryngol.* 80, 88–100. doi: 10.1016/j.ijporl.2015.11.011

Lovett, R. E., Kitterick, P. T., Hewitt, C. E., and Summerfield, A. Q. (2010). Bilateral or unilateral cochlear implantation for deaf children: an observational study. *Arch. Dis. Child* 95, 107–112. doi: 10.1136/adc.2009.160325

Loy, B., Warner-Czyz, A. D., Tong, L., Tobey, E. A., and Roland, P. S. (2010). The children speak: an examination of the quality of life of pediatric cochlear implant users. *Otolaryngol. Head Neck Surg.* 142, 247–253. doi: 10.1016/j.otohns.2009.10.045

Lund, E. (2016). vocabulary knowledge of children with cochlear implants: a meta-analysis. *J. Deaf Stud. Deaf Educ.* 21, 107–121. doi: 10.1093/deafed/env060

McGarrigle, R., Gustafson, S. J., Hornsby, B. W. Y., and Bess, F. H. (2019). Behavioral measures of listening effort in school-age children: examining the effects of signal-to-noise ratio, hearing loss, and amplification. *Ear Hear.* 40, 381–392. doi: 10.1097/AUD.0000000000000623

McRackan, T. R., Bauschard, M., Hatch, J. L., Franko-Tobin, E., Droghini, H. R., Nguyen, S. A., et al. (2018). Meta-analysis of quality-of-life improvement after cochlear implantation and associations with speech recognition abilities: QOL improvement after cochlear implantation. *Otol. Neurotol.* 39, 29–36. doi: 10.1097/MAO.0000000000001620

Meserole, R. L., Carson, C. M., Riley, A. W., Wang, N. Y., Quittner, A. L., Eisenberg, L. S., et al. (2014). Assessment of health-related quality of life 6 years after childhood cochlear implantation. *Qual. Life Res.* 23, 719–731. doi: 10.1007/s11136-013-0509-503

Moberly, A. C., Lowenstein, J. H., and Nittrouer, S. (2016). Early bimodal stimulation benefits language acquisition for children with cochlear implants. *Otol. Neurotol.* 37, 24–30. doi: 10.1097/MAO.0000000000000871

Noble, J. H., Hedley-Williams, A. J., Sunderhaus, L., Dawant, B. M., Labadie, R. F., Camarata, S. M., et al. (2016). Initial results with image-guided cochlear implant programming in children. *Otol. Neurotol.* 37, E63–E69. doi: 10.1097/MAO.0000000000000909

Nunes, M. D. R., Jacob, E., Bomfim, E. O., Lopes-Junior, L. C., de Lima, R. A. G., Floria-Santos, M., et al. (2017). Fatigue and health related quality of life in children and adolescents with cancer. *Eur. J. Oncol. Nurs.* 29, 39–46. doi: 10.1016/j.ejon.2017.05.001

Ojelabi, A. O., Graham, Y., Haighton, C., and Ling, J. (2017). A systematic review of the application of wilson and cleary health-related quality of life model in chronic diseases. *Health Qual. Life Outcomes* 11:241. doi: 10.1186/s12955-017-0818-2

Percy-Smith, L., Cayé-Thomasen, P., Gudman, M., Jensen, J. H., and Thomsen, J. (2008). Self-esteem and social well-being of children with cochlear implant compared to normal-hearing children. *Int. J. Pediatr. Otorhinolaryngol.* 72, 1113–1120. doi: 10.1016/j.ijporl.2008.03.028

Quitmann, J., Rohenkohl, A., Sommer, R., Bullinger, M., and Silva, N. (2016). Explaining parent-child (dis)agreement in generic and short stature-specific health related quality of life reports: do family and social relationships matter? *Health Qual. Life Outcomes* 14:150.

Rachakonda, T., Jeffe, D. B., Shin, J. J., Mankarious, L., Fanning, R. J., Lesperance, M. M., et al. (2014). Validity, discriminative ability, and reliability of the hearing-related quality of life questionnaire for adolescents. *Laryngoscope* 124, 570–578. doi: 10.1002/lary.24336

Raj, M., Sudhakar, A., Roy, R., Champaneri, B., Joy, T. M., and Kumar, R. K. (2017). Health-related quality of life in Indian children: a community-based cross-sectional survey. *Indian J. Med. Res.* 145, 521–529. doi: 10.4103/ijmr.IJMR-447-16

Rajmil, L., López, A. R., López-Aguilá, S., and Alonso, J. (2013). Parent–child agreement on health-related quality of life (HRQOL): a longitudinal study. *Health Qual Life Outcomes* 11:101. doi: 10.1186/1477-7525-11-101

Ravens-Sieberer, U., Devine, J., Bevans, K., Riley, A. W., Moon, J., Salsman, J. M., et al. (2014a). Subjective wellbeing measures for children were developed within the PROMIS project: presentation of first results. *J. Clin. Epidemiol.* 67, 207–218. doi: 10.1016/j.jclinepi.2013.08.018

Ravens-Sieberer, U., Karow, A., Barthel, D., and Klasen, F. (2014b). How to assess quality of life in child and adolescent psychiatry. *Dialogues Clin. Neurosci.* 16, 147–158.

Ravens-Sieberer, U., Ottova, V., Hillebrandt, D., Klasen, F., and Hbsc-Team Deutschland, (2012). Health-related quality of life and mental health of children and adolescents in Germany: results from the German HBSC Study 2006-2010. *Gesundheitswesen* 74(Suppl.), 33–41. doi: 10.1055/s-0032-1312641

Razafimahefa-Raoelina, T., Farinetti, A., Nicollas, R., Triglia, J. M., Roman, S., and Anderson, L. (2016). Self- and parental assessment of quality of life in child cochlear implant bearers. *Eur. Ann. Otorhinolaryngol. Head Neck Dis.* 133, 31–35. doi: 10.1016/j.anorl.2015.10.002

Rebok, G., Riley, A., Forrest, C., Starfield, B., Green, B., Robertson, J., et al. (2001). Elementary school-aged children's reports of their health: a cognitive interviewing study. *Qual. Life Res.* 10, 59–70.

Riley, A. W. (2004). Evidence that school-age children can self-report on their health. *Ambul. Pediatr.* 4, 371–376. doi: 10.1367/a03-178r.1

Roman, A. S., Pisoni, D. B., Kronenberger, W. G., and Faulkner, K. F. (2017). Some neurocognitive correlates of noise-vocoded speech perception in children with normal hearing: a replication and extension. *Ear Hear.* 38, 344–356. doi: 10.1097/AUD.0000000000000393

Ruben, R. J. (2018). Language development in the pediatric cochlear implant patient. *Laryngoscope Investig. Otolaryngol.* 3, 209–213. doi: 10.1002/lio2.156

Sach, T. H., and Barton, G. R. (2007). Interpreting parental proxy reports of (health-related) quality of life for children with unilateral cochlear implants. *Int. J. Pediatr. Otorhinolaryngol.* 71, 435–445. doi: 10.1016/j.ijporl.2006.11.011

Samuel, V., Gamble, C., Cullington, H., Bathgate, F., Bennett, E., and Coop, N. (2016). Brief assessment of parental perception (BAPP): development and validation of a new measure for assessing paediatric outcomes after bilateral cochlear implantation. *Int. J. Audiol.* 55, 699–705. doi: 10.1080/14992027.2016.1204669

Sarant, J. (2012). "Cochlear implants in children: a review," in *Hearing Loss*, ed. S. Naz (Rijeka: InTech), 406. Available at: http://www.intechopen.com/books/hearing-loss/cochlear-implants-inchildren-a-review.

Sarantopoulos, G., Lykoudis, S., and Kassomenos, P. (2014). Noise levels in primary schools of medium sized city in Greece. *Sci. Total Environ.* 48, 493–500. doi: 10.1016/j.scitotenv.2013.09.010

Schorr, E. A., Roth, F. P., and Fox, N. A. (2009). Quality of life for children with cochlear implants: perceived benefits and problems and the perception of single words and emotional sounds. *J. Speech Lang. Hear. Res.* 52, 141–152. doi: 10.1044/1092-4388(2008/07-0213)

Silva, N., Crespo, C., Carona, C., Bullinger, M., and Canavarro, M. C. (2015). Why the (dis)agreement? Family context and child–parent perspectives on health-related quality of life and psychological problems in paediatric asthma. *Child Care Health Dev.* 41, 112–121. doi: 10.1111/cch.12147

Sparreboom, M., Snik, A. F., and Mylanus, E. A. (2012). Sequential bilateral cochlear implantation in children: quality of life. *Arch. Otolaryngol. Head Neck Surg.* 138, 134–141. doi: 10.1001/archoto.2011.229

Speaker, R. B., Roberston, J., Simoes-Franklin, C., Glynn, F., Walshe, P., and Viani, L. (2018). Quality of life outcomes in cochlear implantation of children with profound and multiple learning disability. *Cochlear Implants Int.* 19, 162–166. doi: 10.1080/14670100.2018.1434451

Stacey, P. C., Fortnum, H. M., Barton, G. R., and Summerfield, A. Q. (2006). Hearing-impaired children in the United Kingdom, I: auditory performance, communication skills, educational achievements, quality of life, and cochlear implantation. *Ear Hear.* 2, 161–186. doi: 10.1097/01.aud.0000202353.37567.b4

Sullivan, J. R., Osman, H., and Schafer, E. C. (2015). The effect of noise on the relationship between auditory working memory and comprehension in school-age children. *J. Speech Lang. Hear. Res.* 58, 1043–1051. doi: 10.1044/2015_JSLHR-H-14-0204

Taitelbaum-Swead, R., and Fostick, L. (2017). Audio-visual speech perception in noise: implanted children and young adults versus normal hearing peers. *Int. J. Pediatr. Otor.* 92, 146–150. doi: 10.1016/j.ijporl.2016.11.022

Umansky, A. M., Jeffe, D. B., and Lieu, J. E. (2011). The HEAR-QL: quality of life questionnaire for children with hearing loss. *J. Am. Acad. Audiol.* 22, 644–653. doi: 10.3766/jaaa.22.10.3

Upton, P., Lawford, J., and Eiser, C. (2008). Parent-child agreement across child health-related quality of life instruments: a review of the literature. *Qual. Life Res.* 17, 895–913. doi: 10.1007/s11136-008-9350-5

Wallander, J. L., and Koot, H. M. (2016). Quality of life in children: a critical examination of concepts, approaches, issues, and future directions. *Clin. Psychol. Rev.* 45, 131–143. doi: 10.1016/j.cpr.2015.11.007

Warner-Czyz, A., Loy, B., Pourchot, H., White, T., and Cokely, E. (2018). Effect of hearing loss on peer victimization in school-age children. *Except. Child.* 84, 280–297. doi: 10.1177/0014402918754880

Warner-Czyz, A. D., Loy, B., Tobey, E. A., Nakonezny, P., and Roland, P. S. (2011). Health-related quality of life in children and adolescents who use cochlear implants. *Int. J. Pediatr. Otorhinolaryngol.* 75, 95–105. doi: 10.1016/j.ijporl.2010.10.018

Werfel, K. L., and Hendricks, A. E. (2016). The relation between child versus parent report of chronic fatigue and language/literacy skills in school-age children with cochlear implants. *Ear Hear.* 37, 216–224. doi: 10.1097/AUD.0000000000000242

Wilson, I. B., and Cleary, P. D. (1998). Linking clinical variables with health-related quality of life. A conceptual model of patient outcomes. *JAMA* 273, 59–65. doi: 10.1001/jama.273.1.59

World Health Organization [WHO], (1948). *WHO Definition of Health, Preamble to the Constitution of the World Health Organization as Adopted by the International Health Conference*. Geneva: World Health Organization.

World Health Organization [WHO], (1994). *Measurement of Quality of Life in Children. MNH/PSF/94.5*. Geneva: World Health Organization.

Yorgun, M., SürmelioƏlu, Ö, Tuncer, Ü, Tarkan, Ö, Özdemir, S., and Çekiç, E. (2015). Quality of life in pediatric cochlear implantations. *J. Int. Adv. Otol.* 11, 218–221. doi: 10.5152/iao.2015.730

Zaidman-Zait, A., Curle, D., Jamieson, J. R., Chia, R., and Kozak, F. K. (2017). Health-related quality of life among young children with cochlear implants and developmental disabilities. *Ear Hear.* 38, 399–408. doi: 10.1097/AUD.0000000000000410

Zhao, Y., Li, Y., Zheng, Z., Li, J., Nie, X., and Jin, S. (2018). Health-related quality of life in mandarin-speaking children with cochlear implants. *Ear Hear.* 40, 605–614. doi: 10.1097/AUD.0000000000000633

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"*I Must Try Harder*": Design Implications for Mobile Apps and Wearables Contributing to Self-Efficacy of Patients With Chronic Conditions

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Background: Diverse wellness-promoting mobile health technologies, including mobile apps and wearable trackers, became increasingly popular due to their ability to support patients' self-management of health conditions. However, the patient's acceptance and use depend on the perceived experience and the app appropriateness to the patient's context and needs. We have some understating of the experience and factors influencing the use of these technologies in the general public, but we have a limited understanding of these issues in patients.

Objective: By presenting results from an explorative study, this paper aims to identify implications for the design of mobile apps and wearables to effectively support patients' efforts in self-management of health with a special emphasis on support for self-efficacy of activities contributing to health.

Methods: An explorative mixed-method study involving 200 chronically ill patients of Stanford Medical Center (Stanford, CA, United States) was conducted between mid-2016 and end of 2018. Amongst these, 20 patients were involved in a 4-weeks study, in which we collected the underlying wearable device use logs (e.g., Fitbit) and subjective use experience [via an Ecological Momentary Assessment (EMA)], as well as patients' momentary perception of general self-efficacy in their natural environments and different daily contexts.

Results: The results indicate that mobile apps for health and wearables have the potential to enable better self-management and improve patients' wellbeing but must be further refined to address different human aspects of their use. Specifically, the apps/wearables should be easier to use, more personalized and context-aware for the patient's overall routine and lifestyle choices, as well as with respect to the momentary patient state (e.g., location, type of people around) and health(care) needs. Additionally, apps and devices should be more battery efficient and accurate; providing timely, non-judgmental feedback and personalized advice to the patients anywhere-anytime-anyhow. These results are mapped on major sources of the individuals' self-efficacy.

Conclusion: Our results show how the apps/wearables that are aimed at supporting the patients' self-management should be designed to leverage and further improve the patients' general self-efficacy and self-efficacy of activities contributing to chronic disease management.

Keywords: self-efficacy, digital health, mhealth, self-management, technology acceptance, behavior assessment, health apps, user experience

INTRODUCTION

Smartphone and wearable usage is growing rapidly. Currently, more than 2.5 billion people use smartphones with this number projected to reach 5 billion in 2025 (GSM Association, 2018). Along the same trend we observe almost an exponential increase in the number of individuals diagnosed with chronic diseases like diabetes, cardiovascular disease or chronic obstructive pulmonary disease (Antó et al., 2001; Zheng et al., 2017; Piché et al., 2018). The proposed Chronic Care Model aims at better management of these individuals and includes recommendations for all different components of care, including the implementation of the health system itself, the design and delivery of decision support systems, the design of clinical information systems, the support for patient self-management, community resources and their delivery system design (Wagner et al., 2001). Smartphone and wearable devices have the potential to influence all aspects of this model, especially patient self-management support and community resources. Specifically, smartphones and wearable devices enable more convenient delivery of services for patients' education, coaching, self-monitoring, personal goal-setting and social support.

Self-management of health implies management of activities contributing to health including physical activity, nutrition, stress, sleep, medication intake, and management of symptoms (Morgan et al., 2017; Powers et al., 2017). Self-management for chronically ill patients is highly suggested and even required, especially for patients who see their specialist occasionally and need to manage their condition daily (Wagner et al., 2001). Self-management has been shown to play a role in the reduction of disease exacerbations in chronically sick patients and improve adherence to rehabilitation (Bodenheimer, 2002; Gallagher et al., 2008; Duscha et al., 2018). This is achieved by continuous and unobtrusive monitoring of the patient's health state while enabling the patient to follow an almost-normal daily life routine.

Self-efficacy is the self-belief that an individual can manage his/her daily life and put in effort to get the desired behavioral and health outcomes (Bandura, 1977). General self-efficacy entails general attitudes and self-beliefs to cope with a variety of difficult demands in life. Self-efficacy of health is a complex psychological concept that varies over time for the same person, according to their current health state and treatment plan. It is highly correlated with the patient's self-management efforts and hence their health outcomes (Strecher et al., 1986; Sarkar et al., 2006; Ross and Mirowsky, 2010; Bethancourt et al., 2014). There is a large role of self-efficacy of activities contributing to the long term health state of patients (Lenferink et al., 2017; Cameron et al., 2018).

Self-efficacy has been shown to improve self-management, in direct and indirect ways. A cohort study focused on a chronic disease self-management program found that after 7 weeks of a self-management program with an emphasis on self-efficacy (including problem solving, decision making and confidence building skills), participants made statistically significant improvements in their health status, self-efficacy and health behaviors and had fewer emergency department visits (Lorig et al., 2001). This study illustrates that programs that have a self-efficacy focus can help patients improve their self-management. Self-efficacy can also improve self-management in a more indirect manner. Self-efficacy can lead to an in increase in self-belief that can spillover across other domains of life, contributing to health indirectly, e.g., having better communication and better quality of social interactions (Lauren et al., 2016). It has been shown that patients with greater quality of social interactions are more successful at self-management (Reeves et al., 2014). Additionally self-efficacy can allow individuals to build on successes, tackling easier behaviors successful and spilling over in attempting more challenging behaviors (Lauren et al., 2016). Although self-efficacy has been shown to improve self-management, the rudimentary patient education provided by the current health system is not sufficient to leverage and improve this self-efficacy, hence so many patients relapse over time (Lorig et al., 2001).

The wide use of smartphones and wearables may provide a method for increasing self-efficacy and self-management in patients with chronic conditions, although there is limited research on its efficacy (McCabe et al., 2017). However, we still know little on the role of this technology on patients' self-efficacy of health-related activities and on if/how chronically ill patients use and experience the widely available smartphones/wearables (Wang et al., 2014; Hamine et al., 2015; McCabe et al., 2017). It has even been claimed that current so-called "gadgets" are ignoring large groups of people including physically impaired elderly and chronically ill individuals, the ones who may need the most support (Herz, 2014).

This study presents results from an explorative mixed-method study of 200 chronically ill patients at the Stanford Medical Center (Stanford, CA, United States). Amongst these, 20 patients were involved in a 4-weeks study, in which we collected the underlying wearable device use logs and subjective experience of use, as well as patients' momentary perception of general self-efficacy in their natural environments and different daily contexts. This study is different from previous research in that it correlates *in situ* experiences with technology captured and self-reported self-management efforts, as well as and momentary self-efficacy assessments.

In Ickin et al. (2012), the authors presented factors influencing quality of experience of mobile applications in general public. The study presented in here is largely inspired by this past study (Ickin et al., 2012) and draws comparisons between its findings, but expands toward wearables in users with chronic conditions. The overlapping analyzed factors influencing the user's experience with the mobile applications include: "application interface's design," "application performance," "battery," "phone features," "apps and data connectivity cost," "user's routine," and "user's lifestyle"(Ickin et al., 2012). The study presented in here is bringing these results forward by showing if/how chronically ill patients use and experience the widely available smartphones apps and wearables, and what is the role of technologies in patients' self-management of health, and specifically their self-efficacy of health-related activities.

METHODOLOGICAL APPROACH

Methods

Our research was purely explorative and we use a mixed-methods approach incorporating both qualitative and quantitative methods, and involving patients at different stages, via the following: (i) entry survey/open-ended interview (ii) The Ecological Momentary Assessment (EMA), (iii) The Day Reconstruction Method (DRM), and (iv) The mQoL-Log. (i) The entry survey/open-ended interview on the Stanford-based Website (RedCap), was used to collect the patients' health state and socio-demographics, current self-management behaviors, general self-efficacy and health status, and overall attitudes toward and experiences with mobile apps/wearable (if any) for self-management (**Supplementary Material**). (ii) The Ecological Momentary Assessment (EMA) also referred to as Experience Sampling Method (ESM) (Hektner et al., 2007) was used to gather general self-efficacy (SE) perception (Lorig et al., 2009). It was gathered daily along one randomly selected question from 10 questions (**Appendix 1**) like "*Today, I can manage to solve difficult problems if I try hard enough*"(answer choices ranging from 1 "Not at all true" to 4 "Exactly true") and was asked on smartphone screen at a random time in predefined waking hours of the morning. We designed the EMA questions such that each SE question was asked to each participant in a uniform distribution, i.e., three times along the whole study duration. Additionally, we deployed EMA to evaluate the momentary user's experience (QoE) with a wearable/mobile app, with questions along the Mean Opinion Score (MOS) (International Telecommunication Union, 2015) for ICT-services ("*How would you rate the experience for the application*," with answers ranging from 1 "the worst" to 5 "excellent"). They were asked during the waking hours of a day randomly after closing the fitness app (e.g., Fitbit) on the phone, i.e., the user was not able to predict when, along the app usage, the QoE question will be triggered to him/her. Each rating is purely a subjective, episodic assessment of the event provided on the basis of the given perception of the user in a given context. The EMA method contributes to capturing the momentary "ground truth" SE and user's QoE data in the studies. (iii) The Day Reconstruction Method (DRM) (Kahneman et al., 2004) is a semi-structured interview, which enabled participants to reflect on their recent past user's experiences and attitudes, from the past 24 hours. It puts the EMAs into context and enables us to identify the factors influencing the particular user, which may not be captured automatically. The DRM method contributes to capturing a day-level "ground truth" data in the studies. (iv) The mQoL-Log is a measurements-based Android OS smartphone logger that has been developed and validated in our lab (Manea and Wac, 2018) enabling automatic, continuous and unobtrusive gathering of the smartphone usage data (on, off, apps used, charging, WiFi/Cell ID connectivity), and details about the user's context (physical activity e.g., walking while using phone, location derived from WiFi/Cell ID).

The interviews, surveys and DRMs data were analyzed by grouping words into clusters via an affinity clustering method. The coding and grouping of words into clusters was done by two independent coders. Inter-rater agreement was derived via a joint probability of agreement, i.e., the percentage of the time the raters agree in coding. We then derived statistics of the user's interaction with the mobile app/wearable based on the mQoL-log datasets.

Study Participants

We recruited 200 participants from Stanford Medical Center (Stanford, CA, United States), within the Bariatric and Metabolic Interdisciplinary Clinic or the Multi-Organ Transplantation Clinic. The Institutional Review Board of Stanford University has approved the study (IRB #29414 and #28265). All participants were informed about the goals of the study, the procedure, the data collected, stored and processed for the purpose of research, the risks and benefits of participation, and that they can withdraw from the studies and request his/her data deletion at any point in time, without any negative consequences. Each participant signed the consent form providing the above information in detail. At recruitment, all participants were assigned an anonymous identification code, which was used throughout the study. The collection of personal information (e.g., name, email addresses) was kept to a minimum. Participants were included in the study if they were cognitively intact (assessed through their understanding of the study and consent form) English-speaking adults who used Android OS smartphones daily. Many study participants ($n = 180$) only completed the open-ended interview at the beginning of the study, where they went into length about why/why not they use mobile apps/wearables for self-management. Amongst the 200 participants, the first $n = 20$ participants who had a wearable (e.g., FitBit) or a mobile application that the used for their own health self-management, committed to the 4 weeks or more ($M = 35 \pm 5$ days) data collection part of the study where they answered the EMAs and completed the DRMs and had the mQoL-Log installed on their phones. The convenient sample of $n = 20$ participants was recruited by the team as a follow up and along the 4 weeks of data collection and interviews. Participants' characteristics are shown in **Table 1**. None of the participants had accessibility problems related to their phone use and, when asked, none of them admitted that they are adversely affected by the beliefs regarding Electromagnetic Fields (EMF) health issues for mobile phone usage.

RESULTS

In the following sections we present the results acquired along our study for all participants (*n* = 200), ranging from non-user or limited use and factors influencing that (section "Smartphone, Mobile Apps, and Wearables Non-Use"), to factors influencing the user's experience (section "Use and Experience of Mobile Apps and Wearables by Patients"), to a specific focus on self-efficacy construct and our analysis how does it influence the use of technologies by patients (section "Self-Efficacy").

Smartphone, Mobile Apps, and Wearable Non-use

Some participants (*n* = 10) do not use technologies for self-management of health and admit it, ranging from asking for advice on how it can be used (e.g., they never heard of Fitbit) to denial of its use for their own health. An older male participant, visibly angry to be asked that question, pointed out "I don't mix my smartphone with my health," another female patient said "I do not want a phone reminds me about my disease" and yet another one "I have got a [Fitbit as a] gift and I dropped it." Further, another one visibly amused by question said that "It's all in here" [indicating his/her own head].

Some patients (*n* = 18) may have tried or have some experience with technologies contributing to own self-management, but did not use it regularly at the time our study was conducted and did not have any plans to use it in the near future. The input for these participants we got is that "Privacy is an issue," "It's complicated," "I do not know how to use it," and "I am not a techie." These types of statements apply equally to older male and female patients.

Use and Experience of Mobile Apps and Wearables by Patients

The Mobile Apps and Wearables Being Used

The rest of the participants (*n* = 172) were actively using smartphone apps or wearables for their own use. Most frequently used mobile applications were dieting applications like MyFitnessPal or calorieCounter, or exercise ones (RunKeeper, Endomondo) or the built-in Apple "Health." As the study took place at Stanford, many of the participants (*n* = 48) mentioned Stanford Health Care "My Health" App, enabling them access to their own Stanford Health records. Additionally, they mentioned the importance of Google Search, WebMD, Facebook (for keeping in touch with loved ones), games, notes (to register symptoms), medication reminder apps, calendar, or a bible app (for mental health). **Figure 1** visualizes in a word-cloud the names of health applications mentioned or used by study participants. The word-cloud visualizes the app frequency as a weighted list, as the font sizes are set in relation to the frequency of the corresponding app name.

Many participants (*n* = 27) mentioned that they use the built-in activity tracker apps (Apple Health and Google Fit) and treat their smartphone as a "wearable," even if they are aware of potential inaccuracies as they sometimes forget to take along their phones. The external wearable devices were used include Fitbit, Apple Watch, iFit, JawboneUP, Garmin, Samsung Gear, Nike+. **Figure 2** visualizes in a word-cloud the names of wearables mentioned or used by study participants. From the interviews we also understood that some (especially male) participants stopped using wearables like Garmin/Polar and started to use smartphone built-in activity tracker. Female participants enjoyed the playful jewelry-like design aspects of a wearable and in many cases had other band colors besides the default black for their Fitbit bands.

With respect to how much the wearables and apps were actually used, the results are as follows. From the 4 weeks study we saw that the participants who participated with their own wearable, were not frequently checking the mobile apps to see the results of their steps or calories. This was mostly because either the participants relied on notifications provided by the phone (e.g., for achieved goal of reaching predefined steps by predefined lunch time) or because these wearables have their own screen, where they can see the numbers (e.g., steps) without going into the phone app. In fact, based on datasets collected via mQoL-log we derived that the participants were interacting with a wearable (and specifically with a mobile app associated with a wearable) or a mobile app (like MyFitnessPal) on average less than 5 min a day. When asked for the context of the wearable/apps usage along the DRM, they declared that they usually use these apps when alone or as a distraction when surrounded by others (co-workers, strangers), who are not paying attention to the participant checking his/her phone. None of the participants declared their wearable/app usage and content (e.g., steps in a given day) to be a topic of the social interaction.

Factors Influencing Experience of Mobile Apps and Wearables by Patients

Overall, the experience of using smartphone, apps and wearables was reported as a positive one, as even one of the patients admitted – smartphone apps "Keep me sane" (S5). Along this line, there are multitude of factors influencing the nuances of the user's experience with mobile apps and wearables. We have used 100+ expressions from our 20 patient's weekly DRM interviews, additional 180 patients' interviews in the clinic. **Figure 3** represents all the expressions used by study participants. We have grouped these words into clusters by using affinity clustering method, which we then labeled along the identified factor. The coding and grouping of words into clusters have been done by two independent coders, and their measure of agreement was 87%. The most disagreements were related to person's routines and lifestyle choices, because sometimes it was about framing of e.g., notifications (interface design) or charging patterns (the battery aspect) fitting into the lifestyle choices and user routines.

TABLE 1 | Characteristics of the 20 participants collecting data for at least 4 weeks.

ID	Age range	Gender: M/F	Profession	Mobile provider	QoE at the entry survey	Days participated (*M*: 35 ± 5)	Total no of QoE answers in study	Most frequent QoE-along the study (1–5)	No. of low QoE (MOS = 1,2)	Wearable (W) or mobile health app (A)	Total no. of SE answers in study	SE (*M* ± SD) (1–5)*
S1	36–45	M	Senior engineer	T-Mobile	3	38	46	4 (48%)	8	W: FitBit	20	3.75 ± 2.06
S2	36–45	F	Librarian	T-Mobile	4	26	63	4 (73%)	6	A: MyFitnessPal	17	3.47 ± 1.23
S3	45–55	M	Administrator	Verizon	5	18	63	5 (40%)	7	A: SleepLike Android	6	3.03 ± 1.16
S4	36–45	F	Administrator/clerical	Verizon	4	38	128	5 (88%)	2	W: FitBit	38	3.73 ± 0.86
S5	55–65	F	Professional caregiver	Verizon	5	41	88	4 (61%)	0	A: WebMD	29	3.96 ± 0.90
S6	25–35	M	Designer	AT&T	4	41	95	4 (71%)	0	W: FitBit	36	3.89 ± 1.02
S7	25–35	F	Artist	AT&T	4	15	74	5 (53%)	0	W: Garmin	15	3.80 ± 1.52
S8	18–24	F	Entrepreneur	AT&T	4	44	78	5 (67%)	10	W: Nike+	36	4.00 ± 0.30
S9	36–45	F	Senior manager	Sprint	4	35	120	4 (68%)	2	A: MyFitnessPal	34	2.8 ± 2.88
S10	36–45	M	Mental health counselor	Verizon	5	31	83	3 (41%)	6	W: FitBit	27	3.94 ± 1.12
S11	25–35	M	Office worker	AT&T	4	31	89	4 (67%)	8	W: FitBit	29	3.34 ± 3.27
S12	36–45	F	Nurse	T-Mobile	5	43	33	4 (89%)	0	W: FitBit	2	3.00 ± 3.42
S13	18–24	F	Student	Verizon	4	35	77	4 (87%)	5	A: MyFitnessPal	31	3.61 ± 0.98
S14	45–55	F	Office worker	T-Mobile	5	40	89	5 (58%)	0	W: iFit	26	3.12 ± 3.74
S15	18–24	F	Clerical	T-Mobile	5	33	40	5 (63%)	2	A: MyFitnessPal	30	3.53 ± 2.39
S16	18–24	F	Student	AT&T	4	41	119	5 (74%)	3	W: Nike+	29	2.62 ± 1.72
S17	45–55	M	Professional caregiver	T-Mobile	3	55	155	3 (48%)	12	W: FitBit	101	4.0 ± 1.28
S18	25–35	M	Office worker	AT&T	5	28	99	5 (67%)	1	W: Samsung Gear	21	3.81 ± 1.23
S19	45–55	F	Office worker	Verizon	4	31	117	4 (55%)	4	A: MyFitnessPal	29	2.69 ± 0.66
S20	18–24	F	Clerical	AT&T	4	37	128	5 (70%)	1	W: FitBit	34	2.29 ± 1.61

**SE is considered "very high" if its above 3 (green), "high" for 2.5–3 (yellow), "low" for 2–2.5 (orange), and "very low" for below 2 (red).*

FIGURE 1 | Mobile health applications used by study participants.

We have distinguished the following factors influencing the user's experience and discuss them in light of previous research on factors influencing the experience of commonly used mobile applications as identified in a 2012 study (Ickin et al., 2012). We first discuss the seven factors from the previous research by comparing them with previous results and expanding them toward wearables, and then add three new factors identified explicitly by this research.

Application and wearable interface's design and notifications

In Ickin et al. (2012), it was pointed out that users struggled with the key positioning, web-page scrolling, and screen resizing. Additionally, users found web versions of the applications at times easier to use than mobile versions of the applications (Ickin et al., 2012).

The issue of preferring an input of long text or manual data on laptop (larger screen) is still present. Overall, the application interface in terms of application/wearable interaction was mentioned very often, yet not in negative terms of bad interface design, but in positive terms of application/wearables notifications keeping the user informed and content. Notifications provided by applications where discussed much more often than the application interface itself. Wearables' notifications are there to fit in the routine and unobtrusively support the user's goal matching along a day. For non-routine days, e.g., with less physical activity – the lack of notifications from wearable will be the first indicator of "bad" day in terms of matching the user's goal: "If I do not get notifications along my afternoon, I know I am in trouble" (S12). Additionally, notifications had to be found to be informative. Notifications that did not serve any purpose resulted in participants abandoning the device (e.g., Fitbit) or turning off the notifications completely from these specific applications. An example of a helpful notification was, e.g., "Each 1000 steps I get reminded to drink water" (S10).

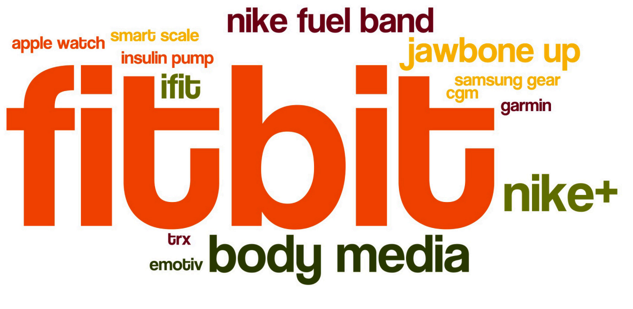


FIGURE 2 | Wearables used by study participants.

Application and wearable performance

In Ickin et al. (2012), it was pointed out that applications did not always meet user's expectations due to typing difficulties, application settings, and network connectivity issues.

In our study, some individuals complained about applications not providing expected services or about the poor performance of their underlying network that influenced the provision of these services. A participant said, the "Internet can be touchy" (S7), to express their concern with the underlying network connectivity. Additionally, the participants complained about the lack or erroneous apps sync, low accuracy of Chinese input recognition, or inaccurate GPS. The lack of constant reliability can be a source of irritation: "When and app doesn't work as it should, my blood pressure skyrockets with the frustration" (S5). Ultimately, participants expressed that if an application is constantly malfunctioning or not refreshing content, they will stop using the application all together.

Smartphone and wearable battery

In Ickin et al. (2012), it was pointed out that battery limited usage, especially later in the day.

Battery efficiency is consistently influencing the experience of the mobile users on a growing scale. Users are using more and more applications and services while continuing to expect that their phone will support them throughout the whole day. One participant was travelling and used an additional battery to support their needs. Overall, users recognized that the battery capacity issue related to usage, e.g., navigation, with screen on, GPS and continuous data and Bluetooth devices' connectivity. Similarly, users also expected wearable charge to last at least the whole day, "if it didn't last the full day (8 hours), then I walked for free" (S3). Additionally, a participant even mentioned that the battery time influenced her activity, "I don't walk when [my wearable] is charging" (S2). Overall, participants mentioned

FIGURE 3 | Expressions in user's interviews and surveys.

having a significantly worse experience if their device did not support their full day of use.

Smartphone and wearable features

In Ickin et al. (2012), it was pointed out that users lacked features deemed necessary including flash player, personalized alarm clock, GPS, and privacy settings.

Mobile users noted missing features of their specific phone, which then hindered their experience, e.g., lack of or a faulty synchronization between Bluetooth devices, and lack of GPS for some older phones, lack of features for privacy settings. Additionally, participants expressed their desire for additionally features including devices that allow for greater personalization of behaviors, automatic nutrition calculations, data fusion between multiple sources (physical activity, nutrition, sleep, medications), a wearable that is waterproof, a wearable that has an ability to assess the swelling of a leg and help to self-manage the CVD patient's fluid retention. Moreover, participants mentioned that a symptoms manager application that derived automatic checklists from notes would be a more effective way of tracking symptoms than through traditional note-taking applications. Nobody mentioned explicitly EMF issues yet two were worrying of too much synchronization, which cannot be disabled (Fitbit).

Apps and data connectivity cost

In Ickin et al. (2012), it was pointed out that cost of applications and data prevented user usage.

Very few participants ($n = 15$) indicated cost as a factor influencing their experience, as they mentioned their inability to purchase a smartphone or mentioned their inability to buy a wearable ($n = 5$). Only one of the participants who owned a wearable mentioned price as a factor influencing their expectations and experience: "it's expensive, it shall work" (S7). Contrastingly, the fact that build-in apps and services are cheap and accessible was emphasized. Very few of the participants followed up with a reflection that given the affordability of the apps and services, the leak of personal data is the price to pay for having the affordable service and that the personal data privacy is definitely an issue (as mentioned earlier).

User's routine

In Ickin et al. (2012), it was pointed out that different applications were used depending time of day and location, implying different mobile user need for services.

The routine of the user implied specific activities being done on weekdays and weekends and specific outcome for physical activity goal achieved at given times of the day. The users' were most critical for their experience of smartphone/mobile apps for their non-routine days, where their decisions relied on information provided by the phone e.g., up to date location, and maps. Mobile devices play a crucial role in the organization of daily activities: "smartphone is my assistant" (S5). Mobile devices reminded users to take their medications, drink water and conduct many other important daily activities (i.e., work-related emails and calls). Mobile devices also allowed users to plan their day by looking at traffic, prices of petrol, designated routes, weather and downloading podcasts ahead of time to listen on the commute. Additionally, some participants indicated that technology helps them set up their routine, while other indicated that they wish that technology could support them in creating a better routine (i.e., better sleep choices). Contrastingly, some users did not use their devices daily. For example, a participant only used their wearable for sport activities, leaving it behind the rest of the day. Another participant only used their smartphone while traveling, leaving it behind when at home or at the office.

User's lifestyle and identity

In Ickin et al. (2012), it was pointed out that users used specific applications that supported their lifestyle choices (i.e., nutrition, exercise) and that were found to be convenient.

Mobile devices and wearables form an important part of users' lives. Applications are there to support healthy (ex. physical activity) or unhealthy (ex. being "lazy" and watching videos on the phone). They can also be modified to fit a user's routine: a clip being put in a pocket, clip (on bra) for users working (ex. in a production line) where they are not allowed to have anything on a wrist; watch for people who are active and wish to get updates on their steps throughout the day (especially female). Besides design modifications for routine, there is also esthetic modifications. Participants mentioned the need for "showing off" to others (via colorful choice of Fitbit bracelet, females mostly, e.g., S4) or hiding from others that a wearable is used (mostly male users). Lifestyle choices are also related to listening to educational/informative podcasts of audiobooks via a smartphone while commuting and having an adequate support for that. Without smartphones, many participants reported feeling "naked" or when a wearable is lost a patient expressed that she "lost her life" (S12).

Smartphone apps and wearable accuracy

This factor was not mentioned in the 2012 paper (Ickin et al., 2012) and constitutes new finding. The accuracy or even a perception of inaccuracy of wearables consistently influences the experience of some of its users. The fact that devices are inaccurate (e.g., Fitbit for assessment of biking) and provide erroneous data (e.g., device registers steps, while the user is driving on a bumpy road) has been noticed by many participants. On the one hand, the users are fully aware that these are not medical accurate devices and they would not expect the medical practitioner to trust only the data acquired to make a clinical decision. Some participant expressed clearly that the device is "accurate enough to recognize my efforts [in exercising more]." On the other hand, the users do not accept the numbers without a critical perspective, and they notice the errors in data. Some participants dropped the wearable use because it was too unreliable for them, e.g., when it consistently did not account for their biking, the user dropped it. One female patient pointed out that her Fitbit experience was fine for few days until she discovered its inaccuracy by comparing it to another wearable: "I have compared [Fitbit] to my husband's Garmin and I was disappointed" [and have stopped using it after a total week of use]. For some interviewed participants who did not own any wearables, the doubt in accuracy of the device became an "excuse" for not using at all.

Willingness to share data with others

This factor has not been mentioned in 2012 paper (Ickin et al., 2012) and constitutes new finding. The study participants were also asked if they are sharing or not their wellness/fitness tracking data from apps and wearables with others and why (or why not). Overall, most of the patients rather not share the data, as they expressed the fact that they are not expecting to compete with others. They fear that sharing this information with friends or family could instead of making the patient feeling better – makes him/her feel worse and inadequate about their progress. One participant pointed out that she feels "enough people are judging offline" (S4); meaning that she is experiencing enough judgment about her condition (obesity) in her daily life and she prefers not be judged online as well. She uses her Fitbit by herself and for herself only.

If the user mentions that he/she shares data with others, they are usually family members, same age and potentially aiming for the same goals (e.g., nutrition or physical activity). The persons with whom the data is shared are there to support the participants' self-management efforts; while the participant supports their efforts. An example is a participant (also a diabetes patient) who shares Fitbit data via setting up competitions with his younger niece living in other state across the country and suffering from bipolar disorder. He pointed out that he knows that physical activity is recommended in her state and he is supporting her from far away.

When commenting on wherever they would share the data with their medical team, they, on the one hand, again point to accuracy, "doctor wont' trust the data." On the other hand, some participants commented that they had not received negative feedback from their medical teams (nurses and clinicians), in contrary, the inputs were positive like "whatever it takes to get you more healthy " or "whatever contributing to your health is good." The participants would be generally accepting to share the data with their doctors.

Self-Efficacy

This factor has not been mentioned in 2012 paper (Ickin et al., 2012) and constitutes new finding, and since is related to the core aim of this paper is presented in a separate section and in great detail. Self-efficacy was a frequent theme of conversation with the participants; discussing their belief that they can manage their own physical activities, nutrition, sleep, medication adherence and other activities contributing to their health self-management with (or without) help of the mobile apps and wearables. There are four main sources of self-efficacy: (i) own past experiences, (ii) experiences of people similar to ourselves, (iii) verbal encouragement from others, and (iv) intrinsic state (Bandura, 1977, 1997). We analyzed the participant data for these factors and present the design implications for mobile apps and wearables contributing or hindering self-efficacy.

Past Experiences

Wearables and mobile device applications are designed to allow users to easily visualize trends. It allows users to see their previous successes as well as previous failures. Although wearables and apps enable users to see the trends, the target levels are predefined. For example, the target step levels are usually at 10,000 steps and some participants admitted that even though that set target was too high for them and they had never been able to achieve this predefined goal, they were not "tech savvy" enough to know how to change the goal. The self-defined targets do not encourage subsequent increases in effort. It was suggested by Kate Lorig verbally that wearable or apps should first monitor the user (based on passive monitoring) and then suggest a feasible goal. This more flexible goal setting, based on user goals, past experiences, trends should allow any user, regardless of their technical skills to benefit, adjust and feel good about achieving their goals.

People Similar to Ourselves

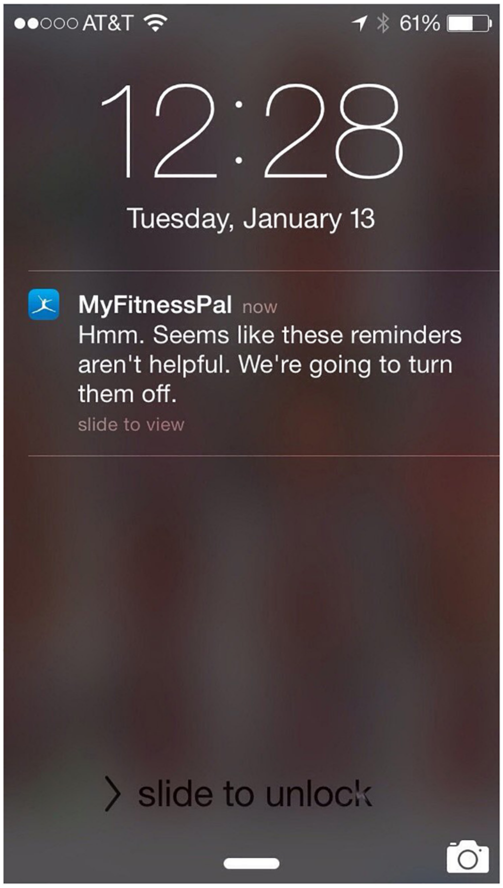
Social networks should theoretically allow and facilitate users to find people living a similar lifestyle and undergoing similar challenges. Although that can be true in some cases, social networks self-representation are not always accurate (Mallan, 2009). Therefore, it can be hard to find people going through similar challenges, not because people are not going through these challenges but because many people may not be posting about it. Weakness, vulnerability, real daily challenges is not the content people want others to see. Additionally, it is not content that people are willing to share due to fear: "enough people judging me offline" (S4). This can make it hard to find other individuals with similar chronic conditions, going through similar daily challenges. Social networks do not always promote self-efficacy, if you feel that everyone is doing better than you and having an easier time with the challenges or if you don't identify with your social group. The design implication is to enable users to connect with others of the same/similar characteristics. Observing others achieving specific goals that we may identify ourselves with, may increase self-efficacy of the individual users.

Verbal Encouragement From Others

There are many applications and wearables that send motivational notifications to users after achieving a certain goal or to remind the user to continue tracking (i.e., track the next meal). These notifications provide users with a reminder to and sometime encouragement to continue their hard work in achieving their goal. Although a lot of these notifications can be helpful, one participant pointed out that the MyFitnessPal coaching feature is "giving up on her" (S9) when she has not logged for few days. That was discouraging and she pointed out that it could be redesigned better – the device should not give up on an individual ever, as it really feels judgmental and discourages the person from progress (**Figure 4**). Now it's kind of supporting the patients' relapse and that's "sad" as the patient said, "The app shall be last one to give up on the patient" (S9).

Individual's Intrinsic State

Current evidence in behavioral medicine and health psychology shows that habits are hard to change (Ouellette and Wood, 1998). It can be hard to start a change and keep it going. Additionally, it can be hard to fail at a new habit and have the courage to restart from the beginning. Wearables and mobile devices allow users to start a goal again and again. It allows the user to suggest their own self-belief in efforts to be put into self-management. For example, a participant said that this feature allowed them to "Know that if I failed yesterday to meet physical activity goal, I can start again tomorrow" (S18). Another participant further echoed this, "I can do 5000 [steps] in a good day. If I do not, I can try again tomorrow." This shows that the ability to keep trying allows people to set up the intrinsic motivation to try again tomorrow. Additionally, some participants admitted that the wearable or application was not at fault for their inability to consistently reach a goal: "I Must try harder[. . .] Device is not faulty of my behavior" (referring to weight gain) (S1).



12:28

Tuesday, January 13

MyFitnessPal now

Hmm. Seems like these reminders aren't helpful. We're going to turn them off.

slide to view

slide to unlock

FIGURE 4 | MyFitnessPal coaching feature turning off after not logging in for a few days.

Additionally, participants reported that their emotional state influenced their daily interactions with the apps/wearables. For example, a participant (S20) discussed that they received the device as a gift. Since it was a gift and something, they did not intend to purchase they do not use it as often. The importance of emotional state was also discussed in terms of daily interactions, participants expressed that they had momentary expression that a wearable is a "friend" or "enemy" depending on if they had met the goal (and felt good) or not (and felt bad).

LIMITATIONS

Limitations of this study include the fact our sample was a convenience sample, included only self-selected participants, limited time and we did not log the content on the health app or wearable used. In terms of the convenience sample, the researchers were only available to talk to participants at certain times of the day, this may have influenced the recruited participants. Participants were self-selected to participate in this study, and this could have influenced the study pool for people with a particular positive or negative view on wearables and applications. We are not able to quantify this bias. Additionally, due to the structure of the clinic, sometimes time was more limited with specific participants. Moreover, participants perceived the EMAs for self-efficacy differently. Some perceived them as encouraging, while some thought these were annoying, as they were tired in the morning and were not in a mood for challenging questions.

CONCLUSION AND AREAS OF FUTURE WORK

Our study illustrates that applications and wearables that are aimed at supporting the users' self-management should leverage and further improve the patients' self-efficacy of activities contributing to self-management of chronic disease. The results indicate that mobile apps for health/wearables have potential to enable better self-management and lead improved wellbeing but must be further refined to address different human aspects of their use. Specifically, the apps/wearables should be easier to use, more personalized and context-aware for the patient's overall routine and lifestyle choices, as well as with respect to the momentary patient state (e.g., internal feeling of self-efficacy – achieved some goals or not) and health(care) needs. Additionally, apps and devices should be more battery efficient and accurate; providing timely, non-judgmental feedback and personalized advice (matching current state and bringing the patient to nest state slowly, along personal relapses and achievements) to the patients anywhere-anytime-anyhow.

Improved belief increased health outcomes, and we must re-engineer technologies to better engage the ones who need the solution the most and even further improve this belief (via increased arousal and self-gamification) and co-design with patients (Norman and Draper, 1986; Schuler and Namioka, 1993; Sanders and Stappers, 2008) (to leverage the self-efficacy sources). The self-efficacy source (people like ourselves) is harder because it depends on others' behavior and how people display those behaviors, this is now over-emphasized in current designs. Current designs assume people want to constantly compete, while some patients do not want or welcome that pressure. Addressing this would require adapting the designs to different personality traits (e.g., openness, agreeableness and neuroticism), which could then be translated into interaction types leading to an increase in the individual's self-efficacy. Knowing what we know now, mobile apps and wearable devices should be designed to leverage and improve the individual's self-efficacy as much as possible to lead to the user to the healthier behaviors in subtle design-based ways.

All our findings point toward a strategy that is well known in the health communication field, which is tailored communication (Hawkins et al., 2008). The interest in increasing self-efficacy because of its potential to positively influence self-management of chronic condition has been clearly stated. Our findings, however, show that pre-conceived design ideas aimed at influencing self-efficacy do not correspond to what users want, as we show the necessity of having a design adapted to different personality traits in order to increase individual's self-efficacy. But also beyond self-efficacy, our research shows how user experience could be positively influenced and sustained by personalized solution in apps and wearables, as well as by personalized feedback. Many behavioral interventions have shown that one size does not fit all and in order to become able to influence behavior we need to tailor the solutions to the individual needs. Mobile and wearables offer an unprecedent opportunity to tailor communication, as personal devices are able to collect data that can be used to this end. If tailored approach has been already proven successful on the web (Lustria et al., 2013), mobiles and wearable have the moral duty to bring this a step forward. This design implication is fundamental for the future.

DATA AVAILABILITY STATEMENT

The datasets generated for this study will not be made publicly available due to study IRB and HIPAA. Requests to access the datasets should be directed to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by David D. Oakes, M.D., Stanford University (Protocol 28265) and Michael D. Amylon, M.D., Stanford University (Protocol 29414). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

KW collected the data and coded it (with MF). KW and SW wrote the first draft of the manuscript. SW, KW, HR, WC, and MF contributed to all versions of the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2019.02388/full#supplementary-material

REFERENCES

Antó, J. M., Vermeire, P., Vestbo, J., and Sunyer, J. (2001). Epidemiology of chronic obstructive pulmonary disease. *Eur. Respir. J.* 17, 982–994.

Bandura, A. (1977). Self-efficacy: toward a unifying theory of behavioral change. *Psychol. Rev.* 84, 191–215. doi: 10.1037/0033-295x.84.2.191

Bandura, A. (1997). *Self-Efficacy: The Exercise of Control*. San Francisco, CA: W.H. Freeman an Company.

Bethancourt, H. J., Rosenberg, D. E., Beatty, T., and Arterburn, D. E. (2014). Barriers to and facilitators of physical activity program use among older adults. *Clin. Med. Res.* 12, 10–20. doi: 10.3121/cmr.2013.1171

Bodenheimer, T. (2002). Patient self-management of chronic disease in primary care. *JAMA* 288:2469. doi: 10.1001/jama.288.19.2469

Cameron, J. E., Voth, J., Jaglal, S. B., Guilcher, S. J. T., Hawker, G., and Salbach, N. M. (2018). "In this together": social identification predicts health outcomes (via self-efficacy) in a chronic disease self-management program. *Soc. Sci. Med.* 208, 172–179. doi: 10.1016/j.socscimed.2018.03.007

Duscha, B. D., Piner, L. W., Patel, M. P., Crawford, L. E., Jones, W. S., Patel, M. R., et al. (2018). Effects of a 12-week mhealth program on functional capacity and physical activity in patients with peripheral artery disease. *Am. J. Cardiol.* 122, 879–884. doi: 10.1016/j.amjcard.2018.05.018

Gallagher, R., Donoghue, J., Chenoweth, L., and Stein-Parbury, J. (2008). Self-management in older patients with chronic illness. *Int. J. Nurs. Pract.* 14, 373–382. doi: 10.1111/j.1440-172X.2008.00709.x

GSM Association, (2018). *The Mobile Economy 2018*. London: GSM Association.

Hamine, S., Gerth-Guyette, E., Faulx, D., Green, B. B., and Ginsburg, A. S. (2015). Impact of mHealth chronic disease management on treatment adherence and patient outcomes: a systematic review. *J. Med. Int. Res.* 17:e52. doi: 10.2196/jmir.3951

Hawkins, R. P., Kreuter, M., Resnicow, K., Fishbein, M., and Dijkstra, A. (2008). Understanding tailoring in communicating about health. *Health Educ. Res.* 23, 454–466. doi: 10.1093/her/cyn004

Hektner, J. M., Schmidt, J. A., and Csikszentmihalyi, M. (2007). *Experience Sampling Method: Measuring the Quality of Everyday Life*. Thousand Oaks, CA: SAGE.

Herz, J. C. (2014). *Wearables Are Totally Failing The People Who Need Them Most*. San Francisco, CA: Wired.

Ickin, S., Wac, K., Fiedler, M., Janowski, L., Hong, J.-H., and Dey, A. (2012). Factors influencing quality of experience of commonly used mobile applications. *IEEE Commun. Mag.* 50, 48–56. doi: 10.1109/MCOM.2012.6178833

International Telecommunication Union, (2015). *BS.1534: Method for the Subjective Assessment of Intermediate Quality Levels of Coding Systems*. Geneva: International Telecommunication Union.

Kahneman, D., Krueger, A. B., Schkade, D. A., Schwarz, N., and Stone, A. A. (2004). A survey method for characterizing daily life experience: the day reconstruction method. *Science* 306, 1776–1780. doi: 10.1126/science.1103572

Lauren, N., Fielding, K. S., Smith, L., and Louis, W. R. (2016). You did, so you can and you will: self-efficacy as a mediator of spillover from easy to more difficult pro-environmental behaviour. *J. Environ. Psychol.* 48, 191–199. doi: 10.1016/j.jenvp.2016.10.004

Lenferink, A., van der Palen, J., van der Valk, P., Cafarella, P., van Veen, A., Quinn, S., et al. (2017). Effects of self-management action plans for COPD patients with comorbidities on health status and self-efficacy. *Eur. Respir. Soc.* 50:A3456. doi: 10.1183/1393003.congress-2017.PA3456

Lorig, K., Ritter, P. L., Villa, F. J., and Armas, J. (2009). Community-based peer-led diabetes self-management: a randomized trial. *Diabetes Educ.* 35, 641–651. doi: 10.1177/0145721709335006

Lorig, K. R., Sobel, D. S., Ritter, P. L., Laurent, D., and Hobbs, M. (2001). Effect of a self-management program on patients with chronic disease. *Eff. Clin. Pract.* 4, 256–262.

Lustria, M. L. A., Noar, S. M., Cortese, J., Van Stee, S. K., Glueckauf, R. L., and Lee, J. (2013). A meta-analysis of web-delivered tailored health behavior change interventions. *J. Health Commun.* 18, 1039–1069. doi: 10.1080/10810730.2013.768727

Mallan, K. (2009). Look at me ! look at me ! Self-representation and self-exposure through online networks. *Digit. Cult. Educ.* 1, 51–66.

Manea, V., and Wac, K. (2018). "mQoL: mobile quality of life lab: from behavior change to QoL," in *Proceedings of the 2018 ACM International Joint Conference and 2018 International Symposium on Pervasive and Ubiquitous Computing and Wearable Computers*, New York, NY.

McCabe, C., McCann, M., and Brady, A. M. (2017). Computer and mobile technology interventions for self-management in chronic obstructive pulmonary disease. *Cochrane Database Syst. Rev.* 5:CD011425. doi: 10.1002/14651858.CD011425.pub2

Morgan, H. M., Entwistle, V. A., Cribb, A., Christmas, S., Owens, J., Skea, Z. C., et al. (2017). We need to talk about purpose: a critical interpretive synthesis of health and social care professionals' approaches to self-management support for people with long-term conditions. *Heal Expect.* 20, 243–259. doi: 10.1111/hex.12453

Norman, D., and Draper, S. (1986). *User Centered System Design; New Perspectives on Human-Computer Interaction*. London: Taylor & Francis.

Ouellette, J. A., and Wood, W. (1998). Habit and intention in everyday life: the multiple processes by which past behavior predicts future behavior. *Psychol. Bull.* 124, 54–74. doi: 10.1037/0033-2909.124.1.54

Piché, M.-E., Poirier, P., Lemieux, I., and Després, J.-P. (2018). Overview of epidemiology and contribution of obesity and body fat distribution to cardiovascular disease: an update. *Prog. Cardiovasc Dis.* 61, 103–113. doi: 10.1016/j.pcad.2018.06.004

Powers, M. A., Bardsley, J., Cypress, M., Duker, P., Funnell, M. M., Fischl, A. H., et al. (2017). Diabetes self-management education and support in type 2 diabetes. *Diabetes Educ.* 43, 40–53. doi: 10.1177/0145721716689694

Reeves, D., Blickem, C., Vassilev, I., Brooks, H., Kennedy, A., Richardson, G., et al. (2014). The Contribution of social networks to the health and self-management of patients with long-term conditions: a longitudinal study. ozakinci G, ed. *PLoS One* 9:e98340. doi: 10.1371/journal.pone.0098340

Ross, C., and Mirowsky, J. (2010). *Why Education is the Key to Socioeconomic Differentials in Health*. Nashville, TN: Vanderbilt University Press.

Sanders, E. B.-N., and Stappers, P. J. (2008). Co-creation and the new landscapes of design. *CoDesign* 4, 5–18. doi: 10.1080/15710880701875068

Sarkar, U., Fisher, L., and Schillinger, D. (2006). Is self-efficacy associated with diabetes self-management across race/ethnicity and health literacy? *Diabetes Care* 29, 823–829. doi: 10.2337/diacare.29.04.06.dc05-1615

Schuler, D., and Namioka, A. (1993). *Participatory Design: Principles and Practices*. London: Taylor & Francis.

Strecher, V. J., McEvoy DeVellis, B., Becker, M. H., and Rosenstock, I. M. (1986). The role of self-efficacy in achieving health behavior change. *Heal Educ. Behav.* 13, 73–92. doi: 10.1177/109019818601300108

Wagner, E. H., Austin, B. T., Davis, C., Hindmarsh, M., Schaefer, J., and Bonomi, A. (2001). Improving chronic illness care: translating evidence into action. *Health Aff.* 20, 64–78. doi: 10.1377/hlthaff.20.6.64

Wang, J., Wang, Y., Wei, C., Yao, N. A., Yuan, A., Shan, Y., et al. (2014). Smartphone interventions for long-term health management of chronic diseases: an integrative review. *Telemede Health* 20, 570–583. doi: 10.1089/tmj.2013.0243

Zheng, Y., Ley, S. H., and Hu, F. B. (2017). Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nat. Rev. Endocrinol.* 14:88. doi: 10.1038/nrendo.2017.151

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

APPENDIX 1: GENERAL SELF-EFFICACY SCALE

The participants were asked daily 1 general self-efficacy question:

1. Today, I can manage to solve difficult problems if I try hard enough.
2. Today, if someone opposes me, I can find the means and ways to get what I want.
3. Today, it is easy for me to stick to my aims and accomplish my goals.
4. Today, I am confident that I could deal efficiently with unexpected events.
5. Today, Thanks to my resourcefulness, I know how to handle unforeseen situations.
6. Today, I can solve most problems if I invest the necessary effort today.
7. Today, I can remain calm when facing difficulties because I can rely on my coping abilities.
8. Today, if I am confronted with a problem, I can find several solutions.
9. Today, if I am in trouble, I can think of a solution.
10. Today, I can handle whatever comes my way.

Response options:
1 = not at all true (low self-efficacy) 2 = hardly true 3 = moderately true 4 = exactly true (high self-efficacy).

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Personality Traits, Perceived Stress, and Tinnitus-Related Distress in Patients With Chronic Tinnitus: Support for a Vulnerability-Stress Model

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Background: Despite vulnerability-stress models underlying a variety of distress-related emotional syndromes, few studies have investigated interactions between personality factors and subjectively experienced stressors in accounting for tinnitus-related distress.

Aim: The present study compared personality characteristics between patients with chronic tinnitus and the general population. Within the patient sample, it was further examined whether personality dimensions predicted tinnitus-related distress and, if so, whether differential aspects or levels of perceived stress mediated these effects.

Method: Applying a cross-sectional design, 100 patients with chronic tinnitus completed the Freiburger Persönlichkeitsinventar (*FPI-R*) measuring personality, the Perceived Stress Questionnaire (*PSQ-20*) measuring perceived stress and the German version of the Tinnitus Questionnaire (*TQ)* measuring tinnitus-related distress. FPI-R scores were compared with normed values obtained from a representative German reference population. Mediation analyses were computed specifying FPI-R scores as independent, PSQ20 scores as mediating and the TQ-total score as dependent variables.

Results: Patients with chronic tinnitus significantly differed from the general population across a variety of personality indices. Tinnitus-related distress was mediated by differential interactions between personality factors and perceived stress dimensions.

Conclusion: In conceptualizing tinnitus-related distress, idiosyncratic assessments of vulnerability-stress interactions are crucial for devising effective psychological treatment strategies. Patients' somatic complaints and worries appear to be partly informed by opposing tendencies reflecting emotional excitability vs. aggressive inhibition – suggesting emotion-focused treatment strategies as a promising new direction for alleviating distress.

Keywords: tinnitus, personality, vulnerability-stress, Tinnitus Questionnaire (TQ), perceived stress, FPI

INTRODUCTION

Tinnitus is a symptom denoting the perception of acoustic sensations without an external sound stimulus. The prevalence in the general population ranges between 4 and 32%, and the levels of reported contemporaneous psychological distress vary considerably (Durai and Searchfield, 2016). Whilst some patients report depression and anxiety associated with the tinnitus percept (Schaaf et al., 2003; Durai and Searchfield, 2016), others report little or no tinnitus-related distress. Tinnitus can be acute or chronic with the latter being defined as a symptom duration of > 3 months (Deutsche Gesellschaft für Hals-Nasen-Ohren-Heilkunde Kopf- und Hals-Chirurgie, 2015). Depending on perceived tinnitus-related distress, tinnitus can also be divided into compensated and decompensated presentations with the latter involving high levels of tinnitus-related distress and associated symptoms of low mood and/or anxiety (Biesinger et al., 1998).

Whilst its causes are not always clearly identifiable and closely interlinked, chronic tinnitus has been associated with numerous risk factors (Haider et al., 2018; Trevis et al., 2018; Boecking et al., 2019) that have partly been interpreted within a vulnerability-stress framework. For example, emotional exhaustion and low emotional well-being were found to predict the risk of developing tinnitus (Hébert et al., 2012) with the former also being shown to predict higher sensitivity to sound following an acute stress task (Hasson et al., 2013). Moreover, several studies have shown that existing emotional distress predicted higher tinnitus-related distress (Bartels et al., 2009; Schaaf et al., 2014; Wallhäusser-Franke et al., 2015; Durai and Searchfield, 2016; Strumila et al., 2017; Sahlsten et al., 2018). On the other hand, high psychological resilience (i.e., an individual's ability to adapt to adverse life conditions) was associated with higher emotional well-being that was – in turn – associated with lower tinnitus-related distress (Wallhäusser-Franke et al., 2014). In line with conceptualizations of other functional syndromes such as chronic pain (Flor, 1991; Linton, 2000; Wittchen and Hoyer, 2011), tinnitus-related distress might be conceptualized as a function of an interaction of pre-existing psychological vulnerability and life stressors that may include – but are not limited to – the tinnitus symptom.

Personality, i.e., the sum of an individual's unique and stable aspects [i.e., personality traits] that describe, explain and predict one's behavior (Asanger and Wenninger, 1999), is a well-established vulnerability factor for developing anxiety and depression following stressful experiences (e.g., Boyce et al., 1991; Kotov et al., 2010). Personality traits are psychological constructs that describe individual differences in perception, experience, emotion, cognition, and behavior on selected parameters. Personality factors could either render an individual vulnerable to developing tinnitus (e.g., Mucci et al., 2014), or facilitate the development and experience of psychological distress that, upon the perception of a tinnitus sound, extends toward the tinnitus percept (Peerenboom et al., 2015). Investigating personality factors bears high importance for understanding all psychological components of tinnitus-related distress and its maintenance, as personality may affect both exposure and reactivity to stressful events as well as differential choices of coping efforts and their differential effectiveness (Bolger and Zuckerman, 1995). Moreover, success rates of treatment approaches such as schema (Jacob and Arntz, 2013) or mentalization-based therapy (Vogt and Norman, 2018) increasingly refute the notion that personality-associated persistent emotional difficulties are stable. These treatments offer promising tools to address personality factors as modifiable treatment targets. Regarding tinnitus, some studies have investigated whether certain personality traits predict the presence or degree of tinnitus-related distress. For example, Weber et al. (2008) applied the Freiburg Personality Inventory (Freiburger Persönlichkeitsinventar, FPI-R, Fahrenberg et al., 2010) to a sample of 121 patients with chronic tinnitus and demonstrated significant differences in between patient groups with low and high tinnitus-related distress in the personality traits life satisfaction, excitability, aggressiveness, strain, somatic complaints, health concerns, and emotionality. Durai and Searchfield (2016) showed that tinnitus-related distress was associated with high neuroticism, low extraversion, high stress reaction, higher alienation, lower social closeness, lower well-being, lower self-control, lower psychological acceptance and presence of a type D personality, i.e., a tendency toward negative affectivity and social inhibition, and externalized locus of control. Moreover, several studies reported positive relations between tinnitus-related distress and a subset of "Big-Five" personality traits, namely low agreeableness, low extraversion and high neuroticism (Langguth et al., 2007; McCormack et al., 2014; Mucci et al., 2014; Dehkordi et al., 2015). Welch and Dawes (2008) stated alongside Durai et al. (2017) that compared to non-tinnitus control groups, tinnitus patients were more socially withdrawn, reactive to stress, and alienated as well as less self-controlled. Compared to an adult reference population, Chung et al. (2017) reported that tinnitus patients showed higher levels of harm avoidance and lower scores for novelty seeking, reward dependence, persistence, cooperativeness and self-transcendence. Overall, studies demonstrated mixed relations between tinnitus-related distress and a variety of personality factors. However, due to heterogeneous operationalizations of the investigated personality constructs, no consistent picture has of yet emerged.

The meaning of "stress" varies widely in the scientific field. It can describe external stimuli, the adaptive reaction to them or resulting physical or mental strain. Longitudinal studies that compare differential stress dimensions with regard to tinnitus or tinnitus-related distress do not yet exist (Boecking et al., 2019). However, several studies have investigated the interaction between personality traits and stressors as influencing psychological distress and somatic symptoms. Almeida (2005) used a diary method approach and reported that psychological resilience and sociodemographic factors predicted the likelihood of exposure, appraisal and reactivity to daily stressors. Personality traits can thus influence daily well-being through their interaction with stressors.

Several other studies further suggest that subjects with high neuroticism are more likely to develop depressive symptoms upon exposure to daily hassles (Hutchinson and Williams, 2007; Vinkers et al., 2014; Hentrich et al., 2016) – to which help-seeking patients with tinnitus have also shown to be susceptible (Scott and Lindberg, 2000). Yang et al. (2013) reported that perfectionism – a trait known to be heightened in individuals with chronic tinnitus (Andersson et al., 2005) – predicted depression in interaction with achievement-related, but not interpersonal hassles. A few more studies showed that interactions between perfectionism, daily hassles or major life events had an influence on the occurrence and maintenance of depressive symptoms (Flett et al., 1997; Yang et al., 2013).

Overall personality traits interact with daily stressors in predicting psychological distress. Applying a psychological vulnerability-stress framework, the current study investigates how personality characteristics (as measured by the FPI-R) interact with perceived stress in explaining tinnitus-related distress in patients with chronic tinnitus.

Hypotheses

We examined the following hypotheses:

(1) There are systematic differences in personality factors between patients with chronic tinnitus and the general population;
(2) There are systematic differences in personality factors between patients with decompensated and compensated chronic tinnitus; and
(3) Within patients with chronic tinnitus, the degree of tinnitus-related distress is a function of differential interactions between personality-factors and differing dimensions of perceived subjective stress.

MATERIALS AND METHODS

Procedure

The current study included $N = 100$ patients with chronic tinnitus who had been referred to the Tinnitus Center at Charité – Universitätsmedizin-Berlin between 2011 and 2012 and who completed [1] the German version of the Tinnitus Questionnaire (TQ) measuring tinnitus-related distress, [2] the Freiburg Personality Inventory (FPI-R) measuring personality factors, and [3] the Perceived Stress Questionnaire – German modified version measuring perceived stress. The reference group for the FPI-R norms consists of 3740 non-institutionalized adult subjects who are representative of the German population (Fahrenberg et al., 2010). The study was carried out in accordance with the recommendations of the German S3 Guideline 017/064: Chronic Tinnitus (Deutsche Gesellschaft für Hals-Nasen-Ohren-Heilkunde Kopf- und Hals-Chirurgie, 2015). Data was collected as part of the clinic's routine diagnostic procedures approved by the Ethics Committee of Charité Universitätsmedizin Berlin (Nr. EA 1/115/15). All participants gave written consent for the use of anonymized data for research purposes in accordance with the Declaration of Helsinki.

Materials

Tinnitus Questionnaire – German Version (TQ; Goebel and Hiller, 1998)

The German version of the Tinnitus Questionnaire is a self-report questionnaire that measures the degree of tinnitus-related distress. The questionnaire consists of 52 items ("disagree" = 0, "partly agree" = 1, "agree" = 2), 40 items of which are included into the total score and two items being entered twice thus yielding a range between 0 and 84 points. The total score can be divided to reflect compensated (slight and moderate tinnitus-related distress, as defined by scores ranging from 0 to 46) and decompensated levels of tinnitus-related distress (severe and catastrophic, as defined by scores ranging from 47 to 84; Biesinger et al., 1998; Goebel and Hiller, 1998). The scale's internal consistency is high ($\alpha = 0.95$; Zeman et al., 2012).

Freiburg Personality Inventory (FPI-R, Freiburger Persönlichkeitsinventar; Fahrenberg et al., 2010)

The Freiburg Personality Inventory consists of 138 items ("not true" = 0, "true" = 1) across 12 personality dimensions that comprise 10 to 14 items each. The inventory has been validated across various languages and populations and the subscales' internal consistencies are sufficient ($\alpha = 0.73$–0.83; Fahrenberg et al., 2010). In the following, the dimensions will be explained in some detail to allow for a psychologically meaningful description of the patient sample. Descriptions have been translated and adapted from the FPI-R handbook (Fahrenberg et al., 2010, pp. 84–90).

Life satisfaction describes feelings of satisfaction, contentment with life, self-acceptance, and an optimistic vision of one's own future. People with lower scores show discontent about past and present life conditions. They lack self-efficacy, tend to ruminate and are often fed up by their circumstances. They express gloomy and unhappy moods, depressiveness and a negative approach to life. People with higher scores are content about their life choices and conditions. They have high self-valuation and show optimism and a positive attitude toward life.

Social orientation describes social solidarity, i.e., one's tendency to be generous, friendly, helping, and warm. Persons with low scores highlight individual responsibility regarding life conditions. They act selfish and with unsympathetic attitudes toward others. Persons with high scores feel a high social responsibility. They express helpfulness, react to worries of others, and are motivated to help, comfort and care. They also tend to feel guilty which motivates them to engage in helping others.

Achievement orientation describes a person's ambition; wish to assert themselves, competition behavior, activism, and determination. Persons with low scores show low competitive behavior and very little ambition. Either because of principles against the competitive vision of life, or because professional and social achievements are not important life goals. People with high scores are achievement orientated and motivated. They are ambitious and solve problems fast and efficient. They also enjoy being in competition, in their profession and social life. Usually they show higher commitment to their profession than to leisure time activities.

Inhibitedness describes hesitant and shy behavior, which is characterized by withdrawal, inhibition, lack of self-confidence, and little development or verbalization capacities. Persons with low scores are easy-going, spontaneous and self-confident in social groups. Persons with high scores feel inhibited in social situations: they are afraid to enter rooms filled with other people, prefer to stay in the background, have difficulties to speak in front of others. They are easily embarrassed, often anxious and blush often. Interactions with strangers are difficult and hard for them. They have difficulties joining conversations or making friends.

Excitability describes impulsive behavior and lack of self-control – with slightly aggressive manifestations. Persons with a lower score are characterized by serenity. They are difficult to provoke or bother, stay calm and patient even in difficult and hectic situations with multiple disturbances. People with higher scores are easily irritated and worked up. They have difficulties to control their anger, show aggressive behavior in improvident statements. They react sensitive and rushed, even in unimportant situations.

Aggressiveness describes verbal or physical aggressive behavior. It describes mainly spontaneous reactive and dominating behaviors. Persons with lower scores show little aggression. They are either reserved, solitary, inhibited in expressing themselves or socially passive and can control their reactions. They do not use physical violence to enforce their needs or rights. Persons with higher scores show willingness to violent behavior. They can experience joy in rude jokes, showing up faults of others or hurting people. They defend themselves with fury and lack of control, perhaps even with physical violence, if they feel insulted or in their rights violated.

Strain describes a personal perception of subjective overload. This induces tension, stress, nervousness, and exhaustion. Persons with lower scores feel less stressed and overworked. They feel equal to their requirements and are able to fulfill their tasks. Persons with higher scores feel highly stressed: they have a lot of tasks, experience high requirements and time pressure.

Somatic complaints describe the subjective disturbance of one's actual state of health. Persons with low scores rarely complain of physical symptoms. Persons with higher scores complain about sleeping disorders, headaches, meteoropathy, arrhythmia, hot flashes, cold extremities, an irritable stomach, a chest tightness, tics, and/or shivering.

Health concerns describe worries about one's present and future state of health irrespective of the actual state of health. Persons with low scores show little worries about their own health. They are unconcerned, robust, and not over-protective. Persons with high scores describe a health orientated, worried behavior. They try to reduce risk of health-related harm, contagion, infection and accidents. They show hypochondriac tendencies, food and lifestyle control and often ask for medical or therapeutic advice.

Frankness describes open, unreserved and unconventional behaviors, which are characterized by straightforwardness. Persons with lower scores try to make good impressions with active impression management. Different motives can explain these behaviors: lack of self-criticism or self-idealization, reticence or conformity. People with higher scores are able to admit everyday mistakes or weaknesses: being late, procrastination, gloating, occasional lies, nasty thoughts, etc. They admit these deviations from the social norm without shame and do not see these norms as important or deviations as flagrant.

Extraversion describes one of the basic dimensions of most personality theories: it captures the difference between sociable, impulsive, active and socially present, dynamic and vivid persons, and reserved, uncommunicative, controlled, introvert ones. People with lower scores are withdrawn in social situations and prefer to be alone. They are calm and serious, uncommunicative, not enterprising and more likely self-controlled than impulsive. People with higher score are sociable and impulsive. They like to go out, varieties, entertainment, make friends fast, enjoy company of others and can be easy-going. They are active, communicative and eloquent in contact with others. They can be prankful, enterprising, energetic and ready to take command.

Emotionality describes the continuum of emotional stability to emotional lability and neuroticism. People with lower scores are satisfied with themselves and their life. They are serene, relaxed, and calm. They are little anxious or sensitive. They show mostly no health concerns, psychosomatic symptoms or inner conflicts. People with high scores show high numbers of problems and inner conflicts. They are excitable and irritable or feel tired, asthenic or indifferent. Their mood switches a lot, but they feel mainly depressed and anxious. They ruminate a lot and feel misunderstood by their peers and relatives. They are stressed, concerned about their health, nervous and psychosomatically accentuated.

Perceived Stress Questionnaire – German Modified Version (PSQ20; Fliege et al., 2005)

The Perceived Stress Questionnaire is a self-report questionnaire measuring perceived stress. The German modified version consists of 20 items with a four-point Likert-type scale ("almost never" = 1, "sometimes" = 2, "often" = 3, "usually" = 4; Fliege et al., 2005). Higher total scores indicate more severe perceived stress. Items are rated across four subscales: worries (worries, anxious concern for the future, and feelings of desperation and frustration), tension (disquietude, exhaustion and the lack of relaxation), joy (positive feelings of challenge, joy, energy, and security), and demands (perceived environmental demands, such as lack of time, pressure, and overload.). The resulting PSQ20 total und subscale scores are linearly transformed to scores ranging from 0 to 1. For the computation of the total score, the scale joy is inversed. The scale "demands" focuses on the subjective perception of external stressors, while the other three scales focus on internal stress reactions (Fliege et al., 2005). Originally designed in English, this instrument has been translated into French, Italian, German and Spanish, and validated in various populations (Kocalevent et al., 2007). The scale's internal consistency is high ($\alpha = 0.90$; Fliege et al., 2005).

Participants

A total of $N = 100$ patients with chronic tinnitus (53% female) completed the TQ, FPI-R and PSQ20. On average, patients were 50 years old ($SD = 12.38$; range = 19–76). Seventy-three patients reported compensated tinnitus whilst 27 reported decompensated tinnitus. To interpret the reported FPI-R scores, scores were compared both with the reference population mean values published in the FPI-R – 8th edition ($N = 3740$) (Fahrenberg et al., 2010) and between patients with compensated vs. decompensated tinnitus.

Statistical Analysis

All analyses were conducted using IBM SPSS Statistics for Windows, version 24. Statistical significance was set at $\alpha = 0.05$. For the comparisons of means, effect sizes (Cohen's d) were also calculated. Effect sizes of Cohen's d are defined as d (0.01) = very small, d (0.2) = small, d (0.5) = medium, d (0.8) = large, d (1.2) = very large, and d (2.0) = huge (Sawilowsky, 2009). *First*, we used descriptive statistics to explore sample descriptors. *Second,* we used the SPSS dummy matrix variable approach and independent samples t-tests to compare our sample means with the summarized data from the FPI-R population norms. *Third*, we used independent samples t-tests to compare decompensated and compensated patients. *Finally*, to explore interaction effects between personality traits (vulnerability) and perceived stress (stress) on tinnitus-related distress, mediation analyses were computed, specifying FPI-R dimensions as independent variables, PSQ20 dimensions as mediating variables and the TQ total score as dependent variable. Here, the PROCESS macro (Hayes, 2018) was used to compute a series of path coefficients: the effect of the independent variable X on the dependent variable Y (total effect, c); the effect of X on the mediator M (path a); the effect of M on Y (path b); the indirect effect (ab); and the total effect adjusted for ab (direct effect, c'). Whenever the effect of X on Y decreases to zero once M is included in the model, "complete mediation" is said to have occurred (James and Brett, 1984). In this case, there is strong evidence that the investigated mediator dominantly accounts for almost all variance in the outcome variable. "Partial mediation" is said to have occurred, if the effect of X on Y decreases significantly, but not necessarily to zero (Judd and Kenny, 1981). In the results section, indirect effects will be reported graphically – for an overview of estimates, see **Appendix A**.

RESULTS

Descriptive Statistics

Table 1 shows sociodemographic factors and means for the TQ (German version), FPI-R, and PSQ20.

TABLE 1 | Sample description.

	N	*M*	*SD*	Min	Max
Gender					
Male	47				
Female	53				
Age	100	50.00	12.38	19	76
TQ_Total score	100	33.71	16.80	0	73
FPI-R					
Life satisfaction	100	7.01	3.28	0	12
Social orientation	100	7.52	2.40	1	12
Achievement orientation	100	7.15	2.68	0	12
Inhibitedness	100	5.57	3.14	0	12
Excitability	100	6.81	3.10	0	12
Aggressiveness	100	3.42	2.42	0	11
Strain	100	7.51	3.80	0	12
Somatic complaints	100	4.31	2.38	0	10
Health concerns	100	5.50	2.79	0	12
Frankness	100	5.81	2.86	1	12
Extraversion	100	6.47	3.54	0	14
Emotionality	100	7.36	3.61	0	14
PSQ20					
Total	99	0.44	0.22	0.01	0.92
Worries	99	0.39	0.25	0.00	1.00
Tension	99	0.52	0.26	0.00	1.00
Joy*	99	0.53	0.26	0.00	1.00
Demands	99	0.50	0.28	0.00	1.00

*M, mean; Min, minimum; Max, maximum; SD, standard deviation; TQ, Tinnitus Questionnaire (German version); PSQ20, Perceived Stress Questionnaire. *Higher values indicate more joy; for the total score, the coding is reversed.*

Comparison of Means

First, we compared FPI-R mean values of tinnitus patients to those of the general population. For the tinnitus patients, results showed significantly elevated values in [+] social orientation ($p = 0.000$, $d = 0.426$), excitability ($p = 0.000$, $d = 0.528$), strain ($p = 0.000$, $d = -0.588$), somatic complaints ($p = 0.000$, $d = 0.282$), emotionality ($p = 0.000$, $d = 0.430$), and significantly lower values in [−] aggressiveness ($p = 0.000$, $d = -0.359$) and health concerns ($p = 0.000$, $d = 0.426$) (see **Figure 1**). Differences in social orientation, aggressiveness, somatic complaints, health concerns and emotionality yielded small effect sizes; differences in excitability and strain medium effect sizes. We then explored Pearson correlations between the personality dimensions that distinguished tinnitus patients from the general population in our sample. Here, coefficients suggested an affectively centered cluster comprising strong correlations between emotionality and excitability, strain and somatic complaints (see **Table 2**).

Third, we compared FPI-R values between decompensated and compensated tinnitus patients. Results showed significantly higher values in [+] excitability, strain, somatic complaints, and emotionality alongside significantly lower values in [−] life satisfaction (**Table 3**). Medium effect sizes emerged for life satisfaction, excitability and strain; large effect sizes for emotionality and somatic complaints.

Mediation Analyses

Exploring possible interactions of vulnerability (personality dimensions) and stress (perceived stress) factors in predicting tinnitus-related distress, we computed sets of mediation analyses specifying those personality factors as independent variables that

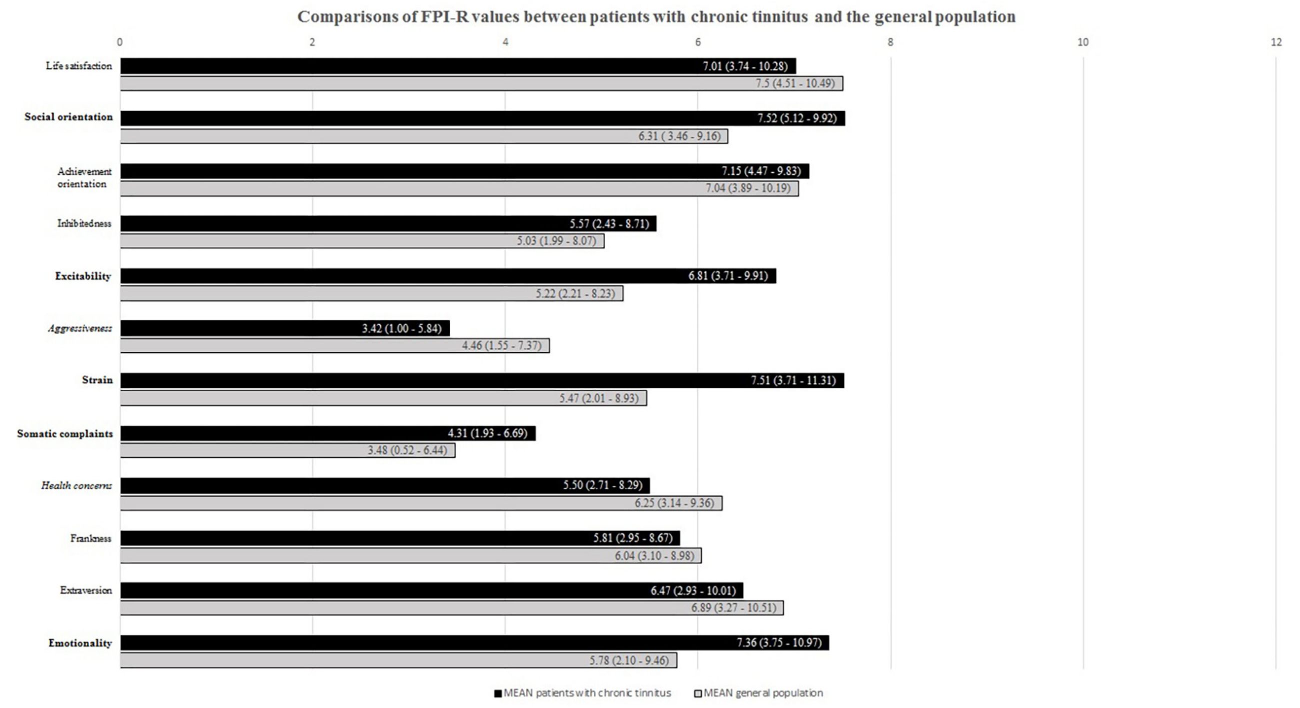

FIGURE 1 | FPI-R values for patients with chronic tinnitus and the general population. Compared to the general population, bold labels indicate significantly higher; italicized labels significantly lower scores for patients with chronic tinnitus.

TABLE 2 | Intercorrelations of factors that distinguish patients with chronic tinnitus from the general population.

	Aggressiveness	Strain	Somatic complaints	Emotionality
Aggressiveness				*0.275***
Strain			0.479**	**0.726****
Somatic complaints				**0.582****
Excitability	*0.256**	**0.495****	0.338**	**0.616****

*Only significant coefficients are reported. *p < 0.05, **p < 0.01 (two-tailed). Italicized values denote small (below ± 0.29), underlined values medium (± 0.30 and ± 0.49), and bold values strong correlations (± 0.50 and ± 1).*

TABLE 3 | Comparisons of FPI-R values between patients with decompensated and compensated chronic tinnitus.

FPI-R scale	*Decompensated* tinnitus patients *n* = 27	*Compensated* tinnitus patients *n* = 73	*p*	*d*
Life satisfaction	**5,67 ± 3,15**	**7,51 ± 3,20**	**0.012**	**−0,577**
Social orientation	7,85 ± 2,41	7,40 ± 2,40	0.408	
Achievement orient.	7,22 ± 2,91	7,12 ± 2,60	0.869	
Inhibitedness	5,41 ± 3,24	5,63 ± 3,13	0.758	
Excitability	**7,89 ± 2,67**	**6,41 ± 3,18**	**0.034**	**0,485**
Aggressiveness	3,56 ± 2,58	3,37 ± 2,37	0.729	
Strain	**9,26 ± 2,40**	**6,86 ± 4,03**	**0.005**	**0,654**
Somatic complaints	**6,11 ± 1,74**	**3,64 ± 2,24**	**0.000**	**1,166**
Health concerns	5,26 ± 2,10	5,59 ± 3,02	0.603	
Frankness	5,56 ± 2,98	5,90 ± 3,02	0.617	
Extraversion	6,67 ± 3,93	6,40 ± 3,41	0.737	
Emotionality	**9,41 ± 2,58**	**6,60 ± 3,66**	**0.000**	**0,825**

Bold values denote significant differences between the groups, p < 0.05.

were found to significantly differ for tinnitus patients compared to the general population (cf. **Figure 1**). As mediators, we specified the total and subscale scores of the PSQ20 questionnaire with the dependent variable being specified as tinnitus-related distress as measured by the TQ total score. **Figure 2** shows the significant effects of the explorative mediation analyses.

Overall, the following indirect effects accounted for the relationship between personality factors and tinnitus-related distress:

(1) For personality traits that were significantly more pronounced in patients with chronic tinnitus compared to the general population:

- Higher excitability interacting with (a) higher perceived tension, (b) higher worries, (c) less joy, and (d) higher demands;
- Higher strain interacting with (a) higher perceived tension and (b) higher worries;
- Higher somatic complaints interacting with (a) higher perceived tension, (b) higher worries, and (c) higher demands; and
- Higher emotionality interacting with (a) higher perceived tension.

(2) For personality traits that were significantly less pronounced in patients with chronic tinnitus compared to the general population:

- Higher aggressiveness interacting with (b) higher worries.

Social orientation and health concerns did not interact with perceived stress in predicting tinnitus-related distress. **Appendix A** reports the detailed results of the mediation analyses (a three-step logistic regression analysis) outlining coefficients "*a*" (effects of the independent variables on the mediators), "*b*" (effect of the mediators on the dependent variable), "*c*" (total effect of the independent variable on the dependent variable), "*c*′" (direct effect; i.e., the total effect adjusted for the indirect effect) and the indirect effect "*ab*" that is tested for significance using a *bootstrapping* approach yielding 95% confidence intervals.

DISCUSSION

The present study investigated interrelations between personality factors as measured by the FPI-R, perceived stress (PSQ20) and tinnitus-related distress (TQ-German version) in a sample of 100 patients with chronic tinnitus.

Comparisons Between Tinnitus Patients and Between Tinnitus Patients and the General Population

> *Hypothesis 1: There are systematic differences in personality factors between patients with chronic tinnitus and the general population.*

Results of this study indicate differences in personality traits between patients with chronic tinnitus and the general population as measured using the FPI-R. Compared to the general population, patients rated themselves as [1] experiencing higher social responsibility and reacting more readily to the worries of others (+ social orientation), [2] being more easily irritated, worked up, sensitive and rushed – with slight aggressive manifestations (+ excitability), [3] having a substantively higher personal perception of subjective overload; including habitual stress, nervousness and exhaustion (+ strain), [4] complaining more about somatic symptoms (+ somatic complaints), [5] being more excitable and irritable *or* tired, asthenic or indifferent and feeling not understood by their peers and relatives (+ emotionality), [6] being more inhibited in expressing themselves and socially passive (− aggressiveness), and, [7] being *less* worried about their personal state of health – possibly underlying fewer health-orientated behaviors (− health concerns).

The results are partly in keeping with previous studies researching relations between tinnitus-related distress and personality factors: in particular, patients' higher emotionality and excitability scores support previous findings reporting higher scores of neuroticism and type D personality characteristics (e.g., Langguth et al., 2007; McCormack et al., 2014; Mucci et al., 2014; Durai and Searchfield, 2016) thereby supporting the importance of these constructs as risk factors for tinnitus-related distress.

> *Hypothesis 2: There are systematic differences in personality factors between patients with decompensated and compensated chronic tinnitus.*

In keeping with results from the comparisons of the overall sample with the general population, patients with decompensated (vs. compensated) tinnitus yielded higher expressions of excitability, strain, somatic complaints and emotionality and lower expressions of life satisfaction. By contrast, we did not find differences in aggressiveness and health concerns between the two subpopulations. These results partly reflect previous findings from Weber et al. (2008) who compared tinnitus patients across severity grades I–IV of the Tinnitus Questionnaire and reported that, compared to grade I patients, grade IV patients had lower life satisfaction and higher excitability, aggressiveness, somatic complaints, and emotionality ratings whilst health concerns were found to differ between grade I and III patients only.

Overall, patients with chronic tinnitus show predispositions toward interpreting and responding to stimuli in a manner characterized by easy irritation, high levels of subjective overload, inner conflict, and higher ruminative tendencies whilst being more inhibited in expressing their emotional needs alongside a guilt-associated tendency to orientate themselves toward others' needs. Interestingly, patients also report a lower degree of health concerns that might interact with higher excitability and higher social orientation in reflecting a coping style potentially aiming to regulate unexpressed emotion such as inhibited aggressivity (e.g., not using hearing protection). Relative to comparisons between tinnitus patients and the general population, the subsample of patients with *decompensated* tinnitus showed a somewhat similar, yet more pronounced profile across the excitability, strain, somatic complaints, and emotionality dimensions. Whilst the distinction between patients with compensated vs. decompensated tinnitus is clinically common (e.g., Stobik et al., 2005; Graul et al., 2008; Heinecke et al., 2008), results of the present study challenge the helpfulness of this dichotomization. Rather, personality traits appear to inform state cognitive-affective reactions to stimuli along a *continuum* of vulnerability-stress interactions with decompensation indicating a more pronounced expression of underlying, yet comparable, processes.

Vulnerability-Stress Interactions

> *Hypothesis 3: Within patients with chronic tinnitus, the degree of tinnitus-related distress is a function of differential interactions between personality-factors and differing dimensions of perceived subjective stress.*

While personality constructs are understood as comparably stable traits of a person, perceived stress – as measured in the present study – can be understood as reflecting negative state stress-related perceptions. The results of the mediation analyses may thus represent vulnerability-stress interactions that contribute to tinnitus-related distress yet do not, however, allow for assuming causality. Results indicated that tinnitus-related distress was predicted by vicious cycles between dispositional patterns of feeling easily irritated, strained, and emotional which interact

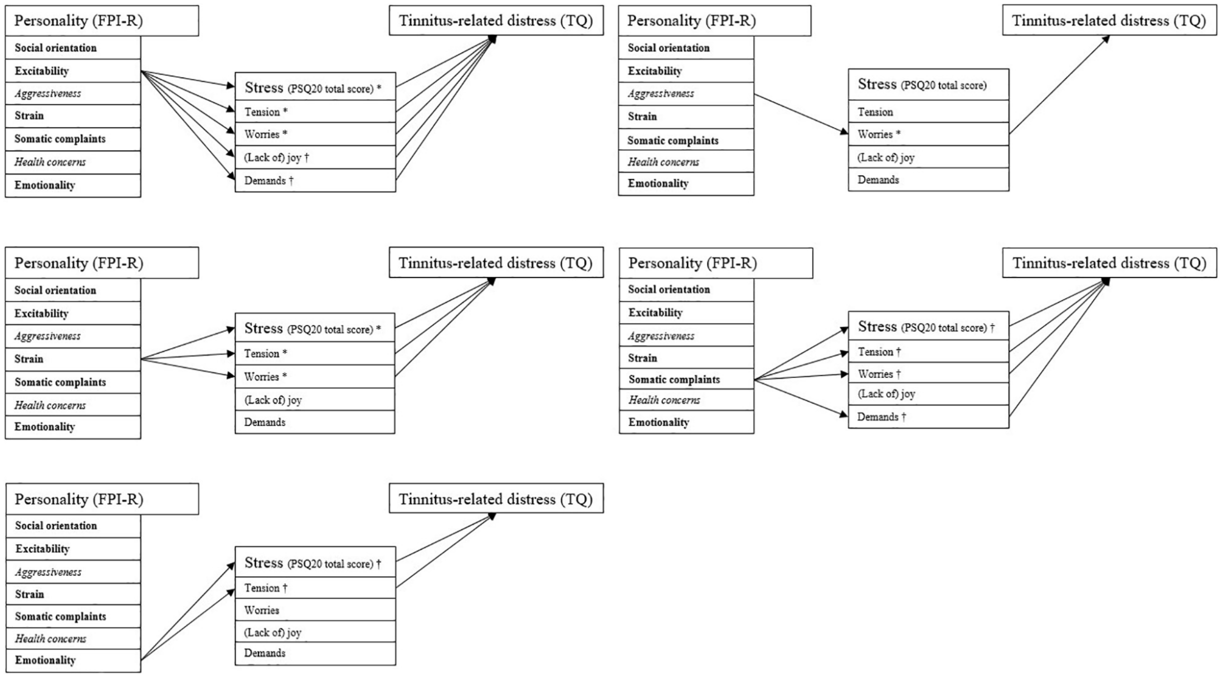

FIGURE 2 | Indirect effects of the mediation analyses. The PSQ20 subscale "joy" was inverted for reasons of consistent presentation (i.e., higher scores indicating higher perceived stress). Arrows indicate significant indirect effects ($p < 0.05$). All path coefficients are positive. Compared to the general population, bold labels indicate significantly higher; italicized labels significantly lower scores for patients with chronic tinnitus. *Complete mediation (total effect reduced to non-significance upon inclusion of *ab*); † partial mediation (total effect not reduced to non-significance upon inclusion of *ab*).

with state experiences of high perceived stress, in particular emotional tension and worries, in response to a variety of stimuli. Thus, tinnitus-related distress appears to be one possible expression of distress within a broader experience of dispositional stimulus-processing and behavioral patterns associated with psychological distress (or the inhibition thereof) and mild risk-taking behaviors.

The relationship between aggressiveness and tinnitus-related distress was found to be mediated by worries against the background of an overall inhibited expression of aggressiveness relative to the general population. Placing this finding in context, patients' high levels of concerns for others, inhibited expression of aggression, and *lower* levels of health anxiety and –related safety behaviors suggest that patients' high levels of worries may be less indicative of illness concerns (of which they express many), but may instead reflect *internal coping attempts to regulate aggressive tendencies*. On the extreme end of this spectrum, vicious cycles between high degrees of (suppressed) aggressiveness, high impulsivity, and high social orientation would be reflected in a clinical presentation of a self-sacrificing patient reporting high levels of tinnitus-related distress and worries that he/she might be attributing to the tinnitus sound, yet which may instead reflect unexpressed aggressive tendencies stemming from a felt need for behaving socially desirable in the face of possibly challenging interpersonal circumstances.

Interestingly, only the relationships between excitability and somatic complaints on tinnitus-related distress were mediated by demands (i.e., the *internal perception of external* stressors). By contrast, most other effects were mediated by patients' experiences of their *internal stress reactions* – notably *emotional tension* and *worries*. We believe that *emotional tension* reflects an affective state that patients with chronic tinnitus attempt to regulate through cognitive avoidance expressing itself in high levels of worry (Borkovec et al., 2004). Clinically, this lends support to the hypothesis that the *inner experience* of distress associated with patients' broader life situations may form a primary target for case conceptualization and intervention in patients with chronic tinnitus. By contrast, patients' frequently reported emphases of somatic symptoms or external stressors should be understood as emotion regulation attempts that are possibly informed by patients' needs for interpersonal support and validation upon struggling with guilt or distress-informed ways of interpreting their internal and external worlds.

Overall, the observed interaction patterns highlight the importance of considering personality traits in interaction with state experiences when trying to explain and treat tinnitus-related distress on a general or individual level. Whilst several studies have demonstrated effects of cognitive-behavioral therapy (CBT) interventions that included "stress management" techniques (Cima et al., 2014), the individual conceptualization of perceived "stress" in the context of dispositional personality traits appears crucial in understanding and meeting the needs of patients with chronic tinnitus. These idiosyncratic conceptualizations ought to consider *individual interactions of early experiences* *and personality traits, and their situational activation and expression across different stimulus-processing contexts that may include, but are not limited to the tinnitus sound* thus allowing for individualized case conceptualizations and derived treatment strategies.

Psychological interventions that aim to encourage and facilitate emotional expression and -regulation may successfully reduce "emotional tension" thus providing a protective shield in the face of perceived stressors – even in the face of more stable personality traits indicating high vulnerability. Crucially, psychological interventions should focus on the *symptom function*, *affective states* and *difficulties in emotion regulation* that are likely to underlie observed (and commonly reported) worries about the tinnitus sound – and not necessarily attempt to address the worries' content "at face value" only. If indicated, treatment approaches should further address personality factors that predispose individuals to reacting toward a broad range of stimuli with high levels of perceived distress. There is now good evidence that personality factors continue to change in adulthood (Roberts and Mroczek, 2008) and psychological treatment approaches for personality problems have shown considerable effects (Cristea et al., 2017). Here, treatment frameworks that are based on third-generation behavior therapy models such as Compassion-Focused Therapy (CFT; Gilbert, 2010) or Schema Therapy (Young et al., 2003) provide useful bases for addressing more engrained stimulus-processing patterns and have been shown to meaningfully improve depression and anxiety-related difficulties (Leaviss and Uttley, 2015; Taylor et al., 2017). Although these approaches have not yet been trialed in patients with chronic tinnitus, preliminary evidence suggests their potential conceptual relevance in patients with somatization disorder (e.g., Davoodi et al., 2018); however, respective research strands are in their infancy.

Limitations

The current study has several limitations: in comparing patients' ratings with the general population, it cannot be ruled out, that a proportion of the FPI-R reference population might have also suffered from tinnitus symptomatology. However, the representative sample was normed against criteria including "state of health," "chronic illness," "hospital admissions," "doctor appointments," and "psychological therapy," rendering an above-chance proportion of chronic tinnitus patients unlikely to have been included. Moreover, whilst clinically common, the subdivision of patients into subgroups with compensated vs. decompensated tinnitus yields several disadvantages. These include, for example, the loss of statistical information and potential miscategorizations of patients close to the cut-off point as different rather than similar (Purgato and Barbui, 2013). The mediation analyses, by contrast, conceptualize tinnitus-related distress as a continuous variable. Owing to the cross-sectional design of the study, however, temporal lags between the formation of personality traits and their interaction with currently perceived stress cannot be established. Similarly, mediation analyses neither imply nor allow for assumptions of causality. Intercorrelations between habitual processing styles and state perceived stress variables are likely confounded; however, provide two different-yet-related targets for reducing tinnitus-related distress within psychological treatment frameworks.

CONCLUSION

Individual personality traits and their differential interactions with subjective experiences of internal or external stimulus-processing contexts provide valuable targets for assessments, case-conceptualizations, and treatments of patients with chronic tinnitus. Whilst the literature on personality factors and tinnitus-related distress is mixed, theorization and empirical investigation of vulnerability-stress models offers a more nuanced and ultimately more meaningful way of modeling and predicting tinnitus-related distress within a broader psychological conceptualization framework. Moreover, psychological trait x state models offer helpful ways of identifying and clustering patient-subpopulations that may benefit from respectively matched treatment protocols. Future studies ought to conceptualize tinnitus-related distress and psychological trait and state variables as continuous, interacting factors in order to predict, prevent or treat maladaptive exacerbations of psychological distress pathways.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Charité Universitätsmedizin Berlin EA 1/115/15. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

RB: literature review, data analysis, data interpretation, and co-wrote article (Introduction, Materials and Methods, and Results). BB: literature review, devised data analysis strategy, data analysis, data interpretation, wrote substantive section of article (Abstract, Introduction, Materials and Methods, and Discussion), and addressed reviewer comments. PB: idea for study conceptualization/design, first data analysis, and commented on previous draft of the manuscript. RG: responsible for data collection. BM: idea for study conceptualization/design, supervision of publication, and head of department.

REFERENCES

Almeida, D. (2005). Resilience and vulnerability to daily stressors assessed via diary methods. *Curr. Dir. Psychol. Sci.* 14, 64–68.

Andersson, G., Airikka, M. L., Buhrman, M., and Kaldo, V. (2005). Dimensions of perfectionism and tinnitus distress. *Psychol.Health Med.* 10, 78–87.

Asanger, R., and Wenninger, G. (1999). *Handwörterbuch Psychologie*. Weinheim: Beltz.

Bartels, H., Pedersen, S., van der Laan, B., Staal, M., Albers, F., and Middel, B. (2009). The impact of type D personality on health-related quality of life in tinnitus patients is mainly mediated by anxiety and depression. *Otol. Neurotol.* 31, 11–18. doi: 10.1097/MAO.0b013e3181bc3dd1

Biesinger, E., Heiden, C., Greimel, V., Lendle, T., Höing, R., and Albegger, K. (1998). Strategien in der ambulanten behandlung des Tinnitus. *HNO* 46, 157–169.

Boecking, B., Brüggemann, P., and Mazurek, B. (2019). Tinnitus: psychosomatische aspekte. *HNO* 67, 137–152.

Bolger, N., and Zuckerman, A. (1995). A framework for studying personality in the stress process. *J. Personal. Soc. Psychol.* 69, 890–902.

Borkovec, T., Alcaine, O., and Behar, E. (2004). "Avoidance theory of worry and generalized anxiety disorder," in *Generalized Anxiety Disorder: Advances in Research and Practice*, eds R. Heimberg, C. Turk, and D. Mennin, (New York, NY: Guilford Press), 77–108.

Boyce, P., Parker, G., Barnett, B., Cooney, M., and Smith, F. (1991). Personality as a vulnerability factor to depression. *Br. J. Psychiatry* 159, 106–114.

Chung, J. H., Byun, H., Lee, S. H., Park, C. W., and Jang, E. Y. (2017). Temperament and character traits in patients with tinnitus: a prospective case series with comparisons. *Clin. Otolaryngol.* 42, 397–403. doi: 10.1111/coa.12805

Cima, R., Andersson, G., Schmidt, C., and Henry, J. (2014). Cognitive-behavioral treatments for tinnitus: a review of the literature. *J. Am. Acad. Audiol.* 25, 29–61. doi: 10.3766/jaaa.25.1.4

Cristea, I. A., Gentili, C., Cotet, C. D., Palomba, D., Barbui, C., and Cuijpers, P. (2017). Efficacy of psychotherapies for borderline personality disorder: a systematic review and meta-analysis. *JAMA Psychiatry* 74, 319–328.

Davoodi, E., Wen, A., Dobson, K. S., Noorbala, A. A., Mohammadi, A., and Farahmand, Z. (2018). Early maladaptive schemas in depression and somatization disorder. *J. Affect. Disord.* 235, 82–89. doi: 10.1016/j.jad.2018.04.017

Dehkordi, M. A., Javanbakht, M., Moghadam, S., Meshkat, M., and Abolbashari, S. (2015). Personality Traits in Patients with Subjective Idiopathic tinnitus. *Iran. J. Otorhinolaryngol.* 27, 369–375.

Deutsche Gesellschaft für Hals-Nasen-Ohren-Heilkunde Kopf- und Hals-Chirurgie (2015). *S3-Leitlinie 017/064: Chronischer Tinnitus. Frankfurt/Main: Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e. V*. German: AWMF.

Durai, M., O'Keffe, M. G., and Searchfield, G. (2017). The personality profile of tinnitus sufferers and a nontinnitus control group. *J. Am. Acad. Audiol.*28, 271–282. doi: 10.3766/jaaa.15103

Durai, M., and Searchfield, G. (2016). Anxiety and depression, personality traits relevant to tinnitus: a scoping review. *Int. J. Audiol.* 55, 605–615. doi: 10.1080/14992027.2016.1198966

Fahrenberg, J., Hampel, R., and Selg, H. (2010). *Freiburger Persönlichkeitsinventar (FPI-R). 8., Erweiterte Auflage. Manual*. Göttingen: Hogrefe.

Flett, G., Hewitt, P., Garshowitz, M., and Martin, T. (1997). Personality, negative social interactions, and depressive symptoms. *Can. J. Behav. Sci.* 29, 28–37.

Fliege, H., Rose, M., Arck, P., Walter, O., Kocalevent, R.-D., Weber, C., et al. (2005). The perceived stress questionnaire (PSQ) reconsidered: validation and reference values from different clinical and healthy adult samples. *Psychosom. Med.* 67, 78–88.

Flor, H. (1991). *Psychobiologie des Schmerzes*. Bern: Huber.

Gilbert, P. (2010). *The Compassionate Mind*. London: Constable & Robinson.

Goebel, G., and Hiller, W. (1998). *Tinnitus-Fragebogen. Ein Instrument zur Erfassung von Belastung und Schweregrad bei Tinnitus*. Göttingen: Hogrefe.

Graul, J., Klinger, R., Greimel, K. V., Rustenbach, S., and Nutzinger, D. O. (2008). Differential outcome of a multimodal cognitive-behavioral inpatient treatment for patients with chronic decompensated tinnitus. *Int. Tinnitus J.* 14, 73–81.

Haider, H., Bojić, T., Ribeiro, S., Paço, J., Hall, D., and Szczepek, A. (2018). Pathophysiology of subjective tinnitus: triggers and maintenance. *Front. Neurosci.* 12:866. doi: 10.3389/fnins.2018.00866

Hasson, D., Theorell, T., Bergquist, J., and Canlon, B. (2013). Acute stress induces hyperacusis in women with high levels of emotional exhaustion. *PLoS One* 8:e52945. doi: 10.1371/journal.pone.0052945

Hayes, A. (2018). *Introduction to Mediation, Moderation, and Conditional Process Analysis. A Regression-Based Approach*, 2nd Edn. New York, NY: Guildford Press.

Hébert, S., Canlon, B., and Hasson, D. (2012). Emotional exhaustion as a predictor of tinnitus. *Psychother. Psychosom.* 81, 324–326.

Heinecke, K., Weise, C., Schwarz, K., and Rief, W. (2008). Physiological and psychological stress reactivity in chronic tinnitus. *J. Behav. Med.* 31, 179–188. doi: 10.1007/s10865-007-9145-0

Hentrich, S., Zimber, A., Sosnowsky-Waschek, N., Kellner, M., and Petermann, F. (2016). Wechselwirkungen zwischen Arbeit, Persönlichkeit und psychischer Gesundheit Vulnerabilitäts- und Resilienzfaktoren bei der Entstehung von Burnout und depressiven Symptomen bei Führungskräften. *Z. Psych. Psychol. Psychother.* 64, 299–309.

Hutchinson, J., and Williams, P. (2007). Neuroticism, daily hassles, and depressive symptoms: an examination of moderating and mediating effects. *Personal. Individ. Differ.* 42, 1367–1378.

Jacob, G. A., and Arntz, A. (2013). Schema therapy for personality disorders-A review. *Int. J. Cogn. Ther.* 6, 171–185.

James, L. R., and Brett, J. M. (1984). Mediators, moderators, and tests for mediation. *J. Appl. Psychol.* 69, 307–32.

Judd, C. M., and Kenny, D. A. (1981). Process analysis: estimating mediation in treatment evaluations. *Eval. Rev.* 5, 602–619.

Kocalevent, R., Levenstein, S., Fliege, H., Schmid, G., Hinz, A., Brähler, E., et al. (2007). Contribution to the construct validity of the perceived stress questionnaire from a population-based survey. *J. Psychosom. Res.* 63, 71–81.

Kotov, R., Gamez, W., Schmidt, F., and Watson, D. (2010). Linking "big" personality traits to anxiety, depressive, and substance use disorders: a meta-analysis. *Psychol. Bull.* 136, 768–821. doi: 10.1037/a0020327

Langguth, B., Kleinjung, T., Fischer, B., Hajak, G., Eichhammer, P., and Sand, P. (2007). Tinnitus severity, depression, and the big five personality traits. *Prog. Brain Res.* 166, 221–225.

Leaviss, J., and Uttley, L. (2015). Psychotherapeutic benefits of compassion-focused therapy: an early systematic review. *Psychol. Med.* 45, 927–945. doi: 10.1017/S0033291714002141

Linton, S. (2000). A review of psychological risk factors in back and neck pain. *Spine* 25, 1148–1156.

McCormack, A., Edmondson-Jones, M., Fortnum, H., Dawes, P., Middleton, H., Munro, K., et al. (2014). The prevalence of tinnitus and the relationship with neuroticism in a middle-aged UK population. *J. Psychosom. Res.* 76, 56–60. doi: 10.1016/j.jpsychores.2013.08.018

Mucci, S., Geocze, L., Abranches, D. C., Antúnez, A. E., and Penido Nde, O. (2014). Systematic review of evidence on the association between personality and tinnitus. *Braz. J. Otorhinolaryngol.* 80, 441–447. doi: 10.1016/j.bjorl.2014.05.031

Peerenboom, L., Collard, R., Naarding, P., and Comijs, H. (2015). The association between depression and emotional and social loneliness in older persons and the influence of social support, cognitive functioning and personality: a cross-sectional study. *J. Affect. Disord.* 182, 26–31. doi: 10.1016/j.jad.2015.04.033

Purgato, M., and Barbui, C. (2013). Dichotomizing rating scale scores in psychiatry: a bad idea? *Epidemiol. Psychiatry Sci.* 22, 17–19. doi: 10.1017/S2045796012000613

Roberts, B. W., and Mroczek, D. (2008). Personality trait change in adulthood. *Curr. Dir. Psychol. Scie.* 17, 31–35.

Sahlsten, H., Taiminen, T., Karukivi, M., Sjösten, N., Nikkilä, J., Virtanen, J., et al. (2018). Psychiatric (Axis I) and personality (Axis II) disorders and subjective psychiatric symptoms in chronic tinnitus. *Int. J. Audiol.* 57, 302–312. doi: 10.1080/14992027.2017.1409440

Sawilowsky, S. (2009). New effect size rules of thumb. *J. Mod. Appl. Stat. Methods* 8, 597–599.

Schaaf, H., Dölberg, D., Seling, B., and Märtner, M. (2003). Komorbidität von Tinnituserkrankungen und psychiatrischen Störungen. *Der Nervenarzt* 74, 72–75.

Schaaf, H., Flohre, S., Hesse, G., and Gieler, U. (2014).Chronic stress as an influencing factor in tinnitus patients. *HNO* 62, 108–114

Scott, B., and Lindberg, P. (2000). Psychological profile and somatic complaints between help-seeking and non-help-seeking tinnitus subjects. *Psychosomatics* 41, 347–352.

Stobik, C., Weber, R. K., Münte, T. F., Walter, M., and Frommer, J. (2005). Evidence of psychosomatic influences in compensated and decompensated tinnitus. *Int. J. Audiol.* 44, 370–378.

Strumila, R., Lengvenyte, A., Vainutiene, V., and Lesinskas, E. (2017). The role of questioning environment, personality traits, depressive and anxiety symptoms in tinnitus severity perception. *Psychiatr. Q.* 88, 865–877. doi: 10.1007/s11126-017-9502-2

Taylor, C. D., Bee, P., and Haddock, G. (2017). Does schema therapy change schemas and symptoms? A systematic review across mental health disorders. *Psychol. Psychother.*90, 456–479.

Trevis, K., McLachlan, N., and Wilson, S. (2018). A systematic review and meta-analysis of psychological functioning in chronic tinnitus. *Clin. Psychol. Rev.* 60, 62–86. doi: 10.1016/j.cpr.2017.12.006

Vinkers, C., Joëls, M., Milaneschi, Y., Kahn, R., Penninx, B., and Boks, M. (2014). Stress exposure across the life span cumulatively increases depression risk and is moderated by neuroticism. *Depress. Anxiety* 31, 737–745. doi: 10.1002/da.22262

Vogt, K. S., and Norman, P. (2018). Is mentalization—based therapy effective in treating the symptoms of borderline personality disorder? A systematic review. *Psychol. Psychother.*.92, 441–464.

Wallhäusser-Franke, E., Delb, W., Balkenhol, T., Hiller, W., and Hörman, K. (2014). Tinnitus-related distress and the personality characteristic resilience. *Neural. Plasticity* 2014:370307. doi: 10.1155/2014/370307

Wallhäusser-Franke, E., Repik, I., Delb, W., Glauner, A., and Hörmann, K. (2015). Langzeit-Entwicklung von akutem Tinnitus. *Laryngorhinootologie* 94, 759–769.

Weber, J., Jagsch, R., and Hallas, B. (2008). The relationship between tinnitus, personality and depression. *Z. Psychosom. Med. Psychother.* 54, 227–240.

Welch, D., and Dawes, P. J. (2008). Personality and perception of tinnitus. *Ear. Hear.* 29, 684–692. doi: 10.1097/AUD.0b013e318177d9ac

Wittchen, H., and Hoyer, J. (2011). *Klinische Psychologie & Psychotherapie.* Heidelberg: Springer-Verlag.

Yang, L., Wang, Y., and Deng, J. (2013). Relationship among perfectionism, stress and depression. *Chin. J. Clin. Psychol.* 21, 272–276.

Yang, L., Qi, Z., and Deng, J. (2013). A study on the mediating effect of daily hassles between perfectionism and depression. *Chin. J. Clin. Psychol.* 21, 95–100.

Young, J., Klosko, J., and Weishaar, M. (2003). *Schema Therapy: A Practitioner's Guide*. New York, NY: Guildford Press.

Zeman, F., Koller, M., Schecklmann, M., Langguth, B., and Landgrebe, M. (2012). Tinnitus assessment by means of standardized self-report questionnaires: psychometric properties of the Tinnitus Questionnaire (TQ), the tinnitus handicap inventory (THI), and their short versions in an international and multi-lingual sample. *Health Q. Life Outcomes* 10:128. doi: 10.1186/1477-7525-10-128

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

APPENDIX

TABLE A1 | Path coefficients, confidence intervals and indirect effects for mediation analyses with FPI-R [independent variables], PSQ20 [mediators] and TQ total score indices [dependent variable].

	FPI-E	PSQ20	Path *a*	*LLCI*	*ULCI*	Path *b*	*LLCI*	*ULCI*	*ab*	*LLCI*	*ULCI*	Path *c*	*LLCI*	*ULCI*	Path *c'*	*LLCI*	*ULCI*
Excitability		total	0.0381	0.0264	0.0497	36.7785	21.0639	52.4931	1.4001	0.7353	2.1866	2.0471	1.0468	3.0473	0.6470	−0.4408	1.7349
		worries	0.0414	0.0276	0.0551	28.8191	15.3195	42.3186	1.1919	0.6227	1.9099	2.0471	1.0468	3.0473	0.8552	−0.2235	1.9339
		tension	0.0419	0.0274	0.0565	28.7590	16.0916	41.4264	1.2057	0.6152	1.9383	2.0471	1.0468	3.0473	0.8414	−0.2153	1.8982
		joy	−0.0399	−0.0543	−0.0254	−19.8637	−33.2608	−6.4666	0.7916	0.1728	1.5300	2.0471	1.0468	3.0473	1.255	0.1543	2.3566
		demands	0.0359	0.0193	0.0525	16.6896	4.9618	28.4114	0.5997	0.1297	1.1395	2.0471	1.0468	3.0473	1.4474	0.3933	2.5015
Aggressiveness		worries	0.0221	0.0020	0.0422	34.2950	22.3140	46.2761	0.7576	0.0367	1.6186	0.7878	−0.5889	2.1645	0.0302	−1.1960	1.2564
Strain		total	0.0456	0.0388	0.0523	37.3904	15.1495	59.6312	1.7032	0.6465	2.8026	2.0217	1.2364	2.8070	0.3185	−0.9405	1.5774
		worries	0.0435	0.0337	0.0534	24.7134	9.3000	40.1269	1.0760	0.3779	1.8164	2.0217	1.2364	2.8070	0.9457	−0.0614	1.9528
		tension	0.0521	0.0432	−0.0610	26.8539	9.7738	43.9340	1.3981	0.5777	2.3826	2.0217	1.2364	2.8070	0.6230	−0.5421	1.7881
Somatic complaints		total	0.0474	0.0317	0.0631	23.8626	10.0870	37.6382	1.1313	0.4422	1.8991	4.3041	3.1714	5.4367	3.1727	1.9154	4.4301
		worries	0.0537	0.0355	0.0720	18.2776	6.2707	30.2844	0.9821	0.3330	1.7301	4.3041	3.1714	5.4367	3.3220	2.0570	4.5870
		tension	0.0575	0.0386	0.0764	18.3932	6.8327	29.9537	1.0581	0.4651	1.7433	4.3041	3.1714	5.4367	3.2460	1.9745	4.5175
		demands	0.0412	0.0188	0.0636	11.9519	1.9955	21.9082	0.4921	0.0805	1.0327	4.3041	3.1714	5.4367	3.8120	2.6321	4.9919
Emotionality		total	0.0456	0.0380	0.0533	23.0133	2.9236	43.1031	1.0500	0.0164	1.9647	2.5071	1.7300	3.2842	1.4571	0.2657	2.6484
		tension	0.0504	0.0402	0.0606	18.0812	3.1095	33.0529	0.9109	0.1592	1.6423	2.5071	1.7300	3.2842	1.5962	0.5264	2.6661

All analyses were computed using the PROCESS macro (Hayes, 2018); resampling procedures (bootstrapping) comprised 10000 replicates. LLCI = Lower level confidence interval (95%), ULCI = Upper level confidence interval (95%). Path a denotes the effect of the independent variable on the mediator; path b the effect of the mediator on the dependent variable; ab denotes the product term, i.e., indirect effect. Path c denotes the total effect of the independent variable on the dependent variable; path c′ the direct effect; i.e., the total effect adjusted for ab.

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Body-Centered Interventions for Psychopathological Conditions: A Review

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World-wide, billions of dollars are spent each year on body-centered interventions to alleviate both physical and psychological pathologies. Given the high demand and increasing popularity of body-centered interventions, there is need for a systematic organization of empirical evidence associated with body-centered therapies. This article reviews the psychological effects of body-centered interventions on emotional well-being, including both self and other-administered (receptive) therapies. Theory behind body-centered interventions rely upon the bidirectional communication pathway between the brain and body. We investigated the bidirectional communication pathway between the brain and body by evaluating evidence across multiple body-centered therapies. The research reviewed includes studies that investigate effects of massage therapy, reflexology, acupuncture, functional relaxation, emotional freedom technique, Rolfing, yoga, tai-chi, and dance/movement therapy on psychological conditions across the lifespan. Results demonstrated that overall, massage therapy, tai-chi, dance/movement therapy, functional relaxation, reflexology, acupuncture and emotional freedom technique seem to alleviate stress, depression, anxiety, bipolar disorder and facilitate pain reduction. Of these, the most robust evidence available was for massage therapy, indicating it is an effective intervention for numerous age groups and populations. Rolfing and reflexology had the least amount of support, with few studies available that had small sample sizes. Although these conclusions are limited by scarcity of high-quality empirical data and contradictory findings, available evidence indicates that body-centered interventions can be effective in reducing psychopathology and supports the proposed mechanism of the bidirectional pathway between the brain and body: the body holds the potential to influence the mind. Integrating body-centered therapies in both clinical settings and as self-care could lead to better outcomes. Lastly, we propose the first taxonomy of body-centered interventions and empirical evidence of their effectiveness for clinicians and researchers.

Keywords: body-centered, interventions, taxonomy, brain-body communication, therapies alternatives

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INTRODUCTION

Body-centered therapies and interventions have always been an integral part of traditional medical systems. Restoration of the balance between bodily humors and Nature were important to Hippocrates (460-377 B.C.) and ancient Greek physicians who believed in the healing effect of laying-on-of-hands and the importance of touch (Calvert, 2002). Later in Rome, Asclepiades promoted naturalistic therapeutic methods such as a healthy diet, massage and physical exercise. Healing through a holistic approach of integrating mind and body was also emphasized in the Traditional Chinese Medicine (Abbott and Lavretsky, 2013), Ayurveda (Mishra et al., 2001), and Traditional Arabic and Islamic Medicine (Al-Rawi and Fetters, 2012).

Much of the developing world continues to rely on traditional medical practices (World Health Organization, 2013, 2019), and in Western countries, a majority of the population has utilized some form of complementary medicine including body-centered therapies in lieu of or in conjunction with conventional biomedical interventions for both emotional and physical relief (Tracy et al., 2005). The 2007 National Health Interview Survey found that Americans spent $33.9 billion in the previous year on complementary or alternative medicine practices which include numerous body-centered interventions such as yoga, tai-chi, Qi Gong and relaxation techniques (Barnes et al., 2009). On massage therapy alone, Americans spent more than $14.2 billion and in total, $11.9 billion was spent on complementary practitioner visits, which amounts to one-quarter of total out-of-pocket spending on physician visits for the year. Given the high demand and increasing popularity of body-centered interventions, there is need for a systematic organization of empirical evidence associated with body-centered therapies (Röhricht, 2009). This review synthesizes the empirical evidence of major body-centered interventions and their effectiveness on psychological conditions and mental health, crafting a taxonomy of these heterogeneous somatic interventions.

The central nervous system's control of the body and somatic functioning forms the basis for understanding the etiology and treatment of diseases in the modern biomedical system. Typical treatment of a disease, after diagnosis, entails matching the condition with the appropriate therapy or intervention. A particular psychological condition is most likely treated with a psychological therapy while a physical ailment involves direct intervention of the body (see **Figure 1A**). Research and practice of clinical psychology and psychiatry tend to focus on the impact of the brain/mind on mental states (e.g., Cognitive Behavioral Therapy for depression). The impact of changing cognitive framework on the body (e.g., Cognitive Behavioral Therapy to reduce stress response or chronic pain) has also been studied extensively (Cherkin et al., 2016). However, the effects of body-centered therapies on mental states have not been extensively studied even though the benefits of physical exercise on neuroplasticity, cognition and mood have been demonstrated (Salmon, 2001; Hötting and Röder, 2013). To summarize, the literature on the role of the brain/mind-based therapies on psychological disorders is robust. The literature on the role of the brain/mind-based therapies on the body is also quite robust. However, the literature on the role of body-centered therapies on psychological disorders is not well defined; this is the focus of our review.

Most of the abovementioned therapies assume that the relationship between the body and the brain is unidirectional—the brain controls and influences the body. However, there is growing evidence that there exists a communication pathway between the brain and body that is not limited to one direction but rather, is bidirectional; the brain not only influences and controls the body but the body communicates to the brain (Lutz et al., 2007). One theory behind body-centered interventions relies upon this bidirectional relationship between the brain and body suggesting that through the body one can alter or influence the brain and emotions yielding positive health benefits. These bidirectional communications (i.e., from the brain to the body, and from the body to the brain) are thought to takes place via three routes: the autonomic nervous system, the endocrine system and the immune system (Lutz et al., 2007). In this review, we aimed to expand our understanding of the bidirectional communication pathway between the brain and the body by focusing on the crucial influence of the body on the brain and presenting evidence across multiple body-centered interventions. With this goal, we investigated the effectiveness of body-centered, somatic interventions upon psychopathology.

To accomplish this goal, we developed a taxonomy of body-centered interventions and evaluate existing empirical evidence for each of them regarding *psychological* benefits. We organized each therapy according to three different factors: movement, method, and tactile involvement. The first factor of utilization of movement (or lack of movement) is important for physicians and patients who are seeking a body-centered therapy but cannot generate somatic movements. In this way, distinctions between movement and non-movement therapies is critical. Next, each body-centered intervention was further classified according to the administration method: delivered by another person or through self-administration. This categorization was employed because there are different known neurological effects for active versus passive movements (Shimada et al., 2010). Finally, each body-centered intervention was grouped according to tactile involvement—the therapy either utilizes touch or is non-tactile. Again, this categorization is important because (as we discuss below) traumatic events hold the potential to create touch-aversion (Rothschild, 2014). Lastly, for each body-centered intervention, definitions, quality of available empirical evidence, and proposed or known mechanisms were expounded (see **Figure 1B**).

Literature searches and the procuring of research articles were conducted with PubMed, Web of Science and Google Scholar. Priority was given to meta-analyses and Cochrane reviews above individual empirical studies.

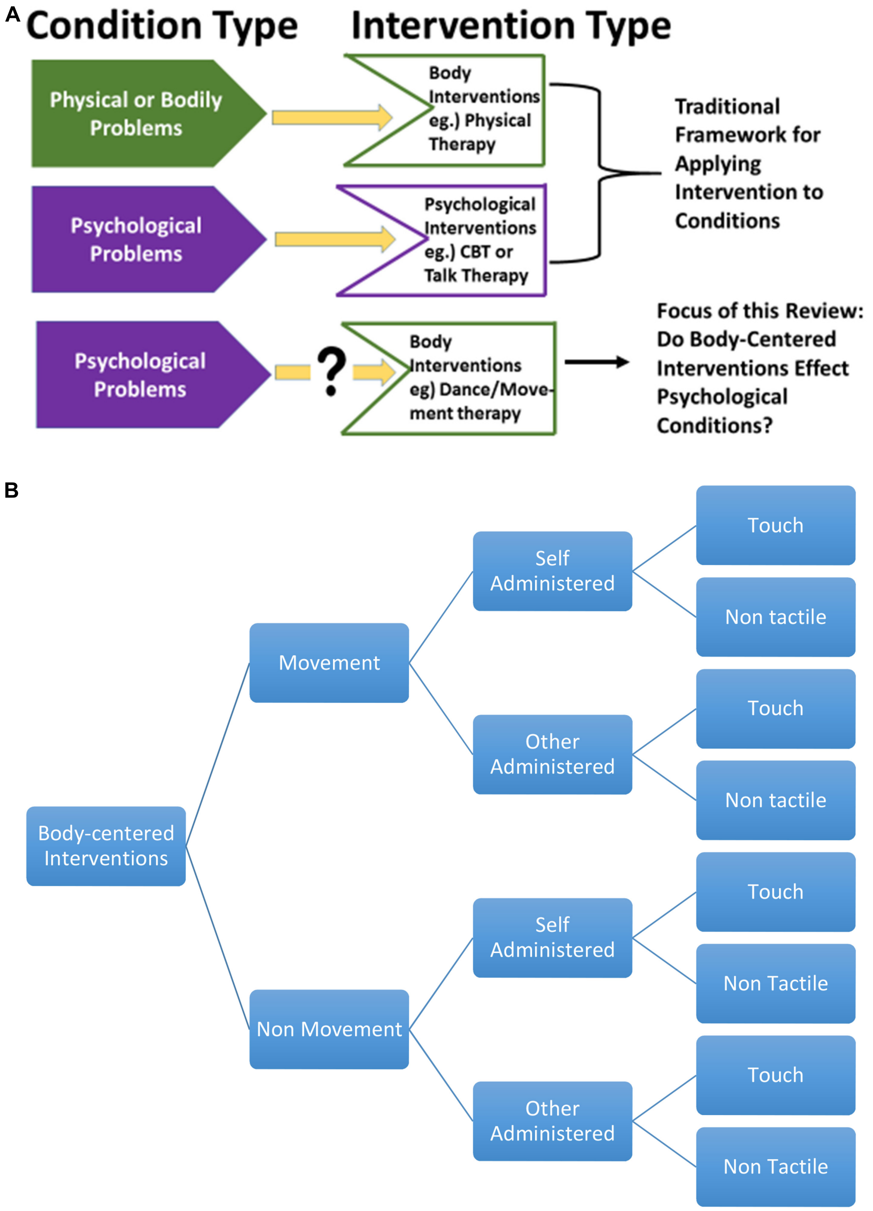

FIGURE 1 | (A) Mind-body targeted interventions. **(B)** Classification of psychological and body-centered interventions.

NON-MOVEMENT THERAPIES

Massage Therapy: Tactile, Other-Administered

Massage therapy is the manual manipulation of soft tissue for healing or well-being (Moyer et al., 2004) and has been shown to alleviate a variety of symptoms across the lifespan from premature infants to the elderly (Field, 2014; Nakano et al., 2019). Its effectiveness has been demonstrated for migraines, depression, asthma, low-birth weight in infants, general pain reduction, fibromyalgia, high blood pressure, stress reduction, and overall increase in well-being and immune functioning (Cady and Jones, 1997; Field, 1998; Moyer et al., 2004; Ernst et al., 2007; Russell et al., 2008; Lee et al., 2010; Li et al., 2014). Additionally, it is effective at reducing pain in cases of physical injury or surgery (Diego et al., 2002; Hernandez-Reif et al., 2005; Bauer et al., 2010; Cutshall et al., 2010), and enhancing immunological function with the added benefit of simultaneously reducing negative emotional symptomology such as anxiety, depression and anger (Cassileth and Vickers, 2004; Hernandez-Reif et al., 2004; Kutner et al., 2008; Ernst, 2009). Thus, massage therapy carries a twofold physical and emotional benefit; it alleviates not only somatic symptomology but enhances psychological well-being.

The twofold physical and emotional pain alleviating attribute of massage therapy makes sense in light of the underlying circuitry involved in the brain's representation of pain. Neuroimaging reveals that the circuitry involved in induction of both emotional pain, such as social rejection, and physical pain evoke activation of similar neurological regions (Eisenberger and Lieberman, 2004). In both situations, the dorsal subdivision of the anterior cingulate cortex, areas 240 and 320, and right ventral prefrontal cortex are activated (Eisenberger et al., 2003). Neurologically, both social/emotional and physical pain involve similar neural processes, suggesting that the activation of pain, rather than the source, is the key. In the brain, pain is recognized as pain regardless of its source, be it emotional or physical. However, only social pain involves the reliving of this pain each time memory is recalled (Chen et al., 2008; Jin and Josephs, 2016). This physical-social pain overlap in the brain becomes important when evaluating the effectiveness and mechanisms of massage therapy. Due to the neurological overlap in the brain in perceiving both emotional and physical pain, massage therapy's twofold effectiveness at relieving physical pain and enhancing emotional well-being is expected.

Massage Therapy for Infants and Children

The benefits of massage therapy are not limited to the adult population but extend to both children and elderly persons. Massage therapy for infants has generated much research in the previous three decades demonstrating a significant decrease in physical and emotional stress. Following intervention, preterm infants demonstrate an increase in insulin and insulin-like growth factor 1 (Field et al., 2008), increase in body temperature (Diego et al., 2008), alleviation of sleep problems (Field and Hernandez-Reif, 2001; Mindell et al., 2018), and reduction in stress by means of increased vagal tone (Field et al., 2010a) and increase in triglycerides, an important benefit for premature infants (Field et al., 1996, 2010b; Field, 2019). Due to the number of benefits and its effects on physical and emotional states, massage could be utilized to facilitate emotional regulation in infants.

For older children, massage therapy has been used as either a supplemental or alternative treatment for asthma, autism and ADHD. Both children with ADHD and autism benefited from massage therapy and exhibit a decrease in anxiety and cortisol levels and increase in overall positive mood and attention; also, in both groups, teachers and parents report better communication and task-oriented attention (Field et al., 1998; Escalona et al., 2001; Khilnani et al., 2003). Other studies show that asthmatic children demonstrate an immediate decrease in cortisol, behavioral anxiety and increase in pulmonary functioning following massage therapy (Field, 1998; Moyer et al., 2004; Abdel Fattah and Hamdy, 2011).

A handful of studies that have investigated the benefits of massage therapy on elderly and found that hand massage therapy immediately and significantly reduced aggressiveness in nursing home residents compared to music therapy alone (Remington, 2002). Massage therapy also significantly reduced anxiety and depression and increased well-being, general health and perceived stress compared to guided relaxation (Sharpe et al., 2007).

Mechanisms

Possible mechanisms by which massage therapy induces these emotional and biophysiological changes have been proposed. Some suggest that pressure applied during massage stimulates parasympathetic activity and/or increases vagal tone (Diego et al., 2004; Moyer et al., 2004). Increasing vagus nerve stimulation, also known as the tenth Cranial Nerve, and consequently reducing symptoms of psychopathology aligns with previous research investigating respiratory sinus arrhythmia (RSA), the online biomarker of parasympathetic functioning (Beauchaine, 2015). According to the Polyvagal theory (Porges, 1985, 1995, 2007, 2011), the vagus nerve (measured via RSA functioning) serves as the critical mechanism of attention, emotion, self-regulation, communication, social behavior and adaptability. Consequently, the vagus nerve is operative in multiple psychopathological conditions (Beauchaine and Thayer, 2015). The proposed mechanism is that massage increases vagal functioning which is a means of increasing parasympathetic function and ameliorating symptoms associated with dysregulated autonomic activity.

Field (2010) suggested that the pain-relieving property of massage therapy is attributed to a reduction in substance P and increase in serotonin and highlights that the overall benefits of positive touch include specific physiological changes. Others suggest that possible changes in body chemistry, such as the release of the endorphin serotonin into the bloodstream, ameliorates pain and provides feelings of relief or well-being (Andersson and Lundeberg, 1995).

Price (2007) argues that in adults, the therapeutic recovery process is intrinsically related to the integration of the self, specifically the integration of sensory and emotional experience. She argues that as a protective mechanism, victims of abuse (i.e., sexual abuse) dissociate these aspects of the self, derailing healthy functioning in adulthood. Consequently, massage therapy is used as a means of integrating the individual's emotional and somatic experiences, catalyzing greater awareness of both phenomena. Field et al. (1997) demonstrated that massage therapy mitigates the effects of sexual abuse such as decreasing cortisol, depression, and anxiety. At the end of 1 month receiving massages, women with a history of sexual abuse exhibited a 31% decrease in urine cortisol levels, even in the midst of on-going life stresses.

Whereas more research is needed to investigate the emotional and somatic integration of massage therapy and possible mechanisms, there is growing evidence that massage therapy does increase serotonin and decrease cortisol yielding an alleviation of negative emotional symptomology such as depression, anger and enhancement of positive mood (Field et al., 2005; Field, 2010). However, more research is necessary to establish the dosage (or amount) and type (hand, foot, etc.) of massage therapy that is needed for each population and/or condition. In addition, most massage studies utilize cross-sectional rather than longitudinal designs and consequently, the durations of massage therapies effects are not established. Further, if massage therapy is to be implemented as a supplementary therapy, that is, a therapy that is given in addition to typical biomedical practices, more research is needed to understand possible interactions between massage therapy and other interventions such as pharmacological agents, physical and nutritional therapies.

Functional Relaxation Therapy: Non-tactile, Self-Administered

Relaxation therapy is defined as a pedagogical approach toward inducing a reduction of tension without using external resources, utilizing techniques such as holding a representation, image or word in one's mind, contracting and relaxing specific muscles, breathing and sometimes, small movements or posture changes (van Dixhoorn and White, 2005). Typically taught in an intense period spanning several months, relaxation therapy can be taught individually or in a group and is often referenced as stress management, psychological or nursing intervention and to some, relaxation therapy is synonymous with meditation. However, contrary to typical meditative practices, relaxation therapy emphasizes awareness of low and high tension in daily life and coaches individuals in how to unwind from stressful episodes.

Across studies, there is a lack of precision regarding functional relaxation therapy and how it differentiates from other therapies. In addition, for those studies using functional relaxation therapy and integrating breathing techniques, the alteration of RSA needs be taken into consideration, in addition to other pathways, as the neurobiological mechanism by which symptoms are reduced.

This body-oriented psychologic therapy has been found to be effective in reducing tension headaches, non-cardiac (non-specific) chest pain, psychosomatically influenced asthmatic diseases and irritable bowel disease (Loew et al., 2000, 2001; Lahmann et al., 2008a,b, 2009). In addition to alleviating physiological symptoms, functional relaxation therapy significantly reduced anxiety and stress, both chronic and circumstantial, in the above-mentioned studies. However, more precision regarding functional relaxation therapy is needed and more random controlled trials with larger samples are needed to further investigate its effectiveness on psychological conditions.

Acupuncture: Tactile, Other-Administered

A healing modality utilized for more than 2,000 years, acupuncture is considered a premier medical skill in Eastern Asian medicine and has gained popularity in western countries in the last few decades with an estimated 3 million Americans a year pursuing acupuncture treatment (Bai and Lao, 2013). The methodology behind acupuncture includes the insertion of fine needles into an individual in specified, defined areas with the aim of relieving pain. There is evidence from animal models that demonstrate that acupuncture evokes the release of different neuropeptides, such as the analgesic adenosine, into the central nervous system. Experimental studies show that 50–70% of patients report a decrease in chronic pain after short-term acupuncture treatment (Murray, 1995). Acupuncture has been effective at reducing tension headaches/migraines, Parkinson's disease symptoms, fibromyalgia, chronic neck and back pain, osteoarthritis pain and ineffective at reducing symptoms of carpel tunnel, abdominal pain due to surgery and consistent, long-term general pain reduction (Murray, 1995; Chou et al., 2008; Reinhold et al., 2008; Plank and Goodard, 2009; Cho et al., 2012). Regarding psychopathology, acupuncture has demonstrated promising results for alleviating depression, bipolar disorder and mood associated with premenstrual disorder (Zhong et al., 2008; Dennehy et al., 2009; Zhang et al., 2010; Armour et al., 2018). Two meta-analyses demonstrated that acupuncture effectively treats major depressive disorder (MDD) and post-stroke depression (PSD) and should be considered an alternative treatment to antidepressants. Zhong and colleague's meta-analysis (2008) found that acupuncture was as effective as the antidepressant fluoxetine. Acupuncture seems to be a safe and cost-effective form of treatment for MDD, PSD and bipolar disorder but the mechanisms by which acupuncture is effective for some—either through physiological, psychological or emotional alterations—is still debatable and more research is needed to unravel its authentic effects.

One issue with acupuncture is the placebo effect and a few studies have investigated this utilizing neuroimaging. Evidence from these studies show that expectations during acupuncture or sham (placebo control) has a physiological effect on the brain network, the same network that mediates a non-specific clinical response to acupuncture (Middlekauff et al., 2001; Qin et al., 2008; Harris et al., 2009). Bai and Lao (2013) suggest that divergent neural mechanisms exist and may possibly mediate specific aspects of acupuncture effects compared to placebo effects. Consequently, because a placebo effect or psychological expectation seems to play a role in the effectiveness of acupuncture, research design and control groups pose a challenge in researching authentic benefits. Specifically, the challenge is two-fold: does the mode of stimulation or the location of the acupuncture point bear physiological/psychological effects? Further research that has control groups with less confounding variables are needed to clarify the effectiveness of acupuncture and fine-tune the populations or conditions that benefit most from this ancient therapy.

Reflexology: Tactile, Other-Administered

Reflexology requires applied pressure and manipulation of soft tissue, involving stimulation of reflex points on the feet and hands which are thought to correspond somatotopically to specific areas and organs of the body (Stephenson et al., 2007; Miller et al., 2013). Unlike acupuncture, there is less empirical evidence for the benefits and effectiveness of reflexology as an intervention. In 2007, a Cochrane review on reflexology did not find sufficient evidence to support its use and subsequent investigations after the review show conflicting evidence for its effectiveness as an alternative therapy (Wang et al., 2008; Miller et al., 2013). Some studies show that reflexology significantly decreased pain in cancer patients and women experiencing postmenstrual syndrome (Stephenson et al., 2000) and other studies show that reflexology does not have lasting effects on pain reduction (post 3 h stimulation) (Oleson and Flocco, 1993; Stephenson et al., 2003). Another study utilized the cancer patient's partner as the reflexology administer and found that cancer patients reported a significant decrease in pain intensity and anxiety (Stephenson et al., 2007). Cancer patients reported a reduction in nausea, vomiting and fatigue after reflexology treatments (Yang, 2005). A more recent study found that for psychological factors, reflexology may effectively reduce stress in pregnant women (McCullough et al., 2018). Thus, reflexology is seen as a supplemental or self-care intervention that could relieve symptoms of pain, anxiety and/or stress but conflicting evidence exists for its authentic therapeutic effectiveness and few suggest that reflexology carries long-term healing properties or should replace medical intervention (Miller et al., 2013).

Rolfing: Tactile, Other-Administered

Rolfing involves the myofascial structural integration or manipulation of muscle and soft tissue with the goal of loosening fascia layers, reposition muscles and aid body alignment (Hansen et al., 2014). Few studies have investigated the therapeutic effectiveness of Rolfing. Of these few, Weinberg and Hunt (1979) found that Rolfing helped reduce anxiety and suggests that Rolfing "releases" stored emotional tension in soft tissue. Hansen and colleague studied the effects of Rolfing on children ($n = 2$) with spastic cerebral palsy and found improvement in cadence and support time after 3 months of treatment.

Due to the scarcity of research and small sample sizes, more research is needed to investigate the effects of fascia and muscular manipulation. Some suggested hindrances to investigating Rolfing stem from a lack of congruence between the scientific and practitioner communities (Grimm, 2007). In order to further research investigating the effectiveness of Rolfing, efforts to bridge communication and cooperation between both fields is needed.

MOVEMENT THERAPIES

Dance/Movement Therapy: Tactile and Non-tactile, Other-Administered

Dance/movement therapy is one of the creative art therapies (music, art, poetry and drama therapy included) that uses movement and dance in a psychotherapeutic context, utilizing motion and emotion as a vehicle through which a person can gain a clearer definition of self (Payne, 2003). Dance/movement therapy originated in the United States in the 1940's as a mind-body medical modality. Dance/movement therapy traces its roots to ancient forms of therapy that were utilized for healing, fertility enhancement, birth, and rituals involving sickness and death (Ritter and Low, 1996). Non-invasive and cost-effective, dance/movement therapy is used as an intervention for people with an array of emotional, cognitive and physical challenges and previous history of trauma (Serlin, 2007).

In the last 50 years, most research assessing dance therapy as an effective intervention focused on qualitative descriptions and case studies, asking questions about general well-being and subjective experience. The reason for an emphasis on qualitative rather than quantitative research was attributed to the nature of the creative arts therapies, which underscores creativity and subjective ways of knowing (Koch et al., 2014).

Research shows that dance/movement therapy affects mental, emotional and physical health by means of facilitating vestibular coordination, decreasing depressive symptoms (both in clinical and subclinical populations), enhancing psychological well-being in survivors of childhood sexual abuse, reduces anxiety, facilitates heart health in chronic heart failure patients and improves overall well-being in cancer patients (Couper, 1981; Lesté and Rust, 1990; Mills and Daniluk, 2002; Koch et al., 2007; Kiepe et al., 2012; Neto et al., 2014).

Jeong et al. (2005) propose that one possible mechanism by which dance/movement therapy is an effective form of treatment is in its ability to stabilize the sympathetic nervous system. The group measured plasma serotonin and dopamine concentrations pre and post dance/movement therapy in depressed adolescents and found an increase in serotonin and decrease in dopamine, suggesting that dance therapy ameliorates depressive symptoms by means of sympathetic influence.

Others suggest dance/movement therapy works to ameliorate negative symptomology, specifically those induced from previous traumatic experiences, through the therapeutic process of integrating emotions, cognitions and movement. Pierce (2014) highlights the imperative stages of effective dance/movement therapy: the first stage incorporates establishing trust between the client and dance therapist facilitating a sense of safety and stability, the second stage involves integration of previous traumatic events and the third stage is oriented toward rehabilitation and building the relational self through the context of other dance/movement therapy group members.

Several studies have demonstrated that dance/movement therapy is particularly effective at enhancing positive mood, well-being and body image while mending negative symptomology such as depression, anxiety and loneliness (Koch et al., 2014; Ho et al., 2018; Lange et al., 2018).

Emotional Freedom Technique: Tactile, Self-Administered

Callahan (1985) originally developed a technique for self-tapping on acupuncture points as a means to decrease unwanted emotions or stress and Craig and Fowlie (1995) later simplified this method calling it the Emotional Freedom Technique (EFT) (Lint et al., 2006). This newer method involves concentrating on a specific psychological issue while simultaneously self-tapping on specified meridians on the body.

More novel than the aforementioned therapies, EFT significantly reduced symptoms in patients with PTSD. Church et al. (2013) found 90% of PTSD veterans no longer met PTSD clinical criteria with sustained effects at 3 (86%) and 6 months (80%) follow up. These findings are consistent with other studies that show positive long-term effects of EFT for trauma victims or PTSD patients (Church et al., 2009; Church, 2010).

While the mechanisms behind EFT are unknown, one study suggests that acupuncture meridians are not essential in therapeutic effectiveness. Waite and Holder (2003) found that tapping on parts of the body other than meridian points also elicited effects similar to those found in previous EFT studies. However, a more recent study found epigenetic changes may serve as the mechanisms by which EFT effectively reduces PTSD symptoms (Church et al., 2018). While more research is needed to extrapolate EFT's treatment effects and the mechanisms by which it alters symptoms, one cogent advantage of EFT is ease of administration. Intrinsically a self-administered therapy, EFT is versatile and can be self-administered in a variety of settings. This aspect of EFT must be considered when examining its effectiveness with psychological disorders. More studies are needed to investigate EFT's effectiveness upon psychopathological conditions other than stress, anxiety and trauma.

Tai-Chi: Non-tactile, Self-Administered

Originating from China, Tai-Chi is a combination of meditative movements and martial arts that utilizes slowly performed, dance-like postures and movements. Tai-Chi also integrates relaxation of muscles and breathing and incorporates mental concentration.

A meta-analysis investigating tai-chi with elderly patients found beneficial effects on measures of general psychological well-being, depression, anxiety, general stress management and exercise self-efficacy (Chou et al., 2004). Their meta-analysis included three random control trials that used depression as an outcome measure (ES = −5.97; 95% CI −7.06 to −4.87), with $I^2 = 0\%$). Other studies further support tai-chi and its effectiveness at reducing anxiety and stress (Wang et al., 2004; Taylor-Piliae et al., 2006).

Tai-chi is also effective in promoting psychological well-being across cultures, including Western and Eastern samples. Wang et al. (2010) examined quantitative effect sizes for tai-chi on several measures of psychological functioning and found moderate to large effects sizes for reduction of stress (effect size [ES], 0.66; 95% confidence interval [CI], 0.23 to 1.09), anxiety (ES, 0.66; 95% CI, 0.29 to 1.03), and depression (ES, 0.56; 95% CI, 0.31 to 0.80), and enhanced mood (ES, 0.45; 95% CI, 0.20 to 0.69).

Mechanisms

Several possible mechanisms have been suggested as neurobiological contributors to the effectiveness of tai-chi in reducing symptomatology. Because tai-chi invokes physical relaxation, changes in brain waves (Field et al., 2013), decreased systolic and diastolic blood pressure and reduced cholesterol (Ko et al., 2006; Wolf et al., 2006) are suggested. These changes to autonomic and endocrine functioning by means of tai-chi through the combination of relaxation, movement, mental concentration and agility are also influenced by physical and mental training.

In summary, tai-chi is an effective body-centered therapy at reducing the psychopathological conditions of depression and anxiety. More research is needed explore the effects of tai-chi on other conditions and the mechanisms by which tai-chi is operative.

Yoga: Non-tactile, Self-Administered

Yoga is a body-centered intervention designed to foster balance and health to the physical, mental, emotional and spiritual aspects of the individual. This body-centered intervention takes into account both physical postures, breath control, control of the senses, concentration and meditation (Ross and Thomas, 2010).

Yoga has been utilized as an alternative or complementary therapy for a variety of conditions and there exist conflicting evidence for its effectiveness at improving mental and physical health. Some populations seems to benefit from yoga, such as patients with chronic pain (Desveaux et al., 2015). A Cochrane review (Broderick et al., 2015) that included 8 studies found that yoga benefited individuals with schizophrenia on several mental health metrics including mental states (positive and negative syndrome scale), social functioning and overall quality of life but cautions results based upon low to moderate quality of evidence. They suggest there was insufficient evidence to consider yoga as superior to standard care for schizophrenics. Other Cochrane reviews support these findings regarding the limited strength of yoga in treating schizophrenia compared to standard care (Broderick and Vancampfort, 2017; Broderick et al., 2017).

Other populations seem to experience benefits that are similar to exercise alone, such as patients with bipolar disorder or lower back pain (Sherman et al., 2010; Cramer et al., 2013; Uebelacker et al., 2014). Buffart et al. (2012) found that cancer patients reported a decrease in stress and anxiety post yoga treatments and only a moderate change in fatigue, quality of life, and social and emotional functioning. Thus, both the population and disease condition in which yoga is applied seems to be a fundamental factor in determining effectiveness. More research is needed to examine those populations that seem to benefit most from yoga and more studies are needed to ascertain when alternative treatments such as exercise or meditation alone are equally as effective.

One possible factor that might explain the variability of yoga's effectiveness is the component of meditation. As seen in patients with schizophrenia, mediation can catalyze psychotic experiences by inducing hyper-awareness of one's internal state (Sethi and Bhargava, 2003; Kuijpers et al., 2007). Thus, utilizing yoga as an effective and beneficial treatment for differing conditions requires the assessment of both physical exercise and meditation upon that condition.

Basic Body Awareness Therapy: Tactile, Other Administered

Basic Body Awareness Therapy (BBAT) is a form of body physiotherapy that aims to normalize body posture and increase overall balance and awareness of the body, both in relation to others and one's environment. Common in Nordic countries, BBAT enhances awareness of one's movement with the overall aim of integrating and facilitating bodily control by means of grounding/breathing exercises, massage and movement (Gard, 2005; Eriksson et al., 2007). There exists discrepancy within the literature regarding the usage and definition of either Body Awareness Therapy (BAT) or BBAT and its administration in either an individual or group setting such as Basic Body Awareness Group Therapy (BAGT). More precise terminology is needed to differentiate between these two psychosomatic physiotherapeutic treatments. However, there does exist two

TABLE 1 | Taxonomy of body-centered interventions.

Therapy	Administration type	Tactile form	Symptoms influenced	Evidence
Movement				
Dance	Self	Both tactile and non-tactile	Enhances well-being and positive emotions, reduces negative emotions	Couper, 1981; Lesté and Rust, 1990; Mills and Daniluk, 2002; Koch et al., 2007; Kiepe et al., 2012; Neto et al., 2014
Emotional Freedom Technique	Self	Tactile	Decreases PTSD symptoms, anxiety, fear, stress	Church et al., 2009; Church, 2010
Yoga	Self	non-tactile	chronic pain reduction, increase physical health, potential to reduce stress and anxiety	Desveaux et al., 2015
Tai-Chi	Self	Non-tactile	Depression, increases general well-being	Chou et al., 2004; Field et al., 2013
Basic Body Awareness Therapy	Other	Tactile	Decrease in mood, stress-induced somatoform disorders, behavioral and personality disorders; schizophrenia; major depression and anorexia nervosa	Gyllensten et al., 2003, 2009; Hedlund and Gyllensten, 2010; Catalan-Matamoros et al., 2011; Danielsson et al., 2014
Non-movement				
Acupuncture	Other	Tactile	Reduces tension headaches/migraines, Parkinson's disease symptoms, fibromyalgia, chronic neck and back pain, osteoarthritis pain	Middlekauff et al., 2001; Qin et al., 2008; Harris et al., 2009
Functional Relaxation	Self	Non-tactile	Reduces non-specific chest pain, asthma, and tension headaches	Loew et al., 2000, 2001; Lahmann et al., 2008a, 2009
Massage	Other and Self	Tactile	Increased weight and growth in pre-term infants, decreased cortisol and dopamine, increased serotonin, increased positive mood, decreased negative emotions, decrease in stress, increase in immunological response, increase in vagal tone	Field et al., 2005, 2010b; Field, 2010
Reflexology	Other and Self	Tactile	Decreases anxiety and stress	Wang et al., 2008; Miller et al., 2013
Rolfing	Other	Tactile	Decreases anxiety, improved gait in children with spastic cerebral palsy	Weinberg and Hunt, 1979; Hansen et al., 2014

types of metrics which assess the effectiveness of BAT: the body awareness scale and the resource oriented body examination which measure body posture, muscle tension, respiration and heart palpitations (Eriksson et al., 2007).

BBAT has been effective at reducing physiological conditions such as fibromyalgia, chronic pain, irritable bowel syndrome and non-specific musculoskeletal problems (Gard, 2005; Eriksson et al., 2007) and more recent studies demonstrate potential mood altering effectiveness as well. One study found that BBAT improved major depressive symptoms (Danielsson et al., 2014) and others studies have investigated its effectiveness at reducing schizophrenic and anorexia nervosa symptoms (Hedlund and Gyllensten, 2010; Catalan-Matamoros et al., 2011). Two studies have investigated the use of BBAT in psychiatric clinics with patients who experienced mood, stress-related somatoform, behavioral and personality disorders. Both investigations found a significant decrease in symptoms and reduction in overall use and cost of psychiatric services (Gyllensten et al., 2003, 2009).

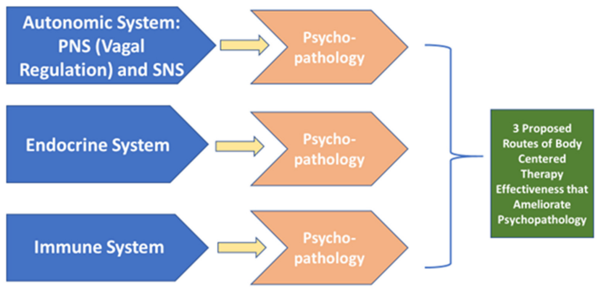

FIGURE 2 | Possible routes by which body-centered therapies operate to ameliorate psychopathology.

Thus, the administration of BBAT in psychiatric outpatient clinics seems to be the most promising line of research and more investigation is needed to evaluate its effectiveness within specific subpopulations. Further, more clarification is needed within the literature to not only define BAT or BBAT but evaluate the most effective form of BBAT as either a group or individual therapy.

CONCLUSION

This review highlights a number of different body-centered therapies, namely interventions that have generated a substantial amount of research, and their effectiveness at reducing psychopathological conditions. There are additional body-centered interventions that seem to be gaining popularity that have yet to be investigated including hakomi, concentrative movement therapy, biosynthesis therapy, and character analytic vegetotherapy. However, of the interventions reviewed here, the most robust evidence was found for massage therapy because the higher number of meta-analyses and Cochrane reviews available (Moyer et al., 2004; Field, 2010, 2014, 2016; Hillier et al., 2010; Miozzo et al., 2016). Converging evidence from these studies and meta-analyses indicate massage was an effective intervention across age, including infants—premature and full-term—and elderly patients and effectively reduces varying psychopathological symptoms. Body-centered therapies with the least amount of evidence were Rolfing and reflexology. Studies examining these interventions had smaller sample sizes and no meta-analyses were available.

Taken together, the evidence provided here indicates that certain body-centered therapies are effective at reducing certain psychopathological conditions (please refer to **Table 1**). Because there is converging evidence from several different therapies that body-centered interventions can reduce psychopathological conditions, there is evidence that suggests the body can communicate/influence the brain and alter psychopathological states. This suggests that alterations could be made to the brain and emotions by means of the body, providing some support that body-centered interventions act as effective interventions. Again, three possible routes are suggested as possible mechanisms by which the brain and body communicate: the autonomic system, the endocrine system and the immune system. We propose that if a body-centered intervention operates via one of these three routes and the targeted condition exists within these limits, a desirable health benefit could result. However, if both the targeted condition and body-centered intervention do not utilize one of these routes, then the therapy is theorized to yield ineffective results. Please see **Figure 2**.

We speculate that of the body-centered interventions mentioned that are found to be effective, the administration type seems to be critical. Self-administered therapies such as EFT, yoga, and dance therapy seem to hold two added variables that may contribute to their effectiveness: ease of administration (self) and focus of cognitive training and attention. We suggest that these additional factors may contribute to underlying mechanisms involved. Through cognitive training and attention, a possible fine-tuning of emotional regulation might be taking place.

In addition, evidence from body-centered interventions addresses the relationship between the body and the self. When the body and self are properly connected and integrated, healthy physiology and psychological functioning results. However, a rift between the body and the self creates a lack of integration and subsequently, inadequate communication between the two. The result is lack of control over the body or self, yielding pathological responses rather than proper functioning. In light of the body-self relationship, this generates more questions regarding the effectiveness of self versus other administered therapies and more research is needed to evaluate this.

Clinical Application: Integrative Methodology and Toolbox Approach

Evidence from the abovementioned interventions indicates that certain populations can benefit from body-centered interventions as complimentary therapies. Due to the large number of individuals who already seek alternative therapies while undergoing traditional medical intervention, a novel treatment paradigm is needed. In addition to more research investigating the specific effectiveness of body-centered interventions, we suggest an integrative approach toward clinical intervention. This model emphasizes an interdisciplinary methodology in which physicians and therapists work together to generate a treatment plan for an individual. Rather than compartmentalizing symptoms and conditions, a dialogue between professionals is needed in which they collaboratively craft a treatment plan that incorporates body-centered interventions.

In order to properly tailor the treatment plan to the individual, we suggest considering the array of body-centered interventions as a toolbox of interventions. Rather than viewing body-centered interventions as a whole, each therapy should be considered in terms of desired effects, symptomology and the individual's history. If one particular body-centered intervention does not generate desired results, a different therapy could be implemented. Also, the toolbox of body-centered interventions can be viewed as progressive: patients can move from less intensive to more intensive therapies. An example of this would be a patient with a history of physical/sexual abuse and a progressive treatment plan of (1) EFT, then once comfortable, moving to (2) reflexology and finally, (3) full body massage.

Further, as demonstrated herein, these interventions are currently recognized as alternative or complementary interventions. As empirical evidence grows and clarifies which interventions are effective or not and which populations benefit from such treatments, we propose that these interventions move from being seen as "alternative" to more primary in the construction of an individual's medical treatment plan. For a clinical example of the effectiveness of a body-centered intervention, please see **Appendix A**.

In conclusion, body-centered therapies are a promising line of intervention that augments the role of the body within the bidirectional communication pathway between the brain and body. These interventions alleviate physical and emotional symptoms via the manipulation of the body, which, in turn, supports the body-self connection. Further research is needed to disentangle the mechanisms underlying body-centered interventions and consider an integrative approach that includes body-centered interventions in treatment plans for psychological disorders.

AUTHOR CONTRIBUTIONS

MT investigated empirical evidence, organized and wrote the manuscript. SP provided theoretical framing. ST provided clinical vignette.

REFERENCES

Abbott, R., and Lavretsky, H. (2013). Tai Chi and Qigong for the treatment and prevention of mental disorders. *Psychiatr. Clin. North Am.* 36, 109–119. doi: 10.1016/j.psc.2013.01.011

Abdel Fattah, M., and Hamdy, B. (2011). Pulmonary functions of children with asthma improve following massage therapy. *J. Altern. Complement. Med.* 17, 1065–1068. doi: 10.1089/acm.2010.0758

Al-Rawi, S., and Fetters, M. D. (2012). Traditional arabic & islamic medicine: a conceptual model for clinicians and researchers. *Global J. Health Sci.* 4, 164–169.

Andersson, S., and Lundeberg, T. (1995). Acupuncture—From empiricism to science: functional background to acupuncture effects in pain and disease. *Med. Hypotheses* 45, 271–281. doi: 10.1016/0306-9877(95)90117-5

Armour, M., Ee, C. C., Hao, J., Wilson, T. M., Yao, S. S., and Smith, C. A. (2018). Acupuncture and acupressure for premenstrual syndrome. *Cochrane Database Syst. Rev.* 8, CD005290.

Bai, L., and Lao, L. (2013). Neurobiological foundations of acupuncture: the relevance and future prospect based on neuroimaging evidence. *Evid. Based Complement. Altern. Med.* 2013:812568. doi: 10.1155/2013/812568

Barnes, P. M., Bloom, B., Nahin, R. L., and Stussman, B. J. (2009). *). Costs of complementary and alternative medicine (CAM) and frequency of visits to CAM practitioners, United States, 2007*. Available at: https://stacks.cdc.gov/view/cdc/11548 (accessed March 25, 2018).

Bauer, B. A., Cutshall, S. M., Wentworth, L. J., Engen, D., Messner, P. K., Wood, C. M., et al. (2010). Effect of massage therapy on pain, anxiety, and tension after cardiac surgery: a randomized study. *Complement. Ther. Clin. Pract.* 16, 70–75. doi: 10.1016/j.ctcp.2009.06.012

Beauchaine, T. P. (2015). Respiratory sinus arrhythmia: a transdiagnostic biomarker of emotion dysregulation and psychopathology. *Curr. Opin. Psychol.* 3, 43–47. doi: 10.1016/j.copsyc.2015.01.017

Beauchaine, T. P., and Thayer, J. F. (2015). Heart rate variability as a transdiagnostic biomarker of psychopathology. *Int. J. Psychophysiol.* 98, 338–350. doi: 10.1016/j.ijpsycho.2015.08.004

Broderick, J., Crumlish, N., Waugh, A., and Vancampfort, D. (2017). Yoga versus non−standard care for schizophrenia. *Cochrane Database. Syst. Rev.* 2017:CD012052. doi: 10.1002/14651858.CD012052.pub2

Broderick, J., Knowles, A., Chadwick, J., and Vancampfort, D. (2015). Yoga versus standard care for schizophrenia. *Cochrane Database. Syst. Rev.* 2015:CD010554. doi: 10.1002/14651858.CD010554.pub2

Broderick, J., and Vancampfort, D. (2017). Yoga as part of a package of care versus standard care for schizophrenia. *Cochrane Database. Syst. Rev.* 2017:CD012145. doi: 10.1002/14651858.CD012145.pub2

Buffart, L. M., Van Uffelen, J. G., Riphagen, I. I, Brug, J., van Mechelen, W., Brown, W. J., et al. (2012). Physical and psychosocial benefits of yoga in cancer patients and survivors, a systematic review and meta-analysis of randomized controlled trials. *BMC Cancer* 12:559. doi: 10.1186/1471-2407-12-559

Cady, S. H., and Jones, G. E. (1997). Massage therapy as a workplace intervention for reduction of stress. *Percept. Mot. Skills* 84, 157–158. doi: 10.2466/pms.1997.84.1.157

Callahan, R. (1985). *Five Minute Phobia cure: Dr. Callahan's Treatment for Fears, Phobias and Self-Sabotage*. Virginia City, NEV: Enterprise Publishing.

Calvert, R. N. (2002). *The History of Massage: an Illustrated Survey From Around the World*. Rochester, VT: Inner Traditions/Bear & Co.

Cassileth, B. R., and Vickers, A. J. (2004). Massage therapy for symptom control: outcome study at a major cancer center. *J. Pain Symptom Manag.* 28, 244–249. doi: 10.1016/j.jpainsymman.2003.12.016

Catalan-Matamoros, D., Helvik-Skjaerven, L., Labajos-Manzanares, M. T., Martínez-de-Salazar-Arboleas, A., and Sánchez-Guerrero, E. (2011). A pilot study on the effect of basic body awareness therapy in patients with eating disorders: a randomized controlled trial. *Clini. Rehabil.* 25, 617–626. doi: 10.1177/0269215510394223

Chen, Z., Williams, K. D., Fitness, J., and Newton, N. C. (2008). When hurt will not heal exploring the capacity to relive social and physical pain. *Psychol. Sci.* 19, 789–795. doi: 10.1111/j.1467-9280.2008.02158.x

Cherkin, D. C., Sherman, K. J., Balderson, B. H., Cook, A. J., Anderson, M. L., Hawkes, R. J., et al. (2016). Effect of mindfulness-based stress reduction vs cognitive behavioral therapy or usual care on back pain and functional limitations in adults with chronic low back pain: a randomized clinical trial. *JAMA* 315, 1240–1249. doi: 10.1001/jama.2016.2323

Cho, S., Shim, S., Rhee, H. Y., Park, H., Jung, W., Moon, S., et al. (2012). Effectiveness of acupuncture and bee venom acupuncture in idiopathic parkinson's disease. *Parkinsonism Relat. Disord.* 18, 948–952. doi: 10.1016/j.parkreldis.2012.04.030

Chou, K. L., Lee, P. W., Yu, E. C., Macfarlane, D., Cheng, Y. H., Chan, S. S., et al. (2004). Effect of Tai Chi on depressive symptoms amongst Chinese older patients with depressive disorders: a randomized clinical trial. *Int. J. Geriat. Psychiatry* 19, 1105–1107. doi: 10.1002/gps.1178

Chou, L., Hong, J. Y., and Hong, C. (2008). A new technique for acupuncture therapy and its effectiveness in treating fibromyalgia syndrome: a case report. *J. Musculoskelet. Pain* 16, 193–198. doi: 10.1080/10582450802161978

Church, D. (2010). The treatment of combat trauma in veterans using EFT (Emotional Freedom Techniques): a pilot protocol. *Traumatology* 16:55Y65.

Church, D., Hawk, C., Brooks, A. J., Toukolehto, O., Wren, M., Dinter, I., et al. (2013). Psychological trauma symptom improvement in veterans using emotional freedom techniques: a randomized controlled trial. *J. Nervous Ment. Dis.* 201, 153–160. doi: 10.1097/NMD.0b013e31827f6351

Church, D., Yount, G., Rachlin, K., Fox, L., and Nelms, J. (2018). Epigenetic effects of PTSD remediation in veterans using clinical emotional freedom techniques: a randomized controlled pilot study. *Am. J. Health Promot.* 32, 112–122. doi: 10.1177/0890117116661154

Church, D., Geronilla, L., and Dinter, I. (2009). *Psychological Symptom Change in Veterans After Six Sessions of Emotional Freedom Techniques (EFT): An Observational Study*. Wholistic Healing Publications, 9. Available at: https://s3.amazonaws.com/eft-academic-articles/marshall.pdf.

Couper, J. L. (1981). Dance therapy effects on motor performance of children with learning disabilities. *Physical. Therapy* 61, 23–26.

Craig, G., and Fowlie, A. (1995). *Emotional Freedom Techniques. Self-Published Manual*. Sea Ranch, CA: Gary Craig.

Cramer, H., Lauche, R., Klose, P., Langhorst, J., and Dobos, G. (2013). Yoga for schizophrenia: a systematic review and meta-analysis. *BMC Psychiatry* 13:32.

Cutshall, S. M., Wentworth, L. J., Engen, D., Sundt, T. M., Kelly, R. F., and Bauer, B. A. (2010). Effect of massage therapy on pain, anxiety, and tension in cardiac surgical patients: a pilot study. *Complement. Ther. Clin. Pract.* 16, 92–95. doi: 10.1016/j.ctcp.2009.10.006

Danielsson, L., Papoulias, I., Petersson, E. L., Carlsson, J., and Waern, M. (2014). Exercise or basic body awareness therapy as add-on treatment for major depression: a controlled study. *J. Affect. Disord.* 168, 98–106. doi: 10.1016/j.jad.2014.06.049

Dennehy, E. B., Schnyer, R., Bernstein, I. H., Gonzalez, R., Shivakumar, G., Kelly, D. I, et al. (2009). The safety, acceptability, and effectiveness of acupuncture as an adjunctive treatment for acute symptoms in bipolar disorder. *J. Clin. Psychiatry* 70, 897–905. doi: 10.4088/JCP.08m04208

Desveaux, L., Lee, A., Goldstein, R., and Brooks, D. (2015). Yoga in the management of chronic disease: a systematic review and meta-analysis. *Med. Care* 53, 653–661. doi: 10.1097/MLR.0000000000000372

Diego, M. A., Field, T., Hernandez-Reif, M., Hart, S., Brucker, B., Field, T., et al. (2002). Spinal cord patients benefit from massage therapy. *Int. J. Neurosci.* 112, 133–142. doi: 10.1080/00207450212023

Diego, M. A., Field, T., and Hernandez-Reif, M. (2008). Temperature increases in preterm infants during massage therapy. *Infant Behav. Dev.* 31, 149–152. doi: 10.1016/j.infbeh.2007.07.002

Diego, M. A., Field, T., Sanders, C., and Hernandez-Reif, M. (2004). Massage therapy of moderate and light pressure and vibrator effects on EEG and heart rate. *Int. J. Neurosci.* 114, 31–44. doi: 10.1080/00207450490249446

Eisenberger, N. I., and Lieberman, M. D. (2004). Why rejection hurts: a common neural alarm system for physical and social pain. *Trends Cogn. Sci.* 8, 294–300. doi: 10.1016/j.tics.2004.05.010

Eisenberger, N. I., Lieberman, M. D., and Williams, K. D. (2003). Does rejection hurt? An fMRI study of social exclusion. *Science* 302, 290–292. doi: 10.1126/science.1089134

Eriksson, E. M., Moller, I. E., Soderberg, R. H., Eriksson, H. T., and Kurlberg, G. K. (2007). Body awareness therapy: a new strategy for relief of symptoms in irritable bowel syndrome patients. *World J. Gastroenterol.* 13, 3206–3214.

Ernst, E. (2009). Massage therapy for cancer palliation and supportive care: a systematic review of randomised clinical trials. *Support. Care Cancer* 17, 333–337. doi: 10.1007/s00520-008-0569-z

Ernst, E., Pittler, M. H., Wider, B., and Boddy, K. (2007). Massage therapy: Is its evidence-base getting stronger. *Complement. Health Pract. Rev.* 12, 179–183. doi: 10.1177/1533210107306090

Escalona, A., Field, T., Singer-Strunck, R., Cullen, C., and Hartshorn, K. (2001). Brief report: improvements in the behavior of children with autism following massage therapy. *J. Autism Dev. Disord.* 31, 513–516.

Field, T. (2010). Touch for socioemotional and physical well-being: A review. *Dev. Rev.* 30, 367–383. doi: 10.1016/j.dr.2011.01.001

Field, T. (2014). Massage therapy research review. *Complement. Ther. Clin. Pract.* 20, 224–229. doi: 10.1016/j.ctcp.2014.07.002

Field, T. (2016). Massage therapy research review. *Complement. Ther. Clin. Pract.* 24, 19–31. doi: 10.1016/j.ctcp.2016.04.005

Field, T. (2019). Social touch. *Dev. Rev.* 51, 123–145. doi: 10.1016/j.dr.2019.01.002

Field, T., Diego, M., Delgado, J., and Medina, L. (2013). Tai chi/yoga reduces prenatal depression, anxiety and sleep disturbances. *Complement. Ther. Clin. Pract.* 19, 6–10. doi: 10.1016/j.ctcp.2012.10.001

Field, T., Diego, M., and Hernandez-Reif, M. (2010a). Moderate pressure is essential for massage therapy effects. *Int. J. Neurosci.* 120, 381–385. doi: 10.3109/00207450903579475

Field, T., Diego, M., and Hernandez-Reif, M. (2010b). Preterm infant massage therapy research: a review. *Infant Behav. Dev.* 33, 115–124. doi: 10.1016/j.infbeh.2009.12.004

Field, T., Diego, M., Hernandez-Reif, M., Dieter, J. N., Kumar, A. M., Schanberg, S., et al. (2008). Insulin and insulin-like growth factor-1 increased in preterm neonates following massage therapy. *J. Dev. Behav. Pediatr.* 29, 463–466. doi: 10.1097/DBP.0b013e3181856d3b

Field, T., and Hernandez-Reif, M. (2001). Sleep problems in infants decrease following massage therapy. *Early Child Dev. Care* 168, 95–104. doi: 10.1080/0300443011680106

Field, T., Hernandez-Reif, M., Diego, M., Schanberg, S., and Kuhn, C. (2005). Cortisol decreases and serotonin and dopamine increase following massage therapy. *Int. J. Neurosci.* 115, 1397–1413. doi: 10.1080/00207450590956459

Field, T., Hernandez-Reif, M., Quintino, O., Drose, L. A., Field, T., Kuhn, C., et al. (1997). Effects of sexual abuse are lessened by massage therapy. *J. Bodywork Mov. Ther.* 1, 65–69. doi: 10.1016/s1360-8592(97)80002-2

Field, T. M. (1998). Massage therapy effects. *Am. Psychol.* 53, 1270–1281.

Field, T. M., Quintino, O., Hernandez-Reif, M., and Koslovsky, G. (1998). Adolescents with attention deficit hyperactivity disorder benefit from massage therapy. *Adolescence* 33, 103–108.

Field, T. M., Schanberg, S., Davalos, M., and Malphurs, J. (1996). Massage with oil has more positive effects on normal infants. *J. Prenat. Perinat. Psychol. Health* 11, 75–80.

Gard, G. (2005). Body awareness therapy for patients with fibromyalgia and chronic pain. *Disabil. Rehabil.* 27, 725–728. doi: 10.1080/09638280400009071

Grimm, D. (2007). Cell biology meets Rolfing. *Science* 218, 1234–1235. doi: 10.1126/science.318.5854.1234

Gyllensten, A. L., Ekdahl, C., and Hansson, L. (2009). Long-term effectiveness of basic body awareness therapy in psychiatric outpatient care. A randomized controlled study. *Adv. Physiother.* 11, 2–12. doi: 10.1080/14038190802242061

Gyllensten, A. L., Hansson, L., and Ekdahl, C. (2003). Outcome of basic body awareness therapy. A randomized controlled study of patients in psychiatric outpatient care. *Adv. Physiother.* 5, 179–190. doi: 10.1186/s13063-016-1347-8

Hansen, A. B., Price, K. S., Loi, E. C., Buysse, C. A., Jaramillo, T. M., Pico, E. L., et al. (2014). Gait changes following myofascial structural integration (rolfing) observed in 2 children with cerebral palsy. *J. Evid. Based Complement. Altern. Med.* 19, 297–300. doi: 10.1177/2156587214540466

Harris, R. E., Zubieta, J.-K., Scott, D. J., Napadow, V., Gracely, R. H., and Clauw, D. J. (2009). Traditional Chinese acupuncture and Placebo (Sham) acupuncture are differentiated by their effects on μ-Opioid Receptors (MORs). *NeuroImage* 47, 1077–1085. doi: 10.1016/j.neuroimage.2009.05.083

Hedlund, L., and Gyllensten, A. L. (2010). The experiences of basic body awareness therapy in patients with schizophrenia. *J. Bodywork Mov. Ther.* 14, 245–254. doi: 10.1016/j.jbmt.2009.03.002

Hernandez-Reif, M., Field, T., Ironson, G., Beutler, J., Vera, Y., Hurley, J., et al. (2005). Natural kiler cells and lymphocytes increase in women with breast cancer following massage therapy. *Int. J. Neurosci.* 115, 495–510. doi: 10.1080/00207450590523080

Hernandez-Reif, M., Ironson, G., Field, T., Hurley, J., Katz, G., Diego, M., et al. (2004). Breast cancer patients have improved immune and neuroendocrine functions following massage therapy. *J. Psychos. Res.* 57, 45–52. doi: 10.1016/s0022-3999(03)00500-2

Hillier, S. L., Louw, Q., Morris, L., Uwimana, J., and Statham, S. (2010). Massage therapy for people with HIV/AIDS. *Cochrane Database Syst. Rev.* 1:CD007502.

Ho, R. T. H., Fong, T. C. T., Chan, W. C., Kwan, J. S. K., Chiu, P. K. C., Yau, J. C. Y., et al. (2018). Psychophysiological effects of dance movement therapy and physical exercise on older adults with mild dementia: a randomized controlled trial. *J. Gerontol. B Psychol. Sci. Soc. Sci.* gby145. doi: 10.1093/geronb/gby145

Hötting, K., and Röder, B. (2013). Beneficial effects of physical exercise on neuroplasticity and cognition. *Neurosci. Biobehav. Rev.* 37, 2243–2257. doi: 10.1016/j.neubiorev.2013.04.005

Jeong, Y. J., Hong, S. C., Lee, M. S., Park, M. C., Kim, Y. K., and Suh, C. M. (2005). Dance movement therapy improves emotional responses and modulates neurohormones in adolescents with mild depression. *Int. J. Neurosci.* 115, 1711–1720. doi: 10.1080/00207450590958574

Jin, E. S., and Josephs, R. A. (2016). "Acute and chronic physiological consequences of social exclusion," in *Ostracism, Social Exclusion, and Rejection*, eds K. D. Williams, and S. A. Nida, (New York, NY: Taylor & Francis).

Khilnani, S., Field, T., Hernandez-Reif, M., and Schanberg, S. (2003). Massage therapy improves mood and behavior of students with attention-deficit/hyperactivity disorder. *Adolescence* 38, 623–638.

Kiepe, M., Stöckigt, B., and Keil, T. (2012). Effects of dance therapy and ballroom dances on physical and mental illnesses: a systematic review. *Arts Psychother.* 39, 404–411. doi: 10.1016/j.aip.2012.06.001

Ko, G. T., Tsang, P. C., and Chan, H. C. (2006). A 10-week Tai Chi program improved the blood pressure, lipid profile and SF-36 scores in Hong Kong Chinese women. *Med. Sci. Monit.* 12, 196–199.

Koch, S., Kunz, T., Lykou, S., and Cruz, R. (2014). Effects of dance movement therapy and dance on health-related psychological outcomes: a meta-analysis. *Arts i Psychother.* 41, 46–64. doi: 10.1016/j.aip.2013.10.004

Koch, S. C., Morlinghaus, K., and Fuchs, T. (2007). The joy dance: Specific effects of a single dance intervention on psychiatric patients with depression. *The Arts in Psychotherapy* 34, 340–349.

Kuijpers, H. J. H., van, D. H., Tuinier, S., and Verhoeven, W. M. A. (2007). Meditation-induced psychosis. *Psychopathology* 40, 461–464. doi: 10.1159/000108125

Kutner, J. S., Smith, M. C., Corbin, L., Hemphill, L., Benton, K., Mellis, B. K., et al. (2008). Massage therapy versus simple touch to improve pain and mood in patients with advanced cancer: a randomized trial. *Ann. Int. Med.* 149, 369–379.

Lahmann, C., Loew, T. H., Tritt, K., and Nickel, M. (2008a). Efficacy of functional relaxation and patient education in the treatment of somatoform heart disorders: a randomized, controlled clinical investigation. *Psychosomatics* 49, 378–385. doi: 10.1176/appi.psy.49.5.378

Lahmann, C., Nickel, M., Schuster, T., Sauer, N., Ronel, J., Noll-Hussong, M., et al. (2009). Functional relaxation and guided imagery as complementary therapy in asthma: a randomized controlled clinical trial. *Psychothe. Psychos.* 78, 233–239. doi: 10.1159/000214445

Lahmann, C., Schoen, R., Henningsen, P., Ronel, J., Muehlbacher, M., Loew, T., et al. (2008b). Brief relaxation versus music distraction in the treatment of dental anxiety: a randomized controlled clinical trial. *J. t Am. Dental Assoc.* 139, 317–324. doi: 10.14219/jada.archive.2008.0161

Lange, G., Leonhart, R., Gruber, H., and Koch, S. (2018). The effect of active creation on psychological health: a feasibility study on (therapeutic) mechanisms. *Behav. Sci.* 8:E25. doi: 10.3390/bs8020025

Lee, M. S., Kim, J. I., and Ernst, E. (2010). Massage therapy for children with autism spectrum disorders: a systematic review. *he J. Clin. Psychiatry* 72, 406–411. doi: 10.4088/jcp.09r05848whi

Lesté, A., and Rust, J. (1990). Effects of dance on anxiety. *Am. J. Dance Ther.* 12, 19–25. doi: 10.1007/bf00844312

Li, Y. H., Wang, F. Y., Feng, C. Q., Yang, X. F., and Sun, Y. H. (2014). Massage therapy for fibromyalgia: a systematic review and meta-analysis of randomized controlled trials. *PloS One* 9:e89304. doi: 10.1371/journal.pone.0089304

Lint, G. A., Lammers, W., and Mitnick, D. G. (2006). Emotional freedom techniques: a safe treatment intervention for many trauma based issues. *J. Aggress.Maltreat. Trauma* 12, 125–150. doi: 10.1300/j146v12n01_07

Loew, T. H., Sohn, R., Martus, P., Tritt, K., and Rechlin, T. (2000). Functional relaxation as a somatopsychotherapeutic intervention: a prospective controlled study. *Altern. Ther. Health Med.* 6, 70–75.

Loew, T. H., Tritt, K., Siegfried, W., Bohmann, H., Martus, P., and Hahn, E. G. (2001). Efficacy of 'functional relaxation'in comparison to terbutaline and a 'placebo relaxation' method in patients with acute asthma. *Psychother. Psychos.* 70, 151–157. doi: 10.1159/000056241

Lutz, A., Dunne, J. D., and Davidson, R. J. (2007). "Meditation and the neuroscience of consciousness," in *Cambridge Handbook of Consciousness*, eds P. Zelazo, M. Moscovitch, and E. Thompson, (Cambridge: Cambridge University Press), 499–555.

McCullough, J. E., Liddle, S. D., Close, C., Sinclair, M., and Hughes, C. M. (2018). Reflexology: a randomised controlled trial investigating the effects on beta-endorphin, cortisol and pregnancy related stress. *Complement. Ther. Clin. Pract.* 31, 76–84. doi: 10.1016/j.ctcp.2018.01.018

Middlekauff, H. R., Yu, J. L., and Hui, K. (2001). Acupuncture effects on reflex responses to mental stress in humans. *Am. J, Physiol. -RegulatoryInt. Comp. Physiol.* 280, R1462–R1468.

Miller, L., McIntee, E., and Mattison, P. (2013). Evaluation of the effects of reflexology on quality of life and symptomatic relief in multiple sclerosis patients with moderate to severe disability; a pilot study. *Clin. Rehabil.* 27, 591–598. doi: 10.1177/0269215512469383

Mills, L. J., and Daniluk, J. C. (2002). Her body speaks: the experience of dance therapy for women survivors of child sexual abuse. *J. Couns. Dev.* 80, 77–85. doi: 10.1002/j.1556-6678.2002.tb00169.x

Mindell, J. A., Lee, C. I., Leichman, E. S., and Rotella, K. N. (2018). Massage-based bedtime routine: impact on sleep and mood in infants and mothers. *Sleep Med.* 41, 51–57. doi: 10.1016/j.sleep.2017.09.010

Miozzo, A. P., Stein, C., Bozzetto, C. B., and Plentz, R. D. M. (2016). Massage therapy reduces pain and anxiety after cardiac surgery: a systematic review and meta-analysis of randomized clinical trials. *Clin. Trials Regul. Sci. Cardiol.* 23, 1–8. doi: 10.1016/j.ctrsc.2016.11.003

Mishra, L. C., Singh, B. B., and Dagenais, S. (2001). Ayurveda: a historical perspective and principles of the traditional healthcare system in India. *Altern. Ther. Health Med.* 7, 36–42.

Moyer, C. A., Rounds, J., and Hannum, J. W. (2004). A meta-analysis of massage therapy research. *Psychol Bull.* 130, 3–18. doi: 10.1037/0033-2909.130.1.3

Murray, J. B. (1995). Evidence for acupuncture's analgesic effectiveness and proposals for the physiological mechanisms involved. *J. Psychol.* 129, 443–461. doi: 10.1080/00223980.1995.9914980

Nakano, H., Kodama, T., Ueda, T., Mori, I., Tani, T., and Murata, S. (2019). Effect of hand and foot massage therapy on psychological factors and eeg activity in elderly people requiring long-term care: a randomized cross-over study. *Brain Sci.* 9:E54. doi: 10.3390/brainsci9030054

Neto, M. G., Menezes, M. A., and Carvalho, V. O. (2014). Dance therapy in patients with chronic heart failure: a systematic review and a meta-analysis. *Clin. Rehabil.* 28, 1172–1179. doi: 10.1177/0269215514534089

Oleson, T., and Flocco, W. (1993). Randomized controlled study of premenstrual symptoms treated with ear, hand, and foot reflexology. *Obstet. Gynecol.* 82, 906–911.

Payne, H. (2003). *Dance Movement Therapy: Theory And practice*. Abingdon: Routledge.

Pierce, L. (2014). The integrative power of dance/movement therapy: Implications for the treatment of dissociation and developmental trauma. *Arts Psychother.* 41, 7–15. doi: 10.1016/j.aip.2013.10.002

Plank, S., and Goodard, J. (2009). The effectiveness of acupuncture for chronic daily headache: an outcomes study. *Mil. Med.* 174, 1276–1281. doi: 10.7205/milmed-d-00-5709

Porges, S. W. (1985). "Respiratory sinus arrhythmia: an index of vagal tone," in *Psychophysiology of Cardiovascular Control: Models, Methods, and Data*, eds J. E. Orlebeke, G. Mulder, and L. J. P. Van Dornen, (NewYork, NY: Plenum), 437–450.

Porges, S. W. (1995). Orienting in a defensive world: mammalian modifications of our evolutionary heritage. *Polyvagal Theory. Psychophysiol.* 32, 301–318. doi: 10.1111/j.1469-8986.1995.tb01213.x

Porges, S. W. (2007). The polyvagal perspective. *Biol. Psychol.* 74, 116–143. doi: 10.1016/j.biopsycho.2006.06.009

Porges, S. W. (2011). *The Polyvagal Theory*. New York, NY: Norton.

Price, C. (2007). Dissociation reduction in body therapy during sexual abuse recovery. *Complement. Ther. Clin. Pract.* 13, 116–128. doi: 10.1016/j.ctcp.2006.08.004

Qin, W., Tian, J., Bai, L., Pan, X., Yang, L., Chen, P., et al. (2008). FMRI connectivity analysis of acupuncture effects on an amygdala-associated brain network. *Mol. Pain* 4:5. doi: 10.1186/1744-8069-4-55

Reinhold, T., Witt, C. M., Jena, S., Brinkhaus, B., and Willich, S. N. (2008). Quality of life and cost-effectiveness of acupuncture treatment in patients with osteoarthritis pain. *Eur. J. Health Econ.* 9, 209–219. doi: 10.1007/s10198-007-0062-5

Remington, R. (2002). Calming music and hand massage with agitated elderly. *Nurs. Res.* 51, 317–323. doi: 10.1097/00006199-200209000-00008

Ritter, M., and Low, K. G. (1996). Effects of dance/movement therapy: a meta-analysis. *Arts Psychother.* 23, 249–260. doi: 10.1016/0197-4556(96)00027-5

Röhricht, F. (2009). Body oriented psychotherapy. The state of the art in empirical research and evidence-based practice: a clinical perspective. Body. *Mov. Dance Psychother.* 4, 135–156. doi: 10.1080/17432970902857263

Ross, A., and Thomas, S. (2010). The health benefits of yoga and exercise: a review of comparison studies. *J. Altern. Complement. Medi.* 16, 3–12. doi: 10.1089/acm.2009.0044

Rothschild, B. (2014). "Body psychotherapy without touch: Applications for trauma therapy," in *Body Psychotherapy*, ed. T. Staunton, (Abingdon: Routledge), 113–127.

Russell, N. C., Sumler, S., Beinhorn, C. M., and Frenkel, M. A. (2008). Role of massage therapy in cancer care. *J. Altern. Complement. Med.* 14, 209–214. doi: 10.1089/acm.2007.7176

Salmon, P. (2001). Effects of physical exercise on anxiety, depression, and sensitivity to stress: a unifying theory. *Clin. Psychol. Rev.* 21, 33–61. doi: 10.1016/s0272-7358(99)00032-x

Serlin, I. (2007). The arts therapies: Whole person integrative approaches to healthcare. *Whole Person Healthcare* 107–121.

Sethi, S., and Bhargava, S. C. (2003). Relationship of meditation and psychosis: case studies. *Aust. N. Z. J. Psychiatry* 37:382. doi: 10.1046/j.1440-1614.2003.11721.x

Sharpe, P. A., Williams, H. G., Granner, M. L., and Hussey, J. R. (2007). A randomised study of the effects of massage therapy compared to guided relaxation on well-being and stress perception among older adults. *Complement. Ther. Med.* 15, 157–163. doi: 10.1016/j.ctim.2007.01.004

Sherman, K. J., Cherkin, D. C., Cook, A. J., Hawkes, R. J., Deyo, R. A., Wellman, R., et al. (2010). Comparison of yoga versus stretching for chronic low back pain: protocol for the Yoga Exercise Self-care (YES) trial. *Trials* 11:36. doi: 10.1186/1745-6215-11-36

Shimada, S., Qi, Y., and Hiraki, K. (2010). Detection of visual feedback delay in active and passive self-body movements. *Exp. Brain Res.* 201, 359–364. doi: 10.1007/s00221-009-2028-6

Stephenson, N., Dalton, J. A., and Carlson, J. (2003). The effect of foot reflexology on pain in patients with metastatic cancer. *Appl. Nurs. Res.* 16, 284–286. doi: 10.1016/j.apnr.2003.08.003

Stephenson, N. L., Weinrich, S. P., and Tavakolil, A. S. (2000). The effects of foot reflexology on anxiety and pain in patients with breast and lung cancer. *Oncol. Nurs. Forum Oncol. Nurs. Soc.* 27, 67–76.

Stephenson, N. L. N., Swanson, M., Dalton, J., Keefe, F. J., and Engelke, M. (2007). Partner-delivered reflexology: effects on cancer pain and anxiety. *Oncol. Nurs. Forum* 34, 127–132. doi: 10.1188/07.onf.127-132

Taylor-Piliae, R., Haskell, W., Waters, C., and Froelicher, E. (2006). Change in perceived psychological status following a 12-week Tai Chi exercise programme. *J. Adv. Nurs.* 54, 313–329. doi: 10.1111/j.1365-2648.2006.03809.x

Tracy, M. F., Lindquist, R., Savik, K., Watanuki, S., Sendelbach, S., Kreitzer, M. J., et al. (2005). Use of complementary and alternative therapies: a national survey of critical care nurses. *Am. J. Crit. Care* 14, 404–414.

Uebelacker, L. A., Weinstock, L. M., and Kraines, M. A. (2014). Self-reported benefits and risks of yoga in individuals with bipolar disorder. *J. Psychiat. Pract.* 20, 345–352. doi: 10.1097/01.pra.0000454779.59859.f8

van Dixhoorn, J, and White, A. (2005). Relaxation therapy for rehabilitation and prevention in ischaemic heart disease: a systematic review and meta-analysis. *Eur. J. Cardiovasc. Prev. Rehabil.* 12, 193–202. doi: 10.1097/01.hjr.0000166451.38593.de

Waite, W. L., and Holder, M. D. (2003). Assessment of the emotional freedom technique: an alternative treatment for fear. *Sci. Rev. Ment. Health Pract.* 2, 20–26.

Wang, C., Schmid, C. H., Rones, R., Kalish, R., Yinh, J., Goldenberg, D. L., and McAlindon, T. (2010). A randomized trial of tai chi for fibromyalgia. *N. Eng. J. Med.* 363, 743–754. doi: 10.1056/NEJMoa0912611

Wang, M. Y., Tsai, P. S., Lee, P. H., Chang, W. Y., and Yang, C. M. (2008). The efficacy of reflexology: systematic review. *J. Adv. Nurs.* 62, 512–520. doi: 10.1111/j.1365-2648.2008.04606.x

Wang, Y., Taylor, L., Pearl, M., and Chang, L. (2004). Effects of Tai Chi exercise on physical and mental health of college students. *Am. J. Chi. Med.* 32, 453–459. doi: 10.1142/s0192415x04002107

Weinberg, R. S., and Hunt, V. V. (1979). Effects of structural integration on state-trait anxiety. *J. Clin. Psychol.* 35, 319–322. doi: 10.1002/1097-4679(197904)35:2<319::aid-jclp2270350220>3.0.co;2-3

Wolf, S., O'Grandy, M., Easley, K. Guo, Y., Kressig, R., and Kutner, M. (2006). The influence of intense Tai Chi training on physical performance and hemodynamic outcomes in transitionally frail older adults. *J. Gerontol.* 2006 184–189. doi: 10.1093/gerona/61.2.184

World Health Organization (2013). *WHO Traditional Medicine Strategy 2014-2023*. Geneva: World Health Organization.

World Health Organization (2019). *WHO Global Report on Traditional and Complementary Medicine 2019*. Geneva: World Health Organization.

Yang, J. H. (2005). The effects of foot reflexology on nausea, vomiting and fatigue of breast cancer patients undergoing chemotherapy. *Taehan Kanho Hakhoe Chi* 35(1), 177–185.

Zhang, Z., Chen, H., Yip, K., Ng, R., and Wong, V. T. (2010). The effectiveness and safety of acupuncture therapy in depressive disorders: systematic review and meta-analysis. *J. Affect. Disord.* 124, 9–21. doi: 10.1016/j.jad.2009.07.005

Zhong, B., Huang, Y., and Li, H. (2008). The effectiveness and safety of acupuncture for depression: a systematic assessment. *Chin. Ment. Health J.* 22, 641–647.

Conflict of Interest: ST was employed by Dancing Dialogues.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

APPENDIX A

Clinical Vignette

Identifying features have been altered to maintain confidentiality.

> *An Application of Dance/Movement Therapy*
> *Integration of Somatic and Cognitive Experience in the Therapeutic Process*

Jerry is a 35 years old female, tall and of average weight, who works as an executive in a large business and typically enjoys an active physical life. She began experiencing pain and a restricted range of motion in her right shoulder, procured medical attention and received a diagnosis of frozen shoulder. Following medical advice, she undergoes physical therapy for 4 months and experiences no improvement. Her primary physician refers her to dance/movement therapy.

At the first therapy session, Jerry briskly enters the office holding her right arm tightly across her chest with the palm of her hand snuggled next to her clavicle. She cautiously sits down, bracing her upper torso and holding her body upright away from the back of the chair. The flow of Jerry's breath was short and shallow, seemingly contained in her upper torso.

Jerry describes her situation as follows;

> "*I don't understand what has happened to me. My life has always revolved around physical activities and pushing myself to do my best. I grew up in a family that was all about achievement. Everyone in my family works really hard and we all succeed. I learned early on that being physical has been a core way that I balance my emotional and work life. I have not been able to do anything these four months and I'm depressed and discouraged.*"

The goal of the dance/movement therapy was to help Jerry become aware of the interconnections among her bodily sensations, personal movement style, emotional reactions and thoughts that create an embodied sense of herself. During the initial stage of treatment, Jerry learned to identify how she holds her breath when experiencing stress and what aspects of her life are most distressful. First, Jerry was asked to deepen her breath in vertical, sagittal and horizontal directions that promotes calmness while listening to gentle flowing harp music. As her torso became more relaxed, she begins to recall that she learned to "*hold myself so erect and tightly as a child, trying to keep up with all my family's expectations of achievement.*"

Then, accompanied by music with a strong beat, Jerry was asked to explore an erect posture, while holding her right arm across her chest and listening to music with a strong beat. During this movement improvisation, Jerry spontaneously stretched her right arm out in front of her, extending her elbow and making a pulsing gesture with her hand, pushing away from her torso. She suddenly stopped, drawing her arm back across her chest, her hand by her heart, hollowing her upper torso. She began to cry. The therapist changed back to the harp music and supported her, enabling her to connect to the flow of her breath.

In this moment, her body, emotions and thoughts were connected and integrated, allowing Jerry to recall the feeling of being overwhelmed as a child, and needing to protect her heart from family pressure. She yearned for affection when feeling overwhelmed, but her achievement-oriented parents viewed this need as a weakness. By exploring and identifying the metaphors associated with her frozen shoulder, Jerry was able to be kinder to herself, and ask for physical affection from her spouse when stressed. Her frozen shoulder improved and she was able to resume an active, balanced life.

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Building Wellbeing in People With Chronic Conditions: A Qualitative Evaluation of an 8-Week Positive Psychotherapy Intervention for People Living With an Acquired Brain Injury

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Research indicates that Acquired Brain Injury (ABI) is associated with significant and chronic impairment across multiple areas of functioning including physical, cognitive, emotional and behavioral domains. Whilst impairments associated with ABI can be ameliorated, cure is seldom possible. The emergence of positive psychology reflects a paradigm shift in health and wellbeing research, highlighting the role of character strengths, positive emotions, meaning, and resilience. Positive psychology interventions have been demonstrated to improve wellbeing in a variety of populations, although research investigating the impact of positive psychotherapy for people living with ABI are sparse. Here we characterize the experience of an 8-week positive psychotherapy intervention for 13 people living with ABI including four mentors and nine participants using thematic analysis of transcripts collected during mini-groups and one-to-one interviews. Six main themes were identified including empowerment, social opportunity, coping, cultivation of positive emotion, consolidation of skills and barriers. Results indicated that wellbeing can be promoted and improved in individuals with ABI. Recent theoretical developments in wellbeing science highlight scope to improve the intervention by connecting individuals to their communities and spending time in nature.

Keywords: acquired brain injury, ABI, chronic conditions, positive psychotherapy, PPT, healthcare improvement

INTRODUCTION

Acquired Brain injury (ABI) refers to injury to the brain that occurs after birth and can be subdivided Traumatic Brain Injury (TBI) or Non-traumatic Brain Injury (NTBI; Saatman et al., 2008). TBIs occur when an external force injures the brain. NTBIs occur both from an internal or external source, but are not directly caused by external force, (e.g., stroke, hypoxia, encephalitis, etc.). ABI can be associated with significant and chronic impairments across multiple areas of functioning including physical, cognitive, emotional, behavioral and social domains (Milders et al., 2003; Barman et al., 2016; de Freitas Cardoso et al., 2019; Kane et al., 2019). Critically, the psychological consequences of ABI are generally hidden and are associated with poor involvement in rehabilitation, hospital re-admission, long-term disability, limited social activity, reduced ability to manage physical conditions, increased health service usage, suicide and a general increase in risk for mortality (Gillen et al., 2001; Naylor et al., 2012; Ayerbe et al., 2013; van Eeden et al., 2016). People affected by ABI – as with other chronic conditions – have little access to psycho-social interventions to address ongoing holistic needs: almost three- quarters of people living with ABI feel that their psychological needs are not met (McKevitt et al., 2011; Oyesanya, 2017). The main goal of the present study therefore is to report a qualitative evaluation of routinely collected data on participant experience of an 8-week positive psychotherapy intervention.

Healthcare systems are typically founded on the acute medical model, which tackle illnesses and conditions by adopting a "find it and fix it" approach (Keller and Carroll, 1994). Although a disease focus is advantageous when delivering life-saving care and attempting medical stability in the acute stage, this model does not adequately support the holistic needs of individuals during the post-acute and community-based stages. For example, disease focused approaches aim to reduce impairment or distress associated with a disease but do not seek to build wellbeing, facilitate psychological adjustment and community re-integration. With respect to ABI, neurorehabilitation services typically adopt a disease focus with an emphasis on reducing impairment through compensatory or restorative techniques. The dominant model used to treat psychological difficulties post ABI has been Cognitive Behavioral Therapy (CBT). CBT aims to alter unhelpful negative thoughts in order to reduce negative affect and psychological distress. These disease focused approaches are underpinned by the assumption that eradication or reduction of impairment will improve health and wellbeing. However, this is problematic for two reasons; firstly, chronic conditions cannot be "fixed" and secondly, the absence of impairment does not equate to wellbeing (Anderson, 1995). Accordingly, there is a need for services to focus on reducing impairment, while also focusing on creating a context for acceptance and wellbeing despite impairment (Schretlen and Shapiro, 2003; Dikmen et al., 2009).

It is now widely accepted that health and wellbeing are no longer tied to the presence or absence of illness or disease (Anderson, 1995). The World Health Organisation (WHO) defined health as "a state of complete physical, mental and social wellbeing and not merely the absence of disease or infirmity" (World Health Organization [WHO], 1948). Whilst this definition goes beyond defining health as an absence of disease, as per the medical model, there are several issues. Striving for "complete" health as a goal for health pathologizes suboptimal health states, thereby contributing to the over-medicalization of society (Hanslik and Flahault, 2016). In addition, the word "complete" is arbitrary, it is difficult to ascertain a "complete" sense of wellbeing and implies that most of us are unhealthy, most of the time. This approach to health and wellbeing is particularly problematic for people with chronic conditions who experience issues in physical, mental and social domains. Under this definition, wellbeing is not attainable for people with chronic conditions. Fortunately, research has highlighted the shortcomings of the WHO definition of health and wellbeing, giving rise to alternate theories and subsequent definitions.

Here we highlight two approaches to the study of wellbeing: hedonic and eudaimonic theories. Hedonic theories of wellbeing, such as Subjective Wellbeing theory (SWB; Diener, 1984), focus on three main components: a cognitive aspect involving global appraisals of life satisfaction and two emotional components, including positive affect and negative affect (Diener, 1984). Another well described hedonic theory of emotion is Barbara Fredrickson's *Broaden and Build Model* (2001), which highlights a role for positive emotions in broadening our thought-action repertoire leading to more creative and flexible actions. This model further emphasizes the role of positive emotions in building cognitive, psychological, social and personal resources that promote wellbeing and psychological resiliency. Research has identified links between positive emotion, positive health outcomes and increased social connectedness (DuBois et al., 2012). Positive psychological attributes – including optimism and curiosity – have also linked to a decreased risk for disease development and increased engagement in positive health behaviors (Boehm and Kubzansky, 2012; Richman et al., 2005). By contrast, eudaimonic theories, such as Psychological Wellbeing theory (PWB; Ryff, 1995), emphasise purpose and meaning in life. Intriguingly, recent epidemiological research on the United States Health and Retirement Study has identified associations between stronger life purpose and lower mortality (Alimujiang et al., 2019), highlighting an intimate connection between mental wellbeing and physical health. Ryff (1995) proposed six components of PWB which include; self-acceptance, positive relationships with others, autonomy, personal growth, environmental mastery and purpose in life. In 2011, Martin Seligman introduced the *PERMA model*, which combines hedonic and eudaimonic aspects of wellbeing, presenting a model of wellbeing that is comprised of positive emotions, engagement, relationships, meaning and accomplishments. These five core elements of wellbeing according to PERMA theory are not mutually exclusive, and Seligman has argued that flourishing arises when a person excels across all five of these pillars.

All these models of wellbeing present evidence-based factors that contribute to wellbeing (**Figure 1**). A commonality between these three models is that they all adopt principles relating to Positive Psychology (PP). Positive Psychology is a unique discipline that focuses on identifying human strengths and factors that contribute to a life well-lived (Seligman, 2011). A key principle of PP is that strengths and virtues can be mobilized to develop wellbeing. For example, strategies include practicing optimistic thinking and mindfulness (James, 2011), savoring positive events through diary writing (Sherliker and Steptoe, 2000; Harris et al., 2003; Ben-Shahar, 2010; Jose et al., 2012), making a gratitude visit, (Emmons and Crumpler, 2000; Sansone and Sansone, 2010; Emmons and Stern, 2013),

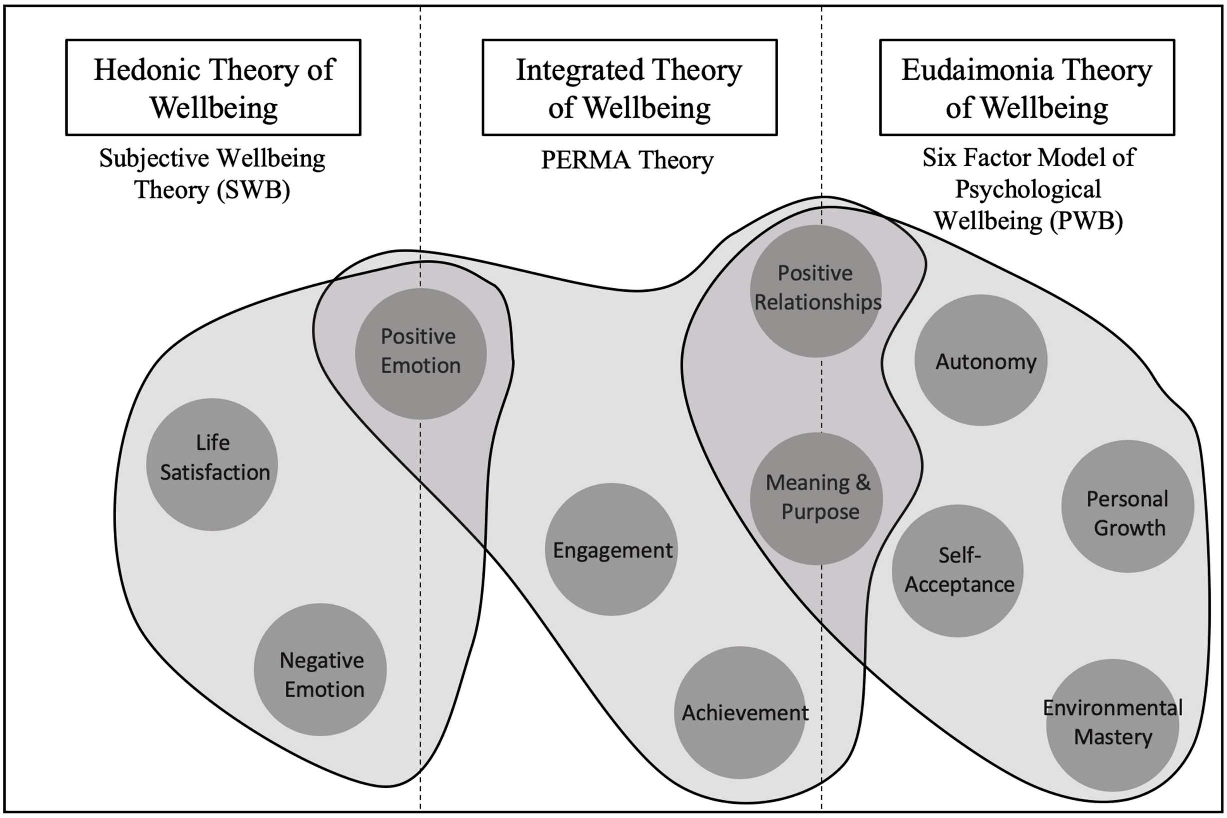

FIGURE 1 | Factors of Wellbeing According to Hedeonic (Subjective Wellbeing Theory), Eudaimonic (Six factor model of Psychological Wellbeing) and Integrated Approaches (PERMA Theory).

discovering and employing character strengths, (Tedmanson and Guerin, 2011; Panter-Brick and Leckman, 2013), and using relaxation techniques such as guided imagery (Larsson and Starrin, 1992; Gedde-Dahl and Fors, 2012). Published meta-analyses of techniques report enhanced wellbeing and decreased depressive symptoms (Sin and Lyubomirsky, 2009; Bolier et al., 2013; Chakhssi et al., 2018).

The emergence of positive psychology, and related bodies of literature including Quality of Life (QoL), patient centerd care and patient activation reflect a paradigm shift in health and wellbeing research. There is now a focus on creating a context for wellbeing that spans beyond attempts to simply eradicate or reduce impairment. For example, developments in QoL literature for those living with ABI emphasize the need for more comprehensive assessments that include social inclusion, community integration, human rights and personal development (Fernández et al., 2019). This psychosocial approach to assessment reaches beyond disease-specific assessments (Sánchez, 2010). Additionally, recent research on patient-centerd rehabilitation is closely tied with the concept of flourishing. Cogan (2016) notes that in order to promote unique capabilities, goals and potential in those living with ABI, clinicians must provide individualized care in which treatment is collaborative between the provider and the recipient. Such care focused on understanding patient's lives, their relationships with others and the way in which they want to live. In line with the goals of positive psychology, this research emphasises a shift toward focusing on wellness instead of illness.

Theoretical frameworks of wellbeing and evidence from the field of Positive Psychology and its application through Positive Psychotherapy suggest that people with chronic conditions may benefit from interventions that not only focus on symptom reduction, but also on creating a context for wellbeing. For example, it has been well established that people living with ABI are often socially isolated, with fewer positive relationships, fewer opportunities for meaning and lower community integration (Barber et al., 2018). Thus, increasing opportunities for wellbeing in the ABI population – including enhancing opportunities for positive social connections, developing meaning and purpose in life, and community engagement – has much potential to improve people's lives.

That said, there is a paucity of research investigating the promotion of wellbeing in the context of ABI. Group and one-to-one positive psychotherapy (PPT) have been reported to increase happiness (Andrewes et al., 2014; Cullen et al., 2018) and reduce symptoms of anxiety (Cullen et al., 2018). These studies reported that the feasibility and effectiveness of PPT in this population is promising. Bertisch et al. (2014) showed a relationship between key constructs in positive psychology (character strengths, resilience, and positive mood states) and factors affecting rehabilitation outcome (i.e., perception of functional abilities post-injury and beliefs about treatment) for people with ABIs. These factors affecting rehabilitation outcome are important in determining treatment success and quality of life outcome in rehabilitation settings and could potentially be impacted on by positive psychotherapy.

Our study builds on these initial promising findings and emerging evidence base by reporting on the findings from detailed qualitative evaluation of the perceptions of people living with ABI following group-based positive psychotherapy. The research question of this study was as follows: Is it possible to build wellbeing in people living with ABI through group-based positive psychotherapy? We review mini-group and interview data against the background of the prevailing approaches that span subjective and psychological wellbeing.

MATERIALS AND METHODS

Ethical Considerations

Service evaluations conducted in the United Kingdom are excluded from ethical review under official policy (GAfREC 2.3.12)[1]. The United Kingdom-based Health Research Authority online decision-making tool confirmed that ethical review was not required[2]. Service evaluations are characterized by minimal risk and therefore fall outside the remit of research ethics committees in the United Kingdom. This exemption was subsequently confirmed by our Research and Development Officer in Swansea Bay University Health Board, provided that data is anonymized or pseudonymized when writing up results for publication.

Design

The service in which the study took place has historically adopted a participatory approach to service development and evaluation. Service users are involved at a transactional level in the implementation of new initiatives focusing on wellbeing. The present study investigated the experience of service users who completed an 8-week Positive Psychology Intervention (PPI) run in 2017, offered by a community neurorehabilitation service in a major hospital located in South Wales, United Kingdom. A qualitative evaluation (QE) design was employed (Tayabas et al., 2014) to gather in-depth accounts of service user's experience of the PPI, consistent with United Kingdom National Health Service requirements of evaluating services and patient experience, in keeping with a participatory and context-sensitive approach. QE designs are used to evaluate programmes or services and can employ diverse approaches, including participatory action and interpretative methods, focused on understanding processes in context.

Our study utilized Thematic Analysis (TA) since it allows for large amounts of data collected from multiple participants in naturalistic settings to be analyzed and synthesized into meaningful accounts (Braun and Clarke, 2006). One advantage of thematic analysis is that it is not wedded to any epistemological frameworks and therefore provides flexibility in application. In line with our QE design, a critical realist epistemological perspective was employed in the present study (Bhaskar et al., 1998; Archer et al., 2013). According to this approach, knowledge or "truth" may be shared across individuals, although each individual will have their experience and perspectives, which will be dependent on context.

In line with overarching aims, context and the critical realist approach of the study, we draw on the quality frameworks as suggested by Yardley (2000), which includes four characteristics of good qualitative analysis; sensitivity to context, commitment and rigor, transparency and coherence, and impact and importance.

Participants

Participants were initially contacted face-to-face by the clinician from a Community Neurorehabilitation Service (CNS) based in South Wales, after which letters were sent including details relating to time, date and location of the PPI. A total of 19 participants were purposively invited to attend the course and 13 accepted the invitation. Reasons for not accepting the invitation included other commitments, employment, travel difficulty, and surgery. Once the course had begun, there were no dropouts. Four out of the 13 participants had attended a course previously, and were subsequently invited to become mentors. These individuals were trained by a member of the clinical team to deliver some of the practical aspects of the intervention and asked to share their own lived experiences of using some of the PP techniques that had learnt. One participant was lost to follow up due to being discharged from the CNS. Details of the twelve participants who participated in this study are included in **Table 1**. Participants are referred to as pseudonyms in the manuscript, categorized according to mentor or participant status, followed by an identification number (e.g., "M1," "P1").

All participants had a confirmed diagnosis of ABI, had experienced psychological difficulties and/or reduced social participation and had received rehabilitative treatment before participating in the study. The recruitment process was pragmatic in nature and involved the clinician selecting individuals whom she had worked with from within the CNS. The clinician exercised judgment relating to participants' capacity to benefit from the course, as well as the likelihood of disrupting the learning opportunity for others. The decision process was centerd around the following inclusion and exclusion criteria.

Inclusion criteria included age greater than 18; confirmed diagnosis of ABI; ability to actively engage in the intervention as determined by their clinician; living in the community; evidence of psychological difficulties during the initial clinical interview when patients access the brain injury service; living within the catchment area of the participating health boards; at least 3-month post-injury at recruitment, allowing time for spontaneous recovery and for the person to become aware of their difficulties and the implication of these on their lives. Exclusion criteria including receptive or expressive language difficulties, or extremely low memory function that may preclude people from engaging meaningfully; medical or psycho-social

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[1] https://tinyurl.com/rcp2cqe

[2] https://tinyurl.com/wdrydgg

TABLE 1 | Participant characteristics.

	Sex	Age	Injury	Comments
M1	Female	53	Inflammatory idiopathic left limbic encephalitis	M1 was interviewed with 3 other mentors in a mentor-only mini group interview
M2	Female	62	Moderately severe traumatic brain injury	M2 was interviewed with 3 other mentors in a mentor-only mini group interview
M3	Female	60	Suspected encephalitis	M3 was interviewed with 3 other mentors in a mentor-only mini group interview
M4	Female	50	Mild Traumatic Brain Injury	M4 was interviewed with 3 other mentors in a mentor-only mini group interview
P1	Male	68	Severe traumatic brain injury	P1 was interviewed in mini group for participants along with P2, P3, P4 and P5.
P2	Female	53	Moderate traumatic brain injury	P2 was interviewed in mini group for participants along with P1, P3, P4 and P5.
P3	Male	58	Severe traumatic brain injury	P3 was interviewed in mini group for participants along with P1, P2, P4 and P5.
P4	Male	29	Moderate to severe traumatic brain injury	P4 was interviewed in mini group for participants along with P1, P2, P3 and P5.
P5	Male	55	Severe Traumatic brain injury	P5 was interviewed in mini group for participants along with P1, P2, P3 and P4.
P6	Female	73	Moderate traumatic brain injury	P6 was interviewed individually using a face-to-face interview with an assistant psychologist who had been present for some of the group sessions.
P7	Female	34	Suspected hypoxic brain injury	P7 was interviewed individually using a face-to-face interview with an assistant psychologist who had been present for some of the group sessions.
P8	Female	37	Cerebellar infarct following a traumatic artery dissection.	P8 was interviewed individually using a face-to-face interview with an assistant psychologist who had been present for some of the group sessions.

reasons, based on risk assessments by the referring clinician; potentially disruptive to other group members as determined by their clinician; not able to provide informed consent. Mentors were subject to the same inclusion criteria as participants with the exception of showing "evidence of psychological distress." Mentors were also subject to the following additional inclusion criteria: demonstrated ability to be responsive and sensitive to the needs of others; known to and recommended by their referring clinical team; good interpersonal skills; willing and able to commit to training as well as attending all eight PPT sessions.

Intervention

The positive psychology course was developed in partnership between clinical and academic psychologists. The course was delivered in a semi-structured format and was designed to incorporate aspects of subjective wellbeing (Diener, 1984; Fredrickson, 2001), psychological wellbeing (Ryff, 1989) and PERMA theory (Seligman, 2011; **Table 2**). Participants were given a resource booklet which outlined the structure of the course as well as pages for note-taking and completion of written activities. The course was structured to include psychoeducation and practical elements, allowing participants to engage in a range of activities designed to improve wellbeing after being provided with relevant background and context. While the clinician ensured that all course content was delivered, open discussion was encouraged. The semi-structured nature of the course promoted a transactional approach between the clinician delivering the course and participants. Discussions enabled participants to share their own stories relating to their experience of ABI, facilitating group bonding and positive social ties. Sessions were typically 2 h long with a break in the middle. Additional breaks were given if required.

Data Collection

Semi structured interviews were carried out across two separate mini-groups, one for the mentors ($n = 4$) and the other for participants ($n = 5$). Three additional individual ($n = 3$) interviews were separately conducted to accommodate those individuals who requested that they be interviewed separately. All interviews were conducted in a hospital, within a Community Neurorehabilitation Service where the intervention had taken place, following the positive psychotherapy intervention. Participants were initially invited to attend the interviews face-to-face at the end of the course, subsequently letters were sent to participants detailing the time, location and date. All interviews were conducted by a single Assistant Psychologist (AP) (female) with postgraduate training in psychology. The AP had established relationships with the participants over the 8-week period by attending groups and greeting participants when they visited the clinic. During interviews, only the AP and the participants were present; clinical staff (ZF, HB) were outside of the room, but nearby for governance reasons. Field notes were made during interviews by the AP to include overall impressions of perceived improvements to wellbeing according to individual representation and possible improvements to future services. These notes were then passed to the leading clinician to guide future interventions.

Before the interviews began, participants were informed of the purpose of the interviews and that anonymized data may be used for evaluative purposes. Verbal consent was then obtained. Each interview followed a similar pattern, beginning by exploring the initial hopes of the group versus experiential gains, inviting individuals to give feedback regarding the group and its delivery, commenting on salient aspects and whether the course had impacted upon future recovery. Questions for participants were open-ended and were developed iteratively over the course of the discussions, consistent with the need to be flexible and responsive to material in qualitative research. The interviewer sought to promote group discussion by asking others if they agreed with the points that were raised and by asking participants to engage in discussion.

All interviews were recorded using a "Voice Memos" application. Verbal consent was gathered from all participants for the recordings to be transcribed and analyzed. Audio data of interviews totaled 3 h and 1 min. Interviews were 36 min in duration on average and ranged from 20 min to 1 h and 3 min.

TABLE 2 | Structure of positive psychotherapy intervention.

Week	Focus	Comment
1	Introduction to positive psychology	This session focuses on introducing participants to the course. They are given an informational booklet outlining the course structure which also has worksheets and note-taking spaces, for each session. Models of wellbeing are taught including; hedonic, eudaimonic and PERMA. Participants are asked to complete a "wheel of wellbeing" which outlines the 5 pillars of the PERMA model to encourage participants to think about how these relate to their own lives.
2	Relaxation	This session focuses on learning about the role and function of stress and anxiety and learning how to activate the relaxation response using exercises of relaxation techniques, such as diaphragmatic breathing and guided imagery. Participants are given CD's with guided relaxations including a loving kindness exercise which encourages participants to think about and feel love for important people in their lives. Participants complete a guided imagery exercise of a safe place.
3	Character Strengths	Participants complete the VIA character strengths and explore their top strengths (Peterson and Seligman, 2004). They write examples of when they have used them in their lives prior to the course and think of new ways to mobilize them in future.
4	Positive emotions	Participants are to learn the role and function of emotions and explore negativity bias' and the benefits of increasing frequency of positive emotional experiences. Participants complete a gratitude exercise; participants note down three positive things they are grateful in their day-to-day lives. Participants are encouraged to complete this exercise daily over the course of a week and take note of this in their information booklet. Participants are encouraged to complete one random act of kindness a day and record this exploring Barbara Fredrickson's Theory of love in terms of shared experiences to facilitate positive emotions, bio-behavioral synchrony and mutual care and concern. Participants then experience a loving-kindness meditation.
5	Optimism	Participants learn about optimism, learned helplessness and learned optimism. Participants learn how to alter thinking styles using CBT to adopt a more optimistic outlook. Participants complete activities relating to the ABCDE model of optimism.
6	Mindfulness	Participants learn about the four key elements of mindfulness according to Hölzel et al. (2011) and how to apply these to everyday life. Participants complete two exercises at home as instructed in their workbook; to use mindfulness when eating and mindful meditation. Mindful meditation. Participants then complete a grounded exercise which evokes the five senses when meditating.
7	Connection between body and mind	Educational information on sympathetic and parasympathetic nervous system and responses to antecedents are delivered to participants as well as discussions on the effects of chronic stress. Participants are taught about the vagus nerve, heart rate variability and their connections to health outcomes. Positive health behaviors are explored. Participants then complete exercises to increase HRV e.g., exercise followed by deep breathing with prolongation of the outbreath.
8	Making positive changes	Participants learn about habits and how to move away from bad habits, to good habits. Willpower and the path of least resistance is explored and reducing activation energy for desired behavior. Participants are invited to discuss how they can apply these principles to their own lives.

The interview audio files were then transcribed orthographically so that the true essence of the data would be captured by incorporating utterances such as "ah, um etc.," as well as utilizing grammatical correctness to indicate pauses, end of statements and exclamations. Interviews were transcribed verbatim except for the names of participants, staff names and locations, which were omitted to ensure anonymity.

Data Analysis

The software ATLAS.TI was used to manage the data at the coding stage, after which established codes were organized into categories and then managed using Microsoft Excel. All categories were then referenced against original codes in ATLAS to check for consistency and appropriateness of categorization. The analysis of the data followed a guide introduced by Braun and Clarke (2006), which outlines a 6-step procedure to good Thematic Analysis (see **Table 3**).

Braun and Clarke (2006) note that qualitative research will inevitably involve a mixture of both inductive and deductive approaches. In line with the quality criteria set out by Yardley (2000), coding applied "bracketing" to maintain critical awareness of the basis for sense making, and allowed the researcher to choose to focus on use of positive psychology theory in the data, or to bracket or suspend this in order to maintain sensitivity to the meanings and experiences of participants (Tufford and Newman, 2012). Data was not coded by a second coder because – in line with, Braun and Clarke (2006) – measures of inter-rater reliability between multiple coders simply reflect the degree to which coders follow the same procedure, rather than accuracy of the coding process, *per se*.

RESULTS

Recurrence of themes was noted during analysis, and participants' experiences could be coded within a common or shared set of themes and sub themes (**Tables 4**, **5**).

TABLE 3 | Braun and Clarke (2006) 6-step Guide to Good Thematic Analysis.

Phase	Examples of Procedure for Each Step
1. Familiarization	Transcribing data: reading and re-reading; noting down initial codes
2. Generating Initial Codes	Coding interesting features in the data in a systematic fashion across the data set, collating data relevant to each code
3. Searching for Themes	Collating codes into potential themes, gathering all data relevant to each theme
4. Involved Reviewing Themes	Checking if the themes work in relation to the coded extracts and the entire data-set; generate a thematic map
5. Defining and Naming Themes	Ongoing analysis to refine the specifics for each theme; generation of clear names for each theme
6. Producing the Report	Final Opportunity for Analysis selecting appropriate extracts; discussion of analysis; relate back to the research question or literature; produce report

TABLE 4 | Themes and Subthemes for Thematic Analysis for non-mentor participants.

Theme	Subthemes
Empowerment	Achievement
	Confidence
	Sense of transformation
Social Opportunity	Relatedness with others (ABI and non-ABI)
	Understanding the self through others
Coping	
Cultivating Positive Emotion	
Barriers	Stage in recovery
	Location/Environment of intervention

TABLE 5 | Themes and Subthemes for Thematic Analysis for Mentors.

Theme	Subthemes
Empowerment	Meaning through providing support Achievement
	Feeling Valued
	Confidence
Social Opportunity	Relatedness with others (ABI and non-ABI)
	Helping others
Coping	Reframing
	Mobilization of character strengths
Consolidation of skills	
Cultivating Positive Emotion	
Barriers	Stage in recovery
	Location/Environment of intervention

For non-mentor participants, Thematic Analysis (TA) identified the following themes: (1) Empowerment; (2) Social Opportunity; (3) Coping; (4) Cultivating Positive Emotion; and (5) Barriers (see **Table 4**).

For mentors, TA identified the following themes: (1) Empowerment; (2) Social Opportunity; (3) Coping; (4) Consolidation of skills; (5) Cultivating Positive Emotion; and (6) Barriers (see **Table 5**).

Themes for mentors and participants were then converged onto a single thematic map (see **Figure 2**). This convergence process was achieved by collapsing identical themes and then converging respective sub-themes. Links between themes were then included to the relationships between themes and sub-themes.

A full description of themes and sub-themes is provided in **Supplementary Materials**, while the reported results below have been shortened, describing only the main themes and observations, for brevity.

Empowerment Theme

This theme captured an overall sense of empowerment experienced by both mentors and participants. A combination of enhanced confidence; sense of achievement; feeling valued by others, gaining meaning by helping others and a sense of transformation all contributed to an overall sense of empowerment. Achievements such as gaining new skills and overcoming challenges, facilitated a sense of independence and control over personal circumstances.

> *"I'd lost my husband in the supermarket and I didn't have a panic attack. I just didn't move from where I was, I just waited for him to come back to where he last saw me. And then I said to him. . .I said no I'm going to go shopping on my own and it was a huge, huge thing. . . I came out and I must have felt about ten foot tall."* (P6).

Individuals became more resourceful and welcomed situations in which they would be able to further develop confidence, such as speaking to members of the public.

> *"its given me more confidence to try things that I wouldn't have had the confidence to do before. I would have automatically gone into something thinking I can't do that and now I'm sort of open to try things. And I've tried a lot of things. Most of them haven't worked, but you know, I've tried them"* (M3).

People living with ABI were eager to give back to their community by helping others, an experience that was facilitated by participating in the positive psychotherapy group as mentors. This opportunity to help others by drawing on their experience of living with an ABI gave them meaning and purpose by feeling valued and by adopting the view that their purpose within the intervention was to provide support and hope for positive change.

> *"when I am mentoring, I do feel valued. I feel somebody, you know, I've got a bit of self-worth again, which you tend to lose"* (*M1*).

Mentors remarked that their purpose is to make others feel safe and valued;

> *"It's about making them feel safe and valued"* (*M1*).

Mentors had experienced positive change themselves through completing the course. This positive change was reflected with a sense of transformation described by both mentors and participants, often explaining that their life had changed for the better and that personal development was evident through gains in ability, implementation of coping strategies, increased self-efficacy, confidence and acceptance of injury.

> *"I went in thinking that can you really learn happiness, and I learnt about positivity. . . and to walk away as a happier person, I mean you can't give a medicine for that"* (*P8*).

Social Opportunity Theme

This theme captured participants sense of better understanding of the self, relatedness with others, and for mentors, the sense that they were helping others. Participants explained that having a shared understanding of ABI facilitates a comfortable, judgment-free and acceptance-based atmosphere, which in turn promotes of sense of unity based on equality;

> *"I think if you want to express something you can talk to somebody here and they can understand it. And they don't judge you. . ."* (*P1*); *"Everyone comes in at the same level"* (*P3*).

Mentors were viewed as inspirational, as participants felt that they had made significant progress in their recovery;

> *"Yeah it's exactly the same with the mentors as well. You can see them and say 'right okay the level of improvement they have made and [see what] we can get to"* (*P4*).

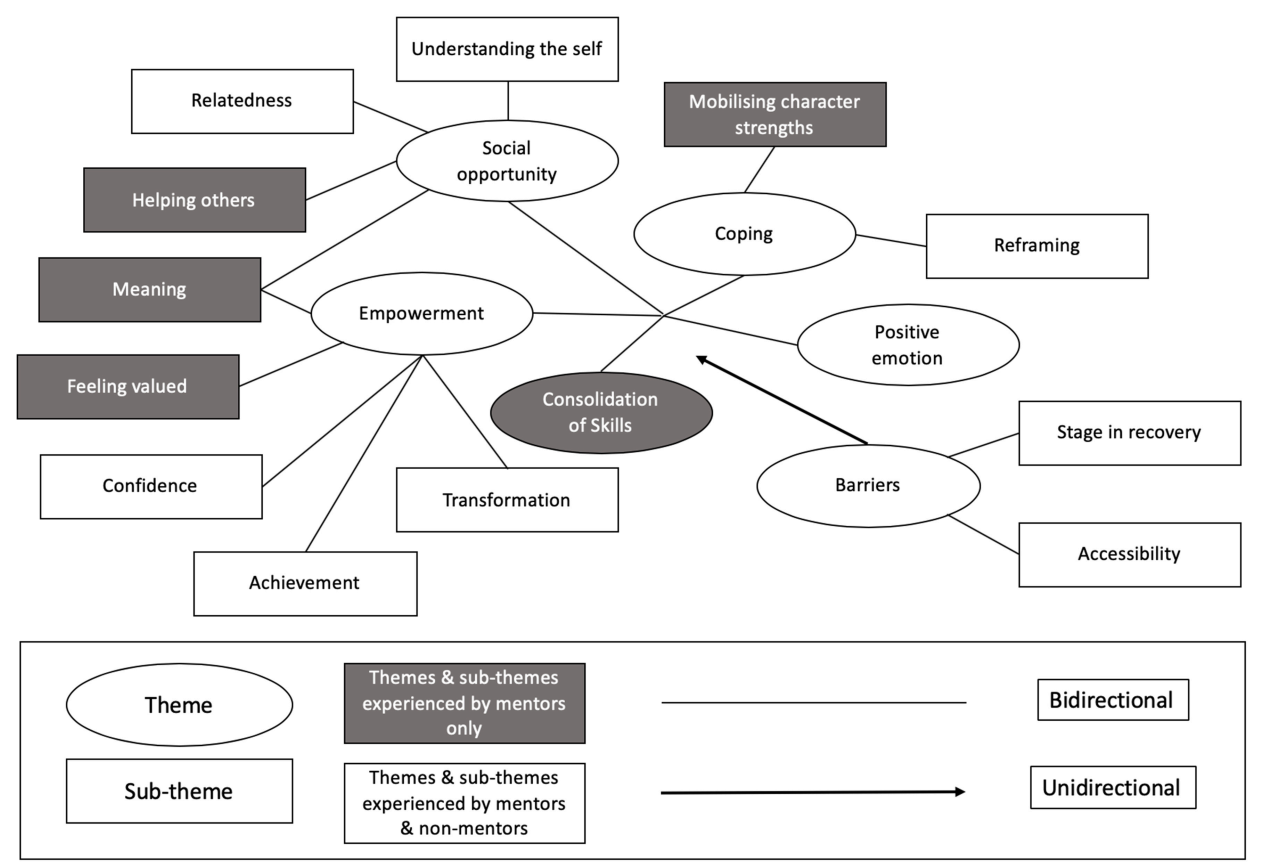

FIGURE 2 | Visualization of themes and sub-themes identified in thematic analysis of transcripts collected during focus groups and interviews on people living with ABI following positive psychotherapy.

Participants described that group membership allowed them to explore their individual symptomology. Participants were able to explore confusing and difficult behavior in a comfortable social arena;

> "*I couldn't explain myself before, whereas now I have outbursts of where I have got no breaks of… before I would say things and I would get so upset that I wouldn't get over it, why have I done that? I didn't understand why I was doing it. And I sort of isolated myself then. Sort of punishing myself. Whereas now I think it's okay to have that blip.*" (*P2*).

Coping Theme

This theme captures the sub-themes of positive reframing and mobilization of character strengths. Coping strategies learned during the intervention included grounding techniques, gratitude techniques, and humor;

> "*I am a lot happier, and because I have gone back to basics and hearing other people's stories at how they appreciate just the simple things you know… I'm putting a positive slant on things rather than a negative slant and I've been trying to do that a lot more.*" (P8).

The ability to reframe thoughts led to individuals viewing anxious situations as a marker for challenge;

> "*everybody has to fight their own battle, but you can get there and I think you can be happy no matter what.*" (*P8*);

Coping mechanisms such as reframing were underpinned by mobilization of character strengths (for mentors). The shift in attention from negative to positive emotion was reinforced by recognizing strength, instead of weakness;

> "*think when you've had an illness, and like us with the brain damage, afterward everything is negative. Because you're focusing on what you used to do and you can't do it anymore. But then you read your strengths and you think 'oh hang on a minute, you know*" (M2).

Cultivation of Positive Emotion Theme

Positive emotions were cultivated when experiencing empowerment, social opportunity, coping and consolidation of skills. For example, achieving the ability to execute tasks was associated with happiness and joy;

> "*I sat in the car and had this huge great big grin on my face…I didn't want to go I just felt so so amazing, so happy, I literally I felt so happy because to me I had achieved something*" (*P2*).

The creation of a new social network and social participation also lead to an increased sense of happiness;

> "*the friendships you make, and to walk away as a happier person*" (*P8*).

Helping others was associated with positive feelings;

> "*it's helped me put it into perspective and it sounds awful but that made me feel good*" (*M3*).

Positive emotions were also used as a coping mechanism when dealing with difficult situations;

> "*sometimes I may laugh at something I done whereas before I would cry.*" (*P2*).

Consolidation of Skills Theme

Mentoring allowed individuals to reinforce knowledge, serving as a reminder to maintain skills;

> "*I'd started to only see the negatives again. Whereas this has helped me to see the positives as well as the negatives and then deal with the negatives then, isn't it...It's like layers, like I'm building upon layers and then I think oh yeah, I remember now. I almost needed it [positive psychotherapy] to consolidate the information myself.*" (M2).

Revisiting the course several times over through mentoring also allowed mentors to absorb new information that they believed they had missed during prior courses;

> "*You just get little nuggets of information. Like somebody will say, just as a throwaway line, and you'll think- what? And you say, sorry can you repeat that? And you think- Ah! I forgot all about that! Why aren't I doing that? Um so I just get as much from it, well, probably more.*" (M4).

Barriers to Efficacy Theme

These theme captures two sub-themes including 'stage in recovery' and accessibility issues'. One participant (P7) noted that her stage in recovery impacted on how beneficial she found the group. She commented;

> "*I think if I'd have had this 5 years ago, 4 years ago, even 2 years ago when I was at rock bottom. I think it would have been such a great help...*" (P7).

However, P7 explained that although she felt further along in recovery and part of the course was less relevant to her, she still found it helpful to compare her own progress with others. In that sense, she felt grateful for her own progress;

> *"I feel further along with it. And I felt that even though it was really good for me to see that actually I'm not as bad as I think, other people."*

Many participants noted that the location of the intervention was difficult to access. The course was not located in proximal locations for some, which meant traveling long distances to participate in the course. Participants further noted that parking facilities at the location were extremely limited. Even with disabled badges, parking was still considered to be an issue;

> *"she had a disability badge and she still wouldn't be able to park so well... parking was a major thing there."* (*P7*).

DISCUSSION

This study explored whether positive psychotherapy might promote wellbeing in people living with ABI, and examined participants' experience of the intervention against the background of prevailing theoretical models. Thus, during analysis, concepts relating to these wellbeing models were identified and subsequently organized into themes within the context of ABI. The six themes identified in this paper included; empowerment, social opportunity, coping, consolidation of skills, cultivation of positive emotion and barriers to the efficacy of positive psychotherapy.

In line with Subjective Wellbeing (SWB; Diener, 1984; Fredrickson, 2001), Psychological Wellbeing (PWB; Ryff, 1989) and PERMA theory (Seligman, 2011), results indicate that positive psychotherapy promoted wellbeing in people living with ABI. Elements of both eudaimonic and hedonic aspects of wellbeing were identified in the analyzed transcripts. Consistent with eudaimonic theories of wellbeing, participants derived a sense of purpose and meaning through course participation. Mentors characterized their purpose as helping others by providing hope for future recovery as well as providing a unique perspective of ABI that only comes with lived experience. Participants derived purpose and meaning by developing skills and abilities, with an eye toward personal recovery so that they could eventually help others in similar situations.

Consistent with hedonic theories of wellbeing, the cultivation of positive emotion was associated with experiencing positive emotions due to learning and applying new skills, overcoming challenges, building and strengthening social ties and recognizing progress in one's recovery. Moreover, participants used coping skills to manage negative emotions by accepting them and refocusing attention on positive elements, suggesting that they had achieved greater emotional control. Central to SWB theory, emotional control led to the experience of low negative affective and high positive affect, promoting a sense of wellbeing. Consistent with Fredrickson's (2001) broaden and build theory, and Seligman's PERMA model (2011), a sense of achievement was usually accompanied with positive emotion, which spurred individuals to seek more situations in which they could experience the positive emotions associated with achievement, thus broadening their thought-action repertoire.

Factors associated with Ryff's Psychological Wellbeing theory (Ryff, 1989) such as self-acceptance, personal growth, purpose, environmental mastery and positive relations; and Seligman's PERMA model (2011) were discussed by participants. For example, participants experienced improvement in abilities, such as communication skills and the ability to overcome challenges, deriving a sense of achievement when doing so. A sense of achievement was associated with increased independence and autonomy for some. Gains in ability to execute a task resulted in reduced need for support. Participants described positive life changes due to personal development including gain in abilities, the development and employment of coping mechanisms, recognition of improvement and behavior over time and alterations in beliefs and attitudes toward challenges. The theme of "Social Opportunity" captured the positive relationships that participants experienced where they described feeling reciprocal support and empathy from others.

Thus, in terms of the aforementioned wellbeing theories, positive psychotherapy enhanced wellbeing for people living with Acquired Brain Injuries (ABI). In addition, this study also outlined context-specific factors that contributed to enhancing wellbeing. For example, within the theme "Social Opportunities" positive relationships were fostered leading to a sense of togetherness and a shared experience of living with ABI. Sharing of information related to symptoms, recovery and support, facilitated group bonding and strengthened relationships between participants. These findings are in line with other research on relatedness and ABI which suggests that a sense of belongingness is associated with psychosocial wellbeing (Bay et al., 2002, 2012). Individuals noted that the sense of relatedness was a core feature of the intervention as they described a sense of misunderstanding and stigmatization from individuals living without brain injury. Research has previously demonstrated that stigmatization of brain injury is reflected in negative attitudes toward survivors (McLellan et al., 2010). In addition, research has shown that the adverse effects of brain injury, such as anxiety and speech difficulties, are compounded by people's misunderstandings of brain injury as individuals attempt to minimize perceived mistakes leading overcompensation or societal withdrawal (McClure et al., 2006). Participants felt that their actions would not be wrongly judged by others in the group, providing them with a safe and comfortable space in which to explore their authentic self. In turn, participants described "feeling okay" to act outside of their comfort zone, promoting further opportunity for growth.

In addition, individuals in this study described learning and employing various coping skills. Participants found coping strategies to be beneficial when experiencing fatigue, a common symptom of ABI (Belmont et al., 2006). Research has demonstrated that the development of coping skills can help people with ABI adopt a more active lifestyle, as they learn strategies to manage the demands of the environment (Tomberg et al., 2005). The coping skills developed over the course of positive psychotherapy helped participants to reconcile loss relating to ability, social network, social participation and identity. Participants describe employing acceptance-based strategies, such as gratitude techniques and mindfulness, when becoming frustrated or distressed with loss. Through reframing, participants were able to focus on the positive aspects of one's life, giving rise to a new sense of appreciation for one's residual abilities. This process of reframing and accepting loss is consistent with Gracey et al. (2009) "Y-Shaped" model. According to this model, the process of adaptation and reintegration into society following brain injury involves identifying, understanding and resolving social and psychological discrepancies. These discrepancies can include a lack of understanding from others or stigmatization of ABI, withdrawal from social participation, and identified differences between pre-injury and current sense of self. As an individual works to resolve these discrepancies, aspects of continuity of self are discovered and developed leading to new, adaptive meanings associated with the self.

Consistent with the "Y-Shaped" model, the present study found that mentors were able to mobilize character strengths to underpin coping efforts. The sub-theme "Mobilization of Character Strengths" denotes how mentors first identified their character strengths, then understood how to employ them after which strength mobilization helped to create a more meaningful sense of identity. For example, mentors reported knowing themselves better and feeling more adaptive to situations. Mentors were then afforded the opportunity to consolidate their skills revisiting the course and absorbing new information. In addition, mentors consolidated their sense of meaning, to help others and provide hope for the future, with each course.

The theme relating to barriers outlined some of the issues raised by participants that may impact on the efficacy of the intervention. Relating to the sub-theme "stage in recovery" one participant in particular, noted that she felt further along in her recovery than her peers, resulting in frustration with elements of the intervention. She believed that the discussion of negative emotion, such as depression and anxiety in a group setting, did not facilitate positive change, instead viewing this as an example of "emotional dwelling." The frustration experienced early in the intervention resulted in reduced participation with other aspects of the course, such as the session on mindfulness. She explained that her reduced participation was a result of not wanting to dwell on negativity. Sessions were semi-structured, allowing for user-led discussions, so that participants could explore ideas salient to them. Holding the view that she was further in recovery, she noted that she did not relate to these ideas at her stage of recovery. However, this participant also described several positive experiences including comparing her progress to others who were less advanced in their recovery. According to social comparison theory (Festinger, 1954) downward social comparison is used as a means of self-evaluation, to compare the self with others that are considered to be worse-off to feel better about the self or personal circumstances (Tesser et al., 1988). This individual also noted that she had made a close friend in the group who was regarded as being at her level of recovery and described feeling a sense of relatedness and self-esteem as the only outcomes of the intervention for her. This suggests that group facilitators need to consider perceived stages in recovery in future psychotherapy and to group individuals according to their preferred stage when possible.

Another barrier was captured by the subtheme of "accessibility and location." Several participants noted that it was difficult for them to access the course, often traveling several hours each way in attendance. In addition, several participants described a lack of service provision in their local area, noting that accessing any type of community care-based therapy is difficult. Whilst, this issue did not translate to drop-outs in the present study, the mention of accessibility was recurrent, suggesting it was a salient concern for participants. The lack of service provision and long travel distances reflects the so-called treatment gap and lag (Wang et al., 2004; Patel et al., 2010), highlighting a need for major reform of current mental health treatment and its availability, especially when considering ongoing challenges associated with the increasing burden of chronic disease (GBD 2013 Mortality and Causes of Death Collaborators, 2014; Vos et al., 2015). Treatment gap refers to the numbers of people needing treatment and not receiving it, while the treatment lag refers to the amount of time taken to receive care when it does exist. Studies suggest that the mental health treatment gap exceeds 50% in all countries, and 90% in those countries with less resources (Patel et al., 2010), while the treatment lag can be as long as 10 years (e.g., Wang et al., 2004).

Recent criticism of wellbeing models has emphasized their individualistic focus and a lack of consideration of community, the environment within which individuals live, wider societal influences and socio-structural factors such as community resources and inequality (e.g., Carlisle et al., 2009; Ehrenreich, 2010; Davies, 2015; Frawley, 2015). Unfortunately, this has led to a tired debate between proponents of individualist versus structural approaches to health promotion, ignoring a need for their combination. In response, we have proposed a model of health and wellbeing, the GENIAL model, that spans both approaches (Kemp et al., 2017; Mead et al., 2019), emphasizing a role for the individual, community and the wider environment. Our model and its recent iteration (Kemp et al., 2017; Mead et al., 2019) characterizes socio-structural influences over individual health-related behaviors and subsequent wellbeing, emphasizing an important role for community cohesion and collective efficacy to support individual health-related goals. In doing so, our model emphasizes important roles for novel vehicles for change such as task shifting and partnership working to improve individual wellbeing and longevity. Further research is also needed on the role community organizations can play in the health and wellbeing of people living with ABI to support interventions such as positive psychotherapy.

With respects to limitations, the study was based on qualitative analysis of a service-user evaluation, and conclusions are therefore restricted to the service from which data was collected. However, results are interpreted in the context of available theory and therefore lay useful foundations for healthcare service improvement. Data collection was also restricted to a single timepoint as it was not pragmatic to carry out repeat interviews. One advantage of repeat interviews is the ability to explore processes over time. Whilst this will be important for future work, our goal was to identify the factors that contribute to wellbeing in participants and mentors living with ABI. Future studies should consider exploring how these processes change over time. Similarly, when conducting interviews, it was not feasible or pragmatic to return transcripts to participants for comment. However, our service is underpinned by a participatory and collaborative approach to service development and improvement. We note further that findings have been shared with and positively received by the brain injury community, demonstrating enthusiasm for improving the healthcare of people living with ABI by focusing on wellbeing rather than a restricted focus on impairment. Another limitation is relatively small sample size, which comprised those who access the service, as well as subsequent inclusion and exclusion criteria. However, recurrence of themes was noted during analysis, and participants' experiences could be coded within a common or shared set of themes and sub themes. We further note that there has been debate over application of the principle of saturation by qualitative researchers who have recognized that complete saturation is rarely possible (Charmaz, 2006) and may not always be appropriate (O'Reilly and Parker, 2012; Malterud et al., 2016). Finally, it is recognized that the use of mini-groups and individual interviews are distinct tools, however we adopted a mixed approach to ensure that the needs and preferences of all service users were met. Carlsson et al. (2007) note that those with ABI are often excluded from qualitative enquiry due to the methodological challenges incurred from communication issues or fatigue. As such, it is recommended that individuals with ABI are supported throughout the interview process. In this case, we sought to provide individuals with a choice over interview type in order to provide more individualized communication support. In this way, we have followed the guidance of Carlsson et al., and employed adjustments to our methodological approach in order to capture the voices of individuals who are otherwise marginalized (Paterson et al., 2001).

In summary, this study provides new qualitative data to support the use of positive psychotherapy for enhancing wellbeing in individuals living with ABI. Importantly, and for the first time, certain themes (i.e., consolidation of skills) and sub-themes (helping others, meaning, feeling valued and mobilization of character strengths) were identified, emphasizing the benefits associated with acting as mentors for those experiencing positive psychotherapy. These findings suggest that mentors may provide the healthcare sector with an underutilized community resource for ensuring that mental health services for people living with ABI are more sustainable and may help to bridge the treatment gap and better support service users including mentors and participants at the same time. Further research exploring these novel insights is warranted. Critically, our findings indicate that it is possible to improve the wellbeing of people with ABI, despite the impairments caused by their condition. In terms of healthcare, this suggests a need for more effective models of care for people with chronic conditions (including ABI) which not only focus on reducing impairment, but also on improving wellbeing. Given, emerging evidence that health and wellbeing is contingent on individual, community and environmental factors (see Mead et al., 2019 for review), "health and wellbeing" should no longer be thought of as "the remit" of the health service. There is a need for greater partnership working between health services, universities and community organizations to create evidenced-based environments designed to improve health and wellbeing.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements.

AUTHOR CONTRIBUTIONS

ZF and AK conceptualized, planned and supervised the project supported by JP, FG, and JT. ZF was responsible for delivery of the intervention, supported by AK, HB, and LW. CT completed this study in partial fulfilment of her MSc degree. All authors edited the manuscript for intellectual content and approved the final version prior to submission.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2020.00066/full#supplementary-material

REFERENCES

Alimujiang, A., Wiensch, A., Boss, J., Fleischer, N. L., Mondul, A. M., McLean, K., et al. (2019). Association between life purpose and mortality among US adults older than 50 years. *JAMA Netw. Open* 2:e194270. doi: 10.1001/jamanetworkopen.2019.4270

Anderson, R. M. (1995). Patient empowerment and the traditional medical model: a case of irreconcilable differences? *Diabetes Care* 18, 412–415. doi: 10.2337/diacare.18.3.412

Andrewes, H. E., Walker, V., and O'Neill, B. (2014). Exploring the use of positive psychology interventions in brain injury survivors with challenging behaviour. *Brain Injury* 28, 965–971. doi: 10.3109/02699052.2014.888764

Archer, M., Bhaskar, R., Collier, A., Lawson, T., and Norrie, A. (2013). *Critical Realism: Essential Readings*. Abingdon: Routledge.

Ayerbe, L., Ayis, S., Wolfe, C. D., and Rudd, A. G. (2013). Natural history, predictors and outcomes of depression after stroke: systematic review and meta-analysis. *Br. J. Psychiatry* 202, 14–21. doi: 10.1192/bjp.bp.111.107664

Barber, S., Bate, A., Adcock, A., Harker, R., Roberts, N., Woodhouse, J., et al. (2018). *House of Commons Library, Debate Pack: Acquired Brain Injury*. Available at: http://researchbriefings.files.parliament.uk/documents/CDP-2018-0145/CDP-2018-0145.pdf (accessed October 5, 2018).

Barman, A., Chatterjee, A., and Bhide, R. (2016). Cognitive impairment and rehabilitation strategies after traumatic brain injury. *Indian J. Psychol. Med.* 38, 172–181. doi: 10.4103/0253-7176.183086

Bay, E., Hagerty, B. M., Williams, R. A., Kirsch, N., and Gillespie, B. (2002). Chronic stress, sense of belonging, and depression among survivors of traumatic brain injury. *J. Nurs. Scholarsh.* 34, 221–226. doi: 10.1111/j.1547-5069.2002.00221.x

Bay, E. H., Blow, A. J., and Yan, X. (2012). Interpersonal relatedness and psychological functioning following traumatic brain injury: implications for marital and family therapists. *J. Marit. Fam. Therapy* 38, 556–567. doi: 10.1111/j.1752-0606.2011.00231.x

Belmont, A., Agar, N., Hugeron, C., Gallais, B., and Azouvi, P. (2006). Fatigue and traumatic brain injury. *Ann. Readapt. Med. Phys.* 49, 370–374.

Ben-Shahar, T. (2010). *Even Happier: A Gratitude Journal for Daily Joy and Lasting Fulfillment*. New York, NY: McGraw-Hill.

Bertisch, H., Rath, J., Long, C., Ashman, T., and Rashid, T. (2014). Positive psychology in rehabilitation medicine: a brief report. *Neurorehabilitation* 34, 573–585. doi: 10.3233/nre-141059

Bhaskar, R., Collier, A., Lawson, T., and Norrie, A. (1998). "Critical realism," in *Proceedings of the Standing Conference on Realism and Human Sciences* (Bristol: IEEE).

Boehm, J. K., and Kubzansky, L. D. (2012). The heart's content: the association between positive psychological well-being and cardiovascular health. *Psychol. Bull.* 138, 655–691. doi: 10.1037/a0027448

Bolier, L., Haverman, M., Westerhof, G., Riper, H., Smit, F., and Bohlmeijer, E. (2013). Positive psychology interventions: a meta-analysis of randomized controlled studies. *BMC Public Health* 13:119. doi: 10.1186/1471-2458-13-119

Braun, V., and Clarke, V. (2006). Using thematic analysis in psychology. *Qual. Res. Psychol.* 3, 77–101. doi: 10.1191/1478088706qp063oa

Carlisle, S., Henderson, G., and Hanlon, P. W. (2009). 'Wellbeing': a collateral casualty of modernity? *Soc. Sci. Med.* 69, 1556–1560. doi: 10.1016/j.socscimed.2009.08.029

Carlsson, E., Paterson, B. L., Scott-Findlay, S., Ehnfors, M., and Ehrenberg, A. (2007). Methodological issues in interviews involving people with communication impairments after acquired brain damage. *Qual. Health Res.* 17, 1361–1371. doi: 10.1177/1049732307306926

Chakhssi, F., Kraiss, J., Sommers-Spijkerman, M., and Bohlmeijer, E. (2018). The effect of positive psychology interventions on well-being and distress in clinical samples with psychiatric or somatic disorders: a systematic review and meta-analysis. *BMC Psychiatry* 18:211. doi: 10.1186/s12888-018-1739-2

Charmaz, K. (2006). *Constructing Grounded Theory: A Practical Guide Through Qualitative Analysis*. Thousand Oaks: Sage.

Cogan, A. (2016). From surviving to flourishing: using narrative as a tool for patient-centered care. *J. Hum. Rehabil.* 1–10.

Cullen, B., Pownall, J., Cummings, J., Baylan, S., Broomfield, N., Haig, C., et al. (2018). Positive psychotherapy in ABI Rehab (PoPsTAR): a pilot randomised controlled trial. *Neuropsychol. Rehabil.* 28, 17–33. doi: 10.1080/09602011.2015.1131722

Davies, W. (2015). *The Happiness Industry*. London: Verson Books.

de Freitas Cardoso, M. G., Faleiro, R. M., de Paula, J. J., Kummer, A., Caramelli, P., Teixeira, A. L., et al. (2019). Cognitive impairment following acute mild traumatic brain injury. *Front. Neurol.* 10:198. doi: 10.3389/fneur.2019.00198

Diener, E. (1984). Subjective well-being. *Psychol. Bull.* 95, 542–575.

Dikmen, S. S., Corrigan, J. D., Levin, H. S., Machamer, J., Stiers, W., and Weisskopf, M. G. (2009). Cognitive outcome following traumatic brain injury. *J. Head Trauma Rehabil.* 24, 430–438. doi: 10.1097/HTR.0b013e3181c133e9

DuBois, C. M., Beach, S. R., Kashdan, T. B., Nyer, M. B., Park, E. R., Celano, C. M., et al. (2012). Positive psychological attributes and cardiac outcomes: associations, mechanisms, and interventions. *Psychosomatics* 53, 303–318. doi: 10.1016/j.psym.2012.04.004

Ehrenreich, B. (2010). *Smile or Die: How Positive Thinking Fooled America and the World*. London: Granta.

Emmons, R. A., and Crumpler, C. A. (2000). Gratitude as a human strength: appraising the evidence. *J. Soc. Cli. Psychol.* 19, 56–69. doi: 10.1521/jscp.2000.19.1.56

Emmons, R. A., and Stern, R. (2013). Gratitude as a psychotherapeutic intervention. *J. Clin. Psychol.* 69, 846–855. doi: 10.1002/jclp.22020

Fernández, M., Gómez, L. E., Arias, V. B., Aguayo, V., Amor, A. M., Andelic, N., et al. (2019). A new scale for measuring quality of life in acquired brain injury. *Qual. Life Res.* 28, 801–814. doi: 10.1007/s11136-018-2047-5

Festinger, L. (1954). A theory of social comparison processes. *Hum. Relat.* 7, 117–140. doi: 10.1177/001872675400700202

Frawley, A. (2015). Happiness research: a review of critiques. *Sociol. Compass* 9, 62–77. doi: 10.1111/soc4.12236

Fredrickson, B. L. (2001). The role of positive emotions in positive psychology: the broaden-and-build theory of positive emotions. *Am. Psychol.* 56, 218–226. doi: 10.1037/0003-066x.56.3.218

GBD 2013 Mortality and Causes of Death Collaborators (2014). Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the global burden of disease study 2013. *Lancet* 385, 117–171. doi: 10.1016/s0140-6736(14)61682-2

Gedde-Dahl, M., and Fors, E. A. (2012). Impact of self-administered relaxation and guided imagery techniques during final trimester and birth. *Complement. Ther. Clin. Pract.* 18, 60–65. doi: 10.1016/j.ctcp.2011.08.008

Gillen, R., Tennen, H., McKee, T. E., Gernert-Dott, P., and Affleck, G. (2001). Depressive symptoms and history of depression predict rehabilitation efficiency in stroke patients. *Arch. Phys. Med. Rehabil.* 82, 1645–1649. doi: 10.1053/apmr.2001.26249

Gracey, F., Evans, J. J., and Malley, D. (2009). Capturing process and outcome in complex rehabilitation interventions: a "Y-shaped" model. *Neuropsychol. Rehabil.* 19, 867–890. doi: 10.1080/09602010903027763

Hanslik, T., and Flahault, A. (2016). Overmedicalization: when too much medicine harms. *La Rev. Med. Intern.* 37, 201–205. doi: 10.1016/j.revmed.2015.10.009

Harris, C., Daniels, K., and Briner, R. B. (2003). Short research paper A daily diary study of goals and affective well-being at work. *J. Occup. Organiz. Psychol.* 76, 401–410. doi: 10.1348/096317903769647256

Hölzel, B. K., Carmody, J., Vangel, M., Congleton, C., Yerramsetti, S. M., Gard, T., et al. (2011). Mindfulness practice leads to increases in regional brain gray matter density. *Psychiatry Res. Neuroimaging* 191, 36–43. doi: 10.1016/j.pscychresns.2010.08.006

James, C. (2011). Law student wellbeing: benefits of promoting psychological literacy and self-awareness using mindfulness, strengths theory and emotional intelligence. *Legal Educ. Rev.* 21, 217–233.

Jose, P. E., Lim, B. T., and Bryant, F. B. (2012). Does savoring increase happiness? A daily diary study. *J. Posit. Psychol.* 7, 176–187. doi: 10.1080/17439760.2012.671345

Kane, A. W., Diaz, D. S., and Moore, C. (2019). Physical therapy management of adults with mild traumatic brain injury. *Semin. Speech Lang.* 40, 36–47. doi: 10.1055/s-0038-1676652

Keller, V. F., and Carroll, J. G. (1994). A new model for physician-patient communication. *Patient Educ. Couns.* 23, 131–140. doi: 10.1016/0738-3991(94)90051-5

Kemp, A. H., Arias, J. A., and Fisher, Z. (2017). "Social ties, health and wellbeing: a literature review and model," in *Neuroscience and Social Science*, eds A. Ibáñez, L. Sedeño, and A. García (Cham: Springer), 397–427. doi: 10.1007/978-3-319-68421-5_17

Larsson, G., and Starrin, B. (1992). Relaxation training as an integral part of caring activities for cancer patients: effects on wellbeing. *Scand. J. Caring Sci.* 6, 179–185. doi: 10.1111/j.1471-6712.1992.tb00149.x

Malterud, K., Siersma, V., and Guassora, A. (2016). Sample size in qualitative interview studies. *Qual. Health Res.* 26, 1753–1760. doi: 10.1177/1049732315617444

McClure, J., Devlin, M. E., McDowall, J., and Wade, K. (2006). Visible markers of brain injury influence attributions for adolescents' behaviour. *Brain Injury* 20, 1029–1035. doi: 10.1080/02699050600909870

McKevitt, C., Fudge, N., Redfern, J., Sheldenkar, A., Crichton, S., Rudd, A. R., et al. (2011). Self-reported long-term needs after stroke. *Stroke* 42, 1398–1403. doi: 10.1161/STROKEAHA.110.598839

McLellan, T., Bishop, A., and McKinlay, A. (2010). Community attitudes toward individuals with traumatic brain injury. *J. Int. Neuropsychol. Soc.* 16, 705–710. doi: 10.1017/s1355617710000524

Mead, J., Fisher, Z., Wilkie, L., Gibbs, K., Pridmore, J., Tree, J., et al. (2019). Rethinking wellbeing: toward a more ethical science of wellbeing that considers current and future generations. *Authorea* doi: 10.22541/au.156649190.08734276

Milders, M., Fuchs, S., and Crawford, J. R. (2003). Neuropsychological impairments and changes in emotional and social behaviour following severe traumatic brain injury. *J. Clin. Exp Neuropsychol.* 25, 157–172. doi: 10.1076/jcen.25.2.157.13642

Naylor, C., Parsonage, M., McDaid, D., Knapp, M., Fossey, M., and Galea, A. (2012). *Long-Term Conditions and Mental Health: The Cost of Co-Morbidities*. London: The Kings Fund.

O'Reilly, M., and Parker, N. (2012). 'Unsatisfactory Saturation': a critical exploration of the notion of saturated sample sizes in qualitative research. *Qual. Res.* 13, 190–197. doi: 10.1177/1468794112446106

Oyesanya, T. (2017). The experience of patients with ABI and their families during the hospital stay: a systematic review of qualitative literature. *Brain Injury* 31, 151–173. doi: 10.1080/02699052.2016.1225987

Panter-Brick, C., and Leckman, J. F. (2013). Editorial commentary: resilience in child development–interconnected pathways to wellbeing. *J. Child Psychol. Psychiatry* 54, 333–336. doi: 10.1111/jcpp.12057

Patel, V., Maj, M., Flisher, A. J., De Silva, M. J., Koschorke, M., Prince, M., et al. (2010). Reducing the treatment gap for mental disorders: a WPA survey. *World Psychiatry* 9, 169–176.

Paterson, B. L., Thorne, S. E., Canam, C., and Jillings, C. (2001). *Meta-Study of Qualitative Health Research: A Practical Guide to Meta-Analysis and Meta-Synthesis*, Vol. 3. Thousand Oaks: Sage.

Peterson, C., and Seligman, M. E. P. (2004). *Character Strengths and Virtues: A Handbook and Classification*. New York, NY: Oxford University Press.

Richman, L. S., Kubzansky, L., Maselko, J., Kawachi, I., Choo, P., and Bauer, M. (2005). Positive emotion and health: going beyond the negative. *Health Psychol.* 24, 422–429. doi: 10.1037/0278-6133.24.4.422

Ryff, C. D. (1989). Happiness is everything, or is it? Explorations on the meaning of psychological well-being. *J. Pers. Soc. Psychol.* 57, 1069–1081. doi: 10.1037/0022-3514.57.6.1069

Ryff, C. D. (1995). Psychological well-being in adult life. *Curr. Direct. Psychol. Sci.* 4, 99–104. doi: 10.1111/1467-8721.ep10772395

Saatman, K. E., Duhaime, A. C., Bullock, R., Maas, A. I., Valadka, A., and Manley, G. T. (2008). Classification of traumatic brain injury for targeted therapies. *J. Neurotrauma* 25, 719–738. doi: 10.1089/neu.2008.0586

Sánchez, L. E. G. (2010). *Consideraciones Conceptuales y Metodológicas Sobre el Desarrollo de Escalas Multidimensionales de Calidad de Vida Centradas en el Contexto*. Doctoral dissertation, Universidad de Salamanca, Salamanca.

Sansone, R. A., and Sansone, L. A. (2010). Gratitude and well being: the benefits of appreciation. *Psychiatry* 7, 18–22.

Schretlen, D. J., and Shapiro, A. M. (2003). A quantitative review of the effects of traumatic brain injury on cognitive functioning. *Int. Rev. Psychiatry* 15, 341–349. doi: 10.1080/09540260310001606728

Seligman, M. (2011). *Flourish*. New York, NY: Free Press.

Sherliker, L., and Steptoe, A. (2000). Coping with new treatments for cancer: a feasibility study of daily diary measures. *Patient Educ. Counsel.* 40, 11–19. doi: 10.1016/s0738-3991(99)00047-6

Sin, N. L., and Lyubomirsky, S. (2009). Enhancing well-being and alleviating depressive symptoms with positive psychology interventions: a practice-friendly meta-analysis. *J. Clin. Psychol.* 65, 467–487. doi: 10.1002/jclp.20593

Tayabas, L. M., Castillo Leon, T., and Monarrez Espino, J. (2014). Qualitative evaluation: a critical and interpretative complementary approach to improve health programs and services. *Int. J. Qual. Stud. Health Well Being* 9:24417. doi: 10.3402/qhw.v9.24417

Tedmanson, D., and Guerin, P. (2011). Enterprising social wellbeing: social entrepreneurial and strengths based approaches to mental health and wellbeing in "remote" Indigenous community contexts. *Austral. Psychiatry* 19, S30–S33. doi: 10.3109/10398562.2011.583078

Tesser, A., Millar, M., and Moore, J. (1988). Some affective consequences of social comparison and reflection processes: the pain and pleasure of being close. *J. Pers. Soc. Psychol.* 54, 49–61. doi: 10.1037/0022-3514.54.1.49

Tomberg, T., Toomela, A., Pulver, A., and Tikk, A. (2005). Coping strategies, social support, life orientation and health-related quality of life following traumatic brain injury. *Brain Injury* 19, 1181–1190. doi: 10.1080/02699050500150153

Tufford, L., and Newman, P. (2012). Bracketing in qualitative research. *Qual. Soc. Work* 11, 80–96. doi: 10.1177/1473325010368316

van Eeden, M., van Mastrigt, G. A., Evers, S. M., van Raak, E. P., Driessen, G. A., and van Heugten, C. M. (2016). The economic impact of mental healthcare consumption before and after stroke in a cohort of stroke patients in the Netherlands: a record linkage study. *BMC Health Serv. Res.* 16:688. doi: 10.1186/s12913-016-1915-3

Vos, T., Barber, R. M., Bell, B., and Bertozzi-Villa, A. (2015). Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the global burden of disease study 2013. *Lancet* 2015, 743–800.

Wang, P. S., Berglund, P. A., Olfson, M., and Kessler, R. C. (2004). Delays in initial treatment contact after first onset of a mental disorder. *Health Serv. Res.* 39, 393–416. doi: 10.1111/j.1475-6773.2004.00234.x

World Health Organization [WHO], (1948). *Preamble to the Constitution of the World Health Organization as Adopted by the International Health Conference, New York, 19-22 June, 1946; Signed on 22 July 1946 by the Representatives of 61 States (Official Records of the World Health Organization, no. 2, p. 100) and Entered into Force on 7 April 1948.* Geneva: WHO.

Yardley, L. (2000). Dilemmas in qualitative health research. *Psychol. Health* 15, 215–228. doi: 10.1080/08870440008400302

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Gender Differences in Dysfunctional Attitudes in Major Depressive Disorder

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Background: Dysfunctional attitudes play a key role in the development and prognosis of depression. Gender also plays an important role in many clinical features of major depressive disorder (MDD). This study is aimed at investigating the gender differences in dysfunctional attitudes in patients with MDD.

Methods: One hundred and seventy-two patients with MDD and 159 healthy controls (HCs) were enrolled in this study. Dysfunctional attitudes were assessed by the Chinese version of the dysfunctional attitude scale—form A (C-DAS-A) and depression severity was assessed by the 24-item Hamilton rating scale for depression ($HAMD_{24}$). The 14-item Hamilton Anxiety Rating Scale ($HAMA_{14}$) was used to measure anxiety. Factorial analysis of variance (ANOVA) of gender and diagnosis on C-DAS-A total and factor scores was adopted with age, education, and body mass index (BMI) controlled. Multiple linear regression analyses of DAS were performed in the MDD group.

Results: First, the C-DAS-A score in the MDD group was increased significantly than HCs. Second, female patients with MDD showed significantly higher scores in C-DAS-A total and three-factor scores (seeking applause, dependence, and self-determination attitude), while no significant difference between female HCs and male HCs was detected. Third, five variables (age, gender, smoking history, $HAMD_{24}$, and $HAMA_{14}$) had predictive effects on and gender showed the greatest contributions to C-DAS-A total and three-factor scores (seeking applause, dependence, and self-determination attitude).

Conclusion: Females with MDD may be linked to more severe cognitive distortion than their male counterparts in seeking applause, dependence, and self-determination attitude, supporting the reasonableness for gender-specific psychosocial interventions.

Keywords: major depressive disorder, dysfunctional attitudes, gender differences, seeking applause, dependence, self-determination attitude, gender-specific interventions

INTRODUCTION

According to Beck's cognitive model, depression results from an interaction of negative thinking styles and stressful events (1). These negative thinking styles are typically conceptualized as dysfunctional attitudes, which are rigid and maladaptive beliefs about oneself, the world, and the future. Previous studies have shown that dysfunctional attitudes play a central role in the development and prognosis of depression (2). Specifically, subjects with dysfunctional attitudes are associated with higher risk and poorer prognosis of major depressive disorder (MDD) (3), including more severe depression (4), poorer response to antidepressant treatment (5), shorter time to (6–8), and higher risk of (6) relapse and/or recurrence.

On the other hand, gender also plays a major role in many clinical features of MDD. The lifetime prevalence of depression in females is twice as that in males (9, 10). Females with MDD tend to show younger age of onset (11), longer duration (12), more severe and recurrent episodes (13), higher comorbidity of anxiety, lower comorbidity of substance use, greater functional impairment (11), and lower quality of life (14) than male patients. In the clinical symptomatology, females with MDD report higher rates of increased appetite and weight gain, somatic concern, and hypochondriasis than their male counterparts (12, 15). Taking the roles of gender and dysfunctional attitudes in depression together, it is of particular interest whether there may as well be gender differences in the dysfunctional attitudes of MDD.

Several studies have investigated gender differences in dysfunctional attitudes in the general population and patients with MDD, but the results are mixed. A study recruiting 644 college students showed that there is no gender difference in the dysfunctional attitude scale (DAS) (16). Two studies found no gender difference in dysfunctional attitudes in depressed patients (17, 18), while the other two studies found more dysfunctional attitudes in female patients than in male patients. Specifically, Farmer et al. (19) found that female patients and their siblings show more dysfunctional attitudes on dependence as compared with their male counterparts. Ou et al. (20) found that female patients with hypertension comorbid with depression show significantly higher scores in five factors (attraction and repulsion, compulsion, seeking applause, dependence, self-determination attitude) and lower scores in one factor (cognition philosophy) of the DAS than male patients. These findings indicate that gender differences in dysfunctional attitudes may vary across samples with different characteristics or diagnoses.

Given the key role of dysfunctional attitudes in MDD and the common gender differences in the clinical features of depression, we conducted this study to investigate gender differences in dysfunctional attitudes in a Chinese adult MDD sample. Based on the poorer prognosis of female MDD patients than male MDD patients, we hypothesized that females with MDD would show more dysfunctional attitudes than their male counterparts.

MATERIALS AND METHODS

Subjects

The data reported in this paper comes from a large-sample, longitudinal project investigating the biological and psychological mechanisms of MDD (hypothalamic-pituitary-adrenal axis function and magnetic resonance imaging study of trauma-related depression, registration number: ChiCTR1800014591). We used structural and functional magnetic resonance imaging (MRI) to investigate the neural substrates of MDD and to assess the correlations between clinical and psychological variables (including dysfunctional attitudes) and neural substrates in MDD. We also assessed the hypothalamic-pituitary-adrenal axis function in MDD patients.

One hundred and seventy-two patients were recruited from the Zhumadian Psychiatric Hospital, Henan, China. The participant enrollment procedure took place from January 2013 to December 2018. Patients were diagnosed by two experienced psychiatrists based on the Structured Clinical Interview for DSM-IV (SCID-IV). The severity of depression was moderate-to-severe with a 24-item Hamilton rating scale for depression ($HAMD_{24}$) total score > 19. Patients meeting the following criteria were excluded: 1) met the diagnostic criteria of other psychiatric disorders excepting for generalized anxiety disorder (GAD); 2) had substance abuse history apart from tobacco dependence; 3) had a history of severe physical condition; and 4) had significant suicide ideation or suicide attempts. One hundred and fifty-nine healthy controls (HCs) with a $HAMD_{24}$ total score < 8 were enrolled from the nearby communities of the Zhumadian Psychiatric Hospital. None of them had a current or lifetime diagnosis of any psychiatric disorders or substance abuse except for tobacco dependence. All of the participants aged 18–55 years. A more detailed description of the inclusion and exclusion criteria of participants has been reported in another paper of this project (21).

The present study was approved by the ethics committee of the Second Xiangya Hospital of Central South University and the ethics committee of the Zhumadian Psychiatric Hospital. Written informed consent was obtained from all of the participants after a detailed explanation of the purpose and procedure of the study.

Measures

Dysfunctional Attitudes

Dysfunctional attitudes are usually assessed by DAS (22). Two forms of DAS have been developed: form A (DAS-A) and form B (DAS-B). Between them, DAS-A is used much more frequently than DAS-B since both of them have similar psychometric properties but DAS-A has much fewer items and takes a much shorter time than DAS-B. In this study, we used the Chinese version of the dysfunctional attitude scale—form A (C-DAS-A), which has shown good reliability and validity in a Chinese MDD sample (23, 24). The C-DAS-A is a self-report scale consisting of 40 items. Each item consists of a statement about the subject and a 7-point Likert scale assessing the extent of agreement (7 = fully

TABLE 1 | Demographics and clinical information of major depressive disorder (MDD) and healthy control (HC) groups.

Item	MDD		P_1	HC		P_2	P_3
	Male (n = 75)	Female (n = 97)		Male (n = 74)	Female (n = 85)		
Age (years)	33.25 ± 9.86	36.55 ± 9.32	**.026**	30.04 ± 8.00	38.48 ± 8.20	**< .001**	.591
Gender (%)	43.6	56.4	–	46.5	53.5	–	.592
Education (years)	10.87 ± 3.63	9.79 ± 3.30	**.045**	11.96 ± 3.00	10.35 ± 3.90	**.004**	**.032**
BMI (kg/m^2)	21.91 ± 2.97	22.08 ± 3.11	.718	24.53 ± 3.14	22.87 ± 2.62	**< .001**	**< .001**
First episode age (years)	29.86 ± 9.93	32.30 ± 10.12	**.027**	–	–	–	–
HAMD$_{24}$	30.89 ± 6.76	32.20 ± 7.70	.482	1.11 ± 1.71	2.02 ± 2.73	.091	**< .001**
HAMA$_{14}$	17.58 ± 5.47	18.85 ± 6.67	.331	0.89 ± 1.58	1.81 ± 2.37	.206	**< .001**

Data are presented as mean ± SD; Bold values indicate statistical significance; MDD, major depressive disorder; HC, healthy control; BMI, Body mass index; HAMD$_{24}$, 24-item Hamilton Rating Scale for Depression; HAMA$_{14}$, 14-item Hamilton Anxiety Rating Scale; P_1, statistical significance of MDD group; P_2, statistical significance of HC group; P_3, statistical significance of MDD and HC groups.

agree; 1 = fully disagree). Ten items are scored reversely (item 2, 6, 12, 18, 24, 29, 30, 35, 37, 40). The higher the total score, the more dysfunctional attitudes. In the study of the reliability and validity of the C-DAS-A for Chinese MDD patients, an eight-factor structure (24) of C-DAS-A was proposed and adopted widely in later studies (20, 25, 26), which was also used in the present study. The eight factors are vulnerability (vulnerable self-confidence such as hold an attitude that "People will probably think less of me if I make a mistake"), attraction and repulsion (believe that happiness depends on other's love, e.g., "If others dislike you, you cannot be happy"), perfectionism (pursuit perfection immoderately like "It is difficult to be happy unless one is good looking, intelligent, rich and creative"), compulsion (selective or overly generalization like "To be a good, moral, worthwhile person, I must help everyone who needs it"), seeking applause (has a rigid tendency to pursue the approval of others like "My value as a person depends greatly on what others think of me"), dependence (lack of self-independence like "If you don't have other people to lean on, you are bound to be sad"), self-determination attitude (casting one's value to comparison with others like "If I do not do as well as other people, it means I am an inferior human being"), and cognition philosophy (positive attitudes such as "Happiness is more a matter of my attitude toward myself than the way other people feel about me"). Items categorized into each factor were reported in Chen et al. (24)

Depression

Depression was assessed by the HAMD$_{24}$, which is the most widely used clinician-report scale of depression.

Anxiety

The 14-item Hamilton Anxiety Rating Scale (HAMA$_{14}$) was used to assess anxiety. The total score of HAMA$_{14}$ > 14 means definite anxiety symptoms.

Data Analysis

Firstly, two-sample independent t-tests and chi-square tests were used to assess the differences in the demographic information between different groups. Analysis of covariance (ANCOVA) was performed to assess the differences in the clinical information between different groups with unmatched demographic variables as covariance respectively. Secondly, factorial analysis of variance (ANOVA) of gender and diagnosis on C-DAS-A total and factor scores was performed with age, education, and body mass index (BMI) controlled. When there was a significant interaction effect between gender and diagnosis, the simple effects of gender on C-DAS-A total and factor scores were analyzed in the MDD group and HC group separately. Lastly, to investigate the effects of age, gender, education, BMI, smoking history, HAMD$_{24}$, HAMA$_{14}$ predicting dysfunctional attitudes in MDD patients, multiple linear regression analyses were used. Statistical significance was set as a two-tailed P ≤ .05.

RESULTS

Demographic and Clinical Information of MDD and HC Groups

Demographic and clinical information of MDD patients and HCs are shown in **Table 1**. In the MDD group, gender differences were shown in age, education, and first episode age (P_1 = .026, .045, .027, respectively). There were no differences in BMI, HAMD$_{24}$, and HAMA$_{14}$ (all P_1 > .05). In subgroup analyses of MDD patients, 114 patients are moderate MDD and 58 patients are severe MDD. We defined that consuming tobacco in a lifetime or currently smoking any amount as having a smoking history and there are 155 patients with no smoking history and 17 with a smoking history. 126 patients are comorbid with GAD and 46 patients are not comorbid with GAD. No significant difference was found in C-DAS-A total score between subgroups of moderate or severe patients, patients with or without GAD, as well as patients with and without smoking history (**Table S1**). The differences in demographic and clinical information of different severity of MDD patients and HC groups are shown in **Table S2**.

In the HC group, males and females showed significant differences in education, age, and BMI (P_2 = .004, < .001, < .001, respectively). Distribution of HAMD$_{24}$ and HAMA$_{14}$ was balanced between males and females (all P_2 > .05). No statistical significance was noted in age and gender between MDD and HC groups (all P_3 > .05). MDD group had lower education years (P_3 = .032) and BMI (P_3 < .001). Moreover, patients with MDD showed significantly higher $HAMD_{24}$ and $HAMA_{14}$ total score than the HC group (all $P_3 < .001$).

ANCOVA of C-DAS-A Total and Factor scores of MDD and HC Groups

Table 2 shows the ANCOVA of C-DAS-A total and factor scores of MDD and HC groups. Patients with MDD showed higher scores in C-DAS-A and all of its eight factors than that of HCs (all $P < .001$). Female MDD patients had higher mean C-DAS-A total and factor scores than their male counterparts judging by scores only.

Factorial ANOVA of Gender and Diagnosis on C-DAS-A Total and Factor Scores

Table 3 presents the main and interaction effects of gender and diagnosis as well as the simple effects of gender in MDD and HC groups separately. As shown in **Table 3**, diagnosis showed main effects on C-DAS-A total and all of the 8-factor scores (all $P <$ .001). Gender showed no main effect on C-DAS-A total or any of the 8-factor scores. Gender and diagnosis showed significant interaction effects on C-DAS-A total and 3-factor scores (seeking applause, dependence, and self-determination attitude) ($P = .029$, .033, .020, .004, respectively), with females with MDD showing significantly higher scores on C-DAS-A and three of its factors (seeking applause, dependence, and self-determination attitude; $P = .035$, .036, .028, .021, respectively), while no gender difference shown in C-DAS-A total or any of its factor scores in HCs.

We also performed subgroup analyses of gender differences on C-DAS-A total and factor scores adding to the supplementary materials (**Table S3** and **Table S4**). The results of factorial ANOVA of gender and diagnosis on C-DAS-A total and factor scores in patients with moderate MDD and HC groups are shown in **Table S3**. Gender and diagnosis showed significant interaction effects on the self-determination attitude ($P = .002$). The simple effects of gender on the self-determination attitude ($P = .011$) showed that females with moderate MDD had higher self-determination attitude scores than that in males. The results of factorial ANOVA of gender and diagnosis on C-DAS-A total and factor scores in patients with severe MDD and HC groups are shown in **Table S4**. As shown in **Table S4**, gender and diagnosis had significant interaction effects on C-DAS-A total and three factor scores (compulsion, seeking applause, and dependence) (all $P < .05$). The simple effects of gender on the compulsion showed that females with severe MDD had higher compulsion scores ($P = .021$).

Multiple Linear Regression Analyses of DAS in MDD Group

In **Table 4**, we investigated the effects of age, gender, education, BMI, smoking history, $HAMD_{24}$, $HAMA_{14}$ predicting C-DAS-A total and three-factor scores in the MDD group. In the model of C-DAS-A total score, three variables (gender, smoking history, and $HAMD_{24}$) had statistical significance ($P = .002$, .010, .030, respectively) and they explained 9.9% variation of C-DAS-A total score ($R^2 = .099$, $P = .015$). Age, gender and smoking history entered into the model of seeking applause ($P = .039$, .002, .029, respectively) with $R^2 =.102$. In the model of self-determination attitude, three variables (gender, smoking history, and $HAMA_{14}$) showed significance (all $P < .05$, $R^2 = .112$). Gender contributed most in each model (standardized $\beta = .254$, .253, .259, respectively). Although the model of dependence had no significance, gender was the only one showing significance among these variables ($P = .027$).

DISCUSSION

To the best of our knowledge, this is the first study to investigate gender differences in dysfunctional attitudes in Chinese adult MDD patients. First, we found that MDD patients showed significantly higher C-DAS-A scores than HCs. Second, we observed significant gender differences in C-DAS-A total and three-factor scores (seeking applause, dependence, and self-determination attitude) in MDD patients, with women scoring higher than men. Third, five variables (age, gender, smoking history, $HAMD_{24}$, and $HAMA_{14}$) had predictive effects on and

TABLE 2 | Analysis of covariance (ANCOVA) of Chinese version of the dysfunctional attitude scale—form A (C-DAS-A) total and factor scores of major depressive disorder (MDD) and healthy control (HC) groups.

Item	MDD		HC		P
	Male (n = 75)	Female (n = 97)	Male (n = 74)	Female (n = 85)	
Total score	150.17 ± 25.98	160.05 ± 28.98	126.92 ± 29.94	123.73 ± 22.30	**<.001**
Factor scores					
Vulnerability	17.25 ± 4.42	18.72 ± 4.67	14.68 ± 4.95	14.81 ± 4.13	**<.001**
Attraction and repulsion	18.12 ± 5.04	18.53 ± 6.25	12.77 ± 5.26	12.93 ± 4.76	**<.001**
Perfectionism	18.21 ± 5.29	19.19 ± 5.94	15.15 ± 5.96	14.64 ± 4.06	**<.001**
Compulsion	18.28 ± 4.50	19.55 ± 4.62	16.15 ± 4.30	16.34 ± 3.71	**<.001**
Seeking applause	18.45 ± 5.16	20.40 ± 5.47	16.74 ± 8.41	15.59 ± 4.91	**<.001**
Dependence	18.67 ± 4.00	20.36 ± 5.23	15.78 ± 5.09	14.86 ± 4.15	**<.001**
Self-determination attitude	21.07 ± 5.95	23.03 ± 5.28	18.49 ± 5.53	17.24 ± 4.62	**<.001**
Cognition philosophy	20.12 ± 5.08	20.28 ± 5.62	17.16 ± 5.37	17.33 ± 4.73	**<.001**

Data are presented as mean ± SD; Bold values indicate statistical significance; P showed the difference in the C-DAS-A total and factor scores between MDD and HC groups; ANCOVA, analysis of covariance; C-DAS-A, Chinese version of the dysfunctional attitude scale – form A; MDD, major depressive disorder; HC, healthy control.

TABLE 3 | Factorial analysis of variance (ANOVA) of gender and diagnosis on Chinese version of the dysfunctional attitude scale—form A (C-DAS-A) total and factor scores.

Item	Main effects of diagnosis		Main effects of gender		Interaction effects (gender & diagnosis)		Simple effects of gender	
	F	*P*	F	*P*	F	*P*	MDD *P*	HC *P*
Total score	87.59	**<.001**	0.46	.499	4.79	**.029**	**.035**	.332
Factor scores								
Vulnerability	39.00	**<.001**	2.05	.153	1.48	.224	–	–
Attraction and repulsion	76.72	**<.001**	0.06	.807	0.14	.707	–	–
Perfectionism	41.50	**<.001**	0.43	.513	0.82	.366	-	-
Compulsion	26.06	**<.001**	0.12	.728	2.17	.141	-	-
Seeking applause	19.17	**<.001**	0.50	.479	4.59	**.033**	**.036**	.358
Dependence	60.31	**<.001**	0.41	.524	5.51	**.020**	**.028**	.271
Self-determination attitude	47.75	**<.001**	0.06	.801	8.41	**.004**	**.021**	.084
Cognition philosophy	16.43	**<.001**	0.01	.908	0.03	.857	–	–

Bold values indicate statistical significance; ANOVA, analysis of variance; C-DAS-A, Chinese version of the dysfunctional attitude scale – form A; MDD, major depressive disorder; HC, healthy control.

gender showed greatest contributions to C-DAS-A total and three-factor scores (seeking applause, dependence, and self-determination attitude).

Gender Differences in Dysfunctional Attitudes in MDD Patients

Consistent with our hypothesis, our results revealed that females with MDD showed more dysfunctional attitudes in seeking applause, dependence, and self-determination attitude factors than male patients. Our results are also partially in line with the findings of two previous studies (19, 20). One study demonstrated that depressed women are associated with more dysfunctional attitudes in the dependence factor (19). The other study found that women with hypertension comorbid with depression show more dysfunctional attitudes in five factors of DAS (attraction and repulsion, seeking applause, compulsion,

TABLE 4 | Multiple linear regression analyses for assessing effects of age, gender, education, BMI, smoking history, 24-item Hamilton rating scale for depression ($HAMD_{24}$), and 14-item Hamilton anxiety rating scale ($HAMA_{14}$) predicting dysfunctional attitudes in major depressive disorder (MDD) patients.

	Variables	Unstandardized β	Standardized β	T	*P*	R^2	F	*P*
C-DAS-A total score	Age	−.082	−.028	−.350	.727	.099	2.584	**.015**
	Gender	14.349	.254	3.116	**.002**			
	Education	−.108	−.013	−.168	.867			
	BMI	−.227	−.025	−.323	.747			
	Smoking history	19.777	.211	2.624	**.010**			
	$HAMD_{24}$	.836	.218	2.186	**.030**			
	$HAMA_{14}$	−.868	−.191	−1.907	.058			
Factor scores								
Seeking applause	Age	−.094	−.169	−2.085	**.039**	.102	2.665	**.012**
	Gender	2.745	.253	3.100	**.002**			
	Education	−.037	−.024	−.299	.765			
	BMI	−.007	−.004	−.055	.956			
	Smoking history	3.189	.177	2.200	**.029**			
	$HAMD_{24}$	.124	.168	1.689	.093			
	$HAMA_{14}$	.001	.001	.007	.995			
Dependence	Age	−.025	−.051	−.615	.539	.040	.985	.444
	Gender	1.814	.188	2.234	**.027**			
	Education	−.007	−.005	−.064	.949			
	BMI	.032	.020	−.256	.798			
	Smoking history	.311	.019	.234	.815			
	$HAMD_{24}$	.077	.118	1.147	.253			
	$HAMA_{14}$	−.065	−.084	−.807	.421			
Self-determination attitude	Age	.045	.077	.956	.341	.112	2.970	**.006**
	Gender	2.937	.259	3.192	**.002**			
	Education	.229	.141	1.780	.077			
	BMI	−.076	−.041	−.538	.591			
	Smoking history	3.412	.181	2.267	**.025**			
	$HAMD_{24}$	.089	.116	1.168	.245			
	$HAMA_{14}$	−.191	−.209	−2.099	**.037**			

Bold values indicate statistical significance; BMI, body mass index; $HAMD_{24}$, 24-item Hamilton Rating Scale for Depression; $HAMA_{14}$, 14-item Hamilton Anxiety Rating Scale; MDD, major depressive disorder; C-DAS-A, Chinese version of the dysfunctional attitude scale—form A.

dependence, and self-determination attitude) than men (20). Although specific factors showing differences vary across different studies, these studies together with our study all support gender differences in dysfunctional attitudes in depression.

The reason why females with MDD exhibit more dysfunctional attitudes than males is unclear, particularly in the context that no gender difference in the dysfunctional attitudes in HCs is observed, which is consistent with the previous finding that there is no gender difference in DAS score of college students (16). One possible explanation is that the gender differences in dysfunctional attitudes in MDD may be associated with gender differences in neuroticism, which is a personality more commonly seen in females than in males (27–31). Previous studies have demonstrated that dysfunctional attitudes are closely linked to neuroticism (8, 32–35). Some items of DAS, such as "If you don't have other people to lean on, you are bound to be sad" and "If I fail at my work, then I am a failure as a person", reflect thinking styles commonly seen in subjects with neuroticism personality. Moreover, neuroticism has a close relationship with depression (36–38). We hypothesized that in depression, the depressed mood may interact with neuroticism and bring about more dysfunctional attitudes in females (39), particularly in the attitudes closely related to neuroticism, like seeking applause, dependence, and self-determination attitude. Although the specific factors showing differences vary across subgroups of patients with different severity, these results all support our main argument that there are gender differences in dysfunctional attitudes in patients with MDD.

An understanding of gender differences in dysfunctional attitudes in MDD may facilitate our understanding of and guide our treatment for depression in clinical practice. On one hand, the gender differences in dysfunctional attitudes in MDD may contribute to the gender differences in the development and prognosis of MDD. On the other hand, the gender differences in dysfunctional attitudes in MDD call for gender-specific interventional approaches in the treatment of depression, particularly in the interventions targeting the distorted cognition, like cognitive behavioral therapy (CBT). Our results suggest that CBT therapists should pay greater attention to the dysfunctional attitudes when working with female MDD patients.

The Predictive Variables for Dysfunctional Attitudes in MDD Patients

Although each regression model accounted for only about 10% of the variance for dysfunctional attitudes, it had pointed out that age, gender, smoking history, $HAMD_{24}$, and $HAMA_{14}$ had an association with dysfunctional attitudes. Particularly, gender made the greatest contribution in each regression model, which is consistent with our finding that female MDD patients have higher DAS scores. As shown in the model, age had a negative prediction for the score of seeking applause, which is inconsistent with the demographic information of this study that female patients were older than males while with higher seeking applause score. The reason for consistency is unknown, possibly because the role of gender in seeking applause is greater than that of age.

Meanwhile, smoking history is an important predictor for dysfunctional attitudes, which is consistent with a previous study reporting worse cognitive function in smokers (40). However, the predictive effect of smoking history is relatively small and the results of subgroup analyses revealed no significant difference in C-DAS-A total score between MDD patients with and without a smoking history. The $HAMD_{24}$ total score had a positive prediction for dysfunctional attitudes, which is consistent with previous studies (20, 24, 41) showing a close relationship between dysfunctional attitudes and severity of depression. We also found that the $HAMA_{14}$ total score had a negative correlation with the self-determination attitude. Considering the relatively small predictive effects of these variables, future studies are needed to investigate additional effective predictive variables for dysfunctional attitudes.

Limitations

There are a few limitations in this study and caution should be raised when interpreting the results of this study. First, the investigative data represent only the adult population of China in the age range of 18–55. It remains unknown whether the findings are suitable for geriatric or adolescent MDD patients. Second, the number of subjects is relatively small and the area distribution of participants is concentrated, which questions the representativeness of this sample for the general Chinese population. Thus, future studies should recruit geriatric or adolescent participants and more subjects from broader areas. Third, we are unable to provide the exact reason why DAS-A score of females with MDD is higher than that in males. Future studies investigating the mechanism of gender differences in dysfunctional attitudes in MDD patients are needed. Fourth, the recruitment of this study spanned 6 years, which means that the subjects of the same age may represent different generations and cognitive backgrounds. Shorten the duration of enrollment will deserve consideration in the future.

Conclusions

There are gender differences in dysfunctional attitudes in MDD. Female patients have more dysfunctional attitudes than male patients, particularly in seeking applause, dependence, and self-determination attitude. A better understanding of the gender differences in dysfunctional attitudes in MDD may be useful for understanding the gender differences in clinical features of MDD and for developing gender-specific interventional approaches in the future.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding authors.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee of the Second Xiangya Hospital of Central South University and the Ethics Committee of the Zhumadian Psychiatric Hospital. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

LL and BL co-designed the topic. JS, MW, XL, QD, LZ, JL, YJ, PW, HG, FZ, and YZ are responsible for participant recruitment and data collection. XQ and JS undertook the statistical analyses and wrote the initial draft of the manuscript. BL contributed substantial revisions to the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2020.00086/full#supplementary-material

REFERENCES

1. Beck AT, Rush AJ, Shaw BF, Emery G. *Cogn Ther Depress*. New York: Guildford Press (1979).
2. Luty SE, Joyce PR, Mulder RT, Sullivan PF, McKenzie JM. The relationship of dysfunctional attitudes to personality in depressed patients. *J Affect Disord* (1999) 54(1-2):75–80. doi: 10.1016/s0165-0327(98)00136-0
3. Beck AT, Bredemeier K. A unified model of depression: integrating clinical, cognitive, biological, and evolutionary perspectives. *Clin Psychol Sci* (2016) 4 (4):596–619. doi: 10.1177/2167702616628523
4. Fava M, Bless E, Otto MW, Pava JA, Rosenbaum JF. Dysfunctional attitudes in major depression. changes with pharmacotherapy. *J Nerv. Ment. Dis.* (1994) 182(1):45–9.
5. Peselow ED, Robins C, Block P, Barouche F, Fieve RR. Dysfunctional attitudes in depressed patients before and after clinical treatment and in normal control subjects. *Am J Psychiatry* (1990) 147(4):439–44. doi: 10.1176/ajp.147.4.439
6. Lam DH, Green B, Power MJ, Checkley S. Dependency, matching adversities, length of survival and relapse in major depression. *J Affect Disord* (1996) 37(2-3):81–90. doi: 10.1016/0165-0327(95)00075-5
7. Rush AJ, Weissenburger J. Do thinking patterns predict depressive symptoms. *Cogn Ther Res* (1986) 10(2):225–36. doi: 10.1007/bf01173727
8. Beck AT, Brown G, Steer RA, Weissman AN. Factor analysis of the dysfunctional attitude scale in a clinical population. *J Consulting Clin Psychol* (1991) 3(3):478–83. doi: 10.1037/1040-3590.3.3.478
9. Oldehinkel AJ, Bouma EM. Sensitivity to the depressogenic effect of stress and HPA-axis reactivity in adolescence: a review of gender differences. *Neurosci Biobehav Rev* (2011) 35(8):1757–70. doi: 10.1016/j.neubiorev.2010.10.013
10. Eaton WW, Shao H, Nestadt G, Lee HB, Bienvenu OJ, Zandi P. Population-based study of first onset and chronicity in major depressive disorder. *Arch Gen Psychiatry* (2008) 65(5):513–20. doi: 10.1001/archpsyc.65.5.513
11. Schuch JJ, Roest AM, Nolen WA, Penninx BW, de Jonge P. Gender differences in major depressive disorder: results from the Netherlands study of depression and anxiety. *J Affect Disord* (2014) 156:156–63. doi: 10.1016/j.jad.2013.12.011
12. Marcus SM, Young EA, Kerber KB, Kornstein S, Farabaugh AH, Mitchell J, et al. Gender differences in depression: findings from the STAR*D study. *J Affect Disord* (2005) 87(2-3):141–50. doi: 10.1016/j.jad.2004.09.008
13. Brailean A, Curtis J, Davis K, Dregan A, Hotopf M. characteristics, comorbidities, and correlates of atypical depression: evidence from the uk biobank mental health survey. *Psychol Med* (2019) 1–10. doi: 10.1017/S0033291719001004
14. Kornstein SG, Schatzberg AF, Thase ME, Yonkers KA, McCullough JP, Keitner GI, et al. Gender differences in chronic major and double depression. *J Affect Disord* (2000) 60(1):1–11. doi: 10.1016/s0165-0327(99)00158-5
15. Marcus SM, Kerber KB, Rush AJ, Wisniewski SR, Nierenberg A, Balasubramani GK, et al. Sex differences in depression symptoms in treatment-seeking adults: confirmatory analyses from the sequenced treatment alternatives to relieve depression study. *Compr Psychiatry* (2008) 49(3):238–46. doi: 10.1016/j.comppsych.2007.06.012
16. Zhu X, Cai L, Yi J, Yao S, Luo Y. Predictive value to depressive symptoms of dysfunctional attitudes in collegc students a multi-wave longitudinal study. *Chin Ment Health J* (2011) 25(8):606–9. doi: 10.3969/j.issn.1000-6729.2011.08.012
17. Zlotnick C, Shea MT, Pilkonis PA, Elkin I, Ryan C. Gender, type of treatment, dysfunctional attitudes, social support, life events, and depressive symptoms over naturalistic follow-up. *Am J Psychiatry* (1996) 153(8):1021–7. doi: 10.1176/ajp.153.8.1021
18. Spangler DL, Simons AD, Monroe SM, Thase ME. Gender differences in cognitive diathesis-stress domain match: implications for differential pathways to depression. *J Abnorm Psychol* (1996) 105(4):653–57. doi: 10.1037//0021-843x.105.4.653
19. Farmer A, Harris T, Redman K, Mahmood A, Sadler S, McGuffin P. The cardiff depression study: a sib-pair study of dysfunctional attitudes in depressed probands and healthy control subjects. *Psychol Med* (2001) 31 (4):627–33. doi: 10.1017/s0033291701003932
20. Ou J, Duan S, Zhao S. A study on the dysfunctional attitudes of hypertension patients with depression. *Chin J Clin Psychol* (2009) 17(4):487–8. doi: 1005-3611(2009)04-0487-02
21. Liu J, Dong Q, Lu X, Sun J, Zhang L, Wang M, et al. Exploration of major cognitive deficits in medication-free patients with major depressive disorder. *Front Psychiatry* (2019) 10:836. doi: 10.3389/fpsyt.2019.00836
22. Weissman AN, Beck AT. Development and Validation of the Dysfunctional Attitude Scale a Preliminary Investigation. In: *The 62nd Annual Meeting of the American Educational Research Association*; 1978 March 27–31; Toronto, Ontario, Canada. (1978).
23. Wong DF, Chan KS, Lau Y. The reliability and validity of the chinese version of the dysfunctional attitudes scale form a (das-a) in a community sample. *Int J Psychiatry Med* (2008) 38(2):141–52. doi: 10.2190/PM.38.2.b
24. Chen Y, Xu J, Yan S, Xian Y, Li Y, Chang X, et al. A study of the dysfunction attitude scale. *Chin Ment Health J* (1998) 12(5):265–8.

25. Cui L, Shi G, Zhang Y, Yu Y. A study of the integrated cognitive model of depression for adolescents and its gender difference. *Acta Psychologica Sin* (2012) 44(11):1501—14. doi: 10.3724/SP.J.1041.2012.01501
26. Cong Z, Chen L, Cong Q, Tian W. Association between depression and the cognitive model including automatic thoughts and dysfunctional attitudes of freshmen in a medical university. *J China Med Univ* (2018) 47(7):597–600. doi: 10.12007/j.issn.0258-4646.2018.07.006
27. Dunkley DM, Sanislow CA, Grilo CM, McGlashan TH. Validity of DAS perfectionism and need for approval in relation to the five-factor model of personality. *Pers Individ Dif* (2004) 37:1391–400. doi: 10.1016/j.paid.2004.01.009
28. Kendler KS, Gatz M, Gardner CO, Pedersen NL. Personality and major depression: a Swedish longitudinal, population-based twin study. *Arch Gen Psychiatry* (2006) 63(10):1113–20. doi: 10.1001/archpsyc.63.10.1113
29. Lahey BB. Public health significance of neuroticism. *Am Psychol* (2009) 64 (4):241–56. doi: 10.1037/a0015309
30. Weisberg YJ, Deyoung CG, Hirsh JB. Gender differences in personality across the ten aspects of the big five. *Front Psychol* (2011) 2:178. doi: 10.3389/fpsyg.2011.00178
31. Sutton JM, Mineka S, Zinbarg RE, Craske MG, Griffith JW, Rose RD, et al. The relationships of personality and cognitive styles with self-reported symptoms of depression and anxiety. *Cognit Ther Res* (2011) 35(4):381–93. doi: 10.1007/s10608-010-9336-9
32. Sahin NH, Sahin N. How dysfunctional are the dysfunctional attitudes in another culture? *Br J Med Psychol* (1992) 65(Pt 1):17–26. doi: 10.1111/j.2044-8341.1992.tb01680.x
33. Parker G, Bradshaw G, Blignault I. Dysfunctional attitudes: measurement, significant constructs and links with depression. *Acta Psychiatr Scand* (1984) 70(1):90–6. doi: 10.1111/j.1600-0447.1984.tb01186.x
34. Reda MA, Carpiniello B, Secchiaroli L, Blanco S. Thinking, depression, and antidepressants: modified and unmodified depressive beliefs during treatment with amitriptyline. *Cogn Ther Res* (1985) 9(2):135–43. doi: 10.1007/bf01204845
35. Farabaugh A, Mischoulon D, Schwartz F, Pender M, Fava M, Alpert J. Dysfunctional attitudes and personality disorder comorbidity during long-term treatment of MDD. *Depress Anxiety* (2007) 24(6):433–9. doi: 10.1002/da.20174
36. Speed D, Hemani G, Speed MSMajor Depressive Disorder Working Group of the Psychiatric Genomics C, Borglum AD, Ostergaard SD. Investigating the causal relationship between neuroticism and depression *via* Mendelian randomization. *Acta Psychiatr Scand* (2019) 139(4):395–7. doi: 10.1111/acps.13009
37. Cloninger CR, Svrakic DM, Przybeck TR. Can personality assessment predict future depression? a twelve-month follow-up of 631 subjects. *J Affect Disord* (2006) 92(1):35–44. doi: 10.1016/j.jad.2005.12.034
38. Farmer A, Redman K, Harris T, Mahmood A, Sadler S, Pickering A, et al. Neuroticism, extraversion, life events and depression the cardiff depression study. *Br J Psychiatry* (2002) 181:118–22. doi: 10.1017/S0007125000161823
39. Farmer A, Redman K, Harris T, Mahmood A, Sadler S, Pickering A, et al. Neuroticism, extraversion, life events and depression. the cardiff depression study. *Br J Psychiatry* (2002) 181:118–22. doi: 10.1017/s0007125000161823
40. Depp CA, Bowie CR, Mausbach BT, Wolyniec P, Thornquist MH, Luke JR, et al. Current smoking is associated with worse cognitive and adaptive functioning in serious mental illness. *Acta Psychiatr Scand* (2015) 131 (5):333–41. doi: 10.1111/acps.12380
41. Dobson KS, Shaw BF. Cognitive assessment with major depressive disorders. *Cogn Ther Res* (1986) 10(1):13–29. doi: 10.1007/bf01173379

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CORRECTION
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Corrigendum: Gender Differences in Dysfunctional Attitudes in Major Depressive Disorder

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A Corrigendum on

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In the original article, there was a mistake in **Table 2** as published. A *P*-value was missing in **Table 2**, on the row “Compulsion”. The corrected **Table 2** appears below. Meanwhile, the full name showed as “14-item Hamilton rating scale for depression” of the $HAMA_{14}$ was wrong in the title of Table 4. The corrected title of Table 4 is as following: Multiple linear regression analyses for assessing effects of age, gender, education, BMI, smoking history, 24-item Hamilton rating scale for depression ($HAMD_{24}$), and 14-item Hamilton anxiety rating scale ($HAMA_{14}$) predicting dysfunctional attitudes in major depressive disorder (MDD) patients.

We apologize for these errors and these do not change the scientific conclusions of the article in any way. The original article has been updated.

TABLE 2 | Analysis of covariance (ANCOVA) of Chinese version of the dysfunctional attitude scale – form A (C-DAS-A) total and factor scores of major depressive disorder (MDD) and healthy control (HC) groups.

Item	**MDD**		**HC**		***P***
	Male (n = 75)	**Female (n = 97)**	**Male (n = 74)**	**Female (n = 85)**	
Total score	150.17 ± 25.98	160.05 ± 28.98	126.92 ± 29.94	123.73 ± 22.30	**<.001**
Factor scores					
Vulnerability	17.25 ± 4.42	18.72 ± 4.67	14.68 ± 4.95	14.81 ± 4.13	**<.001**
Attraction and repulsion	18.12 ± 5.04	18.53 ± 6.25	12.77 ± 5.26	12.93 ± 4.76	**<.001**
Perfectionism	18.21 ± 5.29	19.19 ± 5.94	15.15 ± 5.96	14.64 ± 4.06	**<.001**
Compulsion	18.28 ± 4.50	19.55 ± 4.62	16.15 ± 4.30	16.34 ± 3.71	**<.001**
Seeking applause	18.45 ± 5.16	20.40 ± 5.47	16.74 ± 8.41	15.59 ± 4.91	**<.001**
Dependence	18.67 ± 4.00	20.36 ± 5.23	15.78 ± 5.09	14.86 ± 4.15	**<.001**
Self-determination attitude	21.07 ± 5.95	23.03 ± 5.28	18.49 ± 5.53	17.24 ± 4.62	**<.001**
Cognition philosophy	20.12 ± 5.08	20.28 ± 5.62	17.16 ± 5.37	17.33 ± 4.73	**<.001**

Data are presented as mean ± SD; Bold values indicate statistical significance; P showed the difference in the C-DAS-A total and factor scores between MDD and HC groups; ANCOVA, analysis of covariance; C-DAS-A, Chinese version of the dysfunctional attitude scale – form A; MDD, major depressive disorder; HC, healthy control.

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ORIGINAL RESEARCH
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I Wasn't at War With the Noise: How Mindfulness Based Cognitive Therapy Changes Patients' Experiences of Tinnitus

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Objectives: Intrusive tinnitus is a challenging, life-changing experience for which traditional medical treatment does not yet have a cure. However, Mindfulness Based Cognitive Therapy for tinnitus (MBCT-t) is effective in reducing tinnitus-related distress, disability and intrusiveness. It is a priority to understand patients' experience of MBCT-t and active processes which they regarded as underpinning the changes they experienced. Semi-structured interviews were conducted 6 months after participants had completed MBCT as part of a randomized controlled trial (RCT), with a focus on exploring their experiences of the course, what they felt had changed and how they felt such changes had occurred.

Methods: Nine participants took part and Interpretative Phenomenological Analysis (IPA) was used to analyze the interview transcripts.

Results: Four overarching themes emerged: (1) Relating to Tinnitus in a New Way, (2) Holistic Benefits, (3) Connection, Kindness and Compassion, and (4) Factors Supporting Engagement and Change.

Conclusion: All participants reported benefits from MBCT-t, based on a radically new relationship with tinnitus. It was no longer characterized by "fighting it" and was instead based on "allowing" tinnitus to be present. Changes were supported by the development of open, stable, present-moment awareness and attitudes of equanimity, kindness, and compassion. Practices encouraging focus on sound (including tinnitus) were challenging, but essential to learning this new way of being with tinnitus. MBCT-t had a huge range of benefits including reduced distress and enhanced wellbeing. The group nature of MBCT-t was an integral part of the therapeutic process. A number of clinical and research implications are discussed.

Keywords: tinnitus, mindfulness, mindfulness based cognitive therapy, MBCT, IPA

INTRODUCTION

Tinnitus is the internal sensation of sound that has no external cause. It is extremely common, with prevalence at 30% (McCormack et al., 2016), and with severe tinnitus reported by 1–2% of the population, it represents a significant public health problem, with millions seeking treatment annually across the globe. Comorbid anxiety, depression, stress, insomnia, poor concentration, and functional disability are commonplace (Baguley et al., 2013). Conventional biomedical approaches fail to "silence" tinnitus and the strongest evidence base is for psychological intervention based on cognitive behavioral therapy (CBT) (Martinez-Devesa et al., 2010; Fuller et al., 2020; and more recently, mindfulness interventions (Rademaker et al., 2019).

Recent clinical standards and guidelines indicate psychological therapies for tinnitus (e.g., Cima et al., 2019). However, patient experiences are not yet in line with recommendations, and a recent review found that the majority of tinnitus patients do not receive sufficient therapeutic assistance for tinnitus (McFerran et al., 2019). Within the UK, only 11% of patients receive CBT and 9% mindfulness meditation, with the majority receiving written information (67%), sound therapy (35%), listening strategies (29%), or relaxation (23%) (McFerran et al., 2018). Thus although guidelines recommend psychological treatments for tinnitus, the standard care available for patients is far more likely to involve strategies based on acoustic approaches and relaxation.

Mindfulness Based Programmes (MBPs) systematically train participants in mindfulness. The best known structured training programme is Mindfulness Based Stress Reduction (MBSR) with decades of evidence in the treatment of chronic illness (Kabat-Zinn, 1990). Mindfulness Based Cognitive Therapy (MBCT) combines this with CBT and was originally developed to treat depressive disorder and relapse (Kuyken et al., 2016). MBCT and MBSR have small to moderate effects on psychological wellbeing in chronic medical conditions (Bohlmeijer et al., 2010).

Mindfulness has been defined as "a way of being in a wise and purposeful relationship with one's experience… cultivated by systematically exercising one's capacity for paying attention, on purpose, in the present moment and non-judgmentally" (Mindful Nation UK, 2015). Kabat-Zinn (1990) highlights seven attitudinal foundations for mindfulness (acceptance, non-judging, patience, letting-go, trust, beginner's mind, and non-striving). Other definitions focus on self-regulation, requiring *sustained attention* (to recognize what arises in each moment), *attentional switching* (flexibility) and *inhibition of secondary elaborative processing* (noticing experience without thinking about it). Integrating several models, Kuyken and Feldman (2019, p. 14) offer a five-faceted definition of mindfulness as:

1. A *state* of being present, a *process* of unfolding moment-by-moment experience *and a faculty* that can be cultivated and applied.
2. Based upon intentionality (about the placement of attention and awareness),
3. Imbued with attitudinal qualities (curiosity, patience, friendliness, care, trust and equanimity).
4. Something that requires effort to cultivate.
5. Intrinsically ethical (i.e., deployed to reduce suffering and enhance wellbeing).

Cultivating mindfulness is proposed to benefit health and wellbeing through various processes. Crane et al. (2017) suggest that it teaches *discernment*: People learn to recognize automatic behaviors and related distress arising from unhelpful habits of mind and choose to respond in more skilful ways, with less reactivity. Supported by empirical study, outcomes in MBPs have been shown to be mediated by reduced cognitive and emotional reactivity, repetitive negative thinking and increased self-compassion and psychological flexibility (e.g., Alsubaie et al., 2017). Probably, universal and specific features of MBCT/MBSR will be differentially relevant across conditions, with acceptance and exposure important in physical conditions (Carlson, 2012) characterized by avoidance, selective attention and catastrophic thinking (e.g., tinnitus; McKenna et al., 2014). Thus processes of change must be examined in specific groups to refine particular applications of MBPs.

Tinnitus distress is maintained by repetitive, catastrophic and negative thinking leading to unhelpful fear-based strategies of suppression, avoidance and distraction (McKenna et al., 2014; Marks et al., 2019). Unhelpful attentional processes include purposeful and automatic selective attention *toward* the feared tinnitus, and difficulties with sustaining attention elsewhere or switching attention away from tinnitus (as attention is "captured" by tinnitus). Unfortunately, early advice given to tinnitus patients often causes iatrogenic distress, as they are told to "just learn live with it, because there is no cure." This results in feeling both hopeless and responsible for getting rid of or suppressing the noise, which fuel the unhelpful strategies described above (Marks et al., 2019). Standard treatments (with a poor evidence base) can likewise promote unhelpful behaviors by encouraging tinnitus avoidance (e.g., masking, distraction), without targeting underlying cognitive behavioral processes. In contrast, CBT for tinnitus focuses on changing the content of cognitions about tinnitus, reducing stress and increasing exposure to tinnitus.

Mindfulness is a unique approach to tinnitus because it directly targets key processes of sustained and flexible attention. Based on standard MBCT (Segal et al., 2012), MBCT for tinnitus (MBCT-t) includes adaptations focusing on sound and the cognitive model of tinnitus (McKenna et al., 2017). Participants practice developing mindful awareness toward all experience, including tinnitus and practice approaching tinnitus rather than avoiding it. Unlike CBT, the relationship to negative thoughts is changed, rather than the content of them. Participants practice using sustained and flexible attention, choosing to pay attention in a way that is based on choice, receptivity and non-judgment, rather than fear. One might be concerned that paying more attention toward tinnitus would exacerbate distress. However, theoretically, it is the distressing cognitions and stress arousal that drive distress, and narrow attention onto tinnitus. Since mindfulness practice redeploys attention by widening the attentional "spotlight" to include other events and experiences as well as tinnitus, it should result in less distress and awareness of more stimuli than just tinnitus. Any distortion in the perception of tinnitus as a consequence of selective attention and resistance is reduced.

MBCT-t and CBT for tinnitus overlap, sharing an underpinning theory that cognitive-behavioral responses to tinnitus maintain distress. Both therapies thus target cognition (albeit in ostensibly different ways – CBT through challenging the content of the cognition and MBCT through changing the relationship to the cognition). Importantly, they both encourage patients to stop avoiding tinnitus, and to approach it instead. MBCT and CBT are thus radically different from the treatments most often available as standard for tinnitus patients (which as we have seen tend to involve information, acoustic strategies, and relaxation) (McFerran et al., 2018).

By reducing avoidance, MBCT could be regarded as a type of "exposure." MBCT also teaches individuals to relate differently to inner experience (particularly thoughts), and theoretically this should reduce emotional distress. Such reductions in distress may then create a condition in which habituation is further supported, in turn driving a "virtuous cycle" leading to greater tinnitus acceptance. Other known outcomes from MBCT (increased metacognitive awareness, reduced repetitive negative thinking, and self-compassion) are also likely to benefit tinnitus patients. This study aimed to explore what participants experienced in MBCT-t and how their understanding of what, how and why any changes occurred with treatment.

This study adopted qualitative methods which could assess contextual aspects of the intervention likely to affect treatment successful, and guide future research into mechanism. The participants' voices articulate what MBCT-t is like and thus show new ways out of distress which can refine and improve the approach. Interpretative Phenomenological Analysis (IPA) is appropriate for exploring the lived experience of an individual when they are participating in a psychological intervention (Smith et al., 2009). Within this approach the knowledge and expertize of the researcher become an important part of the interpretation of the data and its meaning.

MATERIALS AND METHODS

The participants in this study had all completed MBCT-t as part of a Randomized Controlled Trial (RCT), and the full details of this procedure (including inclusion criteria) can be found in the article describing this trial (McKenna et al., 2017). This RCT has already shown that MBCT-t is effective in reducing tinnitus severity in chronic and distressed tinnitus patients, as well as reducing tinnitus-catastrophising and fear and increasing tinnitus acceptance, when compared to an active control condition (relaxation training). This study aimed to explore how and why MBCT-t might have this effect using a qualitative approach focused on the individuals' experiences.

MBCT-t involved 8 weekly sessions of 120 min, and an overview of the treatment can be found in **Supplementary Material**. The majority of MBCT-t focuses on learning mindfulness and meditation and how to apply this to tinnitus. In addition there are specific references to the cognitive model: In week 2, Cognitive Theory is described and applications to tinnitus discussed, in week 4 the cognitive model of tinnitus is presented and in week 6 participants explore new ways of responding to challenging thoughts using mindfulness.

Participants completed MBCT-t (8 weeks of treatment). After this there was no additional treatment other than two follow-up sessions (at 1 and 6 months after treatment). Only once participants had completed their 6 months follow up were they given information about this interview study. Participants expressing interest in this study were invited to take part and provided full informed consent. Participants were only eligible for this interview study if they had completed MBCT-t as part of the RCT. The first nine respondents were included. Ages, gender, Social Economic Status, and tinnitus duration varied; the latter was of at least 6 months and all tinnitus subtypes were permitted (see **Table 1**). Names have been changed to ensure confidentiality.

Procedure

Participants were invited to take part following their 6 months follow-up and the initial nine respondents were interviewed. Interviews were based on a semi-structured interview schedule following guidelines for IPA (Smith et al., 2009). The first author (EM), one of the trial clinicians, conducted the interviews. The interview had two parts. The part reported here focused on their experiences and effects of MBCT, the other part focusing on their healthcare journey has been reported elsewhere (Marks et al., 2019). The interview schedule asked participants to reflect on their experiences of MBCT-t including the practices, teachings requirements, group setting, application of mindfulness to tinnitus and other aspects of their life, changes they noticed, external issues affecting their experiences and any longer term effects since completing the course. They were asked to reflect on how and why they felt MBCT-t had the impact it did and what they might say to others considering the course. An overview of the interview schedule is available in **Supplementary Material**. Ethical approval was provided by local UK NHS research ethics.

Interviews were transcribed verbatim by the lead author and analyzed with IPA, in line with the four-stage process of by Smith et al. (2009): (1) Interpretative reading of transcripts, notation of initial responses; (2) Identifying emergent themes; (3) Reviewing themes and mapping thematic connections; (4) Aligning sub-ordinate themes within super-ordinate themes. Cases were analyzed one at a time in this way, then across-case patterns were detected, creating a set of themes for the whole group. Repeated discussion and checking of themes and data by the second author occurred through an iterative process.

TABLE 1 | Characteristics of participants (anonymized).

	Age	Gender	Tinnitus duration (months)	Tinnitus severity (pre-treatment TQ score)	Tinnitus severity (6-month follow up TQ score)
Sarah	59	F	120	34	7*
Kelly	52	F	74	56	47
Joe	67	M	120	28	12*
Adam	58	M	360	52	13*
Matthew	54	M	128	27	14*
Peter	64	M	360	50	37*
Sam	35	M	18	57	39*
James	54	M	36	43	36
Damien	36	M	204	59	19*

Clinically significant change on TQ (11 point reduction).

RESULTS

Four superordinate themes were identified: Two describing *what* changed: "Relating to Tinnitus in a New Way" and "Holistic Benefits," and two describing *how* this was cultivated: "Connection, Kindness and Compassion" and "What supports engagement and change" (see **Supplementary Material** for a summary).

Supraordinate Theme 1: Relating to Tinnitus in a New Way

All participants described a radical change in their relationship to tinnitus and how this reduced their distress. Some reported tinnitus reducing in volume or pitch, but this was secondary to their transformed relationship with tinnitus. Changes involved recognizing how their existing coping strategies (of resistance and attempts to control tinnitus) paradoxically exacerbated their difficulties, whilst experimentation with allowing, accepting and turning toward tinnitus reduced their suffering. They cultivated new ways of being with tinnitus by staying present, having more open, stable and flexible awareness, without fighting tinnitus, and reclaiming life.

> *Sarah*: I wasn't at war with the noise. . . That was the main bit. . . . . . in a way I've controlled it by not controlling it. . . at the start I knew I had to control it, because otherwise how am I going to manage it, and I didn't know any different at the start of the programme. I thought, *I'm going to learn to control it,* but actually what you do is learn to let it go, and just if it's there, it's there.

Staying Present

Prior to MBCT-t, most participants reacted to tinnitus by striving to keep it away, through "*ignoring. . . putting on the TV. . . being busy hard at work*" (Sam). MBCT-t changed this, inviting a gentler approach of paying attention to one's present moment experience and "*actually being aware of what's inside you*" (Matthew). This improved and was seen as fundamentally different from distraction which was "*not deep enough. . . you haven't developed any skills*" (Sarah). Mindfulness is "*awareness*" (Kelly) or "*noticing*" (Peter) for all participants except Joe, who found the attentional training actually improved his ability to distract away from tinnitus.

> *Damien:* I don't think it's a distraction from your tinnitus because ideally you're sitting there quietly, focusing. So I think actually I'm more aware of my tinnitus when I'm doing the mindfulness. . . focusing on the tinnitus is what separates that from doing any relaxation exercises.

Thus MBCT taught participants to stay present with all experiences, including difficult tinnitus. This was initially challenging, as tinnitus felt intolerably unpleasant. Time, repetition and the use of specific, tangible objects as the focus of attention (sights, breath, body sensations, the soundscape) helped with learning this skill. Participants felt less overwhelmed by tinnitus when they were able to keep refocusing attention onto one particular aspect of experience. This practice meant they were less caught up by repetitive negative thinking, challenging emotions and tinnitus "spikes." Although effort was required to develop this skill, once learnt, it required far less effort than pre-existing strategies of avoidance and distraction and strikingly, this meant that many participants reported the novel experience of feeling peaceful and relaxed even when aware of tinnitus.

> *Matthew:* I still get annoyed by things now and again, but things don't fester any more, like they used to do. . . It's like, let it pass. . . it's almost stopping thinking too much, letting be. . . I wouldn't say it's sort of an aggressive or forced act... It's not STOP, I'm forcing myself to stop now. It just like, okay, leave it. . . become aware of breathing, trees, birds singing, sky, whatever.

Growing awareness of one's body helped with staying present, and this feeling of being "*more solid. . . functioning... whole*" was "*quite a revelation*" (Matthew) that gave participants the power to stay peacefully with whatever arose in each moment. There was a "*power of being aware of yourself and how you've got choices in how you deal with things*" (Kelly), which made participants more curious about their selves.

> *Matthew*: (Mindfulness) brings a new layer of awareness and focus and peacefulness into all of it. . . your inner self maybe has got so many parts to it that you explore and certain things you do help you to explore certain parts of that inner self.

Joe understood the process of MBCT-t differently from the others, seeing it as distraction, but he still had a similar experience, noting that "*the effect of tinnitus was dramatically less*" during meditation because "*while you're focused on something else you're (not) worried by your tinnitus*." This indicates how actively doing meditation matters more than understanding it. Mindfulness may have different functions for different people at different times; from switching attention between stimuli to expanding attention to include more stimuli.

Staying present with tinnitus challenged the distressing belief that tinnitus must be controlled in order to be tolerated. By observing their automatic reactions to tinnitus during meditation, participants realized that their habitual thoughts and behaviors actually increased suffering. Recognizing how "*your brain defaults to a pattern of behavior*" (Sarah) was liberating, because it meant new thoughts and behaviors could be tried out. Mindfulness didn't stop default patterns from happening in the first place, but rather allowed participants to "*cast them aside*" (Peter) and choose a less reactive and resistant way of being with tinnitus. When awareness of tinnitus increased, it obviously provoked discomfort. But this discomfort was an essential part of learning how to relate to tinnitus differently. By noticing, acknowledging and allowing their discomfort without resistance, participants learnt how to allow themselves to be as they are, a kind act that helped them to heal.

> *Kelly*: allowing. . . when I can bring it to mind. . . gives me permission, either to be angry, to be sad, to be accepting or just be without feeling anything necessarily. . .. Like a relief, a burden is lifted. . . You learn. You can only do that by allowing it. If you don't allow it, you'll never know what it feels like to allow it.

Participants described "open" awareness, a capacity to flexibly notice multiple facets of experience which created an expanded sense of self. This ameliorated tinnitus distress because they no longer felt so "trapped" by tinnitus, a common part of distress (Marks et al., 2019), because when tinnitus feels bigger than the self, it is overwhelming. Attention expanded around tinnitus, creating inner "*spaciousness*" (Damien).

> *Damien:* "I guess I feel like I'm not thinking so much within my head. I'm focusing on stuff that's outside of my brain. . . especially focusing on breathing and feeling the breath further down the body."

MBCT-t is unique in its repeated invitation to purposefully listen to tinnitus with curiosity. This challenging new idea initially aroused irritation about paying attention "*to a lot of noise that I already know*" (Sarah). But "*listening to the tinnitus. . . being part of the daily landscape*" actually became "*one of the biggest changes*" (Sam). Participants realized that "*what I'm hearing in my own head is not the only thing to be heard*" *(*Kelly) and tinnitus shrank from an all-encompassing monster to one small part of a larger self. Taking "*a step back*," participants could "*see the bigger picture*" (James): Tinnitus shifted from being the index problem, to being regarded "*more globally. . . a symptom of other things*" (Matthew). In contrast to traditional tinnitus treatments, MBCT offered new ways of "thinking about" and "being" with tinnitus, by learning how to stay present with all experience.

Equanimity (Allowing and Letting Be)

By paying close attention participants recognized the ever-present flux of all experience, including tinnitus. Understanding that tinnitus (and all difficult moments) eventually pass on their own, reduced how much participants felt they had to strive fix tinnitus. Catastrophic thinking was replaced by acceptance.

> *Sam*: "accepting that. . . it probably is always going to be there. . . just because it's screaming really badly this morning, doesn't mean you're going to notice it all day long."

This equanimous attitude of allowing tinnitus to be as it is, is purposefully fostered in MBCT-t, with participants experimenting with what happens when they treat pleasant, unpleasant and neutral stimuli with equal respect. It initially required courage to "*to get up close to it*" which was "*quite scary*" (Sarah), but listening to tinnitus was surprisingly "*okay*" (Damien). Tinnitus was less terrible, and more changeable than expected. Paradoxically, paying attention to tinnitus without seeking to change it, changed the experience of tinnitus.

> *Adam:* . . .even the negative side is just a feeling. . . if you can treat everything with the same respect, the good and the bad... it's going to go in a certain amount of time.

Attending to tinnitus meant participants could see their reactions more clearly and gave them an opportunity to update their assumptions about it. They realized that fear of tinnitus is different from the reality that it is "*not yesterday's tinnitus, not tomorrow's tinnitus, but now*" (Sarah). The reality of tinnitus was easier to cope with than the fear of it, and paying attention to it unexpectedly engendered calmness. This was not because "*mindfulness per se*" is relaxing (Sam), but because by learning to "*go with the flow*" (Joe) they were "*less likely to get flustered*" (Damien) by tinnitus. With practice, participants trusted that experiences would come and go of their own accord. Sarah described how reminding herself that "*it's already happened*" allowed her to stop resisting unpleasant experience. This required neither resignation nor blind trust, but a growing clarity grew of understanding what aspects of experience one can and cannot influence.

> *Sarah*: I don't sit and worry. . .. I know what I can do about it and I know what I can't do, so why am I giving it this extra energy? It's already happened. . . I have no control. . . It doesn't mean it doesn't get me down. . . but it will sort itself out."

Participants were striving less and no longer "*at war with the noise*" (Sarah), choosing not to "*expend much energy worrying or getting cross.*" For some, tinnitus itself improved, Sarah stopped having a painful experience of tinnitus "*fireworks*," Damien reported reduce tinnitus "*volume (and) pitch.*"

> *Adam*: It hasn't affected the tinnitus. . . It's the way I think about it and the way I deal with it. . . knowing that in just a few moments it won't be as bad. . . you have to accept that it's there, you have to.

The swiftness and breadth of acceptance varied and Sarah noticed in just 4 weeks that "*I haven't even thought about it today*" and after a few months that "*I don't think I'd class myself any more as having invasive tinnitus.*" Those with smaller and slower changes benefitted too (e.g., Joe may have still had intrusive daytime tinnitus but this disappeared at night). Overall, most participants felt less limited by tinnitus, confident that even if they had a "tinnitus spike," they would cope.

> Damien . . . I've been pushing myself to do more things, so I'm having a better life really... going to concerts. . . flying. . . I think it just gave me a bit of a kick you know.

MBCT-t was not a panacea, and many participants felt resignation as well as acceptance or "*the right mental attitude*" (Sam). Most still wished for a definitive "cure." Yet participants saw the big advantage of mindfulness being it's ability to empower them, offering a tool to "*take away*" (Damien).

Supraordinate Theme 2: Holistic Benefits

MBCT-t was associated with many additional benefits. Distress reduced as negative thinking became less tyrannical, associated emotions (depression, anxiety, frustration, anger), difficulties (stress, insomnia, interpersonal conflict) and avoidance behaviors eased. Enhanced wellbeing developed across life domains with positive states of gratitude and joy flourishing.

> *Sam:* . . .mindfulness in general would appear to me to be a really beneficial thing in real life. . . some of the people who come through the course naturally lean towards depressive tendencies. . .. I kind of just got the sense of there being more than the tinnitus that people are being helped with.

Reduced Distress

Many participants had long-standing anxiety, depression and stress which MBCT-t helped. Adam saw himself "*as being treated for depression*," Sarah became less "*jumpy*," Matthew used mindfulness to "*de-stress*" and Damien "*to manage anxiety.*" MBCT-t is known to reduce psychological distress in tinnitus

(McKenna et al., 2017, 2018b), and participants related this to reduced repetitive negative cognition or "*almost stopping thinking too much*" (Matthew). They learnt to identify and disengage from negative thoughts which reduced negative reactions to events spiraling out of control. Participants had more "*choice*" about how to respond to a situation and "*rather than just going 'poof' straight away*" (Kelly), they could slow down, choose a new perspective and response. This was particularly profound for Sarah, who's recurrent suicidal ("*invasive*") thoughts reduced in frequency, and even when they arose she observed them without being overwhelmed.

> *Sarah*: the rest of me has benefitted... You can't catastrophize over everything else but manage it with your tinnitus. So it's holistic. . . the big thing is the not catastrophizing. . .

Enhanced Wellbeing

MBCT led to more calm, relaxed or tranquil states, offering an "*inner support*" (Kelly), with "*rewards in itself*" (Matthew). This arose naturally, something that "*permeate(s) a lot of things. . . it's a general, more relaxed approach to things*" rather than through trying hard to create a state of relaxation. This coincided with growing equanimity across life domains. By learning that one "*can't prevent things. . . you just have to let them go*" (James) they learnt to relax control. A growing sense of peace was a significant experience for several participants. It is important as many tinnitus sufferers fear that constant tinnitus will prevent them from ever having "peace and quiet" again. Yet experiences in MBCT-t refute this idea, showing it is possible to have peace even as tinnitus continues. Perhaps peacefulness arises not when there is an absence of *sound*, but when there is an absence of *war* (when the fight with tinnitus stops).

Positive behavioral changes were commonplace, supported by greater energy reserves, better mood and growing commitments to self-care. These changes were profound, enriching and "*liberating*" (Kelly) as "*horizons opened*" (Sam). Feeling calmer benefitted participants' interpersonal relationships: Matthew's wife noticed he managed anger better by "*not to get to that tipping point*"*;* Adam noticed less family conflict and Kelly reported calmer interactions at home and work. Again Joe's experience was different, because he felt his tendency to keep emotions "*bottled up*" meant others wouldn't observe changes in him. Improvements in sleep were reported, with Joe describing that he would "*worry less at night. . .(and) fall asleep sooner*." Damien able to "*sleep without (tinnitus) disturbing*" him and Peter replacing sleeping pills with meditation.

Gratitude, appreciation and joy arose during the course, significantly contributing to wellbeing. This was interwoven with other aspects of mindfulness such as paying attention, being less busy and feeling more equanimous and connecting to the world, through "*listening to what is going on around you. . . stuff you don't usually have time for*" (James). At first this required making intentional decisions notice pleasant events, and appreciate fleeting beauty that previously would have been missed. In noticing joy, experiences of struggle and distress reduced.

> *James*: You can appreciate things more. . . whether it be your pet cat or the squirrel running across the world. . . a good day or a bad day. . . if you take time you can appreciate it a bit more.

As mindful awareness became more integrated into their lives, joy and gratitude arose more spontaneously, with gratitude springing from connections with others, seeing kindness and generosity in other people. Simply paying attention transformed experience as "*it just melts everything away for a moment*" (Kelly).

Supraordinate Theme 3: Connection, Kindness, and Compassion

MBCT-t deepened connections with others and the self, particularly through recognition of shared suffering and shared humanity, which generated kindness and compassion toward those suffering. The process of MBCT-t involved increasing sensitivity to suffering and a wish to alleviate or prevent it in oneself and others. This aligns with other group interventions, although specific attitudes of kindness and compassion appeared to be fostered particularly by the foundational attitudes of mindfulness.

With Other People

The community that arose from the group nature of MBCT-t was an essential part of the process. All participants spoke of the value of being with other people with tinnitus, benefitting from consolation, support, motivation, education and insight. Connection was immediate and instinctive, and the group reduced isolation and loneliness, as nobody was "*singled out as only person who has to suffer*" (Matthew). Shared suffering transcended other differences, and everyone felt that the others would understand and accept their distress. This shared connection was an essential element of the therapeutic process, indicating the benefits of offering tinnitus treatments in a group format.

> *Kelly:* there's just an instant connection, even if that person is completely different to you in all other respects, they just know, you know, it's an unsaid thing. . . powerful. . . in some respects it could be quite healing. . . collective of sharing. . . makes you feel like you're not the only one.

MBCT-, with its' focus on skills-learning supported engagement and connection, possibly as it was easier to be in a "*class*" rather than a "*therapy group*." Sharing experiences was "*enlightening and strangely comforting*" and aided learning through "*knowing that other people are maybe coping*" which offered hope they could cope too. Comparing one's own suffering to others', greater struggles put one's own tinnitus in perspective, reducing the sense of overwhelm and stimulating gratitude; both powerful antidotes to negative cognitions. This included a teacher's disclosure of personal experience with tinnitus because "*empathy could be more powerful sometimes than anything else*" (Kelly).

> *Peter*: There's a lot of people with worse things you know. . . to see someone worse off, at least it makes you more aware of what people have to cope with. . . thinking about other people's problems rather than concentrating on your own. . . other people

> can maybe cope with worse than you. . . that should make you able to cope with yours.

Empathy led to compassion, particularly for participants struggling with greater stress (busier lives or worse tinnitus), and from this a real wish for their wellbeing.

> *Adam*: 'The only person I thought who had it worse than me... she did seem to improve as the weeks went on. . . I really really do hope that she improved. . .

Participants learnt from each other in different ways, including observation (such as seeing "*how they were sitting*" (Damien)), listening to their comments ("*negative or positive*" (James)) and hearing the *inquiry* (where teacher and participant discuss experiences together). It was very important for the group to welcome skeptical and negative reactions, probably because it demonstrated that mindfulness was being used authentically. This welcoming of all experience is a key aspect of the MBCT-t group approach (Crane et al., 2010).

> *Adam*: I can understand now how people will be skeptical, but it doesn't matter, because I know, I've seen it work. . . my own experience but from other people's too. . . the group is. . . informative for everybody.

Participants were motivated by "*how much work*" others put in, feeling "*a responsibility*" to do the same. For Damien, this was "*one of the main reasons I started timetabling my mindfulness*" and for Sarah, hearing how people used their own "*personalities and skills to get to grips with the mindfulness*" helped her think about what was best for her. Unlike some group therapies which might focus more stories about the past, MBCT-t supported learning by focusing on how to engage in particular skills and practices in the here and now.

Connections with the service and the teachers were essential for trust, engagement, commitment, hope, and embodied learning. Equally valued were professional expertize (in mindfulness, tinnitus and psychology), and personal attributes (experience of tinnitus, commitment to mindfulness practice, and embodied attitudes of patience, non-striving, non-judging, acceptance and compassion, e.g., Kabat-Zinn, 1990). Being "*professionally run*" (Sarah) within the NHS and specific for tinnitus, with good organization and delivery meant participants felt safe, and could feel both trust and skepticism at the same time. Feeling safe in the group gave participants more confidence to try out new and challenging practices in the belief that they might help. As Adam described, "*(your service is) the best. . . if you can't do something then not many people can*," and there was "*less potential for anything negative to happen*" (Damien). This is important when considering the context of a growing mindfulness industry where levels of regulation and supervision vary enormously, and when research has shown that expectations of therapy correlate with outcome (Greenberg et al., 2006).

> *Damien*: . . .very well set up and appropriate. . . you've adapted the course . . . very clear about objectives. . . The course material was really good. . . really well organized... an NHS project, properly funded.

Participants learnt how to be mindful by observing their teachers' embodiment of mindfulness, as reported elsewhere (Crane et al., 2010). This included teachers balancing gentle permissiveness with structured discipline. For example, through "*being able to sit or lie down wherever*" (Peter) or having meditations guided "*in a sensitive way*" (Matthew). Participants learnt treat themselves in the same way, "*to take what you can and leave the rest*" (Kelly), allowing them "*to work out their own way*" (Adam). Similarly, the teachers' attitude of "*completely non-judging things*" was anathema to participants' habitual "*judging oneself as substandard*" (Kelly), and feeling "*looked after*" (Damien) and accepted by the teachers was the ground upon which participants began to develop compassion for themselves.

> *Kelly:* (the) teacher. . . always been very gentle and very allowing. . . when I can bring it to mind it gives me permission (to be as I am).

Connection and compassion seeped out of relationships within the group into everyday life. Sarah found that her natural empathic nature became increasingly infused with kindness, leading to more compassionate responses to challenging situations. Thus if conflict arose, Sarah felt "*less under attack*" and she had the psychological space to respond wisely. Sam found that MBCT-t increased "*empathy and my psychological understanding of other people's behavior, so I'm more connected*," Adam found it "*makes you want to be a better person*" and James felt that kindness was a "*knock on effect*" as he developed more "*empathy to people, animals, etc.*" Matthew felt "*more empathetic, sympathetic*" toward "*everything: people, animals, the world*" (including himself). Sarah felt connected to even strangers with tinnitus, and marveled at her deep wish for everyone to receive the help she was receiving. In opening to human suffering, compassion bloomed:

> *Kelly:* . . .like if someone's running for a bus and I'll think "ah I really hope that bus waits for them" whereas before I might have been "go on, drive off" (*laughs*).

Feeling kind toward others was supported by the ability to stay present and be less caught up in automatic thinking. Kelly described how she started to notice how she had automatic negative thoughts about other people that made her feel disconnected from them ("*why is he doing that*"). With mindfulness, she stopped being caught up in negative stories and chose instead to notice other people more neutrally ("*oh so and so is doing that*"). She began to feel more curious about others, more willing and able to offer them attention ("*oh well that person is really wanting to know about me and I want to know about them*") and eventually more likely to offer them kindness; for example, she took on a pastoral role at work "*to give something back*."

With One's Self

MBCT-t involved offering compassion "*to me as well*" (Kelly). Most simply, paying attention to oneself and allowing oneself to be is an act of self kindness. This applied to neutral stimuli, such as noticing the breath with an attitude of "*gentleness*" (Sarah) and to aversive stimuli, such as tinnitus, recognizing it as part of oneself and allowing it to be present. These shifts in attitude toward the self and inner-experience laid the groundwork for bigger life-changes.

> *James*: you're giving yourself that time which in everyday life you don't have. . . to actually let things go, breathe easy, express themselves, I think is very important.

Self-kindness changed the habitual language of the "inner critic." The old voice that might say "*oh now look what you've done*" or "*moron*", was replaced with a kinder voice saying "*what you did then you thought was the right thing to do*." Participants learnt to forgive themselves for making mistakes, which made making mistakes and asking for help less threatening (as it was less likely to result in a tsunami of inner-judgement). In realising her difficulties were shared with other humans, Sarah could ask for help without feeling ashamed. In feeling kinder toward himself, Matthew stopped caring about others' judgments, and could do what he wanted, not what he felt others expected of him. Self-compassion could elicit fear, particularly when it threatened high-standards or where over-permissiveness might risk a complete collapse of boundaries: "*what if I allow too much?*" (Kelly). This is an important issue to discuss in the group, as participants find the right boundaries for themselves: "*you learn – you set your own limits which you can only do if you first learn to allow.*"

> *Matthew*: it's about treating yourself well, which you know it's quite easy not to do. It's quite easy to punish yourself, to criticise yourself and not actually congratulate or reward yourself. . . (now) I tend to sort of do what I feel like is right for me, not what I feel like what I'm supposed to be doing.

Mindfulness helped participants to be kinder overall, which in turn freed them up to think differently and move out of familiar patterns of criticism.

Supraordinate Theme 4: Factors Supporting Engagement and Change

Engagement with MBCT-t and sustained practice led to change, and depended upon having an open mind, tempered by welcoming skepticism. Various internal and external supporting factors supported included motivation, personal characteristics, stress levels, time, help and appropriate practices. MBCT-t required perpetual re-balancing of hope with realism and gentleness with discipline.

All interviewees had been committed enough to MBCT-t to complete it, although enthusiasm and skepticism varied. Most had begun the course without knowing what to expect, but reported prior experience of complementary therapies, indicating an open mindedness toward "alternative therapies" which probably helped engagement. This included cranial osteopathy, acupuncture, Tai-Chi (Sarah, Matthew, Kelly, Damien), meditation (Adam, Peter), psychotherapy (Kelly, Matthew) or Buddhism (Sam).

> *Damien*: I'm sceptical about alternative therapies . . . but I found it a quite pleasant experience when I got around the slight weirdness of it. . . Previously I'd had a good experience of an alternative therapy route. I didn't know anything about mindfulness prior, so that's what I thought it was.

MBCT-t appealed as a non-invasive intervention for something which medical or surgical routes had failed to help (Marks et al., 2019). Several people expressed preferences for a therapy helping them to "*get inside (their) head and figure out a way of working with it*" (Kelly), rather than a "*cure*." This is an important point, as participants here recognized that there is no "cure" available to "silence" tinnitus. This is at odds with a growing cultural narrative which claims that medical interventions will always be the preference for everyone.

Skepticism and open-mindedness came together, and both facilitated change. Open mindedness led people to engage, and the permission to express skepticism prevented people from feeling alienated. Adam feared the Buddhist origins of mindfulness might be too spiritual, but decided to "*see what happens*." James, wanting a cure, was "*apprehensive*. . . *didn't think it would benefit me*" and only attended because he had committed to it. Realistic expectations were helpful, as Sam stated, he would recommend it to anyone unless they were "*dead set on treatment that was tantamount to a cure*."

> *Sam*: my wife was doing some research. . . I wasn't sure but I thought I may as well. . . part of me thought that probably it isn't my thing and it probably won't do any good, but actually for me, I was surprisingly open minded to it. . .

Practical factors made important contributions to the experience of MBCT-t, and the biggest one was practice. Commitment and patience were required to allow for slow and "*gradually revealing*," changes, because one "*couldn't expect a miracle too quickly*." Meditation practices tended to be difficult at first, becoming more enjoyable and easeful with growing familiarity.

> *Damien*: I found some of it overwhelming because it's not something I'm really used to. . . I got more used to it over time. Towards the end I was enjoying. . . it, just became a bit more normal.

The structured nature of MBCT-t helped, and attending weekly sessions preserved momentum and learning, because "*the group made mindfulness easier for me than doing it myself*" (Sam). Participants valued having an accessible and welcoming location supported by appropriate equipment (cushions, mats etc.). Background noise in the room (air conditioning), irritated some, exacerbating tinnitus and hearing loss, but consoled others as it "*partially masked the tinnitus*" (Damien). MBCT-t groups should consider advising use of appropriate background noise for classes and home practice.

A unique aspect of MBCT-t that supported change was the focus upon *sound and hearing* meditation and inquiry. This was described as "*the most important*" practice (Kelly), particularly attending to the entire soundscape (not just to tinnitus) and noticing sound directly (rather than thinking about sound). This was very challenging at first, as sitting still with tinnitus usually led to an initial increase in its' prominence. Participants needed commitment and courage to continue, and eventually the benefits unfurled. Meditation became easier, as practice led to benefits which led to more practice. For example, Sarah who had a strong home practice found mindfulness worked "*quickly*. . . *not hearing the tinnitus as quickly*," keeping her very engaged.

> *Damien:* it was important to challenge myself. . . the more I practiced, the more I got out of it. I was determined to give it my best shot. . . practicing outside meant that when I was doing it there it didn't feel so foreign.

Participants re-learnt how to listen, with more expansive awareness of multiple noise: "*voices, traffic and my tinnitus*" (Peter). This helped them to reconnect with the joy and beauty of sound, particularly in pleasant or natural environments.

> *Kelly*: there's lots of birds in our garden, and I love that because I suppose that when I'm listening to that. . . I'm also aware of all the other sounds.

This was not easy, and simply guiding sound meditation was insufficient. Participants wanted repeated, explicit teaching and discussion about how to mindfully attend to sound and how mindfulness applies to tinnitus. Watching an MBCT-t alumni speak of his experiences on film helped with this somewhat.

> *Sam*: Maybe there could have been more to link the mindfulness activity specifically to the tinnitus. . . treating us like idiots and explaining step by step, this is how it can affect your coping with tinnitus.

The more serious aspects of meditation practice could be challenging, and integrating lighter and more humorous attitudes was sometimes helpful, particularly in encouraging gentleness, as seen in Kelly's playful approach to sound meditation.

> *Kelly* 'It's a shift I remember. . . when I'm in the shower I will always try to listen to the water and I might go to this place where I'm going 'water, tinnitus, water, tinnitus' (Laughs).

The demands of daily life made practice difficult, but priorities changed as the benefits were experienced directly. Adam, noticing how his stress increased if he stopped practicing, realized that "*if you don't do it, it doesn't work.*" On seeing benefits, some participants reduced their practice but still felt confident knowing that it "*worked before*. . . *should be able to work again*" (Damien). Practical strategies such as daily schedules reduced cognitive loads of remembering and deciding to practice, which helped.

> *Damien*: other people were saying they were practicing and getting a lot out of it . . . initially I wasn't dedicating enough time to it. . . I had to be quite strict about timetabling it into my day. . . you were investing in me. . . so I felt like I had a responsibility to the group.

People saw a correlation between frequency and duration of practice and quality of their life, particularly when supported by the ongoing sessions.

> *Damien*: I had a better quality of life in that period when I was regularly practicing mindfulness. . . the most at peace and the best I felt were really deep, long meditations.

Clearly, induction to MBCT-t must ensure participants have the time, energy and will to commit to practice. This includes learning to meditate at a point in their life where there is space to practice, because "*meditation is easier*. . . *if you're in a frame of mind to meditate*. . . *you have to be in the right mood*" (Joe). It also includes cultivating an attitude toward practice as something fundamental, part of self-care, health-care and an opportunity to learn something new, rather than just another burden.

> *Sarah:* commit to all the work. . . not to see it as a chore, as I see it as an opportunity to take control, to retrain the brain.

Flexibility in practice was important, and each person discovered how to fit mindfulness to their particular circumstances. This made the shorter and more informal practices popular, including mindful awareness of activities such as "*laying in the bath,*" "*feeling the ground under my feet,*" (James) or existing exercise routines (Peter, Matthew). Portable practice, such as a few minutes on the daily commute "*could be more powerful than doing something for 30 minutes*" (Kelly).

Thus the type, intensity and regularity of practice varied across individuals, with learning occurring in each participant differently, but in equally valid ways. Sarah explained the importance of using "*whatever their learning style is to help them with the meditation*," and how teachers must be able to support participants to use their particular skills and characteristics to "get to grips" with mindfulness. This includes creative approaches to standard exercises such as breath and body awareness.

> *Sarah:* As a visual person. . . I came up with. . . like when you see mercury sliver, fluid. . . I had that image in gold. . . I even used it to move around the blood. . . because the breath on its own I just couldn't get a handle on that.

Unpleasant and aversive experiences were common, with descriptions of the eating meditation as a "*waste of time*" (James) and imagining breath traveling through the body, as "*so silly*" (Joe). Here an open mind and an option to try other exercises helped keep people engaged. The stories and poetry weaved throughout MBCT-t were "*refreshing*. . . *different ways of looking at it all*" (Matthew). However, the CBT specific exercises were rarely recalled by participants unless prompted. These psychological principles "*made sense*" (Matthew, Sam) but didn't seem as critical to learning as other aspects of the group.

DISCUSSION

Four over-arching themes emerged from the IPA: *Relating to Tinnitus in a New Way; Holistic Benefits; Connection, Kindness and Compassion; and Factors Supporting Engagement and Change.* These resonate with qualitative research across other MBPs. The discussion focuses first on how MBCT-t applied to tinnitus followed by some reflections on more general experiences.

How Did MBCT-t Apply to Tinnitus?

Every participant reported a transformation in their relationship with tinnitus. The shift from "being at war with it" to "allowing it" was the core process and outcome shared across the group. A few people reported improvements in tinnitus volume and pitch, but this was not universal. Participants explained how they became aware of automatic thoughts (rumination and catastrophizing) and coping behaviors (resistance, suppression, control) and discerned how these were unhelpful. MBCT-t taught them the theory and skill to relate differently to the experience, by turning toward and allowing tinnitus, without getting caught up in reactive narratives or behaviors. They described making significant efforts to apply mindfulness to the present moment, in an intentional, patient, friendly, trusting and equanimous way, with a view to reducing their suffering and enhancing wellbeing (e.g., Kuyken and Feldman, 2019).

Mindful awareness of tinnitus involved sustaining attention in very different ways from their previous fear-based selective attention and monitoring relationship with tinnitus. This new attentional style involved less cognitive and emotional reactivity. Participants could be purposefully aware of tinnitus without also engaging in catastrophic narratives, a need to make things different or feeling emotionally overwhelmed. This process could be seen as involving "exposure" to noxious stimuli (tinnitus) through the dropping of avoidance and safety-seeking behaviors. The development of meta-cognitive awareness through mindfulness may have led to the development of greater emotional stability which in turn could have supported habituation and tinnitus acceptance. Mindfulness also involved attitudes of gentleness, kindness and permissiveness, potentially enabling acceptance of tinnitus, rather than just tolerance of it, as indicated in other physical health conditions (Carlson, 2012).

Attentional flexibility increased, including the ability to refocus away from, or expand attention around tinnitus. Thus participants were not repeatedly "captured" and "overwhelmed" by tinnitus. Crucially, this did not mean mindful awareness involved refining existing avoidance or management strategies. Nor did it mean resignation or just "learning to live with it" as so many had previously been told to do (Marks et al., 2019). Instead, participants developed a new, acceptance-based perspective on tinnitus. They saw how striving to control tinnitus was often futile and counterproductive, and that the best way out of suffering was to let go of the struggle. By "allowing" tinnitus, they saw that even the worst moments always pass, without them having to do anything to make this happen. This meant they stopped engaging in fear-based catastrophic thinking, and instead chose a more equanimous attitude. Even the most skeptical participant (Joe) learnt how to "*go with the flow*" more often. This new perspective on tinnitus sits comfortably with the definition of mindfulness involving an ability to sustain and switch attention whilst inhibiting secondary elaborative processing.

Sound and hearing meditation were key to change, and although challenging at first, with encouragement and explanation about applying mindful awareness to tinnitus, this critical aspect of MBCT-t helped participants to develop a new relationship with the noise. MBCT-t does not involve learning any particular "acoustic strategies" (such as the "masking" or "partial masking" that characterizes sound therapy), the only acoustic strategy advised in MBCT-t is to encourage participants to approach and allow tinnitus, and to reduce their reliance on sound used for partial masking or distraction.

Of further importance were the location and make-up of the group and expertize of the teachers. Sharing experiences with other tinnitus-sufferers contributed strongly to the therapeutic nature of the intervention, as did having mindfulness teachers with expertize in tinnitus (personal and professional), based in an audiology center. This finding indicates why MBPs may be most effective when designed, tested and delivered in appropriate settings, including the integration of such programmes into holistic care. A biopsychosocial approach to health and illness is advised in tinnitus (McKenna et al., 2018a), and with clear evidence that MBPs are effective in tinnitus (Rademaker et al., 2019) clinical services must make these accessible to patients in the most effective contexts possible. This could include employing psychologists and MBP teachers in audiology services, or even training audiologists to deliver MBPs or work alongside mindfulness teacher, providing an audiological perspective within standard MBPs.

Contextual Factors

The stories of these individuals accentuate how compassion and kindness are integral to both the process of and outcomes from MBCT-t. This particular MBCT-t course included explicit teaching on kindness in week seven (loving-kindness meditation and discussion about compassion). Participants explained how the course allowed them to offer themselves time and space to simply be, without judgment or alteration, including in response to tinnitus. This chimes with broader literature which indicates how increases in self-compassion could be one mechanism of change in MBPs (Kuyken et al., 2010). Self-compassion arose with compassion for other beings, through the recognition of shared human suffering, which allowed perspective taking and healing.

The related constructs, appreciative joy and gratitude, were also present across the different themes, emerging from MBCT-t as perspectives shifted. This included seeing comparing one's tinnitus to the larger context of human suffering and being able to appreciate what aspects of life one is grateful for. This didn't negate the pain of tinnitus, but did reduce negative cognitions and create opportunities to notice and connect with many positive aspects of life that are not limited to tinnitus. MBCT-t explicitly encourages gratitude practice through the use of a "pleasant events diary" in week 2. More recent developments in MBCT-t now include specific gratitude meditations.

MBCT-t involved the creation of a community, which in turn was a hugely therapeutic experience. This is seen in other MPBs (Williams et al., 2011). Developing this community didn't require participants to share long histories about their personal lives and tinnitus, and in fact seemed to flourish through the shared experience of learning a new skill. The knowledge that one would be understood and accepted, and traveling together into new territory was enough to build strong connections across the group, which in turn supported other changes. This finding may indicate how tinnitus support groups will be more effective when the group has a shared goal or learning outcome, rather than simply involving reflection on experiences.

As with most MBPs, benefits extended beyond the primary concern, with improvements in depression, anxiety, stress, sleeping difficulties and interpersonal conflict. This is an important finding because such comorbidities in tinnitus are common (Baguley et al., 2013) and treatment that can ameliorate these will benefit patients.

This study shows how important it is for participants to find their own way through MBCT-t, and for teachers to balance discipline and structure with flexibility, warmth, a light touch and humor. Allowing, acceptance and compassion will flourish only if the individual can apply this to their own practice, experimenting with different postures, practices, learning styles and being able to express understandable skepticism, pain and suffering. All participants benefitted from the group, but in different ways (although Joe may have regarded mindfulness differently from others, he still benefitted). This links with the theory of mindfulness that one's *intention* in the practice will probably shape what one learns. Teachers therefore have a pivotal role in shaping the intention of participants in a way that will bring the most helpful learning to them. Learning, however, did not come only through didactic pedagogy but was dependent upon how the teachers modeled and embodied attitudes and approaches. The ability to teach MBPs in this way requires high-level training alongside sustained personal practice, so MBCT-t will require services to invest in their staff sufficiently. This poses real challenges in current healthcare systems, but the positive outcomes from MBCT-t in the long-term (here at 6 months) indicates how such investment may pay for itself by reducing the "revolving door" of healthcare so many tinnitus patients experience (Marks et al., 2019). The benefits from MBCT-t will be long lasting because they are associated with profound changes in people's attitudes toward and relationships with tinnitus and life more generally, something that current standard treatments fail to offer.

Strengths and Limitations

Strengths of this study are its novelty; no other studies have explored how tinnitus patients experience MBCT-t and these findings offer clear routes for future research and clinical practice. The IPA approach conducted by an experienced clinician offers a significant depth of insight which is valuable in understanding processes of MBCT-t. Although only 9 people were interviewed, these came from two MBCT-t groups and reflected a range of ages and genders. Limitations of this study are that only committed participants (completing MBCT-t and 6-month follow up) were included. However, only 2 people overall (of 39) dropped out of treatment, so this is a minor issue. All participants were Caucasian which may limit extrapolation to a more diverse sample. The age range of those interviewed was 35–67 years, so extrapolation to younger or older patients samples may also be limited (although theoretically we do not envisage this as having a large effect on the processes described, particularly as age was not found to moderate outcome of MBCT-t in the original RCT). Tinnitus subtyping was not conducted as part of this study, and future research could explore whether this has an impact on treatment outcome. There is a risk of bias from the interviewer also being the trial therapist, but awareness of this was accounted for in the analytic approach, participants were willing to discuss their experiences at length and were prompted to report on challenges and negative experiences.

Clinical Suggestions

Table 2 offers guidance for clinicians working with tinnitus sufferers and indicates how MBCT-t could be developed in the future.

CONCLUSION

MBCT-t brings people to a long-lasting, radically different, and more helpful relationship with their tinnitus. They shift from being "at war" with tinnitus to "allowing it to be." Multiple

TABLE 2 | Clinical suggestions for applying mindfulness to tinnitus.

Stop fighting tinnitus, stop being "at war" and instead and turn toward it.	Mindfulness is not a "cure" to silence tinnitus, nor a way of getting better at "ignoring it." It is based on the evidence that fighting tinnitus makes it worse. Conversely, allowing tinnitus to be present and even turning toward tinnitus will alleviate suffering. Paying attention to tinnitus without judgment or attempts to change it will lead to a new relationship with tinnitus where it becomes less intrusive and problematic. This can be done by purposefully listening to tinnitus as part of the soundscape, but without thinking too much 'about' it.
Develop mindful awareness	Standard mindfulness meditation practices (such as focusing on the breath, body, thoughts, emotions and movement) develop one's ability to remain present with experiences. As this ability grows, it can be applied to difficulties such as tinnitus in a helpful way.
Connect with others	Connect with other people who have or understand tinnitus and building a community, such as a therapeutic group. This helps one to feel less alone and isolated. It may be more helpful for the group to focus on learning something new together, rather than focusing only on tinnitus.
Take a broad perspective and practice gratitude	See tinnitus in the bigger context of all human suffering, and gain perspective on the fearful and catastrophic thoughts that might exist about it. Try experimenting with noticing other aspects of life which one can be grateful for.
Develop kindness and compassion for yourself and others	Experiment with approaching all experiences (including tinnitus) with a kinder, more gentle and friendly attitude. Be kind to oneself by engaging in activities that are fun or pleasant. Try practicing Loving-Kindness meditation and offering kindness to other people.
Balance discipline with permissiveness	Learning mindfulness requires a balance of discipline and permissiveness, and regular practice is vital. Sustaining practice will involve finding ways of practicing that suit the individual and their current life circumstances.

processes interweave to lead to these changes in perspective and attitude, including developing mindful awareness, being in a group, embodied teaching, compassion, gratitude and having an open mind. MBCT-t can be successfully applied to a tinnitus population, in a way that changes the factors that maintain tinnitus-related distress (catastrophic thinking, selective attention and anxiety). MBPs should continue to be developed and utilized to offer increasingly effective tinnitus treatments, and made available to tinnitus patients as part of the standard care which is still frequently limited to information, acoustic strategies and relaxation.

DATA AVAILABILITY STATEMENT

The data supporting the conclusions of this article will be made available by the authors, without undue reservation, to any qualified researcher, to be accessed at University College London Hospitals or the University of Bath.

ETHICS STATEMENT

This study involving human participants were reviewed and approved by the Camden and Kings Cross NHS Ethics Committee. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

EM designed the study, conducted and transcribed the interviews, led the analysis, and wrote the manuscript. PS and LM contributed to the analysis of the interviews, in line with standard IPA methods, and commented on the manuscript. All authors approved the final version of the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2020.00483/full#supplementary-material

REFERENCES

Alsubaie, M., Abbott, R., Dunn, B., Dickens, C., Keil, T. F., Henley, W., et al. (2017). Mechanisms of action in mindfulness-based cognitive therapy (MBCT) and mindfulness-based stress reduction (MBSR) in people with physical and/or psychological conditions: a systematic review. *Clin. Psychol. Rev.* 55, 74–91. doi: 10.1016/j.cpr.2017.04.008

Baguley, D., Andersson, G., McFerran, D., and McKenna, L. (2013). Hyperacusis. *Tinnitus Multidiscip. Approach* 22, 133–147.

Bohlmeijer, E., Prenger, R., Taal, E., and Cuijpers, P. (2010). The effects of mindfulness based stress reduction therapy on mental health of adults with a chronic medical disease: a meta-analysis. *J. Psychosom. Res.* 68, 539–544. doi: 10.1016/j.jpsychores.2009.10.005

Carlson, L. E. (2012). Mindfulness-based interventions for physical conditions: a narrative review evaluating levels of evidence. *ISRN Psychiatry* 2012, 1–21. doi: 10.5402/2012/651583

Cima, R. F. F., Mazurek, B., Haider, H., Kikidis, D., Lapira, A., Noreña, A., et al. (2019). A multidisciplinary European guideline for tinnitus: diagnostics, assessment, and treatment. *HNO* 67, 10–42. doi: 10.1007/s00106-019-0633-7

Crane, R. S., Brewer, J., Feldman, C., Kabat-Zinn, J., Santorelli, S., Williams, J. M. G., et al. (2017). What defines mindfulness-based programs? The warp and the weft. *Psychol. Med.* 47, 990–999. doi: 10.1017/S0033291716003317

Crane, R. S., Kuyken, W., Hastings, R. P., Rothwell, N., and Williams, J. M. G. (2010). Training teachers to deliver mindfulness-based interventions: learning from the UK experience. *Mindfulness* 1, 74–86. doi: 10.1007/s12671-010-0010-9

Fuller, T., Cima, R., Langguth, B., Mazurek, B., Vlaeyen, J. W., and Hoare, D. J. (2020). Cognitive behavioural therapy for tinnitus. *Cochrane Database Syst. Rev.* 2010:CD005233.

Greenberg, R. P., Constantino, M. J., and Bruce, N. (2006). Are patient expectations still relevant for psychotherapy process and outcome? *Clin. Psychol. Rev.* 26, 657–678. doi: 10.1016/j.cpr.2005.03.002

Kabat-Zinn, J. (1990). *Full Catastrophe Living: Using the Wisdom of Your Body and Mind to Face Stress, Pain, and Illness*. New York, NY: Dell.

Kuyken, W., and Feldman, C. (2019). *Mindfulness: Ancient Wisdom meets Modern Psychology*. New York, NY: The Guildford Press.

Kuyken, W., Warren, F. C., Taylor, R. S., Whalley, B., Crane, C., Bondolfi, G., et al. (2016). Efficacy of mindfulness-based cognitive therapy in prevention of depressive relapse: an individual patient data meta-analysis from randomized trials. *JAMA Psychiatry* 73, 565–574. doi: 10.1001/jamapsychiatry.2016.0076

Kuyken, W., Watkins, E., Holden, E., White, K., Taylor, R. S., Byford, S., et al. (2010). How does mindfulness-based cognitive therapy work? *Behav. Res. Ther.* 48, 1105–1112. doi: 10.1016/j.brat.2010.08.003

Marks, E., Smith, P., and McKenna, L. (2019). Living with tinnitus and the health care journey: an interpretative phenomenological analysis. *Br. J. Health Psychol.* 24, 250–264. doi: 10.1111/bjhp.12351

Martinez-Devesa, P., Waddell, A., Perera, R., and Theodoulou, M. (2010). Behavioral cognitive therapy for tinnitus. *Cochrane Database Syst. Rev.* 8:CD005233.

McCormack, A., Edmondson-Jones, M., Somerset, S., and Hall, D. (2016). A systematic review of the reporting of tinnitus prevalence and severity. *Hear. Res.* 337, 70–79. doi: 10.1016/j.heares.2016.05.009

McFerran, D., Hoare, D. J., Carr, S., Ray, J., and Stockdale, D. (2018). Tinnitus services in the United Kingdom: a survey of patient experiences. *BMC Health Services Res.* 18:110. doi: 10.1186/s12913-018-2914-3

McFerran, D. J., Stockdale, D. J., Holme, R., Large, C. H., and Baguley, D. M. (2019). Why is there no cure for tinnitus? *Front. Neurosci.* 13:802. doi: 10.3389/fnins.2019.00802

McKenna, L., Handscomb, L., Hoare, D. J., and Hall, D. A. (2014). A scientific cognitive-behavioral model of tinnitus: novel conceptualizations of tinnitus distress. *Front. Neurol.* 5:196. doi: 10.3389/fneur.2014.00196

McKenna, L., Marks, E., and Scott, D. (2018a). "Understanding tinnitus: a psychological perspective," in *Scott Brown's Otorhinolaryngology Head & Neck Surgery: Head & Neck Surgery*, eds J. C. Watkinson, and R. W. Clarke (Boca Raton, FL: CRC Press), 893–900. doi: 10.1201/9780203731017-70

McKenna, L., Marks, E. M., and Vogt, F. (2018b). Mindfulness-based cognitive therapy for chronic Tinnitus: evaluation of benefits in a large sample of patients attending a Tinnitus clinic. *Ear Hear.* 39, 359–366. doi: 10.1097/AUD.0000000000000491

McKenna, L., Marks, E. M., Hallsworth, C. A., and Schaette, R. (2017). Mindfulness-based cognitive therapy as a treatment for chronic tinnitus: a randomized controlled trial. *Psychother. Psychos.* 86, 351–361. doi: 10.1159/000478267

Mindful Nation UK (2015). *Mindful Nation UK – report by the Mindfulness All-Party Parliamentary Group (MAPPG), 2015*. London: Mindfulness Initiative.

Rademaker, M., Stegeman, I., Ho-Kang-You, K., Stokroos, R., and Smit, D. (2019). The effect of mindfulness-based interventions on Tinnitus Burden. A systematic review. *Front. Neurol.* 10:1135. doi: 10.3389/fneur.2019.01135

Segal, Z. V., Williams, J. M., and Teasdale, J. D. (2012). *Mindfulness-Based Cognitive Therapy for Depression*, 2nd Edn. New York, NY: Guilford Press.

Smith, J. A., Larkin, M., and Flowers, P. (2009). *Interpretative Phenomenological Analysis: Theory, Method and Research*. London: Sage.

Williams, M. J., McManus, F., Muse, K., and Williams, J. M. G. (2011). Mindfulness-based cognitive therapy for severe health anxiety (hypochondriasis): an interpretative phenomenological analysis of patients' experiences. *Br. J. Clin. Psychol.* 50, 379–397. doi: 10.1111/j.2044-8260.2010.02000.x

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A Clinician and Service User's Perspective on Managing MS: Pleasure, Purpose, Practice

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There is a growing body of evidence that points to an important role for modification of lifestyle factors and promotion of health-related quality of life in the secondary prevention of disease progression in multiple sclerosis (D'Hooghe et al., 2010; Weiland et al., 2014; Hadgkiss et al., 2015). As a clinical psychologist diagnosed with multiple sclerosis in 2012 I have gained a unique insight into ways in which people living with MS and clinicians can usefully integrate evidence-based lifestyle modifications that enhance self-efficacy and self-management to improve wider psychological and physical health. The framework presented here enables clinicians to engage in salutogenic health promotion by placing value upon the importance of healthy, evidence-based behavior change. Furthermore, the framework provides a structure which can empower and provide guidance for people living with MS on what and how to implement and sustain behavior change and emotional wellbeing in the face of this life-changing diagnosis.

Keywords: multiple sclerosis, lifestyle medicine, psychosocial, self-management, behavior modification

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INTRODUCTION

Multiple Sclerosis (MS) is a chronic inflammatory disorder of the central nervous system and it is most frequently diagnosed in young adulthood. With 2.5 million people diagnosed with MS worldwide (Compston and Coles, 2008) and the prevalence increased by 69% between 1996 and 2013 (Rotstein et al., 2018) there is unprecedented demand for support and intervention. There is corresponding growing evidence that modification of lifestyle factors may reduce relapse rate, improve quality of life and potentially slow the course of the disease (Jelinek and Hassed, 2009; D'Hooghe et al., 2010; Jelinek et al., 2013; Weiland et al., 2014; Hadgkiss et al., 2015). If services are to promote and support healthy behavior change among this rapidly growing group of patients, improved methods to help patients and clinicians understand and utilize evidence-based interventions and research to mobilize self-management, are desperately needed. As a clinical psychologist with experience of working in the National Health Service I understand first-hand the challenges faced by services in promoting behavior change. However, it was not until I was diagnosed with MS, in 2012 that I was able to experience for myself the lack of information and encouragement patients receive in relation to making the lifestyle changes research suggests could benefit their symptoms and disease progression. This lack of information and support undoubtedly heightens patient anxiety and leaves them feeling disempowered; both of which contribute to stress-related illness (Theoharides and Cochrane, 2004) and reduce the likelihood of positive behavior change in health interventions (McGrady et al., 2009).

While medication options have increased significantly over the last decade it has been my observation that patients remain poorly informed about the potential role of specific lifestyle risk factors in MS. This is despite a growing body of evidence demonstrating that modification of lifestyle-related risk factors is associated with improved mental and physical health outcomes in MS (Watt et al., 1998; Stuifbergen and Becker, 2001; D'Hooghe et al., 2010; Levin et al., 2014a,b; Taylor et al., 2014; Jelinek et al., 2016; Fitzgerald et al., 2018a,b) and may provide a promising intervention to manage MS progression (D'Hooghe et al., 2010; Li et al., 2010). Specifically, studies have reported that smoking and low vitamin D levels (Coetzee and Thompson, 2017; Hempel et al., 2017), stress-management and mindfulness -based interventions (MBI; Simpson et al., 2014), healthy dietary habits (Hadgkiss et al., 2015) and increasing physical exercise levels (Marck et al., 2014) are all areas in which individuals could make changes to benefit their MS symptoms and quality of life. These findings are in keeping with meta-analyses on health behaviors which have emphasized the central role of diet (Firth et al., 2019) and physical activity (Chekroud et al., 2018) on our psychological and emotional health. Given this growing body of evidence, it is perhaps little wonder that key stakeholders have highlighted the importance of lifestyle as an essential area for future research (Multiple Sclerosis Research of Australia, 2017; Multiple Sclerosis Society of Canada, 2018).

In an era of austerity among clinical services and the growing patient numbers, empowering individuals to make lifestyle modifications seems of paramount importance. Indeed, beneficial self-management programs have emerged in a range of other health conditions such as cancer (Dodd and Miaskowski, 2000) and coronary heart disease (for review see Anderson et al., 2016). However, outside of organized, facilitated psychosocial interventions, which can be costly to services, I have seen that MS patients continue to face barriers to accessing and understanding literature relating to lifestyle medicine and psychoneuroimmunology. As a result, opportunities for patients to understand literature and implement successful behavior change are often limited. My experiences within the MS community and as an academic and clinician, have highlighted three "themes" which may help people living with MS to facilitate and sustain healthy behavior change. These themes (which will be described in this paper and can be seen in **Figure 1**) may also provide a useful framework through which clinicians can educate and empower their patients. Adopting the accessible approach to health promotion presented below may provide both patients and clinicians with a theoretically and empirically based framework through which healthy behavior change and lifestyle modification may be communicated, implemented and sustained.

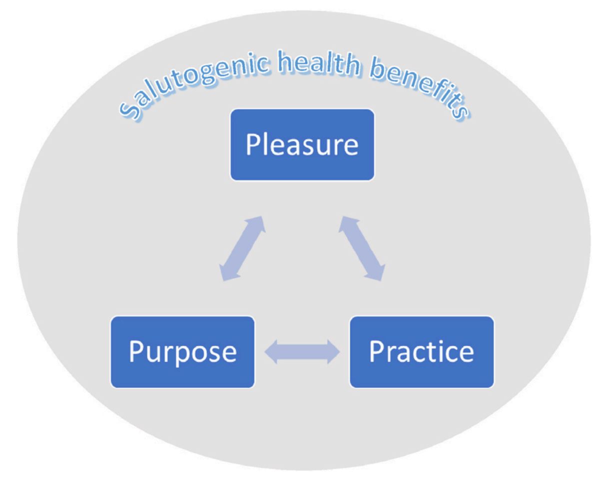

FIGURE 1 | The salutogenic health benefits of the 3P's framework.

Pleasure

Pleasure and positive affect can co-occur with distress (Folkman and Moskowitz, 2000). Moreover, there is growing evidence that experiencing pleasure and positive emotions is essential to help overcome challenges and improve health-related quality of life (Hildon et al., 2008). Indeed, hedonic theories of wellbeing focus on pleasurable experiences to enhance positive affect (Diener, 1984; Fredrickson, 2001). Most recently, the PERMA model associated with positive psychology and developed by Seligman (2011) highlights the importance of integrating positive emotions and experience for wellbeing. What is more, positive feelings motivate protective human behaviors, enhancing performance at work, strengthening relationships, improving our physical health, encouraging optimism (Kun et al., 2017) which are associated with reduced mortality (Chida and Steptoe, 2008; Diener and Chan, 2011) and create opportunities for enhancing the health and wellbeing of people living with chronic conditions (Mead et al., 2019).

When faced with a life-changing diagnosis many people are triggered to re-evaluate their life and ask, "*what truly makes me happy?*" with many going on to make changes to enable that (Linley and Joseph, 2004). Reprioritisation of values and positive changes in relationships are often reported following trauma and adversity, but notably these also can manifest as increased feelings of intimacy, empathy and greater levels of self-disclosure (Tedeschi and Calhoun, 2004). For many people traumatic and life changing experiences trigger improved psychological functioning (Taylor, 2004) and an increased appreciation of life, setting of new life priorities, increased personal strength, identification of new possibilities, improved intimate relationships, and for some, positive spiritual growth (Tedeschi et al., 1998). Providing accurate information at a time when individuals are open to making radical and positive changes to their life could therefore have far-reaching positive effects for their emotional wellbeing, as well as their physical health. Indeed, the model of Salutogenesis encourages a focus upon, and the benefits of, factors that support health and well-being despite stressors and illness (Antonovsky, 1979, 1987). Essentially, the consultation room offers many opportunities to affect changes that the patient may then take forward outside of that meeting and which can have a positive impact upon their physical and emotional health.

Pleasure is an essential component of the promotion and maintenance of change and should not be undervalued. If we can enjoy the changes we make, we are more likely to persevere (Michie et al., 2008), hereby finding creative and alternative solutions that enhance self-efficacy and esteem as we reflect upon what we have achieved and overcome. From a systemic perspective, engaging in activities which we enjoy also connects us to like-minded people through which we may gain or sustain friendship; making us more likely to sustain behavior change *and* avoid social isolation. With increased likelihood of loneliness in those at risk of social isolation (such as people with long-term health conditions and older people; for reviews see Andersson, 1998; Cacioppo et al., 2000, 2015), and established associations between loneliness and mental health problems (Lasgaard et al., 2016), building these social connections and relationships is protective. They provide a buffering effect, increase levels of perceived support and feelings of self-worth, and encourage maintenance of new, positive habits (Tedeschi and Calhoun, 2004; Cacioppo et al., 2015). Moreover, social connectedness and experiences of pleasure can dramatically effect the construction of social and cultural identities, hereby influencing our understandings of health as well as public health interventions (Coveney and Bunton, 2003).

It is important to pause here and consider that working to integrate experiences of pleasure and positive emotions may take conscious effort – especially for those experiencing pain or disability. And as such, they should be encouraged and fully recognized and supported as valuable to improving wellbeing (Folkman and Moskowitz, 2000). It is important to be mindful that experiencing pleasure is *not* a direct result of an absence of distress – people can experience pleasure in spite of pain or disability; in fact this may enable more existential appreciation of life. Moreover, integrating positive experiences and emotions shape an individual's subjective experience and encourages adaptation; the kind of flexibility which defines resilience, described here by Pemberton (2015, page 2) as:

"The capacity to remain flexible in our thoughts, feelings, and behaviors when faced by a life disruption, or extended periods of pressure, so that we emerge from difficulty stronger, wiser, and more able."

As such, integrating positive and pleasurable experiences can help to build resilience and can improve a persons' quality of life when living with an unpredictable chronic condition such as MS. If we consider the high rates of depression reported among people with MS (lifelong prevalence of approx. 50%; Feinstein, 2011) and the inflammatory nature of stress (Slavich and Irwin, 2014), promoting emotional and positive psychological wellbeing can therefore have a multifaceted impact. For example, contributing to minimizing inflammatory disease activity via the vagus nerve (Kemp et al., 2017a,b), *building protective social networks* and buffering stress (Tedeschi and Calhoun, 2004; Cacioppo et al., 2015).

Purpose

The stress-inflammation pathway is widely researched (e.g., Segerstrom and Miller, 2004; Steptoe et al., 2007; Denson et al., 2009; Irwin and Cole, 2011) with chronic inflammation associated with a range of autoimmune conditions, cancers and Alzheimer's disease (Couzin-Frankel, 2010). Cumulative stress and related physiological dysregulation are increasingly regarded as contributing to inflammation, aging and a range of predisposed disease trajectories (Lupien et al., 2009; Juster et al., 2010), even impacting upon gene expression (Zawia et al., 2009; Stankiewicz et al., 2013). As such, person-centered approaches which can contribute to reductions in allostatic load are likely to provide valuable psychosocial interventions for those experiencing stress related illness.

Building a life with the people, purpose and pleasures that are meaningful to you encourages a move away from stressful aspects of your life that may be contributing to chronic stress and perpetuating disease (Slavich and Irwin, 2014). Indeed, interventions that connect to an individual's purpose or promote meaning and accomplishment have been shown to be protective; increasing well-being and reducing symptoms of depression (Giannopoulos and Vella-Brodrick, 2011; Gander et al., 2013). Antonovsky (1996) argued that "salutogenesis" depends on experiencing a strong "sense of coherence" of which a sense of meaning is essential. Indeed, "sense of coherence" is associated with positive health outcomes, strengthens resilience and encourages a positive subjective state of health (Eriksson and Lindström, 2007). Engaging in activities that are both pleasurable and meaningful also provides opportunities for an individual to experience Csikszentmihalyi's (2013) concept of "flow"; "the state in which people are so involved in an activity that nothing else seems to matter," which in turn leads to feelings of happiness (Dodge et al., 2012). Receiving a life-changing diagnosis like MS can lead some individuals to reprioritize and to consider practical changes to their life to make it more fulfilling (Tedeschi and Calhoun, 2006). Such changes in outlook provide opportunity for people to reconnect to the purpose and meaning in their life; resulting in more opportunities for meaningful connection and the positive, protective experience of "flow." Contact with health care professionals often provides an opportunity to reflect upon the psychosocial impact of diagnosis and life with a chronic condition, and currently opportunities are missed to acknowledge and validate the health benefits of making such changes which would undoubtedly reinforce their impact and empower patients.

Practice

The notion that stress may trigger disease activity in MS was first considered by Charcot in 1877, and chronic stress is known to significantly affect the function of the immune system (Tausk et al., 2008). The effect of stress on the central nervous system and on the maintenance of the delicate balance between cell-mediated (Th1) and humoral (Th2) immune responses has been studied widely (for review see Chrousos, 2009) with stress reported to activate inflammatory markers and exacerbate symptoms in a range of autoimmune conditions (Theoharides and Cochrane, 2004; Maté, 2011). Given the widely reported efficacy of mindfulness-based interventions (MBI's) for treating stress, anxiety and recurrent depression in the general population (Goyal et al., 2014) it makes sense that "*MBI's are effective at improving mental well-being in people with MS*" (Simpson et al., 2014).

Mindfulness may have an effect on acute responses to stress, and a wider impact, by inhibiting underlying consequences of chronic exposure to stress. Simple breathing meditations have the potential to alleviate anxiety and also to help an individual develop self-awareness; supporting better integration of the mind and body (Goyal et al., 2014). Mindfulness and meditation are appealing as psychosocial interventions not least because they have no risks, are free and have originated from 2,500-year-old Buddhist traditions, but also because this legacy is now supported by thousands of peer-reviewed papers (for review see Taylor et al., 2014; Baer, 2015). Key to the efficacy of MBI's is the cultivation of habitual or daily practice and the setting of intentions to engage in meditation, which, over time, contributes to a more mindful way of being in the world (Bohlmeijer et al., 2010).

Setting intentions to develop new behaviors can provide a useful framework for people living with chronic conditions to work toward. The evidence suggests that engaging in regular meditation and mindfulness practices are likely to benefit people with MS at an emotional and physiological level (Goyal et al., 2014; Senders et al., 2014) even if delivered virtually or remotely (Frontario et al., 2016). MBIs therefore offer an effective, evidence-based and cost-efficient psychosocial intervention which can be used by individuals at little or no costs to them, or to services. As such, there is now no reasonable excuse for clinicians failing to promote low-risk, MBIs as part of a management plan for stress-related and autoimmune illness if we are to improve the wellbeing of people with MS; the majority of which are of working age and many of whom are seeking ways through which they can actively manage their condition. Furthermore, the notion of "practice" and discipline is a useful notion which can then be extended to other health lifestyle changes – for example, changes to exercise regime or diet. Setting such intentions encourages people to plan how they will implement such changes and helps them to consider how they will overcome barriers and frustrations (Chapman et al., 2009).

Discussion

The framework presented here provides a useful structure for people living with MS, and clinicians working with them, to approach secondary prevention. Advances in medical treatment over the last decade have been hugely positive for the MS community, however, shifts in incorporating evidence relating to lifestyle modifications have lagged behind (Jelinek and Hassed, 2009). This is despite the known benefits of encouraging healthy behavior change (Hadgkiss et al., 2013) and patients demands for non-drug interventions in MS (Leong et al., 2009). The growing numbers of people being diagnosed with MS point to an urgent need to incorporate this information and provide more specific guidance and encouragement regarding self-management. However, as a health professional I know it can be challenging for clinicians to be aware of and/or summarize the rapidly evolving evidence-base, and even harder to develop individualized plans for patients. Austerity measures, alongside people's widening access to health information online provide opportunities for people to autonomously implement healthy changes to their life and clinicians can support and encourage this by using this simple, evidence-based framework.

Communication between "patient" and doctor provides "an important role in educating and motivating patients to take appropriate actions and assist in shared decision-making for improved health outcomes" (Teutsch, 2003). The dissemination of knowledge needs to be enhanced and research evidence needs to be made more accessible (Harzing and Adler, 2016). The promotion of healthy behavior change should not be avoided by clinicians and, based on the empirical knowledge available, to do so neglects the very premise of health care. Indeed disseminating psychological knowledge is a core purpose of the role of a clinical psychologist (British Psychological Society, Biddle et al., 1992) and as such, many clinicians already have a range of skills in their "tool kit" to facilitate the propagation of this information. Patient-doctor communication can play an important role in educating and motivating patients to take appropriate actions and assist in shared decision-making for improved health outcomes. Key health care providers such as neurologists and specialist nurses have the opportunity and potential to empower many patients with MS to take more control of their health by highlighting the benefits of self-efficacy and value of lifestyle modification during consultations – such interactions present important opportunities to acknowledge and place value on the role of specific lifestyle factors such as vitamin D supplementation, exercise, stress management and nutrition. Access to psychological support and targeted health promotion is often inhibited by the limited resources available to clinicians and few MS services are able to provide specialist psychological support to all their patients. As such, the important role that neurologists and nurses can play in promoting and facilitating healthy behavior change in patients must be acknowledged and enhanced. My experience as a patient and professional has shown me that many MS specialist clinicians feel unnecessary discomfort at recommending specific secondary prevention or "lifestyle" interventions and, as a result, avoid discussing anything except the most rudimentary lifestyle factors. This ambiguity can leave patients feeling like they do not have the support of their medical team in making lifestyle and behavior modifications, and/or that such changes are not worthwhile. Opportunities for health promotion are consequently missed as a result of the clinicians reticence and this can have implications for the patients decisions to engage more actively in self-management.

Salutogenic approaches such as the one described here while not widespread are not entirely novel. They have been used in the development of health promotion models (Eriksson and Lindström, 2006), the development of therapeutic practice in health care (Pelikan, 2017), and the design of health-care environments (Wallerstein, 1992; Dilani, 2008). Of particular value in this case is the concept of "sense of coherence" (SOC) which refers to collective coping and acknowledges the ability to mobilize resources in the face of challenge (Taylor, 2004). In particular, SOC highlights the ability for people to understand what happens to them, the extent to which they are able to manage the situation on their own or with the support of community, and the ability to find meaning in the situation (Antonovsky, 1998; Eriksson and Lindström, 2006). Considered alongside the established evidence that interventions which modify self-efficacy are effective in promoting health behavior change

(Sheeran et al., 2016) and the growing numbers of people diagnosed with MS (Rotstein et al., 2018), new approaches to management are essential.

The simple framework described here; "The 3 P's of Secondary Prevention," offers a risk-free structure from which clinicians can encourage and support their patients in evidence-based lifestyle modifications (D'Hooghe et al., 2010; Weiland et al., 2014; Hadgkiss et al., 2015). Moreover, such empowerment carries known health benefits (Wallerstein, 2007) and should not be "*restricted to some disease and treatment-related outcomes, but should be discussed and negotiated with every patient*" (Aujoulat et al., 2007). Engaging people with MS as potential collaborators in their care will not only foster greater patient satisfaction and improve adherence (Martin et al., 2005), it also allows for enhanced understanding of the individuals specific socio-cultural context (Kreps, 2006) and can have potential benefits for individual wellbeing and wider service efficacy (Jahng et al., 2005). However, it is important to consider that the framework is not without its weaknesses. It may, for example, prove difficult for clinicians to feel confidant if patients ask for further information about areas in which the clinician does not feel knowledgeable. There may also be limitations of time within patient consultations which make discussions of secondary prevention difficult. Despite these considerations it is important to hold in mind that for all those patients who are able to independently seek out and decipher up-to-date research evidence and make confidant autonomous decisions about their health care, there are many others for whom this is simply not possible. Clinicians can play an important role in mobilizing patients to engage in salutogenic, health promoting behavior change by making these simple changes in *what* and *how* they communicate with patients. Encouraging patients to take an active role in the management of their MS, which is a life-long chronic condition can have far-reaching positive benefits for their quality of life, physical and emotional wellbeing (Bogosian et al., 2015). If more MS specialist services are able to implement such an approach they may well provide the medical 'approval' the most at-risk patients feel they require to explore and truly engage with and implement such behavior modifications. This may, in the long-term, have the potential to radically change the face of self-management and the quality of life of people living with MS.

AUTHOR CONTRIBUTIONS

The author confirms being the sole contributor of this work and has approved it for publication.

REFERENCES

Anderson, L., Oldridge, N., Thompson, D. R., Zwisler, A. D., Rees, K., Martin, N., et al. (2016). Exercise-based cardiac rehabilitation for coronary heart disease: cochrane systematic review and meta-analysis. *J. Am. Coll. Cardiol.* 67, 1–12. doi: 10.1016/j.jacc.2015.10.044

Andersson, L. (1998). Loneliness research and interventions: a review of the literature. *Aging Ment. Health* 2, 264–274. doi: 10.1080/13607869856506

Antonovsky, A. (1979). *Health, Stress, and Coping*. San Francisco, CA: Jossey-Bass.

Antonovsky, A. (1987). *Unraveling the Mystery of Health: How People Manage Stress and Stay Well*. San Francisco, CA: Jossey-bass.

Antonovsky, A. (1996). The salutogenic model as a theory to guide health promotion. *Health Promot. Int.* 11, 11–18. doi: 10.1093/heapro/11.1.11

Antonovsky, A. (1998). The sense of coherence: an historical and future perspective. *Isr. J. Med. Sci.* 32, 170–178.

Aujoulat, I., d'Hoore, W., and Deccache, A. (2007). Patient empowerment in theory and practice: polysemy or cacophony? *Patient Educ. Couns.* 66, 13–20. doi: 10.1016/j.pec.2006.09.008

Baer, R. A. (ed.) (2015). *Mindfulness-Based Treatment Approaches: Clinician's Guide to Evidence Base and Applications*. Cambridge, MA: Academic Press.

Biddle, S. J., Bull, S. J., and Seheult, C. L. (1992). Ethical and professional issues in contemporary, British sport psychology. *Sport Psychol.* 6, 66–76. doi: 10.1123/tsp.6.1.66

Bogosian, A., Chadwick, P., Windgassen, S., Norton, S., McCrone, P., Mosweu, I., et al. (2015). Distress improves after mindfulness training for progressive MS: a pilot randomised trial. *Mult. Scler. J.* 21, 1184–1194. doi: 10.1177/1352458515576261

Bohlmeijer, E., Prenger, R., Taal, E., and Cuijpers, P. (2010). The effects of mindfulness-based stress reduction therapy on mental health of adults with a chronic medical disease: a meta-analysis. *J. Psychosom. Res.* 68, 539–544. doi: 10.1016/j.jpsychores.2009.10.005

Cacioppo, J. T., Berntson, G. G., Larsen, J. T., Poehlmann, K. M., and Ito, T. A. (2000). The psychophysiology of emotion. *Handb. Emot.* 2, 173–191.

Cacioppo, J. T., Cacioppo, S., Cole, S. W., Capitanio, J. P., Goossens, L., and Boomsma, D. I. (2015). Loneliness across phylogeny and a call for comparative studies and animal models. *Perspect. Psychol. Sci.* 10, 202–212. doi: 10.1177/1745691614564876

Calhoun, L. G., Cann, A., Tedeschi, R. G., and McMillan, J. (2000). A correlational test of the relationship between posttraumatic growth, religion, and cognitive processing. *J. Trauma. Stress* 13, 521–527. doi: 10.1023/a:1007745627077

Carlson, L. E. (2012). Mindfulness-based interventions for physical conditions: a narrative review evaluating levels of evidence. *ISRN Psychiatry* 2012:651583. doi: 10.5402/2012/651583

Chapman, J., Armitage, C. J., and Norman, P. (2009). Comparing implementation intention interventions in relation to young adults' intake of fruit and vegetables. *Psychol. Health* 24, 317–332. doi: 10.1080/08870440701864538

Chekroud, S. R., Gueorguieva, R., Zheutlin, A. B., Paulus, M., Krumholz, H. M., Krystal, J. H., et al. (2018). Physical activity and mental health–Author's reply. *Lancet Psychiatry* 5:874.

Chida, Y., and Steptoe, A. (2008). Positive psychological well-being and mortality: a quantitative review of prospective observational studies. *Psychosom. Med.* 70, 741–756. doi: 10.1097/PSY.0b013e31818105ba

Chrousos, G. P. (2009). Stress and disorders of the stress system. *Nat. Rev. Endocrinol.* 5, 374–381. doi: 10.1038/nrendo.2009.106

Coetzee, T., and Thompson, A. (2017). When are we going to take modifiable risk factors more seriously in multiple sclerosis? *Mult. Scler. J.* 23, 494–495. doi: 10.1177/1352458517694433

Compston, A., and Coles, A. (2008). Multiple sclerosis [seminar]. *Lancet* 9648, 1502–1517.

Couzin-Frankel, J. (2010). Inflammation bares a dark side. *Science* 330:1621. doi: 10.1126/science.330.6011.1621

Coveney, J., and Bunton, R. (2003). In pursuit of the study of pleasure: implications for health research and practice. *Health* 7, 161–179. doi: 10.1177/1363459303007002873

Csikszentmihalyi, M. (2013). *Flow: The Psychology of Happiness*. New York, NY: Penguin Random House.

Denson, T. F., Spanovic, M., and Miller, N. (2009). Cognitive appraisals and emotions predict cortisol and immune responses: a meta-analysis of acute laboratory social stressors and emotion inductions. *Psychol. Bull.* 135, 823–853. doi: 10.1037/a0016909

D'Hooghe, M. B., Nagels, G., Bissay, V., and De Keyser, J. (2010). Modifiable factors influencing relapses and disability in multiple sclerosis. *Mult. Scler.* 16, 773–785. doi: 10.1177/1352458510367721

Diener, E. (1984). Subjective well-being. *Psychol. Bull.* 95, 542–575.

Diener, E., and Chan, M. Y. (2011). Happy people live longer: subjective well-being contributes to health and longevity. *Appl. Psychol. Health Well Being* 3, 1–43. doi: 10.1111/j.1758-0854.2010.01045.x

Dilani, A. (2008). Psychosocially supportive design: a salutogenic approach to the design of the physical environment. *Des. Health Sci. Rev.* 1, 47–55.

Dodd, M. J., and Miaskowski, C. (2000). The PRO-SELF Program: a self-care intervention program for patients receiving cancer treatment. *Semin. Oncol. Nurs.* 16, 300–308. doi: 10.1053/sonu.2000.16586

Dodge, R., Daly, A. P., Huyton, J., and Sanders, L. D. (2012). The challenge of defining wellbeing. *Int. J. Wellbeing* 2, 222–235. doi: 10.5502/ijw.v2i3.4

Eriksson, M., and Lindström, B. (2006). Antonovsky's sense of coherence scale and the relation with health: a systematic review. *J. Epidemiol. Commun. Health* 60, 376–381. doi: 10.1136/jech.2005.041616

Eriksson, M., and Lindström, B. (2007). Antonovsky's sense of coherence scale and its relation with quality of life: a systematic review. *J. Epidemiol. Commun. Health* 61, 938–944. doi: 10.1136/jech.2006.056028

Feinstein, A. (2011). Multiple sclerosis and depression. *Mult. Scler. J.* 17, 1276–1281.

Firth, J., Marx, W., Dash, S., Carney, R., Teasdale, S. B., Solmi, M., et al. (2019). The effects of dietary improvement on symptoms of depression and anxiety: a meta- analysis of randomized controlled trials. *Psychosom. Med.* 81, 265–280. doi: 10.1097/PSY.0000000000000673

Fitzgerald, K. C., Tyry, T., Salter, A., Cofield, S. S., Cutter, G., Fox, R. J., et al. (2018a). A survey of dietary characteristics in a large population of people with multiple sclerosis. *Mult. Scler. Relat. Disord.* 22, 12–18. doi: 10.1016/j.msard.2018.02.019

Fitzgerald, K. C., Tyry, T., Salter, A., Cofield, S. S., Cutter, G., Fox, R., et al. (2018b). Diet quality is associated with disability and symptom severity in multiple sclerosis. *Neurology* 90, e1–e11. doi: 10.1212/WNL.0000000000004768

Folkman, S., and Moskowitz, J. T. (2000). Positive affect and the other side of coping. *Am. Psychol.* 55, 647–654. doi: 10.1037/0003-066x.55.6.647

Fredrickson, B. L. (2001). The role of positive emotions in positive psychology: the broaden-and-build theory of positive emotions. *Am. Psychol.* 56, 218–226. doi: 10.1037/0003-066x.56.3.218

Frontario, A., Feld, E., Sherman, K., Krupp, L., and Charvet, L. (2016). Telehealth mindfulness meditation improves cognitive performance in adults with multiple sclerosis (P3. 092). *Neurology* 86(16 Suppl.):P3-092.,

Gander, F., Proyer, R. T., Ruch, W., and Wyss, T. (2013). Strength-based positive interventions: Further evidence for their potential in enhancing well-being and alleviating depression. *J. Happiness Stud.* 14, 1241–1259. doi: 10.1007/s10902-012-9380-0

Giannopoulos, V. L., and Vella-Brodrick, D. A. (2011). Effects of positive interventions and orientations to happiness on subjective well-being. *J. Posit. Psychol.* 6, 95–105. doi: 10.1080/17439760.2010.545428

Goyal, M., Singh, S., Sibinga, E. M., Gould, N. F., Rowland-Seymour, A., Sharma, R., et al. (2014). Meditation programs for psychological stress and well- being: a systematic review and meta-analysis. *JAMA Intern. Med.* 174, 357–368.

Hadgkiss, E. J., Jelinek, G. A., Weiland, T. J., Pereira, N. G., Marck, C. H., and van der Meer, D. M. (2013). Methodology of an international study of people with multiple sclerosis recruited through web 2.0 platforms: demographics, lifestyle, and disease characteristics. *Neurol. Res. Int.* 2013:580596. doi: 10.1155/2013/580596

Hadgkiss, E. J., Jelinek, G. A., Weiland, T. J., Pereira, N. G., Marck, C. H., and van der Meer, D. M. (2015). The association of diet with quality of life, disability, and relapse rate in an international sample of people with multiple sclerosis. *Nutr. Neurosci.* 18, 125–136. doi: 10.1179/1476830514Y.0000000117

Harzing, A. W., and Adler, N. J. (2016). Disseminating knowledge: from potential to reality—new open-access journals collide with convention. *Acad. Manage. Learn. Educ.* 15, 140–156. doi: 10.5465/amle.2013.0373

Hempel, S., Graham, G. D., Fu, N., Estrada, E., Chen, A. Y., Miake-Lye, I., et al. (2017). A systematic review of modifiable risk factors in the progression of multiple sclerosis. *Mult. Scler.* 23, 525–533. doi: 10.1177/1352458517690270

Hildon, Z., Smith, G., Netuveli, G., and Blane, D. (2008). Understanding adversity and resilience at older ages. *Sociol. Health Illn.* 30, 726–740. doi: 10.1111/j.1467-9566.2008.01087.x

Irwin, M. R., and Cole, S. W. (2011). Reciprocal regulation of the neural and innate immune systems. *Nat. Rev. Immunol.* 11, 625–632. doi: 10.1038/nri3042

Jahng, K. H., Martin, L. R., Golin, C. E., and DiMatteo, M. R. (2005). Preferences for medical collaboration: patient–physician congruence and patient outcomes. *Patient Educ. Couns.* 57, 308–314. doi: 10.1016/j.pec.2004.08.006

Jelinek, G. A., De Livera, A. M., Marck, C. H., Brown, C. R., Neate, S. L., Taylor, K. L., et al. (2016). Lifestyle, medication and socio-demographic determinants of mental and physical health-related quality of life in people with multiple sclerosis. *BMC Neurol.* 16:235. doi: 10.1186/s12883-016-0763-4

Jelinek, G. A., Hadgkiss, E. J., Weiland, T. J., Pereira, N. G., Marck, C. H., and van der Meer, D. M. (2013). Association of fish consumption and Omega 3 supplementation with quality of life, disability and disease activity in an international cohort of people with multiple sclerosis. *Int. J. Neurosci.* 123, 792–801. doi: 10.3109/00207454.2013.803104

Jelinek, G. A., and Hassed, C. S. (2009). Managing multiple sclerosis in primary care: are we forgetting something? *Qual. Prim. Care* 17, 55–61.

Juster, R. P., McEwen, B. S., and Lupien, S. J. (2010). Allostatic load biomarkers of chronic stress and impact on health and cognition. *Neurosci. Biobehav. Rev.* 35, 2–16. doi: 10.1016/j.neubiorev.2009.10.002

Kemp, A. H., Arias, J. A., and Fisher, Z. (2017a). "Social ties, health and wellbeing: a literature review and model," in *Neuroscience and Social Science*, eds A. Ibanez, L. Sedeno, and A. M. Garcia (Berlin: Springer), 397–427. doi: 10.1007/978-3-319-68421-5_17

Kemp, A. H., Koenig, J., and Thayer, J. F. (2017b). From psychological moments to mortality: a multidisciplinary synthesis on heart rate variability spanning the continuum of time. *Neurosci. Biobehav. Rev.* 83, 547–567. doi: 10.1016/j.neubiorev.2017.09.006

Kreps, G. L. (2006). Communication and racial inequities in health care. *Am. Behav. Sci.* 49, 760–774. doi: 10.1177/0002764205283800

Kun, Á., Gerákné Krasz, K., and Balogh, P. (2017). Development of the work-related well-being questionnaire based on Seligman's PERMA model. *Periodica Polytech. Soc. Manag. Sci.* 25, 56–63. doi: 10.3311/PPso.9326

Lasgaard, M., Friis, K., and Shevlin, M. (2016). Where are all the lonely people?" A population- based study of high-risk groups across the life span. *Soc. Psychiatry Psychiatr. Epidemiol.* 51, 1373–1384. doi: 10.1007/s00127-016-1279-3

Leong, E. M., Semple, S. J., Angley, M., Siebert, W., Petkov, J., and McKinnon, R. A. (2009). Complementary and alternative medicines and dietary interventions in multiple sclerosis: what is being used in South Australia and why? *Complement. Ther. Med.* 17, 216–223. doi: 10.1016/j.ctim.2009.03.001

Levin, A. B., Hadgkiss, E. J., Weiland, T. J., and Jelinek, G. A. (2014a). Meditation as an adjunct to the management of multiple sclerosis. *Neurol. Res. Int.* 2014:704691. doi: 10.1155/2014/704691

Levin, A. B., Hadgkiss, E. J., Weiland, T. J., Marck, C. H., van der Meer, D. M., Pereira, N. G., et al. (2014b). Can meditation influence quality of life, depression, and disease outcome in multiple sclerosis? Findings from a large international web-based study. *Behav. Neurol.* 2014:916519. doi: 10.1155/2014/916519

Li, M. P., Jelinek, G. A., Weiland, T. J., Mackinlay, C. A., Dye, S., and Gawler, I. (2010). Effect of a residential retreat promoting lifestyle modifications on health-related quality of life in people with multiple sclerosis. *Qual. Prim. Care* 18, 379–389.

Linley, P. A., and Joseph, S. (2004). Positive change following trauma and adversity: a review. *J. Trauma. Stress* 17, 11–21. doi: 10.1023/b:jots.0000014671.27856.7e

Lupien, S. J., McEwen, B. S., Gunnar, M. R., and Heim, C. (2009). Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nat. Rev. Neurosci.* 10, 434–445. doi: 10.1038/nrn2639

Marck, C. H., Hadgkiss, E. J., Weiland, T. J., Van der Meer, D. M., Pereira, N. G., and Jelinek, G. A. (2014). Physical activity and associated levels of disability and quality of life in people with multiple sclerosis: a large international survey. *BMC Neurol.* 14:143. doi: 10.1186/1471-2377-14-143

Martin, L. R., Williams, S. L., Haskard, K. B., and DiMatteo, M. R. (2005). The challenge of patient adherence. *Ther. Clin. Risk Manage.* 1, 189–199.

Maté, G. (2011). *When the Body Says No: The Cost of Hidden Stress*. New York, NY: W. W. Norton and Company.

McGrady, A., Brennan, J., and Lynch, D. (2009). Effects of wellness programs in family medicine. *Appl. Psychophysiol. Biofeedback* 34, 121–126. doi: 10.1007/s10484-009-9084-3

Mead, J., Fisher, Z. Wilkie, L. Gibbs, K., Pridmore, J., Tree, J., et al. (2019). Rethinking wellbeing: Toward a more ethical science of wellbeing that considers current and future generations. *Authorea* doi: 10.22541/au.156649190.08734276

Michie, S., Johnston, M., Francis, J., Hardeman, W., and Eccles, M. (2008). From theory to intervention: mapping theoretically derived behavioural determinants to behaviour change techniques. *Appl. Psychol.* 57, 660–680. doi: 10.1111/j.1464-0597.2008.00341.x

Multiple Sclerosis Research of Australia (2017). Multiple sclerosis research Australia 2017. *Mul. Scler. J.* 23, NP1–NP29. doi: 10.1177/1352458517734699

Multiple Sclerosis Society of Canada (2018). *Research Priorities*. Toronto ON: Multiple Sclerosis Society of Canada.

Pelikan, J. M. (2017). "The application of salutogenesis in healthcare settings," in *The Handbook of Salutogenesis*, eds M. B. Mittelmark, S. Sagy, M. Eriksson, G. F. Bauer, J. M. Pelikan, B. Lindström, et al. (Cham: Springer).

Pemberton, C. (2015). *Resilience: A Practical Guide for Coaches*. Maidenhead: Open University Press.

Rotstein, D. L., Chen, H., Wilton, A. S., Kwong, J. C., Marrie, R. A., Gozdyra, P., et al. (2018). Temporal trends in multiple sclerosis prevalence and incidence in a large population. *Neurology* 90, e1435–e1441. doi: 10.1212/WNL.0000000000005331

Segerstrom, S. C., and Miller, G. E. (2004). Psychological stress and the human immune system: a meta-analytic study of 30 years of inquiry. *Psychol. Bull.* 130, 601–630. doi: 10.1037/0033-2909.130.4.601

Seligman, M. (2011). *Flourish: A New Understanding of Happiness, Well-Being-and How to Achieve Them*. Boston, MA: Nicholas Brealey Pub.

Senders, A., Bourdette, D., Hanes, D., Yadav, V., and Shinto, L. (2014). Perceived stress in multiple sclerosis: the potential role of mindfulness in health and well-being. *J. Evid. Based Complement. Alternat. Med.* 19, 104–111. doi: 10.1177/2156587214523291

Sheeran, P., Maki, A., Montanaro, E., Avishai-Yitshak, A., Bryan, A., Klein, W. M., et al. (2016). The impact of changing attitudes, norms, and self-efficacy on health-related intentions and behavior: a meta-analysis. *Health Psychol.* 35, 1178–1188. doi: 10.1037/hea0000387

Simpson, R., Booth, J., Lawrence, M., Byrne, S., Mair, F., and Mercer, S. (2014). Mindfulness based interventions in multiple sclerosis-a systematic review. *BMC Neurol.* 14:15. doi: 10.1186/1471-2377-14-15

Slavich, G. M., and Irwin, M. R. (2014). From stress to inflammation and major depressive disorder: a social signal transduction theory of depression. *Psychol. Bull.* 140, 774–815. doi: 10.1037/a0035302

Stankiewicz, A. M., Swiergiel, A. H., and Lisowski, P. (2013). Epigenetics of stress adaptations in the brain. *Brain Res. Bull.* 98, 76–92. doi: 10.1016/j.brainresbull.2013.07.003

Steptoe, A., Hamer, M., and Chida, Y. (2007). The effects of acute psychological stress on circulating inflammatory factors in humans: a review and meta-analysis. *Brain Behav. Immun.* 21, 901–912. doi: 10.1016/j.bbi.2007.03.011

Stuifbergen, A. K., and Becker, H. (2001). Health promotion practices in women with multiple sclerosis: increasing quality and years of healthy life. *Phys. Med. Rehabil. Clin.* 12, 9–22. doi: 10.1016/s1047-9651(18)30081-0

Tausk, F., Elenkov, I., and Moynihan, J. (2008). Psychoneu-roimmunology. *Dermatol. Ther.* 21, 22–31.

Taylor, J. S. (2004). Salutogenesis as a framework for child protection: literature review. *J. Adv. Nurs.* 45, 633–643. doi: 0.1046/j.1365-2648.2003.02954.x

Taylor, K. L., Hadgkiss, E. J., Jelinek, G. A., Weiland, T. J., Pereira, N. G., Marck, C. H., et al. (2014). Lifestyle factors, medications and demographics associated with depression risk in an international sample of people with multiple sclerosis. *BMC Psychol.* 14:327. doi: 10.1186/s12888-014-0327-3

Tedeschi, R. G., and Calhoun, L. G. (2004). Posttraumatic growth: conceptual foundations and empirical evidence. *Psychol. Inq.* 15, 1–18. doi: 10.1207/s15327965pli1501_01

Tedeschi, R. G., and Calhoun, L. G. (2006). Time of change? The spiritual challenges of bereavement and loss. *OMEGA* 53, 105–116. doi: 10.2190/7mbu-ufv9-6tj6-dp83

Tedeschi, R. G., Park, C. L., and Calhoun, L. G. (eds) (1998). *Posttraumatic Growth: Positive Changes in the Aftermath of Crisis*. Hillsdale, NJ: Lawrence Erlbaum Associates, Inc.

Teutsch, C. (2003). Patient-doctor Communication. *Med. Clin. North Am.* 87, 1115–1145.

Theoharides, T. C., and Cochrane, D. E. (2004). Critical role of mast cells in inflammatory diseases and the effect of acute stress. *J. Neuroimmunol.* 146, 1–12. doi: 10.1016/j.jneuroim.2003.10.041

Wallerstein, I. (2007). "The sociologist and the public sphere," in *Public Sociology Fifteen Eminent Sociologists Debate Politics and the Profession in the Twenty-First Century*, eds N. Gerstel, R. Stokes, J. Misra, D. Clawson, and R. Zussman (Berkeley, CA: University of California Press), 169–175.

Wallerstein, N. (1992). Powerlessness, empowerment, and health: implications for health promotion programs. *Am. J. Health Promot.* 6, 197–205. doi: 10.4278/0890-1171-6.3.197

Watt, D., Verma, S., and Flynn, L. (1998). Wellness programs: a review of the evidence. *CMAJ* 158, 224–230.

Weiland, T. J., Hadgkiss, E. J., Jelinek, G. A., Pereira, N. G., Marck, C. H., and van der Meer, D. M. (2014). The association of alcohol consumption and smoking with quality of life, disability and disease activity in an international sample of people with multiple sclerosis. *J. Neurol. Sci.* 336, 211–219. doi: 10.1016/j.jns.2013.10.046

Zawia, N. H., Lahiri, D. K., and Cardozo-Pelaez, F. (2009). Epigenetics, oxidative stress, and Alzheimer disease. *Free Radic. Biol. Med.* 46, 1241–1249. doi: 10.1016/j.freeradbiomed.2009.02.006

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A RE-AIM Analysis of an Intergenerational Dementia Education Program

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Objectives: Children often have a lack of dementia understanding and poor attitudes toward people with dementia. Intergenerational programs are increasingly common, but the effects on knowledge and attitudes related to dementia are mixed, especially in the long-term (6 months). Using a RE-AIM framework, we quantitatively evaluated the effects of an educational dementia program (with and without an intergenerational program) on dementia attitudes in the short and long-term, and qualitatively, which elements of the program facilitated this change.

Methods: Eighty-one children (9.63 ± 0.52 years, 35 males) from three classes participated in an 8-week dementia education program and 52 also interacted with older adults through an intergenerational experience. Program reach was measured as the percentage of children who participated in the study. The Kids Insight into Dementia Survey (KIDS) was implemented to measure dementia knowledge and attitudes: efficacy and maintenance. Qualitative interviews with all participant groups informed both adoption and implementation. Cost-benefit analysis was used as a secondary outcome measure for efficacy.

Results: The program demonstrated strong levels of impact reaching 93% of school children across the three included classes. Efficacy was demonstrated by a positive change in children's dementia knowledge and attitudes immediately post program, which remained increased (as compared to baseline) 6- months post intervention; there were no differences between groups (those who interacted with older adults and those who did not). Interviews identified positive changes in children's empathy and improved community awareness. Barriers to adoption included the project scope, time constraints incurred by school terms and the management of children-to-adult ratios.

Conclusions: These findings provide the first evidence that school-based dementia education improves knowledge of and attitudes toward people with dementia long-term. We demonstrated programs such as this can be successful in both primary school and wider community settings, with support from school and community partners key to the success.

Keywords: intergenerational program, school-based, dementia-friendly communities, program evaluation, RE-AIM

INTRODUCTION

People living with dementia often experience loneliness and stigma, potentially leading to a withdrawal from social activities and delays in seeking a formal diagnosis (1). A lack of community-level dementia knowledge can contribute to misinformation about dementia and its risk factors, as well as propagate unhelpful attitudes and stigmatized views. Evidence suggests that the general public have varying levels of dementia knowledge (2, 3). This knowledge may be influenced by gender, education, or current caring responsibilities of an older adult or a person living with dementia (4, 5). With an increase in the number of people living with dementia worldwide, it is essential that the community have adequate dementia knowledge.

Community education programs have been developed and implemented to improve dementia knowledge and attitudes. Target populations for these programs have typically been general practitioners (6), public health and service workers (7), aged care staff and family members of people with dementia (8). One segment of the population that may be particularly receptive to information about dementia, yet are understudied, are children; who are at an age where their health beliefs and attitudes are malleable (9).

According to one government survey, as many as one-third of British children aged 8–17 years knew someone living with dementia, but two-thirds indicated a lack of dementia knowledge prevented them from assisting these individuals (10). Similarly, in a recent qualitative study, children's misconceptions about dementia were evident in the words they used to describe someone living with dementia, such as "frustrating" and "crazy" (11). To address this lack of knowledge, school-based dementia education programs are now being introduced with success (12, 13). These programs have successfully increased children's dementia knowledge and attitudes at their conclusion compared to the start. Whether this knowledge and attitudinal shift is retained in long-term (e.g., over months), remains unknown.

A second evidence-based method used to increase children's dementia knowledge and attitudes is engaging children and older adults together in structured intergenerational programs (14). The programs are typically mutually beneficial for all participants. Increased activity engagement and reduced social isolation, depression and anxiety has been reported for older participants (15, 16). While the younger participants report more positive attitudes toward people living with dementia, improved social skills, and increased self-confidence (17, 18). Arguably, combining both school-based dementia education alongside an intergenerational program may augment any independent increases in children's dementia knowledge and attitudes. However, to our knowledge, no study has investigated if the addition of an intergenerational component delivered alongside dementia education leads to cumulative benefits on dementia knowledge and attitudes long-term, in school-aged children.

The purpose of this study was to evaluate an 8-week school-based dementia education program with 6-weeks of embedded intergenerational interaction using the RE-AIM framework (19). The program was co-designed and co-implemented by researchers at the University of South Australia and key partners including a local council, a publicly funded primary school and an aged care service provider each based in Adelaide, South Australia. Despite the increasing popularity of intergenerational programs in recent years, there remains a limited understanding of the program specific components that lead to their success.

RE-AIM is an evaluation framework, often used in health promotion, and broad public health initiatives (19). Briefly RE-AIM incorporates five dimensions (Reach, Efficacy, Adoption, Implementation and Maintenance) that assess outcomes in relation to real-world translation and scaling of interventions (19, 20). Reach, is the proportion and characteristics of the target sample who received or were aware of the intervention. Efficacy, is any change (both positive and negative) in the main outcome measure or any secondary outcomes realized for the target population. Adoption, is the number and characteristics of the settings who adopted the planned intervention, with details on any barriers to participation also captured at the organizational level. Implementation, is the extent to which the intervention components have been implemented as originally planned, by adequately trained staff. Finally, Maintenance, assesses the ability to maintain and sustain the program over time (both individually and at the organizational/institution level).

Taken together, the predominant aim of this study was to evaluate the overall real-world sustainability and success of combining school-based dementia education with intergenerational excursions to guide future program development.

METHODS

Participants

Three year 4/5 classes at a publicly funded co-educational primary school participated in an 8-week, school-based dementia educational program. Two classes were also invited to attend six intergenerational excursions held at a social-day program for older adults living in independently in the community with cognitive impairment (commonly dementia).

This study was approved by the University of South Australia Human Research Ethics committee (protocol no. 20070). All participants (children, older adults and staff) provided informed written consent. Where participants were unable to consent for themselves (e.g., children) they provided assent and consent was provided by a parent or legal guardian.

Design

We employed a non-randomized, mixed methods, quasi-experimental evaluation approach whereby all students participated in dementia education lessons and two classes also attended the excursions. The allocation of classes to the excursion was non-randomized based on timetabling and excursion availability.

Dementia Education Program

The dementia education program was modified and extended from the Kids4Dementia (K4D) content previously developed by teachers, children, people living with dementia, carers and academics (13). To complement K4D, other age-appropriate activities were developed by an education student designed around each main lesson theme (see, **Table 1**).

TABLE 1 | Outline of the weekly topics discussed as part of the school-based dementia education program.

Topic	Key resources needed
Week 1: what is dementia?	• Assessment: KIDS Insight into Dementia Survey (KIDS) • Video: kids 4 dementia – module 1 (What is dementia?) • Activity booklet: introduction and title page
Week 2: communication and social interaction	• Video: Kids 4 dementia – module 6 (How does it feel to have dementia?) • Activity booklet: my letter plan
Week 3: environment	• Video: Kids 4 dementia – module 3 (What happens in nursing homes?) • Activity booklet: activity ideas mind map and activity poster
Week 4: memories	• Kids 4 dementia – module 4 (What causes dementia?) • Activity booklet: 3, 2, 1 response (3 dementia facts, 2 insights, 1 question)
Week 5: cognitive reserve	• Video: Kids 4 dementia – module 5 (How can we keep our brains healthy?) • Brain models to show children the different parts of the brain dementia can affect • Activity booklet: prevent dementia by poster proforma
Week 6: sensory changes	• Video: Alzheimer's society (Small changes make a dementia friendly world) and sony aibo technology example • Activity booklet: design technology to support people with dementia
Week 7: role of families and care staff	• Q + A session with a geriatrician • Brainstorm: how to make our environment dementia friendly?
Week 8: prevention (diet and lifestyle)	• Assessment: KIDS • Video: Kids 4 dementia – module 7 (How does it feel for the family?)

Intergenerational Experience

The intergenerational experience was based around "the corner store" theme. This provided an opportunity for participants to discuss their experiences of shopping, and for the older adults, to share with the students how these shopping experiences had changed over their lifetime. Activities were led by Enabling Confidence at Home (ECH) activity and lifestyle staff, and commissioned community artists. Examples included flower pot planting, 8-ball, dyeing fabric (cyanotype) to make re-usable shopping bags, and group singing. Students were split into smaller groups to reduce noise throughout the center. Each student group were assigned a different activity each week, however, there was no structured grouping of children and adults.

Program Rollout

Dementia education was led by University trained lecturers who had research expertise in dementia. One lesson was delivered each week (45 min) for 8 weeks in term 1 2018 (February – April).

Excursions began for two classes ($n = 52$ students) from week 3 of the program. Each excursion was 45 min in duration. The class that did not attend the intergenerational excursions (29 students) participated in similar art activities at the school, facilitated by ECH staff and community artists, but without the older adults.

RE-AIM Measures

Table 2 presents the main outcomes for each RE-AIM dimension and participant group.

Reach

Reach was assessed as the number of children who participated in the classroom lessons. Demographic characteristics (including previous dementia knowledge/familiarity) of the children were self-reported in class before and immediately after the program. Due to fluctuating attendance at the social day program it was not possible to assess the attendance of all older adults who attended the sessions. However, a core group were observed to participate during all sessions.

Efficacy

To assess efficacy or change in children's dementia knowledge and attitudes the Kids Insight into Dementia Survey (KIDS) was completed individually under test conditions in a classroom environment at baseline, program completion and 6-month follow-up. KIDS provides good validity and internal consistency, strong concurrent validity and strong correlations with an adult measure of dementia attitudes in children aged 9–13 years (grades 4–7) (21). The 14 statements included in the KIDS are divided into three factors, personhood, stigma and knowledge. Six of the statements are negatively worded and were reverse-scored prior to analysis. Responses were summed to produce the total KIDS score, with higher scores indicating greater dementia knowledge and more positive attitudes (score range 14–70). Individual factor scores were also calculated for

TABLE 2 | RE-AIM components and associated outcome measures for the program.

RE-AIM component	Outcome measure
Reach	Individual Children: demographic questionnaire and baseline dementia knowledge assessment conducted in class during week 1 of program.
Efficacy	Individual Children: kids insight into dementia survey (KIDS). Overall score and factor scores for personhood, stigma and knowledge. Assessed immediately pre/post educational intervention. In addition, a subgroup of children attended semi-structured interviews with their parent/caregiver to discuss the broader impacts of the program. Parents: Semi-structured interviews with their child to discuss the family impact of the program, including any positive/negative changes in behavior they had identified in their child as a result of the program. Older adults: semi-structured interviews with older adults and their carers (where possible) to discuss their experiences of the program. Organizational Cost and benefit analysis conducted on the whole of program costs at the conclusion of program
Adoption	Organizational School: Number and percentage of classes offered the intervention who agreed to participate. Excursion location: Agreement of organizations approached to facilitate excursion.
Implementation	Organizational Assessed as the number of sessions (both education and excursion) that were delivered as intended. Measured by reports from key project staff.
Maintenance	Individual Children: Score on KIDS, 6-month post intervention (Term 4 2018). Organizational School & Aged care organization: intention and ability to continue with the program (either in full or component parts) after the completion of the intervention.

**Individual and organizational refer to RE-AIM components assessed either individually or at the setting/organizational level.*

TABLE 3 | Demographic characteristics of students participating in the dementia education program.

	Excursion group ($n = 37$)	No excursion group ($n = 22$)	Overall ($n = 59$)
Age (years)*	9.43 ± 0.56	9.95 ± 0.21	9.63 ± 0.52
Gender: male^	65% (24)	50% (11)	59% (35)
Year 5 %^	54% (20)	100.0% (22)	71% (42)
Lesson attendance %	97	94	96
Had dementia knowledge at baseline (amalgamated)^	14% (5)	23% (5)	17% (10)
Heard about dementia^	57% (21)	68% (15)	61% (36)
Seen someone with dementia^	22% (8)	41% (9)	29% (17)
Watched movie/read book about dementia^	27% (10)	36% (8)	30% (18)
Relative with dementia^	11% (4)	9% (2)	10% (6)
Family friend with dementia^	5% (2)	14% (3)	9% (5)
KIDS Baseline Score (Time 1) (range 14–70)*	50.0 (8.7)	52.55 (7.9)	51.0 (8.4)
KIDS post score (Time 2) (range 14–70)*	58.2 (7.1)	57.55 (6.5)	57.9 (6.8)
KIDS longitudinal score (Time 3) (range 14–70)*	59.1 (6.6)	59.3 (7.6)	59.2 (6.9)

**m ± sd, ^% (n).*

personhood, stigma, and knowledge. There was no true control group who did not receive dementia education. The school involved requested all three of their year 5 classes receive the educational content.

Following the removal of incomplete data and outliers, a one-way ANOVA was conducted with KIDS baseline total score as the dependent variable and knowledge or no knowledge of dementia as the independent variable (see **Table 3**). Subsequently, dementia knowledge or familiarity at baseline was included as a covariate in all models.

To investigate if the dementia education program was associated with a change in dementia knowledge and attitudes, the KIDS total and factor scores (for personhood, stigma and knowledge) were analyzed using separate mixed analyses of covariance (ANCOVA). The within-subjects factor was time (three levels: baseline, post-program and 6-month follow-up) and the between subjects factor was condition (two levels: excursion or no excursion). All significant main effects and interactions were explored with *post-hoc* pairwise comparisons adjusted for multiple comparisons with Bonferroni corrections. Normal distribution and homogeneity of variance of the data were assessed using the Kolmogorov-Smirnov test and Levene's statistic, respectively. Effect sizes were estimated with partial eta-squared (partial η^2). In ANCOVAs where assumptions of sphericity were violated, the critical value of F was adjusted using the Greenhouse-Geisser epsilon value. Unless otherwise stated all analyses were performed in SPSS v25 (IBM, Microsoft Corporation). Significance was accepted at $p < 0.05$ (prior to any correction).

In addition to the primary outcome of the KIDS score, secondary outcomes for parents, older adults and carers were assessed through semi-structured qualitative interviews. Parents/guardians and children were interviewed at a neutral location (UniSA, City East Campus) during the school holidays immediately following program completion. Interviews typically lasted 20–30 min and covered topics such as expectations, impact, positives and negatives, potential improvements and examples of program translation to the home setting.

Older adults and their carers' were also interviewed at program completion either within their own home, over the phone or at ECH. Interviews included open-ended and probing questions to gain insights into reasons behind program participation, participant experiences (both positive and negative aspects were probed), suggestions for program improvement and noticeable changes in the older adults observed by carers or family members.

In addition to the interviews above, a cost benefit analysis of the program was also undertaken to provide a transparent method for assessing the "value for money" of the program. Cost data included: information on revenues received to run the program from Office of the Aging and additional in-kind resources reported from interviews with staff. Staff time was costed using data differentiated by Occupation from the Australian Bureau of Statistics Issue 6306.0 – Employee Earnings and Hours, Australia, May 2016. Prices were updated to 2018 prices using the Wage Price Index. Costs associated purely with the evaluation of the program were not included. The costs per unit of benefit were calculated by dividing the total cost of the program by the number of participants in the relevant groups.

Adoption

Interviews with key staff from all contributing organizations were held at the completion of the intervention. Responses to questions pertaining to suggested improvements, successful components and barriers were used to assess adoption through thematic analysis.

Implementation

Implementation was assessed by the project manager, who was onsite for all lessons and excursions. Lesson plans provided a reference for the lesson content that was delivered, and a checklist was developed for excursion activity stations. Key staff were also interviewed following the intervention to discuss issues with implementation at their respective organizations (as detailed in Adoption above).

Maintenance

Individual level maintenance was determined as the 6-month follow up post scores on the KIDS survey for children. At the organizational level, semi-structured interviews with key staff identified the level of program related maintenance occurring at each organization as a result of the intervention.

RESULTS

Reach

The three school classes had a combined enrolment of 87 students. Of these 81 parents provided consent for their child's data to be included in this evaluation (93% total reach). For equity purposes the remaining six children continued to participate in the program but their data were not used in the evaluation. Demographic characteristics for the children are presented in **Table 3**.

Efficacy

Children

Twenty children reported having knowledge of dementia at baseline. Children who had knowledge or dementia familiarity at baseline (**Table 3**), performed better on the KIDS ($F_{[1,\ 76]} = 8.38$, $p = 0.005$).

KIDS scores increased from baseline to post-program and was sustained at the 6-month follow-up (main effect of time: $F_{[1.8,\ 100.9]} = 46.73$, $p < 0.001$, partial $\eta^2 = 0.46$). *Post-hoc* pairwise comparisons revealed improvement in dementia knowledge and attitudes from baseline to post-program ($p = 0.001$) and baseline to six-month follow-up ($p < 0.001$) (**Figure 1**) but no difference from post-program to 6-month follow-up ($p = 0.21$). There was also a main effect of dementia knowledge at baseline ($\mathrm{F}_{[1,\ 56]} = 5.79$, $p = 0.020$, partial $\eta^2 = 0.094$) and a time x dementia knowledge interaction ($\mathrm{F}_{[1.8,\ 100.9]} = 3.24$, $p = 0.048$, partial $\eta^2 = 0.06$). There was no augmentation effect of condition (excursion or no excursion).

For each KIDS factor, there was a main effect of time: personhood ($\mathrm{F}_{[2,\ 112]} = 28.32$, $p < 0.001$, partial $\eta^2 = 0.34$), stigma ($\mathrm{F}_{[1.7,\ 95.86]} = 29.07$, $p < 0.001$, partial $\eta^2 = 0.34$) and knowledge ($\mathrm{F}_{[2,\ 108]} = 22.08$, $p < 0.001$, partial $\eta^2 = 0.29$). For both stigma and knowledge, *post-hoc* pairwise comparisons revealed this was due to significant improvement from pre to post-program (both p's < 0.001), and pre to 6-month follow-up (both p's < 0.001), but not from post to six-months follow-up (both p's $= 1.00$). For personhood, scores increased from pre to post ($p < 0.001$) and long-term follow-up ($p < 0.001$) and also from post to 6-month follow-up ($p = 0.007$). There were no other main effects or interactions for the individual factors (**Figure 1**).

Parents

Fourteen parent and child dyads were interviewed directly after program completion to understand any wider secondary effects of the program on either the family unit, or directly on the child that were not assessed by the KIDS survey and to provide further information/benefits not identified in the KIDS survey. Following transcription and thematic analysis (22), Three of four identified themes pertinent to efficacy were positive changes and effects of completing the program, negative experiences These changes typically included children reporting being more patient with older relatives, and ability to explain the new knowledge gained to friends or family members, and greater empathy and patience in everyday situations. In some cases, children also identified their own improved behaviors (including increased patience and greater understanding while in public and with older family members) as a result of undertaking the program and in particular most children reported on the positive benefits of undertaking the excursions.

> *"just being more careful around other people because they might have dementia but you can't tell by the way they look, or by the way they act."* Child
> *"I think that empathy even just hearing him say, just now, you know not taking people at face value and knowing that there might be underlying stuff."* Parent.

Older Adults and Carers

Twelve older adults and four carers were also interviewed to discuss their experiences with the program. Overall, the intergenerational program was reported as positive, with many adults commenting on experiencing positive emotions, as a direct result of interacting with the children, and positive self-changes.

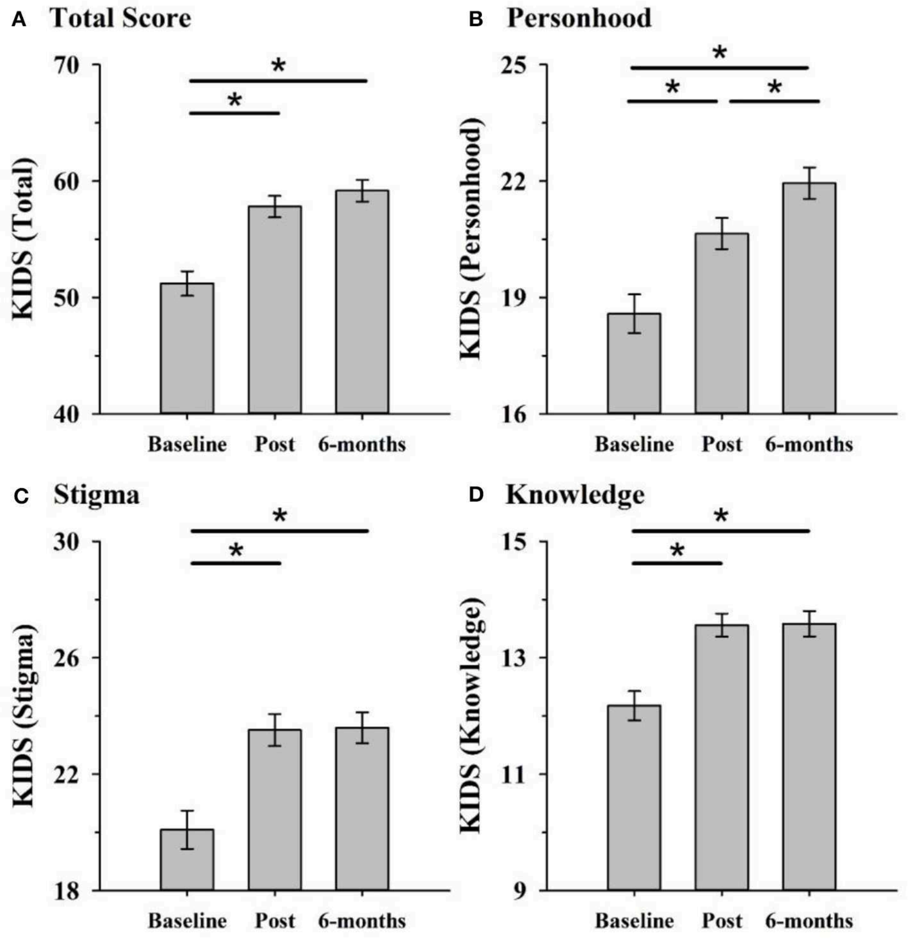

FIGURE 1 | KIDS scores improved in both excursion and non-excursion classes after the program compared to before. Improvements were maintained at 6-months follow-up and occurred across the total score **(A)** and each of the three factors personhood **(B)**, stigma **(C)**, and knowledge **(D)**. $^*p < 0.05$ (after Bonferroni correcting for multiple comparisons).

> *"I really enjoy the children coming in. It's because I've had four of my own… and they say, you're a natural with kids"* Older Adult.
> *"At Easter time, this beautiful boy made him [older adult] an Easter card. Oh, he was just about in tears when he came home"* Carer.

Whilst, there were few negative experiences reported, the large majority older adults reported high levels of noise during the excursions.

> *"The only thing was the noise. That was about it. Otherwise no, there was no negative feedback at all"* Carer.

Some older adults and carers also reported an inability to remember activities that occurred during the program (this was particularly evident in the follow up period). This is likely to be due to a combination of interpersonal complications that occurred during the program, and the progressive nature of participants' condition, rather than a negative effect of the program.

> *"You know sometimes I think I think I've been there, done that and it's out of your mind then, you know… But I can't recall that"* Older Adult.

Cost-Benefit Analysis

The costs associated with delivering the dementia education lessons and intergenerational excursions are estimated in Australian Dollars, AUD. These include both direct and in-direct costs and were estimated at $42,001 for the entire program. The direct costs incurred during the program included, set up and management costs ($2,919), school programming costs ($5, 000) and intergenerational program costs ($12,000). Direct program costs include estimations of implementing the art program (excursions), creating lesson plans and hire of charter buses. Indirect costs related to staff time used for program preparation ($17,064), and implementation of the program ($5,018). Costs for simply running the school-based dementia education program, without the intergenerational component were estimated at $7,919.

The cost-benefit analysis was conducted separately for the children who had data available post program ($n = 70$), and those who had data available at 6-month follow up ($n = 59$). Together per unit of student benefit was estimated at $600 per student who demonstrated an increase in dementia knowledge and attitudes at post program when compared to baseline (direct + indirect costs; **Table 4**). It is important to recognize that this estimate includes a significant proportion of in-kind support from staff in preparation and implementation of the program. This in-kind support equates to 52% of the total cost estimate with most of the in-kind support relating to preparation of the program. It is therefore likely that our initial cost benefit estimate of $600 per student who demonstrated an increase in dementia knowledge and attitudes represents an upper bound. This cost would also likely reduce, if more students had attended school on the day of the 6-month follow up testing. Unfortunately, due to public holidays and end of term, a number of students were absent on the day of 6-month testing and further testing days could not be rescheduled.

The cost-benefit analysis was also calculated examining only the school-related education component (excluding the excursions; **Table 4**). Costs per unit of benefit were estimated at $113 per student who demonstrated an increase in dementia knowledge and attitudes.

Adoption

One school was approached to pilot this intervention and accepted on behalf of their year 5/6 cohort (three classes). The aged care partnership was more problematic, with two community based not for profit organizations offered the same opportunity. Both organizations provided initial quotes for their services (one for education component and one for art program) however due to the project requirements these partners withdrew their interest. A third partner was approached to assist with facilitating the excursions who accepted and was able to provide significant in kind staffing assistance to reduce the costs of excursions.

Interviews with key staff from all organizations were overwhelmingly positive. Staff recognized that the successful partnership between all four organizations (a council, school, aged care facility and university) was key to the success of the project as each partner provided their own lens in design, implementation and program support. Barriers that were raised throughout the interview series included noise at the center, the large number of children and subsequent high ratios of children to older adults (buddying or 2:1 preferable), and the distance to transport students to attend excursions.

Implementation

Education sessions were provided separately for all three classes by trained university researchers. Educational content was mapped to curriculum priority areas and shared with teachers prior to lessons occurring (see **Table 1**). Sessions were supported as a timetabled fixture for the three participating classes with support from the school Principal. As such lessons were delivered as planned, despite any regular teacher absences (i.e., substitute teachers also supported the content delivery when required). Student workbooks used throughout lessons were also scanned for completeness to ensure educational content and activities were delivered as intended.

Similarly, excursions were also supported as a timetabled activity at the aged-care provider. With ECH agreeing to allow full access to their facility for the duration of the program, as well as sufficient time and staffing before and after sessions to allow for set up, and pack down of activity stations and art/music projects.

Maintenance

Results from the follow-up KIDS survey indicated there were no decline in KIDS scores from post-program to 6-month follow-up ($p = 0.21$; **Figure 1**). This indicated that children's knowledge of dementia remained improved from the pre-program baseline, demonstrating a maintenance effect of the education. Organizational maintenance was assessed through key staff interviews at the conclusion of the program. Teaching staff indicated that they planned to continue with the theme of dementia education in later curriculum areas (in particular in relation to social studies activities). Staff at the aged-care provider were positive about the experience and would welcome the opportunity to be involved in similar projects in the future, however due to cost restrictions had no immediate plans to continue the intervention.

TABLE 4 | Benefits and total costs per unit increase in dementia knowledge and attitudes in the children as a result of the program.

Benefit	Number of participants who achieved the benefit	Direct costs for school program per unit of benefit	Direct costs (school program + excursions) per unit of benefit	Total cost per unit of benefit (direct + in kind)
Students who participated across the three classes	88	$90	$226	$477 per student participating
Older people who participated	25	–	$796	$1,680 per older person participating
Students who demonstrated an improvement in dementia knowledge during the program	70	$113	$284	$600 per student with improved dementia knowledge
Students who demonstrated retention of improved knowledge and attitudes at long-term follow up	59	$134	$337	$711 per student with improved dementia knowledge

DISCUSSION

Overall this RE-AIM evaluation has provided strong evidence that dementia education improved children's knowledge and attitudes toward dementia, for at least 6 months. The combination of strong Reach, Adoption and Implementation resulted in significant positive changes in outcomes both immediately post-program, and in the 6-month follow-up. Interestingly, there were no between group differences in dementia knowledge or attitudes in the children who did or did not interact with older adults through the intergenerational experience.

Critical to the success of this program was the combined efforts and shared vision of all partner organizations who accepted invitations to participate. The ability to co-design both the lessons (with class teachers) and activity stations (with aged care staff) was one of the driving factors behind the successful implementation of the project. The co-location of settings, both in the school and in the aged-care facility also helped to ensure strong engagement from both the children and older adults, as they were familiar with the environment and viewed the intergenerational engagement as novel and exciting.

These outcomes align strongly with the aims of the World Health Assembly's Global Action Plan on the public response to dementia 2017–2025 (23). In particular, increasing public dementia awareness, and establishing a dementia friendly society through public awareness campaigns have been identified as important future actions. Our findings here support the embedding of dementia education into the school curriculum as one strategy that facilitates long-term improved knowledge and reduces stigmatization of people living with dementia in a segment of the population who will be future leaders, business owners and health care workers.

The strong maintenance effect at the individual level, as seen in this program is another key strength. It is possible that the detailed program of education, where the children received 6 h of education across 8 weeks led to this effect (45 min × 8 lessons). Across the 8 weeks, children were exposed to a range of topics including communication, environment, memories, cognitive reserve, sensory changes and prevention (**Table 1**). In contrast, dementia education/training in healthcare settings is not mandatory or consistently delivered (24). A recent systematic review identified only 14 studies investigating dementia education for health professionals within general hospital settings. Each of the included studies varied in terms of the program development and delivery, and none included a long-term follow-up (24). Programs varied in length from 2 h of education (25) to 12 days (26). Likewise, dementia education is also delivered inconsistently for pre-registration health care trainees (27). In their review (27), concluded dementia education programs were not consistently undertaken for health care trainees and most were conducted with undergraduate nursing students, whereas only three programs were conducted with medical trainees. Importantly, the most effective programs did not rely on theoretical input alone, but included both theoretical learning, and practice-based experience, by encouraging interactions between students and people living with dementia. The programs employing this combined approach resulted in increased student comfort to interact with people living with dementia, and improvements in confidence and communication at post program compared to pre. Taken together, with our qualitative findings, this body of evidence suggests that whilst improvements in knowledge and attitudes toward dementia can occur with education alone, practical interactions with people living with dementia are critical to increase confidence and enhance communication skills.

It was interesting to note, intergenerational experiences alongside the dementia education lessons did not have cumulative benefits for children's knowledge and attitudes. This suggests that dementia education alone is enough to change children's knowledge and attitudes in the following 6-months. Qualitative interviews with parents and children provided further important insights into the role of the intergenerational experience that were not captured with the KIDS. For example, interviewed parents reported additional benefits directly attributed to the intergenerational excursions such as: improvements in empathy, and reductions in children's negative judgement of older people and people living with dementia, within the community. Assessment of these additional benefits were not specifically targeted in the KIDS. One key difficultly commonly reported in intergenerational literature is how best to operationalise the benefits attributed to intergenerational interactions (12, 28).

The cost burden of these types of studies was the main barrier for future implementation raised by the non-adopters of our program. While our calculations show a $600 AUD cost per student who demonstrated an increase in dementia knowledge/attitudes, there are alternative approaches to assist in reaching an economy of scale. For instance, program preparation has now occurred, with educational content created and mapped to the curriculum. Variable costs including student transport could be reduced or eliminated if school and providers were in close proximity to each other. It is important to note that some fixed costs will remain to ensure participant safety, such as staff to student/older adult ratios.

The costs incurred per child appear to be within the range of similar programs run in pre-school or primary schools in Australia. Total costs for the Cool Little Kids intervention (designed to prevent anxiety and depression in preschool age children and incorporating six 90-min face to face group sessions with a psychologist) were similar at $549 per child (29). The intervention led to a reduction in the number of children diagnosed with anxiety (44.2 vs. 50.2%). Total costs for a school-based healthy eating and physical activity education program in high school students were $1,388 per student (30). Benefits included an increase of 5.2% of students eating more than 2 serves of fruit per day, and a 2.5% increase in students eating more than 4 serves of vegetables per day.

By comparison, the costs appear higher than a volunteer-driven multicomponent intervention for people with dementia and their caregivers (£75 per dyad) (31). However, there is evidence that the costs of programs for people with dementia can reduce overtime from the start-up phase to the continuing phase of the program (likely due to economies of scale and increased efficiency once the program is up and running). For example, the costs of care-coordination programs in people with dementia decreased from between $501–$581 during the start-up phase for the program, to $142–$241 per participant per month once the programs were up and running in a stable phase (all in US dollars) (32). Therefore, similar economies of scale and increased efficiency may occur if the dementia-education program were run again in multiple regions.

Key strengths of our program included its co-design with council, aged care and primary school teachers, co-implementation and evaluation based on the RE-AIM framework. A potential limitation not considered or controlled for in the current study, was how the classroom teachers extended and applied extra dementia education across other aspects of the curriculum, outside of the dementia lessons each week. Indeed, it is possible that the class not attending the excursions were exposed to more dementia education delivered by their classroom teacher, outside of the weekly lessons so the students did not feel disadvantaged by missing out on excursions each week. This may potentially account for the lack of differences we observed between the excursion and non-excursion classes. In future, controlling for, or keeping a record of how much time teachers spent discussing dementia, outside of the program should be considered. Future studies could also consider implementing the program across multiple schools instead of having the excursion and non-excursion groups within the same school.

Implications for Future Research

Whilst we show here that dementia education is sufficient to improve children's knowledge and attitudes 6-months after the completion of the program. It is possible that the specific benefits of the intergenerational excursions were not fully captured in our chosen primary outcome assessment. Building on the novel findings, future studies should consider further refining the intergenerational formats based on identified successful elements of other intergenerational dementia programs (28, 33–35). Taking the findings of our study with the existing extant literature (36, 37), four key successful elements could be considered for future intergenerational programs including (1) buddy systems to foster relationship building; (2) embedding dementia education within intergenerational experiences; (3) considerations around activity set-up (based on participant abilities and preferences); and (4) analysis of student reflective journals to gain a greater insight into the holistic program benefits. It is noted that the sample size of the study is relatively small, and the program conducted only within one primary school and age care facility. An obvious future avenue for research would be to investigate how best to upscale school-based dementia education more broadly including modifying the program for different age-groups. This was beyond the scope of the current study.

Using a RE-AIM evaluation approach, our findings suggest that 8-weeks of school-based dementia education can be successfully presented and implemented in a community setting. Such a program can significantly improve children's knowledge and attitudes toward dementia for at least 6 months. Importantly, improvements were seen for the total KIDS score as well as each of the individual factor scores of personhood, stigma and knowledge and no differences in knowledge or attitudes toward dementia occurred between the groups of students who interacted with older adults and those who did not. Given the absolute increase in the number of people living with dementia worldwide, programs of this nature will be important to improve dementia knowledge and reduce dementia-related misinformation and stigmatization of people living with dementia.

DATA AVAILABILITY STATEMENT

De-identified datasets generated for this study are available on reasonable request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by University of South Australia Human Research Ethics Committee. Written informed consent to participate in the study was provided by all participants. Where participants could not consent for themselves (e.g., children) written assent was obtained from the children and consent to participate in the study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

AS planned the study, supervised the data analysis, and drafted the manuscript. GK, SL, and MH undertook data collection, cleaned the data, performed all statistical analyses, and contributed to revising the paper. JB helped plan the study, informed the educational program, and revised the manuscript. RM and JR supervised the economic analysis and revised the manuscript. TL and HK helped plan the study, contributed to educational program delivery, and revised the manuscript. All authors contributed to the article and approved the submitted version.

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REFERENCES

1. Swaffer K. Dementia: stigma, language, and dementia-friendly. *Dementia.* (2014) 13:709–16. doi: 10.1177/1471301214548143
2. Low LF, Anstey KJ. Dementia literacy: recognition and beliefs on dementia of the Australian public. *Alzheimers Dement.* (2009) 5:43–9. doi: 10.1016/j.jalz.2008.03.011
3. Cahill S, Pierce M, Werner P, Darley A, Bobersky A. A systematic review of the public's knowledge and understanding of Alzheimer's disease and dementia. *Alzheimer Dis Assoc Disord.* (2015) 29:255–75. doi: 10.1097/WAD.0000000000000102
4. Werner P, Goldberg S, Mandel S, Korczyn AD. Gender differences in lay persons' beliefs and knowledge about Alzheimer's disease (AD): a national representative study of Israeli adults. *Arch Gerontol Geriatr.* (2013) 56:400–4. doi: 10.1016/j.archger.2012.11.001
5. Cations M, Radisic G, Crotty M, Laver KE. What does the general public understand about prevention and treatment of dementia? A systematic review of population-based surveys. *PLoS ONE.* (2018) 13:e0196085. doi: 10.1371/journal.pone.0196085
6. Turner S, Iliffe S, Downs M, Wilcock J, Bryans M, Levin E, et al. General practitioners' knowledge, confidence and attitudes in the diagnosis and management of dementia. *Age Ageing.* (2004) 33:461–7. doi: 10.1093/ageing/afh140
7. Smyth W, Fielding E, Beattie E, Gardner A, Moyle W, Franklin S, et al. A survey-based study of knowledge of Alzheimer's disease among health care staff. *BMC Geriatr.* (2013) 13:2. doi: 10.1186/1471-2318-13-2
8. Robinson A, Eccleston C, Annear M, Elliott K, Andrews S, Stirling C, et al. Who knows, who cares? Dementia knowledge among nurses, care workers, and family members of people living with dementia. *J Palliative Care.* (2014) 30:158–65. doi: 10.1177/082585971403000305
9. O'driscoll C, Heary C, Hennessy E, Mckeague L. Explicit and implicit stigma towards peers with mental health problems in childhood and adolescence. *J Child Psychol Psychiatr.* (2012) 53:1054–62. doi: 10.1111/j.1469-7610.2012.02580.x
10. Isaac M, Isaac M, Farina N, Tabet N. Knowledge and attitudes towards dementia in adolescent students. *J Ment Health.* (2017) 26:419–25. doi: 10.1080/09638237.2016.1207234
11. Baker J, Jeon Y, Goodenough B, Low L, Bryden C, Hutchinson K, et al. What do children need to know about dementia? The perspectives of children and people with personal experience of dementia. *Int psychogeriatr.* (2018) 30:673–84. doi: 10.1017/S1041610217002022
12. Atkinson T, Bray J. Dementia awareness & intergenerational exchange in schools: A pioneer project supporting dementia friendly communities. *Association for Dementia Studies & Coventry and Warwickshire NHS Trust, Worcester.* (2013). Available online at: https://www.worcester.ac.uk/documents/Schools_Evaluation_Final_Report.pdf
13. Baker J, Goodenough B, Jeon Y, Bryden C, Hutchinson K, Low L. The Kids$_4$Dementia education program is effective in improving children's attitudes towards dementia. *Dementia.* (2018) 18:1777–89. doi: 10.1177/1471301217731385
14. Galbraith B, Larkin H, Moorhouse A, Oomen T. Intergenerational programs for persons with dementia: a scoping review. *J Gerontol Soc Work.* (2015) 58:357–78. doi: 10.1080/01634372.2015.1008166
15. Heyman J, Gutheil I. "They touch our hearts": The experiences of shared site intergenerational program participants. *J Intergene Relation.* (2008) 6:397–412. doi: 10.1080/15350770802470726
16. Kamei T, Itoi W, Kajii F, Kawakami C, Hasegawa M, Sugimoto T. Six month outcomes of an innovative weekly intergenerational day program with older adults and school-aged children in a Japanese urban community. *Jpn J Nurs Sci.* (2011) 8:95–107. doi: 10.1111/j.1742-7924.2010.00164.x
17. Low LF, Russell F, Mcdonald T, Kauffman A. Grandfriends, an intergenerational program for nursing-home residents and preschoolers: a randomized trial. *J Intergene Relation.* (2015) 13:227–40. doi: 10.1080/15350770.2015.1067130
18. Harris P, Caporella C. Making a university community more dementia friendly through participation in an intergenerational choir. *Dementia.* (2018) 18:2556–75. doi: 10.1177/1471301217752209
19. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. *Am J Public Health.* (1999) 89:1322–7. doi: 10.2105/AJPH.89.9.1322
20. Harden SM, Gaglio B, Shoup JA, Kinney KA, Johnson SB, Brito F, et al. Fidelity to and comparative results across behavioral interventions evaluated through the RE-AIM framework: a systematic review. *Syst Rev.* (2015) 4:155. doi: 10.1186/s13643-015-0141-0
21. Baker J, Low L, Goodenough B, Jeon Y, Tsang R, Bryden C, et al. The kids insight into dementia survey (KIDS): development and preliminary psychometric properties. *Aging Ment Health.* (2018) 22:947–53. doi: 10.1080/13607863.2017.1320703
22. Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol.* (2006) 3:77–101.
23. Dua T, Seeher K, Sivananthan S, Chowdhary N, Pot A, Saxena S. World health organization's global action plan on the public health response to dementia 2017-2025. *Alzheimer's Dementia.* (2017) 13:P1450–1. doi: 10.1016/j.jalz.2017.07.758
24. Scerri A, Innes A, Scerri C. Dementia training programmes for staff working in general hospital settings - a systematic review of the literature. *Aging Ment Health.* (2017) 21:783–96. doi: 10.1080/13607863.2016.1231170
25. Wesson L, Chapman B. A dementia education scheme. *Nurs Older People.* (2010) 22:22–5. doi: 10.7748/nop2010.03.22.2.22.c7565
26. Waugh A, Marland G, Henderson J, Robertson J, Wilson A. Improving the care of people with dementia in hospital. *Nurs Stand.* (2011) 25:44–9. doi: 10.7748/ns.25.32.44.s50
27. Alushi L, Hammond JA, Wood JH. Evaluation of dementia education programs for pre-registration healthcare students-a review of the literature. *Nurse Educ Today.* (2015) 35:992–8. doi: 10.1016/j.nedt.2015.04.006
28. Baker J, Webster L, Lynn N, Rogers J, Belcher J. Intergenerational programs may be especially engaging for aged care residents with cognitive impairment: findings from the avondale intergenerational design challenge. *Am J Alzheimers Dis Other Dementias.* (2017) 32:213–21. doi: 10.1177/1533317517703477
29. Chatterton ML, Bayer JK, Engel L, Rapee RM, Beatson R, Hiscock H, et al. Cost-effectiveness of preventing child internalising problems: results from the translational trial of cool little kids at school entry. *J Anxiety Disord.* (2020) 70:102191. doi: 10.1016/j.janxdis.2020.102191
30. Shrewsbury VA, Venchiarutti RL, Hardy LL, Foley BC, Bonnefin A, Byth K, et al. Impact and cost of the peer-led Students As LifeStyle Activists programme in high schools. *Health Edu J.* (2020) 79:3–20. doi: 10.1177/0017896919856050

31. Milders M, Bell S, Lorimer A, Jackson H, Mcnamee P. Improving access to a multi-component intervention for caregivers and people with dementia. *Dementia.* (2019) 18:347–59. doi: 10.1177/1471301216672745
32. Rosa TD, Possin KL, Bernstein A, Merrilees J, Dulaney S, Matuoka J, et al. Variations in costs of a collaborative care model for dementia. *J Am Geriatr Soc.* (2019) 67:2628–33. doi: 10.1111/jgs.16076
33. Camp CJ, Judge KS, Bye CA, Fox KM, Bowden J, Bell M, et al. An intergenerational program for persons with dementia using Montessori methods. *Gerontologist.* (1997) 37:688–92. doi: 10.1093/geront/37.5.688
34. Chung JC. An intergenerational reminiscence programme for older adults with early dementia and youth volunteers: values and challenges. *Scand J Caring Sci.* (2009) 23:259–64. doi: 10.1111/j.1471-6712.2008.00615.x
35. Camp CJ, Lee MM. Montessori-based activities as a trans-generational interface for persons with dementia and preschool children. *J Intergener Relatsh.* (2011) 9:366–73. doi: 10.1080/15350770.2011.618374
36. Radford K, Gould R, Vecchio N, Fitzgerald A. Unpacking intergenerational (IG) programs for policy implications: a systematic review of the literature. *J Intergener Relation.* (2018) 16:302–29. doi: 10.1080/15350770.2018.1477650
37. Gerritzen EV, Hull MJ, Verbeek H, Smith AE, De Boer B. Successful elements of intergenerational dementia programs: a scoping review. *J Intergener Relation.* (2020) 18:214–45. doi: 10.1080/15350770.2019.1670770

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SYSTEMATIC REVIEW
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A Systematic Review of Associations Between Interoception, Vagal Tone, and Emotional Regulation: Potential Applications for Mental Health, Wellbeing, Psychological Flexibility, and Chronic Conditions

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Background: Interoception and heart rate variability have been found to predict outcomes of mental health and well-being. However, these have usually been investigated independently of one another.

Objectives: This systematic review aimed to explore a key gap in the current literature, that being, identifying whether HRV and interoception predict emotional regulation outcomes and strategies.

Methods: The process of article retrieval and selection followed the PRISMA guidelines. Databases PsychINFO, Web of Science, PubMed, CINAHL, and MEDLINE were scanned for papers published. Preliminary inclusion and exclusion criteria were specified following the PICO framework, whilst the CHARMS framework was used to help formulate the research question, and critically assess for bias.

Results: Two hundred and thirty-seven studies were identified after initial database searches. Of these, eight studies were included in the final selection. Six studies explored the associations between HRV and ER, whilst three investigated the associations between interoception and ER (one study included both). Results show that greater HRV and interoception are associated with better ER. Specifically, high parasympathetic activity largely predicted the use of adaptive ER strategies such as reappraisal, and better acceptance of emotions. High interoception, instead, was predictive of effective downregulation of negative emotions and handling of social uncertainty, there was no association with any specific ER strategy.

Conclusions: Awareness of one's own bodily feelings and vagal activation seem to be of central importance for the effective regulation of emotional responses. However, one limitation is the small sample of studies found, thus more studies in this area are needed in the future.

Keywords: emotional regulation, vagal tone, interoception, chronic conditions, health and well-being, psychological flexibility

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INTRODUCTION

Emotions are a multifaceted construct involving overlapping aspects of the experiential, behavioral, and autonomic systems (Koole et al., 2011). It has been suggested that emotions drive behavioral modification when faced with constantly changing situations and direct individuals toward efficient, goal directed, behavioral responses (Damasio, 1999).

From an evolutionary perspective, emotions may provide a survival advantage as they are an important part of environmental adaptation, whether at a singular (benefiting the individual organism) (Cosmides and Tooby, 2000) or at a multi-level selection level (benefiting the group) (Wilson and Sober, 1994).

Emotions can be defined as self-regulatory, automatic, feeling processes that arise in response to internal, and external environmental stimuli (Thompson, 1994; Mauss et al., 2005), and these can be specific (e.g., angry about missing a bus) or global (e.g., feeling generally stressed and anxious) (Koole et al., 2011).

Both the autonomic nervous system (ANS) and endocrine system mediate allostatic processes necessary to allow for the efficient homeostatic levels necessary for survival (Kreibig, 2010; de Veld et al., 2012). For example, in an emotionally challenging situation, a person's hands may start sweating (to cool the body), their face may become red, their skin may tense, and their heart may beat faster (to ready them for a fight or flight response).

Despite these automated processes of the ANS, individuals have the ability to evaluate situations and adjust their frequency, latency, and intensity toward goal-oriented behavior (Gyurak et al., 2011). Lazarus (1991), one of the early theorists of emotions, defined two temporally distinct emotional responses. A primary response, which entails the raw, sensitivity-driven, response to an emotion-inducing event, and a secondary response, in which individuals are able to make judgements and regulate their emotional responses to cope with the primary response (Baumann et al., 2007).

Individuals have been shown to employ various cognitive-behavioral strategies to regulate emotions, some of which have been linked with positive and others with worse psychological outcomes (Aldao et al., 2010). The attempt to change the moment-to-moment emotional experiences, behavioral expressions, and physiological responses is called emotional regulation (ER) (Gross, 1998; Aldao, 2013). Effective ER is associated with better executive control, decision-making, understanding other's behaviors, and handling of social circumstances (van't Wout et al., 2010; Teper et al., 2013). From a perspective of physical health, more effective forms of ER are associated with reduced mortality, morbidity, cardiovascular issues, and better immune system function (Kiecolt-Glaser et al., 2002; Pressman and Cohen, 2005; Chida and Steptoe, 2009; Song and Chung, 2010). Emotional dysregulation, on the other hand, has been found to lead to inflexible behavioral and autonomic responses, the reinforcement of maladaptive behaviors and thoughts, increased inflammatory states, peripheral and central sensitization, and a negative effect on the overall bodily homeostatic balance (Bradley et al., 2011; Jazaieri et al., 2013).

Gross (1998) developed a process model of ER whereby he suggested that ER strategies can be broadly categorized as either antecedent-focused or response-focused. Antecedent-focused strategies were thought to be aimed at manipulating the inputs of emotion, for instance, by selecting situations with less emotional impact (situation selection), modifying the impact of a given environment (situation modification), shifting the attention away from the arousing event (attentional deployment) or revaluating the situation and thoughts held in relation to it (cognitive change). In contrast, response-focused strategies were thought to be aimed at manipulating the emotional output in order to intensify, diminish, or prolong it (Gross, 1998). Expressive suppression (such as thought suppression) is a response-focused strategy which is intended to be the active inhibition of uncomfortable emotions and thoughts. However, there is evidence that emotional suppression strategies are associated with greater cognitive distress and sympathetic arousal (Aldao et al., 2010). Other expressive suppression strategies such as using anti-anxiety drugs can often lead to the adverse effects of dizziness, headaches, and nausea (Gorman, 2003).

Antecedent-focused strategies are widely considered as the most adaptive ER strategies as they have been shown to provide better affective and physiological regulation with minimal cognitive and physical energetic expenditure (Ochsner and Gross, 2005; Buhle et al., 2014). One example of an antecedent strategy is emotional reappraisal which is the attempt to cognitively reframe an event to reduce its negative impact. This has shown to consistently activate executive function regions (pre-frontal, and temporal cortices) and modulate limbic activity of the amygdala in a beneficial way (Buhle et al., 2014).

Some evidence suggests that the ability to emotionally regulate successfully may be strongly dependent on the moment-to-moment awareness of bodily parameters relayed via interoceptive pathways which are measured through the use of an electrocardiogram (ECG) in the form of interoceptive awareness (IA) (Thayer and Lane, 2000; Craig, 2008). IA, more commonly referred to as interoception, refers to the internal representation of all bodily sensations in any given moment (Craig, 2002) and how the brain evaluates these sensations (Cameron, 2001). In addition to this, it is not limited to that of bodily sensations derived from the afferent component of the ANS, but also has a role in processing emotional, motivational, and behavioral outcomes (Craig, 2014; Owens et al., 2018). Damasio and Carvalho (2013) suggested that the interoceptive system is responsible for creating homeostatic maps of the body and orchestrating regulatory responses both at a conscious level, through emotions and feelings, and at the autonomic level.

Anatomically, the interoceptive system comprises of unmyelinated C and myelinated Aδ fibers converging signals into spinal laminae I and II, and reaching homeostatic centers, namely the hypothalamus, anterior insular and cingulate cortices (Pollatos et al., 2007). Interoceptive inputs stem from many physiological systems including the viscera, thermoregulatory, nociceptive, and endocrine systems. From there, inputs of varying motivational immediacy such as warmth-coldness, prickly-burning pain, taste, need to urinate, hunger, and sensual touch are relayed (Strigo and Craig, 2016). Importantly, these signals are integrated into primary emotional and motivational centers of the limbic system, the anterior insula and cingulate cortices (i.e., the homeostatic sensorimotor cortex), which have been shown to activate during all human emotions and motivational behaviors (Murphy et al., 2003; Craig, 2014). It is theorized that at these centers a meta-representation of the self is defined, allowing formulation of finely-tuned regulatory responses (Damasio and Carvalho, 2013).

In laboratory experiments, interoception is commonly measured as interoceptive accuracy (IAc), or sometimes called interoceptive sensitivity (IS) (these measures are the same). These measures are evaluated by asking participants to count their perceived heart beats which is a validated procedure called the heart beat perception task (Schandry, 1981; Pollatos et al., 2009). Numerous links have been established between altered IAc/IS and psychopathology, for instance in chronic pain, depression, anxiety, and eating disorders (Paulus and Stein, 2010; Klabunde et al., 2013; Di Lernia et al., 2016; Duschek et al., 2017). Generally, psychophysical pathology tends to be associated with reduced IAc/IS scores. It is suggested that the inefficient or impaired relay of interoceptive information from peripheral structures to the higher centers determines dysfunctional "body mapping" and, therefore, dysfunctional self-regulatory processes, with aberrant emotional, behavioral, and autonomic sequelae (Craig, 2008).

In addition to interoception, another psychophysiological factor which may influence the ability to emotionally regulate is the activity of the vagal nerve. The vagus nerve is the 10th cranial nerve (labeled CN X), it is the longest cranial nerve in the body, and the main anatomical component of the parasympathetic nervous system (Walker, 1990). Although often considered solely for its efferent functions, 80% of the fibers of the vagus relay sensory information from viscero-somatic structures (Porges, 2007a). Recently, the scope of the vagus has been expanded beyond visceral homeostatic functions to include social, cognitive, and affective components (Yuan and Silberstein, 2016). As the heart is under dominant tonic inhibitory control of the vagus nerve, electrocardiogram (ECG) measurements can be utilized in order to quantify vagal activity. This measure is an expression of interbeat variation, called Heart Rate Variability (HRV), that has been demonstrated to be a reliable indicator of several psychosomatic functions including emotional and behavioral regulation (Laborde et al., 2018).

More specifically, HRV refers to the variation between each consecutive heartbeat, described as the interval period between sequential R-R peaks in the QRS complex of an ECG measure (1996). The heart receives dual innervation from the sympathetic and parasympathetic nervous system, the former promoting a shortening of the interbeat interval whilst the latter prolongs it. Amongst the methods employed to quantify this construct, the most common measure is the frequency domain index whereby high frequency (HF) domain provides a reliable measure of vagal function (Thayer, 2009). Two additional methods for recording HRV are the Root Mean Square Successive Difference (RMSSD) which utilizes a time-domain, and the Respiratory Sinus Arrhythmia (RSA) measure which provides the value of HRV in synchrony with the respiratory cycle. High HRV is indicative of increased parasympathetic activity whereas low HRV indicates reduced parasympathetic activity and increased sympathetic activity.

In terms of mental health, low HRV has been linked with major psychological disorders such as depression and anxiety disorder (Kemp et al., 2010; Brunoni et al., 2013; Chalmers et al., 2014). Low HRV is also predictive of a first-time cardiovascular event, higher adverse outcomes after myocardial infarction, greater inflammation, and increased mortality (Thayer and Lane, 2007; Buccelletti et al., 2009; Hillebrand et al., 2013). In contrast to this, higher HRV has been found to be associated with better cognitive-behavioral function, including greater executive function, stress management, coping, and social engagement (Beauchaine and Thayer, 2015).

One psychophysiological attempt to provide a theoretical model of this association between HRV and mental as well as physical health, has been provided by Thayer and Lane (2000) through their work on the neurovisceral integration model (NIM). The model delineates an anatomical network of forebrain, brainstem, spinal cord, and the central autonomic network (CAN), which is suggested to be responsible for the integration of sensory-visceral, emotional, and cognitive information, and the subsequent implementation of regulatory actions (Benarroch, 1993). At the forebrain level, within the insular cortex, the anterior cingulate and amygdala, viscero-somatic afferent information is integrated with multi-source inputs of motivational value. Concurrently, nuclei of the hypothalamus integrate autonomic and endocrine inputs to regulate homeostatic functions. At the brainstem level, within the periaqueductal gray matter, pain and stress-related information are also integrated, whereas at the parabrachial nucleus, the nucleus solitarius and medullary reticular formation, the reflexive control of visceral systems takes place.

Sensory information is mostly processed in a sequential-hierarchical fashion through the structures of the CAN, before reaching complete integration and motor output (Riganello et al., 2018). Monitoring the regulatory processes within the CAN are cortical areas, mainly led by the prefrontal cortex. Prefrontal control is essential in order to adaptively regulate self-regulatory responses based on environmental demands (Smith et al., 2017). The NIM posits focus on these cortical processes for the determining of emotional regulation. The inability to exert cortical control has been found to underly inflexible and dysregulated emotional responses (Park and Thayer, 2014). The primary autonomic output resulting from CAN integration takes place at the sinoatrial node of the heart, therefore, HRV can be utilized as an index of these functions. HRV represents the interplay between sympathetic and parasympathetic activity where it has been suggested that greater parasympathetic activity is indicative of effective cortical-inhibitory-control and self-regulation (Jennings et al., 2015).

The second major theory explaining the vagal circuit system is the polyvagal theory (PVT) (Porges, 1991). The PVT describes the development of the ANS from an evolutionary and adaptive perspective. It is theorized that the ventral myelinated aspect of the vagus nerve (which developed evolutionarily most recently) developed in order to promote productive social affiliations

(Porges, 2007b). In doing this, when safe and calm environments are detected, the vagus nerve inhibits primitive defense reflexes of the sympathetic system in favor of metabolically more efficient and soothing functions. When this soothing "social-engagement system" is active there is often an increase in efficient situational judgement, flexible behavioral responses and pro-social traits such as the distension of facial muscles, modulation of speech tone, and greater reception of voices (Lucas et al., 2018). These effects can facilitate individuals into organized societies and communitarian structures, providing an advantage for the survival of the species (Porges and Center, 2018).

The PVT introduces the novel concept of neuroception, which is the subconscious determination of environmental danger as a result of the integration of interoceptive, somatosensory, and endocrine information (Porges, 1991). Visceral interoceptive information is largely conveyed by the afferent fibers of the vagus nerve and subsequently integrated within higher relay areas to produce emotional and behavioral responses. Altered interoceptive pathways may, therefore, cause abnormal neuroceptive states, inflexible emotional responses, and aberrant vagal outputs (Porges, 2017). The ventral area of vagus functions as a constant "brake" over more primitive sympathetic reflexes so that at rest the "vagal brake" is in full function, and is "released" when external and internal stimuli require larger mobilization of energy via the sympathetic nervous system (SNS) (Porges, 2011).

High SNS activity is associated with emotions such as fear and anger, and behaviors directed toward safety and protection which inhibit the promotion soothing, regulatory, functions. When the SNS exhibits long-term dominance over the peripheral nervous system (PNS), individuals are vulnerable to high stress levels and have detrimental effects both at psychological and physical dimensions. This SNS dominance occurs in cases, for example, of chronic pain and post-traumatic stress disorder (PTSD) (Williamson et al., 2015; Kolacz and Porges, 2018). Porges (2011) also defines a third dimension of the vagal system represented by the dorsal vagal complex (DVC). The DVC is activated during situations of extreme danger and mediates shutdown of all autonomic responses (i.e., the freezing response), which explains, for instance, the loss of bladder and bowel control in frightening situations. Porges suggested that the DVC is of paramount importance in the study of trauma such as PTSD, as it explains the protracted defensive behaviors people display after traumatic events.

AIMS AND OBJECTIVES

Given the psychophysiological evidence outlined in the introduction that both interoception and vagal tone (heart rate variability) seem to have important functional roles for emotional regulation, the primary aim of this study was to produce a systematic review to explore and synthesize (see Method section) the available literature which has identified interoception and heart rate variability as predictors (associations) for emotional regulation. These are central regulatory functions (Ceunen et al., 2016; Holzman and Bridgett, 2017) which tend to be studied independently of one another. Although interoception and HRV are two relatively new fields of research, there is much evidence linking these systems both physiologically, such as described through PVT, as well as psychologically such as their shared impact on many aspects of health and disease both central pathology (e.g., anxiety and depression) and peripheral (e.g., chronic pain) (Buccelletti et al., 2009; Di Lernia et al., 2016). So, this systematic review addresses a key gap in the current literature, that is the identifying whether HRV and interoception predict emotional regulation outcomes and strategies.

The specific primary question being asked is: are interoception and HRV predictors (causally associated) for ER in adult healthy and clinical populations? In this case, the predictors interoception and HRV are the independent variables (see Methods section for specific indices included), whilst emotional regulation is the dependent variable (again see Methods section for the indices included). The secondary questions are as follows: Which types of ER strategies would yield a positive metal well-being outcome? Whether HRV or interoceptive indices predict these well-being outcomes or types of ER strategies employed?

The findings from this systematic review could, at a later date, facilitate the development of a unified model of these central regulatory systems to help develop more appropriate clinical diagnostics and therapeutic interventions.

METHODS

This systematic review followed the Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2009) to ensure transparent and comprehensive reporting of the methods and results.

Search Strategy

Electronic-only databases were searched for this review. The selection for this included PsychINFO, Web of Science, PubMed, CINAHL, and MEDLINE. The specific search strings are presented in **Table 1**. Searches in the Boolean format were as follows: interocept* AND heart rate variability AND emotion*. These terms were used to capture the majority of the research relevant to these areas. Searchers were conducted on all fields which includes the title, abstract and the main body of the text. In addition to this, other relevant known papers by the authors were included.

Screening

All of the papers were assessed independently by two reviewers TP and DE by title and abstract initially. Once the relevant papers

TABLE 1 | Search terms used for each database.

Database	Search string
PubMed	[(interocept*) AND heart rate variability] AND emotion* regulation
PsychInfo	(interocept* AND heart rate variability AND emotion*)
Web of Science	TS = (interocept* AND heart rate variability AND emotion*)
CINAHL	(interocept* AND heart rate variability AND emotion*)
MEDLINE	(interocept* AND heart rate variability AND emotion*)

were selected and the duplicates were removed (see PRISMA Table in Results section), the remaining studies were examined in full text format by both TP and DE. Critical appraisal (see Critical Appraisal and Risk of Bias Assessment section) and final selection were assessed by TP and DE independently. In cases where there were discrepancies, the reviewers discussed these until consensus was made.

Inclusion and Exclusion Criteria

As recommended by the Cochrane Handbook for systematic reviews, the PICO framework was utilized to define inclusion and exclusion criteria, and the research question (Higgins and Green, 2011). PICO is an acronym for population (sample type), intervention, comparator (what an intervention is compared to), outcome (what are the outcome measures). As this study did not explore specific interventions or comparators only the population and outcome were identified in the inclusion and exclusion criteria, along with type of study design.

Population

Only human participants were included, animal studies were excluded. Mixed-age adult-only populations were included, whilst study samples comprising of children, adolescent, and elderly populations were excluded as their anatomical, physiological, and psychological characteristics differ greatly from that of the "normal" general population (Banerjee and Chaudhury, 2010). Non-clinical, and clinical study samples were included, however, it was acknowledged that non-clinical samples reduce the number of confounding variables and more accurately represent the general population (Breakwell and Smith, 2012), though clinical samples provide an overview for predictors relating to clinical dysfunction specifically. Clinical populations were only considered if subjects were affected by Axis 1 disorders, which have a clear relationships with emotion regulation (Bradley et al., 2011). Individuals with intellectual disabilities and terminal disorders were excluded as the links between those associated psychological states and aspects of emotion regulation are less defined (Mcclure et al., 2009).

Type of Study

In order to be included, studies needed to be peer reviewed and published in English. Commentaries, books, and dissertations were excluded. Studies involving pharmacological therapies and transcranial brain stimulation, which are out of the scope of this review were also excluded. Clinical and non-clinical randomized controlled trials (RCT) and observational studies were included so as long as these studies had some focus on associations (predictors) between either interoception (independent measure; IV) or heart rate variability (IV) (or bother of these), and emotional regulation (dependent measure; DV). Predictor analysis refers to regression-based studies, however, correlational studies were also included (in a minority of cases), though not strictly predictors, as though they cannot infer causality, they are useful in terms of identifying simple relations between variables. Systematic reviews and meta-analysis studies were not included.

It is important to understand the key differences between the types of studies, as they relate to bias. RCTs examine the efficacy of an intervention on a defined outcome, whereas observational studies are useful for understanding physiological/pathophysiological processes, making predictions, and establishing the strength of association between variables (Faraoni and Schaefer, 2016). Observational studies differ from RCTs as they do not include a strict protocol (RCTs follow CONSORT) such as including a control group, a randomization process, and predefined endpoints, granting wider freedom of enquiry but also greater vulnerability to bias (Sørensen et al., 2006). Two primary types of observational studies are cohort and cross-sectional studies. Cohort and case-control designs allow observations to be made over time, whilst cross-sectional studies report results relating to a specific point in time (Song and Chung, 2010).

Outcome (Association Measures)

The predictor measures (IVs) of interest relate to that of interoception and HRV, whilst the DV (what is being predicted) relates to emotion regulation. Interoception, in this systematic review was indexed as Interoceptive Awareness (IA), Interoceptive Accuracy (IAc), Interoceptive sensibility (ISen), as already defined in the literature (Garfinkel and Critchley, 2013; Forkmann et al., 2016).

Recent work by Garfinkel and Critchley (2013) has suggested that there is a dissociation between these indices in how they are measured and what they predict (Garfinkel et al., 2015). In order to reduce bias across measures, only interoceptive studies which utilized an objective measure of heart rate awareness were selected in this study (i.e., IA and IAc), whereas subjective measures were excluded (ISen). More specifically, only studies which used the mental tracking methods first developed by Schandry (1981) and later slightly modified versions (which often include more trials), were selected. Other objective methods such as Whitehead Heartbeat Discrimination Tasks (Schulz et al., 2013) were excluded from this study in order to reduce bias, as these have been suggested to relate to different underlying processes (Schulz et al., 2013; Garfinkel et al., 2015).

Heart rate variability was indexed by the commonly implemented means of high-frequency domain indices (HF), root mean square of the successive differences (RMSSD), and respiratory sinus arrhythmia (RSA). In some cases, some studies formulated bespoke indices for these (where these are included, they are defined). For both HRV and interoception, participants needed to have been recorded with a heart rate monitor (a pulse monitor or ECG for interoception and an ECG monitor for HRV).

Emotion regulation was index through commonly used and validated measures. This included the emotion regulation questionnaire (ERQ) (Gross and John, 2003) which comprises 6 items measuring reappraisal and 4 items measuring suppression. The ERQ has demonstrated good internal consistency for both subscales and is considered the gold standard measure for ER (Enebrink et al., 2013). Other commonly utilized measures for ER which were included were the difficulties in emotion regulation scale (DERS) (Gratz and Roemer, 2004); the spontaneous affect regulation scale (SARS) (Egloff et al., 2006); the cognitive emotion regulation questionnaire (CERQ) (Garnefski et al., 2001), which utilizes emotion-evoking visual tasks and daily diary reports; and the UWIST Mood Adjective Checklist, which provides a list of mood adjectives (e.g., happy, dissatisfied etc.) to assess the current mood of the individual (Matthews et al., 1990).

Critical Appraisal and Risk of Bias Assessment

As the studies in this review were based on (prediction) regression and correlational analysis, The Checklist for Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modeling Studies (CHARMS) was utilized. This is a tool developed by the Cochrane Collaboration Prognosis Review Method Group (Moons et al., 2014) to critically apprise the quality of reporting and bias. This was used as opposed to the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) and Prediction Model Risk of Bias Assessment Tool (PROBAST) assessments, which, instead, specialize in assessing developing, and updating prediction models (Debray et al., 2017). CHARMS has 10 domains of inquiry, however, two of these sections were not relevant. Specifically, “model evaluation” and “performance” were removed as the studies explored did not utilize model validation assessments. Therefore, the CHARMS framework was adapted and included only the eight relevant domain sections (see **Table 2** for this adapted CHARMS version). **Table 3** shows the risk of bias quality appraisal assessments made. All of the papers were assessed independently by two reviewers TP and DE, then where there were discrepancies the reviewers discussed these until consensus was met. Though there are no formal guidelines for a cut off criteria in the CHARMS literature (evaluation for this is made on a case by case basis), for the purposes of this systematic review, the criteria for inclusion was arbitrarily set through a simple dichotomous split, where papers would have to meet at least 50% of the criteria set by CHARMS in order to be included in the final synthesis of studies (all studies were included).

TABLE 2 | Adapted relevant eight domains of the CHARMS checklist criteria.

Source of the data
Participants
Outcomes to be predicted
Candidate predictors
Sample size
Model development (type of model)
Results
Interpretation and limitations

RESULTS

There were 237 papers initially identified through the databases, 79 through Web of Science, 24 through PubMed, 67 through PsychInfo, nine through CINAHL and 58 through MEDLINE. Three additional papers were identified outside of the initial search. After duplicates were removed 160 articles were screened through their title and abstract. After screening selection, 27 papers were then examined in full text. After critical appraisal analysis and full text assessment for eligibility, eight papers were selected for full analysis (see PRISMA **Figure 1**, and **Table 4** for the summary of results).

HRV and Emotion Regulation

Three papers were identified which explored an association between HRV and emotional regulation. Of these, Geisler et al. (2010) found that participants with higher HRV (HF) had higher subjective well-being as indexed by the UWIST Mood Adjective Checklist. More specifically, HRV (IV) predicted (positively associated) positive hedonic tone (cheerfulness) ($p < 0.05$, adj. $R^2 = 0.02$) and positive tense arousal (calmness) ($p < 0.05$, adj. $R^2 = 0.03$), indicating that parasympathetic activity is

TABLE 3 | Critical appraisal using CHARMs tool for assessing risk of bias.

References	Source of data (specified study design, e.g., cohort, cross-sectional, RCT etc.)	Participant details	Outcomes to be predicted	Candidate predictors	Sample size and missing data	Model development (type of model)	Results (correct presentation)	Interpretation and limitations
Geisler et al. (2010)	Unclear	Low	Low	Low	Low	Low	Low	Low
Williams et al. (2015)	Unclear	Unclear	Low	Low	Low	Low	Low	Low
Koval et al. (2013)	Unclear	Low	Low	Low	Low	Low	Low	Low
Aldao et al. (2016)	Unclear	Low	Low	Low	Low	Low	Low	Low
Stange et al. (2017)	Unclear	Low	Low	Low	Low	Low	Low	Low
Kever et al. (2015)	Unclear	Low	High	High	Low	High	Low	Low
Füstös et al. (2012)	Unclear	Low	High	High	Low	High	Low	Low
Pollatos et al. (2015)	Unclear	Unclear	Low	Low	Low	Low	Low	Low

Low, Low risk of bias; High, High risk of bias; Unclear, Risk of bias is unclear.

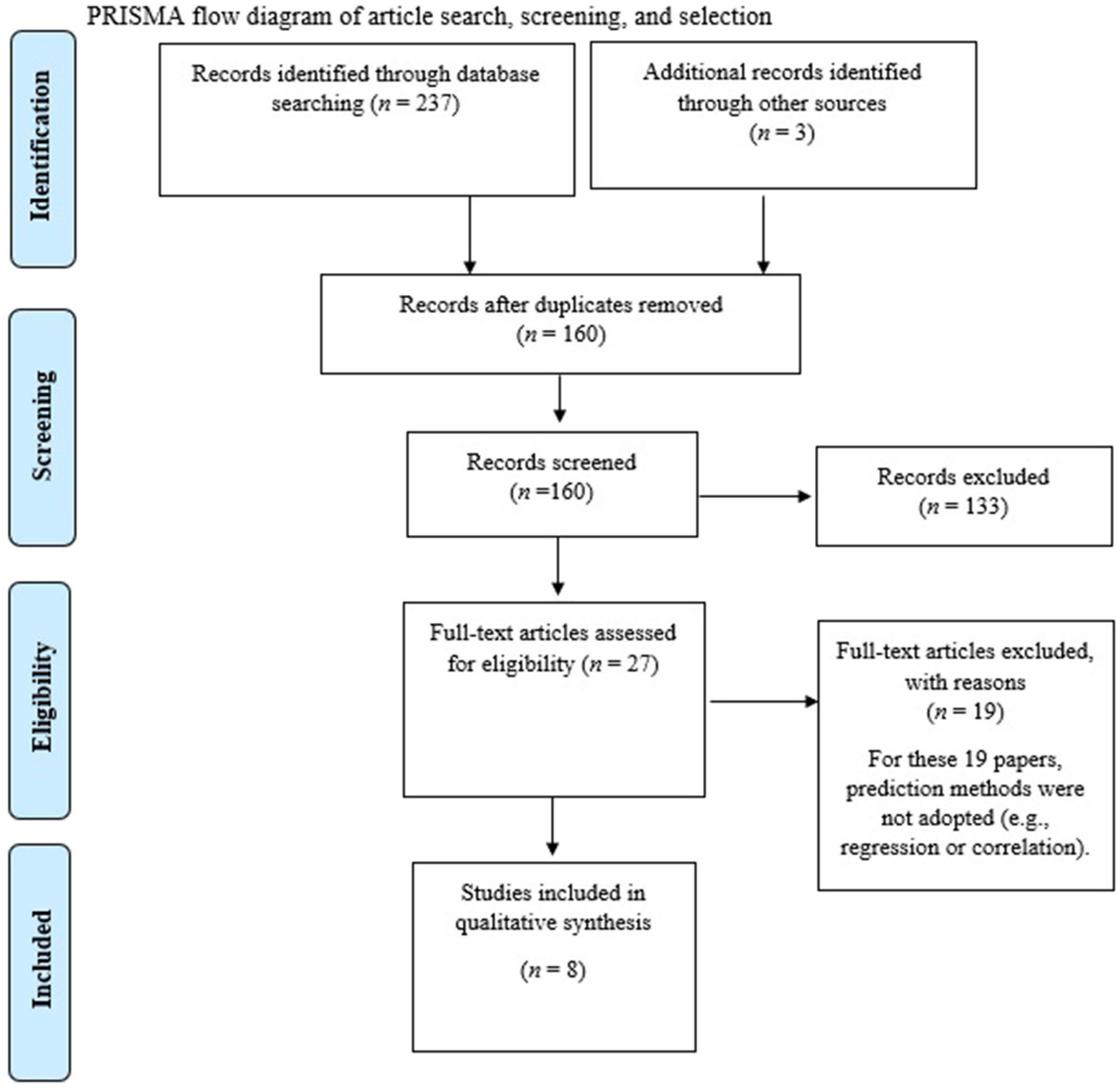

FIGURE 1 | PRISMA flow diagram of article search, screening, and selection.

associated with positive emotions. HRV also predicted the use of executive ER functions (as indexed by the Cognitive Emotion Regulation Questionnaire), and as a mediator (M) between HRV and subjective well-being ($p < 0.01$, adj. $R^2 = 0.04$) but it did not predict the use of non-executive emotion regulation, ($p = 0.54$, adj. $R^2 = 0.00$) (as a mediator between HRV and subjective well-being). In addition to this, HRV (IV) including executive emotion regulation as the mediator (M) predicted positive hedonic tone (DV), ($p < 0.001$, adj. $R^2 = 0.09$), and positive tense arousal (DV), ($p < 0.01$, adj. $R^2 = 0.08$). To extend the ecological validity of the results, the authors recorded HRV over a full day, confirming that HRV is associated with higher DERS scores over this longer period ($r = -0.38$, $p = 0.049$). In terms of life satisfaction, HRV (IV) was not related to past, present, and expected future satisfaction with life, ($p > 0.25$, adj. $R^2 < 0.01$). Though HRV (IV) and executive emotion regulation (M) together predicted present satisfaction with life (DV) ($p < 0.01$, adj. $R^2 = 0.06$), and expected future satisfaction with life (DV), ($p < 0.001$, adj. $R^2 = 0.09$). This indicated that executive emotion regulation significantly mediated the influence of HRV on present and expected future life satisfaction. The authors concluded that HRV could be used as an index of emotional self-regulatory strength.

Williams et al. (2015) also found evidence which supported the idea that HRV and emotional regulation were associated.

TABLE 4 | Summary of findings—relevant articles selected in final included results.

References	Study focus on Interoception or HRV	HRV or Interoception index	Emotional regulation measures	Prediction model used	Results
Geisler et al. (2010)	• HRV	• HF	• Cognitive emotion regulation questionnaire	• Linear regression	• Participants with higher HRV employed greater executive ER functions • HRV was related to positive hedonic tone and positive tense arousal
Williams et al. (2015)	• HRV	• lnRMSSD • RRS • HF	• Emotion regulation scale	• Linear hierarchical regression	• Association between HRV (lnRMSSD) and the difficulties in emotion regulation scale (DERS) total scores • lnRMSSD was significantly associated with scores obtained from the DERS subscales clarity and impulse
Koval et al. (2013)	• HRV	• rMSSD • HF	• Affective instability • ER strategies	Linear regression – multilevel random intercept model	• HRV had a negative association with positive affective (PA) instability • Negative association between rMSSD and positive affect instability • Both rMSSD and HR were negative associated with negative affect
Aldao et al. (2016)	• HRV	• Composite score from HF, mean square difference, percentage of the absolute differences between consecutive IBIs, that are >50ms, and cardiac vagal index	• ER strategies (avoidance)	• Linear regression–GEE analysis	• Spontaneous avoidance was predicted negatively by the HRV index • Spontaneous avoidance in response to disgust eliciting pictures was positively associated by an interaction between the HRV index with the anxiety and depression symptoms score
Stange et al. (2017)	• HRV	• HF • RSA	• Positive or negative affect scale (PANAS) • ER strategies—spontaneous affect regulation scale (SARS) – • To identify ER strategies used (reappraisal, distraction, or suppression)	• Linear regression	• Significant interaction between reappraisal and recovery of HRV, whereby reappraisal predicted greater improvements in NA among those with higher HRV • Interaction between reappraisal and recovery, whereby reappraisal predicted greater improvements in NA for those with higher RSA recovery • Interaction between RSA reactivity and distraction, whereby distraction predicted improvements in NA but only for those with higher RSA reactivity to the sad film • interaction between distraction and recovery of HRV, whereby distraction predicted improvement in NA for those with greater HRV recovery • Suppression associated with increases in NA during recovery for those with lower HRV reactivity to the sad film
Kever et al. (2015)	• Interoception	• Interoceptive sensitivity	• Emotional regulation questionnaire • ER strategies—reappraisal, maintain	Correlation	• IS was higher in participants scoring high in the ERQ • This correlation was the same between IS and those employing greater reappraisal and supression strategies
Füstös et al. (2012)	• Interoception	• Interoceptive awareness	• Emotional arousal • ER strategies—reappraisal, maintain	• Correlation	• Found higher IA was positively correlated with emotional arousal during the negative maintain • When participants passively observing the negative valence images were asked to apply reappraisal ER techniques in the negative reappraisal (NR) condition, IA negatively correlated with emotional arousal • The downregulation in arousal between the passive-observing (NM) condition and the reappraisal (NR) condition (the difference between arousal in the two phases, NM-NR) was highly correlated with IA

(Continued)

TABLE 4 | Continued

References	Study focus on Interoception or HRV	HRV or Interoception index	Emotional regulation measures	Prediction model used	Results
Pollatos et al. (2015)	• Interoception	• Interoceptive sensitivity	• ER strategies—reappraisal, suppression • Emotional regulation questionnaire • Needs-Threat Scale	• Forward selection linear regression	IS predicted higher emotional regulation strategies; reappraisal and suppression

They used a hierarchical regression and found that HRV (InRMSSD; log transformed RMSSD) predicted (association) the outcomes of the difficulties in emotion regulation scale (DERS) total scores ($r_{partial} = -0.222$, $p < 0.01$) after controlling for age, ethnicity, gender, body mass index (BMI), Spielberger trait anxiety inventory (STAI-T) scores, ruminative response scale (RRS) scores, and HF peak (respiration) values. In addition to this, InRMSSD was significantly negatively associated with scores obtained from the subscales; emotional clarity ($r_{partial} = -0.175$, $p < 0.05$) and impulse control ($r_{partial} = -0.155$, $p < 0.05$). It is important to note that high scores of DERS indicate greater difficulties with emotion regulation, so that an inverse association indicates that high HRV is indicative of better emotional regulation. They concluded that their findings supported NIM.

Finally, Koval et al. (2013) explored the mechanisms which underpinned affective instability (mood fluctuations), and used trait HRV (indexed by RMSSD and HF) as a measure of emotion regulation capacity. Koval et al. used a regression multilevel random intercept model and reported that HRV predicted (negatively associated) positive affective (PA) instability ($\beta = -0.18$, $p = 0.010$ and $\beta = -0.17$, $p = 0.006$). Again, it is important to note an inverse association between HRV and affect instability indicates that high HRV is indicative of better emotional regulation. As the authors suggest, affective instability is likely to relate to faulty cortical inhibitory mechanisms central in ER. They also found an association between HRV (RMSSD) and positive affect instability both before ($\beta = -0.16$, $SE = 0.08$, $p = 0.049$) and after controlling for positive affect mean level ($\beta = -0.16$, $SE = 0.08$, $p = 0.044$). Similarly, there was some evidence that HR and positive affect instability were associated both before ($\beta = -0.17$, $SE = 0.08$, $p = 0.045$) and after controlling for PA mean level ($\beta = -0.16$, $SE = 0.09$. $p = 0.061$). In addition to this, after excluding outliers on each index of vagally mediated HRV and controlling for negative affect mean level, there was evidence that both RMSSD and HR were negatively associated with negative affect (NA) (RMSSD: $\beta = -0.25$, $SE = 0.10$, $p = 0.017$; HF: $\beta = -0.32$, $SE = 0.12$, $p = 0.009$). Finally, there was also some weak evidence to suggest that the two HRV indices were negatively associated with the standard deviation of PA (rMSSD: $r = 0.23$, $p = 0.04$; HF: $r = 0.21$, $p = 0.06$).

HRV and Emotion Regulation Strategies

Three studies considered the association between HRV and ER strategies. Of these, Aldao et al. (2016) used a generalized estimation equation (GEE) regression analysis with a HRV index composed of a composite score of four measures (HF, mean square difference, percentage of the absolute differences between consecutive interbeat intervals that were >50 ms, and cardiac vagal index). They found that spontaneous avoidance in response to disgust eliciting pictures was predicted (negatively associated) by resting HRV index (Wald's $\chi^2 = 4.415$, b = -0.091, SE = 0.0435, $p = 0.036$). They also found that spontaneous avoidance in response to disgust eliciting pictures was positively associated by an interaction between the HRV index with the anxiety and depression symptoms score, where resting HRV is low and the symptoms are high (Wald's $\chi^2 = 9.654$, $b = 0.192$, SE = 0.062, $p = 0.002$). This meant that those participants with elevated symptoms of depression and anxiety whilst spontaneously using avoidance were higher in those with low HRV.

Based on these findings that high resting vagal tone (HRV) predicted lower use of spontaneous use of avoidance in response to disgust-eliciting pictures, and to a greater degree than anxiety and depression symptoms, they concluded that vagal tone may therefore be a protective factor against the use of avoidance based strategies in individuals experiencing elevated symptoms of anxiety and depression. They suggested this may have important implications with how to counteract affective disturbances which relate to avoidance such as rigid maladaptive strategies (e.g., avoidance) and underlies many mental health disorders today (Strosahl and Wilson, 1999; Aldao et al., 2010). They also suggested the findings highlighted the importance of using a HRV index as well as subjective measures when studying emotional regulation as the biological measure may be a more reliable predictor of emotion.

Complementing these findings, Stange et al. (2017) explored whether parasympathetic recovery (indexed by fluctuations in HF-HRV and respiration sinus arrhythmia; RSA) moderated associations between spontaneous regulation (ER strategies of reappraisal, distraction, or suppression) to predict affect recovery (improvements in negative affect; NA). They found a significant interaction between reappraisal and recovery of HRV, whereby reappraisal predicted greater improvements in NA among those with higher HRV ($t = 3.86$, $p < 0.005$) but not lower HRV ($t = -0.11$, $p = 0.92$). They also found an interaction between reappraisal and recovery, whereby reappraisal predicted greater improvements in NA for those with higher RSA recovery ($t = 3.86$, $p < 0.05$), but not for those will lower RSA recovery ($t = 0.69$, $p = 0.49$). For distraction, there was an interaction between RSA reactivity and distraction, whereby distraction predicted improvements in NA but only for those with higher RSA reactivity to the sad film ($t = 2.39$, $p = 0.02$) but not lower RSA reactivity ($t = -0.83$, $p = 0.41$). There was also an interaction between distraction and recovery of HRV, whereby distraction predicted improvement in NA for those with greater HRV recovery ($t = 2.50$, $p = 0.01$) but not for those with lower HRV recovery ($t = -1.04$, $p = 0.30$). For suppression, this was associated with increases in NA during recovery for those with lower HRV reactivity to the sad film ($t = -2.36$, $p = 0.02$) but not for higher HRV reactivity ($t = 0.81$, $p = 0.42$). They concluded by suggesting that HRV reactivity protected against the negative effects of suppression on NA recovery.

Koval et al. (2013) utilized two indices of vagally mediated HRV; a time domain measure in the form of rMSSD, and a frequency domain measure in the form of High Frequency component (HF, 0.15–0.40 Hz). They explored, through a multi-level regression, whether participant's daily affective instability was associated with certain "dysfunctional" ER strategies and HRV scores. The study was unable to show any significant association between affective instability and ER strategies such as reappraisal or suppression (measured with the ERQ), nor did HRV predict greater use of reappraisal or suppression.

Interoception, Emotion Regulation, and Emotion Regulation Strategies

Three studies analyzed the relationships between interoception and emotion regulation. Kever et al. (2015) found that IS was higher in participants scoring high in the ERQ. This correlation was the same between IS and those employing greater reappraisal emotional strategies, as well as IS and those employing suppression strategies ($r = 0.17$; $p = 0.001$ for both). They concluded that higher detection of one's own bodily signals (higher interoception) facilitated the implementation of antecedent-focused as well as response focused emotional regulation strategies.

Füstös et al. (2012) analyzed the relationship between IA and emotional arousal in participants viewing pictures with negative valence and found higher IA was positively correlated with emotional arousal during the negative maintain (NM) condition (negative valence pictures but with no reappraisal attempted by the participants) ($r = 0.38$; $p < 0.05$). However, when participants passively observing the negative valence images were asked to apply reappraisal ER techniques in the negative reappraisal (NR) condition, IA negatively correlated with emotional arousal ($r = -0.34$, $p < 0.05$). Moreover, the downregulation in arousal between the passive-observing (NM) condition and the reappraisal (NR) condition (the difference between arousal in the two phases, NM-NR) was highly correlated with IA ($r = 0.59$, $p < 0.01$), which suggests that individuals with greater awareness of body-signals (greater interoception) were more effective at regulating emotions.

Finally, Pollatos et al. (2015) utilized a social-exclusion experiment (Cyberball paradigm) and measured emotional regulation through the ERQ through performing a regression analysis (forward selection). They found that IS predicted higher emotional regulation strategies; reappraisal ($t = 3.14$, $\beta = 0.27$, $p < 0.01$) and suppression ($t = 3.22$, $\beta = 0.28$, $p < 0.01$) scores for the exclusion condition. They concluded that IS can be associated with emotional regulation strategies and having awareness to bodily signals can help reduce aversive states.

DISCUSSION

This systematic review aimed to identify studies which have explored how HRV and interoception predict (associate with) ER and strategies. Interoception and HRV have been explored as biomarkers of health and well-being (such as positive emotional outcomes) previously, however, these have been largely explored independently, there has been no previous attempt to synthesize and compare these outcomes directly, and in the context of ER. They both seem to underlie the homeostatic system where interoception is thought of as the sensory component of the homeostatic system, whereas HRV indexes the primary output of the same homeostatic system in the form of the ANS (Craig, 2008; Park and Thayer, 2014).

The finding from this systematic review suggest that both interoception and vagal tone (HRV) have important functional roles for emotional regulation. The findings also show that some (non-avoidant) ER strategies were associated with better health and well-being, whilst (avoidant) ER strategies led to detrimental effects. More specifically, three of the included studies showed associations between high HRV and better emotion regulation (Geisler et al., 2010; Williams et al., 2015; Visted et al., 2017). One study highlighted the association between higher HRV and better executive-related ER skills, consequently generating better outcomes in mood and life-satisfaction (Geisler et al., 2010). These findings support NIM, as HRV, in that model, is suggested to be reflective of prefrontal-cortex activation which is the region associated with executive-function (Thayer et al., 2009; Fuster, 2015). Additional studies in the literature have demonstrated an association between high-HRV and better executive abilities such as inhibition, working memory, decision-making and general psychological flexibility, suggesting that this has applications for clinical research (Hansen et al., 2007, 2009; Hovland et al., 2012).

Two of the studies identified demonstrated negative associations between HRV and difficulties in regulating one's own emotions, as measured with the DERS (Williams et al., 2015; Visted et al., 2017). Visted et al. highlighted that non-accepting of one's own emotions (avoidance) prevents effective ER and was predicted by low HRV, whilst Williams et al. added strength to this association by controlling for covariates, anxiety, and rumination, and confirming the associations. Non-acceptance of emotions has been extensively linked with emotional inflexibility, leading to intensified emotional responses to stressors, general anxiety disorder, higher depressive symptoms and reduced overall well-being (Mennin et al., 2009; Ford et al., 2018). Conversely, acceptance is a foundational principle of several third-wave psychotherapeutic interventions which have emerged over the last few decades, such as Acceptance and Commitment Therapy (ACT) (Hayes et al., 2009). There is much evidence to suggest that what ACT postulates (acceptance of bad as well as good emotions and thoughts) is a necessary step in the path toward a flexible, purposeful, and values-based life (Hayes and Strosahl, 2004).

Three studies attempted to establish which ER strategy yielded the most positive outcomes (in relation to well-being) and whether HRV indices predicted these outcomes (Koval et al., 2013; Aldao et al., 2016; Stange et al., 2017). Aldao et al. (2016) and Stange et al. (2017) provided evidence of the negative impact of avoidance and suppression on psychological health, which were found to increase anxiety symptoms, depression, and negative affectivity in participants with lower HRV. It was not the same for participants with higher baseline HRV, who engaged in more adaptive ER strategies such as reappraisal. Within the more general literature, suppression has been predominantly linked with adverse psychophysiological outcomes, increased intensity of negative emotions and decreased positive emotionality and life satisfaction (Gross and Levenson, 1993; Gross and John, 2003). These findings were also supported by Stange et al. who demonstrated that people employing reappraisal and distraction strategies better coped with negative emotions and displayed higher HRV (Stange et al., 2017).

Not all of the evidence has supported a relation between ER strategies and emotional well-being. Koval et al. (2013), who collected data over seven consecutive days, found no significant association between suppression or reappraisal and daily affective instability (but they did find a negative association between HRV and positive affect instability). So, the evidence is not unanimously in support of the use of reappraisal over suppression strategies for ER. The benefits of reappraisal seem to be strictly context-dependent, as evidenced by Troy et al. (2013) who found reappraisal to be less adaptive at dealing with controllable stressors, as opposed to dealing with uncontrollable stressors. Moreover, cognitive reappraisal may lead to a heightened risk-taking and inhibit naturally occurring negative emotion (Heilman et al., 2010).

This alternative evidence is also supported by studies which showed that in Chinese populations, emotional suppression was shown to yield best psychological outcomes when compared with other ER strategies (Matsumoto et al., 2008; Soto et al., 2011; Nam et al., 2018). This highlights the need to explore cross-cultural differences as in nations with more rigid (less democratic) hierarchical and centralized societal-structures, emotion suppression may be more adaptive than reappraisal, whilst reappraisal may be more adaptive in libertarian western countries (Langner et al., 2012). Perhaps more flexible ways of regulating emotions, where one responds to situational demands, be it cultural, social, or physiological, in the pursuit of valued goals is important for mental well-being (Bonanno and Burton, 2013). HRV may be usefully applied as a biomarker of psychological and emotional flexibility (Gevirtz, 2015), and should be further explored in clinical settings.

Considerably less studies were identified which explored associations between interoception and ER, when compared to the literature on HRV. One reason may be that the research on interoception has traditionally focused on the neuroanatomical validation of the system, rather than exploring its wider psychosomatic implications (Ceunen et al., 2016). Secondly, the field is still relatively new, and still needs clear differentiation between the distinct facets of interoception, namely IAc, IA, and IS, as well as greater consensus on its heart beat measuring procedure (Kleckner et al., 2015; Forkmann et al., 2016).

Three studies recording baseline interoception were included in this review (Füstös et al., 2012; Kever et al., 2015; Pollatos et al., 2015). Kever and found that IS was greater in individuals applying either reappraisal or suppression strategies, with no statistical difference between the two, and lower in participants with overall reduced ERQ scores. Thus, IS seems to mediate greater ER regardless of the strategy employed by the participants. Furthermore, the results reported that females tend to utilize suppression more than males, highlighting gender differences in the selection of ER strategies. This highlights, again, the need to consider socio-anthropological factors, including socio-economic status and gender in the study of adaptive ER (Troy et al., 2017).

Füstös et al. (2012) showed that greater IA associated with higher emotional arousal when subjects viewed pictures with negative valence. Converging data from imaging studies has also demonstrated that greater interoceptive sensitivity is associated with greater sensitivity to emotional events (Pollatos et al., 2007). Moreover, it seems that increases in IAc drive short-term increases in sympathetic outputs, thus producing momentary reductions in HRV (Pollatos et al., 2012). In addition to this, in the same study by Füstös et al. (2012), when participants applied reappraisal ER to the negative pictures, those with higher IA were able to downregulate emotional arousal significantly better than subjects with lower IA.

Pollatos et al. (2015) demonstrated that people with higher IA were less prone to developing negative feelings when subjected to a social exclusion experiment (Cyberball paradigm), displaying flexible behaviors and ER strategies, as participants equally employed suppression and reappraisal. One expiation or these findings is that at the anterior insular, cingulate, and frontotemporal cortices, interoceptive information is integrated with auxiliary higher-order motivational inputs (Craig, 2009). This allows situational demands to be processed accordingly by executive functions (Garfinkel and Critchley, 2013; Adolfi et al., 2017), allowing for the flexible emotional strategies utilized.

In terms of implications, it is believed that interoceptive inputs are centrally integrated to produce meta-representations of "Self" necessary to mediate emotional responses. These, in turn, manifest via adaptive cognitive, behavioral, and autonomic responses. As the literature shows, dysfunctions within these systems may have pathological consequences both centrally (i.e., depression, anxiety, eating disorders) and peripherally (i.e., chronic pain) (Paulus and Stein, 2010; Klabunde et al., 2013; Di Lernia et al., 2016; Duschek et al., 2017). This work could help with indexing and diagnosing the psychophysiological etiology of the mental health dysfunction, combining with what is understood about HRV. For example, through understanding the individuals resting interoceptive and HRV states and their predicted (associated) outcomes, this may further inform practitioners about how to best to apply therapeutic techniques such as Cognitive Behavioral Therapy (CBT), mindfulness-based interventions, or ACT, which may interact with ER in different ways, thus improving patient-centered care.

Interoception has been linked with aspects of health and psychopathology whilst, concurrently, considerable evidence has explored the salient role of HRV, not only as a bio-marker of psychophysical health, but also as a direct modulator of central regulatory functions (Farb et al., 2015; Kemp et al., 2017). So, by targeting interventions which increase HRV via mind-body practices such as yoga, slow breathing and mindful meditation, beneficial changes can take place at central regulatory centers (Mather and Thayer, 2018), improving ER and ultimately well-being. Evidence has been mounting regarding the effectiveness of mind-body practices such as mindfulness at promoting restorative states alongside greater vagal activation (Sullivan et al., 2018; Zou et al., 2018), so these techniques are promising.

This work may also be considered complimentary to existing models of HRV and well-being. One example of this is the GENIAL (Genomics, Environment, vagus Nerve, social Interaction, Allostatic regulation, Longevity) model, which is behavioral, psychological and physiological model which identifies the vagus nerve indexed by HRV as an important mediator and moderator which influence social ties, subsequent health and well-being, as well as longevity (Kemp et al., 2017). Kemp et al. suggest that future research should initiate a multi-disciplinary focus to develop new lines of inquiry related to this. The findings from this systematic review, may therefore, help facilitate further expansion of the GENIAL model, with the incorporation of the predictive factors of interoceptive and emotional regulatory functions in the context of health and well-being. Such further development of the GENIAL model could help facilitate new diagnostic and prognosis tools in a clinical setting, as well as bespoke patient-centered interventions.

Of course, there are limitations with this study. First of all, the studies identified utilized homogeneous populations of, mostly, university students. Without longitudinal and population-based studies, it cannot be understood the exactly whether these findings can be generalized (Zwahlen and Salanti, 2018). Future studies should focus on longitudinal and population-based studies which incorporate both HRV and interoception in their design methodology. In addition to this, given the relatively small number of papers identified with association analyses between interoception and ER, correlational studies were included, but causality in these cannot be determined. Indeed, the fact that there are a limited number of papers identified in the final output selection means that any interpretations of these findings should be considered cautiously. More studies in the future with larger sample sizes and a greater variety of interoception as well as HRV indices should be considered.

Another potential limitation of this review was it did not identify the distinction between state and trait differences. These have been shown to exist for both HRV (Bertsch et al., 2012) and interoception (Wittkamp et al., 2018), and are typically indices which are stable (trait) or variable (state) over time. HRV and interoception state and trait studies explore temporal differences through latent state trait analysis (such as through repeated subject measures) as opposed to the largely cross-sectional studies explored in this review (only Koval et al. explored HRV as a trait through repeated measures).

These distinctions may be important to explore in the future as studies have suggested that when stable over time HRV, for instance, can be considered a trait characteristic, which can reflect a person's ability to adapt to situations (Thayer et al., 2009). So, the distinction between state and trait may be important when interpreting ER strategies to difficult situations (e.g., when adopting a psychologically flexible vs. avoidant strategy type). Unfortunately, there is simply not enough associational (prediction) studies available at present in order to draw distinctions between state and trait for this type of (prediction based) review. More studies in the future should explore state and trait differences specifically, and within the context of combined interoceptive and HRV associational studies.

A last potential limitation was that ER was assessed in a number of different modalities, comprising various questionnaires, attitudinal and cognitive-behavioral tasks. The lack of a standardized measurement procedure prevents precise comparisons between studies to made. Ideally, measuring methods should all assess the same aspect of ER and present an identifiable aspect of the task, a process defined as metrological traceability (Vesper et al., 2016).

In conclusion, HRV showed significant associations with better ER, largely predicting the use of reappraisal strategies over suppression. These findings are in line with the predominant trend of thought that regards reappraisal as the most adaptive strategy for regulating emotion. Studies considering the long-term regulation of emotions, cross-cultural, and gender differences in ER, however, seem to challenge this trend supporting the need for a flexible approach to emotions, that may involve either suppression or reappraisal dependent on the context. It is concluded here that high HRV should be considered as a biomarker of flexible ER. Despite the fewer studies scrutinizing interoception in ER, people with higher interoception scored higher on the ERQ, better handled negative emotions and feelings of social exclusion. These findings may provide evidence of bottom-up mechanisms of self-regulation and could help facilitate further adaptions on the existing GENIAL model. More research is needed to understand the specific causal order of influence between these constructs, and the peripheral interactions between interoceptive and parasympathetic systems. This may aid in the development of psychological interventions targeted toward these specific functions in a clinical setting and promote more bespoke and patient-centered care options.

AUTHOR CONTRIBUTIONS

TP designed this study with assistance from DE. TP and DE conducted the analysis equally and wrote the paper.

REFERENCES

(1996). Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *Circulation* 93, 1043–1065.

Adolfi, F., Couto, B., Richter, F., Decety, J., Lopez, J., Sigman, M., et al. (2017). Convergence of interoception, emotion, and social cognition: a twofold fMRI meta-analysis and lesion approach. *Cortex* 88, 124–142. doi: 10.1016/j.cortex.2016.12.019

Aldao, A. (2013). The future of emotion regulation research: capturing context. *Perspect. Psychol. Sci.* 8, 155–172. doi: 10.1177/1745691612459518

Aldao, A., Dixon-Gordon, K. L., and De Los Reyes, A. (2016). Individual differences in physiological flexibility predict spontaneous avoidance. *Cogn. Emot.* 30, 985–998. doi: 10.1080/02699931.2015.1042837

Aldao, A., Nolen-Hoeksema, S., and Schweizer, S. (2010). Emotion-regulation strategies across psychopathology: a meta-analytic review. *Clin. Psychol. Rev.* 30, 217–237. doi: 10.1016/j.cpr.2009.11.004

Banerjee, A., and Chaudhury, S. (2010). Statistics without tears: populations and samples. *Ind. Psychiatry J.* 19:60. doi: 10.4103/0972-6748.77642

Baumann, N., Kaschel, R., and Kuhl, J. (2007). Affect sensitivity and affect regulation in dealing with positive and negative affect. *J. Res. Pers.* 41, 239–248. doi: 10.1016/j.jrp.2006.05.002

Beauchaine, T. P., and Thayer, J. F. (2015). Heart rate variability as a transdiagnostic biomarker of psychopathology. *Int. J. Psychophysiol.* 98, 338–350. doi: 10.1016/j.ijpsycho.2015.08.004

Benarroch, E. E. (1993). "The central autonomic network: functional organization, dysfunction, and perspective," in *Paper Presented at the Mayo Clinic Proceedings*. doi: 10.1016/S0025-6196(12)62272-1

Bertsch, K., Hagemann, D., Naumann, E., Schächinger, H., and Schulz, A. (2012). Stability of heart rate variability indices reflecting parasympathetic activity. *Psychophysiology* 49, 672–682. doi: 10.1111/j.1469-8986.2011.01341.x

Bonanno, G. A., and Burton, C. L. (2013). Regulatory flexibility: an individual differences perspective on coping and emotion regulation. *Perspect. Psychol. Sci.* 8, 591–612. doi: 10.1177/1745691613504116

Bradley, B., DeFife, J., Guarnaccia, C., Phifer, J., Fani, N., Ressler, K., and Westen, D. (2011). Emotion dysregulation and negative affect: association with psychiatric symptoms. *J. Clin. Psychiatry* 72, 685–691. doi: 10.4088/JCP.10m06409blu

Breakwell, G. M., and Smith, J, A. (2012). *Research Methods in Psychology:* London: Sage Publications Ltd.

Brunoni, A. R., Kemp, A. H., Dantas, E. M., Goulart, A. C., Nunes, M. A., Boggio, P. S., et al. (2013). Heart rate variability is a trait marker of major depressive disorder: evidence from the sertraline vs. electric current therapy to treat depression clinical study. *Int. J. Neuropsychopharmacol.* 16, 1937–1949. doi: 10.1017/S1461145713000497

Buccelletti, E., Gilardi, E., Scaini, E., Galiuto, L., Persiani, R., Biondi, A., et al. (2009). Heart rate variability and myocardial infarction: systematic literature review and metanalysis. *Eur. Rev. Med. Pharmacol. Sci.* 13, 299–307.

Buhle, J. T., Silvers, J. A., Wager, T. D., Lopez, R., Onyemekwu, C., Kober, H., et al. (2014). Cognitive reappraisal of emotion: a meta-analysis of human neuroimaging studies. *Cerebral. Cortex* 24, 2981–2990. doi: 10.1093/cercor/bht154

Cameron, O. G. (2001). Interoception: the inside story—a model for psychosomatic processes. *Psychosom. Med.* 63, 697–710. doi: 10.1097/00006842-200109000-00001

Ceunen, E., Vlaeyen, J. W., and Van Diest, I. (2016). On the origin of interoception. *Front. Psychol.* 7:743. doi: 10.3389/fpsyg.2016.00743

Chalmers, J. A., Quintana, D. S., Abbott, M. J., and Kemp, A. H. (2014). Anxiety disorders are associated with reduced heart rate variability: a meta-analysis. *Front. Psychiatry* 5:80. doi: 10.3389/fpsyt.2014.00080

Chida, Y., and Steptoe, A. (2009). The association of anger and hostility with future coronary heart disease: a meta-analytic review of prospective evidence. *J. Am. Coll. Cardiol.* 53, 936–946. doi: 10.1016/j.jacc.2008.11.044

Cosmides, L., and Tooby, J. (2000). "Evolutionary psychology and the emotions," in *Handbook of Emotions*, *2nd Edn*, eds M. Lewis and J. M. Havilland-Jones (New York, NY: Guilford), 91–115.

Craig, A. D. (2002). How do you feel? Interoception: the sense of the physiological condition of the body. *Nat. Rev. Neurosci.* 3:655. doi: 10.1038/nrn894

Craig, A. D. (2008). "Interoception and emotion: a neuroanatomical perspective," *Handbook of Emotions* 3, 272–288.

Craig, A. D. (2009). How do you feel–now? The anterior insula and human awareness. *Nat. Rev. Neurosci.* 10, 59–70. doi: 10.1038/nrn2555

Craig, A. D. B. (2014). How do you feel? An interoceptive moment with your neurobiological self. 655–665 doi: 10.23943/princeton/9780691156767.001.0001

Damasio, A. (1999). *The Feeling of What Happens: Body and Emotion in the Making of Consciousness* Boston, MA: Houghton Mifflin Harcourt.

Damasio, A., and Carvalho, G. B. (2013). The nature of feelings: evolutionary and neurobiological origins. *Nat. Rev. Neurosci.* 14:143. doi: 10.1038/nrn3403

de Veld, D. M., Riksen-Walraven, J. M., and de Weerth, C. (2012). The relation between emotion regulation strategies and physiological stress responses in middle childhood. *Psychoneuroendocrinology* 37, 1309–1319. doi: 10.1016/j.psyneuen.2012.01.004

Debray, T. P., Damen, J. A., Snell, K. I., Ensor, J., Hooft, L., Reitsma, J. B., et al. (2017). A guide to systematic review and meta-analysis of prediction model performance. *BMJ* 356:i6460. doi: 10.1136/bmj.i6460

Di Lernia, D., Serino, S., and Riva, G. (2016). Pain in the body. Altered interoception in chronic pain conditions: a systematic review. *Neurosci. Biobehav. Rev.* 71, 328–341. doi: 10.1016/j.neubiorev.2016.09.015

Duschek, S., Montoro, C. I., and Reyes del Paso, G. A. (2017). Diminished interoceptive awareness in fibromyalgia syndrome. *Behav. Med.* 43, 100–107. doi: 10.1080/08964289.2015.1094442

Egloff, B., Schmukle, S. C., Burns, L. R., and Schwerdtfeger, A. (2006). Spontaneous emotion regulation during evaluated speaking tasks: associations with negative affect, anxiety expression, memory, and physiological responding. *Emotion* 6:356. doi: 10.1037/1528-3542.6.3.356

Enebrink, P., Björnsdotter, A., and Ghaderi, A. (2013). The emotion regulation questionnaire: psychometric properties and norms for Swedish parents of children aged 10-13 years. *Eur. J. Psychol.* 9, 289–303. doi: 10.5964/ejop.v9i2.535

Faraoni, D., and Schaefer, S. T. (2016). Randomized controlled trials vs. observational studies: why not just live together? *BMC Anesthesiol.* 16:102. doi: 10.1186/s12871-016-0265-3

Farb, N., Daubenmier, J., Price, C. J., Gard, T., Kerr, C., Dunn, B. D., et al. (2015). Interoception, contemplative practice, and health. *Front. Psychol.* 6:763. doi: 10.3389/fpsyg.2015.00763

Ford, B. Q., Lam, P., John, O. P., and Mauss, I. B. (2018). The psychological health benefits of accepting negative emotions and thoughts: laboratory, diary, and longitudinal evidence. *J. Pers. Soc. Psychol.* 115:1075. doi: 10.1037/pspp0000157

Forkmann, T., Scherer, A., Meessen, J., Michal, M., Schächinger, H., Vögele, C., and Schulz, A. (2016). Making sense of what you sense: disentangling interoceptive awareness, sensibility and accuracy. *Int. J. Psychophysiol.* 109, 71–80. doi: 10.1016/j.ijpsycho.2016.09.019

Fuster, J. (2015). *The Prefrontal Cortex*. Cambridge: Academic Press. doi: 10.1016/B978-0-12-407815-4.00002-7

Füstös, J., Gramann, K., Herbert, B. M., and Pollatos, O. (2012). On the embodiment of emotion regulation: interoceptive awareness facilitates reappraisal. *Soc. Cogn. Affect. Neurosci.* 8, 911–917. doi: 10.1093/scan/nss089

Garfinkel, S. N., and Critchley, H. D. (2013). Interoception, emotion and brain: new insights link internal physiology to social behaviour. Commentary on: "Anterior insular cortex mediates bodily sensibility and social anxiety" by Terasawa et al. (2012). *Soc. Cogn. Affect. Neurosci.* 8, 231–234. doi: 10.1093/scan/nss140

Garfinkel, S. N., Seth, A. K., Barrett, A. B., Suzuki, K., and Critchley, H. D. (2015). Knowing your own heart: distinguishing interoceptive accuracy from interoceptive awareness. *Biol. Psychol.* 104, 65–74. doi: 10.1016/j.biopsycho.2014.11.004

Garnefski, N., Kraaij, V., and Spinhoven, P. (2001). Negative life events, cognitive emotion regulation and emotional problems. *Pers. Individ. Dif.* 30, 1311–1327. doi: 10.1016/S0191-8869(00)00113-6

Geisler, F. C., Vennewald, N., Kubiak, T., and Weber, H. (2010). The impact of heart rate variability on subjective well-being is mediated by emotion regulation. *Pers. Individ. Dif.* 49, 723–728. doi: 10.1016/j.paid.2010.06.015

Gevirtz, R. (2015). Integrating heart rate variability biofeedback into mindfulness-based therapies. *Biofeedback* 43, 129–132. doi: 10.5298/1081-5937-43.3.03

Gorman, J. M. (2003). Treating generalized anxiety disorder. *J. Clin. Psychiatry* 64, 24–29.

Gratz, K. L., and Roemer, L. (2004). Multidimensional assessment of emotion regulation and dysregulation: development, factor structure, and initial validation of the difficulties in emotion regulation scale. *J. Psychopathol. Behav. Assess* 26, 41–54. doi: 10.1023/B:JOBA.0000007455.08539.94

Gross, J. J. (1998). The emerging field of emotion regulation: an integrative review. *Rev. General Psychol.* 2, 271–299. doi: 10.1037/1089-2680.2.3.271

Gross, J. J., and John, O. P. (2003). Individual differences in two emotion regulation processes: implications for affect, relationships, and well-being. *J. Pers. Soc. Psychol*. 85:348. doi: 10.1037/0022-3514.85.2.348

Gross, J. J., and Levenson, R. W. (1993). Emotional suppression: physiology, self-report, and expressive behavior. *J. Pers. Soc. Psychol*. 64:970. doi: 10.1037/0022-3514.64.6.970

Gyurak, A., Gross, J. J., and Etkin, A. (2011). Explicit and implicit emotion regulation: a dual-process framework. *Cognition Emotion* 25, 400–412. doi: 10.1080/02699931.2010.544160

Hansen, A. L., Johnsen, B. H., and Thayer, J. F. (2009). Relationship between heart rate variability and cognitive function during threat of shock. *Anxiety Stress Coping* 22, 77–89. doi: 10.1080/10615800802272251

Hansen, A. L., Johnsen, B. H., Thornton, D., Waage, L., and Thayer, J. F. (2007). Facets of psychopathy, heart rate variability and cognitive function. *J. Pers. Disord.* 21, 568–582. doi: 10.1521/pedi.2007.21.5.568

Hayes, S. C., Strosahl, K. D., and Wilson, K. G. (2009). *Acceptance and Commitment Therapy*. New York, NY: Guilford Press; American Psychological Association.

Hayes, S. C., and Strosahl, K. D. (2004). *A Practical Guide to Acceptance and Commitment Therapy*. Berlin: Springer Science & Business Media. doi: 10.1007/978-0-387-23369-7

Heilman, R. M., Crişan, L. G., Houser, D., Miclea, M., and Miu, A. C. (2010). Emotion regulation and decision making under risk and uncertainty. *Emotion* 10:257. doi: 10.1037/a0018489

Higgins, J. P., and Green, S. (2011). *Cochrane Handbook for Systematic Reviews of Interventions*, Vol. 4. New York, NY: John Wiley & Sons.

Hillebrand, S., Gast, K. B., de Mutsert, R., Swenne, C. A., Jukema, J. W., Middeldorp, S., et al. (2013). Heart rate variability and first cardiovascular event in populations without known cardiovascular disease: meta-analysis and dose–response meta-regression. *Europace* 15, 742–749. doi: 10.1093/europace/eus341

Holzman, J. B., and Bridgett, D. J. (2017). Heart rate variability indices as biomarkers of top-down self-regulatory mechanisms: a meta-analytic review. *Neurosci. Biobehav. Rev.* 74, 233–255. doi: 10.1016/j.neubiorev.2016.12.032

Hovland, A., Pallesen, S., Hammar, Å., Hansen, A. L., Thayer, J. F., Tarvainen, M. P., and Nordhus, I. H. (2012). The relationships among heart rate variability, executive functions, and clinical variables in patients with panic disorder. *Int. J. Psychophysiol.* 86, 269–275. doi: 10.1016/j.ijpsycho.2012.10.004

Jazaieri, H., Urry, H. L., and Gross, J. J. (2013). Affective disturbance and psychopathology: an emotion regulation perspective. *J. Exp. Psychopathol.* 4, 584–599. doi: 10.5127/jep.030312

Jennings, J. R., Allen, B., Gianaros, P. J., Thayer, J. F., and Manuck, S. B. (2015). Focusing neurovisceral integration: cognition, heart rate variability, and cerebral blood flow. *Psychophysiology* 52, 214–224. doi: 10.1111/psyp.12319

Kemp, A. H., Arias, J. A., and Fisher, Z. (2017). Social ties, health and wellbeing: a literature review and model," in *Neuroscience and Social Science* (Berlin: Springer), 397–427. doi: 10.1007/978-3-319-68421-5_17

Kemp, Q.uintana, D. S., Gray, M. A., Felmingham, K. L., Brown, K., and Gatt, J. M. (2010). Impact of depression and antidepressant treatment on heart rate variability: a review and meta-analysis. *Biol. Psychiatry* 67, 1067–1074. doi: 10.1016/j.biopsych.2009.12.012

Kever, A., Pollatos, O., Vermeulen, N., and Grynberg, D. (2015). Interoceptive sensitivity facilitates both antecedent-and response-focused emotion regulation strategies. *Pers. Individ. Dif*. 87, 20–23. doi: 10.1016/j.paid.2015.07.014

Kiecolt-Glaser, J. K., McGuire, L., Robles, T. F., and Glaser, R. (2002). Psychoneuroimmunology: psychological influences on immune function and health. *J. Consult. Clin. Psychol*. 70:537. doi: 10.1037/0022-006X.70.3.537

Klabunde, M., Acheson, D. T., Boutelle, K. N., Matthews, S. C., and Kaye, W. H. (2013). Interoceptive sensitivity deficits in women recovered from bulimia nervosa. *Eat. Behav*. 14, 488–492. doi: 10.1016/j.eatbeh.2013.08.002

Kleckner, I. R., Wormwood, J. B., Simmons, W. K., Barrett, L. F., and Quigley, K. S. (2015). Methodological recommendations for a heartbeat detection-based measure of interoceptive sensitivity. *Psychophysiology* 52, 1432–1440. doi: 10.1111/psyp.12503

Kolacz, J., and Porges, S. W. (2018). Chronic diffuse pain and functional gastrointestinal disorders after traumatic stress: pathophysiology through a polyvagal perspective. *Front. Med.* 5:145. doi: 10.3389/fmed.2018.00229

Koole, S. L., Van Dillen, L. F., and Sheppes, G. (2011). "The self-regulation of emotion," in *Handbook of Self-Regulation: Research, Theory, and Applications* (New York, NY), 2, 22–40.

Koval, P., Ogrinz, B., Kuppens, P., Van den Bergh, O., Tuerlinckx, F., and Sütterlin, S. (2013). Affective instability in daily life is predicted by resting heart rate variability. *PLoS ONE*. 8:e81536. doi: 10.1371/journal.pone.0081536

Kreibig, S. D. (2010). Autonomic nervous system activity in emotion: a review. *Biol. Psychol.* 84, 394–421. doi: 10.1016/j.biopsycho.2010.03.010

Laborde, S., Mosley, E., and Mertgen, A. (2018). Vagal tank theory: the three rs of cardiac vagal control functioning–resting, reactivity, and recovery. *Front. Neurosci.* 12:458. doi: 10.3389/fnins.2018.00458

Langner, C. A., Epel, E. S., Matthews, K. A., Moskowitz, J. T., and Adler, N. E. (2012). Social hierarchy and depression: the role of emotion suppression. *J. Psychol.* 146, 417–436. doi: 10.1080/00223980.2011.652234

Lazarus, R. S. (1991). Progress on a cognitive-motivational-relational theory of emotion. *Am. Psychol.* 46:819. doi: 10.1037/0003-066X.46.8.819

Lucas, A. R., Klepin, H. D., Porges, S. W., and Rejeski, W. J. (2018). Mindfulness-based movement: a polyvagal perspective. *Integr. Cancer Ther*. 17, 5–15. doi: 10.1177/1534735416682087

Mather, M., and Thayer, J. F. (2018). How heart rate variability affects emotion regulation brain networks. *Curr. Opin. Behav. Sci.* 19, 98–104. doi: 10.1016/j.cobeha.2017.12.017

Matsumoto, D., Yoo, S. H., and Nakagawa, S. (2008). Culture, emotion regulation, and adjustment. *J. Pers. Soc. Psychol.* 94:925. doi: 10.1037/0022-3514.94.6.925

Matthews, G., Jones, D. M., and Chamberlain, A. G. (1990). Refining the measurement of mood: the UWIST mood adjective checklist. *British J. Psychol.* 81, 17–42. doi: 10.1111/j.2044-8295.1990.tb02343.x

Mauss, I. B., Levenson, R. W., McCarter, L., Wilhelm, F. H., and Gross, J. J. (2005). The tie that binds? Coherence among emotion experience, behavior, and physiology. *Emotion* 5:175. doi: 10.1037/1528-3542.5.2.175

Mcclure, K. S., Halpern, J., Wolper, P. A., and Donahue, J. (2009). Emotion regulation and intellectual disability. *J. Dev. Disabil.* 15, 38–44.

Mennin, D. S., McLaughlin, K. A., and Flanagan, T. J. (2009). Emotion regulation deficits in generalized anxiety disorder, social anxiety disorder, and their co-occurrence. *J. Anxiety Disord*. 23, 866–871. doi: 10.1016/j.janxdis.2009.04.006

Moher, D., Liberati, A., Tetzlaff, J., and Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann. Intern. Med.* 151, 264–269. doi: 10.7326/0003-4819-151-4-200908180-00135

Moons, K. G., de Groot, J. A., Bouwmeester, W., Vergouwe, Y., Mallett, S., Altman, D. G., et al. (2014). Critical appraisal and data extraction for systematic reviews of prediction modelling studies: the CHARMS checklist. *PLoS Med.* 11:e1001744. doi: 10.1371/journal.pmed.1001744

Murphy, F. C., Nimmo-Smith, I., and Lawrence, A. D. (2003). Functional neuroanatomy of emotions: a meta-analysis. *Cogn. Affect. Behav. Neurosci.* 3, 207–233. doi: 10.3758/CABN.3.3.207

Nam, Y., Kim, Y.-H., and Tam, K. K.-P. (2018). Effects of emotion suppression on life satisfaction in Americans and Chinese. *J. Cross Cult. Psychol.* 49, 149–160. doi: 10.1177/0022022117736525

Ochsner, K. N., and Gross, J. J. (2005). The cognitive control of emotion. *Trends Cogn. Sci.* 9, 242–249. doi: 10.1016/j.tics.2005.03.010

Owens, A. P., Friston, K. J., Low, D. A., Mathias, C. J., and Critchley, H. D. (2018). Investigating the relationship between cardiac interoception and autonomic cardiac control using a predictive coding framework. *Autonomic Neurosci.* 210, 65–71. doi: 10.1016/j.autneu.2018.01.001

Park, G., and Thayer, J. F. (2014). From the heart to the mind: cardiac vagal tone modulates top-down and bottom-up visual perception and attention to emotional stimuli. *Front. Psychol.* 5:278. doi: 10.3389/fpsyg.2014.00278

Paulus, M. P., and Stein, M. B. (2010). Interoception in anxiety and depression. *Brain Struct. Funct.* 214, 451–463. doi: 10.1007/s00429-010-0258-9

Pollatos, O., Füstös, J., and Critchley, H. D. (2012). On the generalised embodiment of pain: how interoceptive sensitivity modulates cutaneous pain perception. *Pain* 153, 1680–1686. doi: 10.1016/j.pain.2012.04.030

Pollatos, O., Gramann, K., and Schandry, R. (2007). Neural systems connecting interoceptive awareness and feelings. *Hum Brain Mapp.* 28, 9–18. doi: 10.1002/hbm.20258

Pollatos, O., Matthias, E., and Keller, J. (2015). When interoception helps to overcome negative feelings caused by social exclusion. *Front. Psychol.* 6:786. doi: 10.3389/fpsyg.2015.00786

Pollatos, O., Traut-Mattausch, E., and Schandry, R. (2009). Differential effects of anxiety and depression on interoceptive accuracy. *Depress. Anxiety* 26, 167–173. doi: 10.1002/da.20504

Porges, S. W. (1991). "Vagal tone: an autonomic mediator of affect," in *Cambridge Studies in Social and Emotional Development. The Development of Emotion Regulation and Dysregulation*, eds J. Garber and K. A. Dodge (Cambridge: Cambridge University Press), 111–128. doi: 10.1017/CBO9780511663963.007

Porges, S. W. (2007a). A phylogenetic journey through the vague and ambiguous Xth cranial nerve: a commentary on contemporary heart rate variability research. *Biol. Psychol.* 74, 301–307. doi: 10.1016/j.biopsycho.2006.08.007

Porges, S. W. (2007b). The polyvagal perspective. *Biol. Psychol.* 74, 116–143. doi: 10.1016/j.biopsycho.2006.06.009

Porges, S. W. (2011). *The Polyvagal Theory: Neurophysiological Foundations of Emotions, Attachment, Communication, and Self-Regulation (Norton Series on Interpersonal* Neurobiology). New York, NY: WW Norton & Company.

Porges, S. W. (2017). "Vagal pathways: portals to compassion," in *The Oxford Handbook of Compassion Science* (Oxford: Oxford University Press). 189–204.

Porges, S. W., and Center, B.-B. (2018). *Polyvagal Theory: A Primer. Clinical Applications of the Polyvagal Theory: the Emergence of Polyvagal-Informed Therapies*. New York, NY: WW Norton & Company.

Pressman, S. D., and Cohen, S. (2005). Does positive affect influence health? *Psychol. Bull* 131:925. doi: 10.1037/0033-2909.131.6.925

Riganello, F., Larroque, S. K., Bahri, M. A., Heine, L., Martial, C., Carrière, M., et al. (2018). A heartbeat away from consciousness: heart rate variability entropy can discriminate disorders of consciousness and is correlated with resting-state fMRI brain connectivity of the central autonomic network. *Front. Neurol.* 9:769. doi: 10.3389/fneur.2018.00769

Schandry, R. (1981). Heart beat perception and emotional experience. *Psychophysiology* 18, 483–488. doi: 10.1111/j.1469-8986.1981.tb02486.x

Schulz, A., Lass-Hennemann, J., Sütterlin, S., Schächinger, H., and Vögele, C. (2013). Cold pressor stress induces opposite effects on cardioceptive accuracy dependent on assessment paradigm. *Biol. Psychol.* 93, 167–174. doi: 10.1016/j.biopsycho.2013.01.007

Smith, R., Thayer, J. F., Khalsa, S. S., and Lane, R. D. (2017). The hierarchical basis of neurovisceral integration. *Neurosci. Biobehav. Rev.* 75, 274–296. doi: 10.1016/j.neubiorev.2017.02.003

Song and Chung. (2010). Observational studies: cohort and case-control studies. *Plast. Reconstr. Surg*. 126:2234. doi: 10.1097/PRS.0b013e3181f44abc

Sørensen, H. T., Lash, T. L., and Rothman, K. J. (2006). Beyond randomized controlled trials: a critical comparison of trials with nonrandomized studies. *Hepatology* 44, 1075–1082. doi: 10.1002/hep.21404

Soto, J. A., Perez, C. R., Kim, Y.-H., Lee, E. A., and Minnick, M. R. (2011). Is expressive suppression always associated with poorer psychological functioning? A cross-cultural comparison between European Americans and Hong Kong Chinese. *Emotion* 11:1450. doi: 10.1037/a0023340

Stange, J. P., Hamilton, J. L., Fresco, D. M., and Alloy, L. B. (2017). Flexible parasympathetic responses to sadness facilitate spontaneous affect regulation. *Psychophysiology* 54, 1054–1069. doi: 10.1111/psyp.12856

Strigo, I. A., and Craig, A. D. (2016). Interoception, homeostatic emotions and sympathovagal balance. *Philos. Trans. Royal Soc. B Biol. Sci.* 371:20160010. doi: 10.1098/rstb.2016.0010

Strosahl, K., and Wilson, K. (1999). *Acceptance and Commitment Therapy: An Experiential Approach to Behavior Change*. New York, NY: Guilford Press.

Sullivan, M. B., Erb, M., Schmalzl, L., Moonaz, S., Noggle Taylor, J., and Porges, S. W. (2018). Yoga therapy and polyvagal theory: the convergence of traditional wisdom and contemporary neuroscience for self-regulation and resilience. *Front. Hum. Neurosci*. 12:67. doi: 10.3389/fnhum.2018.00067

Teper, R., Segal, Z. V., and Inzlicht, M. (2013). Inside the mindful mind: how mindfulness enhances emotion regulation through improvements in executive control. *Curr. Dir. Psychol. Sci.* 22, 449–454. doi: 10.1177/0963721413495869

Thayer, J. F. (2009). "Heart rate variability: a neurovisceral integration model," in *Encyclopedia of Neuroscience*, ed L. R. Squire (Oxford: Academic Press), 1041–1047.

Thayer, J. F., Hansen, A. L., Saus-Rose, E., and Johnsen, B. H. (2009). Heart rate variability, prefrontal neural function, and cognitive performance: the neurovisceral integration perspective on self-regulation, adaptation, and health. *Ann. Behav. Med.* 37, 141–153. doi: 10.1007/s12160-009-9101-z

Thayer, J. F., and Lane, R. D. (2000). A model of neurovisceral integration in emotion regulation and dysregulation. *J. Affect. Disord* 61, 201–216. doi: 10.1016/S0165-0327(00)00338-4

Thayer, J. F., and Lane, R. D. (2007). The role of vagal function in the risk for cardiovascular disease and mortality. *Biol. Psychol.* 74, 224–242. doi: 10.1016/j.biopsycho.2005.11.013

Thompson, R. A. (1994). Emotion regulation: a theme in search of definition. *Monogr. Soc. Res. Child Dev.* 59, 25–52. doi: 10.1111/j.1540-5834.1994.tb01276.x

Troy, A. S., Ford, B. Q., McRae, K., Zarolia, P., and Mauss, I. B. (2017). Change the things you can: emotion regulation is more beneficial for people from lower than from higher socioeconomic status. *Emotion* 17:141. doi: 10.1037/emo0000210

Troy, A. S., Shallcross, A. J., and Mauss, I. B. (2013). A person-by-situation approach to emotion regulation: cognitive reappraisal can either help or hurt, depending on the context. *Psychol. Sci.* 24, 2505–2514. doi: 10.1177/0956797613496434

van't Wout, M., Chang, L. J., and Sanfey, A. G. (2010). The influence of emotion regulation on social interactive decision-making. *Emotion* 10:815. doi: 10.1037/a0020069

Vesper, H. W., Myers, G. L., and Miller, W. G. (2016). Current practices and challenges in the standardization and harmonization of clinical laboratory tests. *Am. J. Clin. Nutr.* 104(Suppl_3), 907S–912S. doi: 10.3945/ajcn.115.110387

Visted, E., Sørensen, L., Osnes, B., Svendsen, J. L., Binder, P.-E., and Schanche, E. (2017). The association between self-reported difficulties in emotion regulation and heart rate variability: the salient role of not accepting negative emotions. *Front. Psychol.* 8:328. doi: 10.3389/fpsyg.2017.00328

Walker, H. K. (1990). "Cranial nerve XI: the spinal accessory nerve," in *Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd edition*. Oxford: Butterworths.

Williams, D. P., Cash, C., Rankin, C., Bernardi, A., Koenig, J., and Thayer, J. F. (2015). Resting heart rate variability predicts self-reported difficulties in emotion regulation: a focus on different facets of emotion regulation. *Front. Psychol.* 6:261. doi: 10.3389/fpsyg.2015.00261

Williamson, J. B., Porges, E. C., Lamb, D. G., and Porges, S. W. (2015). Maladaptive autonomic regulation in PTSD accelerates physiological aging. *Front. Psychol.* 5:1571. doi: 10.3389/fpsyg.2014.01571

Wilson, D. S., and Sober, E. (1994). Reintroducing group selection to the human behavioral sciences. *Behav. Brain Sci.* 17, 585–608. doi: 10.1017/S0140525X00036104

Wittkamp, M. F., Bertsch, K., Vögele, C., and Schulz, A. (2018). A latent state-trait analysis of interoceptive accuracy. *Psychophysiology* 55:e13055. doi: 10.1111/psyp.13055

Yuan, H., and Silberstein, S. D. (2016). Vagus nerve and vagus nerve stimulation, a comprehensive review: part I. *Headache* 56, 71–78. doi: 10.1111/head.12647

Zou, L., Sasaki, J., Wei, G.-X., Huang, T., Yeung, A., Neto, O., et al. (2018). Effects of mind–body exercises (Tai Chi/Yoga) on heart rate variability parameters and perceived stress: a systematic review with meta-analysis of randomized controlled trials. *J. Clin. Med.* 7:404. doi: 10.3390/jcm7110404

Zwahlen, M., and Salanti, G. (2018). Causal inference from experiment and observation. *Evid Based Ment. Health* 21, 34–38. doi: 10.1136/eb-2017-102859

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Physical Comorbidity and Health Literacy Mediate the Relationship Between Social Support and Depression Among Patients With Hypertension

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Depression is a common comorbidity among patients with hypertension. Patients with hypertension and depression have worse health outcomes compared to those without depression. The combined effects of social support, physical comorbidity, and health literacy on depression among individuals with hypertension remain unclear. A survey was conducted between December 2017 and May 2018 to investigate the relationships among social support, physical comorbidity, health literacy, and depression in a population of patients with hypertension in rural areas of Sichuan province, China. Multiple linear regression was used to examine factors that influenced depression, and structural equation modeling (SEM) was used to examine the relationships among the four study variables. The mean scores of 549 patients with hypertension were 37.17 ± 6.84 for social support, 14.62 ± 6.26 for health literacy, and 3.56 ± 3.05 for depression; furthermore, 34.2% of participants had physical comorbidity. Gender and per capita annual family income were significantly associated with depression. Physical comorbidity was directly positively related to depression while health literacy was directly negatively related to depression. Social support had an indirect negative association with depression by the mediating effects of health literacy and physical comorbidity. Adequate social support and health literacy, and less physical comorbidity could potentially contribute to reducing depression. The study highlights the importance of social support in maintaining mental health among patients with hypertension. Strategies that target the enhancement of social support and health literacy should be prioritized to relieve depression among patients with hypertension. More attention should be paid to women, low-income individuals, and patients with physical comorbidities.

Keywords: social support, physical comorbidity, health literacy, depression, hypertension

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INTRODUCTION

Hypertension is one of the most severe chronic diseases and a leading cause of mortality and disability, causing almost 10 million deaths worldwide in 2013 and accounting for 7% of global Disability Adjusted Life Years lost (1). By 2025, ~29% of the world's population is expected to have this disease. In China, successive population surveys have reported an increasing prevalence of hypertension, with the disease affecting 18.8% of the population in 2002 (2) and 27.8% in 2014 (3). Given the rapidly increasing prevalence of hypertension and the burden of disease, its timely and effective control and management has become a basic public health service priority in China.

Depression is recognized as the fourth leading contributor to the global burden of disease (4). By 2020, the burden of depression is projected to account for 5.7% of the total disease burden (1). Clinical depression or depressive disorder is a common comorbidity among individuals with hypertension and epidemiological studies have demonstrated an increased co-occurrence of depression with hypertension (5). Depressive mood is a risk factor for the development of high blood pressure and is known to increase the occurrence of uncontrolled hypertension (6, 7). Patients with hypertension and depression have worse health status, poorer quality of life, impaired well-being, higher health care expenditure, and increased mortality compared to those without depression (7–10). In addition, depression can mask or mimic the symptoms of chronic medical illnesses and anti-depression medications may interact pharmacologically with anti-hypertensive medications, complicating treatment and resulting in poor prognosis (11). These findings emphasize the importance of addressing depression in patients with hypertension.

Social support refers to the "social resources that persons perceive to be available or that are provided to them." Prior studies have demonstrated the association between inadequate social support and depression among patients with hypertension (12–14). Poor social support has also been linked to poor adherence to anti-hypertension treatment and poor blood pressure control (15–17) and may thus cause poor prognosis and eventually affect the mental state of patients with hypertension. In a study of Korean elderly patients with hypertension, both social support and depression were influencing factors of self-care behavior (18).

Physical comorbidity refers to a person suffering from two or more physical diseases at the same time. Physical comorbidity appears to have an impact on depression. In the general population, somatic comorbidity is associated with depression (19). The presence of comorbid chronic diseases is associated with depressive symptoms in older patients with hypertension (12). In addition, persistent depression is significantly more likely to occur in veterans with hypertension and multi-morbidity than in those with only hypertension (20). Health literacy is defined as the "degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions" (21). Previous studies have demonstrated that poor literacy is associated with higher levels of depressive symptoms in populations of US smokers with low socioeconomic status, US adults with addictions, and Korean adults (22–24). Additionally, a study of patients with diabetes indicated that depression may reduce the positive effect of health literacy on self-management (25). Among patients with hypertension, associations between health literacy and medication adherence, hypertension management and control, clinical outcomes (e.g., systolic and diastolic blood pressure), and health-related quality of life have been noted (26–30). However, the relationship between health literacy and depression among patients with hypertension remains unclear.

The prevalence of hypertension in China is increasing more rapidly in rural areas than in urban areas (31). This tendency is related to the adoption of urban lifestyles due to economic development, along with improved diagnostics (32, 33). Due to a lack of contact opportunity, as well as their lower financial and education level, rural individuals with hypertension have poor social support and health literacy (34, 35). Further, hypertension has been effectively controlled in a low percentage of these patients (31), thereby increasing their difficulty in coping with depressive symptoms and the possibility of developing other physical comorbidities. This study focuses on patients with hypertension in rural areas.

Most previous studies examined the associations between social support, physical comorbidity, health literacy, and depression; however, the combined effects of these factors on depression and the underlying mechanisms of those relationships remain unclear. Social support has been positively associated with health literacy among patients with chronic kidney disease and patients with coronary heart disease (36, 37). The mediating role of health literacy between subjective social status and depressive symptoms has also been noted (38). Therefore, we speculated that health literacy may be a potential mediator between social support and depression among hypertensive patients. In addition, prior research has demonstrated the relationship between lower social support and increased comorbidity, as well as the interactions of social support and multiple physical chronic conditions in explaining depression among the elderly (39, 40). Thus, we hypothesized the mediation effect of physical comorbidity on the association between social support and depression among hypertensive patients. Moreover, health literacy has been shown to be independently related to disease knowledge (41). Suffering from physical comorbidity may increase hypertension patients' knowledge of multiple diseases, thus potentially improving their health literacy.

Structural equation modeling (SEM) is an ideal data analytic technique to study the interrelationships between latent variables, which cannot be measured directly. These include social support, health literacy, and depression in the current research. Additionally, this model can be used to test the mediating effect by path analysis (42). We constructed a structural equation model to explore the association between social support and depression, as well as to examine whether this relationship could be explained by the mediation effects of physical comorbidity and health literacy in patients with hypertension. We hope to eventually provide reference for interventions targeting the improvement of the mental health of patients with hypertension. According to the theoretical framework mentioned above, we developed the hypotheses shown in **Table 1**, which correspond to the structural equation model shown in **Figure 1**.

MATERIALS AND METHODS

Sample

We conducted a cross-sectional study in Sichuan Province, China, between December 2017 and May 2018. The sample size

TABLE 1 | The theoretical hypotheses.

1. Social support has a direct negative relationship with depression.
2. Physical comorbidity has a direct positive relationship with depression.
3. Health literacy has a direct negative relationship with depression.
4. Social support has a direct negative relationship with physical comorbidity.
5. Social support has a direct positive relationship with health literacy.
6. Physical comorbidity has a direct positive relationship with health literacy.
7. The relationship between social support and depression is mediated by physical comorbidity.
8. The relationship between social support and depression is mediated by health literacy.
9. The relationship between social support and health literacy is mediated by physical comorbidity.
10. The relationship between physical comorbidity and depression is mediated by health literacy.

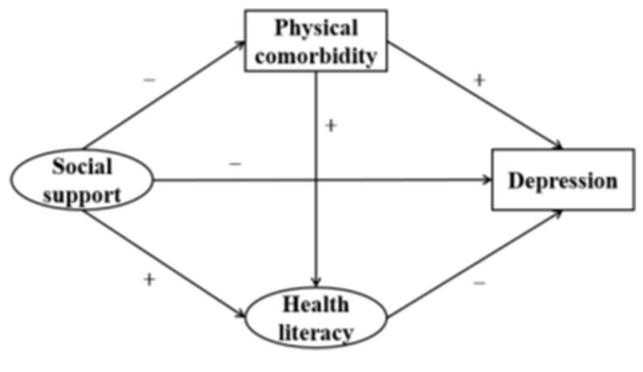

FIGURE 1 | Theoretical model and hypotheses.

was calculated using the formula: $n = \left(\frac{Z\alpha/2}{\delta}\right)^2 \times \pi \times (1-\pi)$; $\pi = 5.7\%$, the depression rate of patients with hypertension in a community-based study conducted in 2014 (43), $\delta = 2\%$, $\alpha = 0.05$, and $Z\alpha/2 = 1.96$. According to the formula, the sample size was calculated as 516. Considering possible dropout, we increased the sample size by 20% to 600. We randomly selected a city in Sichuan Province and 10 townships in rural areas of the city were randomly selected as survey areas. We used systematic sampling to obtain 60 subjects from a database of patients with hypertension established by each township hospital. Therefore, 600 patients with hypertension were interviewed face to face by professionally trained investigators. To ensure the quality of the investigation, we set the following exclusion criteria: (1) patients who could not properly answer questions due to physical disability or cognitive impairment, and (2) those unable to cooperate for personal reasons (they had the freedom to withdraw without consequence). According to these standards, 549 (91.5%) valid responses were ultimately analyzed. All of the participants signed to convey their informed consent before the investigation and were voluntary in their participation. The ethical approval of the data collection was given by the ethics committee of Sichuan University.

Instruments

The questionnaire included five domains: socio-demographics, social support, physical comorbidity, health literacy, and depression.

Socio-Demographics

Socio-demographics consisted of gender, age, education, marital status, per capita annual household income, and living arrangements. Age was categorized as <60, 60–69, 70–79, and ≥80 years. Educational level was divided into "no formal education," "primary school," and "middle school and above." Marital status was defined as a binary variable: "married with spouse" and "divorced, widowed, or unmarried." Per capita annual household income was classified into three categories: <\$750, \$750–1499, and ≥\$1500. Living arrangements were defined as "living with family members" or "living alone."

Social Support

Social support was assessed through The Social Support Rating Scale (44). This scale was specifically designed for use in a Chinese context. It contains three subscales: subjective support (the level of perceived support), objective support (the level of actual or visible support), and support utilization (the degree to which available support was used). Subjective support is assessed via four items, with a possible score range of 8–32; objective support is assessed via three items, with a possible score range of 1–22; and support utilization is assessed via three items, with a possible score range of 3–12. The total score of the scale ranges from 12 to 66, whereby higher scores reflect better social support. It is generally considered that a score from 12 to 22 indicates a low level of social support, 23–44 indicates moderate support, and 45–66 indicates high support (45). This scale had a reported Cronbach's α coefficient of 0.89 and a test–retest reliability of 0.92 in prior research (44).

Health Literacy

A modified version of The Chinese Citizen Health Literacy Questionnaire, developed by the National Health Commission of the People's Republic of China, was used to assess health literacy. Representative questions related to health literacy among patients with hypertension were selected by experts. To improve the study questionnaire, we added questions addressing individuals' knowledge of the prevention and control of common chronic disease. The questionnaire contained three dimensions: knowledge and belief literacy, behavior literacy, and skill literacy, with 33 items and a total possible score of 33. Respondents who correctly answered 80% or more of the questions were regarded as having good health literacy (46). In the current study, this scale has a Cronbach's α coefficient of 0.864.

Physical Comorbidity

The physical comorbidity data concerned physical conditions that had been diagnosed by a health professional and that were expected to persist or had already persisted for 6 months or more. The number of physical comorbidities other than hypertension was calculated and categorized as 0, 1, or 2+.

Depression

Depression was measured using the Centre for Epidemiologic Studies Depression Scale 10-item version (CESD-10), which has been demonstrated to appropriately reflect depressive symptoms experienced in the previous week (47). The CESD-10 includes three items addressing depressed affect, five items addressing somatic symptoms, and two items addressing positive affect. Options for each item range from "rarely or none of the time" (score of 0) to "all of the time" (score of 3). Scoring is reversed for items 5 and 8, which are positive affect statements. Total scores can range from 0 to 30. Scores of 10 or over indicate clinically relevant depression (47). The scale has excellent internal reliability (Cronbach's $\alpha = 0.80$) and good validity (48).

Data Management and Analysis

A database was established using EpiData Version 3.1, and statistical analyses were conducted using SPSS 21.0 and AMOS 20.0. First, descriptive statistics (frequencies, percentages, means, and standard deviations) were calculated to describe the sample. Next, we obtained Pearson correlations to explore the relationships among social support, physical comorbidity, health literacy, and depression. Multiple linear regression was used to estimate associations between the independent variables and depression. Finally, SEM was used to test the hypotheses. We used the subscale scores of social support and health literacy as measurement variables and the total scores of these measures as latent variables. Physical comorbidity and depression were included as measurement variables. Statistical significance was set at $P < 0.05$.

RESULTS

Descriptive Statistics

Descriptive statistics of the sample are displayed in **Table 2**. Our sample contained 343 women (62.5%) and 206 men (37.5%). The highest proportion was 60–69 years old (41.2%), with a primary school education (52.1%). Most were married (78.0%) and lived with family members (90.0%). Most participants had a per capita annual household income in the $750–1499 range (47.0%).

The mean scores for social support, health literacy, and depression were 37.17 ± 6.84, 14.62 ± 6.26, and 3.56 ± 3.05, respectively. The proportion of individuals with a high level of social support was 16.9%, and only 5.6% of the subjects had adequate health literacy. In addition, 6.0% of the patients with hypertension had depressive symptoms. The proportion of participants with physical comorbidity was 34.2%. Type 2 diabetes mellitus ranked first in the number of physical comorbidities. The percentage of people with various physical comorbidities is also displayed in the table.

Correlations Between Study Variables

Correlations between key variables are presented in **Table 3**. Social support was positively correlated with health literacy but negatively correlated with physical comorbidity and depression. There was a significant positive correlation between physical comorbidity and health literacy and depression. Health literacy was significantly negatively correlated with depression.

TABLE 2 | Descriptive results of the sample.

Variable	*N* (%), Mean ± SD
Gender	
Men	206 (37.5)
Women	343 (62.5)
Age (years)	
<60	87 (15.8)
60–69	226 (41.2)
70–79	188 (34.3)
≥80	48 (8.7)
Education	
No formal education	123 (22.4)
Primary school	286 (52.1)
Middle school and above	140 (25.5)
Marital status	
Married have spouses	428 (78.0)
Divorced, widowed, or unmarried	121 (22.0)
Per capita annual household income, $	
<750	124 (22.6)
750–1499	258 (47.0)
≥1500	167 (30.4)
Living arrangements	
Living with family members	494 (90.0)
Living alone	55 (10.0)
Physical comorbidities	
0	361 (65.8)
1	138 (25.1)
2∼	50 (9.1)
Type 2 diabetes mellitus	93 (34.7)
Chronic tracheitis/bronchitis	35 (13.1)
Hyperlipemia	22 (8.2)
Chronic gastrointestinal diseases	21 (7.8)
Hyperosteogeny	20 (7.5)
Coronary disease	19 (7.1)
Lumbar disc protrusion	19 (7.1)
Others	39 (14.5)
Social support	37.17 ± 6.84
Subjective support	22.79 ± 2.42
Objective support	7.91 ± 2.42
Support utilization	6.47 ± 2.08
Health literacy	14.62 ± 6.26
Knowledge and belief literacy	8.60 ± 4.83
Behavior literacy	4.79 ± 1.71
Skill literacy	1.23 ± 0.53
Depression	3.56 ± 3.05

Linear Regression Analysis of Study Variables

Table 4 reveals that depression among patients with hypertension was associated with the two socio-demographic factors of gender and per capita annual household income, in addition to physical comorbidity and health literacy. The depressive symptoms of women with hypertension were more serious than those of men

TABLE 3 | The correlation among key variables.

	Social support	Physical comorbidity	Health literacy	Depression
Social support				
Physical comorbidity	−0.207**			
Health literacy	0.135*	0.127*		
Depression	−0.147*	0.256**	−0.225**	

*$P < 0.01$, **$P < 0.001$.

TABLE 4 | Multiple linear regression analysis of factors associated with depression.

	β	*t*	*P*	95% CI
Constant	4.295	3.462	0.001	1.858, 6.732
Gender				
Men (ref)				
Women	0.725	2.811	0.005	0.219, 1.232
Age				
<60 (ref)				
60–69	−0.104	−0.283	0.777	−0.827, 0.619
70–79	0.593	1.574	0.116	−0.147, 1.334
≥80	0.147	0.272	0.785	−0.911, 1.205
Education				
No formal education (ref)				
Primary school	0.533	1.614	0.107	−0.116, 1.181
Middle school and above	0.554	1.423	0.155	−0.211, 1.319
Marital status				
Married have spouses (ref)				
Divorced, widowed, or unmarried	0.509	1.497	0.135	−0.159, 1.176
Per capita annual household income, $				
<750(ref)				
750–1,499	−0.460	−1.445	0.149	−1.086, 0.165
≥1,500	−0.723	−2.088	0.037	−1.404, −0.043
Living arrangements				
Living with family members (ref)				
Living alone	−0.553	−1.176	0.240	−1.477, 0.371
Physical comorbidity				
0 (ref)				
1	1.316	4.500	0.000	0.741, 1.890
≥2	2.528	5.756	0.000	1.665, 3.390
Social support	−0.025	−1.215	0.225	−0.066, 0.016
Health literacy	−0.116	−5.479	0.000	−0.158, −0.075

(β = 0.725, $P = 0.005$). Compared with the <$750 group, subjects with hypertension with a per capita annual household income of ≥$1500 had fewer depressive symptoms (β = −0.723, $P = 0.037$).

Test of Study Model

We used SEM to test the model shown in **Figure 1**. The path coefficient of the link between social support and depression was not statistically significant. Thus, we revised the model by removing this path. After setting socio-demographic characteristics as covariates, the direction of influence among the key variables remained unchanged and the corresponding coefficients did not change significantly. Thus, the socio-demographic characteristics were not confounding factors and were not considered in the final model. To improve the model fitness, the covariance between measurement errors was set based on the modification indices. **Figure 2** shows the final modified model that tested the associations of social support, physical comorbidity, and health literacy with depression. Standardized coefficients representing the direct associations between variables are displayed over the arrows. The model demonstrated good fit: RMSEA = 0.062, TLI = 0.931, CFI = 0.958, $\chi^2/\text{df} = 3.117$.

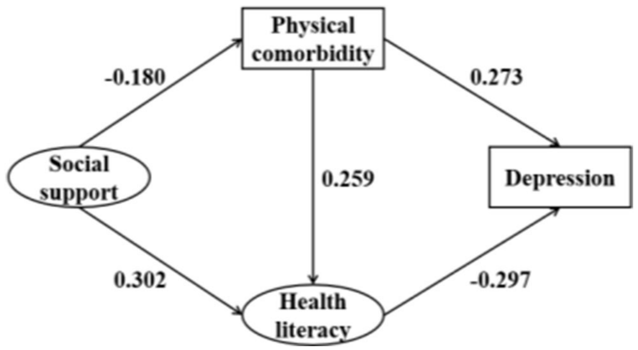

FIGURE 2 | Structural analysis of social support, physical comorbidity, health, literacy, and depression. All coefficients are significant ($P < 0.05$).

The direct, indirect, and total effects of key study variables are displayed in **Table 5**. Physical comorbidity had a direct effect (β = 0.273, 95% CI: 0.219–0.341) on the depression of patients with hypertension, thus supporting Hypothesis 2. Health literacy was directly associated with depression (β = −0.297, 95% CI: −0.381 to −0.197), thus supporting Hypothesis 3. However, social support was only indirectly associated with depression (β = −0.125, 95% CI: −0.162 to −0.077), rather than directly associated, leading us to reject Hypothesis 1. Greater social support was associated with reduced likelihood of having physical comorbidity (β = −0.180, 95% CI: −0.271 to −0.074) and greater health literacy (β = 0.302, 95% CI: 0.188–0.402), thus supporting Hypotheses 4 and 5. Physical comorbidity had a direct association with the health literacy of patients with hypertension (β = 0.259, 95% CI: 0.208–0.319), thus supporting Hypothesis 6.

The results of significance testing of the mediating pathways are displayed in **Table 6**. A mediating effect was considered statistically significant if the 95% confidence interval did not include zero. The results illustrated that the relationship between social support and depression was mediated by physical comorbidity and health literacy (95% CI: −0.160 to −0.045 and −0.282 to −0.097, respectively), thus supporting Hypotheses 7 and 8. In addition, physical comorbidity mediated the relationship of social support with health literacy (95% CI: −0.198 to −0.065), thus supporting Hypothesis 9. Health literacy mediated the relationship between physical comorbidity

TABLE 5 | Direct, indirect, and total effects of key study variables.

Model pathways	Standardized coefficient	95% CI
Total effects		
Social support → Physical comorbidity	−0.180	−0.271 to −0.074
Social support → Health literacy	0.255	0.146 to 0.366
Social support → Depression	−0.125	−0.162 to −0.077
Physical comorbidity → Health literacy	0.259	0.208 to 0.319
Physical comorbidity → Depression	0.196	0.136 to 0.262
Health literacy → Depression	−0.297	−0.381 to −0.197
Direct effects		
Social support → Physical comorbidity	−0.180	−0.271 to −0.074
Social support → Health literacy	0.302	0.188 to 0.402
Physical comorbidity → Health literacy	0.259	0.208 to 0.319
Physical comorbidity → Depression	0.273	0.219 to 0.341
Health literacy → Depression	−0.297	−0.381 to −0.197
Indirect effects		
Social support → Health literacy	−0.047	−0.074 to −0.016
Social support → Depression	−0.125	−0.162 to −0.077
Physical comorbidity → Depression	−0.077	−0.112 to −0.048

TABLE 6 | Significance tests of mediating pathways.

Model pathways	95% CI
Social support → Physical comorbidity → Depression	−0.160 to −0.045
Social support → Health literacy → Depression	−0.282 to −0.097
Social support → Physical comorbidity → Health literacy	−0.198 to −0.065
Physical comorbidity → Health literacy → Depression	−0.473 to −0.240

and depression (95% CI: −0.473 to −0.240), thus supporting Hypothesis 10.

DISCUSSION

To the best of our knowledge, this study is the first to explore the relationships among social support, physical comorbidity, health literacy, and depression in patients with hypertension in China. Hypertension is typically controlled less well in rural residents than in urban residents because of differences in educational level, economic level, and other factors. Furthermore, rural patients with chronic disease tend to have a higher prevalence of depression (49). Depressive symptoms of patients with hypertension may aggravate their health status by lowering therapeutic compliance, limiting health care access, reducing social support, and increasing the incidence of uncontrolled hypertension and comorbidities (7). Thus, it is important to study the factors that affect depression among rural patients with hypertension. In this study, the mean depression score of rural patients with hypertension was 3.56, and 6.0% of patients with hypertension had symptoms of depression.

Physical comorbidities among individuals with hypertension are more common than among those with normal blood pressure (50). A continuous survey of Korean citizens demonstrated that hypertension has a positive association with the risk of comorbidities and patients with hypertension are more than twice as likely to have comorbidities as non-hypertensive adults (51). In the current study, 34.2% of the subjects had physical comorbidity. Previous studies have suggested that the risk of depression increases in the presence of physical illnesses such as myocardial infarct, cerebrovascular disease, and diabetes mellitus (52–54). In the current study, more physical comorbidities were associated with an increased risk of depression among patients with hypertension, which may have resulted from persistent limitations in daily functioning associated with the coexisting diseases. The same conclusion was drawn in another study, which showed an increased severity of depression in patients with hypertension and type 2 diabetes mellitus (55). In addition, comorbidity is not conducive to the control and prognosis of hypertension. A study showed that 60.1% of patients with hypertension and without diabetes achieved their blood pressure control target, compared with just 24.3% of patients with hypertension and diabetes (56).

In this study, the mean health literacy score of patients with hypertension was 14.62 and only 5.6% of the subjects had adequate health literacy, indicating that the health literacy of the sample was rather poor. This is unsurprising given our focus on a rural population, as prior work has revealed poor health literacy in rural patients with hypertension is relatively common (31, 57). A survey conducted in Heilongjiang Province also showed that health literacy, especially regarding hypertension knowledge, was extremely low in rural areas of China (58). In addition, older age and lower education levels have been shown to be associated with poor health literacy in patients with hypertension (59). In this study, the average age of the respondents was relatively old (67.7 ± 8.6 years), and their educational level was generally low (74.5% had an educational level of primary school and below), which may explain the poor health literacy. A lack of health literacy is known to cause poor adherence to medication regimens and, consequently, poor management of hypertension and poor blood pressure control (60); thus, it is essential to promote health literacy among rural patients with hypertension.

The present study represents the first exploration of the association between health literacy and depression among patients with hypertension. The results showed that health literacy was negatively related to depressive symptoms among study samples. Individuals with low health literacy often exhibit poor self-esteem, shame, and embarrassment (61), leading to social isolation and psychological barriers to asking for help, which may contribute to depressive symptoms among this group. Interestingly, our study evidenced the mediating effect of health literacy on the relationship between physical comorbidity and depression. Patients with hypertension and comorbidity may have a better understanding of different diseases, and thus comorbidity may be helpful in improving their health literacy and ultimately reducing their risk of depression. Health literacy is not only directly negatively related to depression but has also been shown to weaken the possible adverse effects of physical comorbidity on depression.

The mean social support score of our study sample was 37.17, and the proportion of individuals with a high level of social support was just 16.9%. Previous studies have reported that subjects with lower levels of social support are more likely to develop cardiovascular disease due to a history of hypertension and are at increased risk of experiencing higher blood pressure, less nocturnal blood pressure decrease, and a worse prognosis after a cardiovascular event (62–64). One study reported a threefold increase in the risk of all-cause mortality among patients with hypertension and poor social support (65). Therefore, the insufficient social support available to patients with hypertension deserves attention. Objective support and support utilization were relatively low in our sample, with scores of 7.91 ± 2.42 and 6.47 ± 2.08, respectively. Objective support refers to individual social networks and actual support received from a spouse, other family members, friends, relatives, workmates, work units, and party committees in the past, especially in times of distress and crisis. Rural hypertensive patients usually work in agriculture, and they lack financial support and support from workmates, work units, or party committees in solving practical problems, which may explain the low levels of objective support. In addition, physical activity and self-efficacy regarding physical exercise levels are generally low in patients with hypertension (66). This weakens their contact with social networks and thus reduces the social support potentially available to them. In this study, the utilization of social support by patients with hypertension was relatively low, consistent with other research (67). The degree of support utilization is associated with patients' compliance with anti-hypertensive therapy and blood pressure control (68). However, patients with hypertension are limited in their activities of daily living due to the illness, which leads to reduced social intercourse (69). This prevents them from making full use of support, even when sufficient resources are present, which is unfavorable in terms of addressing problems and causes negative emotions.

There is an extensive literature documenting that lack of social support is a strong predictor of depression among patients with hypertension (12–14). However, unlike other studies, our study showed that the direct relationship between social support and depression was not significant among study samples. Social support indirectly affected depression by the mediating effects of physical comorbidity and health literacy. A lack of social support was related to a greater likelihood of having multiple physical comorbidities, which may have been because social support can improve therapy adherence among patients with hypertension, thereby reducing the risk of developing other physical illnesses (39). In addition, that greater social support was associated with increased health literacy is consistent with a previous study (70). The mediating pathways suggested that lack of social support may have an impact on the increased risk of physical comorbidity and decreased health literacy, thus potentially leading to a higher prevalence of depression. Our research helps explain the mechanism by which social support influences depression and suggests interventions that may improve the mental health of patients with hypertension.

In addition, the linear regression revealed that gender and per capita annual family income were associated with depression among patients with hypertension. Compared with men, women had a higher degree of depression, consistent with previous studies of patients with hypertension (71, 72). Women have the dual responsibilities and pressures of family and work. Women with chronic disease experience difficulties fulfilling gender-specific social roles, thus increasing the risk of depression (73). In addition, depressive symptoms were fewer among high-income patients with hypertension than among those with low income. Lower income and poorer socioeconomic status have been confirmed as a risk factor for depression in patients with hypertension (74, 75). High-income individuals with hypertension can use more medical resources and health services and thereby obtain better disease control and psychological status (76).

Although our study adds important findings to the literature regarding the factors that influence depression and the mechanisms underlying these factors' relationships among patients with hypertension, we should acknowledge several limitations of this study. First, the cross-sectional design of this study enables the description of relationships between depression and social support, health literacy, and physical comorbidity; it does not enable one to infer causality of the three determinants on depression among individuals with hypertension. Second, this research was carried out in rural areas of Sichuan Province, limiting our ability to generalize the findings to other regions.

Practice Implications

Overall, relieving depressive symptoms among individuals with hypertension requires the enhancement of social support and health literacy. In particular, more attention should be directed toward women, low-income individuals, and patients with physical comorbidities.

More community-based collective activities and social opportunities should be provided for individuals with hypertension, to address the lack of social support caused by disease-related barriers. Moreover, care providers are an important social support resource whose activities in this regard should be encouraged (77).

To enhance the health literacy of patients with hypertension, we suggest that health education programs should be developed to help this population improve their health knowledge and develop self-management behaviors. In addition, training in relaxation techniques or organizational skills for managing daily life activities should also help improve the mental health of patients with hypertension (14).

CONCLUSIONS

Our findings indicated that social support, physical comorbidity, health literacy, gender, and per capita annual family income were significantly related to depression among patients with hypertension. Physical comorbidity had a direct positive relationship with depression, while health literacy was directly negatively associated with depression. Social support was indirectly negatively associated with depression in patients with hypertension, mediated by health literacy and physical comorbidity. Physical comorbidity had an indirect negative effect on depression via health literacy. In addition, female patients and patients with a per capita annual household income of <\$750 had more depressive symptoms.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation, to any qualified researcher.

ETHICS STATEMENT

All of the participants signed an informed consent before investigation. The ethical approval of data collection was from the ethics committee of Sichuan University.

AUTHOR CONTRIBUTIONS

Conceptualization: DL and BZ. Methodology and funding acquisition: DL. Software, formal analysis, and writing—original draft preparation: BZ. Investigation: WZ, XS, and JG. Writing—review and editing: WZ, XS, JG, and DL. All authors contributed to the article and approved the submitted version.

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REFERENCES

1. Long J, Duan G, Tian W, Wang L, Su P, Zhang W, et al. Hypertension and risk of depression in the elderly: a meta-analysis of prospective cohort studies. *J Hum Hypertension.* (2015) 29:478–82. doi: 10.1038/jhh.2014.112
2. Wu Y, Huxley R, Li L, Anna V, Xie G, Yao C, et al. Prevalence, awareness, treatment, and control of hypertension in China: data from the China national nutrition and health survey 2002. *Circulation.* (2008) 118:2679–86. doi: 10.1161/CIRCULATIONAHA.108.788166
3. Li Y, Yang L, Wang L, Zhang M, Huang Z, Deng Q, et al. Burden of hypertension in China: a nationally representative survey of 174 621 adults. *Int J Cardiol.* (2017) 227:516–23. doi: 10.1016/j.ijcard.2016.10.110
4. Organization WH. *The World Health Report 2001: Mental health: New Understanding, New Hope*. World Health Organization (2001).
5. Marazziti D, Rutigliano G, Baroni S, Landi P, Dell'Osso L. Metabolic syndrome and major depression. *CNS Spectrums.* (2014) 19:293–304. doi: 10.1017/S1092852913000667
6. Kaplan M, Nunes A. The psychosocial determinants of hypertension. *Nutr Metab Cardiovasc Dis.* (2003) 13:52–59. doi: 10.1016/S0939-4753(03)80168-0
7. Shao H, Mohammed MU, Thomas N, Babazadeh S, Yang S, Shi Q, et al. Evaluating excessive burden of depression on health status and health care utilization among patients with hypertension in a nationally representative sample from the medial expenditure panel survey (MEPS 2012). *J Nervous Mental Dis.* (2017) 205:397–404. doi: 10.1097/NMD.0000000000000618
8. Scuteri A, Spazzafumo L, Cipriani L, Gianni W, Corsonello A, Cravello L, et al. Depression, hypertension, and comorbidity: disentangling their specific effect on disability and cognitive impairment in older subjects. *Arch Gerontol Geriatr.* (2011) 52:253–7. doi: 10.1016/j.archger.2010.04.002
9. Tsartsalis D, Dragioti E, Kontoangelos K, Pitsavos C, Sakkas P, Papadimitriou G, et al. The impact of depression and cardiophobia on quality of life in patients with essential hypertension. *Psychiatriki.* (2016) 27:192–203. doi: 10.22365/jpsych.2016.273.192
10. Oganov RG, Pogosova GV, Koltunov IE, Romasenko LV, Deev AD, Iufereva IM. Depressive symptoms worsen cardiovascular prognosis and shorten length of life in patients with arterial hypertension and ischemic heart disease. *Kardiologiia.* (2011) 51:59–66.
11. Jefferson WJ. Biologic treatment of depression in cardiac patients. *Psychosomatics.* (1985) 26:31–8. doi: 10.1016/S0033-3182(85)72772-7
12. Ma C. The prevalence of depressive symptoms and associated factors in countryside-dwelling older Chinese patients with hypertension. *J Clin Nurs.* (2018) 27:2933–41. doi: 10.1111/jocn.14349
13. Zhang MY, Yu Z, Yao JG. Relationships of coping style and social support to anxiety or/and depression in patients with hypertension. *J Nanchang Univ.* (2013) 53:33–35. Available online at: http://kns.cnki.net/kcms/detail/detail.aspx?FileName=ZGJK200905004&DbName=CJFQ2009
14. Dennis JP, Markey MA, Johnston KA, Wal JSV, Artinian NT. The role of stress and social support in predicting depression among a hypertensive African American sample. *Heart Lung.* (2008) 37:105–12. doi: 10.1016/j.hrtlng.2007.03.003
15. Weijma M, Janssen V, Doef MVD. *The relationship between social support, adherence and blood pressure control in patients with hypertension* (Master thesis). Department of Psychology, Leiden University, Leiden, Netherlands. (2015).
16. Taher M, Abredari H, Karimy M, Abedi A, Shamsizadeh M. The relation between social support and adherence to the treatment of hypertension. *J Educ Commun Health.* (2014) 1:59–67. doi: 10.20286/jech-010348
17. Ojo OS, Malomo SO, Sogunle PT. Blood pressure (BP) control and perceived family support in patients with essential hypertension seen at a primary care clinic in Western Nigeria. *J Fam Med Prim Care.* (2016) 5:569–75. doi: 10.4103/2249-4863.197284
18. Chang AK, Lee EJ. Factors affecting self-care in elderly patients with hypertension in Korea. *Int J Nurs Pract.* (2015) 21:584–91. doi: 10.1111/ijn.12271
19. Wiltink J, Beutel ME, Till Y, Ojeda FM, Wild PS, Münzel T, et al. Prevalence of distress, comorbid conditions and well being in the general population. *J Affect Disord.* (2011) 130:429–37. doi: 10.1016/j.jad.2010.10.041
20. Findley P, Shen C, Sambamoorthi U. Multimorbidity and persistent depression among veterans with diabetes, heart disease, and hypertension. *Health Soc Work.* (2011) 36:109–19. doi: 10.1093/hsw/36.2.109
21. Medicine NAO. Health literacy: a prescription to end confusion. In: Nielsen-Bohlman L, Panzer AM, Kindig DA, editors. *Institute of Medicine (US) Committee on Health Literacy*. Washington, DC: National Academies Press (2004). p. 389–95.
22. Lincoln A, Paasche-Orlow MK, Cheng DM, Lloyd-Travaglini C, Caruso C, Saitz R, et al. Impact of health literacy on depressive symptoms and mental health-related: quality of life among adults with addiction. *J Gen Intern Med.* (2006) 21:818–22. doi: 10.1111/j.1525-1497.2006.00533.x
23. Rhee TG, Lee HY, Kim NK, Han G, Lee J, Kim K. Is health literacy associated with depressive symptoms among Korean adults? Implications for mental health nursing. *Perspect Psychiatr Care.* (2017) 53:234–42. doi: 10.1111/ppc.12162

24. Stewart DW, Reitzel LR, Correa-Fernández V, Cano MÁ, Adams CE, Cao Y, et al. Social support mediates the association of health literacy and depression among racially/ethnically diverse smokers with low socioeconomic status. *J Behav Med.* (2014) 37:1169–79. doi: 10.1007/s10865-014-9566-5
25. Schinckus L, Dangoisse F, Broucke SVd, Mikolajczak M. When knowing is not enough: emotional distress and depression reduce the positive effects of health literacy on diabetes self-management. *Patient Educ Couns.* (2017) 101:324–30. doi: 10.1016/j.pec.2017.08.006
26. Wannasirikul P, Termsirikulchai L, Sujirarat D, Benjakul S, Tanasugarn C. Health literacy, medication adherence, and blood pressure level among hypertensive older adults treated at primary health care centers. *Southeast Asian J Trop Med Public Health.* (2016) 47:109–20.
27. Shi D, Li J, Wang Y, Wang S, Liu K, Shi R, et al. Association between health literacy and hypertension management in a Chinese community: a retrospective cohort study. *Intern Emerg Med.* (2017) 12:765–76. doi: 10.1007/s11739-017-1651-7
28. Ko Y, Balasubramanian TD, Wong L, Tan M-L, Lee E, Tang W-E, et al. Health literacy and its association with disease knowledge and control in patients with hypertension in Singapore. *Int J Cardiol.* (2013) 168:e116–7. doi: 10.1016/j.ijcard.2013.08.041
29. Park NH, Song MS, Shin SY, Jeong J-h, Lee HY. The effects of medication adherence and health literacy on health-related quality of life in older people with hypertension. *Int J Older People Nurs.* (2018) 13:e12196. doi: 10.1111/opn.12196
30. Johari Naimi A, Naderiravesh N, Safavi Bayat Z, Shakeri N, Matbouei M. Correlation between health literacy and health-related quality of life in patients with hypertension, in Tehran, Iran, 2015-2016. *Electr Phys.* (2017) 9:5712–20. doi: 10.19082/5712
31. TMoHSI C. *An Analysis Report of National Health Services Survey in China, 2008*. Beijing: Peking Union Medical College Press (2009).
32. Sun Z, Zheng L, Wei Y, Li J, Zhang X, Zhang X, et al. The prevalence of prehypertension and hypertension among rural adults in liaoning province of China. *Clin Cardiol.* (2007) 30:183–7. doi: 10.1002/clc.20073
33. Sun Z, Zheng L, Detrano R, Zhang X, Xu C, Li J, et al. Incidence and predictors of hypertension among rural Chinese adults: results from liaoning province. *Ann Fam Med.* (2010) 8:19–24. doi: 10.1370/afm.1018
34. Li X, Yu M, Yinghua L, Junfeng H, Yulan C, Guoyong C, et al. Study on the health literacy status and its influencing factors of urban and rural residents in China. *Chin J Health Educ.* (2009) 25:323–26. Available online at: http://kns.cnki.net/kcms/detail/detail.aspx?FileName=ZGJK200905004&DbName=CJFQ2009
35. Yunhua X, Hong Y. The difference of social support between urban and rural elderly and its influence on health and life satisfaction. *J Huazhong Agric Univ.* (2016) 85–92. doi: 10.13300/j.cnki.hnwkxb.2016.06.012
36. Ho YF, Chen YC, Chi CT, Chen SCJS. Exploring the determinations of health literacy and self-management in patients with chronic kidney disease. In: *26th International Nursing Research Congress.* San Juan (2015).
37. Liu L, Tian JL, Zhang H, Yan-Fei LI, Chen YL, Liu YB, et al. Health literacy and social support among the middle- aged and elderly hospitalized patients with coronary heart disease in Urumqi. *J Nurs Admin.* (2016) 16:7–9.
38. Zou H, Chen Y, Fang W, Zhang Y, Fan X. The mediation effect of health literacy between subjective social status and depressive symptoms in patients with heart failure. *J Psychosom Res.* (2016) 91:33–9. doi: 10.1016/j.jpsychores.2016.10.006
39. Mazzella F, Cacciatore F, Galizia G, Della-Morte D, Rossetti M, Abbruzzese R, et al. Social support and long-term mortality in the elderly: role of comorbidity. *Arch Gerontol Geriatr.* (2010) 51:323–8. doi: 10.1016/j.archger.2010.01.011
40. Ahn SN, Kim S, Zhang H. Changes in depressive symptoms among older adults with multiple chronic conditions: role of positive and negative social support. *Int J Environ Res Public Health.* (2016) 14:16. doi: 10.3390/ijerph14010016
41. Gazmararian JA, Williams MV, Peel J, Baker DW. Health literacy and knowledge of chronic disease. *Patient Educ Couns.* (2003) 51:267–75. doi: 10.1016/S0738-3991(02)00239-2
42. Savalei V, Bentler PM. Structural equation modeling. In Grover R, Vriens M, editors. *The Handbook of Marketing Research: Uses, Misuses, and Future Advances*. Thousand Oaks, CA: Sage (2006). p. 330–64.
43. Liao J, Wang X, Liu C, Gu Z, Sun L, Zhang Y, et al. Prevalence and related risk factors of hypertensive patients with co-morbid anxiety and/or depression in community: a cross-sectional study. *Zhonghua Yi Xue Za Zhi.* (2014) 94:62–6. doi: 10.3760/cma.j.issn.0376-2491.2014.01.018
44. Xiao S. The theoretical basis and application of social support questionnaire. *J Clin Psychol Med*. (1994) 98–100.
45. Ren M, Liu C, Chen Y, Li S. The present situation and influencing factors of social support for the elderly in reclamation area of Shihezi. *Occup Health.* (2019) 35:644–50. doi: 10.13329/j.cnki.zyyjk.2019.017
46. Xue J, Liu Y, Sun K, Wu L, Liao K, Xia Y, et al. Validation of a newly adapted Chinese version of the newest vital sign instrument. *PLoS ONE.* (2018) 13:e0190721. doi: 10.1371/journal.pone.0190721
47. Andresen EM, Malmgren JA, Carter WB, Patrick DL. Screening for depression in well older adults: evaluation of a short form of the CES-D. *Am J Prev Med.* (1994) 10:77–84. doi: 10.1016/S0749-3797(18)30622-6
48. Roberts RE, Vernon SW. The center for epidemiologic studies depression scale: its use in a community sample. *Am J Psychiatry.* (1983) 140:41–6. doi: 10.1176/ajp.140.1.41
49. Wu P, Li L, Sun W. Influence factors of depression in elderly patients with chronic diseases. *Biomed Res.* (2018) 29:945–9. doi: 10.4066/biomedicalresearch.29-17-3442
50. Strandberg AY, Strandberg TE, Stenholm S, Salomaa VV, Pitkälä KH, Tilvis RS. Low midlife blood pressure, survival, comorbidity, and health-related quality of life in old age: the helsinki businessmen study. *J Hypertension.* (2014) 32:1797–804. doi: 10.1097/HJH.0000000000000265
51. Noh J, Kim HC, Shin A, Yeom H, Jang SY, Lee JH, et al. Prevalence of comorbidity among people with hypertension: the korea national health and nutrition examination survey 2007-2013. *Korean Circ J.* (2016) 46:672–80. doi: 10.4070/kcj.2016.46.5.672
52. Carney RM, Blumenthal JA, Diane C, Freedland KE, Berkman LF, Watkins LL, et al. Depression as a risk factor for mortality after acute myocardial infarction. *Am J Cardiol.* (2003) 92:1277–81. doi: 10.1016/j.amjcard.2003.08.007
53. Rotella F, Mannucci E. Diabetes mellitus as a risk factor for depression. A meta-analysis of longitudinal studies. *Diabetes Res Clin Pract.* (2013) 99:98–104. doi: 10.1016/j.diabres.2012.11.022
54. Alexopoulos GS, Meyers BS, Young RC, Campbell S, Silbersweig D, Charlson M. 'Vascular depression' hypothesis. *Arch Gen Psychiatry.* (1997) 54:915–22. doi: 10.1001/archpsyc.1997.01830220033006
55. Li L, Yang J, Yang Y, Zhang Y. A survey and analysis on depression of patients with hypertension or type 2 diabetes mellitus in rural community. *Ningxia Med J.* (2017) 39:430–3. doi: 10.13621/j.1001-5949.2017.05.0430
56. Theng CA, Fah TS, Sazlina SG, Abdul Samad A, Md Sharif S. Blood pressure control among hypertensive patients with and without diabetes mellitus in six public primary care clinics in malaysia. *Asia Pacific J Public Health.* (2015) 27:580–9. doi: 10.1177/1010539513480232
57. Tehrani Bani hashemi S, Amirkhani M, Haghdoost A, Alavian S, Asgharifard H, Baradaran H. Health literacy and the influencing factors: a study in five provinces of Iran. *Strides Dev Med Educ.* (2007) 4:1–9. doi: 10.1007/s12182-011-0118-0
58. Li X, Ning N, Hao Y, Sun H, Gao L, Jiao M, et al. Health literacy in rural areas of china: hypertension knowledge survey. *Int J Environ Res Public Health.* (2013) 10:1125–38. doi: 10.3390/ijerph10031125
59. Zhang Q, An Q, Dai Y, Yang J, Lei Y, Zhang J. The status and related factors of health literacy of community- dwelling hypertensive patients in Urumqi. *J Nurs Admin.* (2014) 14:462–4. doi: 10.3969/j.issn.1671-315X.2014.07.003
60. Kim E-Y, Han H-R, Jeong S, Kim KB, Park H, Kang E, et al. Does knowledge matter?: intentional medication nonadherence among middle-aged Korean Americans with high blood pressure. *J Cardiovasc Nurs.* (2007) 22:397–404. doi: 10.1097/01.JCN.0000287038.23186.bd
61. Parikh NS, Parker RM, Nurss JR, Baker DW, Williams MV. Shame and health literacy: the unspoken connection. *Patient Educ Couns.* (1996) 27:33–9. doi: 10.1016/0738-3991(95)00787-3
62. Blumenthal JA, Burg MM, Barefoot J, Williams RB, Haney T, Zimet G. Social support, type A behavior, and coronary artery disease. *Psychosom Med.* (1987) 49:331–40. doi: 10.1097/00006842-198707000-00002

63. Jürgen B, Sarah S, Roland VKN. Lack of social support in the etiology and the prognosis of coronary heart disease: a systematic review and meta-analysis. *Psychosom Med.* (2010) 72:229–38. doi: 10.1097/PSY.0b013e3181d01611
64. Rosengren A, Hawken S, Ôunpuu S, Sliwa K. Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13648 controls from 52 countries (the INTERHEART study) : case-control study. *Lancet.* (2004) 364:953–62. doi: 10.1016/S0140-6736(04)17019-0
65. Menéndezvillalva C, Gamarramondelo MT, Alonsofachado A, Naveiracastelo A, Montesmartínez A. Social network, presence of cardiovascular events and mortality in hypertensive patients. *J Hum Hypertension.* (2015) 29:417–23. doi: 10.1038/jhh.2014.116
66. Adeniyi A, Idowu O, Ogwumike O, Adeniyi C. Comparative influence of self-efficacy, social support and perceiived barriers on low physical activity development in patients with type 2 diabetes, hypertension or stroke. *Ethiop J Health Sci.* (2012) 22:113–9.
67. Jiang X, Zhang X. A study on the status of social supports for patients with hypertension in the community and nursing interventions. *Chin J Nurs.* (2007) 42:105–9. doi: 10.1016/S1874-8651(08)60050-2
68. Zhang H, Sun J, Zhang H, Zhu Y, Mao X, Ai F, et al. Correlation between compliance in patients with anti-hypertensive therapy and blood pressure control. *Pakistan J Pharm Sci.* (2017) 30:1455–60.
69. Wang J, Wu L, Wang J, Wang P, Zhou Z. Surveying the status of social support on patients with hypertension in communities. *Chin Health Serv Manag.* (2012) 5:394–7. doi: 10.3969/j.issn.1004-4663.2012.05.025
70. Fry-Bowers EK, Maliski S, Lewis MA, Macabasco-O'Connell A, Dimatteo R. The association of health literacy, social support, self-efficacy and interpersonal interactions with health care providers in low-income latina mothers. *J Pediatr Nurs.* (2014) 29:309–20. doi: 10.1016/j.pedn.2014.01.006
71. Neupane D, Panthi B, McLachlan CS, Mishra SR, Kohrt BA, Kallestrup P. Prevalence of undiagnosed depression among persons with hypertension and associated risk factors: a cross-sectional study in urban Nepal. *PLoS ONE.* (2015) 10:e0117329. doi: 10.1371/journal.pone.0117329
72. Ren Y, Huang R, Gao L. Associations between depression and gender and 5-hydroxyptamine/interleukin-6 in elderly patients with hypertension. *Chin Gen Pract.* (2010) 13:2310–12. doi: 10.1016/S1876-3804(11)60004-9
73. Weaver LJ, Hadley C. Social pathways in the comorbidity between type 2 diabetes and mental health concerns in a pilot study of urban middle- and upper-class Indian women. *Ethos.* (2011) 39:211–25. doi: 10.1111/j.1548-1352.2011.01185.x
74. Fan Z, Hu D, Yang J, Xu Y, Li T. Prevalence and risk factors of anxiety and depression in hypertensive patients. *J Capital Univ Med Sci.* (2005) 26:140–2. doi: 10.3969/j.issn.1006-7795.2005.02.011
75. Mahmood S, Hassan SZ, Tabraze M, Khan MO, Javed I, Ahmed A, et al. Prevalence and predictors of depression amongst hypertensive individuals in Karachi, Pakistan. *Cureus.* (2017) 9:e1397. doi: 10.7759/cureus.1397
76. Xu M, Wang X, Wang Z, Li J, Feng R, Cui Y. Equity of outpatient service utilization for hypertensive patients in community. *J Central South Univ Med Sci.* (2018) 43:668–78. doi: 10.11817/j.issn.1672-7347.2018.06.015
77. Chen YC, Chang LC, Liu CY, Ho YF, Tsai TI. The roles of social support and health literacy in self-management among patients with chronic kidney disease. *J Nurs Scholarship*. (2018) 50:265–75. doi: 10.1111/jnu.12377

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STUDY PROTOCOL
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Feasibility and Efficacy of a Psychological Therapy for Patients With a Schizophrenic Psychosis in an Inpatient Setting: Study Protocol of a Randomized Switch Controlled Trial

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Background: Schizophrenic psychoses are severe mental disorders. Despite advances in treatment, outcomes are still unsatisfactory. Pharmacological treatments are still limited, in particular regarding improvements in psychosocial functioning and neuro-cognitive impairment. In recent years new psychological therapies have been developed, demonstrating promising results. However, most of these interventions have been designed for and studied in outpatients; their efficacy and feasibility for patients requiring hospitalization is still unknown. Therefore, we have designed a clinical trial to compare a neuro-cognitive (Integrated Neuro-cognitive Treatment INT); a cognitive-behavioral (Integrated Psychological Therapy IPT); and a control (Cogpack CGP) intervention for patients with a schizophrenic psychosis hospitalized for treatment.

Methods: In a three-parallel-arm, single-blind, randomized, controlled study, we compare INT, IPT, and CGP. Participants will take part in two weekly sessions of one intervention for at least 16 sessions. If due to randomization, participants are allocated to a treatment arm not suitable for them, they are allowed to switch intervention after four sessions. Based on a sample size calculation, recruitment will continue until 30 participants have completed the intervention for each treatment arm.

Outcome Measurement: Primary outcomes are: change in symptom as measured by the Positive and Negative Syndrome Scale (PANSS), change in psychosocial functioning as assessed by the mini ICF-APP and neuro-cognitive performance, assessed by the Matrics Cognitive Consensus Battery (MCCB). Other outcomes of interest are the Brief Symptom Inventory (BSI) and the Health of the Nation Outcome Scales (HoNOS); together with prescribed medication, treatment retention and completion rates. Outcomes will be measured at baseline, 2 weeks into treatment (prior to a potential switch of intervention arm), post-treatment and at 6 and 12-month post-treatment follow-ups.

Expected Outcomes: We expect an overall improvement; however, with differences in specific domains for each treatment arm, with those completing INT showing

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better outcomes than IPT and CGP, respectively. We anticipate that lower functioning participants will drift to CGP and higher functioning participants to INT.

Conclusion: Due to the complexity of treatment for patients with a schizophrenic psychosis, we consider it crucial to compare different treatment options for those more severely affected, therefore, requiring inpatient treatment.

Trial registration: www.clinicaltrials.gov (ID: NCT03316664; 17.10.2017).

Keywords: schizophrenic psychosis, randomized controlled trial, inpatient, CBT for groups, NCR, INT, IPT

BACKGROUND

Schizophrenic psychoses are severe mental disorders, with a heterogeneous combination of symptoms and a lifetime prevalence of around one per cent (1, 2). Characteristic symptoms, albeit not exclusive, are hallucinations, delusions, apathy, blunting of affect, disorganized speech and thinking, together with cognitive impairment (3). Those affected are struck in the prime of life and are frequently unable to cope with the challenges of everyday life; experiencing impairment and disability in multiple domains, including the ability to maintain social relationships, sustain employment, and live independently (1, 2).

The treatment of schizophrenic psychoses remains a challenge; only around half of the patients show substantial clinical improvement (4). Treatment of Schizophrenia still relies predominantly on antipsychotic agents (5). Since their clinical introduction over 60 years ago, the Dopamine D2 receptor antagonism remains the pivotal mechanism of action. Newly developed antipsychotics follow the strategy of maintaining this effect, while attempting to improve tolerability (5). The pharmacological treatment of schizophrenia is often limited due to side-effects (6–8). Overall, antipsychotic agents are most effective in reducing positive symptoms, in comparison other symptom domains, such as psychosocial functioning, negative symptoms, and cognition show minimal improvement (5, 9).

In the past few decades, psychological interventions have been shown to be effective when used in conjunction with pharmacological treatment (10, 11). Psychoeducation, assertiveness training, family therapy, cognitive behavioral therapy, and cognitive remediation treatment programs have been developed and systematically studied and further improved (10–15). Current guidelines recognize their importance for treatment and outcome, correspondingly implementation early on in treatment is recommended, even in hospitalized patients (16–19). However, current evidence regarding the effectiveness of psychotherapeutic interventions has been obtained primarily in studies of outpatient populations; studies in chronic and low functioning patients hospitalized for treatment are sparse (20, 21), with patient recruitment a major challenge (22).

The Integrated Psychological Therapy (IPT) for patients with schizophrenia is one of the first manualized integrated cognitive remediation therapy programs for groups, combining social skills, neuro- and social cognition in a single therapy (23, 24). Since the first trial in 1980, IPT has been extensively studied, with empirical evidence consistently demonstrating its efficacy; consequently, it is currently implemented in clinical practice (25). The further development of IPT has led to Integrated Neurocognitive Therapy (INT) for Schizophrenia, a manualized cognitive remediation therapy, which includes a computerized neurocognitive training component (Cogpack CGP) (26, 27). In clinical trials INT has been shown to not only improve neuro-social-cognitive performance but also to have the potential to improve functional outcome and to reduce negative symptoms (24, 27–29).

Although both INT and IPT seem to be effective treatments for patients with schizophrenia; the therapeutic approaches differ in terms of the symptoms they address, together with how the intervention is delivered (29, 30). Through its plain and straightforward design, IPT is suitable for chronic and hospitalized patients (31). However, IPT does not target all the cognitive domains impacted in schizophrenia (32). In contrast, INT not only integrates these cognitive domains in its therapeutic approach, it also includes elements designed to improve self-awareness and perception of the environment. Furthermore, it includes a computer-based cognitive training, with effects of its own. Consequently, INT is a more complex and challenging intervention than IPT for both therapists and participants (29). Primarily for this reason, INT trials to date have been conducted almost exclusively in outpatient settings (29, 30).

Generally, outpatients are less severely ill (33), which may have implications regarding the implementation of INT for patients requiring hospitalization for treatment. To the best of our knowledge, there have been no trials directly comparing IPT to INT; it is therefore not known if both therapy approaches are equally effective or if one program works better for certain patients or is indeed detrimental for others. Important factors which need to be taken into account are the symptom load and severity in patients requiring hospitalization for treatment, the conditions of the treatment unit, in particular fluctuation in the patient population, together with the presence of patients with disturbing behavior (21).

Therefore, we plan to conduct a single-blind, randomized, controlled trial comparing INT, IPT, and CGP in patients with schizophrenia requiring hospitalization for treatment; to assess the efficacy and feasibility of INT as a treatment programme for such patients. The main outcomes for the assessment of efficacy are changes in symptom load and functionality, together with

TABLE 1 | Inclusion and Exclusion criteria.

Inclusion criteria
Participants are competent to give informed consent, as determined by the referring physician or psychiatrist.
Diagnosis of Schizophrenia or Schizoaffective Disorder according to DSM-5 (34)
Participants are between 18 and 65 years of age.
Completion of regular compulsory education.
German language proficiency as a native speaker or level B1 Common European Framework of Reference for Languages (CEFRL) (35)
Exclusion criteria
Unwilling or unable to comply with study instructions.
Low Intelligence as confirmed by failure to complete regular compulsory education.
Currently in another psychotherapeutic treatment, either in individual or group sessions.
Current consumption of alcohol or illicit drugs.

cognitive performance. Outcomes for feasibility are retention, switch rates, and overall therapy attendance.

METHODS

Design

We have designed an 8-week, randomized, controlled, assessor-blind, three-parallel-arm trial for patients diagnosed with a schizophrenic psychosis. All patients with the diagnosis of a schizophrenic psychosis (according to the DSM 5 Diagnostic criteria) are eligible to participate. In order to allow the participation of chronic and low-functioning patients, the inclusion criteria were deliberately broad (see **Table 1**).

Recruitment

The Center for Integrative Psychiatry [ZIP: (German) Zentrum für Integrative Psychiatrie], is part of the Psychiatric University Hospital of Zurich specializes in treating "heavy-users," i.e., those patients with frequent or long-term hospitalizations for whom outpatient treatment is often insufficient. Participants will be recruited among the patients hospitalized for treatment in the Unit for Psychotic Disorders of the ZIP.

Interventions and Therapists

Cogpack is a computer-based neuropsychological cognitive training program, covering seven domains: visual-motor skills; processing speed; vigilance; executive functions; memory; verbal comprehension and problem- solving (26, 36). Tasks employed will be identical to those used in the INT sessions. The difficulty level of each task is adapted automatically by the program. At the end of each task, the computer program generates a feedback-report for every user on their performance including "percentage correct" and "completion speed." Cogpack will be delivered by a psychiatric medical resident, with cognitive behavioral training and a 2-h introduction to the computer program followed by practical training.

Integrated Psychological Therapy (IPT) is a manualized psychological intervention consisting of five modules (37). The five modules are hierarchically arranged and deal with cognitive deficits, perceptual deficits, verbal communication, social skills, and problem-solving, with successively increasing complexity in each module. The procedure and contents for each module are broadly predefined and can be adapted to each group's specific needs. Therapists delivering IPT are nurses (as IPT has been traditionally delivered) with basic training in cognitive behavioral methods and a 3-day seminar on IPT followed by practical training and regular supervision.

Integrated Neurocognitive Therapy (INT) is a manualized psychological intervention consisting of four modules. Each module consists of neuro- and social-cognitive elements, together with stress and emotional regulation domains. The complexity of the modules increases successively as do the emotional demands. INT has a strategy-based-learning and a drill-and-practice approach, where the same didactic structure is applied to each domain (27, 38). One peculiarity feature of INT is the integration of cognitive domains, together with self-awareness/perception; and computer exercises (CGP) (26). Therapists delivering INT have a psychology and psychotherapy degree and have attended a 3-day seminar on INT, followed by practical training and receive regular supervision.

Taking into account the usual length of stay in our unit, together with current recommendations, we have adapted both IPT and INT to 20 session programmes comprising the contents of all modules, whilst respecting the specifications and recommendations of the manuals. Cogpack modules are analogous to those of INT. For an overview of the parallel interventions according to TIDieR (see **Table 2**).

Randomization and Switch Procedure

Following baseline assessment, patients will be randomly assigned (1:1:1 fashion) to either IPT or INT (active interventions) or Cogpack (control intervention). We expect six to eight participants in each treatment arm. Through randomization, there is the possibility that some participants will experience difficulties with their assigned treatment group. In such cases, patients will be permitted to switch to another treatment arm after 2 weeks. The sole criterion for switching intervention arm is patient preference due to excessive, respectively insufficient demands. We have chosen not to formulate explicit criteria for switching intervention arm for two reasons; first of all to empower patients in their commitment to therapy; second to prevent bias through the delayed selection of participants.

After participation in a minimum of 16 sessions (60–90 min each) in one treatment arm, the intervention will be completed; follow-up assessments will be carried out at 6 and 12 months. For a Study- Flow diagram (see **Table 3** and **Figure 1**).

Ethical and Regulatory Considerations

The study will be conducted in Switzerland in accordance with current regulations. The ethics committee of the Canton of Zurich approved the study protocol (BASEC Nr.: 2017-01351). The study protocol was registered in clinicalTrials.gov

TABLE 2 | Content and chedule of Interventions (ToM: Theory of Mind).

	IPT	INT	CGP
First Block	**Module 1**	**Module A**	**Module A**
Sesion 1	Card sorting	Information processing	Information processing
Sesion 2	Verbal concept	Attention/vigilance	Attention
Sesion 3	Verbal concept	Perception of emotions	Attention
Sesion 4	Search strategies	Perception of emotions	Vigilance
Second Block	**Module 2**	**Module B**	**Module**
Sesion 1	Information collection	Verbal and visual learning	Verbal and visual learning
Sesion 2	Interpretation and discussion	Memory	Memory
Sesion 3	Interpretation and discussion	Social perception (ToM)	Memory
Sesion 4	Title finding	Social perception (ToM)	Verbal and visual learning
Third Block	**Module 3**	**Module C**	**Module C**
Sesion 1	Repetition/paraphrasing	Thinking / problem solving	Thinking / problem solving
Sesion 2	Questions and answers	Problem-solving	Thinking / problem solving
Sesion 3	Asking questions	Problem-solving	Thinking / problem solving
Sesion 4	Focussed communication	Problem-solving	Thinking / problem solving
Fourth Block	**Module 4**	**Module C / Module D**	**Module C /Module D**
Sesion 1	Cognitive processing	Social schemata	Thinking / problem solving
Sesion 2	Cognitive Processing	Social schemata	Thinking / problem solving
Sesion 3	Role-playing games	Working memory	Working memory
Sesion 4	Role-playing games	Working memory	Working memory
Fifth Block	**Module 5**	**Module D**	**Module D**
Sesion 1	Problem identification	Attribution	Working memory
Sesion 2	Generating solutions	Attribution	Working memory
Sesion 3	Generating solutions	Attribution	Working memory
Sesion 4	Implementing solutions	Emotion regulation	Working memory

(NCT03316664; 17.10.2017). Written informed consent will be obtained from the participants before study enrollment.

Assessments of Outcomes, Raters

Study measurement and outcomes will be assessed by raters blinded regarding group allocation and treatment of the participants. Raters have a psychology degree and training in research methods. All raters have been systematically trained in the use of the study instruments. To ensure raters are blind to treatment arm, they will have no access to patient or study records beyond the strict requirements for rating.

Furthermore, rating sessions will be conducted outside the ward and treatment facilities. In the case of a participant revealing treatment arm allocation to the rater this will be documented. Following the completion of the study, such violations of blinding will be analyzed to determine whether they modified the results.

Assessment of Outcome, Instruments

Primary outcomes are change in symptom load as measured by the Positive and Negative Syndrome Scale (PANSS) (39), in level of functioning as assessed by the MINI ICF- APP (40) and performance in the Matrics Cognitive Consensus Battery (MCCB) (32). Other outcomes of interest are symptoms and complaints as measured by the Brief Symptom Inventory (BSI) (41), overall severity (or improvement) as measured by the Clinical Global Impression (CGI) (42) scales, overall functionality as measured by the Global Assessment of Functioning (GAF) (43), along with overall mental health as measured by the Health of the Nation Outcome Scales (HoNOS) (44). An overview of the outcome measurements is given in **Table 4**. Besides these measurement instruments, basic demographic, and clinical characteristics together with medication will also be collected.

Statistical Analysis

We calculated our required sample size using G*Power 3.1 (51) (ANOVA: Repeated measures, three groups, four measurement points; effect size $F = 0.25$; $< = 0.05$; Power $= 0.80$; number of groups $= 3$). Based on that calculation, at least 90 participants (30 in each study arm) completing the intervention are required in order to detect small to moderate size differences. Cohen's d (effect size) will be used to compare the percentage of variation in the groups before and after treatment.

All data sets of participants will be analyzed, on an intention to treat basis. Data at baseline, second week and after the intervention, as well as at 6 and 12-months post-intervention will be considered (see **Table 3**). The demographic and clinical characteristics of the sample will be compared at baseline using an analysis of variance (ANOVA), except for gender and age, which will be assessed using an analysis of covariance (ANCOVA). To compare the overall effect of treatment over time in the three groups, data from the full intent to treat sample

TABLE 3 | Schedule of enrolment, interventions, and assessments.

	Study period						
	Enrolment	**Allocation**	**Post allocation**				**Close-out**
Time Point	**$-t_1$**	**t_0**	**t_1**	**t_2**	**t_3**	**t_4**	**t_5**
Enrolment							
Eligibility screen	X						
Informed consent	X						
Allocation		X					
Switch				X			
Interventions							
INT				●────●			
IPT				●────●			
Cogpack				●────●			
Assessments							
Demographic data	X	X					
Psychopathology			X	X	X	X	X
Psychosocial functionality			X	X	X	X	X
Neurocognition			X	X	X	X	X
Medication			X	X	X	X	X
Safety				X	X		

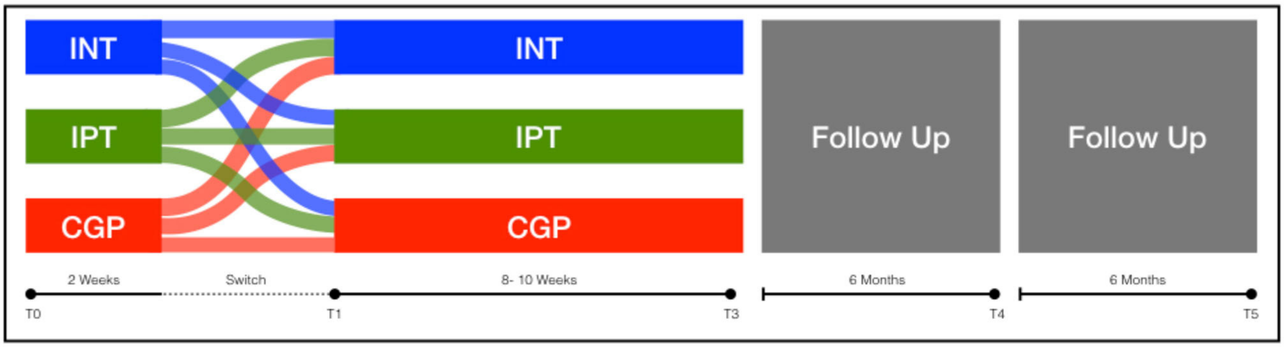

FIGURE 1 | Study flow chart.

will be analyzed using a repeated-measures analysis of variance (ANOVA) with treatment as the intergroup factor and time as the intrasubject factor. *Post-hoc* analyses will be performed using Student's *t*-test for intergroup comparisons. Reported adverse effects and safety-related events will be analyzed separately as will withdrawal from the study or treatment group changes.

Participants Switching Groups, Drop-Outs, and Missing Data

Drop-outs will be replaced until the calculated number of participants has completed the intervention; all enrolled participants will be allowed to complete the intervention. Patient switching therapeutic arm will be considered as drop-outs and will be replaced correspondingly; however, they will be allowed to complete the intervention and outcomes will be assessed as scheduled. For all dropouts, an additional intention to treat, and last observation carried forward analysis will be performed.

In contrast to drop-outs the assessment of outcomes and observation of participants switching groups will be continued. Data prior to switching will be analyzed and reported separately in order to avoid bias duplication of results for a particular participant.

The outcomes of those participants who completed the intervention after switching groups will undergo a *post-hoc* analysis with those who completed their treatment intervention without switching. A multivariate analysis of variance (MANOVA) will be performed, taking into account the switch of intervention together with outcomes measured pre- and post-intervention; i.e., ignoring the outcomes at week two for those not switching intervention arm. Groups for analysis will be constructed according to the number of participants actually switching interventions: the effect of the four first sessions will be categorized according to the change and included in the analysis.

TABLE 4 | Outcome measurements.

Test instrument	Description
Positive and Negative Syndrome Scale (PANSS)	The PANSS is a semi-structured interview designed to measure the severity of psychopathology in adult patients with a psychotic disorder, mainly schizophrenia and schizoaffective disorder (39, 45). It measures symptoms in three domains, positive (seven Items), negative (seven items), and general-non-specific symptoms (16 items). Each item is rated on a seven-point Likert scale: from 1 (not present), and from 2 (present) to 7 (very severe). The PANSS range is from 30 to 210 (39).
Mini ICF—APP	The Mini-ICF-APP was developed (40), as a short observer-rated scale for assessing the level of functioning according to the International Classification of Functioning, Disability, and Health (ICF). It assesses 13 domains of functioning, with anchor definitions provided in the manual. Each item is rated on a five-point Likert scale from 0 (no disability) to 4 (total disability).
MATRICS Consensus Cognitive Battery (MCCB)	The MATRICS (Measurement and Treatment Research to Improve Cognition in Schizophrenia) Consensus Cognitive Battery was developed to provide a relatively brief evaluation of key cognitive domains relevant to schizophrenia and related disorders (46). The test Battery includes 10 tests which represent seven different cognitive domains; the test battery is administered as a unit in a standard order. To facilitate a valid interpretation of test scores psychometric properties and normative data were also analyzed (47).
Clinical Global Impression (CGI)	The CGI scale is a brief, easy to use and pragmatic tool for the assessment of psychiatric illness severity and changes over time (42, 48, 49). The CGI consists of three subscales: 1. Severity of Illness (CGI-S), 2. Global Improvement (CGI-I), and 3. Efficacy Index (CGI-E). CGI-S and CGI-I have a seven-point Likert scale response format. It ranges from 1 representing the "healthy subject" to 7 the "extremely ill subject." The CGI-I ranges from 1 "significant improvement" to 7 "most severe deterioration," whereby a score of 4 indicates no change. The CGI-E relies on several parameters from whom an index is calculated.
Global Assessment of Functioning (GAF)	The GAF is an observer-rated, 100-point single item scale that rates overall functioning on a continuum from mental health to mental illness (43). The scale ranges from 1 (representing the most impaired individual) to 100 (representing the healthiest individual), divided into (10) deciles, 0 denoting insufficient information to make a judgment.
Health of the Nation Outcome Scales (HoNOS)	The HoNOS is an observer-rated scale and consists of 12 items with a five-point Likert scale response format from 0 (no problems) to 4 (severe/very severe problems). Scores above two are considered clinically significant. The items were combined into four dimensions; each subject can be evaluated on items, subscale scores and the total score (44, 50).

If a participant withdraws from the study, his data will be anonymized, and his name will be deleted permanently from the study.

Data Sharing and Publication

After completion of the study, a report for publication in a peer-reviewed journal will be prepared. The manuscript will be edited/compiled according to the CONSORT statement recommendation (52–54). The study protocol has been registered at: www.clinicaltrials.gov (ID: NCT0331664; 17.10.2017). The study protocol was written according to the SPIRIT 2013, statement for reporting of trial protocols (55) and the TIDieR guidelines (56).

TABLE 5 | Expected outcomes.

	Intervention		
Expected outcomes	**INT**	**IPT**	**Cogpack**
Overall improvement (CGI)	+	+	+
Overall functionality (GAF)	+++	++	+
Prescribed medication	+	++	+++
Drop out-switch of treatment group	+++	++	+
Completion of therapy	++	++	+++
Symptom load (PANSS)	+	+	+
Symptom perception (BSI)	++	++	+
Psychosocial functioning (mini ICF)	++	++	+
Psychosocial functioning (HoNOS)	++	++	+
Neurocognitive performance (MCCB)	+++	+	++
Speed of processing	++	+	+++
Verbal learning	+++	++	+
Working memory (non- verbal)	++	+	++
Working memory (verbal)	++	++	+
Reasoning and problem solving	+++	++	++
Visual learning	++	+	+++
Social cognition	++	++	+
Attention/Vigilance	+++	++	+++

Expected Outcomes

We expect all treatment arms to show similar overall rates of improvement; with differences in specific domains. Regarding symptom load, we do not expect any treatment arm to perform significantly better than the others. Regarding psychosocial functioning, we expect INT and IPT to be superior to CGP. Regarding cognitive abilities, we expect that patients participating in INT will perform better than both CGP and IPT participants.

Regarding the feasibility and implementation of the treatment arms, we expect similar retention rates in all treatment arms. Moreover, we anticipate that chronic and lower functioning participants will switch to CGP; whereas higher functioning participants may switch to INT, with lower fluctuation in IPT. Consequently, we anticipate slightly higher retention rates for IPT, followed by INT and CGP. For an overview of the expected outcomes (see **Table 5**).

DISCUSSION

Schizophrenia is a severe chronic disorder; those affected are frequently not able to cope with everyday challenges. Despite advances in treatment and an increase in treatment options the proportion of patients with schizophrenia who fully recover remains practically unchanged, this holds especially true for those requiring hospitalization for treatment (4, 57), however, for methodological reasons, those severely affected by a psychiatric disorder (i.e., those requiring hospitalization) are frequently excluded from studies testing new treatment interventions (58, 59).

The implementation of a new treatment intervention in clinical practice and moreover in an inpatient setting is a major challenge presenting a number of methodological and logistic problems. Firstly, patients hospitalized for treatment are generally more heterogeneous, with several co-morbid conditions, as well as being more severely affected than those typically included in studies. Especially patients with psychotic disorders who are more severely affected tend to have less insight and treatment motivation; consequently, they are less likely to enroll in therapy. Furthermore, the very negative and cognitive symptoms which require treatment may themselves interfere with treatment. Participants may, therefore, be unable to cope with the demands of therapy, leading to demotivation and frustration, which may lead to drop-out from therapy. We have therefore chosen to compare three treatment interventions with similar therapeutic targets and approaches, but differing participation (for patients) and implementation (for therapists) thresholds.

In clinical practice, factors relating to a patient which may affect the therapeutic outcome are considered before initiating treatment. This procedure is, however, incompatible with a randomized assignment of treatment. Furthermore, it makes it impossible to determine if a treatment is really feasible for a group of participants. Therefore, we chose to allow a switch of treatment groups after four sessions, a challenging methodological alternative which should, however, facilitate participants finding the appropriate therapy whilst allowing us to achieve our study goals. The decision to switch from one intervention to another is entirely the participant's choice. This approach strengthens the commitment of participants toward the therapy (60), by reducing feelings of failure or inadequacy which may be raised by psychometric and neurocognitive testing (61). Furthermore, we consider this approach will reduce a potential delayed selection bias.

Taking into account that participants switching treatment arms will continue their treatment, we have decided to continue the assessment of outcomes. Baseline severity will, in such cases, correspond to the time when the main therapy began. This has as a consequence that in addition to the three original treatment arms other treatment arms emerge, namely those of switching from one treatment to another. Since we are not able to accurately foresee how many participants will use this option, and if so to which treatment option they will switch, we have decided to include this in a *post-hoc* analysis. To avoid bias and duplication, we will consider participants switching groups as drop-outs in the primary analysis.

The assessment of outcomes uses a variety of instruments measuring symptom load, neuro-cognitive performance and psychosocial functionality since we expect each treatment arm to show a unique response profile (11). For symptom load, we have chosen to use the PANSS, since it is considered the most specific and validated scale for measuring change in patients with a schizophrenic psychosis (62, 63). The MCCB is regarded as the standard test battery for use with patients diagnosed with schizophrenia; it is claimed as both robust to learning effects and sensitive to change (47). Taking into account that improvements in symptomatology and neuro-cognition should lead to increased autonomy, we have chosen the mini-ICF-APP to assess psychosocial-functioning independently of the main diagnosis (40, 64, 65). Using this set of outcome measures, we expect to assess all facets of the interventions, whilst facilitating the interpretation and comparison of our results with those from previous studies (63).

We anticipate an overall improvement in all participants, regardless of group allocation. This may be attributable to pharmacological treatments administered to the participants. For the same reason, we do not anticipate significant differences in symptom load. However, we do not exclude to find differences in dose equivalents of administered medication, primarily antipsychotics and benzodiazepines. Furthermore, we hope for a reduction of polypharmacy. In order to quantify this effect; medication, respectively dose and dose equivalents, will be taken into account as possible confounders (66). Pharmacological treatment will not be restricted since we consider withholding or delaying pharmacological treatment for methodological or design purposes to be unacceptable; furthermore, in clinical practice, psychological interventions are used as an add-on to pharmacological therapy (11). Offering just a single psychotherapeutic treatment could be ineffective for some patients and at worst detrimental, which could lead to treatment abandonment (67). An intervention which is neither accepted nor tolerated by participants should not be imposed on them.

The allocation of a patient to a treatment arm which does not meet his needs is considered to be unacceptable and may have detrimental effects. To avoid this situation, we have decided to allow participants to switch groups under particular conditions. We consider this approach to be both appropriate and compatible with the trial objectives since we are also interested in evaluating feasibility. In order to minimize the effect of group changes on the primary and secondary outcomes of the study, and to have similar treatment duration and number of sessions, we have chosen to conduct a second assessment prior to a (potential) change of groups. We consider 2 weeks, respectively four sessions, sufficient to determine the suitability and safety of a therapy. INT in outpatient setting shows low drop-out rates and high rates of attendance which indicates a high level of acceptance and motivation and lends support feasibility (29). Another aim of this study is to evaluate whether this also applies to inpatient settings.

Another challenge of this trial was the adaptation of a treatment (INT) designed for outpatients to an inpatient setting (29, 38). The hierarchical structure of the intervention, the density of the therapeutic sessions, and the duration of the therapy had to be taken into account together with the fact that the original therapeutic design foresees closed therapeutic groups (27). For its implementation in an inpatient setting, we subdivided the intervention into modules or blocks comprising of four sessions, allowing the participants to join the therapy at specified times thus allowing for (semi)closed groups. The disadvantage of this approach lies in the hierarchical structure of both INT and IPT interventions (23, 27), which leads participants potentially starting with a more challenging topic; to minimize this effect blocks or modules also had a bottom-up structure allowing new participants to integrate quickly into the group.

Lower functioning patients with low functioning, including those with chronic schizophrenia, seem to benefit from higher frequency psychotherapy (21, 68). We, therefore, concluded that two weekly sessions of 90 min would fulfill this demand. Taking into account the usual length of stay in our unit (6 to 8 weeks), together with current guidelines (17–19) we have chosen to offer at least 16 sessions to participants. For methodological reasons it was not possible to condense both therapeutic interventions to this number of sessions, therefore IPT, INT and CGP have been adapted to 20 sessions programs, respecting the specifications of the treatment manuals.

We considered this to be compatible with the average length of stay in our unit, since some patients remain in treatment for more than 8 weeks. Participants are also encouraged to continue participation after discharge. Although we consider that the completion of a treatment programme to be an important factor determining response, evidence suggests that response is not associated with treatment duration and number of sessions (10).

There is reason to believe that the three treatment arms will differ from one another due to top-down and integration effects on multiple domains. In respect of social- and neuro-cognition, we expect INT and IPT to outperform CGP (36, 69). Nevertheless, we cannot rule out that CGP may also lead to improvements in neuro-cognitive abilities, in particular MCCB domains tested on the computer due to learning and practice effects (12, 70). We expect INT participants to achieve a higher psychosocial performance than CGP, but similar to those of IPT. Although INT and IPT have common roots, applying similar technics for social cognition (23, 27, 37), we expect INT to deliver better outcomes due to its higher complexity and integrative approach (see **Table 5**).

In our study, we wish to evaluate the feasibility of a psychotherapeutic intervention in a unit specialized for the treatment of chronic and low functioning patients with a schizophrenic psychosis. Therefore, the effort required to implement such regular group psychotherapy will also be taken into account. The IPT treatment programme is manualized and has traditionally been delivered by nursing staff after an introductory seminar and workshop (23). The implementation of INT is more challenging since it also requires a trained psychotherapist (27). CGP, on the other hand, is easily implemented and requires practically no training to deliver (26, 71, 72). However, professional experience is a significant factor predicting therapy outcome. Moreover, the therapist variable is an essential factor relating to motivation to participate in the therapy and influencing drop-out rates (73–75). Consequently, all therapists running groups in this study will receive regular supervision and training.

AUTHOR CONTRIBUTIONS

MR wrote the manuscript. DM contributed to the study design and manuscript. ES, SV, and SE contributed to the study design, study protocol and manuscript. All authors contributed to the article and approved the submitted version.

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REFERENCES

1. Van Os J, Kapur S. Schizophrenia. *Lancet.* (2009) 374:635–45. doi: 10.1016/S0140-6736(09)60995-8
2. Kahn RS, Sommer IE, Murray RM, Meyer-Lindenberg A, Weinberger DR, Cannon TD, et al. Schizophrenia. *Nat Rev Dis Primers.* (2015) 1:15067. doi: 10.1038/nrdp.2015.67
3. Tandon R, Gaebel W, Barch DM, Bustillo J, Gur RE, Heckers S, et al. Definition and description of schizophrenia in the DSM-5. *Schizophr Res.* (2013) 150:3–10. doi: 10.1016/j.schres.2013.05.028
4. Hegarty JD, Baldessarini RJ, Tohen M, Waternaux C, Oepen G. One hundred years of schizophrenia: a meta-analysis of the outcome literature. *Am J Psychiatry.* (1994) 151:1409–16. doi: 10.1176/ajp.151.10.1409
5. Leucht S, Leucht C, Huhn M, Chaimani A, Mavridis D, Helfer B, et al. Sixty years of placebo-controlled antipsychotic drug trials in acute schizophrenia: systematic review, Bayesian meta-analysis, and meta-regression of efficacy predictors. *Am J Psychiatry.* (2017) 174:927–42. doi: 10.1176/appi.ajp.2017.16121358
6. Torniainen M, Mittendorfer-Rutz E, Tanskanen A, Bjorkenstam C, Suvisaari J, Alexanderson K, et al. Antipsychotic treatment and mortality in schizophrenia *Schizophr Bull.* (2014) 41:656–63. doi: 10.1093/schbul/sbu164
7. Vanasse A, Blais L, Courteau J, Cohen AA, Roberge P, Larouche A, et al. Comparative effectiveness and safety of antipsychotic drugs in schizophrenia treatment: a real-world observational study. *Acta Psychiatr Scand.* (2016) 134:374–84. doi: 10.1111/acps.12621
8. Goff DC, Falkai P, Fleischhacker WW, Girgis RR, Kahn RM, Uchida H, et al. The long-term effects of antipsychotic medication on clinical course in schizophrenia. *Am J Psychiatry.* (2017) 174:840–9. doi: 10.1176/appi.ajp.2017.16091016
9. Taipale H, Mehtälä J, Tanskanen A, Tiihonen J. Comparative effectiveness of antipsychotic drugs for rehospitalization in schizophrenia—A Nationwide study with 20-year follow-up. *SchizophrBull.* (2017) 44:1381–7. doi: 10.1093/schbul/sbx176
10. Bighelli I, Huhn M, Schneider-Thoma J, Krause M, Reitmeir C, Wallis S, et al. Response rates in patients with schizophrenia and positive symptoms receiving cognitive behavioural therapy: a systematic review and single-group meta-analysis. *BMC Psychiatry.* (2018) 18:380. doi: 10.1186/s12888-018-1964-8
11. Bighelli I, Salanti G, Huhn M, Schneider-Thoma J, Krause M, Reitmeir C, et al. Psychological interventions to reduce positive symptoms in schizophrenia: systematic review and network meta-analysis. *World Psychiatry.* (2018) 17:316–29. doi: 10.1002/wps.20577
12. Mcgurk SR, Twamley EW, Sitzer DI, Mchugo GJ, Mueser KT. A meta-analysis of cognitive remediation in schizophrenia. *Am J Psychiatry.* (2007) 164:1791–802. doi: 10.1176/appi.ajp.2007.07060906
13. Wykes T, Huddy V, Cellard C, Mcgurk SR, Czobor P. A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. *Am J Psychiatry.* (2011) 168:472–85. doi: 10.1176/appi.ajp.2010.10060855
14. Müller DR, Roder V. Vom kognitiven Training zur Kognitiven Remediationstherapie: Nutzen und Grenzen. *Verhaltenstherapie.* (2017) 27:170–9. doi: 10.1159/000479853

15. Prikken M, Konings MJ, Lei WU, Begemann MJH, Sommer IEC. The efficacy of computerized cognitive drill and practice training for patients with a schizophrenia-spectrum disorder: A meta-analysis. *Schizophr Res.* (2019) 204:368–74. doi: 10.1016/j.schres.2018.07.034
16. Lehman AF, Lieberman JA, Dixon LB, Mcglashan TH, Miller AL, Perkins DO, et al. Practice guideline for the treatment of patients with schizophrenia. *Am J Psychiatry.* (2004) 161 (2 Suppl.):1–56.
17. Nice. *Psychosis and Schizophrenia in Adults: Prevention and Management*. National Clinical Practice Guidelines Number *CG*178 (2014).
18. Galletly C, Castle D, Dark F, Humberstone V, Jablensky A, Killackey E, et al. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the management of schizophrenia and related disorders. *Aust N Z J Psychiatry.* (2016) 50:410–72. doi: 10.1177/0004867416641195
19. Kaiser S, Berger G, Conus P, Kawohl W, Müller TJ, Schimmelman BG, et al. *SGPP Behandlungsempfehlungen Schizophrenie.* Bern: SGPP (2016).
20. Grant PM, Huh GA, Perivoliotis D, Stolar NM, Beck AT. Randomized trial to evaluate the efficacy of cognitive therapy for low-functioning patients with schizophrenia. *Arch Gen Psychiatry.* (2012) 69:121–7. doi: 10.1001/archgenpsychiatry.2011.129
21. Grant PM, Bredemeier K, Beck AT. Six-month follow-up of recovery-oriented cognitive therapy for low-functioning individuals with schizophrenia. *Psychiatr Serv.* (2017) 68:997–1002. doi: 10.1176/appi.ps.201600413
22. Boden MT, Gaudiano BA, Walser RD, Timko C, Faustman W, Yasmin S, et al. Feasibility and challenges of inpatient psychotherapy for psychosis: lessons learned from a veterans health administration pilot randomized controlled trial. *BMC Res Notes.* (2016) 9:376. doi: 10.1186/s13104-016-2179-z
23. Roder V, Brenner HD, Kienz N. *Integriertes Psychologisches Therapieprogramm fur Schizophrene Patienten (IPT).* Munich: Psychologie-Verl.; Union Munchen (1988).
24. Roder V, Mueller DR, Schmidt SJ. Effectiveness of integrated psychological therapy (IPT) for schizophrenia patients: a research update. *Schizophr Bull.* (2011) 37(Suppl. 2):S71–9. doi: 10.1093/schbul/sbr072
25. Roder V, Mueller DR, Mueser KT, Brenner HD. Integrated psychological therapy (IPT) for schizophrenia: is it effective? *Schizophr Bull.* (2006) 32(Suppl. 1):S81–93. doi: 10.1093/schbul/sbl021
26. Marker, K. (2003). *COGPACK Manual Version 5.9.* Ladenburg: Marker Software.
27. Roder V, Müller DS, Stefanie J, Lächler M. *INT–Integrierte Neurokognitive Therapie bei Schizophren Erkrankten*. Berlin; Heidelberg: Springer (2013). doi: 10.1007/978-3-642-21440-0
28. Roder V, Müller DR, Schmidt SJ. Empirische Evidenz der INT. In: *INT-Integrierte Neurokognitive Therapie bei Schizophren Erkrankten*. Berlin; Heidelberg: Springer (2013). p. 139–41. doi: 10.1007/978-3-642-21440-0_5
29. Mueller DR, Khalesi Z, Benzing V, Castiglione CI, Roder V. Does Integrated Neurocognitive Therapy (INT) reduce severe negative symptoms in schizophrenia outpatients? *Schizophr Res.* (2017) 188:92–7. doi: 10.1016/j.schres.2017.01.037
30. De Mare A, Cantarella M, Galeoto G. Effectiveness of integrated neurocognitive therapy on cognitive impairment and functional outcome for schizophrenia outpatients. *Schizophr Res Treat.* (2018) 2018:2360697. doi: 10.1155/2018/2360697
31. Roder VB, Hans D, Müller D. *Integriertes Psychologisches Therapieprogramm bei Schizophren Erkrankten IPT*. Weinheim: Julius Beltz (2019).
32. Green MF, Nuechterlein KH. The MATRICS initiative: developing a consensus cognitive battery for clinical trials. *Schizophr Res.* (2004) 72:1–3. doi: 10.1016/j.schres.2004.09.006
33. Rabinowitz J, Reichenberg A, Weiser M, Mark M, Kaplan Z, Davidson M. Cognitive and behavioural functioning in men with schizophrenia both before and shortly after first admission to hospital. Cross-sectional analysis. *Br J Psychiatry.* (2000) 177:26–32. doi: 10.1192/bjp.177.1.26
34. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (DSM-5®).* (2013). Washington, DC: American Psychiatric Association.
35. Verhelst N, Van Avermaet P, Takala S, Figueras N, North B. *Common European Framework of Reference for Languages: Learning, Teaching, Assessment*. Cambridge: Cambridge University Press (2009).
36. Lindenmayer JP, Khan A, Mcgurk SR, Kulsa MKC, Ljuri I, Ozog V, et al. Does social cognition training augment response to computer-assisted cognitive remediation for schizophrenia? *Schizophr Res.* (2018) 201:180–6. doi: 10.1016/j.schres.2018.06.012
37. Roder V, Brenner HD, Kienzle N. *Integriertes psychologisches Therapieprogramm bei Schizophrenen Erkrankten IPT*. Weinheim; Basel: Psychologie Verlagsunion (2008).
38. Mueller DR, Schmidt SJ, Roder V. One-year randomized controlled trial and follow-up of integrated neurocognitive therapy for schizophrenia outpatients. *Schizophr Bull.* (2015) 41:604–16. doi: 10.1093/schbul/sbu223
39. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull.* (1987) 13:261–76. doi: 10.1093/schbul/13.2.261
40. Linden M, Baron S. [The "Mini-ICF-Rating for Mental Disorders (Mini-ICF-P)". A short instrument for the assessment of disabilities in mental disorders]. *Rehabilitation.* (2005) 44:144–51. doi: 10.1055/s-2004-834786
41. Derogatis L, Melisaratos N. The Brief Symptom Inventory: an introductory report. *Psychol Med.* (1983) 3:595–605. doi: 10.1017/S0033291700048017
42. Guy W. *ECDEU Assessment Manual for Psychopharmacology*. Rockville, MD: US Department of Health, Education, and Welfare, Public Health Service, Alcohol, Drug Abuse, and Mental Health Administration, National Institute of Mental Health, Psychopharmacology Research Branch, Division of Extramural Research Programs (1976).
43. Jean Endicott P, Robert L, Spitzer M, Joseph L, Fleiss P, Jacob Cohen P. The global assessment scale. *Arch Gen Psychiatry.* (1976) 33:766–71. doi: 10.1001/archpsyc.1976.01770060086012
44. Wing J, Beevor A, Curtis R, Park S, Hadden S, Burns A. Health of the Nation Outcome Scales (HoNOS). Research and development. *Br J Psychiatry.* (1998) 172:11–8. doi: 10.1192/bjp.172.1.11
45. Leucht S, Kane JM, Kissling W, Hamann J, Etschel E, Engel RR. What does the PANSS mean? *Schizophr Res.* (2005) 79:231–8. doi: 10.1016/j.schres.2005.04.008
46. Nuechterlein KH, Green MF, Kern RS, Baade LE, Barch DM, Cohen JD, et al. The MATRICS Consensus Cognitive Battery, part 1: test selection, reliability, and validity. *Am J Psychiatry.* (2008) 165:203–13. doi: 10.1176/appi.ajp.2007.07010042
47. Green MF, Nuechterlein KH, Kern RS, Baade LE, Fenton WS, Gold JM, et al. Functional co-primary measures for clinical trials in schizophrenia: results from the MATRICS Psychometric and Standardization Study. *Am J Psychiatry.* (2008) 165:221–8. doi: 10.1176/appi.ajp.2007.07010089
48. Berk M, Ng F, Dodd S, Callaly T, Campbell S, Bernardo M, et al. The validity of the CGI severity and improvement scales as measures of clinical effectiveness suitable for routine clinical use. *J Eval Clin Pract.* (2008) 14:979–83. doi: 10.1111/j.1365-2753.2007.00921.x
49. Busner J, Targum SD. The clinical global impressions scale: applying a research tool in clinical practice. *Psychiatry.* (2007) 4:28.
50. Wing J, Curtis R, Beevor A. Health of the Nation Outcome Scales (HoNOS). Glossary for HoNOS score sheet. *Br J Psychiatry.* (1999) 174:432–4. doi: 10.1192/bjp.174.5.432
51. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods.* (2007) 39:175–91. doi: 10.3758/BF03193146
52. Moher D, Schulz KF, Altman D. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. *JAMA.* (2001) 285:1987–91. doi: 10.1001/jama.285.15.1987
53. Moher D, Hopewell S, Schulz KF, Montori V, Gotzsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *BMJ.* (2010) 340:c869. doi: 10.1136/bmj.c869
54. Schulz KF, Altman DG, Moher D. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMC Med.* (2010) 8:18. doi: 10.1186/1741-7015-8-18
55. Chan AW, Tetzlaff JM, Gotzsche PC, Altman DG, Mann H, Berlin JA, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ.* (2013) 346:e7586. doi: 10.1136/bmj.e7586
56. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ.* (2014) 348:g1687. doi: 10.1136/bmj.g1687

57. Jääskeläinen E, Juola P, Hirvonen N, Mcgrath JJ, Saha S, Isohanni M, et al. A systematic review and meta-analysis of recovery in schizophrenia. *Schizophr Bull.* (2012) 39:1296–306. doi: 10.1093/schbul/sbs130
58. Zimmerman M, Clark HL, Multach MD, Walsh E, Rosenstein LK, Gazarian D. Have treatment studies of depression become even less generalizable? A review of the inclusion and exclusion criteria used in placebo-controlled antidepressant efficacy trials published during the past 20 years. *Mayo Clin Proc.* (2015) 90:1180–6. doi: 10.1016/j.mayocp.2015.06.016
59. Zimmerman M, Holst CG, Clark HL, Multach M, Walsh E, Rosenstein LK, et al. The psychiatric inclusion and exclusion criteria in placebo-controlled monotherapy trials of bipolar depression: an analysis of studies of the past 20 years. *CNS Drugs.* (2016) 30:1209–18. doi: 10.1007/s40263-016-0381-0
60. Mitrushina M, Tomaszewski R. The effect of subjective perception of cognition on emotional functioning in adults with long-term neurological and neuropsychiatric disorders. *Disabil Rehabil.* (2019) 1–7. doi: 10.1080/09638288.2019.1585490
61. Borjesson S, Bostrom PK. "I want to know what it is used for": Clients' perspectives on completing a routine outcome measure (ROM) while undergoing psychotherapy. *Psychother Res.* (2019) 30:337–47. doi: 10.1080/10503307.2019.1630780
62. Andreasen NC, Carpenter WTJr, Kane JM, Lasser RA, Marder SR, Weinberger DR. Remission in schizophrenia: proposed criteria and rationale for consensus. *Am J Psychiatry.* (2005) 162:441–9. doi: 10.1176/appi.ajp.162.3.441
63. Van Os J, Burns T, Cavallaro R, Leucht S, Peuskens J, Helldin L, et al. Standardized remission criteria in schizophrenia. *Acta Psychiatr Scand.* (2006) 113:91–5. doi: 10.1111/j.1600-0447.2005.00659.x
64. Pinna F, Fiorillo A, Tusconi M, Guiso B, Carpiniello B. Assessment of functioning in patients with schizophrenia and schizoaffective disorder with the Mini-ICF-APP: a validation study in Italy. *Int J Ment Health Syst.* (2015) 9:37. doi: 10.1186/s13033-015-0030-x
65. Egger ST, Weniger G, Muller M, Bobes J, Seifritz E, Vetter S. Assessing the severity of functional impairment of psychiatric disorders: equipercentile linking the mini-ICF-APP and CGI. *Health Qual Life Outcomes.* (2019) 17:174. doi: 10.1186/s12955-019-1235-5
66. Patel MX, Arista IA, Taylor M, Barnes TR. How to compare doses of different antipsychotics: a systematic review of methods. *Schizophr Res.* (2013) 149:141–8. doi: 10.1016/j.schres.2013.06.030
67. Villeneuve K, Potvin S, Lesage A, Nicole L. Meta-analysis of rates of drop-out from psychosocial treatment among persons with schizophrenia spectrum disorder. *Schizophr Res.* (2010) 121:266–70. doi: 10.1016/j.schres.2010.04.003
68. Rakitzi S, Georgila P. The integrated psychological therapy and treatment-resistant schizophrenia: initial findings. *Psychiatry.* (2019) 1–14. doi: 10.1080/00332747.2019.1616658
69. Aloi M, De Filippis R, Grosso Lavalle F, Chiappetta E, Vigano C, Segura-Garcia C, et al. Effectiveness of integrated psychological therapy on clinical, neuropsychological, emotional and functional outcome in schizophrenia: a RCT study. *J Ment Health.* (2018) 1–8. doi: 10.1080/09638237.2018.1521948
70. Bryce SD, Rossell SL, Lee SJ, Lawrence RJ, Tan EJ, Carruthers SP, et al. Neurocognitive and Self-efficacy benefits of cognitive remediation in schizophrenia: a randomized controlled trial. *J Int Neuropsychol Soc.* (2018) 24:549–62. doi: 10.1017/S1355617717001369
71. Sartory G, Zorn C, Groetzinger G, Windgassen K. Computerized cognitive remediation improves verbal learning and processing speed in schizophrenia. *Schizophr Res.* (2005) 75:219–23. doi: 10.1016/j.schres.2004.10.004
72. Lindenmayer JP, Fregenti S, Kang G, Ozog V, Ljuri I, Khan A, et al. The relationship of cognitive improvement after cognitive remediation with social functioning in patients with schizophrenia and severe cognitive deficits. *Schizophr Res.* (2017) 185:154–60. doi: 10.1016/j.schres.2017.01.007
73. Baldwin SA, Berkeljon A, Atkins DC, Olsen JA, Nielsen SL. Rates of change in naturalistic psychotherapy: contrasting dose-effect and good-enough level models of change. *J Consult Clin Psychol.* (2009) 77:203–11. doi: 10.1037/a0015235
74. Sharf J, Primavera LH, Diener MJ. Dropout and therapeutic alliance: a meta-analysis of adult individual psychotherapy. *Psychotherapy.* (2010) 47:637–45. doi: 10.1037/a0021175
75. Vancampfort D, Rosenbaum S, Schuch FB, Ward PB, Probst M, Stubbs B. Prevalence and predictors of treatment dropout from physical activity interventions in schizophrenia: a meta-analysis. *Gen Hosp Psychiatry.* (2016) 39:15–23. doi: 10.1016/j.genhosppsych.2015.11.008

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Management and Treatment of Patients With Major Depressive Disorder and Chronic Diseases: A Multidisciplinary Approach

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In patients with physical chronic diseases, the prevalence of major depressive disorder (MDD) is approximately 2- to 3-fold higher than in the general population, and it can reach up to 20–40%. The comorbidity of MDD with chronic medical diseases is associated with poorer quality of life, increased medical symptom burden, poor adherence to self-care regimens, increased risk of functional impairment, morbidity, and mortality, and also higher medical costs. Despite this evidence, in routine practice, psychological issues and concerns are frequently inadequately managed. This consensus document proposes that a proper diagnosis, a multidisciplinary approach, and a personalized treatment plan would allow patients with MDD and chronic comorbidities to be more compliant, to improve the outcomes, to reduce possible relapses in the long term, and to prevent or better manage complications and adverse events. This proposal might be useful for any health professionals who deal with patients with chronic diseases, as it can help to pay more attention to the emotional impact of these conditions, in particular in terms of depressive symptoms.

Keywords: depression, major depressive disorder, chronic diseases, diabetes, rheumatoid arthritis, cancer, Parkinson's disease

INTRODUCTION

The prevalence of major depressive disorder (MDD) in the general population is approximately 6.6% (Kessler et al., 2005), with a lifetime prevalence of approximately 11% (Lim et al., 2018). In patients with chronic diseases, MDD prevalence is approximately 2- to 3-fold higher, notably reaching up to 20–40% (Read et al., 2017). A higher prevalence of MDD has been found in patients with a range of chronic conditions, including cardiovascular diseases (Rudisch and Nemeroff, 2003), diabetes (Anderson et al., 2001), arthritis (Matcham et al., 2013), and cancer (Smith, 2015). The WHO World Health Survey (WHS) found a greater prevalence of MDD in people who had at least one chronic condition (9.3–23%), compared to those with none (3.2%; Moussavi et al., 2007). The comorbidity of MDD with chronic diseases has been associated with poorer quality of life, increased symptom burden, poor adherence to self-care regimens, increased risk of morbidity and mortality, and higher medical costs (Moussavi et al., 2007; Katon, 2011; Reddy, 2016). Beyond that, functional impairment is more severe in patients with comorbidity compared to that in patients with either MDD or a chronic disease exclusively (Moussavi et al., 2007; Kang et al., 2015).

Despite this, clinicians frequently fail to address the psychological component of chronic diseases. Depressive symptoms are often inadequately managed because of a lack of training, guidelines, and recommendations (Read et al., 2017). In a fundamental attempt to fill this gap, this multidisciplinary consensus document was produced with two main purposes: (1) to describe the prevalence of MDD in patients with chronic diseases (i.e., diabetes, rheumatoid arthritis, cancer, and Parkinson's disease) and (2) to define guidelines to manage this specific patient population. The multidisciplinary international advisory board was composed of European experts with proven experience in caring for patients with chronic diseases and MDD. The expert consensus statement rests on literature evidence. An extensive review of the literature was performed to identify studies investigating prevalence, clinical manifestation, and impact on outcome of MDD in patients with chronic diseases.

MATERIALS AND METHODS

The review was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009). Four electronic databases (MEDLINE, PubMed, CINAHL, and PsychINFO) were searched to identify studies. The following terms were used in combination with a range of subject headings for each database: (depression OR depressive OR mdd OR mood OR psychiatr* OR psychol*) AND (diabetes OR diabet* OR rheumatoid arthritis OR arthritis OR rheumat* OR cancer OR tumor OR oncol* OR Parkinson's disease OR Parkinson OR chronic illness OR progressive disease).

MDD and Chronic Diseases: A Close Relationship

The relationship between MDD and chronic diseases is bidirectional (Katon, 2011). Physical symptoms can cause or exacerbate depressive symptoms, but the reverse also occurs, with depressive symptoms antedating the onset of health problems (Katon, 2003). The adverse health risk behaviors and the psychobiological changes associated with MDD can increase the risk for chronic diseases, and the biological changes and complications associated with chronic medical conditions can precipitate depressive symptoms leading to MDD (Katon, 2011). Chronic physical morbidity can also lead to MDD through psychosocial factors such as symptom burden, disability, decreased quality of life (Katon, 2003), pain (Bair et al., 2003), dysfunctional beliefs about disease, and ineffective coping (Ziarko et al., 2014). MDD can worsen the outcomes of chronic diseases because of its effect on proinflammatory factors, the hypothalamic-pituitary axis, the autonomic nervous system, and metabolic factors, in addition to being associated with a higher risk of engaging in health risk behaviors (Katon, 2011). Furthermore, poorer disease management may occur in MDD patients, as they less likely adhere to medical regimens (Alexopoulos et al., 2008; Katon, 2011). Although a cause-effect relationship between MDD and chronic diseases has not been established, there is growing evidence that the neurobiological changes of chronic diseases and the associated psychological distress can lead to MDD (Read et al., 2017). Vascular brain lesions, reductions of neurotransmitters in the limbic area, hyperactivity of the hypothalamic-pituitary-adrenal axis, hormonal, metabolic, and immune-inflammatory dysregulations are common in many chronic diseases, and have been linked also to MDD (Nestler et al., 2002; Camus et al., 2004; Freeman et al., 2004; Pariante and Lightman, 2008; Bogdan et al., 2013; Miller and Raison, 2016; Penninx, 2017). A persistent inflammatory status has been frequently found in the course of many chronic diseases and has been associated with a higher risk for MDD (Nestler et al., 2002; Miller and Raison, 2016). As MDD has been linked to low-grade inflammation/dysregulated inflammation, in the long term such condition may predispose to the onset of a chronic disease (Miller and Raison, 2016).

MDD and Diabetes

Patients with MDD and those with diabetes patients share reciprocal susceptibility and a high degree of comorbidity (Canadian Diabetes Association Clinical Practice Guidelines Expert Committee et al., 2013; Pouwer, 2017). The prevalence of depressive symptoms among patients with diabetes is in the range of 30%, and the prevalence of MDD is approximately 10%, which is double the overall prevalence in people without a chronic disease (Canadian Diabetes Association Clinical Practice Guidelines Expert Committee et al., 2013). Risk factors for MDD in patients with diabetes have been identified as female sex, adolescents/young adults and older adults, poverty, few social supports, stressful life events, poor glycaemic control, longer duration of diabetes, and presence of long-term complications, especially painful neuropathy (Mezuk et al., 2008; D'Amato et al., 2016). In addition, the complexity of diabetes treatment regimens might be highly demanding and its burden can lead to depressive reactions. MDD patients have an approximately 60% increased risk of developing type 2 diabetes (Mezuk et al., 2008). The possible mechanisms leading to diabetes in MDD patients involve adverse health risk behaviors (such as physical inactivity and obesity, responsible for insulin resistance) and psychological distress, which causes chronic hypothalamic-pituitary-adrenal activation with subclinical hypercortisolism (Mezuk et al., 2008; Joseph and Golden, 2017). Moreover, long-term use of antidepressants has been related with an increased risk of diabetes (Andersohn et al., 2009). In patients with type 1 diabetes, the presence of MDD has been associated with severe hyperglycaemia and hypoglycaemia (Gilsanz et al., 2018) and with increased cardiovascular mortality (Pouwer, 2017; Farooqi et al., 2019). The prognosis for comorbid MDD and diabetes is worse than when each illness occurs separately: MDD amplifies the diabetes symptom burden and worsens clinical outcomes. On the other hand, MDD tends to be longer and have a higher chance of recurrence (Peyrot and Rubin, 1999; Ludman et al., 2004; Egede et al., 2005).

MDD and Rheumatoid Arthritis

The prevalence of MDD can be as high as 66% in patients with rheumatoid arthritis and almost 17% of rheumatoid arthritis patients have a current MDD (Matcham et al., 2016; Fiest et al., 2017). Chronic pain and depressive symptoms are closely related as regards occurrence, and the coexistence tends to further aggravate the severity of both conditions (Sheng et al., 2017). Although the nature of the relation between pain and MDD remains unclear, recent studies have found considerable overlaps between pain- and depression-induced neuroplasticity and neurobiological changes (Sheng et al., 2017). Many studies have described the associations between peripheral and brain immune responses, which suggest shared pathophysiological mechanisms for immune-mediated inflammatory diseases and MDD (Nerurkar et al., 2019). MDD is associated with adverse outcomes in rheumatoid arthritis: higher levels of pain and disability, lower quality of life, increased disease activity, reduced response to treatment, decreased likelihood of achieving symptom remission, and increased mortality (van den Hoek et al., 2016; Fiest et al., 2017).

MDD and Cancer

The rate of MDD in cancer patients is thought to be up to three times higher than that in the general population (Linden et al., 2012). Depressive symptoms of cancer patients exist on a continuum ranging from non-pathological sadness to an adjustment disorder to subclinical depression to MDD: it has been reported that 0–38% of cancer patients have a concomitant MDD and 0–58% suffer with depressive symptoms (Smith, 2015; Sherrill et al., 2017). MDD rates may vary depending on the site of primary cancer, age, and sex (Linden et al., 2012) and differ over the course of cancer. High rates of MDD are frequent around the time of diagnosis and in patients with advanced disease, while in cancer survivors 5 years after diagnosis, they are comparable to those of the general population (Linden et al., 2012; Smith, 2015). Metastases and pain have been associated with more severe MDD (Ciaramella and Poli, 2001) and the prevalence of MDD is significantly higher in patients with pain, suggesting how pain may have a causative role in MDD onset (Spiegel et al., 1994). MDD in cancer is a multifactorial disorder involving psychosocial (psychological distress, maladaptive coping, previous mental disorders, and social and emotional support), biological (inflammation, hypothalamic-pituitary-adrenal axis activation, neurotransmitters, and hormones changes), and iatrogenic mechanisms (antiemetic drugs and immunotherapy agents, including INF-α; Leonard, 2010; Smith, 2015). MDD in cancer leads to a poorer quality of life, compromises cancer outcomes, and results in higher rates of mortality (Satin et al., 2009; Smith, 2015).

MDD and Parkinson's Disease

The prevalence of MDD in Parkinson's disease (PD) varies between studies (Aarsland et al., 2011). However, a systematic review estimated that 50–70% of PD patients have been affected by MDD (Bomasang-Layno et al., 2015). MDD in PD is more common than in age-matched controls with other chronic diseases, such as diabetes, hypertension, coronary artery disease, or congestive heart failure (Nuti et al., 2004; Egede, 2007; Reijnders et al., 2008; Tan, 2012) and can develop at any phase of the disease. Studies suggested that depressive symptoms may precede the diagnosis of PD by 5 up to 20 years, and MDD has been associated with an increased risk of developing PD with an incidence of 23% (Chaudhuri et al., 2006; Pellicano et al., 2007; Postuma et al., 2012; Chen et al., 2013; Pont-Sunyer et al., 2015). Once PD is diagnosed, the annual rates of newly diagnosed MDD range from 1.86 to 10% (Aarsland et al., 2011; Marsh, 2013; Yapici Eser et al., 2017) and studies have shown that MDD tends to be persistent and worsens over time (Aarsland et al., 2011). Although the exact etiology is unknown, several hypotheses supporting the link between MDD and PD physiopathology have been proposed (Aarsland et al., 2011; Santiago et al., 2017). A significant biological mechanism is more probable than a pure reactive basis and could be a result of damage to serotoninergic neurotransmission, as well as limbic noradrenergic and dopaminergic mechanisms (Chaudhuri et al., 2006). Other factors that might contribute to MDD in PD patients are stress-induced hypercortisolaemia, pain, genetic abnormalities, inflammation and changes in neurotrophic molecules, previous mood disorders, and psychosocial distress (Leonard, 2010; Aarsland et al., 2011; Santiago et al., 2017). In PD, MDD is associated with worse clinical outcomes: when untreated, MDD is related to earlier initiation of dopaminergic therapy, greater functional disability, faster physical and cognitive deterioration, increased mortality, poorer quality of life, and increased distress in caregivers (Aarsland et al., 2011; Marsh, 2013).

MDD in Chronic Diseases: Diagnostic Problems

Although MDD is frequent in chronic disease patients, it remains often unrecognized and, despite the negative consequences on patient health, physicians tend to undertreat it (De Jean et al., 2013). One reason for this could be the diagnostic difficulty experienced by other specialists rather than psychiatrists. MDD may be underdiagnosed when comorbid with a chronic disease, as it may be disguised by other symptoms that draw the attention of both patient and physician. Somatic disturbances such as fatigue, appetite disturbances, and sleep disorders may be sequelae of physical problems rather than symptoms of MDD. In addition, the presence of pain could further complicate the diagnosis. To discern these situations, tools that highlight emotional, cognitive, and somatic aspects of pain are useful; for instance, symptoms such as hypo-volition and anhedonia need to be taken into consideration during anamnesis to establish the presence of depressive symptoms, regardless of pain. Additionally, patients with chronic diseases may deny MDD, whereas clinicians may sometimes have insufficient time to investigate the psychological component. Moreover, the stigmatization of MDD by both physicians and patients may jeopardize diagnoses. Furthermore, MDD is a complex combination of physical and mental symptoms, and when organic factors are involved, as in chronic diseases, patients struggle to accept treatment for psychological comorbidity (De Jean et al., 2013). General practitioners represent the first reference for patients with chronic diseases. However, they seem often unaware that MDD is common among them and that MDD affects the course of the diseases and clinical outcomes. For these reasons, recommendations for MDD diagnostic algorithms and screening practices in chronic diseases are needed.

Management of MDD in Chronic Diseases: The Multidisciplinary Team Approach

The National Institute for Health and Care Excellence (NICE) recommendations state that patients with chronic diseases and moderate to severe MDD, linked with functional impairment, should be treated with a multidisciplinary team approach [National Collaborating Centre for Mental Health (UK), 2010; Kang et al., 2015]. Collaborative care should be part of a stepped-care program and coordinated at the primary and secondary care level; all sectors of care should be integrated in a comprehensive approach to both mental and physical symptoms. A multidisciplinary team (including general practitioners, nurses, specialists, and mental health professionals) coordinated by a case manager should closely collaborate to provide a wide range of interventions [e.g., patient education, psychological and pharmacological interventions, medication management, follow-up controls; National Collaborating Centre for Mental Health (UK), 2010]. This approach has been shown to be more effective than usual care as regards illness burden, physical, and psychological outcomes in patients with MDD and chronic diseases (van Eck van der Sluijs et al., 2018). The first step to manage MDD in chronic diseases patients is the communication of the diagnosis as a step of the whole care process. Physicians should help to understand the complexity of the disease, focusing on the mutual relationship between organic, emotional, and cognitive aspects. A more structured physician-patient relationship has been associated to better outcomes (Linzer et al., 2015). Moreover, well-informed patients tend to be more autonomous and adherent to treatment. A psychological evaluation should be implemented to detect or prevent psychological morbidity. A short preliminary assessment could be performed using rapid screening tools, such as the Hospital Anxiety and Depression Scale (an instrument developed to detect symptoms of anxiety and depression in patient with medical diseases) and the Distress Thermometer [Vodermaier et al., 2009; National Collaborating Centre for Mental Health (UK), 2010]. In case of positive screening, physicians must deepen the assessment and consider a psychological or psychopharmacological intervention, or, when symptoms are more severe, refer the patient to the psychiatrist or clinical psychologist. Educational programs may increase their sensitivity to MDD manifestations in chronic diseases and their comfort in the choice of treatment options. **Table 1** provides a detailed summary of some key-components to implement and sustain a multidisciplinary team approach to manage MDD in chronic diseases.

Management of MDD in Chronic Diseases: The Problem of Patient Adherence

Nearly 50% of patients with chronic diseases fail to adhere to medical directives, regardless of the drug latency or efficacy (Zolnierek and Dimatteo, 2009; Miller, 2016). It is important to pay attention to the psychological status of chronic diseases

TABLE 1 | Key-components to implement and sustain a multidisciplinary team approach to manage major depressive disorder (MDD) in chronic diseases.

Component	Features and methods
Developing a shared individualized care plan	• Collecting a patient's biopsychosocial semi-structured history of MDD and chronic illness (diagnoses, treatments, and complications) from different perspectives (psychiatric, medical, psychological, and nursing) • Understanding and sharing the patient's explanatory model of the disease • Negotiating the therapeutic alliance and identifying goals together with the patient from each perspective • Sharing decision making processes within the team • Explaining all the treatments to the patient in phases as an integrated process • Sharing the information and relevant events within the team and defining a case manager responsible for keeping the team and the patient updated
Systematic monitoring of the care plan	• Tracking the patient's relevant clinical data in an electronic medical record accessible to the team members • Discussing progress, caseload, and resistance encountered by the patient in team supervisions • Assessing the patient's needs and identifying new professionals, roles, and resources outside of the team required to meet them
Support of the patient self-care	• Providing tailored educational materials from each perspective to the patient • Fostering the patient's motivation to get better as a shared message • Monitoring and promoting the patient's adherence to the treatments and prescriptions mutually
Team training	• Organizing face-to-face training sessions to consolidate interprofessional collaboration ties and to develop a common language within the team • Encouraging the expression of needs, doubts, disagreement within the team • Planning scheduled training update sessions based on challenges and success

patients, as MDD has been associated with poor adherence (Moussavi et al., 2007; Katon, 2011; Reddy, 2016). Chronic patients' adherence may be influenced by many factors: understanding of the disease and treatment, beliefs about the benefits and efficacy of prescribed regimens, side effects, financial constraints, psychological conditions, and social support (Miller, 2016). To improve adherence, providing the patient with clear information about disease and treatment is fundamental to promote motivation to heal and appropriate health behaviors and also to reduce drop-out related to side effects or latency of clinical response (Miller, 2016). The relative importance of some symptoms for physicians, patients, and caregivers may be different, and these differences could contribute to explaining the adherence to some prescriptions and the withdrawal of others. Clinicians should keep this in mind. A multidisciplinary team approach may help even in this case, as the whole therapeutic management can be a real challenge for the single physician. More specifically, the adherence to psychological and psychopharmacological treatments in chronic diseases patients with MDD is a delicate matter. Tolerability and compliance should be assessed on the long-term and the multidisciplinary team approach should start from the first visit, where the psychiatrist/psychologist can help patients to understand the therapeutic role and potential side effects of the therapy, increasing adherence (Freedland et al., 2011). To reduce the high number of prescriptions and complexity of whole treatment of chronic diseases, the implementation of drugs targeting different symptoms may also increase adherence. Antidepressants, for example, that are effective in managing pain and depressive symptoms, may be particularly useful in the treatment of patients with diabetes, rheumatoid arthritis, cancer, and Parkinson's disease, where pain and depressive symptoms are frequently concomitant as stated above (Schreiber et al., 2015; Khouzam, 2016).

CONCLUSION

A proper diagnosis, a multidisciplinary team approach, and a personalized treatment plan would allow patients with MDD and chronic diseases to be more compliant, to achieve better results, to reduce possible relapses, and to manage or avoid complications and some adverse events. To provide effective care to patients suffering from chronic diseases, health professionals have to appraise the role of psychosocial factors in the genesis and maintenance of these conditions, while recognizing how emotions and cognitions can influence response to treatment and the course of illness, paying particular attention to the presence of depressive symptoms. Further research on the relationship of MDD and chronic diseases and attention of health policy stakeholders are strongly encouraged.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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REFERENCES

Aarsland, D., Pahlhagen, S., Ballard, C. G., Ehrt, U., and Svenningsson, P. (2011). Depression in Parkinson disease--epidemiology, mechanisms and management. *Nat. Rev. Neurol.* 8, 35–47. doi: 10.1038/nrneurol.2011.189

Alexopoulos, G. S., Raue, P. J., Sirey, J. A., and Arean, P. A. (2008). Developing an intervention for depressed, chronically medically ill elders: a model from COPD. *Int. J. Geriatr. Psychiatry* 23, 447–453. doi: 10.1002/gps.1925

Andersohn, F., Schade, R., Suissa, S., and Garbe, E. (2009). Long-term use of antidepressants for depressive disorders and the risk of diabetes mellitus. *Am. J. Psychiatry* 166, 591–598. doi: 10.1176/appi.ajp.2008.08071065

Anderson, R. J., Freedland, K. E., Clouse, R. E., and Lustman, P. J. (2001). The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care* 24, 1069–1078. doi: 10.2337/diacare.24.6.1069

Bair, M. J., Robinson, R. L., Katon, W., and Kroenke, K. (2003). Depression and pain comorbidity: a literature review. *Arch. Intern. Med.* 163, 2433–2445. doi: 10.1001/archinte.163.20.2433

Bogdan, R., Hyde, L. W., and Hariri, A. R. (2013). A neurogenetics approach to understanding individual differences in brain, behavior, and risk for psychopathology. *Mol. Psychiatry* 18, 288–299. doi: 10.1038/mp.2012.35

Bomasang-Layno, E., Fadlon, I., Murray, A. N., and Himelhoch, S. (2015). Antidepressive treatments for Parkinson's disease: a systematic review and meta-analysis. *Parkinsonism Relat. Disord.* 21, 833–842. doi: 10.1016/j.parkreldis.2015.04.018

Camus, V., Kraehenbühl, H., Preisig, M., Büla, C. J., and Waeber, G. (2004). Geriatric depression and vascular diseases: what are the links? *J. Affect. Disord.* 81, 1–16. doi: 10.1016/j.jad.2003.08.003

Canadian Diabetes Association Clinical Practice Guidelines Expert Committee, Robinson, D. J., Luthra, M., and Vallis, M. (2013). Diabetes and mental health. *Can. J. Diabetes* 37(Suppl. 1), S87–S92. doi: 10.1016/j.jcjd.2013.01.026

Chaudhuri, K. R., Healy, D. G., and Schapira, A. H. V., and National Institute for Clinical Excellence (2006). Non-motor symptoms of Parkinson's disease: diagnosis and management. *Lancet Neurol.* 5, 235–245. doi: 10.1016/S1474-4422(06)70373-8

Chen, H., Burton, E. A., Ross, G. W., Huang, X., Savica, R., Abbott, R. D., et al. (2013). Research on the premotor symptoms of Parkinson's disease: clinical and etiological implications. *Environ. Health Perspect.* 121, 1245–1252. doi: 10.1289/ehp.1306967

Ciaramella, A., and Poli, P. (2001). Assessment of depression among cancer patients: the role of pain, cancer type and treatment. *Psychooncology* 10, 156–165. doi: 10.1002/pon.505

D'Amato, C., Morganti, R., Greco, C., Di Gennaro, F., Cacciotti, L., Longo, S., et al. (2016). Diabetic peripheral neuropathic pain is a stronger predictor of depression than other diabetic complications and comorbidities. *Diab. Vasc. Dis. Res.* 13, 418–428. doi: 10.1177/1479164116653240

De Jean, D., Giacomini, M., Vanstone, M., and Brundisini, F. (2013). Patient experiences of depression and anxiety with chronic disease: a systematic review and qualitative meta-synthesis. *Ont. Health Technol. Assess. Ser.* 13, 1–33.

Egede, L. E. (2007). Major depression in individuals with chronic medical disorders: prevalence, correlates and association with health resource utilization, lost productivity and functional disability. *Gen. Hosp. Psychiatry* 29, 409–416. doi: 10.1016/j.genhosppsych.2007.06.002

Egede, L. E., Nietert, P. J., and Zheng, D. (2005). Depression and all-cause and coronary heart disease mortality among adults with and without diabetes. *Diabetes Care* 28, 1339–1345. doi: 10.2337/diacare.28.6.1339

Farooqi, A., Khunti, K., Abner, S., Gillies, C., Morriss, R., and Seidu, S. (2019). Comorbid depression and risk of cardiac events and cardiac mortality in people with diabetes: a systematic review and meta-analysis. *Diabetes Res. Clin. Pract.* 156:107816. doi: 10.1016/j.diabres.2019.107816

Fiest, K. M., Hitchon, C. A., Bernstein, C. N., Peschken, C. A., Walker, J. R., Graff, L. A., et al. (2017). Systematic review and meta-analysis of interventions for depression and anxiety in persons with rheumatoid arthritis. *J. Clin. Rheumatol.* 23, 425–434. doi: 10.1097/RHU.0000000000000489

Freedland, K. E., Carney, R. M., and Rich, M. W. (2011). Effect of depression on prognosis in heart failure. *Heart Fail. Clin.* 7, 11–21. doi: 10.1016/j.hfc.2010.08.003

Freeman, E. W., Sammel, M. D., Liu, L., Gracia, C. R., Nelson, D. B., and Hollander, L. (2004). Hormones and menopausal status as predictors of depression in women in transition to menopause. *Arch. Gen. Psychiatry* 61, 62–70. doi: 10.1001/archpsyc.61.1.62

Gilsanz, P., Karter, A. J., Beeri, M. S., Quesenberry, C. P. Jr., and Whitmer, R. A. (2018). The bidirectional association between depression and severe hypoglycemic and hyperglycemic events in type 1 diabetes. *Diabetes Care* 41, 446–452. doi: 10.2337/dc17-1566

Joseph, J. J., and Golden, S. H. (2017). Cortisol dysregulation: the bidirectional link between stress, depression, and type 2 diabetes mellitus. *Ann. N. Y. Acad. Sci.* 1391, 20–34. doi: 10.1111/nyas.13217

Kang, H. J., Kim, S. Y., Bae, K. Y., Kim, S. W., Shin, I. S., Yoon, J. S., et al. (2015). Comorbidity of depression with physical disorders: research and clinical implications. *Chonnam Med. J.* 51, 8–18. doi: 10.4068/cmj.2015.51.1.8

Katon, W. J. (2003). Clinical and health services relationships between major depression, depressive symptoms, and general medical illness. *Biol. Psychiatry* 54, 216–226. doi: 10.1016/s0006-3223(03)00273-7

Katon, W. J. (2011). Epidemiology and treatment of depression in patients with chronic medical illness. *Dialogues Clin. Neurosci.* 13, 7–23.

Kessler, R. C., Chiu, W. T., Demler, O., Merikangas, K. R., and Walters, E. E. (2005). Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch. Gen. Psychiatry* 62, 617–627. doi: 10.1001/archpsyc.62.6.617

Khouzam, H. R. (2016). Psychopharmacology of chronic pain: a focus on antidepressants and atypical antipsychotics. *Postgrad. Med.* 128, 323–330. doi: 10.1080/00325481.2016.1147925

Leonard, B. E. (2010). The concept of depression as a dysfunction of the immune system. *Curr. Immunol. Rev.* 6, 205–212. doi: 10.2174/157339510791823835

Lim, G. Y., Tam, W. W., Lu, Y., Ho, C. S., Zhang, M. W., and Ho, R. C. (2018). Prevalence of depression in the community from 30 countries between 1994 and 2014. *Sci. Rep.* 8:2861. doi: 10.1038/s41598-018-21243-x

Linden, W., Vodermaier, A., Mackenzie, R., and Greig, D. (2012). Anxiety and depression after cancer diagnosis: prevalence rates by cancer type, gender, and age. *J. Affect. Disord.* 141, 343–351. doi: 10.1016/j.jad.2012.03.025

Linzer, M., Bitton, A., Tu, S. P., Plews-Ogan, M., Horowitz, K. R., Schwartz, M. D., et al. (2015). The end of the 15-20 minute primary care visit. *J. Gen. Intern. Med.* 30, 1584–1586. doi: 10.1007/s11606-015-3341-3

Ludman, E. J., Katon, W., Russo, J., Von Korff, M., Simon, G., Ciechanowski, P., et al. (2004). Depression and diabetes symptom burden. *Gen. Hosp. Psychiatry* 26, 430–436. doi: 10.1016/j.genhosppsych.2004.08.010

Marsh, L. (2013). Depression and Parkinson's disease: current knowledge. *Curr. Neurol. Neurosci. Rep.* 13:409. doi: 10.1007/s11910-013-0409-5

Matcham, F., Norton, S., Scott, D. L., Steer, S., and Hotopf, M. (2016). Symptoms of depression and anxiety predict treatment response and long-term physical health outcomes in rheumatoid arthritis: secondary analysis of a randomized controlled trial. *Rheumatology* 55, 268–278. doi: 10.1093/rheumatology/kev306

Matcham, F., Rayner, L., Steer, S., and Hotopf, M. (2013). The prevalence of depression in rheumatoid arthritis: a systematic review and meta-analysis. *Rheumatology* 52, 2136–2148. doi: 10.1093/rheumatology/ket169

Mezuk, B., Eaton, W. W., Albrecht, S., and Golden, S. H. (2008). Depression and type 2 diabetes over the lifespan: a meta-analysis. *Diabetes Care* 31, 2383–2390. doi: 10.2337/dc08-0985

Miller, T. A. (2016). Health literacy and adherence to medical treatment in chronic and acute illness: a meta-analysis. *Patient Educ. Couns.* 99, 1079–1086. doi: 10.1016/j.pec.2016.01.020

Miller, A. H., and Raison, C. L. (2016). The role of inflammation in depression: from evolutionary imperative to modern treatment target. *Nat. Rev. Immunol.* 16, 22–34. doi: 10.1038/nri.2015.5

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., and The PRISMA Group (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 6:e1000097. doi: 10.1371/journal.pmed.1000097

Moussavi, S., Chatterji, S., Verdes, E., Tandon, A., Patel, V., and Ustun, B. (2007). Depression, chronic diseases, and decrements in health: results from the World Health Surveys. *Lancet* 370, 851–858. doi: 10.1016/S0140-6736(07)61415-9

National Collaborating Centre for Mental Health (UK) (2010). *Depression in adults with a chronic physical health problem: Treatment and management*. Leicester (UK): British Psychological Society.

Nerurkar, L., Siebert, S., McInnes, I. B., and Cavanagh, J. (2019). Rheumatoid arthritis and depression: an inflammatory perspective. *Lancet Psychiatry* 6, 164–173. doi: 10.1016/S2215-0366(18)30255-4

Nestler, E. J., Barrot, M., DiLeone, R. J., Eisch, A. J., Gold, S. J., and Monteggia, L. M. (2002). Neurobiology of depression. *Neuron* 34, 13–25. doi: 10.1016/s0896-6273(02)00653-0

Nuti, A., Ceravolo, R., Piccinni, A., Dell'Agnello, G., Bellini, G., Gambaccini, G., et al. (2004). Psychiatric comorbidity in a population of Parkinson's disease patients. *Eur. J. Neurol.* 11, 315–320. doi: 10.1111/j.1468-1331.2004.00781.x

Pariante, C. M., and Lightman, S. L. (2008). The HPA axis in major depression: classical theories and new developments. *Trends Neurosci.* 31, 464–468. doi: 10.1016/j.tins.2008.06.006

Pellicano, C., Benincasa, D., Pisani, V., Buttarelli, F. R., Giovannelli, M., and Pontieri, F. E. (2007). Prodromal non-motor symptoms of Parkinson's disease. *Neuropsychiatr. Dis. Treat.* 3, 145–152. doi: 10.2147/nedt.2007.3.1.145

Penninx, B. W. (2017). Depression and cardiovascular disease: epidemiological evidence on their linking mechanisms. *Neurosci. Biobehav. Rev.* 74, 277–286. doi: 10.1016/j.neubiorev.2016.07.003

Peyrot, M., and Rubin, R. R. (1999). Persistence of depressive symptoms in diabetic adults. *Diabetes Care* 22, 448–452. doi: 10.2337/diacare.22.3.448

Pont-Sunyer, C., Hotter, A., Gaig, C., Seppi, K., Compta, Y., Katzenschlager, R., et al. (2015). The onset of nonmotor symptoms in Parkinson's disease (the ONSET PD study). *Mov. Disord.* 30, 229–237. doi: 10.1002/mds.26077

Postuma, R. B., Aarsland, D., Barone, P., Burn, D. J., Hawkes, C. H., Oertel, W., et al. (2012). Identifying prodromal Parkinson's disease: pre-motor disorders in Parkinson's disease. *Mov. Disord.* 27, 617–626. doi: 10.1002/mds.24996

Pouwer, F. (2017). Depression: a common and burdensome complication of diabetes that warrants the continued attention of clinicians, researchers and healthcare policy makers. *Diabetologia* 60, 30–34. doi: 10.1007/s00125-016-4154-6

Read, J. R., Sharpe, L., Modini, M., and Dear, B. F. (2017). Multimorbidity and depression: a systematic review and meta-analysis. *J. Affect. Disord.* 221, 36–46. doi: 10.1016/j.jad.2017.06.009

Reddy, K. S. (2016). Global burden of disease study 2015 provides GPS for global health 2030. *Lancet* 388, 1448–1449. doi: 10.1016/S0140-6736(16)31743-3

Reijnders, J. S., Ehrt, U., Weber, W. E., Aarsland, D., and Leentjens, A. F. (2008). A systematic review of prevalence studies of depression in Parkinson's disease. *Mov. Disord.* 23, 183–189. doi: 10.1002/mds.21803

Rudisch, B., and Nemeroff, C. B. (2003). Epidemiology of comorbid coronary artery disease and depression. *Biol. Psychiatry* 54, 227–240. doi: 10.1016/s0006-3223(03)00587-0

Santiago, J. A., Bottero, V., and Potashkin, J. A. (2017). Biological and clinical implications of comorbidities in Parkinson's disease. *Front. Aging Neurosci.* 9:394. doi: 10.3389/fnagi.2017.00394

Satin, J. R., Linden, W., and Phillips, M. J. (2009). Depression as a predictor of disease progression and mortality in cancer patients: a meta-analysis. *Cancer* 115, 5349–5361. doi: 10.1002/cncr.24561

Schreiber, A. K., Nones, C. F., Reis, R. C., Chichorro, J. G., and Cunha, J. M. (2015). Diabetic neuropathic pain: physiopathology and treatment. *World J. Diabetes* 6, 432–444. doi: 10.4239/wjd.v6.i3.432

Sheng, J., Liu, S., Wang, Y., Cui, R., and Zhang, X. (2017). The link between depression and chronic pain: neural mechanisms in the brain. *Neural Plast.* 2017:9724371. doi: 10.1155/2017/9724371

Sherrill, C., Smith, M., Mascoe, C., Bigus, E., and Abbitt, D. (2017). Effect of treating depressive disorders on mortality of cancer patients. *Cureus* 9:e1740. doi: 10.7759/cureus.1740

Smith, H. R. (2015). Depression in cancer patients: pathogenesis, implications and treatment (Review). *Oncol. Lett.* 9, 1509–1514. doi: 10.3892/ol.2015.2944

Spiegel, D., Sands, S., and Koopman, C. (1994). Pain and depression in patients with cancer. *Cancer* 74, 2570–2578. doi: 10.1002/1097-0142(19941101)74:93.0.CO;2-3

Tan, L. C. (2012). Mood disorders in Parkinson's disease. *Parkinsonism Relat. Disord.* 18(Suppl. 1), S74–S76. doi: 10.1016/S1353-8020(11)70024-4

van den Hoek, J., Boshuizen, H. C., Roorda, L. D., Tijhuis, G. J., Nurmohamed, M. T., Dekker, J., et al. (2016). Association of somatic comorbidities and comorbid depression with mortality in patients with rheumatoid arthritis: a 14-year prospective cohort study. *Arthritis Care Res.* 68, 1055–1060. doi: 10.1002/acr.22812

van Eck van der Sluijs, J. F., Castelijns, H., Eijsbroek, V., Rijnders, C. A. T., van Marwijk, H. W. J., and van der Feltz-Cornelis, C. M. (2018). Illness burden and physical outcomes associated with collaborative care in patients with comorbid depressive disorder in chronic medical conditions: a systematic review and meta-analysis. *Gen. Hosp. Psychiatry* 50, 1–14. doi: 10.1016/j.genhosppsych.2017.08.003

Vodermaier, A., Linden, W., and Siu, C. (2009). Screening for emotional distress in cancer patients: a systematic review of assessment instruments. *J. Natl. Cancer Inst.* 101, 1464–1488. doi: 10.1093/jnci/djp336

Yapici Eser, H., Bora, H. A., and Kuruoglu, A. (2017). Depression and Parkinson disease: prevalence, temporal relationship, and determinants. *Turk. J. Med. Sci.* 47, 499–503. doi: 10.3906/sag-1603-101

Ziarko, M., Mojs, E., Piasecki, B., and Samborski, W. (2014). The mediating role of dysfunctional coping in the relationship between beliefs about the disease and the level of depression in patients with rheumatoid arthritis. *Scientific World Journal* 2014:585063. doi: 10.1155/2014/585063

Zolnierek, K. B., and Dimatteo, M. R. (2009). Physician communication and patient adherence to treatment: a meta-analysis. *Med. Care* 47, 826–834. doi: 10.1097/MLR.0b013e31819a5acc

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SYSTEMATIC REVIEW
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Using Arts-Based Therapies to Improve Mental Health for Children and Young People With Physical Health Long-Term Conditions: A Systematic Review of Effectiveness

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Background: Children with physical health long-term conditions (LTCs) have increased risk of mental health difficulties relative to healthy peers. However, availability of psychological support integrated into pediatric physical health settings is limited, and there are long waiting times for access to child mental health services. Arts-based therapies involve using creative media to develop a therapeutic relationship, and offer a potential alternative to talking-based therapies. The aim of this systematic review is to establish the effectiveness of arts-based therapies for improving the mental health of children with physical health LTCs.

Methods: The review protocol was published on PROSPERO. Four electronic databases were searched (Medline, Embase, Cinahl, and PsycINFO), plus hand searches of two key journals and relevant reviews, and forward/back citations searches of selected articles were conducted. The Effective Public Health Practice Project (EPHPP) Quality Assessment Tool was used to assess bias in selected articles. Second reviewers completed 10% of article screening and 20% of bias assessments. The findings were synthesized narratively.

Results: Sixteen studies met inclusion criteria and demonstrated some improvements on indicators of mental health and well-being including quality of life, coping behaviors, anxiety, self-concept, and mood. However, replication across interventions and outcomes was absent. Overall, the quality of evidence of effectiveness in the studies reviewed was moderate/weak. This was due to bias in study design; other limitations included a lack of detail on intervention components, e.g., use of a manual, and single recruitment sites.

Conclusions: The heterogeneity of existing research evaluating arts-based therapies for children with physical health LTCs limits conclusions about effectiveness. Suggestions are made to inform the design of future research studies to help build a robust evidence base.

Keywords: pediatric, arts-based therapies, physical health long-term conditions, mental health, children

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INTRODUCTION

Pediatric physical health long-term conditions (LTCs) have a childhood onset, require ongoing management over a long period of time, are often multi-system, and typically require complex treatments with both medications and non-pharmacological interventions and services (Mokkink et al., 2008; DoH, 2012). Pediatric physical health LTCs require significant psychological adjustments to symptoms, medical regimes, and pain and may detrimentally affect the well-being of children relative to healthy peers (Denny et al., 2014; Kazak et al., 2015). Children may be isolated from peers during hospital stays and miss participating in activities that contribute to quality of life, and research suggests that children with physical health LTCs are susceptible to poor mental health (Knight et al., 2015; Butler et al., 2018). The prevalence of anxiety and depression is high, and mental health and well-being difficulties are up to four times higher in children with physical health LTCs than in healthy peers (Hysing et al., 2007; Pinquart and Shen, 2011a,b; Ferro, 2016; Brady et al., 2017). Mental health is a key predictor of a successful clinical course; for example, baseline depression in children with rheumatic diseases was associated with higher levels of pain and disability 4 years later (Colver et al., 2018; Gray et al., 2018; Hanns et al., 2018). Good childhood mental health optimizes engagement in daily activities for children and families; facilitates psychosocial development, educational attainment, and increased life-course opportunity; and protects against adult mental health problems (DoH, 2011; Colver et al., 2018; Tollisen et al., 2018). Additionally, parents of children with physical health LTCs are prone to high levels of stress/distress, and poor mental health of their child may be an additional burden on them and on child mental health services, which are under-resourced (Crouch et al., 2019; Rosenberg et al., 2019).

Given the potential burden of poor mental health, UK statutory guidance identifies integration of psychological support into pediatric physical health settings as an indicator of service quality (DoH, 2011; Foster et al., 2017; Parsons et al., 2017; NHSE, 2018). However, evidence suggests that services for pediatric physical health LTCs are not routinely set up in this way, staff time and resources are limited, access to psychological support is patchy, and there are long wait lists for child and adolescent mental health services (Wiener et al., 2015; Cruikshank et al., 2016; Davis et al., 2017). Further, there are currently significant gaps in the evidence base for the best type of psychological support for children with physical health LTCs (Kazak et al., 2015; Knight et al., 2019).

A review evaluating psychological interventions for anxiety and depression in children with physical health LTCs found cognitive behavioral therapy (CBT) effective under certain circumstances—in the short-term for mild/moderate symptoms of depression (Thabrew et al., 2018). A recent evidence synthesis evaluated a range of mental health interventions for children with physical health LTCs, for example, parenting interventions, play therapy, relaxation, and emotional intelligence training (Moore et al., 2019). The review utilized meta-ethnography and identified benefits from the perspectives of patients, families, and practitioners experiencing the interventions (Moore et al., 2019; Shaw et al., 2019). The authors developed a conceptual model of constructs (e.g., empowerment) important for enabling benefit from mental health interventions for children with physical health LTCs (Moore et al., 2019; Shaw et al., 2019). Although some evidence of effectiveness was found for CBT, the review also highlighted an overall lack of quantitative evidence of the effectiveness of mental health interventions for children with physical health LTCs and the absence of trials conducted in the UK (Moore et al., 2019).

The aim of the current review is to inform preparation for a feasibility trial of arts-based therapies in the UK National Health Service (NHS). NICE defines arts-based therapies as psychotherapeutic techniques combined with creative activities to facilitate self-expression and recommends their provision in the management of children with psychosis (NICE, 2016). Arts-based therapies involve using creative media to develop a therapeutic relationship and can be an alternative to talking-therapies through facilitating the expression of inner states that are difficult to articulate verbally (American Art Therapy Association, 2018; Fancourt and Finn, 2019). Although the benefits of arts-based therapies in mental health settings suggest the potential for transferability to physical health services, arts-based therapies are not routinely available as a psychological support in UK NHS physical health settings.

Research has demonstrated some positive effects of arts-based therapies for children with physical health LTCs; however, the evidence base is small (Cohen-Yatziv and Regev, 2019). Previous reviews relevant to this clinical group include two reviews of visual art therapy—one for children with a range of physical health conditions (Clapp et al., 2018) and one focusing on children with cancer (Aguilar, 2017). A systematic review of music interventions for patients with cancer was not specific to children (also included adult samples) and included studies evaluating physical health outcomes (without measurement of mental health outcomes) and studies evaluating music as a distraction (Bradt et al., 2016). These reviews identified some small evidence of effectiveness and some bias in the design of previous studies, and our review builds on the findings of these reviews. Our specific focus is evaluating the potential of arts-based therapies as a psychological support for pediatric physical health settings and the identification of methodological characteristics important to consider in designing future robust research studies to contribute to building an evidence base (Cohen-Yatziv and Regev, 2019). In preparation for a feasibility trial of arts-based therapies in the UK NHS, we reviewed existing arts-based therapy studies in order to help design the trial.

Aims of the Study

The aims of this systematic review are to (i) identify studies evaluating the effectiveness of arts-based therapies for improving the mental health of children with physical health LTCs and (ii) examine the quality of the identified studies using a formal assessment tool.

TABLE 1A | Inclusion criteria.

Inclusion criteria	Population: children (participant mean ≤18 years of age) with physical health long-term conditions (LTCs) Intervention: arts-based therapies Comparator: standard care, none, before/after Outcome: change in mental health symptoms or psychological well-being measured using either (i) an assessment tool (for which published information/psychometric properties is available) or (ii) a formalized assessment method, e.g., time sampling Study design: quantitative Articles published in English since 2000
Exclusion criteria	Babies; passive arts interventions (for distraction or improving skills); unpublished documents; case studies Studies reporting only on mobility, communication, or cognitive functioning; studies combining arts-based therapies with cognitive behavioral therapy

TABLE 1B | Information sources.

Scoping searches	Health and Social Care Information Center Health Management Information Center Cochrane Library [Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Methodology Register, Health Technology Assessment Database]
Formal searches	Electronic databases searched: MEDLINE, EMBASE, PsycINFO, CINAHL
Other sources searched	Reference lists relevant systematic reviews; forward and back citation searches of included studies; Google search of search terms; hand searches in: *International Journal of Art Therapy; Arts and Health. An International Journal for Research, Policy and Practice*

METHODS

A systematic review was reported in accordance with PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-analyses) (Moher et al., 2009). The protocol was published on PROSPERO (CRD registration number: 42019134461).

Inclusion Criteria

Inclusion criteria for the review and PICO components (population, intervention, comparator, and outcome) are shown in **Table 1A**. Inclusion criteria comprised the following: studies recruiting participants ≤18 years of age with pediatric physical health LTCs, defined as requiring ongoing management with medication and/or other treatment interventions over a long period of time (Mokkink et al., 2008; DoH, 2012); studies evaluating arts-based therapies, defined as systematic interventions implemented by a therapist with the aim of improving health through creative expression (for example, drawing, play, photography, movement, music) and a therapeutic relationship promoting communication, connection, and self-awareness (NICE, 2016; Hackett et al., 2017; American Art Therapy Association, 2018); additionally, only articles published after the year 2000 given rapid developments in medical settings and treatment interventions; and finally, those using a published outcome measure or structured assessment (e.g., time sampling) of mental health or well-being.

We conducted the searches in May 2020, and **Table 1B** shows the information sources. We searched four electronic databases, conducted hand searches of two key journals, searched reference lists of relevant reviews, and conducted forward/back citations searches of articles meeting inclusion criteria. The search strategy for Medline is shown in **Table A1**.

Study Selection

One researcher (SW) screened titles and abstracts of articles identified in the searches, with 10% independently screened by a second reviewer (AZ), and the level of agreement was 96%. Ambiguous articles were included. 98 articles were selected for full-text screening. SW carried out full-text screening, with 10% screened independently by a second reviewer (AZ). Agreement was 100%. **Figure 1** shows the selection process to determine the eligibility of articles for inclusion in the review.

Synthesis

Due to high heterogeneity in study design, quantitative synthesis of information was not possible, and we used a narrative synthesis of intervention effectiveness incorporating four elements—intervention conceptualization and theoretical model, tabulation of information, exploring patterns within and across studies, and assessment of methodological quality (Popay et al., 2006).

Intervention Conceptualization and Theoretical Model

Various conceptualizations of arts-based therapies occur in the literature. In this review, we focus on arts-based therapies (visual, drama, music, and play) that include interaction, development of a therapeutic relationship, and facilitating communication and expression (NICE, 2016; Hackett et al., 2017; American Art Therapy Association, 2018). We excluded articles evaluating use of art media for distraction, (e.g., while having an injection), for leisure (e.g., listening to music), or for education. The purpose of the review was to inform the design of a randomized feasibility study of arts-based therapies in the UK NHS. We built a logic model (**Figure 3**) showing areas we felt may be important in a trial evaluating the effectiveness of arts-based therapies in pediatric physical health settings in order to guide information extraction and interpretation of the review findings, and we developed the model informed by the synthesis (Popay et al., 2006).

Assessment of Methodological Quality

Studies were assessed for risk of bias by SW using the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool (Thomas et al., 2004). JB and AZ independently rated 20%, and agreement was 80%.

RESULTS

Key Characteristics of Studies

Three thousand three hundred and fifty articles were identified from the electronic database searches after removal of duplicates. After title/abstract screening, 98 articles were screened in full, and

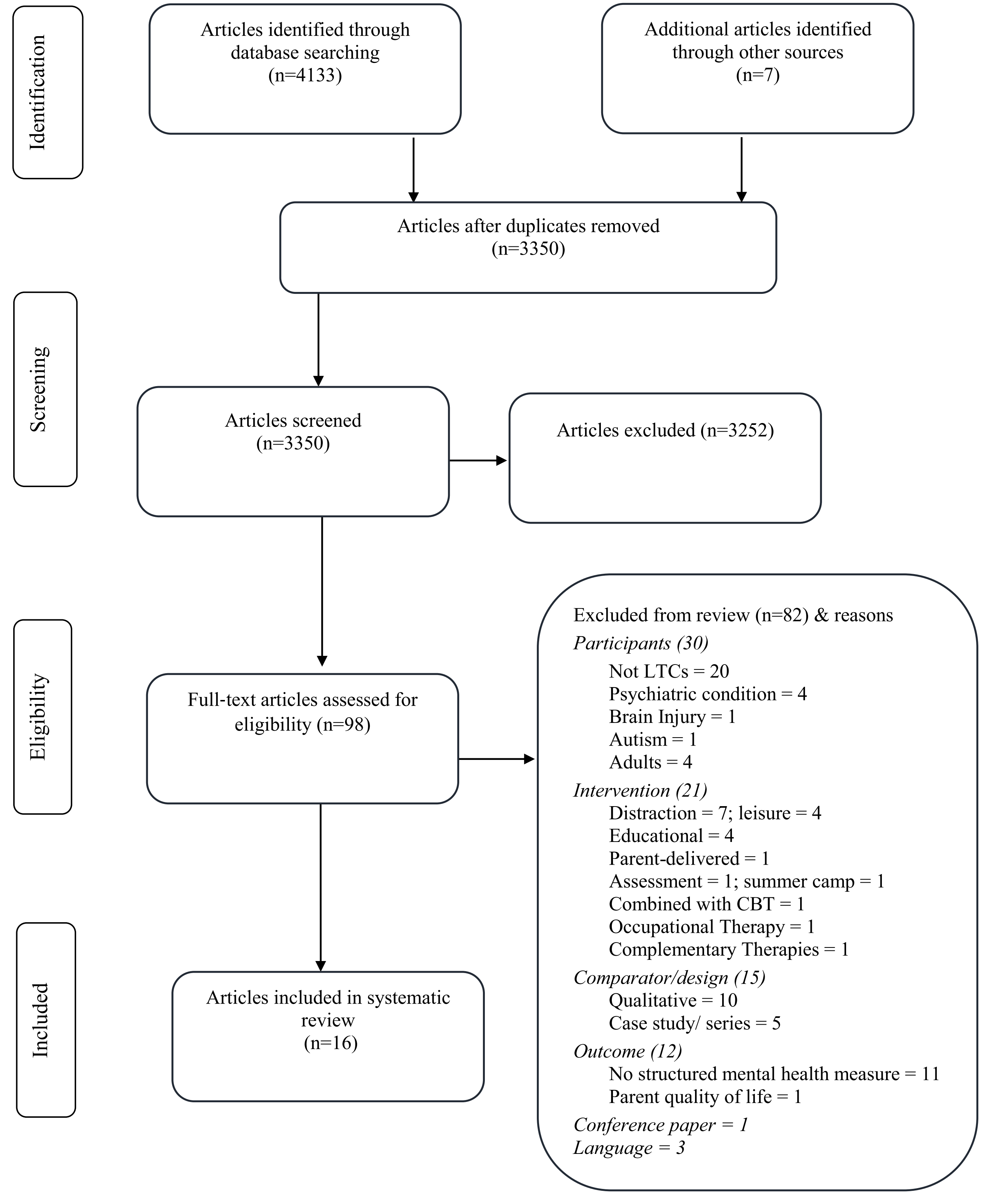


FIGURE 1 | The PRISMA flowchart showing study selection process.

TABLE 2 | Participant, study, and intervention characteristics.

References (country)	N (F)	Age (years) mean (SD); range	Recruitment source	Health condition	Design *Control*	FU (month)	Intervention media	Attrition*
Children with cancer: visual media								
Khodabakhshi Koolaee et al. (2016) (Iran)	30 (16)	10.3 (NR); 8–12	Oncology unit	Leukemia	CCT *TAU*	1	Visual art	NR
Abdulah and Abdulla (2018) (Iraq)	60 (25)	9.5 (2); 7–13	Oncology unit	Heterogeneity of malignancies	RCT *TAU*	0	Visual art	1
Children with cancer: music media								
Robb (2000) (USA)	10 (NR)	NR; 4–11	Oncology isolation	Cancer	Within-subject design	0	Music	NR
Barrera et al. (2002) (Canada)	65 (33)	7 (4.8); 0.5–17	Hematology oncology unit	Heterogeneity of malignancies	Cohort	0	Music	5
Colwell et al. (2005) (USA)	24 (9)	12 (NR); 7–18	Inpatient unit	>75% cancer	CCT *TAU (art)*	0	Music	0
Robb et al. (2008) (USA)	83 (NR)	(NR); 4–7	Inpatient oncology 6 sites	Cancer	RCT *music listening; audio-storybooks*	0	Music	NR
Giordano et al. (2020) (Italy)	48 (NR)	(NR); 2–13	Oncology and hematology ward	Cancer	CCT *TAU*	0	Music	NR
	19		Medical staff					
Children with cancer: composite arts-based therapies (music, movement, and art) and virtual reality play therapy								
Madden et al. (2010) (USA)	18 (4)	5.3 (NR); 2–13	Outpatient oncology; chemotherapy infusion	Cancer	RCT *Attention*	0	Music, movement and visual	2
	32 (14)	8.3 (NR); 3–21			Cohort	0		
			Service providers		Focus groups	12		
Li et al. (2011) (Hong Kong)	122 (57)	12 (2); 8–16	Pediatric oncology ward	Cancer	Quasi-experimental *TAU*	0	Virtual reality play	8
Children with blood disorders and other health conditions: visual media								
Beebe et al. (2010) (USA)	22 (NR)	NR; 7–14	Specialist school clinic	Asthma	CCT *Wait list*	6	Visual art	0
Stafstrom et al. (2012) (USA)	16 (10)	12.8 (2.9); 7–18	Pediatric neurology clinics	Epilepsy	Cohort	0	Visual art	NR
MacDonald et al. (2019) (Canada)	12 (10)	17.75 (NR); 15–21	Provincial diabetes program	Diabetes	Cohort	0	Visual art	5
Children with blood disorders and other health conditions: music media and play therapy								
Colwell et al. (2013) (USA)	32 (17)	11 (3); 6–17	Inpatient unit	Cancer, sickle-cell disease, accidents, infections	CCT (3 groups) Music listening and composition	0	Music	NR
Robb et al. (2014) (USA)	113 (47)	11–24	Multi-site (8 sites)	HSCT	RCT *Audio-books*	3	Music	NR
Tomaj et al. (2016) (Iran)	60 (30)	9.50 (1.74); 7–11	Thalassemia units 2 hospitals	Thalassemia Major	RCT *TAU*	1	Play	2
Uggla et al. (2018) (Sweden)	29 (15)	0–17 (6.6)	Hospital	HSCT	RCT *Wait list*	6	Music	9

*N, number of participants; F, female; CCT, controlled clinical trial; NR, not reported; RCT, randomized controlled trial; C, control; TAU, treatment as usual; FU, follow-up; HSCT, hematopoietic stem cell transplant. *Intervention group.*

16 articles were selected for inclusion in the review. Information was extracted and tabulated, with **Tables 2**, **3** showing study characteristics and **Table 4** showing significant findings from the selected articles.

Eight studies were conducted in the USA (Robb, 2000; Colwell et al., 2005, 2013; Robb et al., 2008, 2014; Beebe et al., 2010; Madden et al., 2010; Stafstrom et al., 2012), two studies were carried out in Canada (Barrera et al., 2002; MacDonald et al., 2019), one in Iraq (Abdulah and Abdulla, 2018), one in Hong Kong (Li et al., 2011), two in Iran (Khodabakhshi Koolaee et al., 2016; Tomaj et al., 2016), one in Italy (Giordano et al., 2020), and one study in Sweden (Uggla et al., 2018).

Quality of Studies Included in This Review

The quality of studies was appraised using structured criteria relevant for intervention effectiveness evaluations, and **Figure 2**

TABLE 3 | Intervention characteristics.

References	Number of sessions; intervention length	Individual (I) group (G)	QI	Intervention
Children with cancer: visual media				
Khodabakhshi Koolaee et al. (2016)	2 per week (1 h); 11 sessions	NR	Y	Painting, collage, drawing
Abdulah and Abdulla (2018)	20 (2 h); 1 month	G	Fine artist	Drawing and craftwork. Encouragement of reflection and description of art work (cardboard, wood, watercolors, markers).
Children with cancer: music media				
Robb (2000)	1 h	I	Y	Control; reading; music; control (15 min each) Intervention schedule: 4–7 and 8–12 years versions
Barrera et al. (2002)	1–3 (15–45 min)	I and family	Y	School age: singing and song writing, improvisation and music listening Pre-school: animated play songs, rhymes, playing instruments Infants: play, songs, lullabies, rhymes, playing instruments. *Instruments: e.g., bells, drums, shakers, guitar, electronic harp/keyboard, songbooks, means of recording and playing music*
Colwell et al. (2005)	45 min	I	Y	Music computer program: CD composition and creation
Robb et al. (2008)	20 min	I and parent	Y	Active music engagement (AME) (music, acoustic guitar, hand instruments, illustrated songbooks, puppets, toys): playing instruments action/illustrated songs. Intervention guide used.
Giordano et al. (2020)	15–20 min 1–6 sessions	I and parent	Y	Individually tailored interactive relational approach with active and receptive techniques, use of musical instruments, improvisation, singing, song writing, creation of/listening to music with the therapist
Children with cancer: composite arts-based therapies (music, movement, and art) and virtual reality play therapy				
Madden et al. (2010)	Randomized group: weekly (1 h ×6) 2 sessions in each CAT modality	I	Y	CAT (movement, music, art) replicated developmental expression from movement, sound, graphics (for each patient in same order)
	Cohort: 1 h session	G		
Li et al. (2011)	30 min × 5 days a week	G	Research nurse	Virtual reality game
Children with blood disorders and other conditions: visual media				
Beebe et al. (2010)	7 × 1 h sessions; 7 weeks	G	Y	Discussion, art-making, sharing feelings. Intervention schedule provided.
Stafstrom et al. (2012)	4 × 1.5 h sessions; 1 month	G	Y	Drawing, painting collage and digital
MacDonald et al. (2019)	12 × 90 min; weekly	I and closed G	N	Relaxation, activities to develop self-awareness, trust, respect Drawing, painting, collage, paper sculpture, clay, fabric, found objects Theoretical model: existential, person-centered, and cognitive behavioral Intervention schedule provided
Children with blood disorders and other conditions: music media and play therapy				
Colwell et al. (2013)	1 × 45 min	I	Y	Orff-based approach: active music making, rhythmic book reading (*Hooray for You! A Celebration of You-ness*) talking about self and goals
Robb et al. (2014)	6 sessions (2 per week)	G	Y	Therapeutic music video (TMV)
Tomaj et al. (2016)	8 × 45–60 min sessions over 1 month	G	Researcher	Playdough, clay, mud, storytelling, and coloring
Uggla et al. (2018)	45 min × twice a week for 4–6 weeks	I	Y	Singing, music playing/listening. Parents could participate.

NR, none reported; CAT, creative art therapy; N, no; Y, yes; QI, qualified interventionist.

shows a summary of the quality assessments (Thomas et al., 2004). None of the studies had global ratings of high quality, 13 studies had a moderate global rating, and 3 studies had weak ratings of quality. All studies had some strong components (e.g., describing participant randomization, use of a published outcome measure); however, the global quality rating of all articles was reduced by specific design limitations. These included confounding variables, a narrow recruitment pool (e.g., one inpatient unit), or a lack of blinding. The purpose of the quality appraisal was to identify areas to address when designing a future trial, and potential bias in the studies reviewed is integrated into the narrative synthesis below and informs the model in **Figure 3**.

Narrative Synthesis

Given that evidence of the effectiveness of psychological interventions for individual pediatric physical health conditions is limited (Moore et al., 2019), we present the results according to health condition.

TABLE 4 | Outcome measures and results.

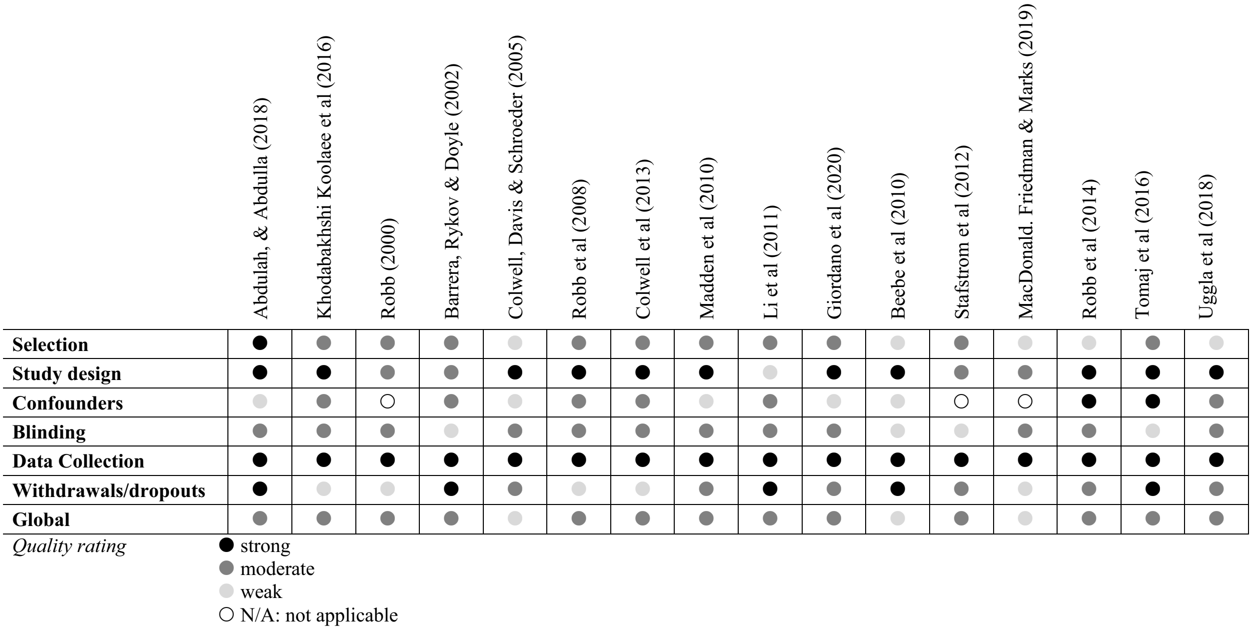
References	Outcome measures	Results
Children with cancer: visual media		
Khodabakhshi Koolaee et al. (2016)	Children's Inventory of Anger (Nelson and Finch, 2000) Spence Children's Anxiety Scale (Spence et al., 2003)	Significant pre/post-intervention reductions in anger ($p = 0.001$), anxiety ($p = 0.001$) in the experimental group
Abdulah and Abdulla (2018)	KIDSCREEN-10 (parent) (Ravens-Sieberer et al., 2010)	Experimental group: significantly more physically active and energetic; less depressed, emotional, and stressed; more enjoyment of social/leisure time and more social participation; improved relationships and better health (all $p < 0.05$)
Children with cancer: music media		
Robb (2000)	Time sampling observations and coding of (i) behavior frequency (activity, attention, choice making, following directions, affective state) and (ii) environment support (verbal directions, activities, choices, positive non/verbal reinforcement, changes initiated by child, positive adult-initiated interaction, attention from adult) Affective Face Scale (McGrath, 1985)	Higher environmental support during music condition Significant main effects for environment ($p < 0.001$) and condition ($p < 0.001$) Significant interaction of condition × environment ($p < 0.001$) Higher behavior scores in music condition Significant main effects for behavior ($p < 0.001$) and condition ($p < 0.001$) Significant interaction of condition × behavior ($p = 0.001$) Significant correlation of environment and behavior: control ($p < 0.001$) and music ($p = 0.002$)
Barrera et al. (2002)	Adapted FACES pain scale (Bieri et al., 1990) Play Performance Scale (Lansky et al., 1987) Satisfaction questionnaire (SQ)	Improved child-reported feelings pre/post ($p < 0.01$) and higher for AME than passively engaged ($p < 0.01$) More parent-reported play after active vs. passive music engagement ($p < 0.01$) and more improvement for adolescents ($p < 0.05$) Satisfaction with music intervention Children <5 years: "I liked the guitar"; children 6–10: "I like the silly songs"; adolescents: "It made my nausea go away" Parents: comforting to child (64%); reducing child anxiety (58%) and own anxiety (49%); comments: "takes their mind off their disease/treatments," "helps children and parents feel less anxious" Staff comments: "The sessions were excellent." "She has such a therapeutic effect on the children and families." "I don't understand what she does."
Colwell et al. (2005)	Piers Harris Children's Self-Concept Scale (Piers and Herzberg, 2002)	*Significant improvements: pre–post-intervention* All subjects: total score ($p = 0.004$) Art: total score ($p = 0.002$) and popularity ($p = 0.009$) Music: school status ($p = 0.02$); physical appearance/attributes ($p = 0.026$) *Significant improvements: between-group differences* Music: greater intellectual/school status ($p = 0.017$) Art group: popularity ($p = 0.021$)
Robb et al. (2008)	Behavioral coding of coping behavior: facial affect, active engagement, initiation	AME: significantly more coping behaviors than ML or ASB Significantly higher positive facial affect and active engagement in AME than ML and ASB ($p < 0.0001$) Initiation significantly higher during AME than ASB ($p < 0.05$)
Giordano et al. (2020)	Modified Yale Pre-operative Anxiety Scale (Jenkins et al., 2014) Interviews with medical staff	Lower anxiety levels in music therapy group >90% medical staff satisfied with music therapy
Children with cancer: composite arts-based therapies (music, movement, and art) and virtual reality play therapy		
Madden et al. (2010)	Pediatric Oncology Quality of Life Inventory (Varni et al., 1998) SQ Faces Scale (McGrath et al., 1996) Emotional Reactions Checklist (Reid et al., 1998)	Randomized phase: parent-reported reduced pain ($p = 0.03$) and nausea ($p = 0.006$) Cohort phase: child-reported improved mood ($p = 0.006$): more excited ($p = 0.04$), happier ($p = 0.02$), less nervous ($p = 0.02$) Positive parent (e.g., "Really good" and "He was able to express feelings and creativity") and provider satisfaction (e.g., "on a busy day it is chaotic if there are drums")
Li et al. (2011)	Short State Anxiety Scale for Children (Li and Lopez, 2007) Center for Epidemiologic Studies Depression Scale for Children (Weissman et al., 1980)	Significantly less depression symptoms in intervention group ($p = 0.02$)
Children with blood disorders and other health conditions: visual media		
Beebe et al. (2010)	Pediatric Quality of Life Asthma Module (Varni et al., 2004) Beck Youth Inventory (Beck et al., 2005) Formal Elements Art Therapy Rating Scale : Draw a Person Picking an Apple from a Tree (Gantt and Tabone, 2003)	Post-intervention and 6 months: improved parent/child-reported quality of life and worry (all $p < 0.05$) Post-intervention: improved self-concept and anxiety; improved anxiety sustained for 6 months (all $p < 0.05$) Improved coping and resourcefulness at post-intervention and 6 months (all $p < 0.05$)

(Continued)

TABLE 4 | Continued

References	Outcome measures	Results
Stafstrom et al. (2012)	Childhood Attitude Toward Illness Scale (CATIS) (Austin and Huberty, 1993)	No differences pre/post-intervention Children and parents positive about art therapy
MacDonald et al. (2019)	Medical Outcomes Study Social Support scale (Sherbourne and Stewart, 1991) Mental Health Continuum Short-Form scale (Lamers et al., 2011) Problem Areas in Diabetes (Polonsky et al., 1995) SQ	29% mental health pre/post-intervention change: languishing/moderate 57% reduced diabetes distress post-intervention 80% intervention acceptable and effective
Children with blood disorders and other conditions: music media and play therapy		
Colwell et al. (2013)	Wong–Baker FACES Pain Rating Scale (Wong and Baker, 2001) State-Trait Anxiety Inventory for Children (Spielberger, 1973) Physiological measures Time sampling engagement/interaction	Intervention group more eye contact with therapist ($p = 0.000$)
Robb et al. (2014)	Measures related to Haase's Resilience in Illness Model	Post-intervention: TMV group (n = 41) significantly better courageous coping ($p = 0.03$) 100 days post-transplant: TMV group (n = 30) significantly better social integration ($p = 0.028$) and family environment ($p = 0.008$)
Tomaj et al. (2016)	Piers Harris Self Concept Scale (Piers and Herzberg, 2002)	Intervention group, significantly higher self-concept pre/post-intervention and 1 month FU ($p < 0.001$)
Uggla et al. (2018)	Pediatric Quality of Life Inventory (generic and cancer module) (Varni et al., 2002) Astrid Lindgren Children's Hospital Pain Scale (Lundqvist et al., 2014)	Music group: higher physical function post-intervention ($p = 0.04$); wait-list control group improved in all domains ($p = 0.015$)

SR, self-report; SD, standard deviation; FU, follow-up; AME, active music engagement; ML, music listening; ASB, audio-storybooks; TMV, therapeutic music video.



	Abdulah, & Abdulla (2018)	Khodabakhshi Koolaee et al (2016)	Robb (2000)	Barrera, Rykov & Doyle (2002)	Colwell, Davis & Schroeder (2005)	Robb et al (2008)	Colwell et al (2013)	Madden et al (2010)	Li et al (2011)	Giordano et al (2020)	Beebe et al (2010)	Stafstrom et al (2012)	MacDonald. Friedman & Marks (2019)	Robb et al (2014)	Tomaj et al (2016)	Uggla et al (2018)
Selection	●	◍	◍	◍	◌	◍	◍	◍	◍	◍	◌	◍	◌	◌	◍	◌
Study design	●	●	◍	◍	●	●	●	●	◌	●	●	◍	◍	●	●	●
Confounders	◌	◍	○	◍	◌	◍	◍	◌	◍	◌	◌	○	○	●	●	◍
Blinding	◍	◍	◍	◌	◍	◍	◍	◍	◍	◍	◌	◌	◍	◍	◌	◍
Data Collection	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Withdrawals/dropouts	●	◌	◌	●	◍	◌	◌	◍	●	◍	●	◍	◌	◍	●	◍
Global	◍	◍	◍	◍	◌	◍	◍	◍	◍	◍	◌	◍	◌	◍	◍	◍

Quality rating
- ● strong
- ◍ moderate
- ◌ weak
- ○ N/A: not applicable

FIGURE 2 | Quality assessment of studies included in the review.

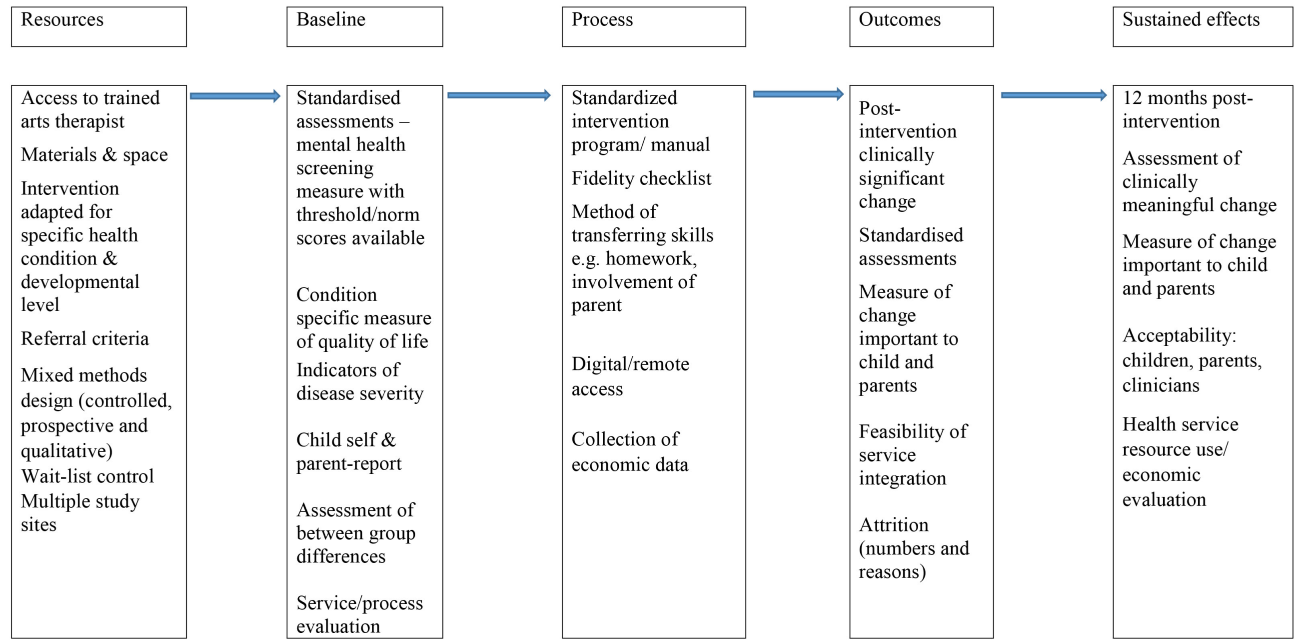


FIGURE 3 | Conceptual model of characteristics important for future research trials evaluating effectiveness of arts-based therapies for mental health and well-being in pediatric physical health settings.

Arts-Based Therapies for Children With Cancer

Nine studies evaluated arts-based therapies for children with cancer. Six studies had controlled designs, three of those describing a randomization process and the remainder having cohort designs.

Children With Cancer: Arts-Based Therapies Using Visual Media

Two studies evaluated visual/craft media (Khodabakhshi Koolaee et al., 2016; Abdulah and Abdulla, 2018). In the first study, parent-reported health-related quality of life measured using a short (10-item) questionnaire improved after a group intervention, though a limitation of the study was no measurement of child-reported outcomes (Abdulah and Abdulla, 2018). The authors stated that the intervention was not provided during chemotherapy, and this level of detail is important information for replication in future research and practice. The second study using visual media demonstrated significantly more reductions in anger and anxiety for the intervention group; a strength of the study was the specific inclusion criteria (scoring above the mean on standardized measures of anxiety and anger) and provision of an intervention schedule (Khodabakhshi Koolaee et al., 2016). The study demonstrated statistically significant post-intervention improvements but did not report whether changes were clinically significant. Both studies recruited narrow age groups relative to other studies reviewed, and this is a strength given developmental differences, though scant detail on intervention components or where to find detailed intervention schedules was a limitation.

Children With Cancer: Arts-Based Therapies Using Music

Five studies evaluated the effectiveness of music-based therapies for children with cancer (Robb, 2000; Barrera et al., 2002; Colwell et al., 2005; Robb et al., 2008; Giordano et al., 2020). The first study provided a detailed protocol and demonstrated that music elicited significantly more engaging behavior but no improvements on an outcome measure of affect (Robb, 2000). Music-based therapy was associated with improvements in feelings (e.g., "It made my nausea go away") for actively involved Canadian pediatric hematology inpatients (Barrera et al., 2002). A limitation was the single-group single-site design, while a strength was the use of child- and parent-reported outcome measures and qualitative assessment of acceptability (Barrera et al., 2002). A third study evaluating music-based therapy for children with cancer recruited from an inpatient service demonstrated significant improvements in self-concept, though the control group had art activities, which may have been a confounder (Colwell et al., 2005). Strengths of the study were the use of a board-certified therapist and a computer music program, suggesting potential for replication. Giordano et al. (2020) evaluated pre-operative music therapy for children with leukemia and parents and found less anxiety relative to a control group, and acceptability to medical staff was high. Finally Robb et al. (2008) demonstrated significantly more positive coping behaviors including smiling and active engagement in music group participants compared to two control groups. Although published outcome measures were not used, the study was included in the review because outcomes were assessed using a formalized behavioral rating system with integrated reliability checks. A strength of the study was the multi-site randomized controlled trial (RCT) design and the use of intervention delivery guides.

Children With Cancer: Composite Arts-Based Therapies (Music, Movement, and Art) and Virtual Reality Play Therapy

One study evaluating a composite arts-based intervention (music, movement, and art) described very specific participant inclusion criteria—those with a brain tumor, receiving treatment for at least 3 months, no less than weekly (Madden et al., 2010). The development of psychological interventions for children with specific physical health conditions has been recommended (Moore et al., 2019). This is therefore a strength of the study, compared to other studies reviewed recruiting children with a heterogeneity of conditions. A limitation was the wide age range of participants, while another study strength was a mixed methods design, including qualitative perspectives of service providers. Service provider perspectives were positive, while child-reported mood and parent-reported pain improved significantly (Madden et al., 2010).

One study evaluated virtual reality play therapy using published measures of anxiety and depression (Li et al., 2011). This is a study strength in relation to other included studies, as limited availability of reliable psychological interventions specifically for anxiety and depression in children with physical health LTCs has been described (Thabrew et al., 2018). There were significantly more reductions in depression symptoms in the intervention group (Li et al., 2011).

In summary, nine studies examined the effectiveness of arts-based therapies on the mental well-being of children undergoing treatment for cancer. Overall, the studies indicated some positive impact; however, the heterogeneity of intervention content and implementation, the outcomes measured, and limitations regarding study quality (e.g., presence of confounding variables, lack of randomization, and single-site evaluations) make it difficult to draw firm conclusions and generalizations or to replicate studies.

Arts-Based Therapies for Children With Blood Disorders and Other Health Conditions

Children With Blood Disorders and Other Health Conditions: Arts-Based Therapies Using Visual Media

Three studies evaluated interventions for children with asthma, epilepsy, and insulin-dependent diabetes (Beebe et al., 2010; Stafstrom et al., 2012; MacDonald et al., 2019).

The first study using visual craft media demonstrated improved mood and quality of life in children with asthma, recruited from a school outpatient clinic (Beebe et al., 2010). Study strengths were measuring child- and parent-report perspectives, providing an intervention schedule, use of health condition–specific outcome measures, controlled design, and data collection 6 months post-intervention.

In the second study, 16 children with epilepsy reported positively on art therapy received; however, outcome measures showed no improvements (Stafstrom et al., 2012). Lastly, 80% of participants with diabetes rated arts-based therapies positively in a satisfaction survey; however, participants were required to attend weekly from remote/rural locations, and attrition was high (MacDonald et al., 2019).

Children With Blood Disorders and Other Health Conditions: Music Media and Play Therapy

Children with a range of health conditions receiving one-to-one music-based therapy demonstrated significant reductions in anxiety or pain but no more so than control groups (music listening/composition) (Colwell et al., 2013). A multi-site music therapy evaluation ($n = 113$) for children with hematopoietic stem cell transplants demonstrated social, family, and spiritual improvements 3 months post-intervention (Robb et al., 2014). A strength of the study was a process for assessing intervention fidelity across sites/therapists.

An RCT of music-based therapy for children receiving hematopoietic stem cell transplants showed improved physical function post-intervention. A study strength was describing parent involvement and the wait-list control design, so all participants had access to the intervention (Uggla et al., 2018).

Finally self-concept was improved 1 month post-intervention (eight play therapy sessions) for 60 children with thalassemia major across two hospital sites (Tomaj et al., 2016).

In summary, seven studies examined the effectiveness of arts-based therapies on the mental well-being of children undergoing treatment for blood disorders and other health conditions. Once again, the studies indicated some positive impact, but significant heterogeneity of intervention characteristics (e.g., whether individual or group format), variety of outcomes measured, and design limitations mean that firm conclusions about effectiveness across studies are not possible.

DISCUSSION

The review identified and appraised 16 articles evaluating the effectiveness of arts-based therapies for improving the mental health of children with physical health LTCs. Some improvements were demonstrated in articles selected, including, for example, improved quality of life, coping behaviors, self-concept, improved mood, and reduced anxiety. Participants included children with a range of physical health LTCs, and interventions comprised arts-based therapies utilizing music, play, and visual media in the context of a therapeutic relationship. However, the heterogeneity in intervention characteristics and design limitations identified mean that it is not possible to make conclusions about effectiveness across studies. Further, the review highlights that the existing evidence base for the effectiveness of arts-based therapies as a psychological intervention for pediatric physical health settings is sparse and requires development (Cohen-Yatziv and Regev, 2019).

A lack of post-intervention positive changes on published outcome measures, in some studies, contrasted with measures of satisfaction (where used), which did indicate benefits. This is in accordance with the findings of a recent evidence synthesis of mental health interventions for children with physical health LTCs, which found meta-ethnographic evidence of benefit but a lack of effectiveness evidence (Moore et al., 2019).

This underlines the importance of measuring outcomes using quantitative and qualitative methods across a range of indicators (e.g., school attendance) and from a range of perspectives when designing future evaluations of arts-based therapies for children with physical health LTCs. The strengths and limitations of the studies reviewed informed a logic model (**Figure 3**), and we use this to make suggestions to guide the design of future research evaluations of the effectiveness of arts-based therapies for children with physical health LTCs in order to help develop the field (Cohen-Yatziv and Regev, 2019). For example, none of the studies reviewed assessed if changes reached minimum thresholds for clinically significant or meaningful change (de Vet et al., 2006); further, most of the effectiveness evaluations in the studies reviewed are cross-sectional. In future studies, quantitative prospective assessments would facilitate evaluating sustained effects after the intervention, and the use of outcome measures with published norm/cut-scores would facilitate more accurate interpretation of any changes in scores resulting from interventions. Most studies recruited participants from a single site. Future research recruiting from multiple sites should incorporate processes for ensuring intervention consistency between sites, evaluation of intervention effectiveness across sites, and feasibility of sustainable integration of arts-based therapies into pediatric physical health LTC service structures, including identification of barriers and facilitators. Most of the studies were conducted in the USA and generalizability to the UK NHS or health services in other countries cannot be assumed, given different health service structures and funding.

REVIEW STRENGTHS AND LIMITATIONS

Limitations of the review include small numbers of studies identified and heterogeneity in their design, so quantitative pooling of results across studies or health conditions was not possible. Arts-based therapies may require tailoring for children with different physical health LTCs; however, an in-depth synthesis of findings on the effectiveness of arts-based therapies for specific health conditions was not possible.

We have taken a reductionist perspective of effectiveness; our inclusion criterion was studies using published mental health outcome measures, and we excluded qualitative studies. We acknowledge that this definition of effectiveness will not capture all effects, mechanisms, and dynamic processes of change occurring during arts-based therapies (Gerber et al., 2018). We did not screen gray literature or include end-user consultation, and we did not have resources to complete full independent screening and quality appraisals or translate and include articles not published in English. These are potential sources of bias in our review.

The aim of the review was to explore the effectiveness of arts-based therapies to improve mental health for children with physical health LTCs. Only one RCT of an arts-based therapy (music) was identified in a recent review of psychological interventions for children with physical health LTCs (Moore et al., 2019). Given this, we looked broadly and included cohort and within-subject designs, which are, however, not strong indicators of effectiveness. Elevated mental health symptoms were not an inclusion criterion for our review, and only one study (Khodabakhshi Koolaee et al., 2016) recruited participants scoring above the mean on standardized measures (of anxiety and anger); this is a limitation of our review with regard to assessing improved mental health. However, given the long wait times for access to child mental health services, it is important to explore the effectiveness of reducing sub-threshold mental health symptoms and any preventative potential of arts-based therapies, and this is a strength of the review (NHS Digital, 2019).

STUDY IMPLICATIONS AND FUTURE RESEARCH

The review identified a number of design limitations important to address in future research, and we have summarized these in a model. Future trials would benefit from including end-user consultation in intervention design and service integration and could evaluate the involvement of parents and online formats of delivery to support transferring acquired/internalized coping skills outside/after intervention and for children in remote locations.

The choice of evidence-based psychological interventions available for children with physical health LTCs is currently small (Moore et al., 2019). Arts-based therapies present a potential option; however, the findings from the review confirm that research is required prior to any sustainable integration into physical heath settings. The review has highlighted some areas to clarify in future research. None of the studies reviewed distinguished between using arts-based therapies as preventative or treatment interventions. Given health service resource constraints, it is unlikely that arts-based therapies can be available to all children in physical health LTC settings, so this distinction requires consideration in future studies. Future research should evaluate how arts-based therapies might be integrated into assessment processes to support clinical teams in identifying mental health difficulties and facilitate children accessing the support they require early. In future research, economic analysis could facilitate examining any savings made by avoiding treatment complications through providing arts-based therapies (Seid et al., 2004; Shaw, 2016). In the absence of any extra health service funding, economic evaluations including an invest-to-save analysis will be important to demonstrate any reduced costs from integrating arts-based therapies in the NHS, e.g., fewer referrals to child and adolescent mental health services (Shaw, 2016). Participant inclusion criteria were not always clear in the studies reviewed. Again, limited health service resources will influence decisions about access to psychological interventions, and identifying the characteristics of children who may benefit most from arts-based therapies is important to clarify in future research and could be explored using mixed methods approaches.

CONCLUSIONS

Integration of psychological support into pediatric physical health settings is an indicator of service quality (DoH, 2011; Foster et al., 2017; Parsons et al., 2017; NHSE, 2018). However, there is limited evidence-based psychological support available for children with physical health LTCs, and this is a barrier to the provision of integrated services (Thabrew et al., 2018; Moore et al., 2019). The findings from this systematic review of effectiveness demonstrated that replication of interventions and outcomes across studies was absent, so conclusions about the effectiveness of arts-based therapies for improving the mental well-being of children with physical health LTCs cannot be made. The findings also highlight design characteristics important to incorporate when developing future trials evaluating the effectiveness of arts-based therapies. If future robustly designed research studies can demonstrate the effectiveness of arts-based therapies for children with physical health LTCs, commissioning is more likely, and this could potentially create increased choice of psychological interventions for children and families, be an alternative to talking-based therapies for children who might find it hard to speak about their difficulties, and increase the resources available for service providers.

DATA AVAILABILITY STATEMENT

All datasets presented in this study are included in the article/supplementary material.

AUTHOR CONTRIBUTIONS

SH, SW, PW, AZ, and SJ conceptualized the review. SW, AZ, and JB analyzed results. SW wrote the first draft of the manuscript. All authors contributed to editing, commenting, and revising manuscript versions, read and approved the submitted version.

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REFERENCES

Abdulah, D. M., and Abdulla, B. M. O. (2018). Effectiveness of group art therapy on quality of life in paediatric patients with cancer: a randomized controlled trial. *Complement. Ther. Med.* 41, 180–185. doi: 10.1016/j.ctim.2018.09.020

Aguilar, B. A. (2017). The efficacy of art therapy in pediatric oncology patients: an integrative literature review. *J. Pediatr. Nurs*. 36, 173–178. doi: 10.1016/j.pedn.2017.06.015

American Art Therapy Association (2018). *About Art Therapy*. Available online at: https://arttherapy.org/about-art-therapy/ (accessed January 31, 2020).

Austin, J. K., and Huberty, T. J. (1993). Development of the child attitude toward illness scale. *J. Pediatr. Psychol*. 18, 467–480. doi: 10.1093/jpepsy/18.4.467

Barrera, M. E., Rykov, M. H., and Doyle, S. L. (2002). The effects of interactive music therapy on hospitalized children with cancer: a pilot study. *Psychooncology* 11, 379–388. doi: 10.1002/pon.589

Beck, J. S., Beck, A. T., and Jolly, J. B. (2005). *Beck Youth Inventories-(BYI-II)*. San Antonio, Tx: PsychCorp. Pearson Clinical.

Beebe, A., Gelfand, E. W., and Bender, B. (2010). A randomized trial to test the effectiveness of art therapy for children with asthma. *J. Allergy Clin. Immunol.* 126, 263–266. doi: 10.1016/j.jaci.2010.03.019

Bieri, D., Reeve, R. A., Champion, G. D., Addicoat, L., and Ziegler, J. B. (1990). The Faces Pain Scale for the self-assessment of the severity of pain experienced by children: development, initial validation, and preliminary investigation for ratio scale properties. *Pain* 41, 139–150. doi: 10.1016/0304-3959(90)90018-9

Bradt, J., Dileo, C., Magill, L., and Teague, A. (2016). Music interventions for improving psychological and physical outcomes in cancer patients. *Cochrane Database Syst. Rev*. 8. doi: 10.1002/14651858.CD006911.pub3

Brady, A. M., Deighton, J., and Stansfeld, S. (2017). Psychiatric outcomes associated with chronic illness in adolescence: a systematic review. *J. Adolesc.* 59, 112–123. doi: 10.1016/j.adolescence.2017.05.014

Butler, A., Van Lieshout, R. J., Lipman, E. L., MacMillan, H. L., Gonzalez, A., Gorter, J. W., et al. (2018). Mental disorder in children with physical conditions: a pilot study. *BMJ Open* 8:e019011. doi: 10.1136/bmjopen-2017-019011

Clapp, L. A., Taylor, E. P., Di Folco, S., and Mackinnon, V. L. (2018). Effectiveness of art therapy with pediatric populations affected by medical health conditions: a systematic review. *Arts Health* 11, 183–201. doi: 10.1080/17533015.2018.1443952

Cohen-Yatziv, L., and Regev, D. (2019). The effectiveness and contribution of art therapy work with children in 2018-what progress has been made so far? A systematic review. *Int. J. Art Ther.* 24, 100–112. doi: 10.1080/17454832.2019.1574845

Colver, A., McConachie, H., Le Couteur, A., Dovey-Pearce, G., Mann, K. D., McDonagh, J. E., et al. (2018). A longitudinal, observational study of the features of transitional healthcare associated with better outcomes for young people with long-term conditions. *BMC Med*. 16:111. doi: 10.1186/s12916-018-1102-y

Colwell, C. M., Davis, K., and Schroeder, L. K. (2005). The effect of composition (art or music) on the self-concept of hospitalized children. *J. Music Ther.* 42, 49–63. doi: 10.1093/jmt/42.1.49

Colwell, C. M., Edwards, R., Hernandez, E., and Brees, K. (2013). Impact of music therapy interventions (listening, composition, orff-based) on the physiological and psychosocial behaviors of hospitalized children: a feasibility study. *J. Pediatr. Nurs.* 28, 249–257. doi: 10.1016/j.pedn.2012.08.008

Crouch, L., Reardon, T., Farrington, A., Glover, F., and Creswell, C. (2019). "Just keep pushing": parents' experiences of accessing child and adolescent mental health services for child anxiety problems. *Child Care Health Dev*. 45, 491–499. doi: 10.1111/cch.12672

Cruikshank, M., Foster, H. E., Stewart, J., Davidson, J. E., and Rapley, T. (2016). Transitional care in clinical networks for young people with juvenile idiopathic arthritis: current situation and challenges. *Clin. Rheumatol*. 35, 893–899. doi: 10.1007/s10067-015-2950-x

Davis, A. M., Rubinstein, T. B., Rodriguez, M., and Knight, A. M. (2017). Mental health care for youth with rheumatologic diseases–bridging the gap. *Pediatr. Rheumatol.* 15:85. doi: 10.1186/s12969-017-0214-9

de Vet, H. C., Terwee, C. B., Ostelo, R. W., Beckerman, H., Knol, D. L., and Bouter, L. M. (2006). Minimal changes in health status questionnaires: distinction between minimally detectable change and minimally important change. *Health Qual. Life Outcomes* 4:54. doi: 10.1186/1477-7525-4-54

Denny, S., de Silva, M., Fleming, T., Clark, T., Merry, S., Ameratunga, S., et al. (2014). The prevalence of chronic health conditions impacting on daily functioning and the association with emotional well-being among a national sample of high school students. *J. Adolesc. Health* 54, 410–415. doi: 10.1016/j.jadohealth.2013.09.010

DoH (2011). *No Health Without Mental Health: A Cross-Government Mental Health Outcomes Strategy for People of All Ages. Supporting Document–The Economic Case for Improving Efficiency and Quality in Mental Health*. Leeds: Department of Health.

DoH (2012). *Long Term Conditions Compendium of Information: Third Edition, 3rd Edn*. Leeds: Department of Health.

Fancourt, D., and Finn, S. (2019). *What is the Evidence on the Role of the Arts in Improving Health and Well-Being. A Scoping Review*. Copenhagen: WHO Regional Office for Europe.

Ferro, M. (2016). Major depressive disorder, suicidal behaviour, bipolar disorder, and generalised anxiety disorder among emerging adults with and without chronic health conditions. *Epidemiol. Psychiatr. Sci.* 25, 462–474. doi: 10.1017/S2045796015000700

Foster, H. E., Minden, K., Clemente, D., Leon, L., McDonagh, J. E., Kamphuis, S., et al. (2017). EULAR/PReS standards and recommendations for the transitional care of young people with juvenile-onset rheumatic diseases. *Ann. Rheum. Dis.* 76, 639–646. doi: 10.1136/annrheumdis-2016-210112

Gantt, L., and Tabone, C. (2003). "The formal elements art therapy scale and "draw a person picking an apple from a tree," in *Handbook of Art Therapy*, ed C. Malchiodi (New York, NY: Guilford), 420–427.

Gerber, N., Bryl, K., Potvin, N., and Blank, C. A. (2018). Arts-based research approaches to studying mechanisms of change in the creative Arts therapies. *Front. Psychol.* 9:2076. doi: 10.3389/fpsyg.2018.02076

Giordano, F., Zanchi, B., De Leonardis, F., Rutigliano, C., Esposito, F., Brienza, N., et al. (2020). The influence of music therapy on preoperative anxiety in pediatric oncology patients undergoing invasive procedures. *Arts Psychother.* 68:101649. doi: 10.1016/j.aip.2020.101649

Gray, S., Cheetham, T., McConachie, H., Mann, K. D., Parr, J. R., Pearce, M. S, et al. (2018). A longitudinal, observational study examining the relationships of patient satisfaction with services and mental well-being to their clinical course in young people with Type 1 diabetes mellitus during transition from child to adult health services. *Diabet. Med.* 35, 1216–1222. doi: 10.1111/dme.13698

Hackett, S. S., Ashby, L., Parker, K., Goody, S., and Power, N. (2017). UK art therapy practice-based guidelines for children and adults with learning disabilities. *Int. J. Art Ther.* 22, 84–94. doi: 10.1080/17454832.2017.1319870

Hanns, L., Cordingley, L., Galloway, J., Norton, S., Carvalho, L. A., Christie, D., et al. (2018). Depressive symptoms, pain and disability for adolescent patients with juvenile idiopathic arthritis: results from the Childhood Arthritis Prospective Study. *Rheumatology* 57, 1381–1389. doi: 10.1093/rheumatology/key088

Hysing, M., Elgen, I., Gillberg, C., Lie, S. A., and Lundervold, A. J. (2007). Chronic physical illness and mental health in children. Results from a large-scale population study. *J. Child Psychol. Psychiatry.* 48, 785–792. doi: 10.1111/j.1469-7610.2007.01755.x

Jenkins, B. N., Fortier, M. A., Kaplan, S. H., Mayes, L. C., and Kain, Z. N. (2014). Development of a short version of the modified yale preoperative anxiety scale. *Anesth. Analg.* 119, 643–650. doi: 10.1213/ANE.0000000000000350

Kazak, A. E., Abrams, A. N., Banks, J., Christofferson, J., DiDonato, S., Grootenhuis, M. A., et al. (2015). Psychosocial assessment as a standard of care in pediatric cancer. *Pediatr. Blood Cancer* 62, 426–459. doi: 10.1002/pbc.25730

Khodabakhshi Koolaee, A., Vazifehdar, R., and Bahari, F. (2016). Impact of painting therapy on aggression and anxiety of children with cancer. *Caspian J. Pediatr.* 2, 135–141.

Knight, A., Vickery, M., Faust, L., Muscal, E., Davis, A., Harris, J., et al. (2019). Gaps in mental health care for youth with rheumatologic conditions: a mixed methods study of perspectives from behavioral health providers. *Arthritis Care Res.* 71, 591–601. doi: 10.1002/acr.23683

Knight, A., Weiss, P., Morales, K., Gerdes, M., Rearson, M., Vickery, M., et al. (2015). Identifying differences in risk factors for depression and anxiety in pediatric chronic disease: a matched cross-sectional study of youth with lupus/mixed connective tissue disease and their peers with diabetes. *J. Pediatr.* 167, 1397–1403. doi: 10.1016/j.jpeds.2015.07.048

Lamers, S. M., Westerhof, G. J., Bohlmeijer, E. T., ten Klooster, P. M., and Keyes, C. L. (2011). Evaluating the psychometric properties of the mental health continuum-short form (MHC-SF). *J. Clin. Psychol.* 67, 99–110. doi: 10.1002/jclp.20741

Lansky, S. B., List, M. A., Lansky, L. L., Ritter-Sterr, C., and Miller, D. R. (1987). The measurement of performance in childhood cancer patients. *Cancer* 60, 1651–1656. doi: 10.1002/1097-0142(19871001)60:7<1651::AID-CNCR2820600738>3.0.CO;2-J

Li, H. C. W., and Lopez, V. (2007). Development and validation of a short form of the Chinese version of the State Anxiety Scale for Children. *Int. J. Nurs. Stud.* 44, 566–573. doi: 10.1016/j.ijnurstu.2005.12.004

Li, W., Chung, J. O., and Ho, E. (2011). The effectiveness of therapeutic play, using virtual reality computer games, in promoting the psychological well-being of children hospitalised with cancer. *J. Clin. Nurs.* 20, 2135–2143. doi: 10.1111/j.1365-2702.2011.03733.x

Lundqvist, P., Kleberg, A., Edberg, A. K., Larsson, B. A., Hellström-Westas, L., and Norman, E. (2014). Development and psychometric properties of the Swedish ALPS-Neo pain and stress assessment scale for newborn infants. *Acta Paediatr.* 103, 833–839. doi: 10.1111/apa.12672

MacDonald, C., Friedman, S., and Marks, S. (2019). Creative arts diabetes initiative: group art therapy and peer support for youth and young adults transitioning from pediatric to adult diabetes care in Manitoba. *Can. J. Diabetes* 34, 377–383. doi: 10.1016/j.jcjd.2019.04.016

Madden, J. R., Mowry, P., Gao, D., McGuire Cullen, P., and Foreman, N. K. (2010). Creative arts therapy improves quality of life for pediatric brain tumor patients receiving outpatient chemotherapy. *J. Pediatr. Oncol. Nurs.* 27, 133–145. doi: 10.1177/1043454209355452

McGrath, P. A. (1985). "Multidimensional pain assessment in children," in *Advances in Pain Research and Therapy*, ed H. L. Fields (New York, NY: Raven Press), 387–393.

McGrath, P. A., Seifert, C. E., Speechley, K. N., Booth, J. C., Stitt, L., and Gibson, M. C. (1996). A new analogue scale for assessing children's pain: an initial validation study. *Pain* 64, 435–443. doi: 10.1016/0304-3959(95)00171-9

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., and Prisma Group (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 6:e1000097. doi: 10.1371/journal.pmed.1000097

Mokkink, L. B., Van Der Lee, J. H., Grootenhuis, M. A., Offringa, M., and Heymans, H. S. (2008). Defining chronic diseases and health conditions in childhood (0–18 years of age): national consensus in the Netherlands. *Eur. J. Pediatr.* 167, 1441–1447. doi: 10.1007/s00431-008-0697-y

Moore, D. A., Nunns, M., Shaw, L., Rogers, M., Walker, E., Ford, T., et al. (2019). Interventions to improve the mental health of children and young people with long-term physical conditions: linked evidence syntheses. *Health Technol. Assess.* 23, 1–164. doi: 10.3310/hta23220

Nelson, W. M., and Finch, A. J. (2000). Children's Inventory of Anger: *ChIA Manual*. Melton South: Western Psychological Services.

NHS Digital (2019). *Waiting Times for Children and Young People's Mental Health Services, 2018 - 2019 Additional Statistics*. Leeds: National Health Service.

NHSE (2018). *NHS England Funding and Resource 2018/19: Supporting 'Next Steps for the NHS Five Year Forward View'*. Wakefield: National Health Service England.

NICE (2016). *Psychosis and Schizophrenia in Children and Young People: Recognition and Management. (NICE Clinical Guideline CG115)*. London: National Institute for Health and Care Excellence.

Parsons, S., Thomson, W., Cresswell, K., Starling, B., McDonagh, J. E., and Barbara Ansell National Network for Adolescent, R. (2017). What do young people with rheumatic disease believe to be important to research about their condition? A UK-wide study. *Pediatr. Rheumatol.* 15, 53–53. doi: 10.1186/s12969-017-0181-1

Piers, E. V., and Herzberg, D. S. (2002). *Piers-Harris Children's Self-Concept Scale: Manual*. Melton South: Western Psychological Services.

Pinquart, M., and Shen, Y. (2011a). Anxiety in children and adolescents with chronic physical illnesses: a meta-analysis. *Acta Paediatr.* 100, 1069–1076. doi: 10.1111/j.1651-2227.2011.02223.x

Pinquart, M., and Shen, Y. (2011b). Depressive symptoms in children and adolescents with chronic physical illness: an updated meta-analysis. *J. Pediatr. Psychol.* 36, 375–384. doi: 10.1093/jpepsy/jsq104

Polonsky, W. H., Anderson, B. J., Lohrer, P. A., Welch, G., Jacobson, A. M., Aponte, J. E., et al. (1995). Assessment of diabetes-related distress. *Diabetes Care* 18, 754–760. doi: 10.2337/diacare.18.6.754

Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., et al. (2006). *Guidance on the Conduct of Narrative Synthesis in Systematic Reviews. A P*roduct *F*rom the ESRC *M*ethods *P*rogramme Version, 1. Lancaster: Lancaster University.

Ravens-Sieberer, U., Erhart, M., Rajmil, L., Herdman, M., Auquier, P., Bruil, J., et al. (2010). Reliability, construct and criterion validity of the KIDSCREEN-10 score: a short measure for children and adolescents' well-being and health-related quality of life. *Qual. Life Res.* 19, 1487–1500. doi: 10.1007/s11136-010-9706-5

Reid, G. J., Gilbert, C. A., and McGrath, P. J. (1998). The pain coping questionnaire: preliminary validation. *Pain* 76, 83–96. doi: 10.1016/S0304-3959(98)00029-3

Robb, S. L. (2000). The effect of therapeutic music interventions on the behavior of hospitalized children in isolation: developing a contextual support model of music therapy. *J. Music Ther.* 37, 118–146. doi: 10.1093/jmt/37.2.118

Robb, S. L., Burns, D. S., Stegenga, K. A., Haut, P. R., Monahan, P. O., Meza, J., et al. (2014). Randomized clinical trial of therapeutic music video intervention for resilience outcomes in adolescents/young adults undergoing hematopoietic stem cell transplant: a report from the Children's Oncology Group. *Cancer* 120, 909–917. doi: 10.1002/cncr.28355

Robb, S. L., Clair, A. A., Watanabe, M., Monahan, P. O., Azzouz, F., Stouffer, J. W., et al. (2008). Randomized controlled trial of the active music engagement (AME) intervention on children with cancer. *Psychooncolgy* 17, 699–708. doi: 10.1002/pon.1301

Rosenberg, A. R., Bradford, M. C., Junkins, C. C., Taylor, M., Zhou, C., Sherr, N., et al. (2019). Effect of the promoting resilience in stress management intervention for parents of children with cancer (PRISM-P): a randomized clinical trial. *JAMA Netw. Open* 2:e1911578. doi: 10.1001/jamanetworkopen.2019.11578

Seid, M., Varni, J. W., Segall, D., and Kurtin, P. S. (2004). Health-related quality of life as a predictor of pediatric healthcare costs: a two-year prospective cohort analysis. *Health Qual. Life Outcomes* 2:48. doi: 10.1186/1477-7525-2-48

Shaw, L., Moore, D., Nunns, M., Thompson, C. J., Ford, T., Berry, V., et al. (2019). Experiences of interventions aiming to improve the mental health and well-being of children and young people with a long-term physical condition: a systematic review and meta-ethnography. *Child Care Health Dev.* 45, 832–849. doi: 10.1111/cch.12708

Shaw, M. J. (2016). An "invest to save" approach to health. *BMJ* 355:i5944. doi: 10.1136/bmj.i5944

Sherbourne, C. D., and Stewart, A. L. (1991). The MOS social support survey. *Soc. Sci. Med.* 32, 705–714. doi: 10.1016/0277-9536(91)90150-B

Spence, S. H., Barrett, P. M., and Turner, C. M. (2003). Psychometric properties of the Spence Children's Anxiety Scale with young adolescents. *J. Anxiety Disord.* 17, 605–25. doi: 10.1016/S0887-6185(02)00236-0

Spielberger, C. D. (1973). *State-Trait Anxiety Inventory for Children*. Palo Alto: Consulting Psychologists Press. doi: 10.1037/t06497-000

Stafstrom, C. E., Havlena, J., and Krezinski, A. J. (2012). Art therapy focus groups for children and adolescents with epilepsy. *Epilepsy Behav.* 24, 227–233. doi: 10.1016/j.yebeh.2012.03.030

Thabrew, H., Stasiak, K., Hetrick, S. E., Donkin, L., Huss, J. H., Highlander, A., et al. (2018). Psychological therapies for anxiety and depression in children and adolescents with long-term physical conditions. *Cochrane Database Syst. Rev.* 2017:CD012488. doi: 10.1002/14651858.CD012488.pub2

Thomas, B., Ciliska, D., Dobbins, M., and Micucci, S. (2004). A process for systematically reviewing the literature: providing the research evidence for public health nursing interventions. *Worldviews Evid. Based Nurs.* 1, 176–184. doi: 10.1111/j.1524-475X.2004.04006.x

Tollisen, A., Selvaag, A. M., Aulie, H. A., Lilleby, V., Aasland, A., Lerdal, A., et al. (2018). Physical functioning, pain, and health-related quality of life in adults with juvenile idiopathic arthritis: a longitudinal 30-year followup study. *Arthritis Care Res.* 70, 741–749. doi: 10.1002/acr.23327

Tomaj, O. K., Estebsari, F., Taghavi, T., Nejad, L. B., Dastoorpoor, M., and Ghasemi, A. (2016). The effects of group play therapy on self-concept among 7 to 11 year-old children suffering from thalassemia major. *Iran. Red Crescent Med. J.* 18:e35412. doi: 10.5812/ircmj.35412

Uggla, L., Bonde, L. O., Hammar, U., Wrangsjö, B., and Gustafsson, B. (2018). Music therapy supported the health-related quality of life for children undergoing haematopoietic stem cell transplants. *Acta Paediatr.* 107, 1986–1994. doi: 10.1111/apa.14515

Varni, J. W., Burwinkle, T. M., Katz, E. R., Meeske, K., and Dickinson, P. (2002). The PedsQL^{TM} in pediatric cancer: reliability and validity of the pediatric quality of life inventory^{TM} generic core scales, multidimensional fatigue scale, and cancer module. *Cancer* 94, 2090–2106. doi: 10.1002/cncr.10428

Varni, J. W., Burwinkle, T. M., Rapoff, M. A., Kamps, J. L., and Olson, N. (2004). The PedsQL^{TM} in pediatric asthma: reliability and validity of the Pediatric Quality of Life Inventory^{TM} generic core scales and asthma module. *J. Behav. Med.* 27, 297–318. doi: 10.1023/B:JOBM.0000028500.53608.2c

Varni, J. W., Katz, E. R., Seid, M., Quiggins, D. J., Friedman-Bender, A., and Castro, C. M. (1998). The Pediatric Cancer Quality of Life Inventory (PCQL). I. Instrument development, descriptive statistics, and cross-informant variance. *J. Behav. Med.* 21, 179–204. doi: 10.1037/t65932-000

Weissman, M. M., Orvaschel, H., and Padian, N. (1980). Children's symptom and social functioning: self-report scales. *J. Nerv. Ment. Disord.* 168, 736–740. doi: 10.1097/00005053-198012000-00005

Wiener, L., Viola, A., Koretski, J., Perper, E. D., and Patenaude, A. F. (2015). Pediatric psycho-oncology care: standards, guidelines, and consensus reports. *Psychooncology* 24, 204–211. doi: 10.1002/pon.3589

Wong, D. L., and Baker, C. M. (2001). Smiling face as anchor for pain intensity scales. *Pain* 89, 295–297. doi: 10.1016/S0304-3959(00)00375-4

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

APPENDIX

Table A1 | Search strategy used for the EBSCO interface and Medline database.

1. (Art therap$ or art psychotherap$ or creative arts therap$). m_titl.	3,337
2. Limit 1 to yr = "2000-Current"	2,662
3. Drama therap$. m_titl.	231
4. Limit 3 to yr = "2000-Current"	163
5. (Music therap$ or music intervention or musical therap$).m_titl.	5,542
6. Limit 5 to yr = "2000-Current"	4,736
7. Play therap$.m_titl.	1,733
8. Limit 7 to yr = "2000-Current"	1,285
9. (Dance therap$ or movement therap$ or dmt).m_titl.	2,676
10. Limit 9 to yr = "2000-Current"	2,397
11. 2 or 4 or 6 or 8 or 10	11,218
12. (Child$ or adolescent$ or youth$ or teenager$).m_titl.	1,937,337
13. Limit 12 to yr = "2000-Current"	1,450,570
14. (Pediatric or child$ or adolescent$).m_titl.	2,138,347
15. Limit 14 to yr = "2000-Current"	1,619,826
16. 13 or 15	1,698,497
17. 11 and 16	2,038

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A Critical Review of Studies Assessing Interpretation Bias Towards Social Stimuli in People With Eating Disorders and the Development and Pilot Testing of Novel Stimuli for a Cognitive Bias Modification Training

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People with eating disorders display a negative interpretation bias towards ambiguous social stimuli. This bias may be particularly relevant to young people with the illness due to the developmental salience of social acceptance and rejection. The overall aim of this study was to systematically develop and validate stimuli for a cognitive bias modification training to reduce a social rejection-related negative interpretation bias in young people with eating disorders. A mixed-methods design was used to achieve this aim. A review of the literature was conducted using EMBASE, MEDLINE, PsycINFO, Web of Science, and PubMed. Six studies were included in the review. Focus groups were held with patients with eating disorders, carers and healthcare professionals. Content analysis was used to identify key themes from the qualitative data. Based on these themes, a total of 339 scenarios were generated by the researchers. Salient themes identified from the focus group data included virtual rejection/exclusion, rejection associated with an aspect of the eating disorder, rejection triggered by ambiguous/benign comments or behaviors of others and rejection perceived when confiding in others. Patients rated these scenarios in terms of their age-relevance and emotional salience and 301 scenarios were included in the final stimulus set. These materials may be used by researchers conducting future experimental research into the potential benefits of interpretation bias training for young people with eating disorders.

Keywords: interpretation bias, eating disorders, social, interpersonal, cognitive bias modification

INTRODUCTION

Mental health disorders place a huge burden on the individuals affected, their families and society (Holmes et al., 2018). Despite the availability of evidence-based psychological treatments, their efficacy is sub-optimal and requires coordinated efforts from researchers and clinicians worldwide to improve (Holmes et al., 2018). The use of evidence-based practice is key to treatment innovation. Evidence-based practice refers to treatment guided by a combined consideration of clinical expertise, research evidence and patient values, preferences and circumstances (American Psychological Association, 2005). Recently, it has been suggested that this approach is particularly suited to improve treatment for conditions characterized by repeated treatment failures and chronicity, such as eating disorders (Peterson et al., 2016; Hilbert et al., 2017). In this study, we will use the evidence-based practice framework to validate the materials for a novel computerized training to improve social functioning in young people with eating disorders.

Eating disorders are psychiatric conditions diagnostically characterized by abnormal eating behaviors and cognitions related to eating, weight and shape (American Psychiatric Association, 2013). These symptoms often appear in adolescence, a time when the pressure for social acceptance is critically high (Somerville, 2013). Among other factors, the onset of abnormal eating behaviors in adolescence has been associated with criticism from others with regards to general aspects of the self, eating, and physical appearance (Jacobi et al., 2011; Copeland et al., 2015; Duarte et al., 2017; Lee and Vaillancourt, 2019; Lie et al., 2019; Okada et al., 2019). Furthermore, the severity of eating disorder symptoms has been linked to greater concerns about appearing nervous or anxious to others (Espel-Huynh et al., 2019). Experimental studies have corroborated the causal role played by interpersonal stress in triggering eating disorder symptoms (Cardi et al., 2018b; Monteleone et al., 2018). For instance, tasks that elicit interpersonal stress increase the desire to binge eat in patients with bulimia nervosa or binge eating disorder (Tuschen-Caffier and Vogele, 1999; Hilbert et al., 2011; Rosenberg et al., 2013), and reduce the liking of food in women with a lifetime diagnosis of anorexia nervosa compared to healthy women (Chami et al., in preparation). The implication of these findings is that decreasing reactivity to interpersonal stress might reduce the severity of eating disorder symptoms.

Recent advances in the field of experimental psychopathology indicate that it is possible to lower patients' sensitivity to negative social feedback by reducing their tendency to interpret ambiguous social information in a negative way (Cardi et al., 2015, 2019; Turton et al., 2018).

Cognitive Bias Modification for Interpretation (CBM-I) is a computerized training developed with the goal of reducing a negative interpretation bias by exposing participants to benign/neutral interpretations of ambiguous social scenarios. Both adults and adolescents with eating disorders display an interpretation bias towards negative social information and this bias is related to self-reported sensitivity to rejection as well as core eating disorder symptoms, such as fear of weight gain and body image disturbance (Cardi et al., 2017). A recent study also indicated that cognitive biases (attention and interpretation biases) towards negative or ambiguous social information are malleable to change after using five training sessions of combined CBM-I and CBM of attention (CBM-A) and that the use of the training is associated with lower levels of anxiety and higher levels of self-compassion in response to critical feedback from an actor (Cardi et al., 2015).

A common limitation of these studies is that they have not measured changes in core eating disorder symptoms following CBM-I. Procedures for CBM-I in other mental health conditions, such as depression and anxiety disorders, seem to produce only a small effect on clinical symptoms (Krebs et al., 2018). A possible reason to explain the lack of generalization effects on clinical symptoms is that training materials are not systematically developed and validated within the target population. Most existing interpretation bias trainings in eating disorders have been adapted from those originally developed for people with anxiety disorders and have been validated in adults. For example, Cardi et al. (2015) adapted stimuli originally developed by Hirsch et al. (2009) which included scenarios covering common worry topics, and tested these in a feasibility study involving a sample of 28 females with anorexia nervosa. Furthermore, these materials were adapted by researchers without the involvement of key stakeholders including patients, health professionals, and carers. These factors limit the ecological validity of the training for the target population within today's social context (Hughes et al., 2016). Based on this hypothesis, this study involved the development of stimuli for a novel CBM-I training for adolescents with eating disorders, and piloting the face validity of these stimuli. The three aims were:

1. To conduct a critical review of the literature on interpretation bias assessment and training towards social stimuli in eating disorders.
2. To conduct focus groups with adolescents with eating disorders, carers and professionals to identify salient themes around the topic of social rejection and generate scenarios (interpretation bias training stimuli) reflecting those themes.
3. To pilot the face validity of these materials, focusing on two key aspects (age-relevance and emotional salience) in the target population (adolescents with eating disorders).

MATERIALS AND METHODS

Aim 1

The literature on interpretation bias towards social stimuli in people with eating disorders or studies involving community samples and included a measurement of eating disorder symptoms were reviewed. An online literature search was conducted using EMBASE, MEDLINE, PsycINFO, Web of Science, and PubMed from database inception – October 2019. Search terms included "interpretation bias" or "biased interpretation" in combination with "anorexia nervosa" or "bulimia nervosa" or "eating disorder" in the Title/Abstract or full-text fields. Publications were included if (1) they were

TABLE 1 | Literature review of materials used for interpretation bias assessment or training.

Materials (Authors)	Population and age group	Description of Material	Development of Material
Summers and Cougle, 2018	Undergraduate female psychology students and women from the community (*N* = 41) with elevated symptoms of Body Dysmorphic Disorder	135 scenarios describing situations involving the risk of social evaluation or exposure to own appearance	Developed by the researchers.
Cardi et al., 2015	Women with anorexia nervosa (*N* = 28)	134 scenarios describing ambiguous situations involving the risk of social rejection	Adapted from Huppert et al., 2007; Hirsch et al., 2009; Hayes et al., 2010
Cardi et al., 2017	Women with anorexia nervosa (*n* = 35) and healthy controls (*n* = 30)	12 scenarios describing ambiguous situations involving the risk of social rejection	Adapted from Huppert et al., 2007; Hayes et al., 2010 Research team (4 individuals) independently chose subgroup of sentences with greatest potential of being interpreted in positive or negative way.
Turton et al., 2018	Women with anorexia nervosa (*N* = 55)	110 scenarios describing ambiguous situations involving the risk of social rejection	Adapted from Huppert et al., 2007; Hirsch et al., 2009; Hayes et al., 2010; Cardi et al., 2015
Matheson et al., 2018	Female undergraduates (*N* = 123)	87 scenarios describing appearance-relevant ambiguous social scenarios	Training stimuli were developed by the researchers and informed by appearance-based feedback and rejection sensitivity scales (Tantleff-Dunn et al., 1995; Altabe et al., 2004; Park et al., 2010; Park, 2013). These were rated by women in a pilot study for relatedness to appearance and affective valence.
Cardi et al., 2019	Adolescent girls with anorexia nervosa (*N* = 24)	112 scenarios describing ambiguous situations involving the risk of social rejection	Adapted from Cardi et al., 2015 in collaboration with five adolescents with anorexia nervosa receiving inpatient care.

published in a peer-reviewed journal and written in English, (2) used an assessment task to measure interpretation bias towards social stimuli or a cognitive bias modification training to reduce negative interpretation bias towards social information and (3) included a sample of children, adolescents or adults with a diagnosis of an eating disorder or included a community sample and a measurement of eating disorder symptoms (**Table 1**). The materials used for the assessment or training task used within each study are summarized in **Table 1**.

Aim 2

In order to address the main research question, "What situations are likely to trigger fear of being rejected/left out/excluded in adolescents with eating disorders?", patients with eating disorders, carers and health professionals were invited to participate in separate, live online group forums which were themed around the topic of social rejection. Participants were recruited via opportunity sampling from a specialist eating disorder intensive treatment service and from a departmental database of patients who had previously participated in research and had opted to be contacted about future studies. Participants were required to be fluent in English and have no severe medical or psychiatric comorbidities in order to take part. Patients' eligibility was assessed by the researcher and the eating disorder diagnosis was confirmed by a Consultant Psychiatrist based on DSM-5 criteria or self-reported by the patient (in three cases). A standard topic guide including questions related to the topic of social rejection was developed (**Table 2**) and the wording was adapted for patients, carers and health professionals. Two separate groups were held for the professionals to accommodate the availability of participants. The forums were hosted on a bespoke research platform that developed for another study running in the department (created by https://www.mindwaveventures.com/ and funded by the National Institute for Health Research - Health Technology Assessment). The forums were live, text-based groups accessible to participants only. All participants were given a participant screen name (e.g., Participant 1) in order to anonymise them. The researcher led the groups by posting open questions and providing participants with time to respond to each question. Each group lasted for one hour. Ambiguous scenarios related to the risk of rejection from others were then generated with consideration of those previously adapted for adolescents with eating disorders (Cardi et al., 2019) and the data derived from the focus groups. Each scenario consisted of a hypothetical ambiguous social situation which was open to the young person for interpretation (e.g., "It is a classmate's birthday and your good friend brings in a cake. You aren't offered a slice and feel awkward. Later you speak to your friend about how this made you feel and they. . .").

Aim 3

Quantitative methods were used to assess the degree to which the scenarios reflected realistic concerns that were both age appropriate and emotionally salient to young people with eating disorders (see **Figure 1**). Girls with eating disorders (*N* = 27) aged 13–17 who participated in the focus groups and girls attending an intensive treatment program who did not participate in the focus groups were invited to rate the scenarios (at this time there were no boys available in the service to rate the scenarios). Participants were provided with paper forms over email, or in person at their

TABLE 2 | Topic guide for focus groups.

What situations can you think of that would involve the chance that you would be rejected by others? This can include being judged, criticized, or left out of a group.
Can you think of some examples of the sorts of things that you have avoided saying or doing in front of others, because you were worried about how others might react? E.g. worried about whether they would judge or criticize you.
What happened the last time you felt excluded / left out of a group?
What happened the last time you avoided a situation because you thought you might be rejected by others?
What would help you to feel more confident (i.e., less fearful or avoidant) in social situations (what could protect you from being rejected)?
How could others (i.e., treatment team, family) help you to feel more confident (less fearful/avoidant) in social situations?

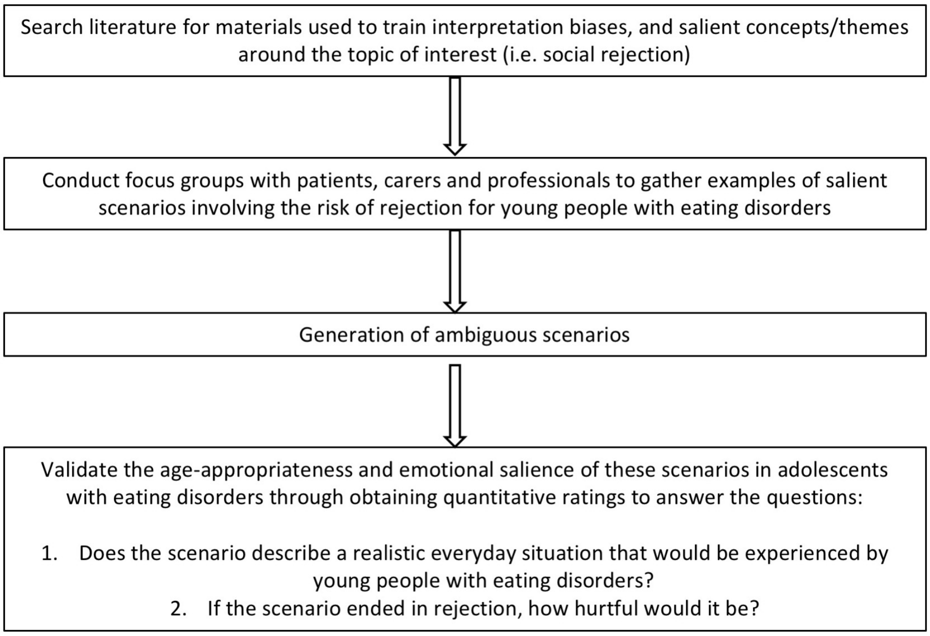

FIGURE 1 | Flow diagram for interpretation bias stimuli development.

treatment center. Each paper form contained a proportion of the scenarios depending on the participants' time availability, and two 5-point Likert-scales which were used to measure the age-relevance and emotional salience of each scenario. The scales ranged from 0 (not at all realistic) to 5 (very realistic) and 0 (not at all hurtful) to 5 (very hurtful). After discussion with the research team, the matrix (**Table 3**) was developed to decide whether to include, modify or exclude each of the scenarios. The scenarios that were considered both realistic and hurtful (scenarios scoring 3 or above on both scales) were included in the final selection of scenarios. The data that support the findings of this study are openly available in [repository name e.g., "figshare"] at http://doi.org/[doi], reference number [reference number].

RESULTS

Results of Aim 1

Six papers meeting the inclusion criteria were identified and reviewed (see **Table 1**). Five studies included adults (N = 312) aged 18–65 and one study included adolescents (N = 24) aged 14–18. With the exception of Cardi et al. (2019) that involved adolescents with lived experience of eating disorders in the process of adapting materials for an interpretation bias modification training, all five studies included stimuli adapted by the researchers that were originally designed for other populations. This presents missed opportunities to tap into concerns around social rejection that may be relevant to people with eating disorders in particular, such as fears around being rejected due to the physical or behavioral symptoms that are specific to anorexia nervosa, and to explore concerns that may be predominantly relevant to adolescents with these conditions.

Results of Aim 2

Five focus groups were held in total. The patient group consisted of eight young people (seven females, one male) aged 13–17 (M = 15.50, SD = 1.22) with anorexia nervosa (n = 6) or bulimia nervosa (n = 2). A separate focus group was held for carers (n = 7) who were females aged 40–58 (M = 50.33, SD = 5.59). Only one of the carer participants was related to one of the patient participants in the study. Two separate groups were held for health professionals who were females aged 23–60 (M = 35.67, SD = 12.02) working within specialist eating disorder services. All participants were living in the United Kingdom. One group

TABLE 3 | Ratings matrix to determine which scenarios would be included, modified or excluded.

Age relevance	**Emotional salience**		
Ratings	**1–2**	**3**	**4–5**
1–2	Exclude	Exclude	Exclude
3	Exclude	Revise and include	Revise and include
4–5	Exclude	Revise and include	Include

included two psychiatrists and two psychologists, and one group included a consultant psychologist, an assistant psychologist and a mental health support worker.

Data collected from the focus group transcripts were analyzed using content analysis to identify recurrent examples of social rejection scenarios (**Table 4**). Two researchers manually coded the data and used the qualitative data analysis software NVivo (Version 13). First the researchers familiarized themselves with the data through repeatedly reading the text of all transcripts and identifying initial codes (i.e., sentence by sentence coding). The researchers then categorized the examples of social rejection described by patients, carers and health professionals into themes, including virtual rejection/exclusion, rejection associated with an aspect of the eating disorder, rejection triggered by ambiguous/benign comments or behaviors from others and rejection perceived when confiding in others (see **Table 4**).

Results of Aim 3

Following Aims 1 and 2, 339 scenarios were generated by the research team. Each patient rated a minimum of 19 and a maximum of 264 scenarios depending on their time availability. The scenarios were then categorized using the ratings matrix (**Table 3**). One-hundred and sixty-six (49%) scenarios were rated high [scoring 4 or 5 on both age-relevance ($M = 4.28$, $SD = 0.71$) and emotional salience ($M = 4.18$, $SD = 0.76$)] and were automatically included in the final set of stimuli. Thirty-eight (11%) scenarios were rated as low (1 or 2) on one or both measures by at least one patient and automatically excluded. One-hundred thirty-five (40%) scenarios were rated as neutral (3) on both aspects and were then revised to increase their age-relevance and emotional salience by the researchers, so that they could be included in the final set of scenarios. Revisions to the neutral scenarios were made by taking aspects from the scenarios rated as high or feedback from young people rating the scenarios and applying them to the neutral scenario. For example, "Your friends are looking at a magazine over lunch at school. One of them turns the page and makes a comment about a thin model, so you ask if they can change the page" was changed to "your friends are looking at Instagram during the school lunchbreak. One of them starts looking at an Instagram feed and makes comments about a thin model, so you ask if they can look at a different account."

The final set of stimuli consisted of 301 scenarios. All scenarios, with ratings for each of them presented separately are openly available in [repository name e.g., "figshare"] at http://doi.org/[doi], reference number [reference number].

DISCUSSION

This study followed the evidence-based practice framework and a systematic process of adapting experimental paradigms to specific populations (Hughes et al., 2016) to develop and validate stimuli for a cognitive bias modification training to reduce interpretation bias towards negative social stimuli in young people with eating disorders. The first aim was to review existing studies that have used cognitive bias assessment or modification procedures to target an interpretation bias towards negative social stimuli in people with eating disorders. The majority of identified studies included only adults and the majority of materials used within the training protocols had been adapted by the researchers from those originally developed for people with anxiety disorders (Cardi et al., 2015, 2017; Summers and Cougle, 2018; Turton et al., 2018). The second aim was to generate real-life examples of scenarios in which individuals with eating disorders feel exposed to social rejection or exclusion. Focus group discussions were held with young people with lived experience of eating disorders, carers and healthcare professionals with experience working with young people with eating disorders in specialist treatment services. Four key themes were identified from the focus groups including (1) virtual rejection/exclusion (2) rejection associated with an aspect of the eating disorder (3) rejection triggered by ambiguous/benign comments or behaviors of others and (4) rejection perceived when confiding in others. The final aim was to obtain quantitative ratings from young people with eating disorders concerning the age-relevance and emotional salience of the scenarios, and to make final adjustments to the scenarios based on this feedback. A total of 301 scenarios were included in the final stimulus set.

The findings from the focus groups with patients, carers and healthcare professionals in this study support the literature on social functioning in young people with eating disorders (Caglar-Nazali et al., 2014; Cardi et al., 2018a,b). All groups agreed that patients perceive rejection when exposed to ambiguous/benign comments or behaviors from others, such as over-thinking the reason for not being invited to a party or receiving a compliment on their physical appearance. These observations corroborate findings from an earlier qualitative study in which young people with anorexia nervosa described a heightened sensitivity to any form of perceived criticism (Patel et al., 2016) and recent quantitative data, which demonstrated that young people with anorexia nervosa on average produced more negative than benign interpretations of ambiguous social scenarios involving the risk of rejection (Cardi et al., 2019).

TABLE 4 | Themes and sub-themes derived from focus groups with patients, carers and professionals.

Theme	Patients	Carers	Professionals
Virtual rejection/exclusion	"oh yeah and like posting photos and seeing how many likes/followers you have seems risky" "or you might worry they think you look fat/might not comment on you being skinny" "after I was discharged from hospital one of my friends always talked about the chat with my other friends who I walked to school with knowing full well I wasn't in the chat"	"with social media, my daughter gets very concerned if she doesn't get immediate responses to messages as she thinks she is being ignored. She doesn't post much and in fact took down most of her social media during her GCSE's." "the "likes" on social media seems to be the way to judge popularity. My daughter used to spend ages trying to take a good photo to put on Instagram and would continuously check the likes and comments" "Yes online media is a nightmare for someone who has major anxieties, low self- esteem etc., Constantly looking for the number of 'likes' - spending hours over which picture to post and which caption she should add in case it is laughed at/ridiculed by others"	"seeing friends message each other on social media and not being included, seeing photos of friends hanging out at parties, etc., that they haven't been invited to" "Not invited to parties and seeing this on the social media or being "blanked" by their peers, getting silent treatment" "friends taking a while to reply to messages" "I have seen young people feel so uncontrollably anxious that they have had panic attacks because friends have not texted them back and they are sure their entire social network has been lost." "they would essentially go into a full-blown panic and experience severe anxiety if they did not receive enough likes on their post or if people unfriended them or unfollowed them or did not follow them back"
Rejection associated with an aspect of the eating disorder	"they go out for a meal but don't invite you I have also had it happen when they go for a meal but don't invite you or your best friend either because they don't want you to feel left out" "Exactly, and sometimes it's not just meals but on someone's birthday they might bring in food but won't ask if you want some or something along those lines" "Another example I had was my close friends all went out to play tennis and didn't even ask as they assumed, I couldn't do it"	"family gatherings with lots of food and expectations were also a problem for us at the time. Harmless statements such as "you're up for dessert seconds" (dessert was never a problem) could send her into a tailspin" "Oh, the stresses of what to wear! it could take hours for her to get ready and the smallest of comments could send her back upstairs to get changed again!" "at present she is isolated and avoiding situations where she feels people are looking at her and judging (to be fair people are looking at her. her BMI is 13 and she looks ill, so it is natural for people to look). Sometimes she has felt excluded so has tried to be popular by dressing up (when she at a healthier weight she is stunning) and getting the boys attention."	"or friends going out for lunch/to a party/to dinner and not inviting them because of the food element" "some negative comments from others about how thin they are, particularly from boys in their school, things like 'you might snap' I have heard quite a few times maybe partly due to fear that their peers would not see them as having an eating disorder, or thinking that they are 'getting better' a person who wasn't selected for their sports team because they really weren't well enough and they really took it to heart - it seemed to really impact their (already low) self-esteem and it was like it was a personal slight against them rather than a reflection of how poorly they were" "there was a lot of assumed rejection or criticism relating to competitiveness - so some young people might sit on the edge of their seat or stand for long periods of time so others would not judge them as lazy or not struggling during meal times, the food would be consumed very slowly, kind of like the opposite of a race"
Rejection triggered by ambiguous/benign comments or behaviors from others	"also people with eating disorders might misinterpret situations and react more negatively compared to people without who might not be upset by it" "Yes I agree with p4 definitely over think the reason you weren't invited." "Yes definitely organizing something with friends because sometimes if they don't reply you might think they don't want to come etc"	"I agree that you have to be very careful what words you use. A friend of mine said my daughter looked really well once and my daughter took that as she had put on too much weight." "yesterday I commented to my daughter that her eyes looked brighter and she didn't look so dehydrated. This translated into her mind as she looks like she has put on weight and looking healthier. she promptly shouted at me that I am triggering and went upstairs to weigh herself" "our daughter was constantly saying that teachers at school gave her "dirty looks" and was convinced that one subject teacher did not want her to study a subject at A	"Yeah, you look well doesn't go down well!" "it is almost like any situation could make them feel rejected depending on even subtle reactions of the people they are with finding friends at lunch times and people not looking up straight away to say hello, or not moving over for them to sit in the group comfortably; peers finishing their conversations with other peers before greeting them; peers not really looking at them when they are talking in a group" people not asking them how they are (yet being asked also causes anxiety); people not making the effort to speak to them first; other ones might include seeing peers whispering and the young people believing they are

(Continued)

TABLE 4 | Continued

Theme	Patients	Carers	Professionals
		Level. I had to ask the School to confirm if that was the case and they said absolutely not and that the teacher had no concerns over her ability"	speaking about them in a negative way, which might make them withdraw from those individuals." "a young person could pay a compliment to another young person about their dress, and then would seek reassurance from a staff member that they have not just made the other young people feel bad/negative about their looks (if that makes sense) - so a lot of second guessing and worrying about what they say and do - and I guess worrying that this would lead to being socially rejected"
Rejection perceived when confiding in others	"when you tell a friend or someone else about the eating disorder and they don't believe you/dismiss it" "I haven't told anyone about my problem sometimes it feels to daunting to confront them about it, so sometimes I just leave it. I wouldn't tell them how I felt because I would fear being rejected yet again by them." "sometimes I try to hide my true feelings from my family and my other friends, and I just hide away"	"my daughter refused to tell anyone what was wrong with her for many years. . .apart from close family. her friends, etc., probably guessed but never asked. As she got older she told a few people. their reactions varied. they usually promised to be there for her and texted her for a week or so after but then that was it. sometimes they told other people which broke her trust. I know many other sufferers who are very open about their illness so I guess that varies for years didn't tell anyone, even when she had long stays as in-patient. now she is 17 and told a few people, but still dificult to be completely up front with people"	"telling even close friends how they really feel" "I have had a few patients who have felt very anxious about letting people know about their eating disorder - understandable- and I guess at least part of that is due to fear of possible rejection, so they end up saying "I'm fine" even to close friends even though they're not if someone is unpleasant or they perceive to have been unpleasant, then they will tell me that they do not know what to say, or only later they will think of something to say, or they will take it out on themselves (self-harm)." "it might be helpful to explicitly provide them with the tools to deal with these situations, e.g., workshops on how to safely confront someone or how to discuss sensitive topics with your peers if you think they are angry with you - basically like survival skills sessions for sensitivity to rejection"

Participants also recalled examples of illness-related rejection experiences, such as being excluded from arrangements to have meals out with friends or not being offered food in social contexts. These findings support other qualitative accounts from young people with anorexia nervosa who have described the impact that their eating disorder and treatment regime had on their social functioning (Lindstedt et al., 2018). Furthermore, the risk of rejection perceived by patients when confiding in others, for example a reluctance to disclose their illness to friends due to a fear of being dismissed or disbelieved, supports the interpersonal model of eating disorders which posits that some problems with social functioning in people with eating disorders may originate in part from maladaptive personality traits, such as the tendency to avoid expressing feelings and the tendency towards interpersonal distrust and negative interactions with others (Arcelus et al., 2013).

Participants referred to several examples of virtual rejection, and over-reactions to this experience such as full-blown panic or severe anxiety if a friend did not reply to their message, or if they did not receive enough likes on their social media posts. These findings are novel in the context of the existing literature on interpretation bias, which has lacked the consideration of exposure to rejection in a virtual environment. However, the findings are in line with what is known about the role of online social interactions in eating disorders. For example, one study found that girls and women with a lifetime diagnosis of an eating disorder reported poorer mood after posting or commenting online, a greater frequency of social comparison, and a greater use of online forums and blogs with more focus on eating disorder-related issues in comparison to a group of age-matched controls (Bachner-Melman et al., 2018). In both groups, these online behaviors correlated with eating disorder symptoms and general psychological health. In another study, the frequency of Facebook use was associated with greater disordered eating, and maintenance of weight/shape concerns and state anxiety compared to an alternative online activity (Mabe et al., 2014). Together, these findings suggest that negative interpretations of social cues online may contribute to feelings of rejection and trigger eating disorder symptoms.

Strengths and Limitations

The main strength of this study is that it is the first study to use a systematic approach to the development of stimuli for an interpretation bias training intervention for people with eating disorders. Other strengths include the involvement of different parties, including patients, carers and professionals (Kimber et al., 2019), to identify the type and content of social situations that trigger social evaluative concerns in adolescents with eating disorders, and the incorporation of both qualitative and quantitative methods in the development and validation of the materials. Furthermore, the large pool of materials developed (N = 301) will be made publicly available, in line with the open science framework and may be used for multi-session interpretation bias training protocols, which have shown advantages over single-session trainings in terms of training efficacy on interpretation bias change (Menne-Lothmann et al., 2014; Cristea et al., 2015; Turton et al., 2018). One limitation of this study was that due to the large number of scenarios and limited availability of patients, quantitative feedback was obtained only from a subgroup of adolescents with eating disorders (girls aged 14–18) and might not be generalisable to other groups of individuals, particularly younger girls or boys who may differ in their experiences of social rejection. Furthermore, some scenarios only had one rating from one participant. The scenarios rated by participants as neutral (n = 135) were revised further by the researchers to increase their age-relevance and emotional salience so that they could be included in the final set of scenarios. Although these adapted neutral scenarios were not included in the pilot study, they will be included in a proceeding study, investigating the feasibility and clinical effectiveness of multi-session cognitive bias modification training.

Clinical Implications

There is increasing interest in the use of treatment enhancers in eating disorders due to their potential to improve clinical outcomes. In the United Kingdom, the National Institute for Health and Care Excellence (NICE) guidelines recommend Family Based Treatment as the first-line treatment for adolescents with eating disorders (National Institute for Health and Care Excellence (NICE), 2017). This therapy aims to improve nutrition and mostly focuses on providing information and support to carers to feed their children (Le Grange and Eisler, 2009; Lock and Le Grange, 2019). Whilst this is the most effective treatment available according to the current evidence base, approximately 20% patients offered Family Based Treatment drop-out (Dejong et al., 2012), between 33% and 42% reach remission by the end of treatment (Lock et al., 2010; Agras et al., 2014), and 40% of patients struggle with significant ongoing psychological distress after treatment (Lock et al., 2006; Wufong et al., 2019). CBM could provide a useful ‘treatment enhancer’ by increasing sensitivity to positive social feedback and reducing sensitivity to social criticism from family and peers, and the online nature of the training may appeal to the younger population.

The large set of stimuli described here has been developed and validated by girls with eating disorders. Multi-session studies combined with follow-up assessments allow for an investigation of the acceptability and effectiveness of the training in the long term. In doing so researchers should consider strategies for facilitating participant engagement with the training over time (Zhang et al., 2018) and to assess whether changes observed in interpretation biases are associated with changes in social perceptions and behaviors, as well as key clinical variables. It will also be important to explore potential pathways through which this training can be related to improvements in symptoms, such as through strengthening responsiveness to social acceptance or support. The training may also provide benefits to individuals at ‘high risk’ of psychopathology through boosting resilience to the risk of social rejection/exclusion.

Conclusion

To date, this is the first study to use a systematic approach to the development of a cognitive bias training targeting an interpretation bias towards negative social stimuli in young people with eating disorders. These materials will be made available to aid researchers in conducting experimental studies to assess the acceptability and clinical effectiveness of multi-session cognitive bias modification training protocols in young people with eating disorders.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

This study was reviewed and approved by London Riverside – Research Ethics Committee. Written informed consent to participate in this study was provided by the participants' or their legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

KR, EW, MS, AH, and VC contributed to the study design. KR and EW performed the data collection and analysis which was supervised by VC. KR, EW, and VC wrote the manuscript with input from MS and AH.

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REFERENCES

Agras, W. S., Lock, J., Brandt, H., Bryson, S. W., Dodge, E., Halmi, K. A., et al. (2014). Comparison of 2 family therapies for adolescent anorexia nervosa: a randomized parallel trial. *JAMA Psychiatry* 71, 1279–1286. doi: 10.1001/jamapsychiatry.2014.1025

Altabe, M., Wood, K., Herbozo, S., and Thompson, J. K. (2004). The physical appearance ambiguous feedback scale (PAAFS): a measure for indexing body image related cognitive bias. *Body Image* 1, 299–304. doi: 10.1016/j.bodyim.2004.05.004

American Psychiatric Association (2013). *Diagnostic and Statistical Manual of Mental Disorders*. Arlington, VA: American Psychiatric Publishing.

American Psychological Association (2005). *Policy Statement on Evidence-Based Practice in Psychology*. Available online at: http://www.apa.org/practice/guidelines/evidence-based-statement (accessed August, 2005).

Arcelus, J., Haslam, M., Farrow, C., and Meyer, C. (2013). The role of interpersonal functioning in the maintenance of eating psychopathology: a systematic review and testable model. *Clin. Psychol. Rev.* 33, 156–167. doi: 10.1016/j.cpr.2012.10.009

Bachner-Melman, R., Zontag-Oren, E., Zohar, A. H., and Sher, H. (2018). Lives on the line: the online lives of girls and women with and without a lifetime eating disorder diagnosis. *Front. Psychol.* 9:2128. doi: 10.3389/fpsyg.2018.02128

Caglar-Nazali, H. P., Corfield, F., Cardi, V., Ambwani, S., Leppanen, J., Olabintan, O., et al. (2014). A systematic review and meta-analysis of 'Systems for Social Processes' in eating disorders. *Neurosci. Biobehav. Rev.* 42, 55–92. doi: 10.1016/j.neubiorev.2013.12.002

Cardi, V., Esposito, M., Bird, G., Rhind, C., Yiend, J., Schifano, S., et al. (2015). A preliminary investigation of a novel training to target cognitive biases towards negative social stimuli in Anorexia Nervosa. *J. Affect. Disord.* 188, 188–193. doi: 10.1016/j.jad.2015.08.019

Cardi, V., Mallorqui-Bague, N., Albano, G., Monteleone, A. M., Fernandez-Aranda, F., and Treasure, J. (2018a). Social difficulties as risk and maintaining factors in anorexia nervosa: a mixed-method investigation. *Front. Psychiatry* 9:12. doi: 10.3389/fpsyt.2018.00012

Cardi, V., Tchanturia, K., and Treasure, J. (2018b). Premorbid and illness-related social difficulties in eating disorders: an overview of the literature and treatment developments. *Curr. Neuropharmacol.* 16, 1122–1130. doi: 10.2174/1570159X16666180118100028

Cardi, V., Turton, R., Brazil, C., Harrison, A., Rowlands, K., Treasure, J., et al. (2019). Training rejection interpretation in eating disorders (TRIER): preliminary findings of a feasibility study in adolescents with anorexia nervosa. *Cogn. Ther. Res.* 43, 1109–1117. doi: 10.1007/s10608-019-10034-x

Cardi, V., Turton, R., Schifano, S., Leppanen, J., Hirsch, C. R., and Treasure, J. (2017). Biased interpretation of ambiguous social scenarios in anorexia nervosa. *Eur. Eat. Disord. Rev.* 25, 60–64. doi: 10.1002/erv.2493

Copeland, W. E., Bulik, C. M., Zucker, N., Wolke, D., Lereya, S. T., and Costello, E. J. (2015). Does childhood bullying predict eating disorder symptoms? A prospective, longitudinal analysis. *Int. J. Eat. Disord.* 48, 1141–1149. doi: 10.1002/eat.22459

Cristea, I. A., Kok, R. N., and Cuijpers, P. (2015). Efficacy of cognitive bias modification interventions in anxiety and depression: meta-analysis. *Br. J. Psychiatry* 206, 7–16. doi: 10.1192/bjp.bp.114.146761

Dejong, H., Broadbent, H., and Schmidt, U. (2012). A systematic review of dropout from treatment in outpatients with anorexia nervosa. *Int. J. Eat. Disord.* 45, 635–647. doi: 10.1002/eat.20956

Duarte, C., Pinto-Gouveia, J., and Stubbs, R. (2017). The prospective associations between bullying experiences, body image shame and disordered eating in a sample of adolescent girls. *Pers. Individ. Dif.* 116, 319–325. doi: 10.1016/j.paid.2017.05.003

Espel-Huynh, H. M., Muratore, A. F., Virzi, N., Brooks, G., and Zandberg, L. J. (2019). Mediating role of experiential avoidance in the relationship between anxiety sensitivity and eating disorder psychopathology: a clinical replication. *Eat. Behav.* 34:101308. doi: 10.1016/j.eatbeh.2019.101308

Hayes, S., Hirsch, C. R., Krebs, G., and Mathews, A. (2010). The effects of modifying interpretation bias on worry in generalized anxiety disorder. *Behav. Res. Ther.* 48, 171–178. doi: 10.1016/j.brat.2009.10.006

Hilbert, A., Hoek, H. W., and Schmidt, R. (2017). Evidence-based clinical guidelines for eating disorders: international comparison. *Curr. Opin. Psychiatry* 30, 423–437. doi: 10.1097/YCO.0000000000000360

Hilbert, A., Vogele, C., Tuschen-Caffier, B., and Hartmann, A. S. (2011). Psychophysiological responses to idiosyncratic stress in bulimia nervosa and binge eating disorder. *Physiol. Behav.* 104, 770–777. doi: 10.1016/j.physbeh.2011.07.013

Hirsch, C. R., Hayes, S., and Mathews, A. (2009). Looking on the bright side: accessing benign meanings reduces worry. *J. Abnorm. Psychol.* 118, 44–54. doi: 10.1037/a0013473

Holmes, E. A., Ghaderi, A., Harmer, C. J., Ramchandani, P. G., Cuijpers, P., Morrison, A. P., et al. (2018). The lancet psychiatry commission on psychological treatments research in tomorrow's science. *Lancet Psychiatry* 5, 237–286. doi: 10.1016/S2215-0366(17)30513-8

Hughes, A. M., Gordon, R., Chalder, T., Hirsch, C. R., and Moss-Morris, R. (2016). Maximizing potential impact of experimental research into cognitive processes in health psychology: a systematic approach to material development. *Br. J. Health Psychol.* 21, 764–780. doi: 10.1111/bjhp.12214

Huppert, J. D., Pasupuleti, R. V., Foa, E. B., and Mathews, A. (2007). Interpretation biases in social anxiety: response generation, response selection, and self-appraisals. *Behav. Res. Ther.* 45, 1505–1515. doi: 10.1016/j.brat.2007.01.006

Jacobi, C., Fittig, E., Bryson, S., Wilfley, D., Kraemer, H., and Taylor, C. B. (2011). Who is really at risk? Identifying risk factors for subthreshold and full syndrome eating disorders in a high-risk sample. *Psychol. Med.* 41, 1939–1949. doi: 10.1017/S0033291710002631

Kimber, M., Dimitropoulos, G., Williams, E. P., Singh, M., Loeb, K. L., Hughes, E. K., et al. (2019). Tackling mixed messages: practitioner reflections on working with adolescents with atypical anorexia and their families. *Eat. Disord.* 27, 436–452. doi: 10.1080/10640266.2018.1542888

Krebs, G., Pile, V., Grant, S., Degli Esposti, M., Montgomery, P., and Lau, J. Y. F. (2018). Research review: cognitive bias modification of interpretations in youth and its effect on anxiety: a meta-analysis. *J. Child Psychol. Psychiatry* 59, 831–844. doi: 10.1111/jcpp.12809

Le Grange, D., and Eisler, I. (2009). Family interventions in adolescent anorexia nervosa. *Child Adolesc. Psychiatr. Clin. N. Am.* 18, 159–173. doi: 10.1016/j.chc.2008.07.004

Lee, K. S., and Vaillancourt, T. (2019). A four-year prospective study of bullying, anxiety, and disordered eating behavior across early adolescence. *Child Psychiatry Hum. Dev.* 50, 815–825. doi: 10.1007/s10578-019-00884-7

Lie, S. Ø., Rø, Ø., and Bang, L. (2019). Is bullying and teasing associated with eating disorders? A systematic review and meta-analysis. *Int. J. Eat. Disord.* 52, 497–514. doi: 10.1002/eat.23035

Lindstedt, K., Neander, K., Kjellin, L., and Gustafsson, S. A. (2018). A life put on hold: adolescents' experiences of having an eating disorder in relation to social contexts outside the family. *J. Multidiscip. Healthc.* 11, 425–437. doi: 10.2147/JMDH.S168133

Lock, J., Couturier, J., and Agras, W. S. (2006). Comparison of long-term outcomes in adolescents with anorexia nervosa treated with family therapy. *J. Am. Acad. Child Adolesc. Psychiatry* 45, 666–672. doi: 10.1097/01.chi.0000215152.61400.ca

Lock, J., and Le Grange, D. (2019). Family-based treatment: where are we and where should we be going to improve recovery in child and adolescent eating disorders. *Int. J. Eat. Disord.* 52, 481–487. doi: 10.1002/eat.22980

Lock, J., Le Grange, D., Agras, W. S., Moye, A., Bryson, S. W., and Jo, B. (2010). Randomized clinical trial comparing family-based treatment with adolescent-focused individual therapy for adolescents with anorexia nervosa. *Arch. Gen. Psychiatry* 67, 1025–1032. doi: 10.1001/archgenpsychiatry.2010.128

Mabe, A. G., Forney, K. J., and Keel, P. K. (2014). Do you "like" my photo? Facebook use maintains eating disorder risk. *Int. J. Eat. Disord.* 47, 516–523. doi: 10.1002/eat.22254

Matheson, E., Wade, T. D., and Yiend, J. (2018). A new cognitive bias modification technique to influence risk factors for eating disorders. *Int. J. Eat. Disord.* 51, 959–967. doi: 10.1002/eat.22938

Menne-Lothmann, C., Viechtbauer, W., Hohn, P., Kasanova, Z., Haller, S. P., Drukker, M., et al. (2014). How to boost positive interpretations? A meta-analysis of the effectiveness of cognitive bias modification for interpretation. *PLoS One* 9:e100925. doi: 10.1371/journal.pone.0100925

Monteleone, A. M., Treasure, J., Kan, C., and Cardi, V. (2018). Reactivity to interpersonal stress in patients with eating disorders: a systematic review and meta-analysis of studies using an experimental paradigm. *Neurosci. Biobehav. Rev.* 87, 133–150. doi: 10.1016/j.neubiorev.2018.02.002

National Institute for Health and Care Excellence (NICE) (2017). *Eating Disorders: Recognition, and Treatment. NICE Guideline [NG69]*. London: NICE Guideline.

Okada, L. M., Miranda, R. R., das Graças Pena, G., Levy, R. B., and Azeredo, C. M. (2019). Association between exposure to interpersonal violence and social isolation, and the adoption of unhealthy weight control practices. *Appetite* 142:104384.

Park, L. E. (2013). Appearance-Based Rejection Sensitivity (Appearance-RS) Scale (Long and Short Form). Measurement Instrument Database for the Social Science. Available online at: www.midss.org (accessed February 27, 2020).

Park, L. E., Calogero, R. M., Young, A. F., and Diraddo, A. M. (2010). Appearance-based rejection sensitivity predicts body dysmorphic disorder symptoms and cosmetic surgery acceptance. *J. Soc. Clin. Psychol.* 29, 489–509. doi: 10.1521/jscp.2010.29.5.489

Patel, K., Tchanturia, K., and Harrison, A. (2016). An exploration of social functioning in young people with eating disorders: a qualitative study. *PLoS One* 11:e0159910. doi: 10.1371/journal.pone.0159910

Peterson, C. B., Becker, C. B., Treasure, J., Shafran, R., and Bryant-Waugh, R. (2016). The three-legged stool of evidence-based practice in eating disorder treatment: research, clinical, and patient perspectives. *BMC Med.* 14:69. doi: 10.1186/s12916-016-0615-5

Rosenberg, N., Bloch, M., Ben Avi, I., Rouach, V., Schreiber, S., Stern, N., et al. (2013). Cortisol response and desire to binge following psychological stress: comparison between obese subjects with and without binge eating disorder. *Psychiatry Res.* 208, 156–161. doi: 10.1016/j.psychres.2012.09.050

Somerville, L. H. (2013). Special issue on the teenage brain: sensitivity to social evaluation. *Curr. Dir. Psychol. Sci.* 22, 121–127. doi: 10.1177/0963721413476512

Summers, B. J., and Cougle, J. R. (2018). An experimental test of the role of appearance-related safety behaviors in body dysmorphic disorder, social anxiety, and body dissatisfaction. *J. Abnorm. Psychol.* 127, 770–780. doi: 10.1037/abn0000387

Tantleff-Dunn, S., Thompson, J. K., and Dunn, M. E. (1995). The feedback on physical appearance scale (FOPAS): questionnaire development and psychometric evaluation. *Eat. Disord.* 3, 332–341. doi: 10.1080/10640269508250063

Turton, R., Cardi, V., Treasure, J., and Hirsch, C. R. (2018). Modifying a negative interpretation bias for ambiguous social scenarios that depict the risk of rejection in women with anorexia nervosa. *J. Affect. Disord.* 227, 705–712. doi: 10.1016/j.jad.2017.11.089

Tuschen-Caffier, B., and Vogele, C. (1999). Psychological and physiological reactivity to stress: an experimental study on bulimic patients, restrained eaters and controls. *Psychother. Psychosom.* 68, 333–340. doi: 10.1159/000012352

Wufong, E., Rhodes, P., and Conti, J. (2019). "We don't really know what else we can do": parent experiences when adolescent distress persists after the Maudsley and family-based therapies for anorexia nervosa. *J. Eat. Disord.* 7:5. doi: 10.1186/s40337-019-0235-5

Zhang, M., Ying, J., Song, G., Fung, D. S., and Smith, H. (2018). Gamified cognitive bias modification interventions for psychiatric disorders: review. *JMIR Ment. Health* 5:e11640. doi: 10.2196/11640

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Neurological Soft Signs and Post-Traumatic Stress Disorder: A Biomarker of Severity?

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Background: The psychophysiological changes for individual suffering from chronic post-traumatic stress disorder (PTSD) raise to the questions of how facilitate recovery and return to work. Negative alterations in neuro-cognition remain a complaint for patients and participate to long-term functional impairments. Neurological soft signs (NSSs) appear as a candidate for better understanding these complaints. They have been reported in several mental disorders. They are found in several behavioral and/or neurocognitive disorders and are taken into account by psychiatric rehabilitation programs to support recovery. As few studies evaluate NSSs in PTSD, our exploratory study aims to assess NSSs in chronic PTSD and their relationships with PTSD severity.

Method: Twenty-two patients with a clinical diagnosis of chronic PTSD were evaluated in terms of PTSD severity (post-traumatic checklist scale, PCL5), NSSs (NSSs psychomotor skills scale, PASS), and well-being upon arrival to the hospital and compared with 15 healthy subjects. Statistical non-parametric analyses assessed the relationships between these variables.

Results: PTSD subjects exhibited higher NSSs compared with healthy subjects. NSSs were positively associated with PTSD severity, with negative alterations in cognition and mood, and with impairment in well-being. They were higher in women compared with men. No impact of age was found. Three groups were identified based on the severity of the PTSD. Severe PTSD exhibited NSSs characterized by motor integration alterations.

Conclusions: This pilot study suggests that NSSs might be a biomarker of PTSD severity. This proof of concept highlights the need for further research for better evaluating the clinical neuro-functional impairment. This will be helping for defining neurological remediation for promoting PTSD recovery.

Keywords: recovery, neurological soft signs, post-traumatic stress disorder (PTSD), cerebellum, gender

INTRODUCTION

Post-Traumatic Stress Disorder

Post-traumatic stress disorder (PTSD) is a debilitating mental disorder that may develop after experiencing or witnessing a life-threatening event. The main characteristics of PTSD are re-experiencing symptoms, avoiding situations that recall the event, negative alterations in cognition and mood and hyperarousal (1). PTSD is associated with impairment in social, occupational and other domains (2) for at least one month. Once those symptoms have been observed for 3 months, PTSD is considered as a chronic disorder (3). Furthermore, the prevalence of comorbidities is high including: depression, substance use disorders and general physical health effects (4, 5).

The lifetime PTSD prevalence was found to range from 1% to 7% in Europe (5). According to the country and the type of trauma, the mean 12-month prevalence of PTSD is between 25% and 50% (6). Among the military, PTSD prevalence is highly dependent on the violence of the mission; the higher the combat exposure is, the higher PTSD prevalence is (up to 20%) (7).

Despite appropriate care, treatment response is variable and almost 20% of the patients do not show condition' improvement. This variability in response treatment arises from (i) the lack of research in precision medicine (i.e., which treatment suits best the patient) and (ii) the nature of the physiopathology of the PSTD (8). In a 20-year longitudinal study conducted on 214 veterans with initial combat stress reaction, Solomon and Mikulincer (2006) highlighted the volatility of chronic stress with a relapse observed in 40% of the recovering subjects within one year of remission (9).

Currently available tools for assessing prognosis when PTSD are inadequate. Impairments in emotional, self-regulatory, and cognitive functions are biomarkers of interest when regarding their critical influence on post-traumatic processing, treatment efficiency and recovery. PTSD has been associated with negative emotions (10), disturbed positive resources (11), as well as impairments in the ability to effectively regulate emotions (12). Moreover, a number of prospective studies indicate that emotional regulation difficulties hinder recovery from PTSD symptoms post-trauma (13).

Putative neural mechanisms underlying the PTSD symptoms involve altered brain regions including the hippocampus and amygdala as well as cortical regions including the anterior cingulate, insula, and orbitofrontal regions (14, 15). These brain alterations have an impact on connection to neural circuits that mediates adaptation to stress and fear conditioning. Altogether, these brain disorders have been proposed to have a direct link to the emotional, self-regulatory, and cognitive impairments in PTSD (16).

Despite advances in the understanding of the neural circuitry associated with emotional, self-regulatory impairments and how they impact prognosis by disturbing treatment outcomes, there is a paucity of research investigating the global cognitive dysfunctions in PTSD. Nevertheless, cognitive deficits are one of the most consistent predictors of chronic disability found among both younger and older people with psychiatric illness (17–19). It is well-known that PTSD is associated with decrements in multiple cognitive systems, including processing speed, learning, memory, and executive function (20–22) and inability to divert attention away from trauma-provoking stimuli (21, 23, 24). Such deficits are well-known to increase the effects of psychosocial stressors related to physical health behaviors (25), academic and vocational productivity (26), and interpersonal relationships (27).

Interestingly, literature reports associations of neurological soft signs (NSSs) with poor cognitive performance in healthy subjects (28–31) as well as in patients with chronic psychiatric diseases, such as schizophrenia (32, 33), and bipolar subjects (34, 35). NSSs are objective performance measures of sensorimotor, reflexive, perceptual, and cognitive capabilities. They reflect minor neurological abnormalities thought to be manifestations of a minor nonspecific cerebral dysfunction (either localized or diffuse) which yield subtle indicators of brain dysfunctions (30). NSSs are different from the "hard" neurological signs. The latter are often indicative of a basic sensory or motor deficit that is considered to be directly related to an injury to a specific brain region. Recent studies using non-clinical samples have suggested that neural correlates of a cognitive function are likely to be distributed throughout the brain rather than localized to specific areas (36, 37). A similar proposal has been considered for NSSs (30), NSSs have been found to be elevated in a variety of mental disorders, with more than 100 studies of NSSs in the psychiatric literature (Pubmed search). A meta-analysis establishes a link between the NSSs and the biological markers of psychiatric vulnerability (38). This shows the interest of NSSs for prognosis of a psychiatric disease all the more that examination of NSSs entails low-tech, inexpensive, relatively brief, and readily administered clinical maneuvers. Furthermore, studies with bipolar suffering suggest that NSSs would progress only minimally with increasing age (35).

Although NSSs have been less investigated in PTSD, they were reported in male veterans with chronic combat-related PTSD (but not in combat-exposed veterans without PTSD) as in adult females with PTSD as a result of childhood sexual abuse (39). In these populations, NSSs were associated with more reported neurodevelopmental problems, e.g., attention deficit, motor hyperactivity, and learning problems (39). However, NSSs were not found in the veteran nurses with PTSD (40). These conflicted results question the role of premorbid neurodevelopment as a risk factor for NSSs in PTSD when traumatic exposure. They also highlight three major gaps in the literature regarding the role of NSSs in PTSD: (1) the pertinence of NSSs as a biomarker of PTSD severity and prognosis, (2) the domain specificity of the involvement of NSSs in cognitive performance, and (3) whether there is sex difference.

This study aims to be a proof of concept in the exploration of the relationship between PTSD severity and NSSs.

MATERIALS AND METHODS

Participants

Two groups of voluntary civilian subjects were recruited: 22 patients suffering from PTSD through the psychiatric consultation in public hospitals of Marseille and Perpignan (France) and 15 healthy subjects matching according to age and gender through the personal from hospitals of Marseille. This study received the agreement of the ethics committee of the French military health service (MHS). After a complete description of the study, written informed consent for participation in this low-risk study was obtained.

Protocol

Informed and volunteer patients with at least one positive response in the criterion A as described in the DSM5 and clinically evaluated by a psychiatrist with a diagnosis of chronic PTSD (more than 6 months since the first psychiatrist PTSD diagnosis without improvement) were included in the study. Self-reported left-handed was a non-inclusion criterion. After their consultation, patients were screened with the following assessments: PTDS severity, well-being and NSSs. These assessments lasted 2h and 30 min.

Informed and volunteer control subjects

Variables

For each subject, the collected socio-demographic included: age, gender, and the number of major stresses encountered in professional and personal environments over subject lifetime.

NSSs were also evaluated using Psychomotor Assessment of the Sweet Signs (PASS) [(41); http://www.psychomot.ups-tlse.fr/EPSID.pdf]. This hetero-questionnaire was developed using the available scale for assessing the NSSs. It was validated in a French population of children and adults. Processing the PASS requires very few materials. Only the test of stereognosies requires the use of the following equipment: a key, a coin, a button, a battery, a dice, a clothespin. Twenty-seven tasks were evaluated and combined in 9 categories of NSSs: (i) walking evaluation implying different types of walking (tasks 1 to 5), (ii) static and dynamic equilibrium (tasks 6 to 8), (iii) perseverance in task (task 9), (iv) tonus (tasks 12 to 15), (v) motor integration included complex and simple sequences of motor coordination (tasks 10, 11, and 19 to 25), (vi) sensory integration (tasks 28–30), (vii) dysrhythmias (tasks 6, 10, 11, and 20 to 25), (viii) synkinesis (tasks 10 and 20–25), and (ix) somatognosis and spatial self-perception (tasks 26–27). A total score is calculated from the 27 tasks. Scores range from 0 (no NSS) to 135 (maximum errors for each evaluated task). An evaluation of manual laterality coefficient (handedness) was realized at the end of the PASS. No cut-off has been validated for this scale.

For PTSD Subjects (PTSD Group)

In addition to the PASS, patients completed the two following questionnaires.

The auto-questionnaire used to assess PTSD severity was the PTSD Check List Scale (PCL-5) (1, 42). It assesses the following four symptoms: re-experiencing symptoms, avoiding situations that recall the event, hyperarousal and impairment of cognitive and emotional affects. Higher scores indicate higher severity. The cut-off point proposed by the National Center for PTSD is a score above or equal to 33.

Well-being was assessed using the Warwick-Edinburgh Mental Well-Being Scale (WEMWBS) (43, 44). This auto-questionnaire covers both affective constructs (including the experience of happiness) and constructs representing psychological functioning and self-realization (45). This is a 14-item scale on thoughts and feelings over the past week; each item ranges from (1) “none of the time” to (5) “all of the time”. Higher scores indicate higher well-being. No cut-off has been validated for this scale.

For Healthy Subjects (Control Group)

In addition to the PASS, healthy subjects were assessed by a psychiatrist using the structured Mini-International Neuropsychiatric Interview (46) to check for the absence of a psychiatric disorder and to screen for potential psychiatric disorders.

Statistical Analysis

Data analyses were performed using the Statistica (Stastsoft France, Maison Alfort, v7.1) software.

The values are expressed as mean ± standard error of mean. Correlations were done using Bravais-Pearson analyses. Comparisons between groups were performed using Pearson’s chi-square test for variables with several modalities and using t-test for the quantitative data or nonparametric Kruskal-Wallis analyses as they did not have a normal distribution.

For the PTSD group, we characterized patients according to PTSD diagnosis and severity. Three groups were defined according to the PCL5 score: a group with a score under 33 (group with minimal PTSD; Minor PTSD), a group with a score under the median of the PCL5 score of our population (group with moderate PTSD; Moderate PTSD), and a group with a score above the median of the PCL5 score of our population (group with severe PTSD; Gr Severe PTSD). Between group comparisons were performed using Kruskal-Wallis test followed by Dunn’s *post-hoc* test (including Bonferroni correction) (47, 48). The statistical threshold of significance was set at $p < 0.05$. The trends are taken in consideration when $p < 0.10$.

RESULTS

Population Description

For the PTSD group, 22 patients were included in the study, 16 females (72.73%) and 6 males (27.27%). They were on average 37.86 (± 12.74) years old aged with a median age of 34.5. The clinical evaluation confirmed PTSD diagnosis for each subjects.

Average score of the clinical severity at PCL5 was 52.35 (± 19.8) and the median value of scores of the PCL5 was 55 (range: 15–84). Negative correlations were found between age and PCL5 score ($r^2 = -0.41$, $p = 0.06$), as between PCL5 score and negative mood and cognition ($r^2 = -0.48$, $p = 0.028$) and hyperarousal ($r^2 = -0.47$, $p = 0.03$) sub-scores.

Average score of the WEMWBS was 47.77 (± 15.15) and the median value of scores of the PCL5 5 was 51.5 (range: 28–60).

Negative correlations were found between WEMWBS and PCL5 scores ($r^2 = -0.61$, $p = 0.003$), as between WEMWBS and negative alterations in cognitions and mood ($r^2 = -0.71$, $p < 0.001$) and hyperarousal ($r^2 = -0.57$, $p = 0.007$) sub-scores. No correlation was found between age and WEMWBS score ($r^2 = 0.25$, $p = 0.26$).

Concerning the PASS evaluation, the laterality coefficient showed that 18 (81.81%) of the patients were right-handed among which 68.18% of the patients had a right handedness coefficient of 100. Three (13.63%) had a coefficient between 20 and 80; one subject (4.54%) had a coefficient of −30, meaning that this patient was left-handed. Average score of the NSSs was 14.04 (± 15.15) and the median value of scores of the PASS is 6.5 (range: 1–45.75) (**Table 1**). Positive correlations were found between PASS and PCL5 scores ($r^2 = 0.69$, $p < 0.001$), as between PASS score and intrusions ($r^2 = -0.48$, $p = 0.028$), negative alterations in cognitions and mood ($r^2 = -0.59$, $p = 0.005$) and hyperarousal ($r^2 = -0.73$, $p < 0.001$) sub-scores. A negative correlation was found between PASS and WEMWBS scores ($r^2 = -0.36$, $p = 0.10$). No correlation is found between age and WEMWBS score ($r^2 = -0.16$, $p = 0.46$).

A gender effect was observed for the NSSs with higher NSSs total score and some of the sub-scores (or tendencies) for females (**Table 1**). Females exhibited higher PCL5 score (W = 16, p = 0.2), with higher alterations in arousal and reactivity (W = 7, p = 0.003) sub-score, and a trend to higher intrusions (W= 24, p = 0.08) sub-score. No gender difference was not found for WEMWBS score (W= 66.5, p = 0.18).

No difference was found between the two centers for each of the scales' score.

For the control group, 15 healthy subjects were included, 8 females (53.33%) and 7 males (46.67%). They were on average 35.8 (± 11.11) years old aged with a median age of 30. The clinical evaluation from the MINI confirmed the absence PTSD and other psychopathological diagnosis for each of the subjects. The number of traumatic life event was zero for each of the subjects.

TABLE 1 | Mean scores, standard deviations (±), medians, and ranges for the main items of the PASS with significant gender effect, with left or right precision when necessary.

		My ± ET	Median	Range Min-Max	Gender effect p
NSSs total score		14.04 ± 15.15	6,5	1–45.75	0.007
Spontaneous tempo (s)		11.03 ± 2.51	11	6.83–14.86	0.028
Fastest tempo (s)		7.05 ± 3.24	5.93	3.02–13	
Walking	Gait	0.26 ± 0.54	0	0–2	
	Gait on tiptoes	0.40 ± 0.66	0	0–2	
	Gait on heels	0.71 ± 0.78	1	0–2	
	Gait with inversion/eversion	1.52 ± 1.57	1	0–5	
	Gait with heel-and-toe	1.14 ± 1.42	0	0–4	
Static and dynamic equilibrium	Jumping up and down on one foot*	1.62 ± 2.42	0.5	0–8	
	Lowest time of unipodal equilibrium (s)**	0.35 ± 0.75	0	0–3	
	Average time of unipodal equilibrium (s)**	35.71 ± 24.21	28.25	3.83–71	0.038 Right 0.077 Left
	Romberg stability*	0.57 ± 0.73	0	0–2	
Protrusion of the tongue	Average of time (s)				
	Abnormal movement (yes or not)				
	Diadochocinesia (s)*	8.47 ± 1.27	0	2.44–21	
	Average time of arm in horizontal position (EO)*	7.88 ± 2.63	8.50	3.01–13.5	0.060 Right
	Opening and closing hands	0.38 ± 0.74	0	0–2	
	Finger-nose pointing EO/EC	0.19 ± 0.43/ 0.36 ± 0.67	0/0	0–1.5/0–2	
	Average time of tapping between thumb and index finger	12.00 ± 4.92	11	4–21.85	0.07 Right
	Tapping	0.68 ± 1.22	0	0-4	0.072 Right
	Average time of thumb fingers (s)	8.99 ± 4.23	9	4–20.5	
	thumb fingers opposition	0.83 ± 1.37	0	0–5	
	Average time of 5 sequences of fist-side-palm	1.84 ± 2.50	0.25	0–8	
	To tap the feet	0.35 ± 0.81	0	0–3	0.063 Left
	Heel-and-toe tap	0.74 ± 1.26	0	0–4	0.09 Right
Sensory integration	Sterognosis (EC)	0.09 ± 0.27	0	0–1	
	Extinction (EC)	0.33 ± 0.59	0	0–2	
	Graphestesia	0.19 ± 0.44	0	0–1.5	
Tonus	Tonicity of upper limb	0.02 ± 0.11	0	0–0.5	
	Upper limb dangling	0.29 ± 0.64	0	0–2	
	Tonicity of lower limb	0.25 ± 0.55	0	0–1.75	
	Lower limb dangling	0.08 ± 0.24	0	0–1	
Somatognosis and spatial perception	Self-right and left evaluation				
	Other-right and left evaluation	0.45 ± 0.83	0	0–3	

*EO, eyes opened; EC, eyes closed. *left and right average. **assessment for dominance laterality. Gray lines indicate that tasks are performed correctly for all subjects with a null score.*

Average score of the NSSs was 1.56 (± 1) and the median value of scores is 1.92 (range: 0–3.27). Control group exhibited a lower NSSs average total score than PTSD group (t = 2.65, p = 0.01).

Impact of PTSD Severity

According to the PCL5 cut-off of 33, five patients (22.72%) were not positive for the psychometric PTSD diagnosis (group called minor-PTSD). No difference was found between the two centers for the number of patients under the cut-off. For the remaining patients with a score above the cut-off, we defined two groups according to the PCL5-median of 58 for these patients; the group called moderate-PTSD consisted of 8 patients (36.36%) with a PCL5 score under 58 and the group called severe-PTSD consisted of 9 patients (40.91%) above or equal to 58.

The three groups differed in terms of age (H = 7.162; p = 0.027) with the highest average age for the minor-PTSD group (51.6 ± 13.83) compared to the moderate- and severe-PTSD groups (33.25 ± 9.88, and 34.33 ± 9.59, respectively). Difference was observed in terms of gender between groups ($X^2 = 6.49$, p = 0.04) with the highest number of women in the severe-PTSD group (100%; 9 women) compared to the moderate-PTSD group with 62.5% of women (5 women) and the minor-PTSD group with 40% of women (2 women). No difference was observed for marital status, and the number of stressor in professional as personal life between the three groups.

Table 2 described the significant differences (or trends) between the three groups for the PCL5, the WEMBS, and the PASS scores and sub-scores. Patients with severe PTSD exhibited the highest symptoms scores, the lowest well-being score and minor-PTSD patients exhibited the lowest symptoms scores, the highest well-being score, and the patients with moderate PTSD were in between. For the significant NSSs differences, the alterations were maximum for the patients with severe PTSD, minimum for minor PTSD patients and in-between for the patients with moderate PTSD. For both the average time of unipodal equilibrium (s) and fastest tempo, alterations were not different between moderate and severe PTSD.

DISCUSSION

This study explored the relationship between PTSD severity and NSSs as a proof of concept.

According to the three major gaps in the literature, main results highlight that (1) NSSs level reflects the severity of PTSD, (2) the prominent NSSs associated with PTSD are related to static and dynamic equilibrium (i.e., motor integration and coordination), and (3) NSSs primarily affect women.

First, PTSD patients exhibited higher NSSs compared with healthy control subjects. Concerning the relationship between PTSD severity and NSSs, results suggest that the alterations in NSSs increase with PTSD severity. Regarding our results, minor PTSD with the lowest NSSs are the oldest patients. This data is not sufficient to affirm that age does not interact with NSSs and further studies are needed to evaluate this relationship, namely, prospective data are needed for describing the co-evolution of clinical symptoms and NSSs. Furthermore, there is some evidence suggesting that some inflammatory mechanism would be a mediator between PTSD clinical severity and NSS (49, 50). An increasing number of studies examining PTSD have either emphasized a relationship between PTSD and a systemically pro-inflammatory state or identified a link between PTSD and chronic disease. Namely, PTSD symptoms constitute a stress-perpetuating syndrome that maintains the individual in a chronic state of sustained stress (51, 52). Emerging evidence suggests that the biological consequences this include elevated systemic levels of inflammation implying in accelerated cellular aging and neuroprogression (52). Consequently, the inflammatory pathological remodeling of neural circuitry should occur over the course of a chronic mental illness.

TABLE 2 | Mean scores and standard deviations (±) according to the three groups for the items of the PCL5, WEMWBS, and PASS with significant group differences.

		Minor PTSD n = 5	**Moderate PTSD n = 8**	**Severe-PTSD n = 9**	**Group effect p**
PCL5	Total	23.4 ± 6.88	50.5 ± 6.89	71.6 ± 10.1	<0.01[a]
	Intrusion	11.6 ± 3.85	13.62 ± 2.72	17.6 ± 5.33	0.054[a]
	Avoidance	3.87 ± 1.3	5.5 ± 1.85	6.9 ± 2.38	0.064[a]
	Negative mood and cognition	2 ± 2.92	15.87 ± 6.24	25.6 ± 4.72	<0.001[a]
	Alterations in arousal and reactivity	6 ± 2.83	15.5 ± 4.63	21.5 ± 3.5	<0.001[a]
WEMWBS		55.2 ± 2.39	51 ± 8.37	40.78 ± 8.64	0.011[a]
NSSs total score		2.06 ± 2.19	12.06 ± 11.5	23.15 ± 18.1	0.022[a]
Fastest tempo (s)		10.6 ± 2.07	5.39 ± 2.84	6.48 ± 2.65	0.020[b]
Static and dynamic equilibrium	Jumping up and down on the right foot	0	0.25 ± 0.53	0.7 ± 0.57	0.036 R[a]
	Average time of unipodal equilibrium (s)*	30 ± 11.54	18.98 ± 17	18.71 ± 18.73	0.023[b]
	Movements during Romberg	0	0.06 ± 0.18	0.29 ± 0.27	0.053 R[a]
		0	0.06 ± 0.18	0.25 ± 0.27	0.086 L[a]
motor integration and coordination	Average time for 10 prosupinations sequences (s)	11 ± 4.24	5.29 ± 2.41	8.53 ± 5.82	0.081 R[a]
		12 ± 4.74	5.43 ± 1.99	9.27 ± 6.43	0.057 L[a]
	Average time for arm in horizontal position (EO) (s)	10.2 ± 2.17	6.7 ± 1.43	7.54 ± 3.31	0.058 R[a]
		10.2 ± 1.64	6.78 ± 1.4	7.6 ± 3.44	0.03 L[a]

[a]Differences (or trends) between the three groups; [b]low PTSD differed (or trended to differ) from moderate and severe PTSD the three groups.
*EO, eyes opened; EC, eyes closed. *dominance laterality. R, right task; L, left task.*

Literature questions how inflammatory processes and chronic disease issues are interrelated: putative causes for inflammation in PTSD and possible consequences of inflammation in this disorder (49). The scarcity of longitudinal data does not establish whether the increase in proinflammatory markers precedes or follows the onset of PTSD.

Concerning the type of NSSs associated with PTSD, two prominent alterations were found: static and dynamic equilibrium as well as motor integration and coordination NSSs. Altogether, these NSSs alterations highlight the role of the cerebellum. While the cerebellum has, until recently, not been considered as a key region in PTSD, there is growing evidence implicating the cerebellar region in the pathophysiology of PTSD (53, 54). Convergent findings from neuroimaging and lesion studies showed that the cerebellum's role is not confined to motor function (55) but is also important in cognition and emotion (56, 57). Thus, some authors proposed that patients with PTSD exhibited alterations in both top-down and bottom-up emotion regulation (53). From the top-down of view, the hypothesis on PTSD is a learned incapacity of top-down structures as prefrontal cortex in inhibition of an "hyper-reactive" amygdala (58, 59). The down-top frame suggests a role of cerebellum deficits to control the hyper-reactivity of amygdala, too (54). Indeed, it is known that the cerebellum receives and sends information to non-motor cortical areas, including prefrontal regions responsible for higher cognitive functions (60) and that both amygdala and cerebellum are crucial sites in fear conditioning (61, 62) and extinction models (63). Furthermore, it has been recently described the relationship. Furthermore, correlations between functional connectivity in the cerebellum, symptoms severity, included the four symptom domains specified in the DSM-5, has been described (54). Altogether, these data led to propose a non-specific role of the cerebellum in PTSD symptomatology with neurological consequences that could be linked to the severity of the PTSD and its prognosis. The left-right asymmetry in the prominent NSSs is difficult to discuss since left and right handedness subjects are included among our cohort. There a need to evaluate the interaction between objective laterality and gender difference in further studies for better describe functional lateralization of the cerebellum (64). This issue is very important and in that respect some studies observed altered functioning of the left cerebellar hemisphere (65) and vermis (66, 67) in PTSD patients. Further studies are needed for better understanding of the cerebellum involvement in the pathophysiology of PTSD. This could helpful for a better evaluation of the relationships between distinct patterns of cerebellar alterations and the clinical severity, included neurological symptoms as for reducing the gap that continue to exist in the understanding of brain structure and function in PTSD.

The issue that NSSs primarily affect women in our study is associated with the highest PTSD severity for the included women. Such results must be considered with caution due to the small size of the sample. Nevertheless, most findings on gender differences in PTSD found that to be a woman is a risk factor for PTSD when trauma: women are approximately twice as likely as men to meet criteria for PTSD following a traumatic event (68), and they are more than four times as likely as men to develop chronic PTSD (69). These data could account for both the 75% women among our PTSD cohort and the disproportionate number of those experiencing severe PTSD. Interestingly, across various studies, women are about one-third less likely than men to report having experienced a trauma (69, 70). These results suggest that the higher rate of PTSD among women cannot be attributed to a greater overall risk of trauma but to a greater vulnerability to PTSD (70). While studies delineate more precisely the ways in which culture, and gender role, alone and in combination shape the gender differences of PTSD (71), neurobiological mechanisms may account for why women reported PTSD more often than men after a trauma. To date, most researchers in this area primarily paid attention to men with only 2% of neurobiological research conducted in females (mainly rats) (69, 70, 72, 73). From a biological point of view, women appear to have a more sensitized hypothalamus–pituitary–axis than men when facing a stressor (69). The oxytocin regulation of fear also differs between men and women (74). These findings indicate that females acquire fear more easily than males (75). Furthermore, gender differences were found in some cerebellum structures with less gray matter volume and less hemispherical asymmetry for women (76). In addition, a gender-related difference in the cerebellar-thalamic-cortical circuitry has been found (77). A developmental hypothesis has also been advanced for gender difference in cerebellar structures and functioning (78). Altogether, these issues highlight the importance of considering gender as a biological variable in cerebellum research for better understanding how gender acts as a susceptibility or resilience factor for PTSD.

This exploratory study has several limits. The first one is the small sample size. Then, results are to be considered as a proof of concept for further studies. Especially, the causal relationship between NSSs and PTSD severity need to be studied. The second one focuses on the sociodemographic characteristics of the population. Both objective right-hander and left-hander PTSD were included. Related to the asymmetrical differences observed in the NSSs among our patients, this points the importance to control the laterality using objective evaluation instead of self-report before exploration of the NSSs. Moreover, women are overrepresented in our sample. Related to the gender differences in PTSD, how gender affects the link between NSSs and PTSD severity, and in what specific ways, need to be further evaluated. Third, evaluation of NSSs was done using the only validated French questionnaire. A need for developing objective scales among countries are needed (i) for better understanding how NSSs are involved in PTSD and (ii) further for comparing NSSs among psychiatric disorders. Such tools will be useful for studying NSSs as subtle indicators of brain dysfunctions and their neurological correlates. Finally, no hypothesis was made on the role of the type of trauma as on the role of the time between the trauma and the clinical inclusion. To confirm whether NSSS are in line with the severity, these factors need to be controlled for future investigations.

CONCLUSION

This study as a proof of concept highlights the interest of studying NSSs in PTSD. These exploratory results found a relationship between the severity of PTSD and the NSSs in terms of static and dynamic equilibrium and motor integration and coordination but they do not preclude generalizability or causal relationship. Regarding the asymmetrical NSSs and the gender effect, this points out the methodological implication for future studies. They provide some convincing arguments for evaluating the NSSs as a prognosis factor in PTSD using longitudinal follow-up.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by 2019-A01232-37. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

CB and MT conceived the study. All authors actively took part in the process. All authors have planned and participated in the statistical analysis. All authors contributed to the article and approved the submitted version.

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REFERENCES

1. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders. 5th edn.* American Psychiatric Publishing (2013).
2. Holowka DW, Marx BG. Assessing PTSD-related functional impairment and quality of life. In: Beck GJ, Sloan DM, Eds. *Oxford handbook of traumatic stress disorders*. New York (NY): Oxford University Press (2011).
3. Bisson JII, Roberts NP, Andrew M, Cooper R, Lewis C. Psychological therapies for chronic post-traumatic stress disorder (PTSD) in adults. *Cochrane Database Syst Rev* (2013) 12, CD003388. doi: 10.1002/14651858.CD003388.pub4
4. Hoge CW, Terhakopian A, Castro CA, Messer SC, Engel CC. Association of posttraumatic stress disorder with somatic symptoms, health care visits, and absenteeism among Iraq war veterans. *Am J Psychiatry* (2007) 164(1):150–3. doi: 10.1176/ajp.2007.164.1.150
5. Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry* (2005) 62(6):617–27. doi: 10.1001/archpsyc.62.6.617
6. Yehuda R, Hoge CW, McFarlane AC, Vermetten E, Lanius RA, Nievergelt CM, et al. Post-traumatic stress disorder. *Nat Rev Dis Primers* (2015) 1:15057. doi: 10.1038/nrdp.2015.57
7. Kok BC, Herrell RK, Thomas JL, Hoge CW. Posttraumatic stress disorder associated with combat service in Iraq or Afghanistan: reconciling prevalence differences between studies. *J Nerv Ment Dis* (2012) 200(5):444–50. doi: 10.1097/NMD.0b013e3182532312
8. NICE. (2018). https://www.nice.org.uk/guidance/ng116. Published date: December 2018.
9. Solomon Z, Mikulincer M. Trajectories of PTSD: a 20-year longitudinal study. *Am J Psychiatry* (2006) 163(4):659–66. doi: 10.1176/ajp.2006.163.4.659
10. McLean CP, Foa EB. Emotions and emotion regulation in posttraumatic stress disorder. *Curr Opin Psychol* (2017) 14:72–7. doi: 10.1016/j.copsyc.2016.10.006
11. Belrose C, Duffaud A, Dutheil F, Trichereau J, Trousselard M. Challenges Associated With the Civilian Reintegration of Soldiers With Chronic PTSD: A New Approach Integrating Psychological Resources and Values in Action Reappropriation. *Front Psychiatry* (2019) 9:737. doi: 10.3389/fpsyt.2018.00737
12. Chesney SA, Gordon NS. Profiles of emotion regulation: understanding regulatory patterns and the implications for posttraumatic stress. *Cognit Emot* (2016) 2016:1–9. doi: 10.1080/02699931.2015.1126555
13. Bardeen JR, Kumpula MJ, Orcutt HK. Emotion regulation difficulties as a prospective predictor of posttraumatic stress symptoms following a mass shooting. *J Anxiety Disord* (2013) 27(2):188–96. doi: 10.1016/j.janxdis.2013.01.003
14. Hayes JP, Hayes SM, Mikedis AM. Quantitative meta-analysis of neural activity in posttraumatic stress disorder. *BMAD* (2012) 2(1):9. doi: 10.1186/2045-5380-2-9
15. Pitman RK, Rasmusson AM, Koenen KC, Shin LM, Orr SP, Gilbertson MW, et al. Biological studies of post-traumatic stress disorder. *Nat Rev Neurosci* (2012) 13(11):769–87. doi: 10.1038/nrn3339
16. Rauch SL, Shin LM, Phelps EA. Neurocircuitry models of posttraumatic stress disorder and extinction: human neuroimaging research-past, present, and future. *Biol Psychiatry* (2006) 60:376–82. doi: 10.1016/j.biopsych.2006.06.004
17. Green MF, Kern RS, Braff DL, Mintz J. Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the"right stuff"? *Schizophr Bull* (2000) 26:119–36. doi: 10.1093/oxfordjournals.schbul.a033430
18. Heaton RK, Pendleton MG. Use of neuropsychological tests to predict patients everyday functioning. *J Consult Clin Psychol* (1981) 49:807–21. doi: 10.1037/0022-006X.49.6.807
19. Twamley EW, Doshi RR, Nayak GV, Palmer BW, Golshan S, Heaton RK, et al. Generalized cognitive impairments, ability to perform everyday tasks, and level of independence incommunity living situations of older patients with psychosis. *Am J Psychiatry* (2002) 159(12):2013–20. doi: 10.1176/appi.ajp.159.12.2013
20. Schuitevoerder S, Rosen JW, Twamley EW, Ayers CR, Sones H, Lohr JB, et al. A meta-analysis of cognitive functioning in older adults with PTSD. *J Anxiety Disord* (2013) 27:550–8. doi: 10.1016/j.janxdis.2013.01.001
21. Qureshi SU, Long ME, Bradshaw R, Pyne JM, Magruder KM, Kimbrell T, et al. Does PTSD Impair Cognition Beyond the Effect of Trauma? *J Neuropsych Clin N* (2011) 23:16–28. doi: 10.1176/appi.neuropsych.23.1.16
22. Aupperle RL, Melrose AJ, Stein MB, Paulus MP. Executive function and PTSD: disengaging from trauma. *Neuropharmacology* (2012) 62:686–94. doi: 10.1016/j.neuropharm.2011.02.008
23. Twamley EW, Allard CB, Thorp SR, Norman SB, Hami-Cissell S, Hughes-Berardi K, et al. Cognitive impairment and functioning in PTSD related to intimate partner violence. *J Int Neuropsychol Soc* (2009) 15:879–87. doi: 10.1017/S135561770999049X
24. Vasterling JJ, Duke LM, Brailey K, Constans JII, Allain ANJr, Sutker PB. Attention, learning, and memory performances and intellectual resources in Vietnam veterans: PTSD and no disorder comparisons. *Neuropsychology* (2002) 16(1):5–14. doi: 10.1037//0894-4105.16.1.5
25. Zen AL, Whooley MA, Zhao S, Cohen BE. Post-traumatic stress dis-order is associated with poor health behaviors: findings from the heart and soul study. *Health Psychol* (2011) 31:194–201. doi: 10.1037/a0025989
26. Kessler RC, Frank RG. The impact of psychiatric disorders on work loss days. *Psychol Med* (1997) 27:861–73. doi: 10.1017/S0033291797004807
27. Karney BR, Crown JS. *Families under stress: an assessment ofdata, theory, and research on marriage and divorce in the military [Mono-graph]*. National

Defense Research Institute, RAND Corporation. Santa Monica, California: RAND Corporation, MG-599-OSD, 2007 (2007). Available at: https://www.rand.org/pubs/monographs/MG599.html. As of January 26, 2020.

28. Alamiri B, Garrett CN, Fitzmaurice M, Murphy JM, Gilman SE. Neurological Soft Signs and Cognitive Performance in Early Childhood. *Dev Psychol* (2018) 54(11):2043–52. doi: 10.1037/dev0000566
29. Chan RC, Rao H, Chen EE, Ye B, Zhang C. The neural basis of motor sequencing: An fMRI study of healthy subjects. *Neurosci Lett* (2006) 398:189–94. doi: 10.1016/j.neulet.2006.01.014
30. Dazzan P, Morgan KD, Chitnis X, Suckling J, Morgan C, Fearon P, et al. The structural brain correlates of neurological soft signs in healthy individuals. *Cereb Cortex* (2006) 16:1225–31. doi: 10.1093/cercor/bhj063
31. Herold CJ, Duval CZ, Lässer MM, Schröder J. Neurological soft signs (NSS) and cognitive impairment in chronic schizophrenia. *Schizophr Res Cognit* (2019) 16:17–24. doi: 10.1016/j.scog.2018.12.002
32. Heinrichs DW, Buchanan RW. Significance and meaning of neurological signs in schizophrenia. *Am J Psychiatry* (1988) 145:11–8. doi: 10.1176/ajp.145.1.11
33. Boks MPM, Russo S, Knegtering R, van den Bosch RJ. The specificity of neurological signs in schizophrenia: a review. *Schizophr Res* (2000) 43:109–16. doi: 10.1016/s0920-9964(99)00145-0
34. Baş TO, Poyraz CA, Baş A, Poyraz BÇ, Tosun M. The impact of cognitive impairment, neurological soft signs and subdepressive symptoms on functional outcome in bipolar disorder. *J Affect Disord* (2015) 174:336–41. doi: 10.1016/j.jad.2014.12.026
35. Goswami U, Gulrajani C, Varma A, Sharma A, Ferrier IN, Young PAH, et al. Soft neurological signs do not increase with age in euthymic bipolar subjects. *J Affect Disord* (2007) 103(1-3):99–103. doi: 10.1016/j.jad.2007.01.009.2006
36. Colom R, Jung RE, Haier RJ. Distributed Brain Sites for the g-Factor of Intelligence. *NeuroImage* (2006) 31:1359–13.65. doi: 10.1016/j.neuroimage.2006.01.006
37. Luders E, Narr KL, Thompson PM, Toga AW. Neuroanatomical Correlates of Intelligence. *Intelligence* (2009) 37(2):156–63. doi: 10.1016/j.intell.2008.07.002
38. Chan RCK, Xu T, Heinrichs RW, Yu Y, Wang Y. Neurological Soft Signs in Schizophrenia: A Meta-analysis. *Schizophr Bull* (2010) 36(6):1089–104. doi: 10.1093/schbul/sbp011
39. Gurvits TV, Gilbertson MW, Lasko NB, Tarhan AS, Simeon D, Macklin ML, et al. Neurologic Soft Signs in Chronic Posttraumatic Stress Disorder. *Arch Gen Psychiatry* (2000) 57(2):181–6. doi: 10.1001/archpsyc.57.2.181
40. Gurvits TV, Carson MA, Metzger L, Croteau HB, Lasko NB, Orr SP, et al. Absence of selected neurological soft signs in Vietnam nurse veterans with post-traumatic stress disorder. *Psychiatry Res* (2002) 110(1):81–5. doi: 10.1016/S0165-1781(02)00026-4
41. Marionneau A, Servant M-L, et Albaret J-M. Échelle Psychomotrice d'évaluation des Signes neurologiques Doux (EPSID) [Neurological Soft Signs Scale]. In: F Giromini, J-M Albaret, P Scialom, editors. *Manuel d'enseignement de psychomotricité*. Paris: De Boeck-Solal (2018). p. 187–200.
42. Ashbaugh AR, Houle-Johnson S, Herbert C, El-Hage W, Brunet A. Psychometric Validation of the English and French Versions of the Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5). *PloS One* (2016) 11(10):e0161645. doi: 10.1371/journal.pone.0161645
43. Tennant R, Hiller L, Fishwick R, Platt S, Joseph S, Weich S, et al. The Warwick-Edinburgh Mental Well-being Scale (WEMWBS): development and UK validation. *Health Qual Life Outcomes* (2007) 5:63. doi: 10.1186/1477-7525-5-63
44. Trousselard M, Canini F, Dutheil F, Claverie D, Fenouillet F, Naughton G, et al. Investigating well-being in healthy population and schizophrenia with the WEMWBS. *Psychiatry Res* (2016) 245:282–90. doi: 10.1016/j.psychres.2016.08.050
45. Keyes CLM. Promoting and protecting mental health as flourishing: A complementary strategy for improving national mental health. *Am Psychol* (2007) 62(2):95–108. doi: 10.1037/0003-066X.62.2.95
46. Lecrubier Y, Weiller E, Hergueta P, Bonora L, Lepine J. The Mini International Neuropsychiatric Interview (M.I.N.I.), a short diagnostic interview: Reliability and validity according to the CIDI. *Eur Psychiatry* (1992) 12:232–41.
47. Dunn OJ. Multiple Comparisons Using Rank Sums. *Technometrics* (1964) 6 (3):241–52. doi: 10.1080/00401706.1964.10490181
48. Kruskal W, Wallis W. Use of Ranks in One-Criterion Variance Analysis. *J Am Stat Assoc* (1952) 47(260):583–621. doi: 10.2307/2280779
49. Hori H, Kim Y. Inflammation and post-traumatic stress disorder. *Psychiatry Clin Neurosci* (2019) 73:143–53. doi: 10.1111/pcn.12820
50. Speer K, Upton D, Semple S, McKune A. Systemic low-grade inflammation in post-traumatic stress disorder: a systematic review. *J Inflammation Res* (2018) 11:111–21. doi: 10.2147/JIR.S155903
51. Miller MW, Lin AP, Wolf EJ, Miller DR. Oxidative Stress, Inflammation, and Neuroprogression in Chronic PTSD. *Harv Rev Psychiatry* (2018) 26(2):57–69. doi: 10.1097/HRP.0000000000000167
52. Miller MW, Sadeh N. Traumatic stress, oxidative stress and posttraumatic stress disorder: neurodegeneration and the accelerated-aging hypothesis. *Mol Psychiatry* (2014) 19(11):1156–62. doi: 10.1038/mp.2014.111
53. Carletto S, Borsato T. Neurobiological correlates of post-traumatic stress disorder: A focus on cerebellum role. *Eur J Trauma Dissoc* (2017) 1:153–7. doi: 10.1016/j.ejtd.2017.03.012
54. Holmes SE, Scheinost D, DellaGioia N, Davis MT, Matuskey D, Pietrzak RH, et al. Cerebellar and Prefrontal Cortical Alterations in PTSD: Structural and Functional Evidence. *Chronic Stress* (2018) 2:1–11. doi: 10.1177/2470547018786390
55. Lee HW, Arora J, Papademetris X, Tokoglu F, Negishi M, Scheinost D, et al. Altered functional connectivity in seizure onset zones revealed by fMRI intrinsic connectivity. *Neurology* (2014) 83(24):2269–77. doi: 10.1212/WNL.0000000000001068
56. MI Botez Cerebellum, VS Ramachandran eds. *Encyclopedia of Human Behavior* Vol. p. New York: Academic Press (1999). p. 2002.
57. Schmahmann JD, Caplan D. Cognition, emotion and the cerebellum. *Brain* (2006) 129:290–2. doi: 10.1093/brain/awh729
58. Nicholson AA, Rabellino D, Densmore M, Frewen PA, Paret C, Kluetsch R, et al. The neurobiology of emotion regulation in posttraumatic stress disorder: Amygdala downregulation via real-time fMRI neurofeedback. *Hum Brain Mapp* (2017) 38(1):541–60. doi: 10.1002/hbm.23402
59. Patel R, Spreng RN, Shin LM, Girard TA. Neurocircuitry models of posttraumatic stress disorder and beyond : a meta-analysis of functional neuroimaging studies. *Neurosci Biobehav Rev* (2012) 36(9):2130–42. doi: 10.1016/j.neubiorev.2012.06.003
60. Schutter DJ, Van Honk J. The cerebellum on the rise in human emotion. *Cerebellum* (2005) 4:290–4. doi: 10.1080/14734220500348584
61. Lange I, Kasanova Z, Goossens L, Leibold N, De Zeeuw CII, van Amelsvoort T, et al. The anatomy of fear learning in the cerebellum: a systematic meta-analysis. *Neurosci Biobehav Rev* (2015) 59:83–91. doi: 10.1016/j.neubiorev.2015.09.019
62. Ernst TM, Brol AE, Gratz M, Ritter C, Bingel U, Schlamann M, et al. The cerebellum is involved in processing of predictions and prediction errors in a fear conditioning paradigm. *ELife* (2019) 8:e46831. doi: 10.7554/eLife.46831
63. Utz A, Thürling M, Ernst TM, Hermann A, Stark R, Wolf OT, et al. Cerebellar vermis contributes to the extinction of conditioned fear. *Neurosci Lett* (2015) 604:173–7. doi: 10.1016/j.neulet.2015.07.026
64. Fan L, Tang Y, Sun B, Gong G, Chen ZJ, Lin X, et al. Sexual dimorphism and asymmetry in human cerebellum: An MRI-based morphometric study. *Brain Res* (2010) 1353:60–73. doi: 10.1016/j.brainres.2010.07.031
65. Osuch EA, Benson B, Geraci M, Podell D, Herscovitch P, McCann UD, et al. Regional cerebral blood flow correlated with flashback intensity in patients with posttraumatic stress disorder. *Biol Psychiatry* (2001) 50(4):246–53. doi: 10.1016/s0006-3223(01)01107-6
66. Pissiota A, Frans O, Fernandez M, von Knorring L, Fischer H, Fredrikson M. Neurofunctional correlates of posttraumatic stress disorder: a PET symptom provocation study. *Eur Arch Psychiatry Clin Neurosci* (2002) 252(2):68–75. doi: 10.1007/s004060200014
67. Baldaçara L, Jackowski AP, Schoedl A, Pupo M, Andreoli SB, Mello MF, et al. Relationship between structural abnormalities in the cerebellum and dementia, posttraumatic stress disorder and bipolar disorder. *Dement Neuropsychol* (2012) 6(4):203–11. doi: 10.1590/S1980-57642012DN06040003
68. Haskell SG, Gordon KS, Mattocks K, Duggal M, Erdos J, Justice A, et al. Gender differences in rates of depression, PTSD, pain, obesity, and military sexual trauma among Connecticut War Veterans of Iraq and Afghanistan. *J Womens Health (Larchmt)* (2010) 19(2):267–71. doi: 10.1089/jwh.2008.1262
69. Olff M. Sex and gender differences in post-traumatic stress disorder: an update. *Eur J Psychotraumatol* (2017) 8(4):1351204. doi: 10.1080/20008198.2017.1351204
70. Hu J, Feng B, Zhu Y, Wang W, Xie J, Zheng X. *Gender Differences in PTSD : Susceptibility and Resilience*. London, UK: IntechOpen (2017). doi: 10.5772/65287

71. Christiansen DM, Hansen M. Accounting for sex differences in PTSD: A multi-variable mediation model. *Eur J Psychotraumatol* (2015) 6(1):26068. doi: 10.3402/ejpt.v6.26068
72. Goos LM, Silverman I. Sex related factors in the perception of threatening facial expressions. *J Nonverbal Behav* (2002) 26(1):27–41. doi: 10.1023/A:1014418503754
73. McClure EB. A meta-analytic review of sex differences in facial expression processing and their development in infants, children, and adolescents. *Psychol Bull* (2000) 126(3):424–53. doi: 10.1037/0033-2909.126.3.424
74. Frijling JL. Preventing PTSD with oxytocin: Effects of oxytocin administration on fear neurocircuitry and PTSD symptom development in recently trauma-exposed individuals. *Eur J Psychotraumatol* (2017) 8(1):1302652. doi: 10.1080/20008198.2017.1302652
75. Inslicht SS, Metzler TJ, Garcia NM, Pineles SL, Milad MR, Orr SP, et al. Sex differences in fear conditioning in posttraumatic stress disorder. *J Psychiat Res* (2013) 47(1):64–71. doi: 10.1016/j.jpsychires.2012.08.027
76. Diedrichsen J, Balsters JH, Flavell J, Cussans E, Ramnani N. A probabilistic MR atlas of the human cerebellum. *NeuroImage* (2009) 46(1):39–46. doi: 10.1016/j.neuroimage.2009.01.045
77. Xin J, Zhang Y, Tang Y, Yang Y. Brain Differences Between Men and Women: Evidence From Deep Learning. *Front Neurosci* (2019) 13:185. doi: 10.3389/fnins.2019.00185
78. Kaczkurkin AN, Raznahan A, Satterthwaite TD. Sex differences in the developing brain: insights from multimodal neuroimaging. *Neuropsychopharmacol* (2019) 44:71–85. doi: 10.1038/s41386-018-0111-z

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Psychological Consequences in Patients With Amputation of a Limb. An Interpretative-Phenomenological Analysis

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The study aimed to identify the psychological changes that result from the amputation of a limb and the ways in which patients coordinate their daily lives. The study uses an interpretative phenomenological analysis (IPA) aimed at understanding individual experiences in seven patients who have suffered limb amputation. The method used consisted of individual, semi-structured interviews, conducted approximately 4 months after surgery, to patients at home or in hospital, at the time of their regular checkup. The interviews were audio recorded, transcribed and, following the qualitative analysis performed, six common themes were identified: emotional impact, negative affects, tendency toward isolation, role constraints and limitations, phantom limb, and emotional balancing. A specific theme for patients who have suffered amputations is phantom limb pain, which has received special attention from researchers. The last topic relates to the tendency toward emotional balancing and psychological calibration to return to normal life.

Keywords: chronic condition, limb amputation, psychological consequences, interpretative phenomenological analyses, negative affectivity, self

INTRODUCTION

Amputation is traumatic both as a surgery itself and also due to its consequences. Perceived as an aggression to bodily integrity, besides physical suffering, it can initiate or aggravate a series of disharmonies that disrupt the patient's well-being. Desmond and MacLachlan (2002) consider that amputations cause considerable changes in everyday life of the patient, and especially in psychosocial relationships. Physical disability can lead to despair, depression, nervousness, anxiety, loss of self-esteem, stigma, isolation, and the recognition of weakness (Khan et al., 2018). The decision to amputate a limb is difficult for both medical staff, the patient, and his/her family (Boccolini, 1995). The fear of losing a visible part of the body leads to a true sense of body disintegration (Bergo and Prebianchi, 2018). However, amputation may be necessary to save a life. That is why a closer approach to this issue is needed.

Amputation may have multiple causes including burns, frostbite, peripheral vascular disease trauma, infections, and tumors (Simsek et al., 2017). As a surgical procedure, it is done to save life, control pain, malignancy or gangrene in an affected member (Waqar et al., 2015). It can also have a preventative role. An 18 months longitudinal study, according to the WHO (Seidel et al., 2006), found that 14.1% of the amputees reported depression (5.8% in males and 9.5% in females). Another study (McKechnie and John, 2014) found that the levels of anxiety and depression are significantly higher in amputees than the general population. Horgan and MacLachlan (2004) estimate that depression and anxiety are moderately elevated up to 2 years after amputation. Physicians should take this into account in addition to amputation treatment.

This study confirms the meta-analysis of Bergo and Prebianchi (2018) who, quoting Rodrigues (2011), concluded that the emotional responses following amputation differ from patient to patient, and are influenced by a constellation of factors: the etiology of amputation, elements of personal life, the social-historical moment, the pathogenicity of the disease, and the patient's interpretation of the symptoms. Patients who suffer from amputation due to a vascular disorder that causes unbearable pain will feel relieved. Similarly do those who, in this way, hope to attain the healing of bone cancer. Conversely, those traumatized react differently and live the uncertainty of their future prospects. The sooner a prosthesis is applied, the associated psychological problems diminish.

Knowing the psychological consequences of limb amputation is useful for practitioners in the medical field because it helps them develop effective counseling and rehabilitation programs. Various studies investigated the psychological consequences of limb amputations (Khan et al., 2018). Almost all of them relied on a cross-sectional design by administering psychometric questionnaires to the participants. Even if this method generates important empirical evidence when it comes to the psychological consequences in patients with amputation of a limb, it has its limitations. For example, such an approach, limits participants to the information captured by the psychometric measure, while information that may be relevant to psychological consequences of limb amputation, not encompassed in the measure, cannot be reported by participants. Therefore, we think that pursuing a qualitative approach, such as the interpretative phenomenological analysis (IPA) would provide richer and more insightful information, which should help to better understand the consequences of limb amputation.

Even though the previous studies on this topic offer valuable information in understanding the various psychological consequences of limb amputation, these studies did not provide a robust theoretical framework that could serve for the interpretation of the identified psychological consequences. We consider that Self psychology model of Kohut (1966) may be used as a theoretical framework to explain the psychological consequences of limb amputation. This theory describes the self as a collection of self-representations. These collections are understood in terms of representing the cognitive-affective structure of one's identity, being named "the representational world" – that is, people's representations of the self and others (Sandler and Rosenblatt, 1962). This representational world develops as a consequence of the interaction between the individual and his parents, family and the people around him in his childhood (Kohut, 1966). This theoretical model describes the self as bipolar, with ambitions on one side, ideals on the other, and talents and skills driven by these two poles arched between them. The degree to which individuals develop these characteristics depends on the extent to which their caregivers, in the first years of life, are empathic in their response to the children's need for mirroring, support and idealization of caregivers, thus transmitting their own sense of security and self-esteem to them (Kohut and Wolf, 1978).

Although the self of one individual is stab across adulthood (Markus and Kunda, 1986), it may be subjected to important changes and variations as a result of traumatic life experiences (Saakvitne et al., 1998). Because limb amputation is perceived as traumatic (Desmond and MacLachlan, 2002), we consider that it should lead to shifts and modifications on the individual self-structure. Because it affects the integrity of the body, the talents, and skills, which are components of the self-structure, are affected. As a consequence, the "representational world" of the individual is subjected to important modifications. Therefore, the affected individual perceived himself as different and usually inferior compared to the period before amputation, and this perception may activate negative cognitions associated with catastrophizing regarding his future functionality and adaptation. These negative cognitions usually lead to exaggerated negative affectivity such as anger, anxiety, hostility, or depressive tendencies (Beck et al., 2005). Further, negative affectivity tends to lead to maladaptive behaviors (Beck, 2011).

Therefore, relying on the previous rationale, we hypothesize that the psychological consequences of limb amputation can be clustered in negative cognitions such as catastrophizing, negative affectivity such as anger, anxiety, hostility, or depressive tendencies, and maladaptive behaviors.

MATERIALS AND METHODS

Method

The IPA aims to understand each individual experience regarding certain events or common processes. Smith (1995) identifies two aspects of this qualitative method: phenomenology and symbolic interactions. Far from being spectators of their own lives, Smith (2007) believes that individuals are self-analyzing by wanting to understand what is happening to them, by personally and subjectively interpreting the events they are involved in. An IPA study implies an intensive interpretation of the information obtained from a small group of participants linked to a common event in their lives. Semi-structured interviews, focus groups, or journals provide data, which can reveal a comprehensive psychological portrait with generalization value when scientifically processed.

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Ethics Committee of NUPSPA (protocol code no.145, 01.04.2019).

Participants

Specific to qualitative research is the low number of participants, in order to be able to carry out an in-depth analysis of individual experiences. Smith et al. (2009) believe that a number of 3–6 participants in an IPA study would be sufficient. In this case, a number of seven participants, patients of a traumatology hospital in Bucharest, aged between 41 and 75 years, were selected. They were offered the opportunity to volunteer for a research concerning the experience of amputation. In order to ensure confidentiality, an identification number was randomly assigned to each participant and age was considered only for the purpose of establishing a range. All respondents were made aware of these procedures and gave verbal consent to participation. Within this group one participant had the left upper limb amputated, while the rest of the participants had one of the inferior limbs amputated. The causes for amputation were various and are shown in **Table 1**. At the time of the interview none of the participants had yet been given a prosthesis.

Procedure

Data Collection

After giving consent, the participants were interviewed (audio recorded) for about an hour at the hospital or at home. Data was collected in the form of a semi-structured interview, with a flexible interview schedule. The interview schedule was developed according to IPA methodology (Smith et al., 1999, 2009) in order to facilitate a comfortable and productive interaction with the participants. Starting with one research question about the "*emotional experience of the individual after amputation of a limb*," five main topics were selected to provide the overall structure of the schedule. After a consensus was reached between all researchers, the interview was finalized. Its function was to guide and not to prescribe the topics covered by the interview. For each question, prompts have been prepared in case a participant has difficulties responding, and to offer a range of possible directions for investigation. Following IPA methodology and our prior considerations the interview guide was not referred to directly when conducting the interviews. The interviewer's knowledge of the interview guide enabled enough flexibility as to permit substantial room for expression on behalf of the participants within the proposed framework of all investigation. All of the interviews were conducted by one of the authors (CR) who was not known to any of the participants prior to the research interviews. No further inquiries were needed in order to achieve data saturation. All interviews were transcribed verbatim by one researcher (AM).

TABLE 1 | Participants' description.

Participant	Amputation cause
1	Left-side calcal necrosis. Obliteratory arteriopathy of the inferior left limb
2	Myosarcoma inferior left limb
3	Inferior right limb toe necrosis. Unbalanced type 2 diabetes mellitus
4	Traumatic amputation upper left limb
5	Ischemic gangrene inferior right limb
6	Traumatic below knee amputation of inferior left limb
7	Amputation of inferior left limb

Data Analysis

Using IPA (Smith et al., 1999, 2009; Smith and Dunworh, 2003; Reid et al., 2005; Smith, 2007), the extraction of emerging themes was done repeatedly until raw, unprocessed themes were obtained (Smith et al., 2009). The transcripts were read line-by-line, by each individual researcher, focusing on the research question. After completion, the interpretative notes were analyzed to extract themes and sub-themes of interest in relation with the research question. Quotations that were relevant to the extracted themes were then selected and, in the final step, the data was reviewed against all transcripts. This procedure allowed the extraction of recurrent themes about the understanding and meaning that participants give to the amputation experience.

RESULTS

Following the analysis six themes have been highlighted: (1) emotional impact, (2) negative affects, (3) tendency toward isolation, (4) role constraints and limitations, (5) phantom limb phenomenon, and (6) emotional balancing. The examples used in this section were considered to be representative for the themes in question or for a particular manifestation related to these themes.

Emotional Impact

Regardless the reasons for amputation, whether due to traumatic causes or as a consequence of illness, the emotional shock exists. It may have a smaller or larger amplitude depending on a variety of factors such as patient age, medical culture, medical cause etc. As a result of amputation, the research participants' reports were loaded with drama. The first emotional response to amputation was one of despair, a severe sense of self-collapse, something almost unbearable. In this context, the wish for death, as an expression of extreme dread, was mentioned by many of the participants.

> "*I'm a lost man! It will not be how it was!*" (Participant 3)
> "*… awakening from the (induced) coma was a nightmare … I could not move … I wanted to get away … it was terrible! I felt I was in a prison and I could not run. I could see my right hand, but I missed my left hand. Why? For a moment I wanted to die. God, take me! Lord, I cannot live like this!*" (Participant 4).
> "*Well, what can I say … I thought the sky will fall on me … I started crying, I did not want to talk to anybody*" (Participant 2).
> "*At first, I said no, I refused … I thought I'd rather die than… I even told the doctor … I'd rather die than lose my leg*" (Participant 1).

Negative Affects

Anxiety

After surgery, for an extended period of time, the interviewed patients noticed the appearance and increase of anxiety. A lot of negative thoughts invaded their minds. Projections about the future were grim, marked by sadness, helplessness, and even despair. Existential uncertainty, lack of control and further anticipated losses in one's life due to amputation were the primary causes of anxiety and consequently ruminations and insomnia.

> "*We had a time when we were having sleepless nights. I'm still anxious. I'm thinking what's going to happen to me if my wife dies before me. Besides her, I have no one else. Now she lifts me in her arms, puts me in the wheelchair, but if I remain alone, what will I do?*" (Participant 5).
> "*I have insomnia … I can only sleep with medication … I'm anxious. I do not know what's going to happen to me in the future. I have a terrible state of insecurity*" (Participant 4).
> "*I could not sleep more than two hours a night. I'm taking sedatives. I did not accept the idea that I do not have two legs anymore. I was very worried. I was afraid I'd be kicked out of my job. And now, when I have to start work, I wonder if I will be able to handle it*" (Participant 6).

Anger and Hostility

The amputation of a limb is associated not only with physical loss and change in body image but also with an abrupt severing in one's sense of continuity. For participants with amputation as a result of physical trauma the event is often experienced as a transgression and can lead to frustration and anger.

> "*I get angry when I think I can't do what I was doing before*" (Participant 6).
> "*… a terrible frustration. Things were taken from me, my job, my independence … it's a terrible frustration but I am fighting it*" (Participant 4).
> "*… I sometimes get angry because I can't do what I did before … knowing that you could do something without asking for someone's help, now I can't even … it's, yes, a sort of … I get angry when I realize that now I need to call someone for things I used to be able to do on my own before … but I will get used to it, what else can I do?*" (Participant 1).

Hostility toward others makes sense in the context of amputation. Frustration at the loss of a limb can generate a feeling of bitter indignation at having somehow been treated unfairly by fate. Thus, others are at risk of becoming targets of resentment and envy of their "wholeness."

> "*a disabled person becomes more selfish, mournful, mischievous because she is distressed in her own way*" (Participant 5).

Tendency Toward Isolation

Struggle With Depression

Loss of the sense of control left the participants feeling exposed and vulnerable, emotionally and physically, to a world that now seems more dangerous than ever. This abrupt change in one's self state is experienced as a regression to a dependency phase that has crippling emotional effects in the absence of sufficient internal and external resources. Overwhelming distress causes depression and severely hinders the recovery process. Participants with an effective adaptive capacity seemed to fight against depression and to recognize it's damaging capacity.

> "*I cannot afford to fall prey to despair. I'm alone and I have to raise a child on my own. I have to fight. My little girl saw me cry twice, when I could not cope anymore*" (Participant 2).
> "*I have a tortured life. I'm trying not to fall into depression. Looks like I need psychological counseling. I am a strong person on the inside. That does not mean it did not affect me and I do not have moments of despair. But with whom I have to fight … to fight continuously*" (Participant 4).

In the case of elderly participants, a sense of surrender in the face of adversity was present. Given that the feelings of dependency, lack of control and vulnerability are accentuated with age, elderly people already find themselves in a process of adjustment, having to reconcile old and new self-representations. The trauma of amputation in such circumstances can be defeating.

> "*I pray to God I leave this world quicker … so I don't torture my wife anymore*" (Participant 7).
> "*If I was to die, I wouldn't have any regrets … I'm 75 years old … it's enough*" (Participant 5).

Guilt

For some participants amputation of a member was accompanied by the development of a guilt complex. Considering individual psychodynamics, guilt can be a cause and a powerful fuel for depression. In our findings, guilt was related to the realization of a link between their choices and the loss of a limb.

> "*It was only my fault: alcohol. Diabetes brought me here*" (Participant 3);
> "*I smoked for 40 years. That's why*" (Participant 1).
> "*I am guilty. I got off the tractor and did not stop the milling cutter. It was a big mistake. You are not allowed to repair a piece of equipment while functioning*" (Participant 6).

While for one participant, guilt seemed to be needed in an attempt at making sense of the trauma (car accident), in such a way that crucial resources for self-cohesion (in this case religion) remain intact.

> "*I am a religious person. I shouldn't have gone on a trip during Easter … I should have had a different state of mind … not going on a trip*" (Participant 4).

Social Withdrawal

In the case of some participants, the unpleasant image they present to others, the pity that they read in the eyes of friends and acquaintances, further their depression and leads them to social avoidance and retreat. The loss of a limb is also experienced as a narcissistic wound, a dent in the participants' representation of themselves as autonomous, intentional, capable, desirable, and participative beings. This makes them prone to shame.

> "*The fact that I do not have an arm made me isolate myself … I'm embarrassed by the situation I'm in. I do not want them to feel pity for me*" (Participant 4).
> "*After surgery, I shut down my phone because it rang very often and when it did, I started crying badly when I was seeing who was calling me. What should I say to them? That I do not have a leg anymore? And what would they say to me? … That's why I'd rather not answer them. Now when a friend comes and asks … I'm not going into details … exactly what happened etc. … I'm trying to avoid the subject. It hurts me*" (Participant 6).
> "*I'm talking to my brothers on the phone. But they are busy. I do not want to get in touch with a lot of people so they'll say „look at this poor fellow!*" (Participant 1).

At the same time, the need for convalescent isolation comes in conflict with other important necessities, such as resuming previous roles.

> "*A job I was doing with pleasure (teacher) was taken away from me. How can I appear before my students without an arm?*" (Participant 4).
> "*I was selling my vegetables at the market. The first time I went with the crutches it was unbearably shameful… People knew me … But I went. What could I do? I had to go ahead and do it*" (Participant 7).

For another participant, the personal feeling of helplessness and futility was projected outward. While it might not lead to physical isolation, it can, however, create serious barriers in relationships and engaging external resources.

> "*I'm still going out and talking to a neighbor on a bench. I do not tell them anything about me … how can he help me? … But winter is coming, what will I do?*" (Participant 7).

Role Constraints and Limitations

Struggle With a New Normal

Perhaps the most painful thing is that, before a prosthesis, the daily life of the patient with an amputated limb changes dramatically. Certain routine activities can no longer be carried out and with this comes a loss in roles and their contribution to one's self representation.

> "*I suffer that I can't dress properly…*" (Participant 4)
> "*I was taking care of my grandchild who was a year and eight months. He is really restless. I'd go out with him in the park. Now how can I run after him? I had to give up*" (Participant 3).

In addition to having a hard time doing domestic and professional activities, some participants claim to have dropped hobbies and previous physical activities. Also new constraints in one's life now have to be acknowledged and dealt with. For one patient, the struggle to accept the new reality of his options is evident.

> "*I was lively … I'm not the man to stand in one place. I always had to do something. I went on trips to the mountains and the sea. Now I cannot. How do I climb up the mountain or how can I go to the beach without a leg?*" (Participant 1).

Resuming Previous Roles

Focusing on and capacity to reengage in previous roles seemed to provide, for some participants, a shielding effect from the adverse impact of the trauma. If they are active and animated by positive thinking, they can better overcome negative affects and find the opportunity to recover a sense of utility and capacity.

> "*Until now I was helping others. My mother was paralyzed in bed for years and lived with me. I took care of her. She went last year. Now her sister lives with me and she is almost blind. I'm helping her … just like that … without an arm*" (Participant 4).

Fear of losing the active role part of mother seems to be a driving factor in the case of one participant. In order to avoid traumatizing her daughter, she feels compelled to hide her emotional experience from her and continue with previous activities.

> "*My daughter… she saw me cry maybe once or twice. She said 'Please, don't cry! Who's the strongest and bravest on this planet?' and I tell you, this got me… And friends who came and helped me and offered to spend time with my daughter but I wanted to continue our activities so that she does not feel that… She already has a father that she cannot count on, I don't want her to feel the same about me*" (Participant 2).

The importance of maintaining a link with the former self (before trauma) through resuming previous roles is clearly expressed by one patient. He states that in doing so he will avoid losing his mind. Also, he manifests a desire to exert control over his trauma by engaging in the activity that caused his amputation.

> "*I'm still using the tractor. But the wife and the children did not let me operate the milling cutter. It cut my leg off! They called my brother-in-law to operate the milling cutter. I was annoyed and said, 'Leave me, do not try to convince me!' … She pulls me back all the time. I'll go crazy and it will be worse!*" (Participant 6).

Social and Family Ties

There is a difference in coping for participants assisted by family members and those who are alone. In the case of the former, we found the same feeling of embarrassment and frustration. Feeling helpless and unable to fulfill the role of provider, one participant had difficulties in accepting the support his family offered.

> "*My whole family was next to me… my wife and father-in-law took turns staying with me at the hospital. I was embarrassed. Instead of me helping them, they were helping me*" (Participant 6).

With little to look forward to, an elderly participant was deeply affected by his state of dependency, which he saw as a hinder to his family.

> "*I never thought I would become a burden for my family*" (Participant 5).

In the case of those who live alone or do not have a solid system of support in place, it is much more difficult. The feeling of being abandoned by friends and family might seriously affect their psychological recovery. Some participants expressed sadness at the idea of being abandoned and losing social support. Also, there was a reluctancy in asking for help.

> "*At first, the few friends and neighbors took great care of me. Now they're coming less and less often. They also have their problems*" (Participant 3).
> "*I am a widower for 11 years. I do not have children. I have three brothers and two sisters, all married and with families. In the hospital all came to see me. There was no room in the hospital ward. Don't worry, they would say, it'll be good, we'll help you. Then they got busy … I rarely get a phone call. I get the help of a niece. But she is busy as well … She has her concerns*" (Participant 1).
> "*I had a lot of support … Friends were there for me during this really difficult time and also acquaintances and students of mine … there was always someone. It was a strong support for me that I was not left alone. Now a little less … they have their lives and they do what they can. But I need someone on a regular basis not on and off, you know?*" (Participant 4).

Phantom Limb

False Sensations

Only two participants in this research, Participants 3 and 7 claim they have not had false perceptions about the amputated limb. The other participants either had these manifestations immediately after surgery or still have them. For one participant, the phantom limb phenomenon was the cause of new injury.

> "*After I got home, I woke up one morning, I was rushing and when I got out of bed I fell straight onto the stump. They took me back to the hospital. Another misfortune … and now almost a year after surgery, I tend to sit one foot over another as I once did*" (Participant 6).

Other participants find these false perceptions to be a hindering factor in their daily activities. When implicit memory kicks in and habitual reactions take over one's mode of being, they are again confronted with their new reality.

> "*Yes, I feel it now. I'm tickling my toe, my thigh, my fingers … I want to massage it, but I realize it's not there. If someone sits beside me on the bed, I tend to protect it. I am stressed because it physically doesn't hurt, but it does psychologically, and I say: leave me alone, ghost!*" (Participant 1).
> "*After the (car) crash I felt pain and my hand getting numb, I still have the numbness. I've been taking drugs for nine months now. I try to change my thoughts and then the pain stops, but the numbness remains. I tend to lean in it, grab the objects with both hands, cut my nails …*" (Participant 4).

One participant reports false sensations especially when he gets angry or at night.

> "*I feel chills, pain …*" (Participant 5).

Body Representation in Dreams

Also, in relation to body representation, some participants reported dreams in which their bodies were intact. Their dreams seem to express a desire for erasing the trauma and regaining normality.

> "*I dream that I have my left arm … that I am normal. I dream I am whole … I never dream of me without my arm*" (Participant 4).
> "*In my dreams I have my leg, I'm running… I never dream of myself without my leg*" (Participant 2).

Emotional Balancing

Determination

Getting accustomed to the new condition made some participants slowly come back to their previous mental state, and even hope that 1 day they will be almost as they were. One participant showed a strong drive toward recovery and overcoming the obstacles that his new condition brought. A strong will to overcome the trauma and repossess what he felt was taken from him.

> "*Now, yes, I'm past this … I do not want to remember. I have to go ahead. I changed my car. I got a special one so I don't have to rely on others. I want to take my life back*" (Participant 6).

For another participant, exposure to successfully adapted people in similar situations seemed to have a positive psychological effect. The idea of the prosthesis revived the possibility of a reduced gap between the old and new self. Also, in this case, other beneficial aspects were acknowledging the trauma and focusing on what remains rather than on what was lost.

> "*Deep down I am optimistic. Even if I'm alone, I hope I can handle it. There are so many people living worse than me, with both legs amputated or an arm and a leg … I happened to meet a former colleague who had an accident 27 years ago. He got hit by a train and his left leg had to be amputated, just like mine. He has a prosthetic one and walks as if he was normal. He told me that some things change, but if I take it seriously, I will succeed …. We must believe in something. I know I'm not going to grow my leg back, but if I can get along well with the prosthesis, and … I'm not going to run, but do the things I need … I'll be happy!*" (Participant 1).

Hope

Hope, determination to prevail, putting your faith in something, internal or external, and the capacity for humor seem to constitute strengths in the adjustment process of some participants.

> "*God? … If He makes miracles He should have done so before my amputation … now all I can do is pray for my leg to grow back! (laughs) … and that's not going to happen. But man must believe in something, if we would not believe in something then we could not hope … So, I live with hope, as any man… not to grow my leg back but to be able to accommodate to my prosthesis … not running, but, you know, to be able to do what I need, even if slower*" (Participant 1).

Feeling acknowledged and valued by her social environment, one participant regained hope for the future. Insofar as events in one's life are believed to be a manifestation of God, this positive context allowed her, through her beliefs, to maintain self-cohesion and to gradually reengage in her former life.

> "*I perceived it as a supernatural intervention … I mean, I did a lot of good in my life. God knows the good that I have done. And God did not forsake me, that's clear … because when I went back to my work from recovery everyone was there for me and that was extraordinary … Joy and gratefulness*" (Participant 4).
>
> "*In fact, faith has helped me. I rely on God. If I did not have this belief, I think I would have gotten to despair*" (Participant 4).

DISCUSSION

The main purpose of this study was to explore psychological consequences in patients with limb amputation. Six main themes emerged from the qualitative data, each with related secondary themes. Given the relative short amount of time passed since amputation (approximately 4–8 months on average), the main focus of the participants was found to revolve around acceptance of loss, mourning, attempts at dealing with negative emotions and regaining their autonomy. The process of constructing a new self-representation was thus in its early stages with most participants still adjusting to the new reality of their life. In this stage, the patients struggled with their new physical appearance, functional limitations, uncertainty about the constraints on their future opportunities, activities, personal agency, social ties, and the impact that these changes have on their internal representational world. For some participants in our study, this impact seemed to be devastating thus leading to a state of denial and continual struggle with negative affects and cognitions. As such, they gave the impression of being stuck in the initial shock and unable to engage in a healthy mourning process and available resources. At the same time, other participants manifested traces of hope for the future and determination to regain a sense of agency and self-worth. One important factor to consider here is the absence of the prosthesis among the participants. According to findings of Lundberg et al. (2011), the experience of the prosthesis ranges from viewing it as a valuable tool to almost becoming a part of the body. It seems that, apart from being a functional element, the prosthesis can also facilitate a psychological continuity, or link with the former self-representation, perhaps easing the transition and integration of a new self-representation.

Initial Impact

In general, amputations are performed due to traumatic causes or planned medical reasons (Ali et al., 2017), the most favorable situation being when the patient is convinced that only by amputation, he/she can survive and thus wishes to amputate, as was the case for two of the participants in this study. The unexpected sudden loss of a member without prior counseling severely disrupts the psychological harmony of the patient. The results in this study show similarities to findings in other studies regarding the emotional reaction to amputation. Patients can have different responses such as sadness, hate, shock, anger, suicidal ideation, or non-acceptance of the situation (Senra et al., 2012). In our study, participants reported experiencing a state of dread after surgery, one that seriously threatened the integrity of the self, almost as if the loss of a limb was announcing the danger of losing self-cohesiveness, a state of disintegration of the self. This in turn enables the mobilization of defenses against this intolerable state, looking to restore a sense of internal coherence and vitality. It is within this psychological setting that participants managed to view their loss as a partial one and gradually relate emotionally to it in more sophisticated ways, enabling the start of the mourning process.

The Need for Retreat

For several of the participants in this study, having suddenly found themselves in a state of dependency and helplessness stirred up deep feelings of embarrassment and anger. As the perspective shifts from total loss to partial loss, participants saw their amputation as a horrible defect that is to be pitied and looked down upon. This state of humiliation rendered the much-needed post-surgery support of family and friends into a pitiful situation, difficult to tolerate for the wounded self. It is perhaps one reason why participants felt the need to isolate themselves, whenever possible, from human contact.

Being upset when stared at by others, perceiving one's body as defective and the need for isolation are common findings among studies in this field (Ostler et al., 2014; Khan et al., 2018). Their need to avoid contact with other people seemed to serve important temporary defensive functions for the vulnerable recovering self, shielding it from experiencing shame and hostility as a result of anticipation of negative attitudes or actual negative attitudes of others (Murray and Forshaw, 2013). This finding is supported by other authors (Bergo and Prebianchi, 2018) who consider that separation from social networks (a recurring theme among amputees) is temporary, being specific to the immediate post-operative period. With time and especially after prosthesis, the patient becomes accustomed to the situation and begins to resume the old connections.

Living in One's Own Head

However, necessary isolation may be in the beginning, it also has the potential to become a pathological element. Lack of significant human interaction means lack of a healthy feedback loop, of opportunities for changes in one's perspective. Thus, the mind is left to answer its own questions, to circle its own fears and unknowns. The scope of existence narrows and several participants in our study were struggling not to "fall prey to despair." For two elderly participants this struggle seemed lost, as they could find no rewarding perspectives of their future. Ruminations about their own guilt in bringing about the amputation was another factor that caused emotional distress. Anxiety was also present in some participants, mainly regarding the uncertainty of the future, being alone, losing their jobs and means of existence. This uncertainty was manifested as a sense of threat, of imminent danger that compels vigilance and thus caused insomnia, negative cognitions, rumination, stress, and irritability.

Almost all previous studies on the psychological aspects of amputation reported a noticeable decrease in the psychological well-being and quality of life (Desmond and MacLachlan, 2002; Schofield et al., 2006; Waqar et al., 2015; Ali et al., 2017; Khan et al., 2018). According to some authors depression and anxiety are moderately high up to 2 years after amputation (Waqar et al., 2015) and so the risk of depression does not diminish as an amputation becomes more remote in time (Rybarczyk et al., 2004). From our theoretical viewpoint, the existence of an adequate interpersonal relationships system (family and friends) is critical in providing the self-object needs that the development of a healthy self requires, including the need for security and soothing. Here, we consider that a basic training of family members regarding medical and psychological issues associated with amputation is recommended and can encourage more realistic and balanced attitudes and responses, while diminishing the risk of actually amplifying existing feelings of helplessness, anger, and despair.

A New Frustrating Reality

In our study anger was often the response to realizations of constraints and limitations that the new condition brought to the participants. In some cases, the perceived unfairness of the trauma exacerbated feelings of anger and opened the way for resentment and envy towards other people. For others, confronting their impaired capacity to fully engage in previous daily activities and roles was a great frustration that left them feeling angry and bitter. Also, the realization that previous pleasurable activities and hobbies were now off limits was a source of great distress. Another hindering aspect for the participants in our study was the difficulty associated with discovering and integrating the limits of the new body scheme within the self, in terms of functionality. Phantom limb sensations coupled with automatic reactions were often the cause of cognitive dissonance and even injury, as was the case with one of the participants. Pain from the phantom limb may also exacerbate feelings of depression (Murray and Forshaw, 2013), cause mood dysregulation (Trevelyan et al., 2016) and predispose the person to accidents (Senra et al., 2012). Generally, these false sensations are reported in 50–85% of amputees, with varying intensity and duration, spanning weeks or months after surgery (Margalit et al., 2013). This aspect of amputation generates frustration and stress and it can become a threat to the rehabilitation process and the psychological and physical well-being of the person.

(Not So) New Horizons

Despite obstacles, some the participants in our study showed an increased desire to return to previous roles and activities. This seemed to provide a shielding effect from the negative effects of the trauma. The need for self-restoration, as manifested through resuming previous activities, can be seen as a denial of reality but at the same time it provided participants with the opportunity to adjust and also re-instantiate connections with their former ambitions and goals. This helped them somewhat establish a sense of continuity. Adjustment and regaining a sense of normality is often seen as a re-negotiation of self-identity (Hamill et al., 2010; Senra et al., 2012). This means aligning the "internal self," the existing self-representation, to the "external self," the person with a disability and altered body image. This process could be more effective if there is an opportunity to resume previous roles, given that the additional constraints are not entirely prohibitive. In such circumstances, the new reality might be less alienated, less disconnected from past experience thus facilitating psychological health and enabling the person to access available internal and external resources. These findings are supported by previous results (Murray, 2010; Dunne et al., 2014; Zhu et al., 2020) showing that the desire to connect with previous interests and activities was a way to recover a feeling of normality. From our theoretical viewpoint, involving the amputee in a process of reality negotiation (Carpenter, 1994) and the gradual accommodation of a new self-representation is crucial. In time, the integration of trauma is possible thus further strengthening the continuity in the sense of self by decreasing dissociation. For example, one participant felt that his efforts toward resuming previous activities were being sabotaged by his family which gave him serious distress.

Hence, these findings suggest that such endeavors on the part of amputees should be encouraged and provided with an adequate support and oversight.

In or Out

In our study, the degree to which one has sufficiently internalized self-object functions or relies on external sources of sustainment, seems to be linked to the mourning process, consequent adaptation capacity, and psychological well-being. Acknowledging the trauma and focusing on current resources and faith in one's strengths seemed to have a positive effect for some participants. Those that were more optimistic about the future were more inclined to explore existing possibilities for improving their condition and to engage their environment. For example, one participant had modifications done to his vehicle in order to be able to drive, while another found hope in the idea of having prosthesis and resuming physical activities in the future. Previous studies (Hall et al., 2005; Zhu et al., 2020) have had similar findings regarding the rehabilitation process. They found that the ability to self-manage and make adjustments influenced how easily one could regain a sense of normality and balance in their lives.

The support of family, friends, and colleagues, as well as faith in God were pillars of strength for one participant. In her situation, the source of self-cohesion came from outside, from people who provided essential functions of validation and appreciation, and through them, the belief in the divine was maintained. For another participant, the strength to overcome obstacles came from her fear of traumatizing her supportive daughter. For her, succumbing to adversity was not an option. Similar to findings in other studies (Murray and Forshaw, 2013; Khan et al., 2018), some participants in our research benefited from the assistance of friends and family, especially in the restoration of the sense of self-worth. For another participant, the interventions of the family were felt as overprotective, this being in line with the idea that the quality of the relationships is of significant importance (Hamill et al., 2010). The feeling of abandonment by friends and family was also present among our participants. This comes to reinforce the fears of participants of being left alone to dread the existential uncertainty. A complex picture about the experience of participants emerges here, one that takes into account apparently contradictory needs, such as need for isolation, passive-dependent needs and need for autonomy. From a Self psychology perspective, this becomes less paradoxical if all these needs are allowed to manifest in the context of a supporting self-object matrix.

Assessing the dynamics of the self, in relation to self-object needs, could prove very useful in determining the kind of support one requires in the case of amputation. These findings could encourage specialists working with amputees to take into consideration case by case evaluations form a Self psychology perspective in order to develop targeted plans for individual recovery.

Regardless of the circumstances that led to amputation, it brings a dramatic change in the life of the individual that undergoes a shock phase, acceptance and finally adapting to the new situation. But long after surgery, patients, in addition to physical and mental suffering, face a number of difficult problems: the cost of the prosthetic limb, the pursuit of compensation in the case of car or work-related accidents, continuing treatment for chronic disease (such as diabetes), decreased sexual activity, especially in young people, and, in particular, uncertainty about the future. The latter is the most commonly reported feeling (Galván et al., 2009; Sales et al., 2012; Simsek et al., 2017; Bergo and Prebianchi, 2018) and it was also present in the findings of our study. It stands to reason that in order for the person to regain a sense of normality and to be able to develop an adaptive new self-representation as a participative active being in the environment, a complex system of support and resources must be in place.

CONCLUSION AND LIMITATIONS

This study presents an idiographic analysis, wishing to draw attention on the need to develop intervention and support plans by physicians and therapists for patients who have undergone amputations, based on identifying the psychological consequences of limb amputation.

In a qualitative study (Franchini and Savoia, 2013; Bergo and Prebianchi, 2018), it was observed that patients who participated in group psychotherapy became more independent and showed greater acceptance, faster rehabilitation, and positive thinking. Therefore, the efficacy of such programs may be enhanced if the practitioners know the phenomenology of the various psychological consequences in the case of patients with limb amputation. Presenting to patients the situations of people who have successfully adapted to this disability and direct interaction with such people, often result in providing inspirational motivation, optimism, and balance.

Also, the present study wants to raise awareness among medical staff about the psychological problems faced by amputees. Understanding them, the trauma associated with amputation, the loss and the permanent suffering will generate attachment, respect and compassion, improving the medical approach. Consequently, it is necessary to set up a multidisciplinary team (surgeons, neurologists, psychologists, physiotherapists, and orthotists) in order to develop informed interventions aimed at diminishing the undesirable effects of amputation and enabling the patient to resume a normal life. In this respect, a Self psychology perspective could help to better differentiate the psychological needs that individuals have in regard to their adjustment process. Also, this approach could also be useful in informing family members, caregivers, or healthcare professionals about how empathic understanding of the amputee's experience can facilitate appropriate responses, this in turn providing a more adequate environment for the gradual restoration of self-agency and self-worth, while diminishing the risk of negative reactions.

A closely related approach to the one proposed here is founded in the Self-determination theory (SDT) developed by Deci and Ryan (1985). This macro theory of human motivation and personality has focused on need support as a process that facilitates internalization (autonomous self-regulation) and the development of adequate motivation and well-being. Over the last two decades, research testing the applicability of SDT within health contexts has provided good evidence for a variety of health outcomes including depression, anxiety, somatization, and quality of life (Williams and Deci, 2001; Ryan et al., 2008; Williams et al., 2009; Ng et al., 2012; Chemtob et al., 2019). One of the main features of SDT is its understanding of the importance that the social context plays in the process of internalization. Self-psychology, as a developmental model, goes one step further and provides a higher resolution framework that can help practitioners in health care contexts better connect to the patient-professional experience. We think this aspect is useful since, given the time constraints one usually encounters in the medical system, designed interventions, focused on types of action and language, for example, may acquire a stereotypical quality.

However, the limitations of this study warrant further investigation. First, the small number of participants limits the ability of this study to touch upon different types of experiences regarding amputation and possible differences that could emerge due to age, gender, socioeconomic and ethnic background, cause and type of amputation or time elapsed since amputation. However, the aim of IPA is to investigate how individuals experience a particular phenomenon and, as such, a sample as the one used in our study is justified. Second, the relative short amount of time passed since amputation narrows the scope of the research and leaves out opportunities for exploring subsequent themes. A follow-up study would be needed in order to assess the outcomes of the participant's adjustment efforts. Nevertheless, this time frame provided the opportunity to extract a more actual and accurate account of the experience and psychological impact of amputation.

All things considered, the findings in this study support the existing literature and also offer insight into how self-representation is affected by the loss of a limb. Also, it draws attention to the complexity of the adjustment process and the need for addressing it on multiple levels of analysis.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because of the sensitive and confidential nature of the information. Requests to access the datasets should be directed to catalina.rosca@politice.ro.

ETHICS STATEMENT

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Ethics Committee of NUPSPA (protocol code no. 145, April 01, 2019). All respondents were made aware of the procedures and gave verbal consent to participation. Written informed consent from the participants was not required to participate in this study in accordance with the institutional requirements.

AUTHOR CONTRIBUTIONS

All authors have made substantial and equal contribution in all stages of the present study. All authors read and approved the final version of the paper.

REFERENCES

Ali, S., Kaniz, S., and Haider, F. (2017). Psychological adjustment to amputation: variations on the bases of sex, age and cause of limb loss. *J. Ayub Med. Coll. Abbottabad* 29, 303–307.

Beck, J. S. (2011). *Cognitive Behavior Therapy: Basics and Beyond*. New York: Guilford Press.

Beck, A. T., Emery, G., and Greenberg, R. L. (2005). *Anxiety Disorders and Phobias: A Cognitive Perspective*. New York, NY, US: Basic Books.

Bergo, M., and Prebianchi, H. B. (2018). Emotional aspects present in the lives of amputees: a literature review. *Revista Psicologia: Teoria e Prática* 20, 47–60. doi: 10.5935/1980-6906/psicologia.v20n1p47-60

Boccolini, F. (1995). "Reabilitação do amputado," in *Doenças Vasculares Periféricas. 2nd Edn*. ed. H. A. MaffeiF (Tijuca: MEDSI), 257–281.

Carpenter, C. (1994). The experience of spinal cord injury: the individual's perspective – implications for rehabilitation practice. *Phys. Ther.* 74, 614–628. doi: 10.1093/ptj/74.7.614

Chemtob, K., Rocchi, M., Arbour-Nicitopoulos, K., Kairy, D., Fillion, B., and Sweet, S. N. (2019). Using tele-health to enhance motivation, leisure time physical activity, and quality of life in adults with spinal cord injury: a self-determination theory-based pilot randomized control trial. *Psychol. Sport Exerc.* 43, 243–252. doi: 10.1016/j.psychsport.2019.03.008

Deci, E. L., and Ryan, R. M. (1985). *Intrinsic Motivation and Self-Determination in Human Behavior*. New York, NY: Plenum.

Desmond, D., and MacLachlan, M. (2002). Psychological issues in prosthetic and orthotic practice: a 25 year review of psychology in prosthetics and orthotics international. *Prosthetics Orthot. Int.* 26, 182–188. doi: 10.1080/03093640208726646

Dunne, S., Coffey, L., Gallagher, P., and Desmond, D. (2014). "If I can do it I will do it, if I can't, I can't": a study of adaptive self-regulatory strategies following lower limb amputation. *Disabil. Rehabil.* 36, 1990–1997. doi: 10.3109/09638288.2014.885993

Franchini, M. G., and Savoia, M. G. (2013). Psicoterapia de Grupo para pacientes diabéticos amputados e seus cuidadores. *Arq. Med. Hosp. Fac. Cienc. Med. Santa Casa São Paulo* 58, 10–17.

Galván, G. B., Amiralian, M. L., and Moraes, T. (2009). Corpo e identidade: reflexões acerca da vivência de amputação. *Estud. Psicol.* 26, 391–398. doi: 10.1590/S0103-166X2009000300012

Hall, N. J., Rubin, G. P., Dougall, A., Hungin, A. P. S., and Neely, J. (2005). The fight for "health-related normality": a qualitative study of the experiences of individuals living with established inflammatory bowel disease (IBD). *J. Health Psychol.* 10, 443–455. doi: 10.1177/1359105305051433

Hamill, R., Carson, S., and Dorahy, M. (2010). Experiences of psychosocial adjustment within 18 months of amputation: an interpretative phenomenological analysis. *Disabil. Rehabil.* 32, 729–740. doi: 10.3109/09638280903295417

Horgan, O., and MacLachlan, M. (2004). Psychosocial adjustment to lower-limb amputation: a review. *Disabil. Rehabil.* 26, 837–850. doi: 10.1080/09638280410001708869

Khan, M. J., Dogar, S. F., and Masroor, U. (2018). Family relations, quality of life and post-traumatic stress among amputees and prosthetics. *Pak. Armed Forces Med. J.* 68, 125–130.

Kohut, H. (1966). Forms and transformations of narcissism. *J. Am. Psychoanal. Assoc.* 14, 243–272. doi: 10.1177/000306516601400201

Kohut, H., and Wolf, E. (1978). The disorders of the self and their treatment: an outline. *Int. J. Psychoanal.* 59, 413–425.

Lundberg, M., Hagberg, K., and Bullington, J. (2011). My prosthesis as a part of me: a qualitative analysis of living with an osseointegrated prosthetic limb. *Prosthetics Orthot. Int.* 35, 207–214. doi: 10.1177/0309364611409795

Margalit, D., Heled, E., Berger, C., and Katzir, H. (2013). Phantom fighters: coping mechanisms of amputee patients with phantom limb pain: a longitudinal study. *Open J. Orthop.* 3, 300–305. doi: 10.4236/ojo.2013.37055

Markus, H., and Kunda, Z. (1986). Stability and malleability of the self-concept. *J. Pers. Soc. Psychol.* 51:858. doi: 10.1037/0022-3514.51.4.858

McKechnie, P. S., and John, A. (2014). Anxiety and depression following traumatic limb amputation: a systematic review. *Injury* 45, 1859–1866. doi: 10.1016/j.injury.2014.09.015

Murray, C. D. (ed.) (2010). "Understanding Adjustment and Coping to Limb Loss and Absence Through Phenomenologies of Prosthesis Use," in *Amputation, Prosthesis Use, and Phantom Limb Pain: An Interdisciplinary Perspective*. New York: Springer, 81–99.

Murray, C. D., and Forshaw, M. J. (2013). The experience of amputation and prosthesis use for adults: a metasynthesis. *Disabil. Rehabil.* 35, 1133–1142. doi: 10.3109/09638288.2012.723790

Ng, J. Y. Y., Ntoumanis, N., Thøgersen-Ntoumani, C., Deci, E. L., Ryan, R. M., Duda, J. L., et al. (2012). Self-determination theory applied to health contexts: a meta-analysis. *Perspect. Psychol. Sci.* 7, 325–340. doi: 10.1177/1745691612447309

Ostler, C., Ellis-Hill, C., and Donovan-Hall, M. (2014). Expectations of rehabilitation following lower limb amputation: a qualitative study. *Disabil. Rehabil.* 36, 1169–1175. doi: 10.3109/09638288.2013.833311

Reid, K., Flowers, P., and Larkin, M. (2005). Exploring lived experience. *Psychologist* 18, 20–23.

Rodrigues, S. R. (2011). Uma psicanalista em uma equipe multidisciplinar: atendimento a pacientes com amputação em reabilitação com prótese (Dissertação de Mestrado). Instituto de Psicologia, Universidade de São Paulo, São Paulo-SP.

Ryan, R. M., Patrick, H., Deci, E. L., and Williams, G. C. (2008). Facilitating health behaviour change and its maintenance: interventions based on self-determination theory. *Eur. J. Health Psychol.* 10, 2–5.

Rybarczyk, B., Edwards, R., and Behel, J. (2004). Diversity in adjustment to a leg amputation: case illustrations of common themes. *Disabil. Rehabil.* 26, 944–953. doi: 10.1080/09638280410001708986

Saakvitne, K. W., Tennen, H., and Affleck, G. (1998). Exploring thriving in the context of clinical trauma theory: constructivist self development theory. *J. Soc. Issues* 54, 279–299. doi: 10.1111/0022-4537.661998066

Sales, L. M. R., Leite, R. F. B., Coura, A. S., and Muniz, C. M. C. (2012). Repercussões psicossociais da amputação: concepções de pessoas que as vivenciam. *Rev. pesqui. cuid. fundam.* 4, 315–326.

Sandler, J., and Rosenblatt, B. (1962). The concept of the representational world. *Psychoanal. Study Child* 17, 128–145.

Schofield, C. J., Libby, G., Brennan, G. M., MacAlpine, R. R., Morris, A. D., and Leese, G. P. (2012). Beyond the body image: a qualitative study on how adults experience lower limb amputation. *Clin. Rehabil. J.* 26, 180–190. doi: 10.1177/0269215511410731

Seidel, E., Lange, C., Wetz, H. H., and Heuft, G. (2006). Anxiety and depression after loss of a lower limb. *Orthopade* 35, 1152–1158. doi: 10.1007/s00132-006-1017-8

Senra, H., Oliveira, R. A., Leal, I., and Vieira, C. (2012). Beyond the body image: a qualitative study on how adults experience lower limb amputation. *Clin. Rehabil. J.* 26, 180–190. doi: 10.1177/0269215511410731

Simsek, N., Ozturk, G. K., and Nahya, Z. N. (2017). Psychosocial problems and care of patients with amputation. *EJMI* 1, 6–9. doi: 10.14744/ejmi.2017.22931

Smith, J. A. (1995). "Semi-Structured Interviewing and Qualitative Analysis," in *Rethinking Method in Psychology*. eds. J. A. Smith, R. Harré and L. Van Langehhore (London: Sage Publication), 9–27.

Smith, J. A. (2007). Hermeneutics, human sciences and health: linking theory and practice. *Int. J. Qual. Stud. Health Well Being* 2, 3–11. doi: 10.1080/17482620601016120

Smith, J., and Dunworh, F. (2003). "Qualitative Methodology," in *Handbook of Developmental Psychology*. eds. K. Connoly and J. Valsiner (London: Sage Publication).

Smith, A. J., Flowers, P., and Larkin, M. (2009). *Interpretative Phenomenological Analysis. Theory, Method and Research*. London: Sage Publication.

Smith, J., Jarman, M., and Osborne, M. (1999). "Doing Interpretative Phenomenological Analysis," in *Qualitative Health Psychology*. eds. M. Murry and K. Chamberlain (London: Sage Publication).

Trevelyan, E. G., Turner, W. A., and Robinson, N. (2016). Perceptions of phantom limb pain in lower limb amputees and its effect on quality of life: a qualitative study. *Br. J. Pain* 10, 70–77. doi: 10.1177/2049463715590884

Waqar, S., Noor, R., and Khan, M. M. H. (2015). Depression, anxiety & psychological adjustment among amputees. *IJRS* 4, 14–18.

Williams, G. C., and Deci, E. L. (2001). Activating patients for smoking cessation through physician autonomy support. *Med. Care* 39, 813–823. doi: 10.1097/00005650-200108000-00007

Williams, G. C., Niemiec, C. P., Patrick, H., Ryan, R. M., and Deci, E. L. (2009). The importance of supporting autonomy and perceived competence in facilitating long-term tobacco abstinence. *Ann. Behav. Med.* 37:315. doi: 10.1007/s12160-009-9090-y

Zhu, X., Jia Goh, L., Chew, E., Lee, M., Bartlam, B., and Dong, L. (2020). Struggling for normality: experiences of patients with diabetic lower extremity amputations and post amputation wounds in primary care. *Prim. Health Care Res. Dev.* 21:e63. doi: 10.1017/S146342362000064X

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SYSTEMATIC REVIEW
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Systematic Review of Efficacy of Interventions for Social Isolation of Older Adults

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Background: The social isolation of older people is a growing public health concern. The proportion of older people in society has increased in recent decades, and it is estimated that ∼40% of the population will be aged 50 or above within the next few decades. This systematic review aims to summarize and renew knowledge of the effectiveness of existing interventions for alleviating social isolation of older adults.

Methods: Relevant electronic databases, including Cochrane Library, CINAHL, SCOPUS, and Web of Science, were searched by a systematic evaluation method. Eligible randomized controlled trial (RCT) studies were published between 1978 and 2021 in English or Chinese. The primary and secondary outcomes were social isolation and loneliness. The quality of the included RCTs was scored by the Cochrane risk-of-bias tool to assess their quality. Two independent reviewers extracted data, using a standardized form. Narrative synthesis and vote-counting methods were used to summarize and interpret study data.

Results: Twenty-four RCTs were finally included in this review. There was evidence of substantial heterogeneity in the interventions delivered. The overall quality of included studies indicated a low-to-medium risk of bias. Eighteen of 24 RCTs showed at least one dimension effect on reducing social isolation. The interventions with accurate targeting of clients in social and public places had more obvious effect. The interventions in which older people are active participants also appeared more likely to be effective. In addition, group intervention activities and individual intervention interviews were effective in improving structural social support; mixed intervention, and group intervention on training support significantly improved functional social support.

Conclusions: This study suggests that group and mixed intervention targeting of older adults could be helpful for alleviating social isolation problems. The use of modern technology for remote services could also present good results. More well-conducted RCTs of the effectiveness of social interventions for alleviating social isolation are needed to improve the evidence base. Especially as the debating results of remote interventions, further research in this field should be conducted.

Keywords: social isolation, loneliness, older adults, health, systematic review, intervention

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BACKGROUND

Social isolation is a major threat to the health of older adults. There are many risk factors in social isolation in old age, including the lack of family members, rare or no daily communication with friends, depression, and a solitary lifestyle (Iliffe et al., 2007). Studies have indicated that social isolation and loneliness are common negative emotions, and social states among older adults that could lead, without timely intervention, to even more serious situations (Laursen and Hartl, 2013). Subsequently, research has indicated that 40% of adults over the age of 50 often felt lonely (Ferreiraalves et al., 2014). Although "loneliness" is often co-emergent and mutually influential with "social isolation," they are two different concepts (Grenade and Boldy, 2008). Loneliness relates specifically to negative feelings of one about a situation. It may reflect social isolation or a sense of abandonment, resulting from an excessive gap between expectations and reality (Petersen et al., 2020) and increase with age (Li and Zhou, 2002), while the definitions of social isolation incorporate "structural" and "functional" social support (Lu et al., 2013). Social isolation is, therefore, multidimensional and includes the lack of structural and functional social support (Lubben and Gironda, 2003; Victor et al., 2010). In this research, social isolation was divided into two dimensions: "structural social support" and "functional social support." Structural social support is an objective evaluation of the scale or frequency of social support participation (Lubben and Gironda, 2003; Victor et al., 2010); and functional social support is a subjective judgment on the quality of social support, including feelings, tools, and information provided by the perceived responses of others (Hall et al., 2019). According to this definition, social isolation is a multidimensional concept, which results from the lack of quality and quantity of social support (Petersen et al., 2020). The current study adopted this definition as the basis for research.

Social isolation is an essential threat to the health of older adults, and many scholars have provided evidence for methods of alleviating this problem. A meta-analysis conducted in 2010 ($n = 308$, mean age = 64 years; Lunstad et al., 2010) indicated that social isolation of people with strong social relationships might decrease by 50%. The compound variables used to calculate "strong social relationships" included loneliness and social isolation. Specific studies assessing the relationship between social isolation and health have reached different conclusions. For example, social isolation can lead to increased mortality, worse self-rated health (Cornwell and Waite, 2009), more susceptibility to Alzheimer's disease (Fratiglioni et al., 2000), and an increased rate of disability in older adults (Lund et al., 2010). A recent study suggested that social isolation was negatively correlated with health-related quality of life and health status of older adults (Hawton et al., 2010). Much evidence has accumulated to indicate that social isolation can affect the health of an individual. Therefore, it is an important public health problem. Moreover, the results of interventions for social isolation must be scientifically evaluated to reduce its negative impact.

There are several systematic reviews of this topic. For example, one study summarized interventions for loneliness. However, it does not fully address the effectiveness of interventions for social isolation (Masi et al., 2011). In this article, data were integrated from heterogeneous samples and included out-of-school children, homeless teenagers, and older adults. Moreover, the interventions included online chat rooms, exercise, social events, and training support. Although there is a debate about the appropriateness of meta-analysis of heterogeneous data, this kind of systematic evaluation of outcome research has seldom been reported. Recently, two systematic reviews have been conducted that included studies before 2016 (Stojanovic et al., 2016; Poscia et al., 2018). However, in these two systematic reviews, there was no quality evaluation process, and RCTs were not included. Moreover, they did not search the three main databases of PsycINFO, PubMed, and Proquest. Since then, many changes have taken place in the social environment. Remote services have been widely adopted, especially with the rapid development of information technology. Remote and other new-tech intervention RCTs targeting social isolation in older adults have been published until 2021, which necessitates updating of current knowledge.

Outcomes regarding structural social support and functional social support are important indicators of effect in the multidimensional definition of social isolation used in our review. In addition, reporting on loneliness may also contribute to the understanding of intervention effects. Therefore, this systematic review was designed to summarize and update the current knowledge about the efficacy of existing interventions for alleviating social isolation and loneliness among older adults.

METHODS

Search Strategy

The literature published from January 1978 to January 2021 was systematically retrieved, using ENDNOTE X6, to manage the literature. Electronic database retrieval included PsycINFO, PubMed, Proquest, Cochrane Library, Applied Social Sciences Index and Abstracts (ASSIA), CINAHL databases, SCOPUS, Web of science, China National Knowledge Infrastructure (CNKI), and Wanfang Data Knowledge Service Platform (WANGFANG). Another search retrieved social isolation and/or loneliness in the review and has been included in the study of the reference literature; retrieval from the University of Southern California Social Work Institute database, evidence-based medicine research center of Lanzhou University, and Population Research Institute of Southwestern University of Finance and Economics. Contacts were made with scholars within the network of the authors to obtain information about ongoing studies. Search words used were as follows: older/elder/senior/aged/geriatric, isolation/isolate/isolated, lone/loneliness/alone/solitude/solitary, social support/network/relations, psychosocial intervention, treatment/therapy, clinical trial, explanatory trial, pragmatic trial, and randomized controlled trial. Search terms used were as follows: (isolation/isolate/isolated) or (lone/loneliness/alone/solitude/solitary) or (social support/network/relations) and (older/elder/senior/aged/geriatric) and (intervention/therapy/clinical trial/explanatory trial) or (explanatory trial/pragmatic trial/randomized controlled trial). The search terms in different databases were slightly different. Therefore, we also searched through the reference lists of systematic review articles on social isolation.

Review Strategy

According to the research topic and summary, two researchers (FT and CLY) made a preliminary identification of study criteria. The third researcher (FF) read the abstract of the indeterminate literature and determined the specific discussion about the disagreement. A pair of independent raters selected abstracts for full review based on inclusion/exclusion criteria. Two independent reviewers extracted data, using a standardized form. Due to the heterogeneity of different outcome indicators (e.g., family ties increased, feeling of social support, social relationship), meta-analysis is not suitable for use. According to the analysis method of the three previous evaluations (Díaz and García, 2016; Canedo-García et al., 2017; Li et al., 2018), narrative synthesis and vote-counting methods were used to summarize and interpret study data. The current review was reported in accordance with the latest PRISMA guidance (Page et al., 2021).

Inclusion and Exclusion Criteria

The primary and secondary outcomes are social isolation and loneliness. All papers selected for final inclusion met the following criteria: (i) older adults over 50 years of age with no mental illness or cognitive impairment; (ii) the purpose of the intervention was to alleviate social isolation or loneliness; (iii) the results of social isolation intervention were reported; (iv) there were randomized controlled trials but no drug trials; and (v) the paper was written in Chinese or English. Exclusion criteria for the study: (i) study samples aged younger than 50 years; (ii) not used a randomized controlled trial (RCT); (iii) drug intervention was used; and (iv) outcomes reporting only on loneliness but no social isolation.

The Quality Evaluation of the Research

Because of the heterogeneity of the intervention types and results of the trial, quantitative analysis of data was not used in the review, so the method of narrative synthesis was applied to analyze the effect of interventions. In the quality evaluation of open randomized controlled trials, we chose not to use the Jadad standard (Berger, 2006) as this is focused on blind and random sequences; therefore, the Cochrane risk-of-bias tool was deemed more appropriate (Ma et al., 2012). In this paper, based on the Cochrane risk of bias, the quality of the randomized control trial and the bias risk level were identified, and the grading principle of JADAD was used to evaluate the overall research quality. The Cochrane bias-risk tool evaluation principle involves six aspects: selection bias, implementation bias, measurement bias, data bias, publication bias, and other bias (Higgins et al., 2011). The system evaluation report is based on the PRISMA (preferred reporting items for systematic reviews and meta-analyses) standard (Page et al., 2021).

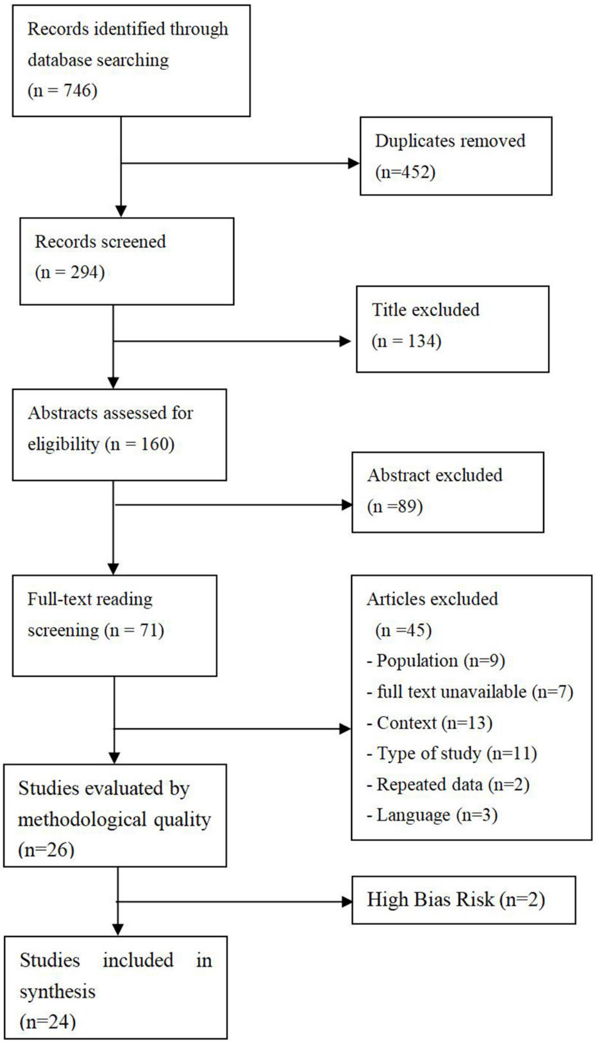

FIGURE 1 | Eligibility and screening of studies considered for the systematic review.

RESULTS

About 746 items were found in the related research, with 452 duplicates removed, 268 of the studies excluded as they did not meet the selection criteria. Two studies were excluded because of high-bias risk. Twenty-four studies were eventually included (**Figure 1**).

Inclusion of the Study

A total of 24 randomized controlled trial studies were included with a total of 4,078 subjects, each involving 26–708 cases. **Table 1** (including two high-bias risks) introduces the characteristics of these studies in accordance with the principle of PICOS, including: population, intervention, comparison, outcomes, and study type (Methley et al., 2014).

Of all the studies, there were only two studies from mainland China (Hang et al., 2011; Yi et al., 2012), and one of them

TABLE 1 | Characteristics of studies stratified by PICOS.

Authors, time (country)	Population	Intervention	Comparison	Outcome	Study type
Harris and Bodden (1978) (USA)	102 cases of incapacitating elderly in the community The mean age is 77	Group intervention activities	Conventional intervention	Chicago Social Activity Scale	Community/public places
Constantino (1988) (USA)	150 widowed women I1 (50)/I2 (50)/C (50) The mean age is 58	Group intervention activities	Not described	RSAS,E(DACL)	School/established place
Lökk (1990) (Sweden)	65 cases of community living disabled elderly (33/C (32) Average age I (76)/C (78) Female ratio I (52%)/C (50%)	Group intervention activities	Standard recovery project	Outdoor activity index, social network index	Care center
Ollonqvist et al. (2008) (Finland)	708 cases of community elderly I (343)/C (365) Average age 78 Female ratio I (85%)/C (87%)	Group intervention activities	No intervention	Loneliness, satisfaction with contact with children, the number of friends and relatives	Rehabilitation center
Routasalo et al. (2009) (Finland)	235 cases of community living in the elderly with lonely orientation I (117)/C (118) Average age 80 Female ratio I (74%)/C (73%)	Group intervention activities	No intervention	UCLA, Lubben's social networking scale, and social activity and mental health status	Community center/public place
Black et al. (2014) (USA)	26 Tai chi elderly people scored ≥40 loneliness scale	Group intervention activities	Not described	psychological Stress Scale, social network index	Community
Chan et al. (2017) (HongKong)	48 elderly persons, not engaged in any social activities Mean age: 77.3 years Women:76%	Group intervention activities	Regular home visits by social workers.	The Lubben social network, De Jong Gieveld loneliness scales, social support questionnaire	Home, community
Ristolainen et al. (2020) (Finland)	345 elderly persons, age 65+ I(159)/C(186); famle radio I (82.2%)/C(83.6%)	Group intervention activities	No intervention	UCLA DOM3	Not clear
Fukui et al. (2003) (Japan)	50 cases of early breast cancer women I (25)/C (25) Average age is 53	Group intervention training support	Candidate interventions	UCLA, questionnaire	Hospital
Savelkoul and de Witte (2004) (Norway)	168 cases of chronic rheumatic patients with I (56)/C1 (56)/C2 (56) Average age 53/52/51 Female ratio I (77%)/C1 (59%)/C2 (73%)	Group intervention training support	Mutual help group	de Jong Gierveld, social support interactive table	Not clear
Kremers et al. (2006) (Norway)	142 Community Single Women I (63)/C (79) Average age I (63)/C (66)	Group intervention training support	No intervention	de Jong Gierveld	Not clear
Bøen et al. (2012) (Norway)	138 patients from 14 elderly centers (77)/C (61). Intervention group 80 years old accounted for 60%, controlled group 80 + accounted for 50% Female ratio I (60%)/C (55%)	Group intervention training support	No intervention/daily activities	SF-36, CES-D, HSCL-10	Geriatric center
Saito et al. (2012) (Japan)	63 elderly people who have settled for more than 2 years after migration (42)/C (21) Mean age I (73)/C (73) Female ratio I (60%)/C (70%)	Group intervention training support	Waiting list	LSI-A,GDS, AOK, and loneliness and social support	Established public place

(Continued)

TABLE 1 | Continued

Authors, time (country)	Population	Intervention	Comparison	Outcome	Study type
White et al. (2002) (USA)	100 nursing homes and concentrated elderly people I (51)/C (49) Average age I (71)/C (72) Female proportion I (71%)/C (82%)	Groups intervene in remote services	Conventional care	UCLA, Number of close friends, CES	In nursing homes/housing
Schulz (1976) (USA)	Residents I1 (10)/I2 (10)/C1 (10)/C2(10) of 40 churches Average age I1 (85)/I2 (80)/C1 (83)/C2 (78) Women 90%	Individual intervention interview	(1) random access (2) no intervention	The activity index, Wohlford hope scale	Geracomium
MacIntyre et al. (1999) (Canada)	26 home care or home care beneficiaries were I (15)/C (11) The mean age was I (80) and/C (79) The female ratio was I (58%)/C (80%)	Individual intervention interview	Routine intervention	Personal resource questionnaire	Private residence
Yi et al. (2012) (China)	144 cases of community aged and elderly living in the home were I (74)/C (70) The mean age was I (85) and /C (84) The female ratio was I (80%)/C (76%)	Individual intervention interview	Door-to-door service according to demand.	GDS-15, UCLA	Private residence
Heller et al. (1991) (USA)	565 cases of low-income families female I (291)/C (274)	Individual intervention in remote service	No intervention	Paloutzian and ellison loneliness scale, CES-D, SSRS	Private residence
Brennan et al. (1995) (USA)	102 patients with community-owned Alzheimer's disease (AD) patients I (51)/C (51) Average age is 64 Female Proportion is 67%	Individual intervention in remote service	Local community service	CES-D, Instruments and emotional social support scale, social contacts, and records of medical services	Private residence
Morrow et al. (1998) (USA)	61 elderly patients with suicidal tendencies were I (30) and/C (31) The average age was 76 The female ratio was 85%	Individual intervention in remote service	Waiting list	GDS, OARS, Social isolation	Private residence
Slegers et al. (2008) (Norway)	107 cases without Internet experience community elderly I (62), /C1 (45)/C2 (68), /C3 (61)	Individual intervention in remote service	Remote service not accepted	de Jong Gierveld, SF-36, The symptom checklist	Private residence
Mountain et al. (2014) (UK)	70 subjects, with good cognitive function, lived independently in a British city. Women's ratio I (66%)/ C (51%)	Mixed intervention in remote service	Not described	SF-36,MH	Home
Czaja et al. (2017) (USA)	300 elderly people at risk of social segregation, Average age I (76.9)/C (75.3) Proportion of women I (79.3%)/C (76.7%)	Mixed intervention in remote service	No intervention	Social isolation Index, Social support Index, computer proficiency Index and attitude toward Technology	Personal residence

(Continued)

TABLE 1 | Continued

Authors, time (country)	Population	Intervention	Comparison	Outcome	Study type
Drentea et al. (2006) (USA)	Of 183 patients with Alzheimer disease (AD), I (94)/C (89) The mean age was I (73) and/C (71) The female ratio was I (58%)/C (66%)	Mixed intervention	conventional therapy	SSNL, Social support satisfaction	Private residence
Hang et al. (2011) (China)	There were 80 empty nest elderly patients with depressive symptoms, I (40), and/C (40) The mean age was I (72) and/C (71) The female ratio was I (58%)/C (50%)	Mixed intervention	No intervention	GDS, UCLA, MUNSH	Community (Group)/private residence (individual)
Lai et al. (2020) (Canda)	60 community-dwelling older Chinese immigrants aged 65 and older I (30)/C (30). The female ratio I(66.7%)/C(60%)	Mixed intervention	Received brief telephone calls	DJLS-6, LSNS	Not clear (Group)/private residence (individual)

I (N), intervention group (N), C (N), control group (N); N, number of objects or proportion; subjects were the number of baseline or pretest interventions. RSAS, the social adaptation scale; BDI, Duke depression scale; (DACL), E; depression adjective checklist; GDS, geriatric depression scale; SF, short form health survey; CES-D, CES-D; HSCL psychological symptom checklist, self-rating scale; DJLS-6, De Jong loneliness scale-6; OARS, Duke University table SSNL; social network scale; LSI-A, self-rating scale, life satisfaction index; AOK loneliness scale; MUNSH, Memorial University of Newfoundland scale of happiness.

belonged to high risk of bias. The rest of the studies were from Hong Kong, Europe, and other developed countries. The United States occupied 10 studies, while the low-risk bias research was mostly from Finland (Ollonqvist et al., 2008; Routasalo et al., 2009).

In terms of the intervention forms, there were three main categories: group intervention, individual intervention, and mixed intervention. Fourteen studies were conducted using group interaction interventions (e.g., Harris and Bodden, 1978; Constantino, 1988; Lökk, 1990; Ollonqvist et al., 2008; Routasalo et al., 2009), seven studies used individual interventions (e.g., Schulz, 1976; Heller et al., 1991; Brennan et al., 1995; MacIntyre et al., 1999; Yi et al., 2012), and five studies combined the above two approaches (Drentea et al., 2006; Hang et al., 2011). The three intervention types could be subclassified into seven subtypes: intervention activities provided, group intervention training support, group intervention in remote service, face-to-face individual intervention, individual interventions in remote service, mixed interventions in remote service, and mixed interview intervention. Among them, seven items were group intervention activities-provided studies (e.g., Harris and Bodden, 1978; Constantino, 1988; Lökk, 1990; Ollonqvist et al., 2008; Routasalo et al., 2009), eight items were group intervention training support studies (Fukui et al., 2003; Savelkoul and de Witte, 2004; Kremers et al., 2006; Bøen et al., 2012; Saito et al., 2012), one item was a group intervention in remote service study (White et al., 2002), three items were face-to-face individual intervention studies (Schulz, 1976; MacIntyre et al., 1999; Yi et al., 2012), four items were individual interventions in remote service studies, two items were mixed interventions in remote service studies (Mountain et al., 2014; Czaja et al., 2017), two items were mixed interventions in remote service studies (Drentea et al., 2006; Hang et al., 2011), and three items were mixed interview intervention studies.

With regard to the time and frequency of intervention, most of the intervention frequency was regular, one time or two times per week. Most interventions lasted from 6 weeks to 1 year, and there was one study that lasted 5 years (Drentea et al., 2006); one study did not elaborate on the intervention frequency information (Heller et al., 1991). Among them, the primary recipient of the intervention included caregivers, disabled people, family members, older adults, and older adults living alone in the community. Only 50% (13/26) of the studies were specifically focused on social isolation or isolation (e.g., Harris and Bodden, 1978; Savelkoul and de Witte, 2004; Routasalo et al., 2009; Black et al., 2014; Chan et al., 2017), while the rest of the studies were secondary or indirect observations of variables. Intervention practitioners were health commissioners or professional social workers (e.g., Lökk, 1990; Savelkoul and de Witte, 2004; Ollonqvist et al., 2008; Routasalo et al., 2009; Saito et al., 2012), teachers (White et al., 2002; Czaja et al., 2017), students (Schulz, 1976; Constantino, 1988; MacIntyre et al., 1999), or experts. One study involved all of the above staff (Bøen et al., 2012), and one study did not specify the identity of the intervention practitioner (Harris and Bodden, 1978).

TABLE 2 | Quality of RCT studies included in the systematic review.

Authors	Random allocation sequence	Allocation concealment	Blinding	Completeness of outcome data	Selective reporting	Other sources of bias	Scoring
Harris and Bodden (1978)	Unclear	Unclear	Unclear	Unclear	Yes	Unclear	7
Constantino (1988)	Yes	No	Unclear	Unclear	Yes	Yes	8
Lökk (1990)	Unclear	Unclear	Unclear	Unclear	Yes	Yes	8
Ollonqvist et al. (2008)	Yes	Yes	Yes	Unclear	Yes	Yes	11
Routasalo et al. (2009)	Yes	Yes	Unclear	Unclear	Yes	Yes	10
Black et al. (2014)	Yes	Unclear	Unclear	Yes	Yes	No	8
Chan et al. (2017)	Yes	Unclear	Yes	Yes	Yes	Unclear	10
Ristolainen et al. (2020)	Yes	Unclear	Unclear	Unclear	Yes	Unclear	8
Fukui et al. (2003)	Unclear	Unclear	Unclear	Yes	Yes	Yes	9
Savelkoul and de Witte (2004)	Unclear	Yes	Yes	Yes	Yes	Yes	11
Kremers et al. (2006)	Unclear	Unclear	Unclear	Unclear	Yes	Yes	8
Bøen et al. (2012)	Unclear	Yes	Unclear	Yes	Yes	Yes	10
Saito et al. (2012)	Unclear	Unclear	No	Yes	Yes	Yes	8
White et al. (2002)	Unclear	Unclear	Unclear	Yes	Yes	Unclear	8
Schulz (1976)	Unclear	Unclear	Unclear	Unclear	No	No	4
MacIntyre et al. (1999)	Unclear	Unclear	Unclear	Yes	Yes	Unclear	8
Yi et al. (2012)	Yes	Unclear	Unclear	Unclear	No	No	7
Heller et al. (1991)	Unclear	Unclear	Unclear	Unclear	Yes	Yes	7
Brennan et al. (1995)	Unclear	Unclear	No	Yes	Yes	Unclear	7
Morrow et al. (1998)	Unclear	Unclear	Unclear	Yes	No	Unclear	6
Slegers et al. (2008)	No	Unclear	Unclear	Yes	Yes	No	6
Mountain et al. (2014)	Yes	Unclear	No	Yes	Yes	Yes	9
Czaja et al. (2017)	Yes	Yes	Unclear	Unclear	Yes	No	8
Drentea et al. (2006)	Unclear	Unclear	Unclear	Unclear	Yes	Yes	8
Hang et al. (2011)	Unclear	Unclear	No	Yes	No	No	4
Lai et al. (2020)	Yes	Unclear	Unclear	Yes	Yes	Unclear	9

In studies that featured control conditions, the control or comparison intervention included setting the control group (e.g., Constantino, 1988; Kremers et al., 2006; Ollonqvist et al., 2008; Routasalo et al., 2009; Black et al., 2014), conventional care, and waiting-list control; four studies used a variety of cross interventions (Schulz, 1976; Savelkoul and de Witte, 2004; Slegers et al., 2008; Mountain et al., 2014); and six studies conducted remote interventions (e.g., Heller et al., 1991; Brennan et al., 1995; Morrow-Howel et al., 1998; Slegers et al., 2008; Mountain et al., 2014). In addition, between 6 months and 3 years after the baseline review, seven studies conducted only one follow-up (e.g., Schulz, 1976; Harris and Bodden, 1978; MacIntyre et al., 1999; Ollonqvist et al., 2008; Black et al., 2014). Thirteen studies included two to four follow-up visits in 2 years after the intervention (e.g., Constantino, 1988; Lökk, 1990; Routasalo et al., 2009; Chan et al., 2017). One of the studies collected follow-up data 11 times during the 5 years of the study (Drentea et al., 2006).

Methodological Quality

In order to evaluate study quality and risk of bias, the Cochrane risk-of-bias tool was applied (see **Table 2**). Seven studies were classified as low risk of bias (e.g., Savelkoul and de Witte, 2004; Ollonqvist et al., 2008; Routasalo et al., 2009; Bøen et al., 2012; Chan et al., 2017), two studies were classified as high risk of bias (Schulz, 1976; Hang et al., 2011), and the rest of the 17 studies were rated as moderate risk of bias. Two studies with high-bias risk will not be discussed further. The remaining 24 studies will be discussed in the following.

The overall quality of the study continued to improve over time. Seven out of the eight intervention studies before 2000 (e.g., Schulz, 1976; Harris and Bodden, 1978; Constantino, 1988; Lökk, 1990; MacIntyre et al., 1999) were rated as moderate risks. Since 2000, 10 of the 18 studies were moderate bias risk; among which, seven were low bias risk.

Intervention Characteristics and Effects

Overall, outcomes labeled with “Y” means the intervention had significant effect on this variable, while “N” indicates no significant effect. Nineteen of the 24 intervention studies showed improvement in social isolation in at least one dimension (e.g., Harris and Bodden, 1978; Constantino, 1988; Lökk, 1990; Routasalo et al., 2009; Black et al., 2014). There was a diversity of definitions and methods of measuring social isolation where it was unclear on how best to categorize all outcomes that were grouped as "social isolation." Where there was sufficient information about type of a social isolation outcome being measured, studies were categorized as structural social support (such as emotional or psychological support) or functional social support (such as instrumental support) (**Table 3**).

Intervention Effects According to Intervention Methods

Generally, according to the classification of different intervention methods, there are 14 group interventions, 8 of them were group activities, 5 of them focus on social support training, and 1 was conducted in a remote manner. Moreover, there are six individual interventions; two of them are interviews, and the rest of four are remote service. In addition, there are four mixed interventions, and two of them are remote service.

As to intervention methods, six of the eight group intervention activities improved structural social support (Harris and Bodden, 1978; Constantino, 1988; Lökk, 1990; Routasalo et al., 2009; Black et al., 2014; Lai et al., 2020), while various forms of outcome measures were conducted. For instance, one low-risk physical exercise study showed no obvious improvement in loneliness and structural social support (Ollonqvist et al., 2008), while Taiji physical exercise showed great effect (Black et al., 2014; Chan et al., 2017). Three group interventions focused on functional social support reported significant improvements (Fukui et al., 2003; Bøen et al., 2012; Saito et al., 2012). Four structural social support studies (Fukui et al., 2003; Savelkoul and de Witte, 2004; Kremers et al., 2006; Saito et al., 2012) reported that two out of four patients had no improvement effect or the effect disappeared over time, while a few studies reported significant effects (Fukui et al., 2003; Saito et al., 2012). A moderate risk bias group intervention conducted earlier with remote services found no improvement (White et al., 2002), while another mixed remote service intervention had effects on structural social support (Mountain et al., 2014). Two individual studies that involved face-to-face interviews showed significant improvement in structural social support (MacIntyre et al., 1999; Yi et al., 2012). One of the four older (before 2010) individuals involved in a remote service study (Heller et al., 1991; Brennan et al., 1995; Morrow-Howel et al., 1998; Slegers et al., 2008) showed improvement effects on structural social support, but the follow-up effect was very short (Morrow-Howel et al., 1998). Two studies with moderate risk bias conducted by mixed intervention showed improvement in functional social support (Czaja et al., 2017; Lai et al., 2020).

Intervention Effects According to Intervention Environment

The external environment of intervention, such as the intervention practitioner, the place of intervention, and the client, was also an important factor in the effect of intervention. Five of the six interventions provided by experts showed improved outcomes (Heller et al., 1991; Fukui et al., 2003; Kremers et al., 2006; Mountain et al., 2014; Czaja et al., 2017). Seven of the 10 interventions provided by health or social workers were also effective (Lökk, 1990; Ollonqvist et al., 2008; Saito et al., 2012; Black et al., 2014; Chan et al., 2017; Lai et al., 2020; Ristolainen et al., 2020). Four interventions provided by teachers or students of the education community presented improved results (Constantino, 1988; MacIntyre et al., 1999; White et al., 2002; Slegers et al., 2008). In addition, one study multiple types of intervention practitioners (Bøen et al., 2012), another study didn't specifically described the information of intervention providers (Harris and Bodden, 1978).

As for the field of intervention, five studies took place in schools or public places (Harris and Bodden, 1978; Constantino, 1988; Routasalo et al., 2009; Black et al., 2014; Chan et al., 2017), and 1∼2 dimensions were improved. Five studies were professional treatment interventions (e.g., senior center, rehabilitation center, and hospital) (Lökk, 1990; Ollonqvist et al., 2008; Routasalo et al., 2009; Bøen et al., 2012; Black et al., 2014), and all of these showed improvements in 1∼3 dimensions. In six individual studies of private residences (Heller et al., 1991; Brennan et al., 1995; Morrow-Howel et al., 1998; MacIntyre et al., 1999; Yi et al., 2012; Lai et al., 2020), only two intervention studies presented no improved effects, even any dimension (Heller et al., 1991, Brennan et al., 1995). The other three studies did not provide evidence of the implementation environment (Savelkoul and de Witte, 2004; Kremers et al., 2006; Ristolainen et al., 2020). In addition, studies precisely targeting clients with social isolation or loneliness problems had better effects on all dimensions (e.g., Harris and Bodden, 1978; Savelkoul and de Witte, 2004; Routasalo et al., 2009; Bøen et al., 2012; Saito et al., 2012). By contrast, the studies without specific targets showed a worsened effect (Savelkoul and de Witte, 2004).

Intervention Effects According to Duration of Effect

Among the 14 studies reporting structural social support effect, three of them used social support as the outcome (Saito et al., 2012; Chan et al., 2017; Czaja et al., 2017), two studies observed the change of new friend number as an outcome (Routasalo et al., 2009; Bøen et al., 2012). One study showed that 45% of the participants made new friends in 1 year (Routasalo et al., 2009), while another showed that 40% of the participants made new friends in 1 year (Bøen et al., 2012), two studies reported using social contact as an outcome (Harris and Bodden, 1978; Morrow et al., 1998). And all studies reporting functional social support effect took completely different indicators during 6–12 months.

DISCUSSION

This study found substantial heterogeneity in the interventions delivered, and the overall quality of included studies indicated a low to medium risk of bias. Also, group intervention activities and individual intervention were effective in improving structural social support; mixed intervention and group intervention on training support significantly improved functional social support. We found that the interventions with accurate targeting of clients in social and public places had

TABLE 3 | Study results for outcomes of loneliness, structural social support, and functional social support.

Author, time (country)	Intervention methods	Bias risk	Loneliness	Structural social support	Functional social support	Remarks
Harris and Bodden (1978) (USA)	Group intervention activities	Medium	–	Y 6 weeks social contact d = 12	–	Social isolation improved within 6 weeks
Constantino (1988) (USA)	Group intervention activities	Medium	–	Y RSAS 6 weeks; 12 months d = −0.65; d = −0.27	–	In 12 months, social isolation improved, especially at week 6; all time periods, the intervention group was superior to the controlled group
Lökk (1990) (Switzerland)	Group intervention activities	Medium	*N*	Y Social network index 6 weeks; 12 weeks d = 0.8; d = 1.3	Y Availability of social contacts 24 weeks d = 6.6	At sixth weeks, social networks widened; at twelfth weeks, the effect disappeared; at twenty-fourth weeks, close friends increased
Ollonqvist et al. (2008) (Finland)	Group intervention activities	Low	N	N	–	Within 12 months, participants in the intervention group were less likely to suffer from loneliness
Routasalo et al. (2009) (Finland)	Group intervention activities	Low	N	Y found new friends 45%	–	Within 12 months, the number of friends increased
Black et al. (2014) (USA)	Group intervention activities	Medium	Y	Y	–	TCC has the capacity to alter stress levels in lonely older adults and to attenuate the rate of increase in a key transcription factor
Chan et al. (2017) (China)	Group intervention activities	Low	Y loneliness 6 months d = −1.84	Y social support 6 months d = 5.4	Y social network 6 months not clear	Reported a significantly greater improvement on the loneliness scale
Ristolainen et al. (2020) (Finland)	Group intervention activities	Low	Y UCLA(loneliness) 6 months d = −0.1	Y social relationship 6 months d = 2.5	–	Within 6 months, loneliness were improved but social contect were not improved
Fukui et al. (2003) (Japan)	Group intervention training support	low	Y UCLA(loneliness) 6 months d = −2.9	Y the number of confidants 6 months d = 1.8	Y the satisfaction with confidants 6 months d = 0.4	Within 6 months, loneliness was reduced, self-confidence increased, and mutual satisfaction improved
Savelkoul and de Witte (2004) (Norway)	Group intervention training support	Low	N	N	–	Within 6 months, only social skills increased, while loneliness, social networks, and well-being were not improved

(Continued)

TABLE 3 | Continued

Author, time (country)	**Intervention methods**	**Bias risk**	**Loneliness**	**Structural social support**	**Functional social support**	**Remarks**
Kremers et al. (2006) (Norway)	Group intervention training support	low	Y social loneliness 6 weeks d = −2.0	N	–	Within 6 months, overall efficacy and emotional isolation were not improved; Social isolation improved for sixth weeks, and disappeared within sixth months.
Bøen et al. (2012) (Norway)	Group intervention training support	Low	–	Y made new friends 40%	Y feeling of social support 12 months d = 0.65	Within 12 months, social support improved significantly, depression increased, life satisfaction decreased, the intervention group was better than the control group, and there was no change in health status
Saito et al. (2012) (Japan)	Group intervention training support	Low	Y AOK loneliness scale 6 months d = −1.0	Y social support 6 months d = 0.6	-	6 months, increased social support, social contact, and social activities to improve is not obvious, increased awareness of community service, increased loneliness, depression has not changed.
White et al. (2002) (USA)	Groups intervene in remote services	Low	N	N	–	Within 5 months, loneliness was not improved, and the number of intimate friends remained unchanged
MacIntyre et al. (1999) (Canada)	Individual intervention interview	Low	–	Y social integration 6 weeks d = 3.08	N	Within six weeks, social inclusion has enhanced, there is no improvement in intimacy and so on.
Yi et al. (2012) (China)	Individual intervention interview	low	Y UCLA 6months d = −8.09	–	Y family ties increased not clear	Within 6 months, loneliness and depression were significantly improved, and family ties increased
Heller et al. (1991) (United States)	Individual intervention in remote service	Low	N	–	N	Loneliness was not improved in 20 or 30 weeks, and friends and relatives showed no improvement
Brennan et al. (1995) (USA)	Individual intervention in remote service	Low	N	–	–	12 months, the social loneliness has no effect

(Continued)

TABLE 3 | Continued

Author, time (country)	Intervention methods	Bias risk	Loneliness	Structural social support	Functional social support	Remarks
Morrow et al. (1998) (USA)	Individual intervention in remote service	Low	N	Y person contact 4 months not clear	N	Within 4 months, social contacts increased, but social satisfaction was not improved, and unmet need declined within 8 months
Slegers et al. (2008) (Norway)	Individual intervention in remote service	low	N	N	–	Within 12 months, there was no improvement in loneliness or social network across all 3 control groups
Mountain et al. (2014) (UK)	Mixed intervention in remote service	Low	N	Y social function 6 months d = 13.4	–	Within 6 months, there was no improvement in loneliness, but the social function was improved
Czaja et al. (2017) (USA)	Mixed intervention in remote service	Low	Y loneliness 12 months d = −2.5	Y social support 6 months 1.33	–	Access to technology applications such as PRISM may enhance social connectivity and reduce loneliness among older adults
Drentea et al. (2006) (United States)	Mixed intervention	Low	–	–	Y satisfaction with social support not clear	Within 5 years, social support satisfaction improved
Lai et al. (2020) (Canda)	Mixed intervention	medium	Y loneliness 10 weeks d = −0.63	Y barriers to social participation 10 weeks d = 0.43	–	Within 10 weeks loneliness and barriers to social participation were improved

–, no report; Y had statistical significance; N, no statistical significance.

more obvious effect. Interventions in which older people were active participants also appeared more likely to be effective. In addition, professionals were better than teachers and students in conducting intervention. The findings provide a tentative indication of the potential benefits of specific types of intervention for improving loneliness/social isolation, advancing theory-informed development of interventions and improving design of evaluation studies. The remote service interventions were debatable, as the recent studies have showed improvement in structural social support, but no effect on older studies. Because of the contradictory results, more research is needed to examine the complexity of "remote interventions" from the perspective of process evaluation. Interventions conducted in social and public places had better effects, and interventions with accurate targeting of clients had more obvious effects. Studies evaluating interventions delivered by professional practitioners appeared to yield better outcomes than those where the intervention was delivered by non-professionals. Effective intervention for older adults in isolation not only improved structural social support, functional social support, and mitigation of loneliness but also promoted the health of older adults.

In the experimental studies, there were a variety of interventions on social isolation. Although experimental design is not always feasible or accepted by participants, this kind of study can provide a scientific and normative reference for the implementation process and assessment report, promote the utilization of randomized control trials, improve the design level, standardize the research process, improve the quality of evidence, and provide a reference for policy-making. We advocate professionals to provide face-to-face intervention in the field of daily life rather than in the home environment and recommend that more efficient remote interventions within smart terminals be developed to achieve better results.

In real life, the environment preference of older adults has an obvious effect on their social interaction. Older adults who enjoy being alone are more likely to be socially isolated. The incidence of social isolation among older adults in different living conditions was also different, with those who were widowed, had low income, and in poor health, more likely to feel lonely and socially isolated. In addition, as age increases, older adults can be more dissociated from social interaction and prefer to be isolated (Lu et al., 2013). Therefore, when we design social isolation interventions, it is essential to consider personal preference, living status, and physiological characteristics of older adults and adjust measures accordingly so as to promote the effectiveness of the intervention. In addition, well-designed remote intervention system, such as personal reminder information and social management (PRISM) system, has the potential to change attitudes toward technology and increase technology self-efficacy.

At the policy level, the establishment of social support systems is imminent (Liu and Ni, 2002). With the advancement of family planning policy, such as China, the aging of the population is becoming more and more serious, and the "4-2-1" or "4-2-2" family pattern (4-grandparent, 2-parent, and 2- or 1-child) has gradually formed (Nan and Dong, 2019). Family support functions have greatly weakened, and, especially, the needs for social interaction and spiritual comfort are not satisfied. Therefore, we must establish a community-based pension support service platform, develop professional social work vigorously, cooperate with research institutes to obtain scientific evidence in order to address the problem of social isolation of older adults, improve their physical and mental health, as well as quality of life, and promote the healthy aging of the population.

LIMITATIONS AND FUTURE RESEARCH DIRECTIONS

In this study, the inclusion literature was defined as older adults over age 50, who have been in isolation or loneliness. However, the relevant research on the concept of social isolation does not use a standardized and unified definition, so inclusion bias may have been incorporated. Although the inclusion criteria were designed to reduce social isolation or loneliness, only 14/24 studies specifically addressed the problem (e.g., Constantino, 1988; Li and Zhou, 2002; Savelkoul and de Witte, 2004; Kremers et al., 2006; Chan et al., 2017). The study may also have the potential risk that the assessment of social isolation or loneliness was due to other characteristics of the target client (Liu and Ni, 2002). Restricting the study language to English and Chinese may have increased the inclusion bias. The quality and expression of the research in the historical period also limited the quality of this study. Some studies conducted a qualitative report rather than quantitative data. It is not appropriate to use quantitative methods as well as meta-analysis due to the heterogeneity of the study subjects.

At the same time, we found that most pieces of randomized controlled trial research in this field were from developed countries. Future research not only needs to enrich the original evidence from all over the world but especially from developing countries. In addition, most of the pieces of research from Finland, Norway, the United States, and other developed countries were different from developing countries due to legal or volunteer service organizations; thus, the applicability and the effectiveness of the evidence are worth discussing further. Moreover, more refined subgroups of systematic review can be done in the near future; for example, systematic review could be used to quantify the effect of intervention on a certain type of intervention.

CONCLUSION

The findings provide a tentative indication of the potential benefits of specific types of intervention for improving loneliness/social isolation, advancing theory-informed development of interventions, and improving design of evaluation studies.

Firstly, this study suggests that group and mixed intervention targeting of older adults could be helpful for alleviating social isolation problems. The use of modern technology for remote services could also present good results. Moreover, our systematic review has identified a need for well-conducted studies to improve the evidence base regarding the effectiveness of social interventions for alleviating social isolation. However, more well-conducted RCTs of the effectiveness of social interventions for alleviating social isolation are needed to improve the evidence base.

Because of the debating results, further research is needed to examine the effect of remote interventions from the perspective of process evaluation.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS

FT is responsible for analyzing data and writing the draft of the results. CLY is responsible for analyzing the data. FF is responsible for revising the manuscript and submitting the paper. LSW is responsible for writing the literature review. IC is responsible for providing suggestions for revising the paper. All authors contributed to the article and approved the submitted version.

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REFERENCES

Berger, V. W. (2006). Is the Jadad score the proper evaluation of trials? *J. Rheumatol.* 33, 1711–1712.

Black, D. S., Irwin, M. R., Olmstead, R. E., Ji, E., Breen, E. C., and Motivala, S. (2014). Tai chi meditation effects on nuclear factor-κB signaling in lonely older adults: a randomized controlled trial. *Psychother. Psychosomat.* 83, 315–317. doi: 10.1159/000359956

Bøen, H., Dalgard, O. S., Johansen, R., and Nord, E. (2012). A randomized controlled trial of a senior centre group programme for increasing social support and preventing depression in elderly people living at home in Norway. *BMC Geriat.* 12:20. doi: 10.1186/1471-2318-12-20

Brennan, P. F., Moore, S. M., and Smyth, K. A. (1995).The effects of a special computer network on caregivers of persons with Alzheimer's disease. *Nurs. Res.* 44, 166–172. doi: 10.1097/00006199-199505000-00007

Canedo-García, A., García-Sánchez, J. N., and Pacheco-Sanz, D. I. (2017). A systematic review of the effectiveness of intergenerational programs. *Front. Psychol.* 8:1882. doi: 10.3389/fpsyg.2017.01882

Chan, A., Yu, D., and Kai, C. (2017). Effects of tai chi qigong on psychosocial well-being among hidden elderly, using elderly neighborhood volunteer approach: a pilot randomized controlled trial. *Clin. Intervent. Aging* 12, 85–96. doi: 10.2147/CIA.S124604

Constantino, R. E. (1988). Comparison of two group interventions for the bereaved. *J. Nurs. Scholar.* 20, 83–87. doi: 10.1111/j.1547-5069.1988.tb00036.x

Cornwell, E. Y., and Waite, L. J. (2009). Social disconnectedness, perceived isolation, and health among elder adults. *J. Health Soc. Behav.* 50, 31–48. doi: 10.1177/002214650905000103

Czaja, S. J., Boot, W. R., Charness, N., Rogers, W. A., and Sharit, J. (2017). Improving social support for older adults through technology: findings from the PRISM randomized controlled trial. *Gerontologist* 58, 1–11. doi: 10.1093/geront/gnw249

Díaz, C., and García, J. N. (2016). Identification of relevant elements for promoting effective interventions in old age. *Revista de Psicodidáctica*, 21, 1–17. doi: 10.1387/RevPsicodidact.13854

Drentea, P., Clay, O. J., Roth, D. L., and Mittelman, M. S. (2006). Predictors of improvement in social support: five-year effects of a structured intervention for caregivers of spouses with Alzheimer's disease. *Soc. Sci. Med.* 63, 957–967. doi: 10.1016/j.socscimed.2006.02.020

Ferreiraalves, J., Magalhães, P., Viola, L., and Simões, R. (2014). Loneliness in middle and old age. *Arch. Gerontol. Geriatr.* 59, 613–623. doi: 10.1016/j.archger.2014.06.010

Fratiglioni, L., Wang, H. X., Ericsson, K., Maytan, M., and Winbiad, B. (2000). Influence of social network on occurrence of dementia: a community-based longitudinal study. *Lancet* 355, 1315–1319. doi: 10.1016/S0140-6736(00)02113-9

Fukui, S., Koike, M., Ooba, A., and Uchitomi, Y. (2003). The effect of a psychosocial group intervention on loneliness and social support for Japanese women with primary breast cancer. *Oncol. Nurs. Forum* 30, 823–830. doi: 10.1188/03.ONF.823-830

Grenade, L., and Boldy, D. (2008). Social isolation and loneliness among elder people: issues and future challenges in community and residential settings. *Austral. Health Rev.* 32, 468–478. doi: 10.1071/AH080468

Hall, R. K., Davenport, C. A., Sims, M., Colón-Emeric, C., Washington, T., Russell, J., et al. (2019). Association of functional and structural social support with chronic kidney disease among African Americans: the Jackson Heart study. *BMC Nephrol.* 20:262. doi: 10.1186/s12882-019-1432-9

Hang, R. H., Liu, X. M., Feng, L. P., and Xing, J. (2011). The effects of psychological intervention on the community Empty Nester the symptoms of depression, loneliness and happiness. *China J. Gerontol.* 31, 2723–2725. doi: 10.3969/j.issn.1005-9202.2011.14.054

Harris, J. E., and Bodden,. J. L. (1978). An activity group experience for disengaged elderly persons. *J. Counsel. Psychol.* 25, 325–330. doi: 10.1037/0022-0167.25.4.325

Hawton, A., Green, C., Dickens, A. P., Richards, S. H., Taylor, R. S., Greaves, C. J., et al. (2010). The impact of social isolation on the health status and health-related quality of life of elder people. *Qual. Life Res.* 20, 57–67. doi: 10.1007/s11136-010-9717-2

Heller, K., Thompson, M. G., Trueba, P. E., Hogg, J. R., and Vlachos-Weber, I. (1991). Peer support telephone dyads for elderly women: was this the wrong intervention? *Am. J. Community Psychol.* 19, 53–74. doi: 10.1007/BF00942253

Higgins, J. P., Altman, D. G., Getzsche, P. C., Juni, P., Moher, D., Oxman, A. D., et al. (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 343:d5928. doi: 10.1136/bmj.d5928

Iliffe, S., Kharicha, K., Harari, D., Swift, C., Gillmann, G., and Stuck, A. E. (2007). Health risk appraisal in older people 2: the implications for clinicians and commissioners of social isolation risk in older people. *Br. J. General Practice* 57, 277–282. doi: 10.1016/S0212-6567(07)70882-X

Kremers, I. P., Steverink, N., Albersnagel, F. A., and Slaets, J. P. (2006). Improved self-management ability and well-being in older women after a short group intervention. *Aging Mental Health* 10, 476–484. doi: 10.1080/13607860600841206

Lai, D. W., Li, J., Ou, X., and Li, C. Y. (2020). Effectiveness of a peer-based intervention on loneliness and social isolation of older Chinese immigrants in Canada: a randomized controlled trial. *BMC Geriat.* 20:356. doi: 10.1186/s12877-020-01756-9

Laursen, B., and Hartl, A. C. (2013). Understanding loneliness during adolescence: developmental changes that increase the risk of perceived social isolation. *J. Adolesc.* 36, 1261–1268. doi: 10.1016/j.adolescence.2013.06.003

Li, J., Ye, H., Tang, Y., Zhou, Z., and Hu, X. (2018). What are the effects of self-regulation phases and strategies for chinese students? A meta-analysis of two decades research of the association between self-regulation and academic performance. *Front. Psychol.* 9:2434. doi: 10.3389/fpsyg.2018.02434

Li, Z., and Zhou, L. (2002). Epidemiological study on the loneliness of old age. *Chinese J. Mental Health* 26, 658–662. doi: 10.3969/j.issn.1000-6729.2012.09.004

Liu, Z. R., and Ni, J. (2002). Relevant factors and countermeasures of loneliness among urban elderly. *J. Anhui J. Prevent. Med.* 8, 326–328. doi: 10.3969/j.issn.1672-6634.2001.02.030

Lökk, J. (1990). Emotional and social effects of a controlled intervention study in a day-care unit for elderly patients. *Scand. J. Primary Health Care* 8, 165–172. doi: 10.3109/02813439008994951

Lu, R. M., Lin, M. X., and Liu, Y. Z. (2013). On the social isolation and loneliness of the elderly in the urban community, a case study of Yantai city of Shandong province. *J. North China Univ. (social science edition)* 14, 132–136. doi: 10.3969/j.issn.1009-5101.2013.02.029

Lubben, J., and Gironda, M. (2003). "Centrality of social ties to the health and well-being of older adults," in *Social work and health care in an aging world*, eds, B. Berkman and L. Harooytan (New York, NY: Springer), 319–350.

Lund, R., Nilsson, C. J., and Avlund, K. (2010). Can the higher risk of disability onset among elder people who live alone be alleviated by strong social relations? A longitudinal study of non-disabled men and women. *Age Ageing* 39, 319–326. doi: 10.1093/ageing/afq020

Lunstad, J., Smith, T. B., and Layton, J. B. (2010). Social relationships and mortality risk: a meta-analytic review. *PLoS Med.* 7:e1000316. doi: 10.1371/journal.pmed.1000316

Ma, J., Liu, Y., Zhong, L. P., Zhang, C. P., and Zhang, Z. Y. (2012). Comparison of Jadad scale and Cochrane bias risk assessment tool in quality evaluation of randomized controlled trials. *China J. Oral Maxillofacial Surg.* 10, 417–422. Available online at: http://en.cnki.com.cn/Article_en/CJFDTOTAL-ZGKQ201205026.htm.

MacIntyre, I., Corradetti, P., Roberts, J., Browne, G., Watt, S., and Lane, A. (1999). Pilot study of a visitor volunteer programme for community elderly people receiving home health care. *Health Soc. Care Commun.* 7, 225–232. doi: 10.1046/j.1365-2524.1999.00178.x

Masi, C. M., Chen, H. Y., Hawkley, L. C., and Cacioppo, J. T. (2011). A meta-analysis of interventions to reduce loneliness. *Personal. Soc. Psychol. Rev.* 15, 219–266. doi: 10.1177/1088868310377394

Methley, A. M., Campbell, S., Chew-Graham, C., Mcnally, R., and Cheraghi-Sohi, S. (2014). Pico, picos and spider: a comparison study of specificity and sensitivity in three search tools for qualitative systematic reviews. *BMC Health Serv. Res.* 14:579. doi: 10.1186/s12913-014-0579-0

Morrow, D. A., Rifai, N., Antman, E. M., Weiner, D. L., and Braunwald, E. (1998). C-reactive protein is a potent predictor of mortality independently of and in combination with troponin t in acute coronary syndromes: a timi 11a substudy. thrombolysis in myocardial infarction. *J. Amer. Cardiol.*, 31, 1460–1465.

Morrow-Howel, N., Becker-Kemppainen, S., and Judy, L. (1998). Evaluating an intervention for the elderly at increased risk of suicide. *Res. Soc. Work Practice* 8, 28–46. doi: 10.1177/104973159800800104

Mountain, G., Hind, D., Gossage-Worrall, R., Walter, S. J., Duncan, R., Newbould, L., et al. (2014). 'Putting Life in Years' (PLINY) telephone friendship groups research study: pilot randomised controlled trial. *Trails* 15:141. doi: 10.1186/1745-6215-15-141

Nan, J. J., and Dong, B. (2019). Research on the pension problem of rural one-child family from the perspective of social work – taking a village in Shandong Province as an example. *Aging Res.* 6, 31–36. doi: 10.12677/AR.2019.63005

Ollonqvist, K., Palkeinen, H., Aaltonen, T., Pohjolainen, T., Puukka, P., and Hinkka, K. (2008). Alleviating loneliness among frail elder people–findings from a randomised controlled trial. *Int. J. Mental Health Promot.* 10, 26–34. doi: 10.1080/14623730.2008.9721760

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., et al. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Syst. Rev.* 1:89. doi: 10.1186/s13643-021-01626-4

Petersen, N., Knig, H. H., and Hajek, A. (2020). The link between falls, social isolation and loneliness: a systematic review. *Arch. Gerontol. Geriatrics* 88:104020. doi: 10.1016/j.archger.2020.104020

Poscia, A., Stojanovic, J., La Milia, D., Duplaga, M., Grysztar, M., Moscato, U., et al. (2018). Interventions targeting loneliness and social isolation among the older people: an update systematic review. *Exp. Gerontol.* 102, 133–144. doi: 10.1016/j.exger.2017.11.017

Ristolainen, H., Kannasoja, S., Tiilikainen, E., Hakala, M., Närhi, K., and Rissanen, S. (2020). Effects of participatory group-based care managementon well-being of older people living alone: A randomized controlled trial. *Arch. Gerontol. Geriatr.* 89:104095. doi: 10.1016/j.archger.2020.104095

Routasalo, P. E., Tilvis, R. S., and Kautiainen, H. (2009). Effects of psychosocial group rehabilitation on social functioning, loneliness and well-being of lonely, elder people: randomized controlled trial. *J. Adv. Nurs.* 65, 297–305. doi: 10.1111/j.1365-2648.2008.04837.x

Saito,T., Kai, I., and Takizawa, A. (2012). Effects of a program to prevent social isolation on loneliness, depression, and subjective well-being of elder adults: a randomized trial among elder migrants in Japan. *Arch. Gerontol. Geriatr.* 55, 539–547. doi: 10.1016/j.archger.2012.04.002

Savelkoul, M., and de Witte, L. P. (2004). Mutual support groups in rheumatic diseases: effects and participants' perceptions. *Arthritis Rheum.* 51, 605–608. doi: 10.1002/art.20538

Schulz, R. (1976). Effects of control and predictability on the physical and psychological well-being of the institutionalized aged. *J. Personal. Soc. Psychol.* 33, 563–573. doi: 10.1037/0022-3514.33.5.563

Slegers, K., van Boxtel, M. P. J., and Jolles, J. (2008). Effects of computer training and Internet usage on the well-being and quality of life of elder adults: a randomized, controlled study. *J. Gerontol. Series B Psychol. Sci. Soc. Sci.* 63, 176–184. doi: 10.1007/BF03324898

Stojanovic, J., Collamati, A., La Milia, D., Borghini, A., Duplaga, M., Rodzinka, M., et al. (2016). Targeting loneliness and social isolation among the elderly: an update systematic review. *Europ. J. Public Health* 26(suppl_1), 10–11. doi: 10.1093/eurpub/ckw164.010

Victor, C., Scambler, S., Bond, J., and Bowling, A. (2010). Being alone in later life: loneliness, social isolation and living alone. *Rev. Clin. Gerontol.* 10, 407–417. doi: 10.1017/S0959259800104101

White, H., McConnell, E., Clipp, E., Branch, L. G., Sloane, R., Pieper, C., et al. (2002). A randomized controlled trial of the psychosocial impact of providing internet training and access to elder adults. *Aging and Mental Health* 6, 213–221. doi: 10.1080/13607860220142422

Yi, J. N., Chen, L. Q., Jia, S. M., Lu, M. M., and Gou, X. Q. (2012). The influence of community nurse led general practitioner team home visiting service on the psychological status of elderly people living in the elderly. *Nurs. Res.* 26, 975–978. doi: 10.3969/j.issn.1009-6493.2012.11.006

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BRIEF RESEARCH REPORT
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Being There: Exploring Virtual Symphonic Experience as a Salutogenic Design Intervention for Older Adults

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This co-design study examined salutogenic potential of mobile virtual reality (VR) experiences as an alternative to participation in a community-based symphonic engagement program (B Sharp), previously found to benefit people with dementia (PWD) and their informal caregivers. Six focus groups were conducted with sixteen adults aged 76–90; three participants had dementia, and two were informal spousal caregivers. No participants had prior VR experience. The study assessed the feasibility of replicating the community-based-arts program in VR, with the goal of enhancing its salutogenic qualities (e.g., positive distraction, engagement, and social connection). Video-recordings of participants while using a mobile head-mounted display (HMD) were analyzed using qualitative thematic analysis to compare perceptions of different virtual experiences, including replication or enhancement of B Sharp and a campus tour. Findings suggest participants had positive perceptions of enhanced VR experiences with no adverse effects, although PWD were less enthusiastic and HMD usability was complicated by eyewear use and comfort with technology. Participants reacted most favorably to the enhanced symphonic experience, where they were "virtually" onstage during the performance, suggesting unique experiences beyond what is possible in the real world have the greatest potential for deep immersion for older adults. Results suggest VR has strong potential to replicate and enhance salutogenic qualities of community-based programming by enabling greater access to experiences for older adults and by increasing enjoyment and engagement through experiences not otherwise feasible. Furthermore, this study illuminates advantages of a user-centered, co-design approach when developing VR experiences with community partners and older adults.

Keywords: dementia, Alzheimer's disease, healthy aging, virtual reality, psychosocial intervention, salutogenic design

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INTRODUCTION

Age-related cognitive decline is a significant global health challenge (World Health Organization, 2015). Cognitive function, essential for independent living and intertwined with physical health (Li and Lindenberger, 2002; Gross et al., 2011), typically declines from the 7th decade[1] (Li et al., 2004). However, with dementia, it deteriorates rapidly and at an earlier age (Bayles et al., 1987).

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[1] Cognitive abilities vary across adulthood. For instance, executive functions and working memory usually peak in the 3rd decade of life and decline thereafter. This decline becomes especially prominent from the 7th decade of life onward.

Dementia is a degenerative condition involving cognitive impairments that interfere with a person's ability to live independently and reduce their quality of life (McKhann et al., 2011). Pharmaceuticals intended to slow dementia-related decline have limited efficacy, problematic side effects, and poor compliance (Serafino, 2018; Davalos et al., 2019). Conversely, participation in enriching activities (e.g., music and arts programming) have shown delayed or reduced functional decline without adverse effects (Raglio et al., 2012; Dyer et al., 2018; Davalos et al., 2019).

Our team studies impacts of community-based arts programming (CBAP), including symphony (Davalos et al., 2019; Faw et al., 2021), dance, theater, and craft (Griggs et al., 2020) experiences on cognitive function and quality of life for people with dementia (PWD) and their caregiving partners (CPs). Our symphonic program, B Sharp, involves PWDs and CPs who receive symphony season tickets. Dyads complete cognitive assessments and quality of life surveys at the beginning and end of each season. Results from the program's first year found overall cognitive performance improved for PWD over the 10-month season (Davalos et al., 2019), with greater improvements for more frequent attendees. Additionally, dyads expressed high motivation to participate due to restorative and engaging program aspects, including a sense of "being away" and social connection (Faw et al., 2021). Despite program benefits, some dyads reported challenges related to transportation, performance timing, and other barriers to attendance. These findings, along with challenges of the recent COVID-19 pandemic, underscore the need for programming that can be delivered while adhering to safe social distancing and in accessible environments (Armitage and Nellums, 2020).

VR is an increasingly-accessible and moderately-priced technology that can enable frequent exposure to symphonic performances and provide access to those unable to attend live events. VR head-mounted displays (HMDs) enable dynamic immersion in digitally created experiences (Parsons, 2015) and are rapidly gaining popularity in clinical and research settings (Parsons, 2015; Hoffman et al., 2019; Kourtesis et al., 2019). Therapeutic applications include the use of VR to treat phobias (Diemer et al., 2013; Malbos et al., 2013), post-traumatic stress disorder (Rothbaum et al., 2014; Norrholm et al., 2016; Beidel et al., 2019), psychotic disorders (du Sert et al., 2018; Pot-Kolder et al., 2018), stroke (Threapleton et al., 2017), and pain management (Gomez et al., 2017; Kourtesis et al., 2019). VR applications have also been used to enhance cognition for PWD (Optale et al., 2010; Man et al., 2012; Manera et al., 2016; Doniger et al., 2018; Gamito et al., 2018).

Although these studies suggest VR's therapeutic benefits, its salutogenic potential remains underexplored. Salutogenesis emphasizes examining factors that support health as opposed to focusing on causes of a disease (Antonovsky, 1979). Salutogenic design is an evidence-based approach to constructing environments that alleviate stress and promote increased engagement and social connection (Mazzi, 2020), thereby enhancing wellbeing, including specific strategies for older adults (Burzynska and Malinin, 2017) and PWD (Mobley et al., 2017). Preliminary evidence from a study by Man et al. (2012) suggests VR can improve objective memory in older adults at risk of developing dementia; however, a key aspect of salutogenic design is to create environments that people enjoy and choose to engage by incorporating human-centered, co-design processes (Burzynska and Malinin, 2017; Mobley et al., 2017; Tsekleves and Cooper, 2017; Cinderby et al., 2018). Co-design involves end-users as collaborators during the design and evaluation of products or services and is particularly useful for surfacing technological challenges and preferences specific to older adults (Sumner et al., 2021). Thus, a salutogenic approach differs from other VR programs. Currently, limited research examines whether older adults find VR enjoyable—an important motivator for participation—and how they perceive VR simulations versus enhanced experiences, which allow them to experience situations unfeasible in real life (Lee et al., 2019). Our co-design study explores the potential of VR to simulate real-world experiences as well as to enhance them, building upon salutogenic effects found in real-world CBAP.

The purpose of our study was to engage older adults, including PWD and CPs, in simulated and enhanced VR-prototype experiences to assess their perceptions. It can be challenging and costly to create VR experiences; thus, we consider this study one step in an iterative, co-design process. A primary goal was to get participant feedback early in the design process to identify affordances and constraints of VR features toward improving participant engagement in the final design. Our project sought to answer the following questions:

(1) How do older adults, including PWD and CPs, perceive simulated and enhanced VR experiences?
(2) To what extent do participants perceive salutogenic design qualities (e.g., social connection and/or enjoyment) in the simulated versus enhanced VR experiences?
(3) Do perceptions and experiences of PWD differ from other participants?
(4) What desires do older adults have for future VR experiences?

MATERIALS AND METHODS

This study was conducted in two parts. All procedures received ethical approval from an institutional review board. The first three focus groups compared experiences with 360° video of a symphony performance intended to *simulate* the B Sharp experience and an *enhanced* campus tour. All participants (n = 16) in six focus groups (**Table 1**) consented to video recording and answered open-ended questions. Based on feedback from focus groups 1–3, an *enhanced* symphonic video replaced the simulated symphony video for focus groups 4–6. In total, three VR experiences (**Table 2**) were examined across the six focus groups. All VR experiences were recorded with 4 k resolution.

Participants wore Oculus Go HMDs, selected because they are stand-alone, lightweight, with integrated speakers and high visual resolution screens, and moderately priced ($500). The HMD uses a single LCD at 2,560 × 1,440 (which amounts to

TABLE 1 | Focus group participant information.

Focus group (length)	Location	Participants	VR experiences
Focus group 1 (59:26)	Private meeting room at an independent living center	Fred (PWD), Anne (CP), Robert (PWD), Peggy (CP), and Ken *Note: Anne and Fred had met the research team previously through another research study.*	Replication symphony campus tour
Focus group 2 (51:12)	Private meeting room at an independent living center	Sheila, Evelyn, and Gene	Replication symphony campus tour
Focus group 3 (41:43)	Private meeting room at an independent living center	Margaret, Leann, and June (PWD)	Replication symphony campus tour
Focus group 4 (46:58)	Participant Leann's private residence	Leann and Betty	Enhanced symphony campus tour
Focus group 5 (38:58)	Private meeting room at a local senior center	Carl and Hal	Enhanced symphony campus tour
Focus group 6 (55:54)	Private meeting room at a local senior center	Darla and Nora	Enhanced symphony campus tour

1,280 × 1,440 per eye) with a refresh rate of 60 Hz and field of view of about 101°, which gives a display fidelity of 12.67 pixels per degree. The HMD is a three-degrees of freedom headset, tracking rotations along the X, Y, and Z axis. It does not use an interpupillary distance (IPD) adjustment wheel but does have spacers to accommodate eyeglasses.

Participants

Participants, recruited via convenience sampling using flyers and in-person announcements at local senior living and recreation centers, could not have a history of seizures or severe motion sickness. In total, six focus groups were conducted with 16 participants aged 76–90 years ($M = 83.00$, $SD = 4.40$); one person participated in both parts. A majority ($n = 11$) indicated some vision and/or hearing impairments; those with impairments participated with appropriate corrective measures (e.g., glasses, hearing aids). Ten participants were female and three were diagnosed with advanced dementia (no longer capable of independent living). Two PWDs attended with their CPs. None of the participants had prior experience using VR. Two knew the researchers prior to study participation through another research study. Researchers obtained written, informed consent from all participants. Participants were given pseudonyms and researchers anonymized identifiable information.

Focus Group Procedures

Focus groups lasted approximately 50 mins (range = 38:58–59:26 mins) and followed a semi-structured protocol (**Table 3**). Focus groups were led by the first and second author (two women: a faculty member with doctorate degree and a graduate student) and attended by research assistants. All members of the research team had extensive experience interacting with older adults and leading qualitative projects. One team member had significant experience in co-design approaches. Participants talked with each other during the focus group, and this cross-talk was a valuable component of the focus groups (Greenbaum, 1998). Participants were asked about their initial impressions of VR and the HMD. Participants were then instructed to put on the HMD and relay their opinions regarding its comfort. Then, research assistants helped them enter the symphonic VR experience. All participants engaged in the virtual experience at the same time. Participants then removed the headset and responded to several questions (see **Table 3**). Next, participants entered the headset again and participated in the VR tour, after which they provided thoughts about the experience and their comfort level. Finally, participants evaluated their general impressions of VR and their desires for future VR

TABLE 2 | Virtual reality experience descriptions.

Experience	Goal	Description
Replication symphony experience	To examine whether a VR experience *replicating* that of a typical symphony concert would be immersive and enjoyable	This experience featured an audience-viewpoint intended to *replicate* the real-world viewpoint of a typical B Sharp participant. 360° footage was recorded in front of the soundboard, located in the middle of the auditorium. Participants were exposed to approximately 10 mins of a single symphonic movement. The movement was selected for its engaging nature and higher volume level
Enhanced symphony experience	To examine whether a VR experience *enhancing* a symphony concert (by placing participants center stage in close proximity to the musicians) would be immersive and enjoyable	This 360° video was recorded on stage directly in front of the conductor, intending to *enhance* the B Sharp experience by surrounding the viewer with the musicians. Participants viewed approximately 8 mins of a symphonic movement that involved string instruments and was upbeat and rhythmic
Enhanced campus tour experience	To examine whether a VR experience that was more active (i.e., moving around campus) and featured enhanced experiences (i.e., flying across campus and hovering above buildings) would be immersive and enjoyable. This experience also helped the researcher evaluate if participants would experience adverse effects from a more active VR experience (such as motion sickness). It also prompted participants to consider the types of enhancements they might enjoy in VR	The campus tour was an 8-min video featuring many activities across a local college campus. It included VR enhancements that people would not typically experience in real life, such as riding a golf cart through campus areas and flying above campus. It also featured more interactive activities, such as throwing confetti at a graduation celebration

TABLE 3 | Focus group protocol and sample questions.

Focus group phase	Goal	Sample questions
Pre-engagement	Inform participants about the goals and purpose of the research; obtain informed consent Assess participant familiarity and comfort with VR Introduce the headset and have participants try it on Gather initial impressions of the headset	How would you describe your comfort level with technology? When your hear the term "virtual reality", what comes to mind? Have you ever tried VR before? What do you think about this headset? What do you notice about it? How did the headset feel?
Post-symphony VR experience questions	Assess participant responses to the VR experience Evaluate for positive/negative outcomes from engaging in the VR experience	How was your experience? What do you most remember about your VR experience? What did you like about it? What did you dislike about it? Did you feel immersed in the environment?
Post-campus tour VR experience questions	Assess participant responses to the VR experience Evaluate for positive/negative outcomes from engaging in the VR experience Compare participant perceptions of the symphony versus the tour experience	How was your experience? What do you most remember about your VR experience? What did you like about it? What did you dislike? Did you feel immersed in the environment?
De-brief questions	Evaluate participants' overall impressions of VR Assess interest in future VR experiences	Did you enjoy this experience? Is this something you would want to do again? Would you feel comfortable using VR on your own? What about with training? Do you think others would enjoy this experience? If we were to design future VR experiences, what would you like for us to do?

TABLE 4 | Summary of research findings.

Research question	Associated findings
RQ1: How do older adults, including PWD and CPs, perceive simulated and enhanced VR experiences?	Participants perceived *enhanced experiences* (i.e., experiences that exceeded the opportunities in real life) as more immersive and enjoyable when compared with *simulated*. They reported fewer complaints about the HMDs and visual/auditory issues when engaged with enhanced experiences
RQ2: To what extent do participants perceive salutogenic design qualities (e.g., sense of "being away", social connection, and/or enjoyment) in the simulated versus enhanced VR experiences?	With enhanced experiences, participants reported escaping or feeling immersed in a new environment (e.g., Hal talked about "going away" to the symphony when experiencing the enhanced symphony VR environment). Participants also felt more connected to musicians and the conductor in the enhanced symphony, and they reported more enjoyment in the enhanced experiences
RQ3: Do perceptions and experiences of PWD differ from other participants?	PWD reported lower levels of immersion and engagement with the VR experiences. They also experienced greater technology challenges when compared with other participants
RQ4: What desires and expectations do older adults have for future VR experiences?	Participants desired enhanced experiences. They specifically asked for opportunities to engage in activities no longer available to them (like travel or outdoor recreation). They also saw VR as a potential avenue for connecting with friends and family across distance

experiences. In total, participants spent 15–20 mins in VR during the focus groups.

Data Analysis

Focus group video recordings and detailed notes were analyzed using thematic analysis and the constant comparative method (Braun and Clarke, 2006; Saldana, 2012). Two researchers first reviewed all data independently and identified broad themes that emerged. They then shared their initial findings, discussed their codes, and reviewed the data a second time. At the end of this second coding, the researchers worked to eliminate disagreements through conversation, and arrived at a set of findings guided by the research questions.

RESULTS

RQ 1: Simulated Versus Enhanced Virtual Reality

Analysis (see **Table 4**) found that participants preferred enhanced experiences over the simulated experience, and all preferred the enhanced symphony over the campus tour. In part one, many participants (*n* = 7) perceived the simulated symphony as poor video quality (although all videos were 4 k resolution) and were disappointed by the lack of environmental immersion. Some (*n* = 3) thought the experience was no better (and, in some cases, worse) than watching a concert on television. Ken (FG1) explained, "You just feel like you're watching a picture or video. I never saw anyone around me." Gene (FG2) was also disappointed: "It felt like we were in the cheap seats." Evelyn (FG2) agreed: "The picture was blurry. If you looked down, you could see the heads of the people in the audience, but just a little. It made it a little more realistic, but it was a fuzzy picture [. . .] The sound sounded like a recording [. . .] You miss a lot because you're not there." June (FG2) kept asking if the volume could be adjusted; she explained, "I don't feel I heard the music very well [. . .]"

In part two, participants were much more pleased with the enhanced symphony, where they were positioned on center stage and music direction varied according to instrument positionality. Additionally, participants had fewer complaints about audio-visual quality or HMD comfort. All participants in the last three focus groups had visual impairments (*n* = 6), yet only two reported issues seeing musicians and instruments. However, both participants noted that when images became unclear, they could adjust the headset to make them clear, demonstrating blurry images were not due to video quality and they were motivated to improve the visual experience.

All participants experienced the virtual campus tour. Participants in focus groups 1–3 who experienced the replication symphony preferred the campus tour (except one PWD who declined to participate in the tour); those in focus groups 4–6 all preferred the enhanced symphony over the tour. Leann (FG3) described her preference for the tour over the simulated symphony: "[It was] fascinating! It felt like you were right there, and you could see everything. When the handle came out right in front of you, I wanted to grab it!" Conversely, all participants (n = 6) who experienced the enhanced symphony preferred it over the tour. Betty (FG4) talked about her desire to spend more time at the symphony, "I preferred the symphony, because it was just that. And then you could do your looking [around], and you could 'Oh, I want to see who's directing?' And you could turn around. Or you could 'Oh, I want to see if [musician] is there!' [. . .] You could concentrate more on it." Leann, the only participant to experience all three virtual experiences, changed her preference from the tour (FG3) to the enhanced symphony (FG4): "It's so wonderful! It was very interesting and very exciting! It felt so real! You felt like you were part of the orchestra! I'd like to stay there for a longer time."

RQ 2: Perceptions of Salutogenic Design Qualities

Participants expressed positive distraction and greater engagement in both enhanced VR experiences and improved social connectedness in the enhanced symphony experience. Participants were less likely to comment about HMD discomfort or audio-video dissatisfaction during enhanced VR experiences, suggesting increased immersion. In the enhanced symphony, participants described a strong sense of social connectedness with musicians and the conductor. For example, Leann (FG4) talked about proximity and connection with the musicians, "Oh my goodness! [The musicians] are so close to me! Oh, this is wonderful!" Darla (FG6) watched the conductor —a perspective she could not experience at a live concert: "And to turn around and watch the director! I thought it was interesting because each director has their own hand signals." Similarly, Hal (FG5) expressed his engagement, "The focus, the sound, the vision of being able to watch and observe the orchestra. You're right there. They're right in front of you. I wouldn't change anything. It's amazing!" As his focus group continued, Hal kept commenting on how "wonderful" the symphony was. Several times he joked about stealing a headset so that he could spend his free time "at the symphony," demonstrating his ability to escape and feel fully immersed.

RQ 3: Similarities and Differences in Experiences of People With Dementia

People with dementia participated in the first (Fred and Robert) and third (June) focus groups, which compared the simulated symphony and enhanced campus tour. At times, PWD echoed the experiences of other participants. For example, Fred talked about his desire for clearer images and more interactive environments after the replication symphony: "It's not quite as interactive as I'd like." At other times, specific challenges arose for PWD. For example, when asked about what she liked about the replication symphony, Jane explained that she could not remember much—a common occurrence resulting from dementia. In FG1, both Fred and Robert struggled to work the headset more than other participants. At one point, Fred expressed frustration, "I don't think I'm doing anything right!" Eventually, Fred was able to experience the virtual campus tour, and described it as disappointing, "I'm really not comfortable with [the headset]. I'm not sure what I can get out of it. I heard some of the music loud enough, so it was easy to spot it and all that, but I didn't know what to do with it. So, I got it moving around a little bit, but I didn't feel like it was doing anything I asked it to do." Similarly, Robert experienced the replication symphony after overcoming some initial hesitancy. He provided limited feedback and then declined to try the headset again. Robert was the only participant who declined a second virtual experience. In general, PWD expressed less sense of VR immersion and engagement and greater technology challenges.

RQ 4: Desires and Expectations for Future Virtual Reality Experiences

After engaging in the VR experiences, participants provided suggestions for future experiences. In general, participants desired experiences aligning with salutogenic design principles that could increase their engagement beyond real-world limitations and allow greater personal control. For example, several (n = 4) participants who viewed the enhanced symphony noted that they could still see the symphony live; however, they could not view a performance from center stage. They all acknowledged the potential for VR to connect them with activities that they could not do. Participants talked about going surfing, skiing, or hiking: "There's things I've never experienced that I would love to do still, you know, even at my age. [Skiing] would be exciting [. . .]" (Sheila, FG2). Several (n = 7) participants also talked about using VR to drive or travel, activities they missed. A few (n = 4) talked about the potential to watch sporting events, as Leann (FG3) explained: "I think viewing sports would be great for people who are stuck in their homes and can't get out." In general, participants saw VR's potential, and most were excited by opportunities to overcome their limitations in virtual spaces. Carl (FG5) talked about his desire to use VR to connect with his family: "[. . .] I have a lot of grandkids and children that live elsewhere, spread around. It'd be nice to actually see them." Indeed, several participants talked about VR as a way to connect with others that would be more immersive than phone calls or text messages. Finally, one participant suggested greater control (i.e., improving self-efficacy) in the VR experiences: "I think what I would like is for each person to have more control [.] over what I was looking at. To stay longer on one thing and then maybe switch to another thing." (Leann, FG4).

DISCUSSION

Research suggests that non-pharmacological interventions have salutogenic potential to delay cognitive decline and enhance quality of life among older adults (Davalos et al., 2019;

Faw et al., 2021). There is a critical need to develop effective, accessible, and enjoyable interventions to help preserve cognition. Results from six focus groups exploring three VR experiences indicates important opportunities and challenges for developing VR as a salutogenic strategy for enhancing wellbeing among older adults. An important conclusion from this research is that VR is a viable intervention for older adults with and without dementia, and co-design processes may be critical for improving salutogenic design features. Importantly, co-design processes revealed that older adults perceived VR experiences positively but do not want virtual experiences that merely simulate real-world ones. Participants during the first three focus groups universally identified the replication symphony experience as underwhelming. Conversely, participants in the last three focus groups praised the enhanced symphony experience, describing it as immersive and exhilarating. It is also important to note that participants found the immersive symphony experience *more* engaging and enjoyable than the activities in the campus tour. Our long-term goal has been to recreate real-world symphony experiences, including walking into the concert hall, virtual interactions with audience members before the concert, etc. However, given participants' desire for enhanced experiences, we believe continued co-design to explore their reactions to these simulated elements is essential in building out future VR experiences. Notably, PWD experienced less immersion and more technology challenges than others, suggesting co-design with PWD is both feasible and important for understanding barriers and opportunities specific to this population. Furthermore, co-design with PWD at different disease stages is needed to better understand how to design VR to enhance its salutogenic potential. Involving older adults as collaborators to co-design technologies at all stages (e.g., from pre-design through prototype testing and iteration, to product evaluation and impacts on wellbeing) is essential for improving salutogenic potential (Sumner et al., 2021). With this in mind, we make the following recommendations:

Practical Suggestions for Future Virtual Reality-Enhanced Experiences With Older Adults

Engage Older Adults in the Co-design of Virtual Reality Experiences

Virtual reality interventions are viable for older adults; participants were willing and excited to use VR with assistance. As Hal (FG5) said, "I gotta tell ya, this is a winner for us seniors." However, there remains little research about how to design engaging VR experiences for older adults. Prior to conducting the focus groups, we anticipated that participants would feel socially connected by "virtually" sitting in the audience during a symphony performance. However, this was not the case; social connection was fostered when video was captured from center stage. This highlights the value of early and frequent engagement with older adults and suggests co-design during pre-design phases may be useful for identifying VR experiences older adults would find most engaging.

Consider the Unique Needs of People With Dementia, Including How These Change With Disease Progression

Based on prior research, we anticipated that PWDs would have greater challenges with technology; however, we did not anticipate that their sense of immersion would be lower than others. Frustration with technology may have mediated engagement in VR. However, sense of immersion and engagement might also have been affected by stage of disease progression, suggesting more co-design research with PWD is needed to understand what types of salutogenic interventions may be beneficial. PWD may be particularly sensitive about being embarrassed if they find the VR experience confusing, meriting special design attention (Hodge et al., 2018; Lee et al., 2019).

Salutogenic Design Principles May Be Useful for Creating Virtual Reality Experiences

Immersive VR involves complicated aspects of film and environmental design. Salutogenic design is a human-centered, evidence-based approach to designing environments to promote wellbeing. Our study considered only a few aspects of salutogenic design (positive distraction, environmental engagement, and social connectedness). Future projects may find salutogenic design a useful framework and, in turn, findings from VR research (where experimental control is more feasible) may help to inform salutogenic design strategies for real-world settings.

Consider Technology Access, Affordances, and Limitations

There were several practical challenges with our study's headsets. At least three participants noted that the headsets felt heavy, forcing them to limit their time in the headset. Additionally, all participants hesitated to use the headsets without guidance, indicating a barrier to adoption. Nevertheless, several participants mentioned interest in being able to check out VR headsets from the library and in buying a headset for personal use. From a research standpoint, VR is a beneficial tool as it puts participants in controlled environments and gives researchers the ability to generate varied and immersive stimuli for them. VR technology is rapidly evolving, and, since our pilot study, new, lighter headsets have come to market with improved graphics. Additionally, a viable VR experience for older adults would require significant time to train participants to use HMDs without assistance. Studies that have included training protocols found improved VR comfort and usability (Optale et al., 2010; Wen et al., 2018), thus investing time and resources into training older adults may be beneficial in overcoming VR adoption limitations.

Limitations and Directions for Future Research

While our study presents valuable data, it is not without limitations. First, these results represent a small, homogenous sample drawn from one region of the United States. To fully capture the potential of VR interventions, researchers should test VR designs across a broader sample, including individuals from different racial and cultural backgrounds. Second, this study used three specific VR experiences. The fact that our study used three designs (and made adjustments based on participant feedback during the project) is both a strength and a limitation. It allowed our participants more than one experience to reflect on when sharing their impressions. However, these experiences are not representative of the diverse VR content available. As such, researchers should explore how older adults respond to different VR experiences, especially by engaging them early in co-design. We hope to see future projects co-create VR experiences that are tailored to participants' unique background and personal preferences, as this might be particularly valuable for PWD. Additionally, PWD and CPs only experienced the simulated symphony and campus tour, giving us limited insight regarding how they might respond to other enhanced experiences (like the enhanced symphony). Another limitation was the fact that PWD participants were not tested for their dementia stage. As dementia is a degenerative condition, it is possible that PWD at earlier stages might experience VR differently and appreciate varying VR dimensions than PWD at more advanced stages. Continued co-design with PWD can attend to these issues more carefully, working to develop recommendations designed to highlight best VR practices across the dementia spectrum.

CONCLUSION

The present study used salutogenic design principles and co-design methods to explore older adults' reactions to three VR experiences. Across focus groups, participants preferred enhanced experiences and benefited from the salutogenic design properties of social connection, immersion, and engagement. Participants expressed their desires for enhanced experiences in future VR interventions. PWD and CPs experienced greater technology challenges and lower levels of immersion, indicating that additional co-design research with these populations is needed to produce to more effective interventions that attend to their unique needs.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Colorado State University Institutional Review Board. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

MF and TB conducted all the focus groups and analyzed the focus group data. MF and LM secured funding for the project. All authors contributed to the conception and design of the study, wrote, read, and approved the final manuscript version.

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REFERENCES

Antonovsky, A. (1979). *Health, stress, and coping*. San Francisco: CA: Jossey-Bass Publishers.

Armitage, R., and Nellums, L. B. (2020). COVID-19 and the consequences of isolating the elderly. *Lancet* 5:E256. doi: 10.1016/S2468-2667(20)30061-X

Bayles, K. A., Kaszniak, A. W., and Tomoeda, C. K. (1987). *Communication and cognition in normal aging and dementia*. Boston, MA: Little, Brown & Co.

Beidel, D. C., Frueh, B. C., Neer, S. M., Bowers, C. A., Trachik, B., Uhde, T. W., et al. (2019). Trauma management therapy with virtual-reality augmented exposure therapy for combat-related PTSD: A randomized controlled trial. *J. Anxiety Disord.* 61, 64–74. doi: 10.1016/j.janxdis.2017.08.005

Braun, V., and Clarke, V. (2006). Using thematic analysis in psychology. *Qualitat. Res. Psychol.* 3, 77–101. doi: 10.1191/1478088706qp063oa

Burzynska, A. Z., and Malinin, L. H. (2017). Enriched Environments for Healthy Aging: Qualities of Seniors Housing Designs Promoting Brain and Cognitive Health. *Seniors Housing Care J.* 25, 15–37.

Cinderby, S., Cambridge, H., Attuyer, K., Bevan, M., Croucher, K., Gilroy, R., et al. (2018). Co-designing urban living solutions to improve older people's mobility and well-being. *J. Urban Health* 95, 409–422.

Davalos, D. B., Luxton, I., Thaut, M., and Cross, J. E. (2019). B Sharp-cognitive effects of a community music program for people with dementia-related disorders. *Alzheimer's Dement. Translat. Res. Clin. Intervent.* 5, 592–596. doi: 10.1016/j.trci.2019.08.004

Diemer, J., Domschke, K., Mühlberger, A., Winter, B., Zavorotnyy, M., Notzon, S., et al. (2013). Acute anxiolytic effects of quetiapine during virtual reality exposure—A double-blind placebo-controlled trial in patients with specific phobia. *Eur. Neuropsychopharmacol.* 23, 1551–1560. doi: 10.1016/j.euroneuro.2013.01.001

Doniger, G. M., Beeri, M. S., Bahar-Fuchs, A., Gottlieb, A., Tkachov, A., Kenan, H., et al. (2018). Virtual reality-based cognitive-motor training for middle-aged adults at high Alzheimer's disease risk: A randomized controlled trial. *Alzheimer's Dement. Translat. Res. Clin. Intervent.* 4, 118–129. doi: 10.1016/j.trci.2018.02.005

du Sert, O. P., Potvin, S., Lipp, O., Dellazizzo, L., Laurelli, M., Breton, R., et al. (2018). Virtual reality therapy for refractory auditory verbal hallucinations in schizophrenia: A pilot clinical trial. *Schizophrenia Res.* 197, 176–181. doi: 10.1016/j.schres.2018.02.031

Dyer, S. M., Harrison, S. L., Laver, K., Whitehead, C., and Crotty, M. (2018). An overview of systematic reviews of pharmacological and non-pharmacological interventions for the treatment of behavioral and psychological symptoms of dementia. *Int. Psychogeriatr.* 30, 295–309. doi: 10.1017/S1041610217002344

Faw, M. H., Cross, J., Luxton, I., and Davalos, D. (2021). Surviving and Thriving: Exploratory Results from a Multi-Year, Multidimensional Intervention to Promote Well-being among Caregivers of Adults with Dementia. *Int. J. Environ. Public Health* 18:4755.

Gamito, P., Oliveira, J., Morais, D., Coelho, C., Santos, N., Alves, C., et al. (2018). Cognitive stimulation of elderly individuals with instrumental virtual reality-based activities of daily life: Pre-post treatment study. *Cyberpsychol. Behav. Soc. Netw.* 22, 69–75. doi: 10.1089/cyber.2017.0679

Gomez, J., Hoffman, H. G., Bistricky, S. L., Gonzalez, M., Rosenberg, L., Sampaio, M., et al. (2017). The use of virtual reality facilitates Dialectical Behavior Therapy® "observing sounds and visuals" mindfulness skills training exercises for a latino patient with severe burns: A case study. *Front. Psychol.* 8:01611. doi: 10.3389/fpsyg.2017.01611

Greenbaum, T. L. (1998). *The handbook for focus group research*, 2nd Edn. Thousand Oaks, CA: Sage.

Griggs, A., Faw, M. H., and Malinin, L. H. (2020). "The Art of Love: Using Participatory Community Arts Engagement to Facilitate Relational Maintenance among Couples with Dementia," in *More Than Words: Expressive Therapeutic Narrative Praxis in Educational, Clinical, and Everyday Settings*, eds K. Afary and A. Fritz (Boulder, CO: Lexington).

Gross, A. L., Rebok, G. W., Unverzagt, F. W., Willis, S. I., and Brandt, J. (2011). Cognitive predictors of everyday functioning in older adults: Results from the ACTIVE cognitive intervention trial. *J. Gerontol. Ser. B* 66B, 557–566. doi: 10.1093/geronb/gbr033

Hodge, J., Balaam, M., Hastings, S., and Morrissey, K. (2018). Exploring the design of tailored virtual reality experiences for people with dementia. *Proc. 2018 CHI Confer. Hum. Factors Comput. Syst. CHI* 18, 1–13. doi: 10.1145/3173574.3174088

Hoffman, H. G., Rodriguez, R. A., Gonzalez, M., Bernardy, M., Peña, R., Beck, W., et al. (2019). Immersive virtual reality as an adjunctive non-opioid analgesic for pre-dominantly latin american children with large severe burn wounds during burn wound cleaning in the intensive care unit: A pilot study. *Front. Hum. Neurosci.* 13:00262. doi: 10.3389/fnhum.2019.00262

Kourtesis, P., Collina, S., Doumas, L. A. A., and MacPherson, S. E. (2019). Technological competence is a pre-condition for effective implementation of virtual reality head mounted displays in human neuroscience: A technological review and meta-analysis. *Front. Hum. Neurosci.* 13:00342. doi: 10.3389/fnhum.2019.00342

Lee, L. N., Kim, M. J., and Hwang, W. J. (2019). Potential of augmented reality and virtual reality technologies to promote wellbeing in older adults. *Appl. Sci.* 9:3556.

Li, K. H.-Z., and Lindenberger, U. (2002). Relations between aging sensory/sensorimotor and cognitive functions. *Neurosci. Biobehav. Rev.* 26, 777–783. doi: 10.1016/S0149-7634(02)00073-8

Li, S.-C., Lindenberger, U., Hommel, B., Aschersleben, G., Prinz, W., and Baltes, P. B. (2004). Transformations in the couplings among intellectual abilities and constituent cognitive processes across the life span. *Psychol. Sci.* 3, 155–163. doi: 10.1111/j.0956-7976.2004.01503003.x

Malbos, E., Rapee, R. M., and Kavakli, M. (2013). A controlled study of agoraphobia and the independent effect of virtual reality exposure therapy. *Austral. N. Z. J. Psychiatry* 47, 160–168. doi: 10.1177/0004867412453626

Man, D. W., Chung, J. C., and Lee, G. Y. (2012). Evaluation of a virtual reality-based memory training programme for Hong Kong Chinese older adults with questionable dementia: A pilot study. *Int. J. Geriatric Psychiatry* 27, 513–520. doi: 10.1002/gps.2746

Manera, V., Chapoulie, E., Bourgeois, J., Guerchouche, R., David, R., Ondrej, J., et al. (2016). A feasibility study with image-based rendered virtual reality in patients with mild cognitive impairment and dementia. *PLoS One* 11:e0151487. doi: 10.1371/journal.pone.0151487

Mazzi, A. (2020). Toward a Unified Language (and Application) of Salutogenic Design: An Opinion Paper. *HERD Health Environ. Res. Design J.* 2020:1937586720967347.

McKhann, G. M., Knopman, D. S., Chertkow, H., Hyman, B. T., Jack, C. R., Kawas, C. H., et al. (2011). The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's Dement.* 7, 263–269. doi: 10.1016/j.jalz.2011.03.005

Mobley, C., Leigh, K., and Malinin, L. (2017). Examining relationships between physical environments and behaviors of residents with dementia in a retrofit special care unit. *J. Interior Design* 42, 49–69.

Norrholm, S. D., Jovanovic, T., Gerardi, M., Breazeale, K. G., Price, M., Davis, M., et al. (2016). Baseline psychophysiological and cortisol reactivity as a predictor of PTSD treatment outcome in virtual reality exposure therapy. *Behav. Res. Therapy* 82, 28–37. doi: 10.1016/j.brat.2016.05.002

Optale, G., Urgesi, C., Busato, V., Marin, S., Piron, L., Priftis, K., et al. (2010). Controlling memory impairment in elderly adults using virtual reality memory training: A randomized controlled pilot study. *Neurorehabil. Neural Repair* 24, 348–357. doi: 10.1177/1545968309353328

Parsons, T. D. (2015). Virtual reality for enhanced ecological validity and experimental control in the clinical, affective and social neurosciences. *Front. Hum. Neurosci.* 9:00660. doi: 10.3389/fnhum.2015.00660

Pot-Kolder, R. M. C. A., Geraets, C. N. W., Veling, W., van Beilen, M., Staring, A. B. P., Gijsman, H. J., et al. (2018). Virtual-reality-based cognitive behavioural therapy versus waiting list control for paranoid ideation and social avoidance in patients with psychotic disorders: A single-blind randomised controlled trial. *Lancet Psychiatry* 5, 217–226. doi: 10.1016/S2215-0366(18)30053-1

Raglio, A., Bellelli, G., Mazzola, P., Bellandi, D., Giovagnoli, A. R., Farina, E., et al. (2012). Music, music therapy and dementia: A review of literature and the recommendations of the Italian Psychogeriatric Association. *Maturitas* 72, 305–310. doi: 10.1016/j.maturitas.2012.05.016

Rothbaum, B. O., Price, M., Jovanovic, T., Norrholm, S. D., Gerardi, M., Dunlop, B., et al. (2014). A randomized, double-blind evaluation of d-cycloserine or alprazolam combined with virtual reality exposure therapy for posttraumatic stress disorder (ptsd) in iraq and Afghanistan war veterans. *Am. J. Psychiatry* 171, 640–648. doi: 10.1176/appi.ajp.2014.13121625

Saldana, J. (2012). *The Coding Manual for Qualitative Researchers* (2nd Ed.). Thousand Oaks, CA: Sage Publications.

Serafino, P. (2018). *Another Alzheimer's drug fails as Lilly, Astra Halt Tests*. New York, NY: Bloomberg.

Sumner, J., Chong, L. S., Anjali Bundele, B. D. S., and Lim, Y. W. (2021). Co-designing technology for aging in place: A systematic review. *Gerontologist* 61, e395–e409. doi: 10.1093/geront/gnaa064

Threapleton, K., Newberry, K., Sutton, G., Worthington, E., and Drummond, A. (2017). Virtually home: Exploring the potential of virtual reality to support patient discharge after stroke. *Br. J. Occupat. Therapy* 80, 99–107. doi: 10.1177/0308022616657111

Tsekleves, E., and Cooper, R. (2017). Emerging trends and the way forward in design in healthcare: An expert's perspective. *Design J.* 20, S2258–S2272.

Wen, D., Lan, X., Zhou, Y., Li, G., Hsu, S.-H., and Jung, T.-P. (2018). The study of evaluation and rehabilitation of patients with cognitive impairment phases based on virtual reality and EEG. *Front. Aging Neurosci.* 10:00088. doi: 10.3389/fnagi.2018.00088

World Health Organization (2015). *World report on aging and health, 2015*. Geneva: World Health Organization.

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