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Psychosocial aspects of skin conditions and diseases

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Psychosocial aspects of skin conditions and diseases

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Role of burn severity and posttraumatic stress symptoms in the co-occurrence of itch and neuropathic pain after burns: A longitudinal study

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Itch and pain are common after burns. Neuropathic mechanisms may underlie both modalities but remain not well-understood. This study aims to prospectively document neuropathic pain symptoms and to identify potential itch symptom profiles that differ regarding duration and co-occurrence with neuropathic pain which may inform underlying pathophysiological mechanisms and respond to different treatments. Adult burn survivors (n = 192) self-reported itch and neuropathic pain at 2 weeks post-discharge, 3, 6, 12, and 18 months post-burn. Based on the presence of itch and pain symptoms over time, participants were allocated to one itch profile: transient itch/pain, chronic itch, or chronic *itch & pain*. Profiles were compared on itch *intensity* over time using General Linear Modeling. Age, gender, burn severity, posttraumatic stress (PTS) symptoms and baseline itch intensity were examined as potential predictors of the profiles in a Multi-nominal regression analysis. Neuropathic pain occurred in 54% after discharge which decreased to 24% 18 months later. Itch intensity was highest in the chronic *itch & pain* profile. Compared to the transient itch profile, the chronic *itch & pain* profile was associated with higher burn severity and more PTS symptoms. Compared to the chronic itch profile, the chronic *itch & pain* profile was associated with more PTS symptoms. Findings suggest that biological and psycho-dermatological processes underlie both chronic neuropathic pain and itch processes in burn scars. Further research should elucidate the mechanisms underlying the different itch profiles, with specific focus on skin innervation and psychological factors.

KEYWORDS

pruritus, neuropathic pain, scars, posttraumatic stress symptoms, burns

Introduction

Over the past decade, studies have shown that prevalence rates of pain and itch after the acute phase of burn injury continue to be high. During hospitalization, most patients suffer from pain and itch (1, 2). Although the vast majority of studies shows a subsequent symptom decrease along with scar maturation processes (3, 4), a subgroup develops chronic itch and pain (1, 5) that seems localized within the scars (3, 6). Typically, prevalence rates of itch exceed those of pain [e.g. (7, 8)], indicating itch profiles co-occurring with and without pain. Because pain and itch intensity are highly correlated (9) and share common predictors, severity of both pain and itch may be linked. Examples are e.g., burn severity, particularly related to depth of the wound (1, 3, 10) and posttraumatic stress (PTS) symptoms (10–12). There is convincing evidence for an entangled relationship between chronic pain and PTS symptoms across many patient groups (13). Evidence for a connection between chronic itch and PTS symptoms has also been described (14), but far less studies are currently available compared to pain.

A neuropathic mechanism is assumed to underlie both pain and itch after burns. Neuropathic pain symptoms such as pins and needles, shooting, and burning pain have been described (15, 16), qualifying as spontaneous pain sensations (stimulus-independent) or paresthesia (e.g., burning pain, electric shocks) (17–19). Also itch is assumed neuropathic, particularly after the acute phase when the role of histamine and substance P have abated (20), subscribing that chronic itch seems mostly non-histaminergic (21). Both neuropathic pain and itch can develop after a lesion of the somatosensory system, with involvement of both peripheral and central processes (17, 22). Although peripheral nerve fibers may regenerate after burns, abnormal nerve fiber density in scars has been reported (23). In general, it is assumed that itch is predominantly peripherally activated because, as yet, central sensitization could not be established (6, 24).

Within a neuropathic pathology, also after burns, itch and pain temporally and spatially concur (9). But the underlying neuronal pathways are not fully understood. Current theories, e.g., the labeled line, selectivity, and pattern theory, propose that itch can result from various neuronal pathways, amongst which itch-specialized primary afferent neurons (pruriceptors) and nociceptors are involved (25, 26). Pruriceptors are assumed to transduce itch when being activated by specific molecular markers (e.g., IL-31) (26, 27). Nociceptors may respond to both algogens and pruritogens and are supposed to be differentially activated based on spatial (e.g., focal nociceptive input will produce itch) and temporal aspects of the peripheral input; hence the experienced pain or itch results from the combination of activated fibers (26, 28). Additionally, via inhibitory spinal interneurons, pain signals may inhibit itch transmission. However, in neuropathic itch, it has been put forward that the co-occurrence of itch and pain may result from impaired spinal inhibition, despite current inconclusive evidence (25, 28). Based on the current theories, one may argue that chronic itch and pain after burns may be related and explained by those various mechanisms. Therefore, identifying sensory profiles of itch and pain symptom and biological and psychological differences across the profiles may further elucidate underlying mechanisms.

This 18-months multi-center longitudinal study aims to document neuropathic pain prevalence as well as potential symptom profiles of itch and neuropathic pain that may present after burns, and to explore potential predictors, such as burn severity, age, gender and PTS symptoms potentially related to the symptom profiles.

Methods

Patients

This study was part of a larger longitudinal multi-center project examining pain after burn injuries. Previous papers about this project described pain measured with the Brief Pain Inventory (2, 12, 29) but did not focus on itch and neuropathic pain. Patients were included in the study between April 2010 and December 2012 from five burn centers in the Netherlands and in Belgium. Adult patients admitted to the burn centers for >24 h were eligible for inclusion in the study. Exclusion criteria included poor Dutch proficiency, acute or chronic cognitive problems, or when the injury was deliberate. Patients requiring mechanical ventilation were invited to participate as soon as they were able to provide informed consent. During the study period, 340 patients met the inclusion criteria of which 84 declined participation and 40 were missed. A group of 216 patients signed informed consent (64%). They did not differ from the 124 patients not included in the study in terms of age, gender, and affected body area [see also (12)].

Measures

Neuropathic pain and itch were measured using an adapted version of the self-report Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale (30), a validated screening questionnaire for neuropathic pain (31). The original scale measures the presence (present yes/no) of five symptoms: unpleasant sensations (pricking, tingling, pin-pricks), color differences (motted and looking more red), abnormally sensitive to touch, pain comes suddenly and in bursts (electric shocks), perceived skin temperature (hot or burning). We added to the original version: (1) as part of the item perceived skin temperature, cold sensations were added (original scale only includes hot or burning), (2) a sixth item measuring itch, and (3) in the case that the participant scored "yes," the intensity

of the symptom was scored on a 7-point Likert scale ranging from 0 (not troublesome) to 6 (severely troublesome) which allows to measure the intensity of the symptom, and (4) items were adapted in order to measure pain related to the scars. e.g., "Does the pain feel like a strange and unpleasant sensation *in your scars*?," and "Does the pain cause *the scar* to look different to normal skin or to that of *scars* that are not painful?." Unlike the original LANSS, physical assessments of allodynia and altered pin-prick thresholds were not tested in this study because patients self-reported their symptoms. The scale was translated into Dutch by two researchers and back-translated by a native English speaker.

Posttraumatic stress (PTS) symptoms were measured using the Impact of Event Scale-Revised (IES-R) (32). The IES-R measures intrusive, avoidant and hyperarousal symptoms associated with a traumatic event. The original 15 items of the IES (33) and the seven hyperarousal items of the IES-R were used and scored with a 4-point scale (0-1-3-5). The construct validity and reliability of the Dutch version of the IES-R was acceptable (34). Cronbach's alpha was high (0.96). In this study, the 3-month measurement indicative of PTS symptoms rather than acute traumatic stress symptoms was used as a predictor.

Demographic characteristics (i.e., gender and age) and burn severity (i.e., percentage total body surface area (TBSA) burned as well as skin graft procedures) were recorded from the medical file. TBSA burned is the estimated percentage body surface area affected by partial and full-thickness burns.

Procedure

The study was approved by an ethics committee in the Netherlands (METC Noord-Holland NL27996.094.09) and Belgium (Ghent University B670201112923) and by local institutional review boards of the participating hospitals, and was conducted in accordance with the Helsinki Declaration. Eligible patients were identified by local researchers during admission to the hospital. Oral and written information was provided. Written informed consent was obtained from each patient. Patients completed printed questionnaires in-hospital (e.g., psychological questionnaires), 2 weeks after discharge (T1), 3 months (T2), 6 months (T3), 12 months (T4), and 18 months (T5) after the burn event.

Data analysis

First, descriptive analyses were performed and patients with complete follow-up were compared with patients who had incomplete follow-up on burn characteristics and demographics using student *t*-tests. Second, itch and neuropathic pain profiles were examined. Two persons (NVL and AvL) independently categorized patients according to the duration of itch and pain [based on literature (3), we used 6 months as cutoff point for chronic itch post-burn which is associated with scar maturation, in contrast to 6 weeks akin the definition of chronic itch resulting from other causes (35)], and potential co-occurrence of neuropathic pain into the following groups: (1) patients reporting itch and/or pain that disappeared after 6 months (*transient itch/pain*); (2) patients reporting itch but never reported pain after 3 months postburn (because we can not exclude that patients may have had small wounds in the postacute phase) (*chronic itch*); (3) patients reporting itch and pain at least 2 out of 5 measurements of which at least once after 6 months (*chronic itch* & *pain*). Beyond the scope of this paper, other profiles included: (4) patients reporting only pain (*chronic pain*); (5) patients reporting no pain or itch (*no pain/itch*). Discrepancies in the categorization of patients were resolved by discussion.

Third, to examine potential differences in the course of itch intensity for the three itch profiles (independent variable), General Linear Modeling (GLM) for repeated measures was conducted with SPSS Statistics for Windows (Version 27.0. Armonk, NY: IBM Corp) with itch intensity over time (T1–T5) as the within-subjects dependent variable and the three itch profiles as independent variable. To investigate potential predictors of the three itch profiles, multi-nominal logistic regression analysis, which uses maximum likelihood estimation to evaluate the probability of categorical membership (of the three itch profiles), was used. Established predictors of both itch and neuropathic pain after burns (age, gender, TBSA burned, surgeries and PTS symptoms) controlling for T1 itch intensity were examined.

Results

Patients

Informed consent was provided by 216 patients, but 24 did not complete any of the measurements leaving a final sample size of 192. At discharge (T1), 177 assessments (92%) were available, 166 (86%) at 3 months (T2), 155 (81%) at 6 months (T3), 152 (79%) at 12 months (T4) and 146 (76%) at 18 months (T5). The 146 patients who completed T5 were older [$t_{(213)} = -4.585$, $p < 0.001$], and had higher TBSA burned [$t_{(213)} = -2.779$, $p = 0.006$] and more surgeries [$t_{(213)} = -2.415$, $p = 0.017$] compared to 46 patients lost to follow-up between T2 and T5.

Of the participants, 129 (67%) were male and 63 (33%) were female. Participants were on average 41.56 years old (SD = 15.58). TBSA burned ranged from 1 to 75% ($M = 9.34$, $SD = 8.85$). Ninety participants (46.9%) did not require surgery, 102 (53.1%) needed one or more skin graft procedures. The mean score indexing PTS symptoms was 21.46 ($SD = 23.89$) at 3 months post-burn.

Itch and pain co-occurrence and itch profiles

The percentage of patients reporting itch decreased over time from 78% (T1) to 43% (T5). For pain, this was 54% (T1) and 24% (T5). Figure 1A presents the prevalence rates of itch and neuropathic pain symptoms (percentage reporting the symptom was present) at the respective time points for the total sample. Whereas itch prevalence rates decreased steadily, pain symptom prevalence remained relatively stable. Figure 1B presents the intensity of itch and pain symptoms measured using a 7-point Likert scale. The blue bars show that itch intensity in the total sample decreased over time, mainly due to the increasing number of patients in which itch disappeared. The orange bars show that itch intensity in the subgroup that also experienced neuropathic pain symptoms was higher on average and more stable. The varying number of patients for every symptom over time can be found in Supplementary Table 1, also presenting additional descriptive details such as mean, standard deviation and median.

Categorization into the different itch profiles was as follows: 51 patients (26.6%) reported *transient itch/pain*, 46 patients (24.0%) reported *chronic itch*, 41 patients (21.4%) reported *chronic itch* & *pain*, 7 patients (3.6%) reported *chronic pain*, 11 patients (5.7%) never reported pain or itch. Twenty-seven patients (14.0%) had no measurements after 6 months, or the symptom pattern could not be attributed to the aforementioned groups ($n = 9$; 4.6%). Table 1 presents the means and standard deviations of the predictor variables for the different profiles. The *chronic itch* & *pain* profile included most patients that needed surgery, had more PTS symptom and comprised more women.

Itch intensity trajectories

GLM was used to study possible differences in itch intensity over time across the three itch profiles. Figure 2 shows that itch intensity was highest in the *chronic itch* & *pain* profile. The main effect of the profiles was significant, [$F(2, 93) = 44.80$, $p < 0.001$], as was the main linear effect of time, [$F(1, 93) = 36.925$, $p < 0.001$]. This suggests that both the three itch profiles and time explain variation in itch intensity and therefore are relevant to consider. The interaction of these two factors (i.e., the itch profiles and time) was also significant, [$F(2, 93) = 3.409$, $p = 0.037$]. This indicates that the profiles show different patterns of itch intensity over time. Figure 2 shows that patients reporting *transient itch/pain* showed, unsurprisingly, an early steep decline in itch intensity ultimately resulting in complete itch alleviation. Of more interest is the difference between the two chronic profiles, where in both profiles, itch intensity slightly decreased, but remained substantial, with higher itch intensity in the chronic *itch* & *pain* profile than in the chronic itch profile.

Predictors of itch profiles

Using multi-nominal logistic regression analysis, we tested whether the three itch profiles were associated with differences regarding gender, burn severity (TBSA burned and needing surgery) age, PTS symptoms and itch intensity measured post-discharge. The fit between the model containing only the intercept and data improved with the inclusion of the predictor variables [$\chi^2(12, n = 112) = 43.09$, $p < 0.001$, Nagelkerke $R^2 = 0.279$]. This indicates that inclusion of the predictors is meaningful and explains variance across the profiles. In the upper part of Table 2A the *transient itch/pain* profile was the reference group which means that the outcomes of the two chronic itch profiles were compared to the *transient itch/pain* profile. The results revealed that compared to *transient itch/pain* profile, younger patients ($p = 0.045$) and those with a larger TBSA burned ($p = 0.034$), and needing surgery ($p = 0.060$) were more likely to be assigned to *the chronic itch* profile. Needing surgery ($p = 0.004$) and higher levels of PTS symptoms ($p = 0.024$) increased the likelihood to be assigned to the *chronic itch* & *pain* profile. In the lower part of Table 2B, the *chronic itch* & *pain* profile was the reference category which allowed to investigate differences across the two chronic profiles. The results showed one statistically significant difference: PTS symptom levels were higher in the *chronic itch* & *pain* profile ($p = 0.019$).

Discussion

This study prospectively documents itch and neuropathic pain symptom development and investigated itch profiles regarding duration and co-occurrence with neuropathic pain in adult burn survivors. Neuropathic pain symptoms were reported by 54% of the participants at 2 weeks post-discharge which declined to 24% at 18 months postburn. For itch, prevalence rates were 78% at 2 weeks postdischarge and 43% at 18 months postburn. Itch intensity was most severe in the *chronic itch* & *pain* profile. Compared to the *transient itch/pain* profile, both chronic profiles were associated with more severe burns, and the *chronic itch* & *pain* profile was associated with more PTS symptoms.

Patients' symptom profiles differ regarding co-occurrence with neuropathic pain, including *transient itch/pain*, *chronic itch* and *chronic itch* & *pain*. Itch intensity in the *transient itch/pain* profile showed a rapid decrease and the patients had less severe burns. This corroborates earlier findings that partial thickness burns more likely produce temporal itch (3) and may be predominantly histaminergic evoked in the early phase of wound healing streching out to the early remodeling phase in which antihistamines provide relief in a subgroup of patients (20).

Significantly higher itch intensities were perceived by the patients within the *chronic itch* & *pain* profile compared to those

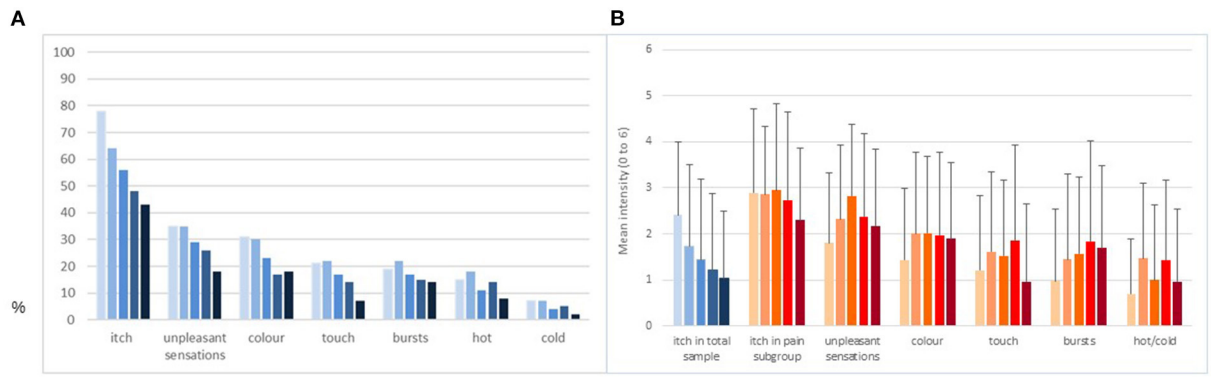

FIGURE 1
Prevalence rates and observed means of itch intensity and neuropathic pain symptom intensity in complete cohort. **(A)** Percentage of patients indicating the symptom was present. **(B)** Observed means of intensity and standard deviations of the symptoms scored on a 7-point Likert scale. Bars from left to right represent the five time points from 2 weeks post discharge (T1, $n = 177$), 3 (T2, $n = 166$), 6 (T3, $n = 156$), 12 (T4, $n = 155$), and 18 (T5, $n = 146$) months post-burn. Blue bars relate to the total sample. Orange bars relate to the subsample experiencing neuropathic pain symptoms.

TABLE 1 Descriptive details of predictors for the different itch profiles.

	Age	TBSA burned	PTS symptoms	Males	≥ One surgeries
Symptom profiles	**M (SD)**	**M (SD)**	**M (SD)**	***N* (%)**	***N* (%)**
Transient itch/pain ($n = 51$)	43.51 (17.79)	7.65 (5.63)	15.06 (20.79)	40 (78.4)	20 (39.2)
Chronic itch ($n = 46$)	38.63 (16.51)	11.78 (8.52)	20.14 (22.31)	31 (67.4)	29 (63.0)
Chronic itch & pain ($n = 41$)	44.24 (15.44)	12.16 (13.19)	30.32 (26.95)	21 (51.2)	31 (75.6)

M, Means; SD, Standard Deviation; N, number.

in the *chronic itch* profile. Provisional support for an association of mixed sensations and symptom severity may come from a study in which patients reporting both neuropathic pain and itch more likey needed both gabapentin and pregabalin compared to patients reporting itch only who received gabapentin to achieve symptom relief (36). Both chronic profiles were associated with more severe burns than the *transient itch/pain* profile. Particularly wounds that needed surgery, i.e., full thickness burns, may have affected skin innervation patterns. The newly regenerating nerve branches may evoke itch and/or pain due to spatial arrangement and spontaneous activity in regenerating sprouts and/or local inflammation (28). When only few epidermal nociceptors are focally activated and many are not, those may produce itch which is described as a "mismatch signal" (25, 37). Possibly, itch-specific pathways are involved in which mediators such as IL-31, pruriceptive neurons, and spinal neurons expressing gastrin-releasing peptide (GRP) play a role, although the latter may also apply to nociceptors (26). Increased levels of IL-31 have been identified in hypertrophic burn scars (38) but the involvement of GRP has not been investigated to our knowledge. What remains unclear is why the co-occurrence of pain and itch produces higher itch intensity. Although speculative, reduced descending inhibition may play a role. Future research may focus on different neuronal pathways in burn scars that may explain variation in itch intensity as well as temporal and spatial co-occurrence of itch and pain.

Higher PTS symptom levels were particularly associated with the *chronic itch* & *pain* profile. This is in line with studies showing a link between PTS symptoms and higher itch intensity (10, 39). Possibly, PTS symptoms affect central processing, potentially decreasing the threshold for pain, and perhaps also for itch. As shown in a study using electroencephalography (EEG) oscillatory activity, itch and pain seem processed differently in burn survivors with PTS symptoms compared to those without PTS symptoms (24). We could speculate that PTS symptoms may influence top-down sensory predictions, which play an important role in symptom perception (40). Due to the repeated peripheral somatosensory input (bottom-up), the brain has learnt to predict upcoming somatosensory sensations. This can result in the actual neurobiological perception of

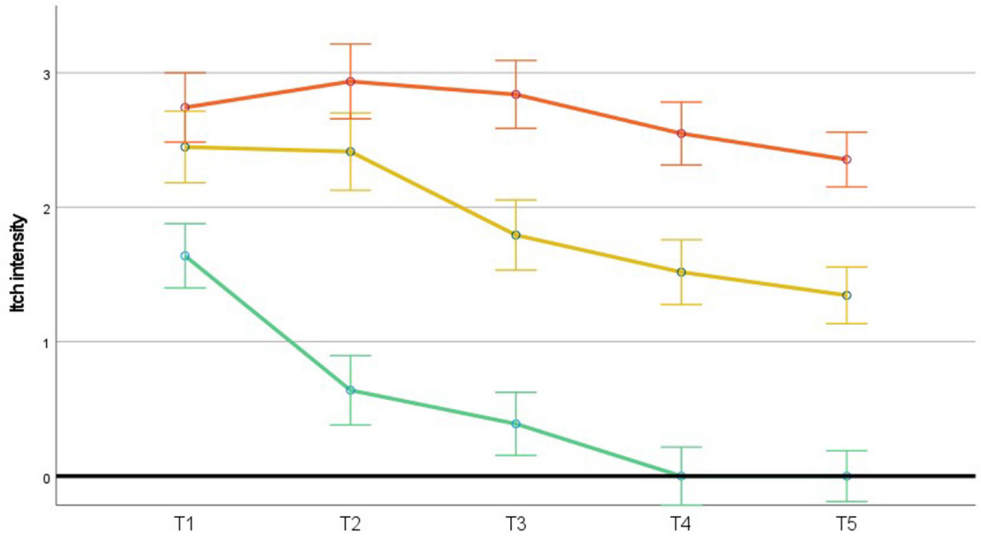

FIGURE 2
Time course of estimated means of itch intensity (ranging from 0 to 6) in the three itch profiles. *N* = 96 (full cases). Upper line (orange) = chronic *itch & pain* (*n* = 31), middle line (yellow) = chronic itch (*n* = 29), lower line (green) = *transient itch/pain* (*n* = 36). Error bars represent 1 standard deviation. T1 = 2 weeks post-discharge, T2 = 3 months post-burn, T3 = 6 months post-burn, T4 = 12 months post-burn and T5 = 18 months post-burn.

symptoms in the brain becoming aligned with the prediction via active interoceptive inference. Especially when sensory input is imprecise and in case of chronic symptoms, predictive processes are supposed to significantly modulate perception (40, 41). In this light, the threat resulting from a traumatic burn event and associated pain may form strong perceptual priors with a high probability, modifying later sensory perceptions, including pain and itch, corroborating that PTS symptoms amplify predictive coding processes (42). Another explanation may relate to increased production of peripheral inflammatory mediators. Elevated corticosteroids and alterations in cytokines related to psychological stress have been associated with slower wound healing (43) and an association between PTS symptoms and lower oxytocin levels in burn wounds have been found (44). This suggest that PTS symptoms can also exert an effect at skin-level through increased production of excitatory skin mediators, one of the mechanisms explaining neuropathic itch (28) and calls for more attention to identify and treat PTS symptoms.

A small effect of younger age was found associated with the categorization to the chronic itch profile, which corroborates earlier findings (1, 45) of which the authors explained the effect of age by neurological and vascular aging of the skin.

The neuropathic pain symptoms prevalence rate of 54% 2 weeks post-discharge was high compared to a study that reported 28% pain at 6 weeks post-burn (9), but 6 to 18 month prevalence rates were within the same range, be it 24% in the current study vs. 21% in the study of Mauck et al. However, it is substantially higher than the 6% prevalence rate (113/1,880 patients) reported in a retrospective chart review study (46). Likely, the prospective and systematic examination of pain symptoms explains the higher prevalence rates. In line with other studies, unpleasant sensations such as pin-pricks was the most frequently reported neuropathic pain symptom, e.g. (15). But also other symptoms such as bursts, sensitive touch, and burning pain were reported which overall indicates that pain symptoms in scars are of neuropathic origin.

This study has clinical and research implications. First, the itch profiles may inform clinical practice and future research into treatments. It is recommended to screen patients for sensory symptoms, specifically focused at the co-occurrence of itch and neuropathic pain, and other risk factors to tailor prescription of for instance gabapentin or pregabalin in an earlier stage (36). Second, more clinical attention to detect and treat PTS symptoms in an early phase is recommended as it may also improve pain and itch outcomes. Third, results call for further exploration of the involvement of different neuronal pathways and contribution of central sensitization processes in the various itch profiles, that may pave the way to conduct targeted medication clinical trials. For example, psychophysically assessing itch and pain modulation may predict course of symptoms and therapeutic (e.g., post-operative) outcomes for both chronic itch and pain (47, 48).

This study also has limitations. First, although the literature is positive about using self-report questionnaires to assess spontaneous pain-related sensations (31), allodynia, and loss of sensory function were not measured because clinical examination is required (49). Loss of sensory function or numbness has been documented in burn scars, indicating its

TABLE 2 Burn characteristics and demographics tested with multi-nominal regression analysis to predict classification into one of the three itch profiles.

	B	SE	Wald	df	Sig	Exp(B)	95% CI	
Reference category is transient itch/pain								
Chronic itch							**Upper**	**Lower**
Intercept	0.992	1.151	0.744	1	0.388			
Age	−0.036	0.018	4.028	1	0.045	0.965	0.931	0.999
Male (=0)	−0.607	0.600	1.025	1	0.311	0.545	0.168	1.765
PTS symptoms	0.001	0.013	0.002	1	0.965	1.001	0.975	1.027
TBSA burned	0.085	0.040	4.512	1	0.034	1.088	1.007	1.176
No surgery (=0)	−1.003	0.534	3.537	1	0.060	0.367	0.129	1.043
Itch T1	0.217	0.200	1.175	1	0.278	1.242	0.839	1.837
Chronic itch & *pain*								
Intercept	0.233	1.246	0.035	1	0.852			
Age	−0.016	0.019	0.672	1	0.412	0.984	0.948	1.022
Male (=0)	−1.065	0.610	3.046	1	0.081	0.345	0.104	1.140
PTS symptoms	0.029	0.013	5.060	1	0.024	1.030	1.004	1.056
TBSA burned	0.052	0.043	1.421	1	0.233	1.053	0.967	1.146
No surgery (=0)	−1.808	0.622	8.461	1	0.004	0.164	0.048	0.554
Itch T1	0.210	0.211	0.987	1	0.320	1.233	0.815	1.866
Reference category is chronic itch & *pain*								
Chronic itch							**Upper**	**Lower**
Intercept	0.759	1.125	0.455	1	0.500			
Age	−0.020	0.018	1.233	1	0.267	0.980	0.946	1.015
Male (=0)	0.458	0.554	0.684	1	0.408	1.581	0.534	4.681
PTS symptoms	−0.029	0.012	5.459	1	0.019	0.972	0.949	0.995
TBSA burned	0.033	0.033	1.014	1	0.314	1.034	0.969	1.102
No surgery (=0)	0.805	0.614	1.720	1	0.190	2.237	0.672	7.449
Itch T1	0.007	0.184	0.001	1	0.971	1.007	0.702	1.445

B represents the regression coefficient. SE, standard error; df, degrees of freedom; Exp (B), exponent B; CI, confidence interval.

relevance (50). Clinical assessments that document stimulus-evoked sensory sensations and temporal summation may inform underlying nerve damage and consequently, therapy (49). Second, the LANSS was modified, including the addition of a 7-point Likert scale, and warrants further validation along with clinical tests to establish its reliability and validity in burn scars. Third, the sample size of the different profiles was small which limits statistical power. Consequently, replication research is warranted. Additionally, the small sample size was deemed too small to use more sophisticated statistical analyses to explore latent classes (read: itch profiles), which could replace the classification of participants based on the duration of the complaints and itch-pain co-occurrence.

In conclusion, the current study shows that the co-occurrence of chronic itch and chronic neuropathic pain is associated with higher itch intensity compared to chronic itch only. This suggests different underlying mechanisms, perhaps related to different neuronal pathways or differences in modulation systems, but this should be considered as hypothesis generating. The role of PTS symptoms may point to altered central processing, which may be another pathway explaining higher itch intensity. Future research focussing on peripheral and central processing of itch from a bio-psychological perspective is warranted. This may ultimately inform pathophysiological and pharmacological mechanisms in future studies—and hence lead to better treatment and improved quality of life of individuals after burn injury.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, upon reasonable request.

Ethics statement

The studies involving human participants were reviewed and approved by METC Noord-Holland, Netherlands & Ghent University, Belgium. The patients/participants provided their written informed consent to participate in this study.

Author contributions

Conception and/or design of the study: NVL, AdJ, and HH. Interpretation of the data and drafted the work: NVL and AvL. Revision the paper: AdJ and HH. All authors approved the final version and agree to be accountable for all aspects of the work.

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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.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2022.997183/full#supplementary-material

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How does self-compassion help people adjust to chronic skin conditions? A template analysis study

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Objectives: Skin conditions can greatly impact people's lives, but greater understanding of the processes involved in positive adjustment is required. Self-compassion has strong links to wellbeing and adaptive functioning and therefore may play an important role in adjustment to skin conditions.

Design: Template analysis was used to explore how self-compassion operates in people living with skin conditions, with reference to existing theories of self-compassion.

Methods: Semi-structured interviews were conducted with highly self-compassionate people with chronic skin conditions (N = 10). Theoretical models of self-compassion were used in the development of the initial template and interview schedule. Participants were purposively selected on the basis of having high scores on a measure of self-compassion.

Results: Participants reported a variety of ongoing skin-related difficulties and their ways of managing these. Sensitivity to distress and care for wellbeing were identified as foundation themes: necessary components of a compassionate response to distress. Eleven types of difficulty-management strategies built upon these foundation themes: empathy, non-judgement, distress tolerance, self-kindness, mindful attention, perspective-taking, self-talk, self-care, using social support, concealment, and idiosyncratic coping strategies.

Conclusions: Components of self-compassion helped people adjust to chronic skin conditions in a wide variety of ways, indicating that psychological adjustment is not a simple, linear process. Sometimes compassionate responses occurred automatically and sometimes with deliberate effort. Further research on compassion-based interventions for people with skin conditions is warranted.

KEYWORDS

self-compassion, template analysis, skin conditions, adjustment, qualitative

1. Introduction

As well as causing physical symptoms, there is substantial evidence that living with a chronic skin condition can impact quality of life. Skin conditions have been found to affect relationships, socializing, work/school, activities of daily living, sleep, finances, and exercise (1–4). Skin conditions can also have a negative impact on mental health, including difficulties with self-esteem, body image, confidence, anxiety, and depression (1). However, there is considerable individual variation in the impact of skin conditions, for example, one study found that 35% of dermatology outpatients reported no impact of their skin condition over the previous week whereas 16% reported a very or extremely large impact (5). Individual variation in the psychological impact of skin conditions cannot be explained merely by condition severity, as previous research has found no association between clinician-assessed severity and psychological morbidity in people with acne, psoriasis and eczema (6). In contrast, self-assessed severity of the skin condition is associated with psychological morbidity (6), which highlights the important role of psychological factors in the impact of skin conditions. To reduce distress and improve quality of life, we first need to understand the psychological processes involved in living with chronic skin conditions.

Adjustment to illness has been described as "the process to maintain a positive view of the self and the world in the face of a health problem" (7, p. 1161) and emerging evidence suggests that positive psychological factors may contribute to adjustment to skin conditions. Psychological flexibility, the ability to consciously engage with the present moment in a way that is consistent with one's values, has been linked with lower appearance anxiety in people with burn injuries (8), and mindfulness and self-compassion have both been linked with lower psychological distress in dermatology patients (9, 10). Furthermore, there is preliminary evidence that mindfulness and compassion-based interventions can reduce shame and depression in people with skin conditions (11, 12). These studies indicate that positive psychological factors show promise as therapeutic targets to promote adjustment to skin conditions but further research is needed to explore how they might promote adjustment. However, previous qualitative work with people who had positively adjusted to appearance-altering conditions, which included participants with skin conditions, identified a range of adaptive strategies used, such as positive cognitive processes that de-emphasize appearance in favor of other aspects of the self (13), drawing on inner strength, using a positive outlook, and active coping (14).

The psychological concept of self-compassion as described by Neff (15), an "emotionally positive self-attitude," may be particularly relevant to adjustment in skin conditions (15, p. 85). Self-compassion is proposed to consist of three components: self-kindness in instances of pain and failure rather than self-judgement, understanding that suffering is a shared human experience rather than feeling isolated by it; and being mindful of distressing thoughts and feelings rather than over-identifying with them (15). As self-compassion is expected to promote behaviors that enhance or maintain wellbeing (15), people with skin conditions who are high in self-compassion are expected to take appropriate steps to manage skin-related distress, thus lessening its impact. Consistent with this notion, there is evidence to suggest that self-compassion helps protect against depression in dermatological outpatients (9).

High self-compassion is expected to facilitate both problem-focused coping and emotional-approach coping (15, 16), that is, individuals with skin conditions taking practical steps to manage their physical symptoms and engaging with any emotional distress associated with the condition, respectively. In other medical populations, self-compassion has been found to be associated with active coping (a problem-focused strategy), acceptance, and positive re-framing (emotion-focused approach strategies) which were, in turn, associated with increased coping efficacy and reduced stress (17). However, living with a skin condition may present challenges that some other health conditions do not. In particular, skin conditions often cause both visible differences and physical symptoms, which can increase the complexity of living with them, and they can have a chronic intermittent course, requiring a flexible approach to their management. Therefore, it is important to research how self-compassion affects coping in a population of people with skin conditions.

Although much research on self-compassion stems from Neff's (15) conceptualization, an alternative perspective on self-compassion has been provided by Gilbert (18), based on evolutionary neuroscience. In Gilbert's model, the attributes of compassion are described as care for well-being, sensitivity to distress, sympathy, distress tolerance, empathy, and non-judgement, with the recognition that these can be directed toward the self as well as others. The conceptualizations of compassion by Gilbert (18) and Neff (15) are therefore organized around different frameworks, but do have overlapping constructs (e.g., both models include a sense of care/kindness and non-judgement). Both models have empirical support for the self-report measures (19, 20) and psychological interventions based upon them (see 21, for a review). However, to our knowledge, no previous study has explored self-compassion using components of both models.

The current study aimed to explore how trait self-compassion operates in the context of living with a chronic skin condition, using existing models of self-compassion (15, 18). Including components of both models in the current study meant that the analysis could draw on either model. The study's objective was to obtain detailed accounts of the processes involved in managing skin conditions and their impacts by

conducting theoretically-informed interviews with participants with chronic skin conditions and high self-compassion.

2. Materials and methods

2.1. Participants and procedure

Participants were adult members of the general population who had chronic skin conditions and exhibited high self-compassion. The study was advertised *via* the University of Sheffield's volunteer list and social media (Facebook and Twitter). Consenting participants from a previous study (9) were also invited to take part. A purposive sample was formed by asking volunteers to complete an online screening survey, which consisted of the Self-Compassion Scale–Short Form (SCS–SF; 22), the PHQ-2 (a depression screener; 23) and questions about the skin condition. The twelve-item SCS–SF has been shown to have good internal consistency, with a Cronbach's alpha of 0.86 (22). Construct and criterion validity have been demonstrated for the two-item PHQ-2 (23). To be eligible for an interview, participants had to have an mean score of 3.75 or more on the SCS–SF and less than a total score of four on the PHQ-2. Neff (24) has stated that for self-assessment, mean self-compassion scores between 3.5 and 5 (on a 1–5 scale) can be considered "high" self-compassion. However, based on previous research (9), a more conservative cut-off value of 3.75 was used, as this represents individuals who are approximately one standard deviation above the mean for self-compassion. The PHQ-2 was used to avoid interviewing participants who were experiencing depressive symptoms, even if they were high in trait self-compassion. This was due to concerns that, as depression commonly includes negative thoughts about oneself, depressive symptoms at the time of the interview might unduly affect participants' reports of their thoughts and feelings toward themselves. On the PHQ-2, the criterion of a total score of 4 or more was considered to be the most appropriate balance of sensitivity and specificity for the current study, based on research recommendations (23). Participants also answered questions relating to the exclusion criteria: whether they had a current mental health diagnosis, a diagnosis of skin cancer, a skin condition caused by an infestation, or were seeking treatment for burns or scarring. However, it was not necessary to exclude any participants on this basis.

Eleven people participated in an interview, although one participant was subsequently excluded from the data analysis as she had not experienced her skin condition for the previous 3 years and therefore could not articulate her previous skin-related difficulties, thoughts, or feelings in depth. The other ten participants had ongoing chronic skin conditions, which required regular treatment at the time of the interviews. Participants ranged from 22 to 65 years of age. Six participants developed their skin condition in childhood, and four participants developed their skin condition as adults. Five participants had eczema, three had psoriasis, one had Darier's disease, and one had urticaria. The sample contained three men, six women, and one person who classed their gender as non-binary. Additional demographic information is shown in Table 1.

TABLE 1 Demographic and clinical characteristics of participants (N = 10).

Characteristic	*n*
Gender	
Female	6
Male	3
Non-binary	1
Employment status	
Employed/self-employed	6
Student	2
Retired	1
Unemployed	1
Relationship status	
Married	6
Non-cohabiting relationship	3
Single	1
Ethnicity	
White	9
Chinese	1
Skin condition(s)[a]	
Atopic eczema	4
Dyshidrotic eczema	1
Chronic plaque psoriasis	3
Guttate psoriasis	1
Darier's disease	1
Urticaria	1
Age (M, SD)	41.8 (13.63)
Skin condition duration, years (M, SD)	26.5 (14.41)
SCS–SF mean score (M, SD)	4.23 (0.26)
PHQ-2 total score (M, SD)	0.55 (1.01)

PHQ-2 = Patient Health Questionnaire 2-item depression screener; SCS–SF = Self-Compassion Scale–Short Form. Possible scores ranged from 0 to 6 on the PHQ-2 and from 1 to 5 on the SCS–SF, with higher scores indicating higher depression/self-compassion.
[a]One participant had chronic plaque and guttate psoriasis.

2.2. Data collection

An interview-specific information sheet was sent to each participant in advance and written consent to participate was collected on the day of the interview. Interviews were conducted face-to-face by the first author, who was a 33-year-old, white woman, with atopic eczema (although not generally visible

TABLE 2 Compassion-related *a priori* codes used in the template analysis.

Code	Description	*n* contributing to each code
Self-kindness[a]	Responding to one's suffering and personal failure with thoughts that demonstrate care, support, tenderness, patience, tolerance, and understanding toward oneself.	7
Common humanity[a]	Viewing suffering and personal failures as normal parts of life, and believing that feelings of failure and inadequacy are shared by most people.	7
Mindful attention[b]	Paying attention in a particular way (on purpose, in the present moment, and non-judgementally) either in normal daily life, during a distressing event or through meditating. Sense of watching events, thoughts or feelings pass by.	10
Care for wellbeing[c]	Believing that being compassionate toward oneself is a desirable attribute. Wanting to care for, nurture and support oneself to promote one's well-being.	10
Sensitivity to distress[c]	Being able to notice and pay attention to one's distress and needs; being attentive to changes in physical feelings, emotions and thoughts (in distressing situations).	10
Sympathy[c]	Being emotionally moved by one's own distress.	0
Distress tolerance[c]	Being able to accept and tolerate distressing feelings as they occur; being familiar with and unafraid of distressing emotions and thoughts.	9
Empathy[c]	Understanding one's thoughts and feelings in distressing situations.	9
Non-judgement[c]	Accepting and not condemning oneself for real or perceived failures or inadequacies.	10

[a]Concept specified by Neff (15).
[b]*Mindfulness* was the concept specified by Neff (15), but the label and description were modified during data analysis, as participants' statements relating to mindfulness were more reminiscent of Kabat-Zinn's conceptualization: "Mindfulness means paying attention in a particular way: on purpose, in the present moment, and non-judgementally" (41, p. 4).
[c]Concept specified by Gilbert (18).

to others), with clinical experience of conducting sensitive interviews. The interviewer's skin condition was not disclosed to participants to avoid unduly influencing the interviews. A reflexive journal was kept by the first author throughout data collection and analysis, which served to increase the research team's awareness of the role that might be played by pre-existing assumptions about the research topic. Interviews were semi-structured, using open-ended questions and probes as necessary. Participants were guided through describing the main impact(s) of their skin condition. Subsequent questions explored strategies that participants used to manage the difficulties of living with their skin conditions. Questions about difficulty-management strategies were structured around Neff's (15, 20) components of compassion (see Supplementary material). Interviews were audio-recorded and transcribed verbatim. Each participant was given a pseudonym to maintain their anonymity, which has been used throughout the results. The study received ethical approval from the University of Sheffield's Research Ethics Committee.

2.3. Data analysis

Interview transcripts were analyzed using template analysis as described by King (25), using *a priori* codes derived from the compassion literature, shown in Table 2. These consisted of theorized components of self-compassion (15, 20) and attributes of compassion (18). Template analysis was selected as the analysis method as it is a flexible approach that can incorporate both inductive and deductive (*a priori*) coding—new codes are devised and *a priori* codes are modified or deleted as fits with the data. NVivo (RRID:SCR_014802) 11 was used for coding and template construction.

An initial coding of all transcripts was carried out using the *a priori* codes. In instances where no *a priori* code was relevant, a new code was devised to encompass this data. An initial template was then produced, which was iteratively developed by comparing it to the transcripts. Codes were inserted, modified or deleted as necessary to encompass the data. In qualitative research, *saturation* is "a criterion for discontinuing data collection and/or analysis" and is commonly used to assess methodological quality (26, p. 1894). In the current study, saturation was conceptualized as an internal process, "the point at which no new information or themes are observed in the data" (27, p. 59). As such, the focus of saturation was on the data analysis rather than data collection. Development of the template ended when saturation of data analysis was considered to have been achieved: when all data were codable using the template (25) and no new codes were emerging from the data (27). The final template was used to interpret findings from the data. An audit trail was kept of the developing templates, showing how the final interpretation of the data was produced (28). This included the use of a codebook of all codes that were applied to the data, which documented

when codes were inserted, modified, merged or deleted. To demonstrate methodological rigor, an audit of the data analysis was conducted by the third author, which included cross-checks between identified themes and interview transcripts (29).

3. Results

Participants reported a wide range of difficulties associated with their skin conditions, consisting of physical symptoms and psychological, social, and practical impacts. All participants experienced negative thoughts and/or emotions relating to their skin condition and all talked about the reactions of others (e.g., strangers or acquaintances) to seeing their skin condition. Differences between past and present impacts were common, with participants' skin conditions often having had more negative impact in the past.

All of the strategies that participants used to manage the difficulties of living with a skin condition were built upon two basic components: sensitivity to distress and care for wellbeing. As such, these were described as *foundation* themes, in that they were the necessary components of a compassionate response to distress. Eleven difficulty-management strategies that built upon sensitivity to distress and care for wellbeing were identified: non-judgement, mindful attention, perspective-taking, empathy, distress tolerance, self-kindness, self-talk, self-care, using social support, concealment, and idiosyncratic coping strategies. These strategies contained cognitive and behavioral elements: participants' attitudes toward themselves, their condition, and the wider world, and choices that required ongoing, deliberate action.

3.1. Foundation themes

3.1.1. Sensitivity to distress

Participants were generally very good at being sensitive to their own distress, whether this was physical symptoms or emotional distress. Once participants had noticed their distress, they then applied one or more specific strategies to try to alleviate it. They were often able to see their distress as a cue for taking holistic remedial action, that is, not simply attending to the skin but to their lives more generally.

> I just see it [psoriasis] as my body telling me that things aren't right, my systems aren't coping, so when it happens I try to think 'right, what can I do to bring my body back into alignment?' (Joanne)

Participants were also able to use sensitivity to distress as a preventative measure: being sensitive to distress had allowed participants to become aware of helpful and hindering factors for their skin conditions, and so could make appropriate choices to try to prevent flare-ups. Furthermore, having sensitivity to distress contributed to participants being skilled at articulating their distressing thoughts and feelings, although often these were historic.

> I think at that time …it [urticaria] did get me really down, 'cos I thought 'I've got no control over it, you know, I'm gonna lose my job because I can't work.…' (Julie)

3.1.2. Care for wellbeing

Behind all the strategies that participants were using to manage their difficulties was a sense of valuing themselves and a consistent desire to look after themselves well.

> [How I treat myself is] just giving myself a bit of space and being kind to myself a bit, doing things that I know probably make me feel good, like go for a run. Yeah.…if I need a bit of peace then I let myself have some peace. So being kind to myself I think. (Helen)

At times, this care for wellbeing required finding a balance between actions that would benefit their physical health and those that would benefit their mental/emotional health. Sometimes this balance also involved choices between short-term and long-term wellbeing.

3.2. Difficulty-management strategies

3.2.1. Non-judgement

All participants expressed and/or demonstrated non-judgement about the skin-related difficulties they experienced. They were often able to talk about their perceived failures and inadequacies without condemnation.

> I guess it [eczema] makes me feel kind of …like I'm missing out. But I don't feel like (pause) I'm of less self-worth. (David)

As part of this non-judgement, participants very commonly expressed an acceptance of their condition, appreciating the futility of wishing that things would be or could have been different.

> I wouldn't change it for instance.…I've just sort of accepted who I am. …That isn't to say that I don't want it to go away or get better, I do want it to get better but I wouldn't change my life history or who I was 'cos that's part of me now. (Martin)

Participants also often reported a lack of self-consciousness about their condition, which in many cases had developed over

time. The appearance of the skin was generally less salient for participants than when the condition first developed.

3.2.2. Mindful attention

All participants used some form of mindfully paying attention to the present moment and were aware that this helped them deal with potentially distressing situations. Sometimes this mindful attention was achieved through formal meditation practices, such as observing the breath or letting go of thoughts and feelings without reacting to them. At other times, mindful attention was used more informally, through focussing attention on current activities, that is, acting with awareness.

> But, you know, just concentrate on actually what you're doing at that time and things like. . . if you're washing pots or anything, just feeling how water feels on your skin. . . and I think that is, that has been a massive help as well. (Julie)

Some participants noted that they found it easiest to use mindful attention while doing yoga or sensory activities, and therefore made time for these. Not paying undue attention to the skin condition and generally having a present-moment focus was also helpful for some.

> I don't really think about it [psoriasis] too much to be honest. (Steve)

3.2.3. Perspective-taking

All participants were able to reflect on their skin-related difficulties from other perspectives, particularly those relating to other people and other times in their lives, and they did this with apparent ease. As a result of these perspective-taking skills, all participants spontaneously expressed a sense of fortune or gratitude for the good things in their lives; very commonly this was for having a supportive family and that the skin condition was not worse in some way. Sometimes this sense of fortune/gratitude included the use of downward social comparison; the appreciation that things are worse for some other people.

> . . . [I]t kind of eases my stress a bit, I guess, to know that people have it worse than me and they're still, they're still living, right. (David)

Common humanity, the understanding that suffering is a normal part of life, was also demonstrated by many participants.

> I mean everybody's got their own problems haven't they, just because you haven't got a skin condition it doesn't mean that you haven't got your own set of problems. (Philippa)

Being able to see their skin-related difficulties from different perspectives meant that participants saw their skin condition as just one aspect of their lives, even though it was difficult to live with at times.

3.2.4. Empathy

Participants were able to understand thoughts and feelings that occur in distressing situations. Participants most often explicitly expressed empathy in the context of understanding others' difficulties, or potential difficulties.

> I think if you were someone that was quite concerned with how you look and that kind of thing I could see that [psoriasis] would affect you a lot more because it'd be (pause) you'd be more conscious and more worried about it I think. (Steve)

However, participants also had good understanding of their own thoughts and feelings about skin-related difficulties. They could use this understanding to decide the best way forward for them, even if it contravened medical advice at times. Having empathy for one's own difficulties—both physical and emotional—contributed to finding the right balance between short-term and long-term consequences of lifestyle choices.

3.2.5. Distress tolerance

Participants very commonly showed distress tolerance: they were able to accept and tolerate distressing feelings and could therefore actively engage with distressing situations, or potentially distressing situations, rather than try to escape or avoid them. For example, some participants chose to exercise despite pain/discomfort due to sweat aggravating the skin condition, and some chose to go into social situations despite feeling self-conscious around others.

This ability to tolerate distress fed into participants' abilities to get on with their lives despite their skin conditions: they frequently chose to do valued activities even though this meant having to accept negative consequences due to the skin condition.

> But I would never say [that] eczema would be a reason why I wouldn't go somewhere or do something. . . like I might, you know, mentally make a few calculations about the pros and the cons but generally there are much *bigger* pros than cons. (Helen)

Another aspect of distress tolerance was willingness to allow limited periods of time to be upset about skin-related

difficulties. After this, participants felt able to get back on with their lives.

> If [my skin]'s really, really, really bad, I'll just shut [myself] off . . . say half an hour, and then I think 'come on, buck up' . . . [and then] I'm alright. (Maureen)

3.2.6. Self-kindness

Participants often reported responding to their difficulties with thoughts that showed self-kindness, that is, directing care and support toward themselves. This self-kindness occurred naturally, without too much conscious effort. However, some participants had experienced previous difficulties with mental health problems and/or self-criticism, which they had worked through to arrive at their current attitude of self-kindness. For other participants, self-kindness seemed to have developed naturally earlier in life.

> That counselling. . . gave me some really good kind of basic tools around not beating yourself up, . . . treat yourself how you'd treat other people. (Emily)

3.2.7. Self-talk

Participants very commonly 'had a word with themselves' when experiencing skin-related problems. When doing this, they were deliberately directing their thoughts in helpful ways and reminding themselves of their coping strategies, often involving trying to take a different perspective.

> I do often think to myself, you know, 'Will this matter in 5 years' time? Will this be important?' (Claire)

As part of their self-talk, participants commonly incorporated a problem-solving approach/wisdom: considering options and being prepared to find out what is helpful.

> [I think about] how to manage. . . . So that could be like medical interventions, what exactly am I going to do medically or biologically to help myself, so am I drinking enough, am I eating the right foods, am I getting enough sleep, anything that will affect my body chemistry. So I think; I strategise. (Martin)

This approach helped participants address the tensions between different choices they might make in terms of their physical and emotional health. It also helped participants respond flexibly to situations, meaning that they could take their current circumstances into account rather than always responding to situations in the same way.

3.2.8. Self-care

All participants used a variety of self-care strategies, in which the sole aim was to look after oneself. Self-care activities either focused on looking after physical health, particularly the skin condition, or were more holistic, leisure activities that incorporated care for emotional health as well, as described below.

3.2.8.1. Physical health care

All participants talked about the specific strategies they used to manage the physical symptoms of their skin conditions. These strategies fell into two categories. First, all participants took steps to manage their skin conditions on a daily basis. Most often this was through the use of moisturizers.

> [Moisturising is] such an everyday part of my life I don't really see it as management, I just see it as part of my everyday life. (Helen)

Using specialist cleansing products, avoiding scratching, taking immunosuppressant medication, and following special diets were other daily management strategies used by participants.

Second, most participants made sure they addressed flares promptly, through a variety of means: increased use of moisturizers or steroid creams, taking antihistamines or steroid tablets, using phototherapy (UVB or PUVA treatments), and by cooling the skin.

All participants chose to avoid certain things that triggered or exacerbated their skin conditions, but these were usually only things that were not highly valued. Most commonly this was avoiding certain physical activities.

> I try and avoid [swimming] just 'cos I just don't like the feeling of it on my skin. . . . but because I don't really like swimming anyway, it doesn't really bother me. (Helen)

Occasionally, participants chose to miss out on valued activities, for example, going away with friends, because of their skin condition and this had a more negative impact on them. However, avoiding such activities was unusual, indicating that participants were responding flexibly to fluctuations in their health.

Sometimes participants avoided social situations because they felt too ill/tired due to their skin condition and wished to protect their health from the demands of socializing. Participants commonly tried to avoid known environmental triggers such as sunlight, heat, pollution, dust, and hard water. Certain fabrics, cosmetics, jewelery, foods, and drinks were also avoided. Although avoiding physical triggers helped minimize the severity of the skin conditions, these choices were not without negative consequences, making normal activities feel difficult.

> I personally can't put much makeup on anymore…so it's quite hard to get excited about going out and socialising when you're not quite as dressed up as everybody else. (Philippa)

Some participants also tried to make sure that they ate healthily (e.g., eating plenty of fruit and vegetables) with the aim of improving their general health, and therefore their skin condition.

3.2.8.2. Leisure activities

Most participants deliberately made time to do enjoyable activities to look after themselves emotionally. Some of these activities were relaxing: reading, knitting, puzzles, baths, reflexology; while others were more active: cooking, playing games, trips out.

> [To manage how I'm feeling] I'll make time for myself. I'll read, 'cos I love reading, and I think when you, when you have got other things on your mind, …you tend not to make time for yourself and I think it's important to just make that time, so I started doing a bit of knitting.… (Julie)

Sometimes there was overlap between the activities that people did anyway and those that they did as a way of improving/maintaining their mood. In these cases, participants made sure that they carried on doing their enjoyable activities despite their skin conditions.

Participants commonly allowed themselves to rest when their skin condition flared, although work commitments could make this feel difficult. Sometimes participants rearranged their work or study schedules to facilitate extra rest.

> [O]kay can I do some, you know, later starts or early finishes [at work] to give myself a bit more time…(Emily)

Some participants with skin conditions that were exacerbated by stress used exercise as a way of caring for themselves. Exercise helped to relieve stress and therefore this had a positive effect on both their mental and physical health.

3.2.9. Using social support

Participants commonly used one or more types of social support to help manage skin-related difficulties. All participants had people in their lives who they described as supportive. Most commonly, participants found it helpful to talk to their significant others about skin-related difficulties, although this was needed infrequently as participants' skin conditions were generally under good control. Some participants identified that simply spending time with others helped them to feel better when they were experiencing skin-related difficulties. When they did this, the focus was not on the skin condition but other everyday things.

> [S]ometimes it's nice having somebody there just to sit and like watch the telly with, or sit and chat to, or go out for a walk with or something like that. (Philippa)

Some participants had used online support, as this was a convenient way of connecting with others with the same skin condition who therefore understood the difficulties involved. Some participants now used online forums to provide support to others who were going through similar difficulties.

3.2.10. Concealment

Although participants were generally coping well with their skin conditions, concealment was commonly used as a strategy for managing potential social difficulties. However, concealment was viewed as a choice, with participants stating that if they did not want to cover their affected skin, they would not. Concealment was only used when convenient, but having the option to conceal seemed to lessen the impact of the skin condition.

> Because I can just wear a shirt and trousers like this at work and no-one asks me about it I kind of can just get on with it. (Steve)

Some participants gave examples of going to greater lengths to conceal their skin condition in the past. Often, this consisted of wearing clothes contrary to their normal preferences in hot weather or on special occasions. However, better control of the skin condition and a change in mindset over time meant that participants no longer felt the need to conceal the skin condition to this extent.

3.2.11. Idiosyncratic coping strategies

Four participants reported idiosyncratic strategies to reduce distress during skin flares. These consisted of using an autonomous sensory meridian response (ASMR), cleaning and tidying, and reading scientific research. All of these strategies were underpinned by being sensitive to distress and caring for wellbeing, but were used by so few participants they could not be incorporated into other themes.

4. Discussion

This study sought to investigate how self-compassion may operate in adjustment to chronic skin conditions. Participants were highly motivated to take good care of themselves, both physically and psychologically, and were proactive in taking measures to promote and maintain their wellbeing. However,

participants still experienced difficulties and psychological distress in connection with their skin conditions, including negative automatic thoughts about their skin from time to time. However, none of them *tried* to think this way, or believed their overly negative thoughts to be accurate on reflection: when they spoke of subsequently 'talking to themselves' it was with helpful, compassionate thoughts. Compassionate thoughts about the skin condition can therefore occur in (at least) two contexts: as compassionate automatic thoughts and as deliberate compassionate 'self-talk' after noticing distress. Some participants had arrived at their current level of self-compassion after overcoming difficulties with anxiety, depression or habitual self-criticism, indicating that such difficulties can provide opportunities for personal growth.

The highly self-compassionate participants in the current study reported using a variety of strategies to deal with the difficulties of living with a skin condition: non-judgement, mindful attention, perspective-taking, empathy, distress tolerance, self-kindness, self-talk, self-care, using social support, and concealment. These strategies may, therefore, constitute adaptive responses for living with skin conditions (although it should be noted that concealment, which can be maladaptive (30), was used in a specific way by participants in this study: as an active choice when it was convenient). Furthermore, all of the difficulty-management strategies were built upon sensitivity to distress and care for wellbeing, either explicitly or implicitly (e.g., if a participant was choosing to rest, this implies an awareness of one's physical needs and the desire to look after oneself). The importance of sensitivity to distress and care for wellbeing suggests that these abilities may be particularly adaptive for people with skin conditions.

More broadly, the current findings suggest that self-compassionate responses to life difficulties are complex and people can and do vary in the compassionate attributes in which they have strengths. For example, some participants appeared to be highly distress tolerant whereas others had strong perspective-taking skills. This suggests potential for compassion-based interventions to help people build on strengths they already possess and develop new skills that are lacking. Indeed, existing compassion-based interventions typically incorporate a variety of techniques (e.g., see 31–33) and the current findings support the benefit of this.

The current findings also offer insights about the relative importance of the different concepts within models of self-compassion. Within Gilbert's (18) conceptualization, sensitivity to distress and care for wellbeing emerged as vital ingredients for self-compassion. Three other components, distress tolerance, non-judgement, and empathy, also played important roles in compassionate responses to skin conditions. However, the final attribute of compassion in this model, sympathy, did not contribute to difficulty-management strategies. Participants never talked about feelings of sympathy for their own distress; rather, their focus was on managing the problem or looking after themselves. It is possible that being sympathetic to one's own distress is implied through care for wellbeing, but sympathy did not translate to any practical strategies for these participants. This finding is consistent with research exploring compassionate attributes expressed by people undertaking a compassion intervention (34). In Gilbert's model (18), sympathy is defined as being emotionally moved by distress, while empathy consists of understanding distress (i.e., understanding the thoughts and feelings connected to it, and why these have arisen). However, Sommers-Spijkerman et al. (34) found that sympathy tends to be expressed alongside empathy rather than on its own, leading the authors to propose a simplified model that incorporates sympathy in the concept of empathy.

Within Neff's conceptualization of self-compassion (15), self-kindness and mindfulness emerged as having greater importance than common humanity. While participants often spontaneously talked about concepts relating to mindfulness and self-kindness, common humanity was less salient, and emerged as part of a higher-order theme of perspective-taking. Participants' use of online peer support could be argued to be partly the result of having a sense of common humanity, that is, knowing other people experience similar difficulties and seeking them out for support. However, due to the small sample and qualitative nature of the study, these findings remain tentative. Further research is needed replicate and quantify these findings, and to explore whether the importance of the components of self-compassion in each of the models varies in different populations.

4.1. Strengths and limitations

A key strength of the study was identifying participants who had lived with their skin condition for a number of years, which meant that they had had time to adjust and so refine their difficulty-management strategies. The use of template analysis was a further strength, as this meant that themes that emerged during analysis could include, but were not limited to, existing concepts from the compassion literature.

A potential limitation was that two of the authors have personal experience of eczema and pre-existing interest in the role of positive psychological variables, which may have influenced data collection and analysis due pre-existing ideas. However, the impact of any preconceptions was mitigated using various quality control processes, including use of a semi-structured interview schedule, use of a reflexive diary, team debriefing within supervision, and use of an audit trail of the codebook and iterative templates. These processes helped to

guard against the research team's experience and expertise in the topic exerting an undue influence on the findings (29).

A limitation of this study was that participants had a relatively small range of skin conditions. A notable absence was acne, which, along with eczema and psoriasis, is one of the most common conditions seen by dermatologists in the UK (35). As psychological experiences may vary with skin condition, the findings of the current study require replication with people who have acne and in a larger sample, given the small sample size.

4.2. Implications

The findings of the current study indicate that self-compassion plays a role in adjustment to chronic skin conditions and is therefore an appropriate therapeutic target for alleviating psychological distress in this population. Findings further suggest that interventions to increase self-compassionate responding in people living with skin conditions should have two key targets: (1) increasing sensitivity to the distress that results from having the skin condition, so that remedial action can be taken, and (2) developing effective care for wellbeing that can negotiate between emotional and physical health demands, and between short-term and long-term wellbeing. Several different compassion-based interventions exist (see 21, for a review) and have been shown to be effective for treating psychological distress (36, 37), including in people with chronic physical health conditions (38). Furthermore, self-compassion interventions have been found to improve the self-regulation of health behaviors (39) and there is emerging evidence that compassion-based interventions can benefit people with skin conditions (11, 12, 40). The current findings provide an increased understanding of how self-compassion translates into adaptive strategies for managing the challenges of living with a skin condition.

4.3. Conclusions

In the context of living with a chronic skin condition, the key processes involved in self-compassion were having sensitivity to skin-related distress and caring for one's physical and mental wellbeing, with a variety of other adaptive strategies being built upon these: non-judgement, perspective-taking and empathy with respect to skin-related difficulties; mindfully attending to the present moment; tolerance of skin-related distress; kind automatic thoughts and deliberately helpful self-talk in response to skin-related difficulties; physical and emotional self-care activities; spending time with others who are supportive about the skin condition; concealment of the skin as a choice; and using idiosyncratic coping strategies.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary materials, further inquiries can be directed to the corresponding author/s.

Ethics statement

This study involving human participants was reviewed and approved by the University of Sheffield Department of Psychology Research Ethics Committee. The participants provided their written informed consent to participate in this study.

Author contributions

EC, PN, and AT contributed to conception and design of the study. EC collected the data and performed the analysis and wrote the first draft of the manuscript. AT conducted the audit of the data analysis. All authors contributed to manuscript revision, read, and approved the submitted version.

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Conflict of interest

Author AT is a topic editor of the Frontiers Research Topic 'Psychosocial Aspects of Skin Conditions and Diseases', was the lead psychological advisor to the recent mental health report produced by the APPGS and has also received honorariums and/or research support from pharmaceutical companies involved in the treatment of skin conditions (including UCB, Novartisis, and Pzifer).

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.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2022.974816/full#supplementary-material

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A mixed methods systematic review of digital interventions to support the psychological health and well-being of people living with dermatological conditions

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Background: Dermatological conditions can have a substantial impact on psychological as well as physical health yet dedicated face-to-face psychological support for patients is lacking. Thus, individuals may require additional support to self-manage dermatological conditions effectively. Digital technology can contribute to long-term condition management, but knowledge of the effectiveness of digital interventions addressing psychological (cognitive, emotional, and behavioural) aspects of dermatological conditions is limited.

Objectives: To identify, determine the effectiveness, and explore people's views and experiences of digital interventions supporting the psychological health of people with dermatological conditions.

Methods: A mixed methods systematic review informed by JBI methodology. The protocol was registered on PROSPERO. Eight electronic databases were searched for papers written between January 2002 and October 2021. Data screening and extraction were conducted in Covidence. The methodological quality of studies were scrutinised against JBI critical appraisal tools. Intervention characteristics were captured using the Template for Intervention Description and Replication checklist and guide. Data were synthesised using a convergent segregated approach. The results were reported in a narrative summary.

Results: Twenty-three papers were identified from 4,883 references, including 15 randomised controlled trials. Nineteen interventions were condition-specific, 13 were delivered online, 16 involved an educational component, and 7 endorsed established, evidence-based therapeutic approaches. Improvements in knowledge, mood, quality of life, the therapeutic relationship, and reduced disease severity in the short to medium term, were reported, although there was substantial heterogeneity within the literature. Thirteen studies captured feedback from users, who considered various digital interventions as convenient and helpful for improving knowledge, emotion regulation, and personal control, but technical and individual barriers to use were reported. Use of established qualitative methodologies was limited and, in some cases, poorly reported.

Conclusion: Some web-based digital psychological interventions seem to be acceptable to people living with mainly psoriasis and eczema. Whilst some digital interventions benefitted cognitive and emotional factors, heterogeneity and inconsistencies in the literature meant definitive statements about their effectiveness could not be drawn. Interdisciplinary and patient-centred approaches to research are needed to develop and test quality digital interventions supporting the psychological health of adults living with common and rare dermatological conditions.

Systematic review registration: [https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=285435], identifier [CRD42021285435].

KEYWORDS

systematic review, dermatology, psychology, digital health, behaviour change

Introduction

Dermatological conditions can impact all aspects of life with people commonly reporting psychological, social, financial, occupational, and educational consequences, plus challenges to daily activities, in addition to their physical manifestations (1–7, 8). Many individuals living with dermatological conditions consider the psychological impact to be most profound (2). In a recent survey of 544 people in the United Kingdom with a skin condition, 97.61% revealed that their emotional wellbeing had been negatively affected as a result of the condition (4). Impaired quality of life (QoL) and a range of mental health issues are recognised in people with dermatological conditions, across the spectrum of psychological conditions, including low mood, anxiety and depression, to suicidality (2) and psychoses (9). Inter-disciplinary and whole person approaches are, therefore, essential for condition management and improving QoL in people with dermatological conditions (7, 10, 11).

The 2013 All-Party Parliamentary Group on Skin report called for more integrated and dedicated psychological support within dermatology (10). The most recent iteration showed little positive change over the previous decade, as the provision of specialist psychological support within dermatology settings, and dedicated psychodermatology services, both remain limited (7). In addition, previous research has shown that dermatology staff report lacking confidence in their ability to address the psychological impact of dermatological conditions (12, 13) and that some dermatologists still fail to recognise (14) and manage dermatological conditions as long-term conditions (15). Thus, inadequacies in education and training for healthcare professionals on the psychological aspects of dermatological conditions persist (7, 10).

Many people with dermatological conditions report not being able to access psychological services (4), or being dismissed (2) by medical professionals who fail to understand (4), or even acknowledge (6) the severity of the psychological impact of dermatological conditions. Individuals report dissatisfaction with the quality of care leaving them feeling unsupported and with no choice but to cope with their condition alone (10, 8). Clearly, additional forms of support are needed to help people to live well with dermatological conditions (16).

Digital technology has transformed healthcare delivery (17), including dermatology (18). For example, both asynchronous and synchronous teledermatology is now widely embedded within dermatology service provision (18), yet the primary focus has been on the assessment, diagnoses, and monitoring of physical symptoms and treatments (18, 19), with little to

no consideration given to the psychological impact of that condition on the individual.

Interventions using digital technology, including the internet and smartphone applications (apps), have proved to be effective in facilitating the management of other long-term conditions (17). For example, people living with type 2 diabetes (20) and cancers (21) consider them a useful and convenient adjunct to standard care that inform, enable and empower individuals to control their health and lifestyle (22). In the context of dermatology, digital health interventions are limited; some have been developed mainly for skin cancer, focusing on primary prevention (23, 24). Digital technology could provide a platform for delivering psychological support to adults with dermatological conditions, but it is not clear what works or what delivery methods are acceptable to this group.

We conducted a mixed methods systematic review to identify existing digital programmes, determine their effectiveness, and explore people's views and experiences of available programmes for supporting the psychological health and well-being of adults living with dermatological conditions.

Methods

The present systematic review was informed by the JBI methodology for conducting mixed method systematic reviews (25).

Eligibility criteria

We developed comprehensive inclusion and exclusion criteria to judge the eligibility of papers for inclusion in this systematic review. The criteria were developed *a priori* based on the results of a preliminary scoping search on the MEDLINE (Ovid) database and were piloted on three papers identified through the initial search. The eligibility criteria were independently applied by RH and one other reviewer (GW or OH). The reviewers discussed potential changes and the eligibility criteria were updated prior to application. The full eligibility criteria are outlined below.

Study design

Qualitative, quantitative, and mixed methods studies written in English were included. Systematic reviews, meta-analyses, study and review protocols, commentaries, editorials, grey literature, conference posters, abstracts, and papers on intervention development, were excluded.

Participants

We included studies concerning adults (18+ years) with a clinician- or self-diagnosed dermatological condition, either with or without established comorbidities. Papers focused on children and adolescents, or people with non-dermatological conditions or mental, psychological, psychiatric disorders only, were excluded.

Interventions

Eligible interventions were those designed for patient use, delivered by digital technology, accessed online or offline, and comprised of at least one of the following interactive components:

- Patient-to-patient communication.
- Patient-to-practitioner communication.
- On-demand information services.
- Personal health tracking.
- Targeted communication.

This definition of digital interventions was adapted from an existing definition (26), which was based on the World Health Organization's classification (27). We extended the existing definition to encompass The Medical Research Council's definition of complex interventions (28).

Digital interventions for detecting, diagnosing, triaging, or assessing physical symptoms, asynchronous telemedicine, and psychological interventions delivered via telephone or email, were not included in this review.

Comparators

Eligible comparators included none or alternative intervention and standard care.

Outcomes

We prioritised psychological outcomes (cognitive, emotional, and behavioural) and considered other outcomes if they were measured alongside a psychological outcome(s). A non-exhaustive list of examples of eligible outcomes are presented in **Table 1**.

Systematic review protocol

The review protocol was registered on PROSPERO in October 2021 (reference number: CRD42021285435).

Search strategy

We ran a preliminary search of MEDLINE (Ovid) on 15th October 2021 to scope the existing literature on the review questions. The scoping exercise helped to ensure there were no current or ongoing reviews on the topic, to refine the aims and eligibility criteria for this systematic review, and to estimate the amount of published work available and, therefore, the resources needed to complete this systematic review. Relevant

TABLE 1 Examples of primary and secondary outcomes.

Category	Examples
Primary outcomes	
Cognitive	Beliefs about illness, beliefs about treatment, knowledge
Emotional	Fear, stress
Behavioural/behaviour change	Diet and weight management, physical activity or exercise, smoking, alcohol consumption, sleep, medication adherence
Other psychological	Adjustment, self-efficacy, self-compassion, motivation, quality of life, health-related quality of life, depression, anxiety
Secondary outcomes*	
Physical	Pain, severity, duration, skin coverage
Usage data metrics	Number of log ins, modules accessed, time spent on/using intervention
Other	Intervention feasibility, acceptability or usability, user satisfaction or engagement

*Only included if measured in addition to at least one psychological outcome.

papers identified from a scoping search of MEDLINE were also used to develop a full search strategy; key words in the titles and abstracts, and the index terms used to describe the papers, were organised into search strings with support from a specialist subject librarian (see **Supplementary material, section 1**).

The search period spanned 1st January 2002 to 29th October 2021. We only included papers published from 2002 onwards because this year followed the publication of an influential paper on defining eHealth (29), which marked the beginning of a global increase in the implementation of eHealth policy and strategies (30).

Data sources

We searched the following electronic databases for peer-reviewed material:

- MEDLINE, EMBASE, Emcare, PsycINFO (Ovid).
- CINAHL (EBSCO).
- Scopus.
- Web of Science.

We also conducted a search of the Open Science Framework Preprint Archive for unpublished papers, but no papers relevant to the review questions were retrieved.

Article screening

References were imported into EndNote X9 (Clarivate Analytics USA), and duplicates were removed. References were subsequently imported to Covidence; an online platform designed to support the conduct of systematic reviews. More potential duplicates were identified automatically in Covidence, which were reviewed and later removed by the review team.

A two-step screening process determined the papers included for analysis. Firstly, titles and abstracts of papers were screened against the eligibility criteria. All were screened independently by RH and one other reviewer (MP, BJ, RP, GW, or OH) using a screening tool developed for the purpose of this systematic review (see **Supplementary material, section 2**). Any conflicts that arose were resolved by a third reviewer (CP, MR, or AT).

The full texts of the remaining papers were screened independently by RH and another reviewer (MP, BJ, RP, GW, or OH), using the screening tool. The reference lists of full texts were also screened to ensure no potentially relevant papers had been missed. Reasons for exclusion were recorded and one reviewer (RP) was responsible for resolving disagreements at this second stage.

The screening process was reported in the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) 2020 flow diagram (31).

Data extraction

Data were independently extracted in Covidence by RH and another reviewer (MP, RP, BJ, GW, or OH). The research team conducted consensus checks and resolved discrepancies through discussion. Intervention characteristics were charted against the Template for Intervention Description and Replication (TIDieR) checklist and guide (32), which we adapted to capture for *whom* interventions were intended. Specific intervention features were captured independently by RH and another reviewer (MP, RP, BJ, GW, or OH) before discrepancies were resolved through team discussion.

Critical appraisal

We assessed the methodological quality of included papers using established JBI critical appraisal tools for the following study designs: Randomised Controlled Trials (RCTs) and quasi-experimental studies (33); analytical cross-sectional studies, case reports, and cohort studies (34); and qualitative research (35).

We adopted the method outlined by Edwards and colleagues (36) to judge quality, and included studies were assessed against the pre-determined criteria. Quantitative and qualitative components of mixed methods studies were appraised separately using the appropriate critical appraisal instruments. Each paper received an overall score based on the number of criteria met (13 for RCTs, 10 for qualitative and cohort studies, 9 for quasi-experimental studies, 8 for analytical

cross-sectional studies and case reports). Studies scored one for each criterion met and zero for any criterion for which the evidence was unclear. If a criterion was considered not applicable to a particular study, a point was deducted from the overall score; for example, if the total possible score was 10, one was deducted reducing the total possible to 9.

Each paper was assessed independently by RH and another reviewer (MP, RP, BJ, GW, or OH) and all scores were checked by a third reviewer. For completeness data were extracted from all papers irrespective of their quality score. In addition, each paper was also assigned to a JBI level of evidence for effectiveness (1 = high, 2 = moderate, 3 = low, 4 = very low) or meaningfulness (1–5), based on the study design reported (37). The purpose was to support healthcare professionals and others working in this area to form preliminary judgements of the rigour of the evidence presented in this review, and facilitate the implementation of quality evidence-based research in clinical and health settings (37).

Data analysis

Papers were imported into NVivo 12 Pro where one reviewer (RH) conducted a content analysis to synthesise the data. This involved assigning codes to parts of the text which captured study and intervention characteristics and results relating to the main aims. The results of the content analysis were verified by two reviewers (CP and CB). The code book is included as **Supplementary material (section 3)**.

One reviewer (RH) employed a convergent segregated approach to synthesise the data; this involved analysing qualitative and quantitative data separately before integrating the results into a narrative summary (38, 39). The summary was scrutinised by the research team for accuracy.

Results

Study selection and characteristics

We screened 4,883 titles and abstracts and assessed 70 full texts for eligibility. Twenty-three papers (40–62) met the eligibility criteria and were included in the review (see **Figure 1**).

The characteristics of studies included in this systematic review are presented in **Table 2**.

We identified experimental studies, including 15 RCTs (40, 41, 43–46, 48, 50, 52, 53, 55, 56, 59, 60, 62), two randomised pilot trials (42, 58), one quasi-experimental design (54), as well as four observational studies (47, 51, 57, 61) and one qualitative study (49). The majority of studies were conducted in western countries; 11 in European countries (42, 44, 48, 50, 51, 54, 55, 57, 59–61) and six in the United States (40, 41, 46, 47, 52, 53).

Various sampling approaches were employed. Eleven studies utilised convenience sampling (41, 42, 44–46, 53, 54, 56, 60–62), four studies relied on voluntary sample (43, 48, 50, 57), and one study sampled purposively (51). Six studies used a combination of two sampling approaches (40, 49, 52, 55, 58, 59). One study did not clearly state how participants were sampled (47).

Twenty papers stated an eligibility criteria for participants, however, two papers (49, 54) did not provide an explicit criteria and one paper noted that the eligibility criteria was reported elsewhere (53). Several studies indicated a diagnosis by a clinician as a requirement for inclusion (43, 50, 57). Other studies specified people with a 'diagnosis' as an inclusion criterion but failed to clarify whether this was a self- or clinician-diagnosis (40, 45–47, 51, 55, 56, 58–61). However, given that research participants were mostly recruited from outpatient dermatology clinics (40–42, 44–46, 54, 55, 61, 62) or using a combination of recruitment methods (52, 53, 58–60), it is reasonable to assume that most studies included people with an established dermatological condition.

Few studies utilised established diagnostic criteria for determining eligibility for inclusion. Two studies relied on criteria for atopic dermatitis; one study (41) used criteria by Hanifin and Rajka (63) and the other study (48) employed The United Kingdom Working Party's Diagnostic Criteria for atopic dermatitis (64). One study (52) determined the eligibility of people with trichotillomania for inclusion using the Diagnostic Statistical Manual of Mental Disorders 5 (DSM-5) criteria (65).

A number of studies only included people with determined severity using the following:

- Psoriasis Area Severity Index (PASI) (66) score of 5–15 (42).
- Mild to moderate psoriasis (43, 59).
- PASI and body surface area scores of >10 (44).
- Mild to moderate psoriasis judged as body surface area score of ≤ 10 (62).
- At least moderate severity according to the Patient-Oriented Eczema Measure (POEM) (67), defined as scores ≥ 8 (48).

The majority of studies were intended for people with specific dermatological conditions, including:

- Psoriasis (40, 42–44, 46, 51, 57, 59, 60, 62).
- Atopic dermatitis (41, 45, 48, 50, 55).
- Melanoma (53, 56).
- Alopecia (49).

One study (52) included people with Trichotillomania. Four studies were not condition-specific and were open to people living with different dermatological conditions, including, but not limited to, acne, vitiligo, hidradenitis suppurativa, and lichen-plan-pilaris, plus visible differences such as birthmarks (47, 54, 58, 61).

TABLE 2 Study characteristics.

References	Country	Condition	Study design	Sampling approach	Recruitment method	Primary outcome	Duration of follow up
Alinia et al. (40)	United States	Psoriasis	RCT	Convenience, purposive	Outpatient clinic	Treatment adherence*	12 months
Armstrong et al. (41)	United States	AD	RCT	Convenience	Outpatient clinic	Disease severity	3 months
Balato et al. (42)	Italy	Psoriasis	Randomised pilot trial	Convenience	Outpatient clinic	Treatment adherence*	3 months
Bundy et al. (43)	United Kingdom	Psoriasis	RCT	Voluntary	Advertisement	Anxiety and depression	6 months
Domogalla et al. (44)	Germany	Psoriasis	RCT	Convenience	Outpatient clinic	Anxiety and depression	60 weeks
Erdil et al. (45)	Turkey	AD (hand)	RCT	Convenience	Outpatient clinic	Unclear	2 months
Hawkins et al. (46)	United States	Psoriasis	RCT	Convenience	Outpatient clinic	Knowledge	Immediately post intervention
Heckman et al. (47)	United States	AD, psoriasis, chronic itch	Cohort study	Unclear	Market research company	Itch-related QoL	1 month
Hedman-Lagerlöf et al. (48)	Sweden	AD	RCT	Voluntary	Online application	Disease severity	12 months
Iliffe and Thompson (49)	United Kingdom	Alopecia	Qualitative	Voluntary, purposive	Social media	Patient experiences	No follow up
Joergensen et al. (50)	Denmark	AD	RCT	Voluntary	Social media	Disease severity, QoL	1 month
Koulil et al. (51)	Netherlands	Psoriasis**	Case report	Purposive	Unclear	Unclear	6 months
Lee et al. (52)	United States	Trichotillomania	RCT	Convenience, voluntary	University campus, mental health providers, online advertisement	Symptom severity, QoL	3 months
Manne et al. (53)	United States	Melanoma	RCT	Convenience	Cancer registry, dermatology clinics, medical centre	Skin self-examinations, sun protection behaviours	11 months
Marasca et al. (54)	Italy	Acne, alopecia, HS, lichen-plan-pilaris, psoriasis	Quasi-experimental study	Convenience	Outpatient clinic	QoL*	1 month
Mollerup et al. (55)	Denmark	AD (hand)	RCT	Convenience, voluntary	Outpatient clinic	Disease severity	6 months
Schuster et al. (57)	Germany	Psoriasis	Analytical cross-sectional study	Convenience, voluntary	Psoriasis	Unclear	No follow up
Sherman et al. (58)	Australia	Visible skin conditions including acne, birthmark, eczema, psoriasis, other	Randomised pilot trial	Convenience, voluntary	University campus, outpatient clinics, social media (Facebook)	Self-compassion*	Immediately post intervention
Svendsen et al. (59)	Denmark	Psoriasis	RCT	Convenience, voluntary	Outpatient clinic, advertisement	Treatment adherence	26 weeks
Russell et al. (56)	Australia	Melanoma	RCT	Convenience	Cancer centre	Unclear	6 weeks
van Beugen et al. (60)	Netherlands	Psoriasis	RCT	Convenience	Outpatient clinic, advertisement	Impact on daily life	6 months
van Cranenburgh et al. (61)	Netherlands	Acne, HS, psoriasis, vitiligo***	Observational pilot study	Convenience	Outpatient clinic	Acceptability, feasibility	2 months
Zhao et al. (62)	China	Psoriasis	RCT	Convenience	Outpatient clinic	Visit adherence*	12 months

AD, atopic dermatitis; HS, hidradenitis suppurativa; RCT, randomised controlled trial; QoL, quality of life.
*Primary outcome not explicitly stated by authors.
**This study also included one person with rheumatoid arthritis, but data were not included.
***Dermatologists were also recruited but data were not included.

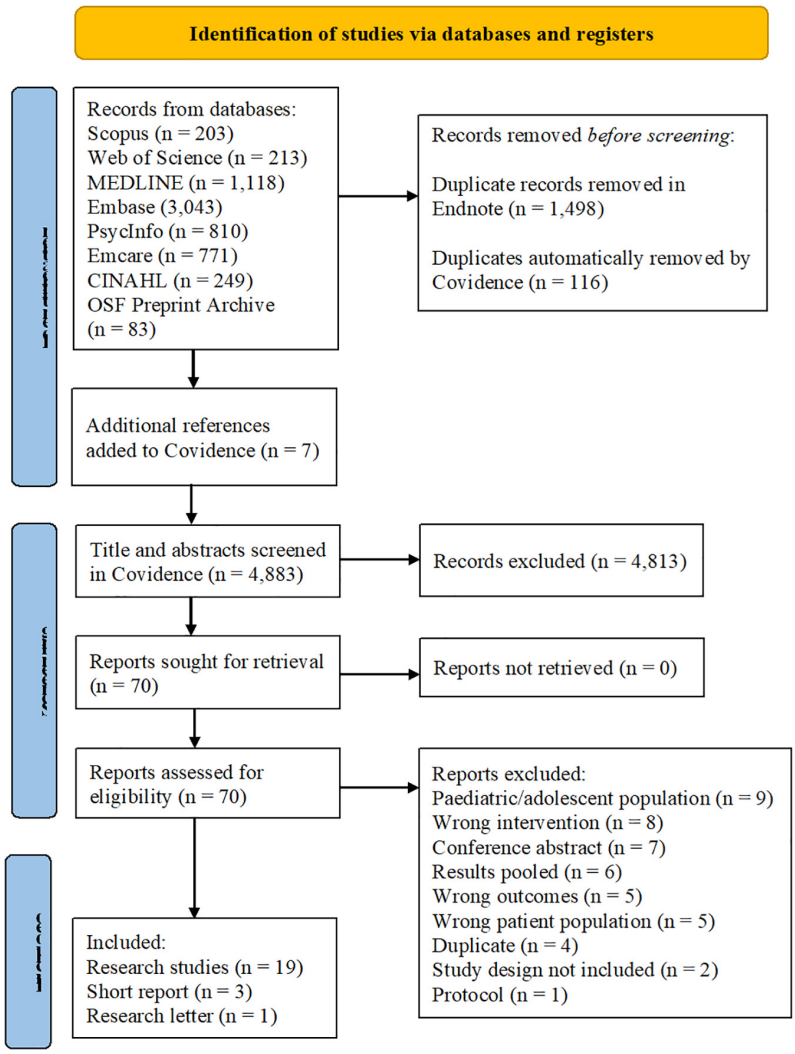

FIGURE 1
Screening process depicted in the PRISMA 2020 flow diagram (31).

One sample included a parent of a person with alopecia (49) and one study recruited dermatologists in addition to patients (61). Another study described the case of a person with rheumatoid arthritis (51). These data were not included in the paper.

Sample sizes ranged from 2 (51) to 441 (53) participants. There were 2,268 participants across the studies and 556 participants were lost to follow-up. The total sample included 933 males and 1,132 females, although two papers did not report gender (46, 61). An overview of the number of participants and dropouts, as well as the gender and mean age of participants, are presented in **Supplementary material, section 4**.

A wide range of outcomes were studied, and a variety of measurement tools were used. Some psychological outcomes were assessed with established measures. For example, nine studies (42–44, 48, 50, 54, 55, 57, 59) measured QoL using the Dermatology Life Quality Index (DLQI) (68). One study (48) also used The Brunnsviken Brief Quality of Life Scale (BBQ) (69), and another study (52) employed the Quality of Life Scale (70). Validated measures of disease severity were also used widely: for example, six studies used the PASI (66); three studies (41, 48, 50) utilised the POEM (67); and four studies (42, 43, 51, 60) collected these data with the Self-Administered Psoriasis Area and Severity Index (SAPASI) (71). Several studies used non-validated self-report measures that had been developed for the purpose of the research being undertaken. These measures comprised of Likert (44, 53, 58, 61), numeric rating (40, 42, 44, 47, 51, 55), and visual analogue (45, 46, 48, 55) scales, as well as multiple choice (42, 46, 53) and true or false questions (45, 53). Fourteen studies (41, 43, 44, 46–50, 52, 53, 55, 59–61) specified at least one primary outcome and five studies alluded to a primary outcome (40, 42, 45, 54, 58, 62). The primary outcome could

not be inferred for four studies (45, 51, 56, 57). All outcome variables studied, and measurement tools used in each study, are presented in **Supplementary material, section 5**.

Eighteen papers (40–45, 47, 48, 50–56, 59, 60, 62) included baseline measures and follow up periods varied substantially. Three papers conducted follow up immediately post-intervention (46, 58), although one study adopted a cross-sectional design meaning there was no baseline data to compare against (57). Other studies conducted follow up assessments after – 4 (47, 50, 54), 6 (56), 8 (13, 24, 26, 40–43, 45, 48, 51–53, 55, 59–62), and 60 (44) weeks post-intervention. Twelve papers assessed key outcomes more than once at the following timepoints:

- 1, 3, 6 and 12 months (40).
- After the 6-week intervention and 12 months (43).
- 12, 24, 36 and 60 weeks (44).
- 4 and 8 weeks (45).
- 3, 6 and 12 months (48).
- 9 weeks and 6 months (51).
- After fifth sessions, immediately post intervention, and 12 weeks following treatment (52).
- 8, 24 and 48 weeks (53).
- 2 and 4 weeks (54).
- 4, 8, and 26 weeks (59).
- 6 and 12 months (60).
- 2, 8, 16, 28, 48, and 52 weeks (62).

Seventeen studies included a comparator (40–46, 48, 50–53, 55, 56, 58–60, 62), mostly standard medical care (51, 56, 60), including drug treatments (40, 59), physical examinations (53), and written information about the condition of interest and treatment (41, 48, 55). Other control conditions included:

- A waitlist control group (43, 52).
- Use of electronic treatment dispensary caps (59).
- In-person follow-up visits (44).
- A standard writing activity (58).
- No intervention (45, 46).
- A matched control group (42).
- Daivobet® (treatment) plus a mobile app without proactive communication with a doctor (62).

One study included two control groups; use of memory buttons only and no intervention (50).

Methodological quality

Scores for methodological quality are presented in **Supplementary material Table 3, section 6**. Total quality scores ranged from two to 10, indicating that no paper met every criterion for their study design.

Levels of evidence

As for levels of evidence for effectiveness, papers were ranked to levels 1 (n = 16), 2 (n = 2), 3 (n = 1), and 4 (n = 2). Rankings ranged from level 1c (high quality) to 4d (very low quality). The two studies involving established qualitative methodology were both ranked to level 3 for meaningfulness (49, 55). Levels of evidence of effectiveness and meaningfulness are presented in **Supplementary material Table 4, section 7**.

Risk of bias

Seven papers (40, 41, 44, 47, 48, 59, 62) reported potential conflicts of interest and fourteen papers (40, 42, 43, 45, 49–51, 53–58, 60, 61) declared none. Two papers provided no information on this (46, 52).

Six studies were funded by pharmaceutical companies (40, 44, 47, 50, 61, 62), seven by public bodies (42, 43, 48, 49, 53, 55, 57), and three studies were funded by a combination of private and public organisations (51, 59, 60). Seven papers did not provide any funding information (41, 45, 46, 52, 54, 56, 58).

Blinding procedures were often poorly described or absent in reports of RCTs; in total, five papers explicitly described blinding procedures for participants (41, 48, 58) and treatment providers (42, 50), and only one paper covered blinding procedures for outcome assessors (42).

Intervention characteristics

Intervention characteristics are presented according to the TIDieR checklist and guide (32) in **Supplementary material, section 8**. All interventions but one (49) were intended for individual use. Most interventions were delivered online via the internet (41, 43, 46–48, 51, 53, 56, 58, 60, 61), including the social media platform Facebook (49, 57). Five interventions utilised mobile technologies, including text messaging (42, 45) and mobile apps (62), or video conferencing software (52, 54). Five interventions comprised of two modes of delivery:

- Electronic medication canisters for monitoring psoriasis treatment, plus online reporting of disease status (40), or treatment information and reminders sent via a mobile app (59).
- Memory buttons and a mobile app for monitoring eczema treatment (50).
- Face-to-face education with an app for monitoring psoriasis (44).
- Face-to-face counselling and a website providing education, self-monitoring, and asynchronous communication for people with hand eczema (55).

Most interventions did not require a provider due to the focus on patient self-management. However, where involved, intervention providers included psychologists (48,

60), advanced graduate students supervised by a licensed psychologist (52), dermatology specialists (44), and nurses (55). The digital components of two interventions were not led by a provider (55, 60) and two papers did not describe the provider (51, 54). Only three papers gave sufficient detail about of the background, expertise, and suitability of the people responsible for intervention delivery (48, 52, 60).

Most interventions provided educational content on dermatological conditions and their management (41–46, 48, 51, 53, 55, 62) or:

- Psychological or social factors and coping (43, 48, 60, 61).
- Biological, psychological and social factors related to itch (47).
- Psychological factors related to trichotillomania and techniques for changing related cognitions and habits (52).
- Mindfulness (56).

Other features of digital interventions included:

- Text or email reminders prompting treatment (42) (45, 62) or intervention use (47, 55, 56).
- General assignments (43) and activities, for example, meditation (56) and writing a self-compassionate letter to oneself (58).
- Contact with intervention providers (44, 48, 51, 52, 55, 62) or patients (49, 55, 57).

Some interventions offered tailored content, including:

- Modules, assignments (55) and feedback, and goal setting (51, 60).
- Tracking physical (40, 44, 53, 55) and psychological (44) symptoms or treatment activity (50, 59).
- Allowing users a choice of modules to complete (61) and respecting personal treatment preferences (50).
- Individual counselling (55).
- Encouragement to verbalise reasons for performing sun protection behaviours and developing action plans (53).

Whilst intervention development was not the focus of this systematic review, we noted any descriptions of the theoretical foundations on which digital interventions were developed. Seven interventions endorsed established, evidence-based therapeutic approaches, including:

- Cognitive Behavioural Therapy (CBT) for psoriasis (43, 51, 60) or eczema (48).
- Acceptance and Commitment Therapy (ACT) Enhanced Behavior Therapy for trichotillomania (52).
- Self-compassion and written emotional disclosure (58).
- A mindfulness-based programme for melanoma (56).
- Habit reversal (51, 52).

Five of these digital interventions were based on existing protocols for face-to-face interventions (43, 48, 51, 52, 60). The authors of the written disclosure intervention (58) had adapted it from an existing intervention for breast cancer survivors. The web-based mindfulness programme (56) was built on a systematic review and the findings of a survey examining knowledge, attitudes and practices of meditation in people with melanoma.

In addition, parts of a web-based intervention (47) were based on the Biopsychosocial Model of chronic itch (72) and offered 'cognitive-behavioural strategies' for coping. One paper referenced using the Preventative Health Model (73) as a conceptual framework on which potential mechanisms of intervention effect could be based (53).

Other digital interventions were developed from:

- Expert medical knowledge of atopic dermatitis and its management (41).
- An existing educational intervention for psoriasis (44).
- A model of a German Tertiary Individual Prevention (TIP) clinical programme (55).
- 'Previous research conducted by the research team', including prototype testing of the electronic foam dispensers (SmarTop^{TM}) and smartphone app (MyPso SmarTop^{TM}) (59).
- An existing dermatology-specific measure of QoL (61) called Skindex-29 (74).

Three studies utilised existing digital technologies as part of their intervention, these included:

- Medication Event Monitoring System (MEMS®) caps (40).
- Memory buttons and a mobile app (50).
- A commercially available smartphone app (62).

The details of the development of some digital interventions were limited or absent from papers. For example, one text-based intervention delivered generic informational and motivational text messages to people with psoriasis, which were based on frequently asked questions and general recommendations for managing psoriasis, but the authors of the paper (42) did not give detail, including whether the motivational messages were underpinned by an existing theory or model of motivation. Another (50) drew links between their combined digital intervention and the Health Belief Model (75) in the discussion section of the paper, but did not expand on this anywhere in the methods section. One study developed an educational video on psoriasis onto an existing educational website for people with dermatological conditions, but no description of the development process was provided (46). The protocol for one intervention offering individual psychological video consultations was also not described (54).

Results of intervention effectiveness

There were small bodies of evidence supporting the effectiveness of digital interventions for improving some 'psycho-educational' outcomes, particularly knowledge (41, 45, 46), mood (47, 51, 58) and the therapeutic relationship (42, 51, 52) to name a few.

The outcome variables studied and the associated findings for each study are presented in **Supplementary material, section 9**. We also recorded results relating to intervention usage, which are reported in **Supplementary material, section 10**.

Knowledge

The three studies (41, 45, 46) that assessed knowledge all reported significant improvements. One study found a significant improvement ($p = 0.007$) in the average knowledge scores between intervention (11/14) and control (9/14) groups immediately post-intervention (46).

Similarly, another study (41) showed significant improvement in knowledge in people who watched an educational video versus those who were given a pamphlet on atopic dermatitis at 12 weeks (3.05 vs. 1.85, $p = 0.011$).

One study (45) reported significant improvements in the knowledge level of people who did (14.8 ± 3.4) and did not (14.6 ± 3.9) receive a text-based intervention from baseline to 4-week follow up ($p < 0.001$ for both groups), although there was no significant difference in the change in knowledge levels between the two groups ($p = 0.23$).

Mood

All three studies (47, 51, 58) measuring affect detected positive results. One study (47) observed significant improvements in mean scores on the emotion subscale of ItchyQoL in people with atopic dermatitis, psoriasis and chronic itch through an educational website called Interactive Toolbox of Comprehensive Health Resources to Enhance Living with Itch (ITCH RELIEF) from baseline to 1 month (33.4 vs. 31.5, $p < 0.01$). A case report of an individual with psoriasis who received Internet-based CBT (ICBT) reported an improvement of at least 30% in negative mood from baseline to post-intervention, and at 6-month follow up (51). Similarly, individuals living with visible skin conditions demonstrated a significant improvement in mean scores for negative (baseline: 24.06 ± 7.90 vs. follow up: 22.21 ± 8.20, $p = 0.028$), but not positive affect, immediately after taking part in an online self-compassion writing activity, compared to those who participated in a standard online writing activity (58).

Therapeutic relationship

Four studies (42, 51, 52, 60) addressed the therapeutic relationship between patients and practitioners. Three of these studies indicated that different types of digital interventions can at least maintain (52), if not improve (42, 51), good working relationships between people with skin conditions and practitioners. One study (52) found mean scores for agreement on tasks and goals and the emotional 'bond' between participants and practitioners before and after treatment were higher than original scores, but no p-value was stated. The second study (51) reported improvements in mean scores pre and post ICBT intervention for agreement on treatment tasks (4.25 vs. 4.75) and goals (4.5 vs. 4.75) yet no p-value was reported. The third study (42), however, did not report the statistics or p-values used to test this variable. The final study found that positive perceptions of the therapeutic alliance at the outset of ICBT treatment predicted significant improvements in physical ($p = 0.02$) and psychological ($p < 0.001$) outcomes (60).

Anxiety

Five studies explored anxiety and reported mixed results. One study (43) observed a significant reduction in mean anxiety scores from baseline (7.6 ± 3.6) to 6-month follow up (6.1 ± 3.5) in people with psoriasis compared to controls ($p < 0.05$), whereas two studies reported no group differences in general anxiety scores ($p = 0.24$) (48) or anxiety as a composite component of psychological functioning ($p \geq 0.20$) (60). One study (51) found improvement of at least 30% in anxiety scores post ICBT treatment but were not maintained long-term follow up, although no significance value was reported. A significant improvement in anxiety scores were found in another study (44) after 12 ($p = 0.02$) and 24 weeks ($p = 0.01$) but not after 36 ($p = 0.08$) or 60 ($p = 0.06$) weeks.

Depression

Similarly, the evidence for depression varied. Significant between-group differences (reductions) in depressive symptoms were reported in people with psoriasis ($p < 0.05$) (44) and atopic dermatitis ($p = 0.008$) (48) from baseline to 12 weeks post treatment.

Another study (43) found that the proportion of people with psoriasis who were considered to be clinically depressed fell from 15.5% to 2.3% following the eTIPs intervention, yet the difference in depression scores between the intervention and control groups was not statistically significant for either the complete cases ($p = 0.088$) or following multiple imputation analysis for missing data ($p = 0.34$). In addition, no significant differences in depression were found between participants who received ICBT and those who did not from baseline to post treatment or 6-month follow up ($p \geq 0.20$) (60). One individual with psoriasis showed an improvement in depression of at least 30% from baseline to post treatment assessment, but no significance value was stated (51).

Treatment adherence and compliance

Eight studies measured adherence to treatment (40, 42, 45, 46, 51, 59, 60, 62). The first study (40) found post-treatment

rates of adherence were significantly higher for participants in the internet survey group compared to the control group from the first to the tenth month ($p = 0.03$), after which adherence rates declined for both groups. The second study (42) found that treatment adherence increased in the experimental group only from 3.86 days per week at enrolment to 6.46 days per week following the text message intervention ($p < 0.01$). Another study (46) reported that participants were not more likely to report using their medication as prescribed after accessing an educational psoriasis website (no significance value given). The next study (59) found, according to the main analysis of chip adherence data, more patients in the intervention group were adherent than patients in the non-intervention group (65% vs. 38%, $p = 0.004$). This study also claimed that patient reported adherence to cutaneous foam was higher in the intervention group (14%) compared to the control (8%) after 1 month, but the difference was not statistically significant ($p = 0.069$) (59). One study (62) found that 13/41 (31.7%) participants who completed a follow up survey at week 12 reported using Daivobet® sometimes or never in the previous 4 weeks. Three studies (45, 51, 60) referred to treatment compliance. One study (45) found no statistically significant difference between the number of participants in the text-based intervention and control groups who forgot to use their medication (52.9% vs. 64.7%, $p = 0.33$). No significant change in the maximal treatment compliance score was observed in an individual with psoriasis from pre to post intervention or follow up (51). Nor did treatment compliance differ significantly between participants who received ICBT or standard care at pre, post or follow up assessment ($p \geq 0.25$) (60).

Skin protection behaviours

As for skin protection behaviours, one study detected significant improvements in moisturiser use from baseline to week 4 ($p < 0.001$) and 8 ($p = 0.020$), in the text-based intervention group (45), although the use of moisturiser was significantly higher in the intervention versus control group at week 4 only ($p = 0.008$). In another study (55) people with hand eczema who received a combined face-to-face counselling and website intervention reported a significant change in the mean scores for performing habits relating to their condition (e.g., using topical steroids and consulting General Practitioner) compared to participants who did not have access to the website (7.9 ± 2.4 vs. 6.6 ± 3.2, $p = 0.024$). This was the case for people with melanoma who participated in the mySmartSkin intervention, who reported performing significantly more sun protection behaviours on average at 24 weeks (i.e., sunscreen use, wearing hats and long sleeves, and seeking shade) compared to controls (3.54 ± 0.74 vs. 3.37 ± 0.84, $p = 0.031$) (53). Greater knowledge of melanoma and increased self-efficacy both partially mediated the relationship between intervention use and performing sun protection behaviours (53). Two studies recorded scratching behaviour using different measures; one study reported significant within-group reductions from baseline to 1-month follow up in mean scores for scratch intensity (12.3 vs. 11.6, $p < 0.05$) and impact (19.8 vs. 17.9, $p < 0.001$), and sleep-related itch and scratch (37.4 vs. 133.3, $p < 0.001$) (47). The other study (51) reported a reduction in scratching behaviour in a person with psoriasis, but the authors did not specify whether the change reached the threshold for statistical significance.

Physical outcomes

A similar picture was observed for physical outcomes. There was clear evidence for improving disease severity in the short term (1–3 months). One study (40) detected significant improvements in PASI, but not Investigator Global Assessment, scores between the intervention and control group after 1 (1.61 vs. −0.12, $p = 0.003$), 3 (2.50 vs. 0.79, $p = 0.025$), and 12 (3.32 vs. 0.34, $p = 0.038$) months. Another study (59) found a significant improvement in psoriasis severity in the intervention group from baseline to week 4. One study found no significant difference between SAPASI scores of participants who tested the eTIPs intervention and those who did not for either the complete cases ($p = 0.67$) data or multiple imputation analysis for missing data ($p = 0.92$) (43). Significant mean reductions in hand eczema severity scores were seen after 8 weeks in participants who received a text message intervention compared to the control group ($70.2\% \pm 35.2$ vs. $38.9\% \pm 67.7$, $p = 0.017$) (45). At 12 weeks, greater improvements in the severity of atopic dermatitis were observed in people who viewed an educational video online compared to those who read an educational pamphlet (3.30 vs. 1.03, $p = 0.0043$) (41). Following receipt of a text-based intervention, people with psoriasis also reported significantly reduced ($p < 0.05$) disease severity [PASI, SAPASI, Physician Global Assessment (PGA), and body surface area] at 12 weeks compared to controls (42). Lastly, significantly larger reductions ($p < 0.005$) in scores of objective measures of disease severity [Eczema Areas Severity Index (EASI) and SCORing Atopic Dermatitis (SCORAD)] were observed in people who received electronic memory buttons plus an app, compared to the two control groups, as was a significant decrease ($p < 0.05$) in subjective POEM scores at the second consultation approximately 1 month after participants began using the intervention (50).

Evidence for effectiveness beyond 6 months was mixed. One study (40) observed a significant improvement in PASI scores in the intervention group at 12-month follow up compared to the control group (3.32 vs. 0.34, $p = 0.038$) until alcohol use and smoking status were included in the analysis as covariates. Similarly, people with eczema who trialled ICBT showed a significantly greater reduction ($p < 0.001$) in average weekly symptoms measured by POEM at 12-month follow up compared to the control group (48). Another

study showed that clinician-assessed disease severity worsened slightly between baseline and 6-month follow up but no significance value was reported (51). One study did not detect a significant difference (p = 0.16) in median hand eczema severity index (HECSI) scores of website and non-website users (55).

Improvements in psoriasis severity were noted in the longer term in two studies; the first study (44) reported significant reductions ($p < 0.001$) in PASI scores in all patients from baseline to follow up at week 60, but no group effect was found. The second study (59) found that the greater improvement in psoriasis severity, measured by the lattice system physicians global assessment (LS-PGA), that was observed in the intervention group in the short term, no longer reached the threshold for statistical significance at week 8 or 26.

Reductions in itch were also seen at 4 weeks ($p < 0.001$) (47), after 6 months (p = 0.052) (55) and 12 months in people with atopic dermatitis (p = 0.01) (48). One study (44) found itch significantly reduced in all participants with psoriasis after 60 weeks, although the difference between the groups was not statistically significant. One study did not control for use of itch medication (47).

Quality of life

As for QoL, two studies (47, 54) reported significant within-group differences from baseline to 4-week follow up. The first study was specific to itch-related QoL (78.9, 95%, confidence interval [CI] = 75.9–81.9) to follow up (75.4, CI = 72.4–78.5, p = 0.007) (47). The second study employed the DLQI (4.4 ± 3.9 vs. 1.6 ± 2.5, $p < 0.05$).

Three studies detected significant between-group differences in QoL favouring the intervention group, from baseline to week 6 (p = 0.042) (43), week 12 ($p < 0.05$) (42), and after 6 months (p = 0.014) (55). One study (48) found a significant between-group difference in QoL favouring the ICBT intervention group with the BBQ (p = 0.001) (69), but not the DLQI (p = 0.07) (68).

Two studies (44, 52) reported improvements in QoL that did not reach statistical significance. Another study noted a reduction in DLQI scores in the intervention group compared to controls at weeks 4 and 8, which relapsed at week 26, yet none of these group differences reached the threshold for statistical significance (59).

Other psychological outcomes

Various psychological concepts were measured in one study only. The high level of heterogeneity in the outcome variables studied meant evidence was often not sufficient to make general claims about specific outcome variables. Statistically significant reductions were found for the following outcomes:

- Perceived helplessness in one individual living with psoriasis (significance value not reported) (51).
- Fear of cancer recurrence in people who received an online mindfulness-based programme, compared to controls (mean difference: −2.55; 95% CI = −4.43 to −0.67; p = 0.008), but only few of these scores fell below the clinical cut-off (≥13) (56).
- Perceived stress (B = 5.09; 95% CI = 1.96–8.21; z = 3.19; p = 0.001) and sleep problems (B = 3.38; 95% CI = 1.28–5.48; z = 3.15; p = 0.002) in people who received ICBT versus the control group (48).
- Trichotillomania severity from pre to post ACT Enhanced Behavior Therapy via telepsychology [slope estimate = −6.13, SE = 1.30, $t(58.48) = -4.72$, $p < 0.001$] (52).

One study observed a statistically significant improvement in mean self-compassion scores (p = 0.006) in people with visible skin conditions following an online self-compassion writing activity (3.33 ± 0.60), compared to those who participated in a standard online writing activity (2.84 ± 0.62) (58).

A number of these papers reported trends towards improvement but were not statistically significant. These outcomes included:

- Self-efficacy for managing eczema in website users versus non-website users (p = 0.093) (55).
- Rumination in people with melanoma following an online mindfulness programme compared to controls (mean difference: −2.76; 95% CI = −6.67 to 1.17; p = 0.169) (56).
- Impairment in daily activities following an educational session via a psoriasis management smartphone app, and participants in the control group (p = 0.63) (44).
- Psychological well-being of people with skin conditions following psychological video consultations (baseline: 68.5 ± 15; week 4: 77.1 ± 16; no p-value reported) (54).
- Psychological flexibility scores post ACT Enhanced Behavior Therapy via telepsychology [$F(1,18) = 3.790$, p = 0.068, ω^2 = 0.064] (52).

There were several psychological outcomes for which no significant between-group differences were reported:

- Perceived stress (p = 0.719) or worry (p = 0.814) in people with melanoma who attempted mindfulness and those in the control group (56).
- Anxiety, depression and negative mood (all $p > 0.20$), or psychological functioning overall (p = 0.32), in people with chronic skin conditions following ICBT and those in the control group (60).
- The rates of hospital visits in people with psoriasis who received a smartphone app with or without prompted communication from doctors (5.2–15.7% vs. 7.5–17.0%,

$p > 0.05$), although older age (50 to 60 years: $P = 0.02$) and greater body surface area (scores 7 to 10: $p = 0.02$), were associated with more hospital visits (62).

One case study tracked changes in psychological and social outcomes overtime in someone with psoriasis who received ICBT and found that high and low levels of social support and stigma (respectively), and maximal impact of psoriasis on daily life, remained unchanged from baseline through to follow up (51).

Individual studies also produced mixed findings for specific outcomes. For example, a study of ACT Enhanced Behavior Therapy delivered via video conferencing showed decreases in shame scores that did not differ significantly when comparing the intervention and control groups. However, when the groups were entered into a combined analysis, a significant change in shame scores was observed from post-treatment to follow up only ($p = 0.002$) (52).

Another study used a composite measure of impact on daily life, which was comprised of physical and psychological functioning and role limitations due to physical and emotional health problems, as a measure of impact on daily activities (60). After 6 months, significant improvements were observed for role limitations due to emotional and physical health problems (both $p = 0.04$) in individuals receiving ICBT, compared to other participants who received care as usual. The improvement in role limitations due to emotional problems was further enhanced at follow up ($p = 0.047$). However, no significant difference ($p \geq 0.17$) in role limitations was found between the groups when baseline values of the dependent variable were included in a secondary analysis.

One study reported that the significant between-group difference in PASI scores favouring the intervention group ($p = 0.038$) at 12 months no longer reached statistical significance when alcohol consumption and smoking status were controlled ($p = 0.07$) (40).

Other independent studies included measures of psychological outcomes but were limited for different reasons. Firstly, one study found that higher levels of Facebook envy were associated with lower levels of life satisfaction (standardised coefficient [β] = −0.38, CI = −0.58 to −0.16) and happiness (β = −0.36, CI = −0.57 to −0.14) in people with psoriasis. This study was cross-sectional and thus Facebook envy and potentially relevant factors could only be measured at one timepoint.

One study measured the average number of minutes that people with melanoma reported meditating per week across a 6-week online mindfulness programme (56). This varied greatly from 64 min in week 2 to 129 min in week 5, but the authors did not test for statistically meaningful differences in the average meditation times at different timepoints.

Lastly, two papers reported measuring psychological outcomes, specifically participants' beliefs about psoriasis (43) and self-efficacy to interact with clinicians (47), but the results for these outcomes were not reported.

User views and experiences

In total, 13 studies explored people's views and experiences of digital psychological interventions (41, 42, 46, 48, 49, 51–53, 55, 56, 59–61). Of these studies, only one adopted a purely qualitative design, (49) and others:

- Included a qualitative component, but only referred to the study as a mixed-methods study in the discussion section (55).
- Described a qualitative content analysis, but did not label the analysis as such (56).
- Did not describe how qualitative data were analysed (46).

The synthesis is reported in relation to acceptability and feasibility, satisfaction, positive feedback, perceived benefits, and barriers to digital intervention use.

In terms of the acceptability and feasibility of digital psychological interventions, two studies (56, 61) explicitly aimed to explore intervention acceptability and feasibility. The first study (56) found that an online mindfulness intervention was acceptable to people with melanoma, as 23/32 (72%) respondents deemed the intervention to be helpful. Furthermore, 70% of participants completed the end-of-study questionnaire and most participants noted that the intervention was simple to use, demonstrating intervention feasibility (56). The second study (61) reported that people with visible skin conditions considered an online educational website appealing and convenient, but overall acceptability was lower than expected because users did not think the website content was relevant to them. It was concluded that this intervention was not feasible overall because users either somewhat or totally agreed that their daily activities prevented regular use (61).

Seven studies measured how satisfied people living with psoriasis (42, 46, 51, 60), atopic dermatitis (41, 48), and trichotillomania (52) were with the interventions they received. These studies indicate high levels of user satisfaction, and that users would recommend, continue using (42, 46), and might prefer online interventions in future (51, 60).

Six studies (41, 42, 46, 51, 52, 60) captured positive feedback from users, which lends further support to the acceptability and feasibility of digital psychological interventions. Users remarked on the user-friendliness (51, 60), appeal (41), convenience (51, 52), and usefulness (42) of digital psychological interventions, particularly for understanding dermatological conditions (46).

A range of perceived benefits of using digital psychological interventions were reported by users across five studies (49, 51, 53, 55, 56). People reported that interventions of this kind

improved their knowledge of their condition and sense of personal control (53, 55).

In addition, these interventions were seen to facilitate positive psychological well-being by helping individuals to accept (56) and regulate their feelings (e.g., helplessness, depression) (49, 51, 53) and behaviour (e.g., itch), and identify coping strategies (51). The benefits of online peer support included facilitating emotional expression, self-confidence and acceptance, and exchanging knowledge, experiences and tips for coping and management (49).

Four studies identified barriers to digital intervention use. These barriers included technical problems (e.g., difficulty accessing and navigating the intervention) and individual factors (e.g., personal priorities, preferences and schedules, physical symptoms, geographical location, and a lack of time) (53, 55, 56, 61). One study (55) found that certain features, specifically digital reminders and interactive activities, facilitated the use of digital interventions.

Integration of qualitative and quantitative results

We identified some overlap between qualitative and quantitative data for some outcomes. Firstly, knowledge of skin conditions and their management. Quantitative data revealed significant improvements in participants' knowledge following the use of digital psychological interventions, including an online educational video on eczema (41), and a text message intervention (45) and an online educational website (46) for psoriasis. Two studies (46, 53) involving patient evaluations also found participants felt more informed about their conditions and how to manage them following intervention use, and a group intervention enabled members to share knowledge and learn from each other (49).

Secondly, we identified some parallels between the quantitative and qualitative data relating to emotions. The former indicated that use of digital interventions, including ICBT (51), online self-compassion writing (58), and an educational website (47) improved negative mood in particular. One qualitative study (49) similarly found that an online support group enabled people to express how they felt about alopecia. In addition, feedback from people with melanoma suggested that they felt calmer, at peace and more at ease after taking part in online mindfulness (56).

Another outcome for which there was congruence was stress. One study (48) found significant reductions in perceived stress among the ICBT intervention group versus controls. This was supported by one study (56) in which eight reports from five participants suggested an online mindfulness intervention helped individuals to manage their stress.

We did not identify any contradictory evidence. Many of the outcome variables measured in quantitative studies were not addressed in the few qualitative studies that were included in this review.

Discussion

As digital technology becomes further embedded in health care generally, this mixed methods systematic review offers valuable insight into the potential effectiveness of digital platforms and content for improving some psychological and physical outcomes in people with dermatological conditions, mainly psoriasis and eczema. There is some support for web-based digital interventions to improve people's knowledge of their skin conditions and its management, and emotional functioning, particularly negative affect. Use of digital interventions also seemed to benefit aspects of disease severity in the short to medium term. These insights align with some of the findings of an earlier meta-analysis of effectiveness of psychological interventions for adults with skin conditions, which detected medium effect sizes for psychological outcomes and skin severity (76).

We identified several digital interventions that focused on treatment non-adherence, a significant problem within dermatology (77). However, most of these interventions did not lead to significant improvements in treatment adherence and therefore a new approach is needed.

Some digital interventions showed improvement in QoL and offers some confidence that digital interventions requiring active involvement from a provider (e.g., ICBT) are at least as good as those delivered in person in terms of facilitating rapport between the people receiving and delivering the intervention. This is a useful finding given that previous research with people with psoriasis (78) and hidradenitis suppurativa (79) have indicated that other forms of digital interventions, including remote consultations via video, and telephone consultations especially, are not conducive to discussing the broader psychological impact of skin conditions or building rapport between patients and clinicians.

Overall, considerable heterogeneity in study designs, measures and outcomes meant there was a lack of sufficient and consistent evidence for many psychological outcomes preventing us making definitive conclusions about intervention effectiveness. The level of diversity within this systematic review mirrors that found in a previous systematic review of psychological therapies in psoriasis management (80). Several papers indicated any suggested improvements did not reach the threshold for statistical significance; it is plausible that some of the studies reviewed were not sufficiently powered, as also suggested by another previous systematic review and meta-analysis of psychological and education interventions for atopic dermatitis specifically (81).

As for people's views and experiences, we found poor reporting of qualitative methodology in some studies that sought patient evaluations. Some, mostly web-based interventions, may be acceptable to people living with different dermatological conditions but personal factors could also present as barriers to intervention use. The main benefits of digital interventions included improved emotional control (82) and confidence to socially interact (83), which echo similar findings of previous research (82, 83). A better understanding of dermatological conditions and approaches to management were also a key benefit of digital interventions. Importantly, some of these key qualitative findings lend support to the positive quantitative results showing improved knowledge and emotional functioning. Furthermore, the qualitative and quantitative insights on user knowledge that we have identified arguably builds on previous research, which was unable to determine the efficacy of educational and psychological approaches for adults with atopic dermatitis (81). The present review gives us some confidence that digital interventions including educational material are likely to be of some benefit to people with dermatological conditions, the next step is to find out what benefit and for whom.

Strengths and limitations

To our knowledge, this is the first mixed methods systematic review investigating *digitally delivered* interventions supporting the psychological health of people with dermatological conditions. The TIDieR checklist and guide (32) provided a comprehensive framework for charting key characteristics of the digital interventions clearly, and identifying gaps in reporting. This review was conducted by a multi-disciplinary team of health and clinical psychologists and a general practitioner, most of whom specialize in dermatology research and practice. It was supported by experts from a JBI Centre of Excellence and followed JBI methodology; JBI is renowned for the conduct of highly rigorous evidence syntheses to promote and implement evidenced-based decisions to improve health and healthcare globally (84). The use of JBI critical appraisal tools allowed for a detailed and nuanced assessment of different study designs. In addition, it has been noted by experts in JBI methodology that the step of corroborating and refuting findings is often lacking or missing entirely from mixed methods systematic reviews (38). We adopted a convergent segregated approach to data synthesis and as a result were able to triangulate some of the key findings relating to cognitions and emotions specifically, further strengthening the present review.

However, our decision to review all eligible studies regardless of quality meant three short reports (42, 47, 54) and one research letter (46) were included, arguably weakening the overall quality of this review. We also opted to include a paper specific to trichotillomania; a complex psychiatric disorder (85). Whilst this inclusion constitutes as a deviation from the protocol, people with trichotillomania often present to dermatology staff, psychiatrists and psychologists (86), reiterating the complex interplay between dermatological and psychological factors. Thus, we argue that the contents of this paper on trichotillomania are likely to be of relevance to the dermatology community, justifying its inclusion in this systematic review. Furthermore, we identified several papers at the full text screening stage which were of some relevance to this review, but these were excluded on the basis that they involved people as young as 12 (15, 87–90) and 16 (91, 92) years old and pooled the results (93–96), preventing us from extrapolating the results specific to our population of interest. It is possible that we missed information related to the review questions by excluding these papers. Lastly, two of the papers included in this review were authored by CB (43) and AT (49), potentially introducing bias. However, we attempted to counter this bias by ensuring that neither author was responsible for reviewing their respective papers at any point in the review process.

Future research

Further work to design and test digital psychological interventions is needed, as is qualitative research, to ensure future interventions are feasible, appropriate, meaningful and effective (84) for people with a broad range of common and rare dermatological conditions (97). We have shown that existing research largely focuses on specific dermatological conditions, mainly psoriasis followed by eczema. Researchers should aim to develop digital interventions targeting other dermatological conditions, such as hidradenitis suppurativa and acne, which carry a substantial psychological burden (8), as well as digital interventions that tackle psychological impacts that are common across dermatological conditions. The TIDieR checklist and guide (32) is likely to be a useful tool for intervention developers to consider when planning, developing, and particularly when reporting, complex digital interventions.

This review highlights that many existing studies lack quality, despite the level of evidence they were assigned to. In the context of RCTs, for example, these studies were ranked to level 1, the highest level of evidence for effectiveness, but most were missing detailed information about standard trial procedures, such as blinding. This criticism aligns with earlier research calling for a higher quality and better reporting of RCTs (76). Underreporting of blinding procedures in RCTs of psychological interventions is not a new finding, but it is paramount that researchers explore all possible avenues for blinding, adequately report blinding

attempts, and acknowledge potential pitfalls where blinding is not possible (98). Greater transparency in the reporting of these procedures could facilitate the development of more robust RCTs in the future, and support healthcare professionals and policy makers to make more informed, evidence-based decisions relating to the care of people with dermatological conditions.

Furthermore, it seems that larger samples might be required for future studies of digital interventions to determine whether their use can significantly improve psychological outcomes (e.g., self-efficacy, well-being, etc.) in people with dermatological conditions, and to establish the magnitude of the effect where one exists.

We also emphasise the need for more qualitative research to further explore intervention barriers and facilitators to using digital psychological interventions and outcomes that are meaningful to patients. Addressing these issues directly with people living with a range of dermatological conditions, as well as ways of overcoming barriers to use, could help to maximise the appropriateness, practicability, and usability of new digital psychological interventions for this population (28). The qualitative data offers some insight into psychological factors (e.g., personal control and acceptance) which might help to explain the mechanisms through which digital interventions work, as does qualitative and quantitative data on self-efficacy and knowledge. It is important to investigate these factors further to determine whether they are indeed mechanisms for change. However, qualitative methodologies were sometimes not acknowledged or described sufficiently by authors. Thus, more explicit and comprehensive reporting of qualitative methodologies is required.

Practical implications

Several studies focused on treatment behaviours. Whilst treatment adherence and skin protection are important for managing dermatological conditions (77), other modifiable dietary and health behaviours, such as smoking, alcohol consumption, and poor sleep are associated with some, mostly inflammatory, dermatological conditions (99), and increased risk of cardiovascular disease (100–102). Digital interventions addressing a variety of health behaviours are, therefore, needed to support a holistic and effective approach to patient self-management.

While many studies in this review included an educational component, the provision of information alone is not always sufficient for eliciting behaviour change; other factors, including personal capabilities, opportunities and levels of motivation, are established drivers of behaviour (103). In the context of treatment adherence, for example, other psychological factors, such as illness and treatment beliefs and concerns, are known to influence behaviour (77). Dermatologists involved in developing digital interventions should address the psychological factors which underpin adherence to dermatological treatments (77), as well as target other related health behaviours.

Whilst intervention development in the usual way was not the focus of this systematic review, it was not always clear from the papers included if or how theoretical frameworks contributed to intervention development, or if the perspectives and needs of the target user were considered throughout this process. Digital behaviour change interventions, like face to face interventions, should be informed by theory in order to determine and test mechanisms for change (104). The Behaviour Change Wheel (BCW) is an example of an established and evidence-based framework for designing behaviour change interventions (103). At the heart of the BCW sits the COM-B Model, which encapsulates three key drivers of behaviour: Capability, Opportunity and Motivation (103). The BCW also specifies nine intervention types and seven policy categories that could aid the design and implementation of new interventions (103). Specialists in dermatology should adopt behavioural science principles, including recognised theories of behaviour change, such as the COM-B Model (103), and a person-based approach from the outset, to ensure digital interventions meet the needs and preferences of people living with dermatological conditions (104). We also advocate for interdisciplinary collaborations between experts in dermatology, technology, and particularly behaviour change, to facilitate better understanding, development and testing of future complex digital interventions (104).

Conclusion

This mixed-methods systematic review shines light on a diverse range of existing digital psychological interventions for some dermatology conditions, as well as substantial heterogeneity and varying quality in the literature. A lack of sufficient and consistent evidence allowed for, at best, tentative conclusions on intervention effectiveness. Whilst digital interventions of this kind are, to some extent, acceptable to patients, there are barriers to their use, and these must be addressed to maximise future use. Collectively, existing evidence underscores the need for quality and interdisciplinary research to develop and test complex digital psychological interventions targeting a broader range of psychological factors, specifically health behaviours, with input from people living with dermatological conditions.

Data availability statement

The original contributions presented in this study are included in the article/**Supplementary material**, further inquiries can be directed to the corresponding author.

Author contributions

RH contributed to the conceptualisation, lead for methodology, material development, database searching, article screening, data extraction, curation, critical appraisal, data synthesis, writing – original draft and review, and editing, and project administration. MP contributed to the database searching, article screening, data extraction, critical appraisal, and writing – review and editing. CP contributed to the conceptualisation, methodology, consensus checks and discrepancy resolution for article screening, data extraction and critical appraisal, and writing – review and editing, and supervision. RP contributed to the conceptualisation, methodology, article screening, data extraction, critical appraisal, discrepancy resolution, consensus checking, and writing – review and editing. BJ contributed to the methodology, material development, article screening, data extraction, critical appraisal, consensus checking, and writing – review and editing. GW and OH contributed to the material development, article screening, data extraction, critical appraisal, consensus checking, and writing – review and editing. MR contributed to the consensus checking and discrepancy resolution for article screening, data extraction and critical appraisal, and writing – review and editing. AT contributed to the consensus checking and discrepancy resolution for article screening and data extraction, and writing – review and editing. CB contributed to the lead for conceptualisation and supervision, supported methodology and writing – review and editing. All authors contributed to the article and approved the submitted version.

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Conflict of interest

RH had received financial support for research from Beiersdorf AG. AT is a Topic Editor of the special article collection title Psychosocial Aspects of Skin Conditions and Diseases in Frontiers in Medicine (Dermatology). He had received workshop and consultancy fees from a number of pharmaceutical companies including UCB (non-specific). He is also receiving research support from Pfizer. He is a scientific advisor for the Vitiligo Society, and a trustee of Changing Faces; and has been psychological advisor to the All-Party Parliamentary Group on Skin. CB had over the last 3 years received funds for research, honoraria or consultancy from the following pharmaceutical companies: Abbvie, Almirall, Amgen (was Celgene), Beiersdorf AG, Janssen, Novartis, Pfizer, UCB.

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.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2022.1024879/full#supplementary-material

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Anxiety, depression, and quality of life in children and adults with alopecia areata: A systematic review and meta-analysis

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Introduction: Alopecia areata (AA) is a non-scarring hair loss condition, subclassified into AA, alopecia universalis, and alopecia totalis. There are indications that people with AA experience adverse psychosocial outcomes, but previous studies have not included a thorough meta-analysis and did not compare people with AA to people with other dermatological diagnoses. Therefore, the aim of this systematic review and meta-analysis was to update and expand previous systematic reviews, as well as describing and quantifying levels of anxiety, depression, and quality of life (QoL) in children and adults with AA.

Methods: A search was conducted, yielding 1,249 unique records of which 93 were included.

Results: Review results showed that people with AA have higher chances of being diagnosed with anxiety and/or depression and experience impaired QoL. Their psychosocial outcomes are often similar to other people with a dermatological condition. Meta-analytic results showed significantly more symptoms of anxiety and depression in adults with AA compared to healthy controls. Results also showed a moderate impact on QoL. These results further highlight that AA, despite causing little physical impairments, can have a significant amount on patients' well-being.

Discussion: Future studies should examine the influence of disease severity, disease duration, remission and relapse, and medication use to shed light on at-risk groups in need of referral to psychological care.

Systematic review registration: [https://www.crd.york.ac.uk/prospero/], identifier [CRD42022323174].

KEYWORDS

alopecia, alopecia areata, psychosocial functioning, anxiety, depression, quality of life, meta-analysis

Introduction

Alopecia areata (AA) is a hair loss condition with a lifetime prevalence of 2.1% (1). AA has a peak onset between 25 and 29 years old, with a median age at diagnosis of 31 for males and 34 for females. It occurs more frequently in people with a non-white ethnicity (2). Males and females appear to be affected equally often (2), however research has also reported females to be slightly more likely to experience AA (2). AA is typically divided into AA (patchy hair loss), alopecia universalis (AU; total loss of scalp hair), alopecia totalis (AT; total loss of body hair) and alopecia ophiasis (band-like hair loss on the temporal and occipital scalp) (3).

Alopecia areata has an unpredictable disease course characterized by relapse and remission (4). Full hair regrowth may be observed in 50–80% of patients (5, 6), but relapse rates of 30–52% have been reported (5) with around 30% of patients with AA eventually progressing to complete hair loss (6). Relapse is more likely in patients with an earlier onset of AA, but is not related to gender, clinical severity and treatment given (5). Furthermore, medication often fails to provide sustained hair regrowth (3).

There are indications that people with AA experience adverse psychosocial outcomes. Qualitative studies, for instance, have shown that patients reported considerable distress (7). Feelings of sadness, insecurity, inadequacy, and self-consciousness (8), as well as feelings of depression, anxiety, and suicidal thoughts (7) were prevalent. The majority of qualitative research highlights that people struggle with everyday activities, such as participating in sports or social events, due to a fear of their appearance being noticed (7–9). The unpredictable nature of AA was also highlighted as a source of distress in particular (7, 8) and women seem to report more stress and distress than men (10, 11).

Most quantitative research has focused on anxiety, depression or quality of life (QoL). For anxiety, a meta-analysis including eight studies by Okhovat et al. (12) showed that people with AA are 2.50 times more likely to experience anxiety. However, it is unclear how the papers were selected and what type of control group was included in the meta-analysis. Other studies have shown that people with AA have a higher chance of being diagnosed with an anxiety disorder than healthy controls (13). When the amount of anxiety symptoms of people with AA is compared to people with other dermatological diagnoses mixed results have been found (14).

When looking at depression, the aforementioned meta-analysis found that people with AA are 2.71 times more likely to experience depression (12). This result is corroborated by other studies reporting people with AA to be more likely to be diagnosed with depression (13, 15). As for anxiety, it is unclear how people with AA compare to people with other dermatological diagnoses (16, 17).

A systematic review conducted in 2018 has shown that AA has a considerable impact on QoL (18). However, it remained unclear how QoL was related to disease severity (18). Furthermore, people with AA were not compared to people with different dermatological diagnoses in this review. More recent research has reported a moderate effect on QoL (19), as well as no effect (20). Comparisons to people with a different dermatological diagnosis have yielded mixed results. For instance, one study comparing people with AA to people with alopecia androgenetica reported people with AA to have better QoL (21), while another study found the opposite result (22).

Although previous systematic reviews on psychosocial consequences of AA have been conducted (e.g., 18, 23), it remains unclear how people with AA compare to people without AA or people with a different dermatological diagnosis. In addition, these reviews have not highlighted the psychosocial impact of AA on different age groups (i.e., children or adults). Therefore, the purpose of the current systematic review and meta-analysis was to update and expand previous systematic reviews, as well as describing and quantifying levels of anxiety, depression, and QoL in patients with AA, AU, or AT. We also aimed to explore whether gender or age would influence the amount of anxiety, depression, and QoL experienced by people with AA. We specifically sought to answer the following research question: What is the impact of living with alopecia areata, alopecia totalis or alopecia universalis on levels of anxiety, depression, and quality of life in children and adults? We also wanted to know how levels of anxiety, depression, and QoL of people with AA compared to people with a different dermatological condition and to healthy controls.

Materials and methods

This article was written in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (24) and was registered prospectively in the international prospective register of systematic reviews, PROSPERO, registration number CRD42022323174. The protocol was registered with a broad focus on psychological impact of AA, as it was unclear how many papers the search would yield. After selection of relevant papers, a decision was made to focus only on anxiety, depression and QoL and a further nine papers were excluded (see **Figure 1**).

Search strategy

As this article was part of a bigger project for the Dutch Alopecia Association, a broad search focusing on the psychosocial impact of living with AA was conducted by a research librarian on 28 March 2022. The following databases

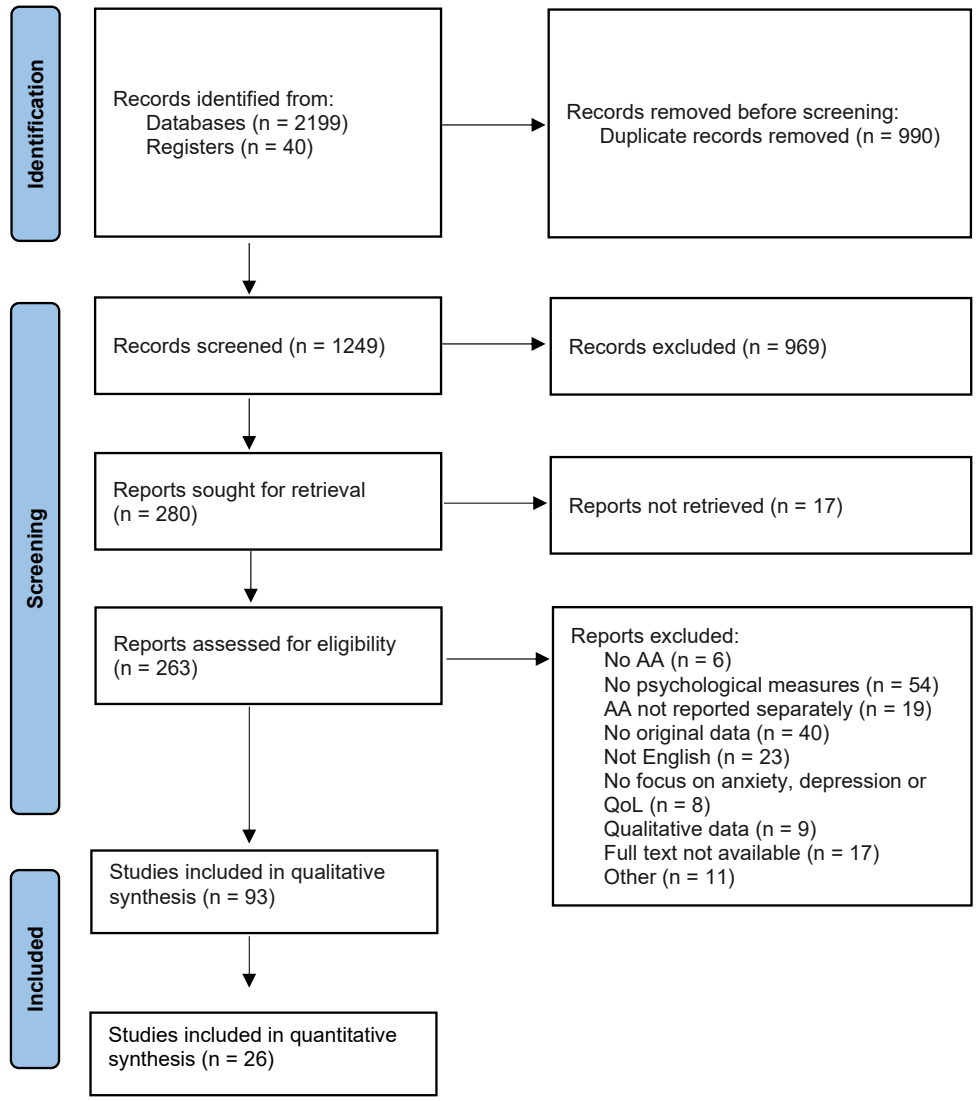

FIGURE 1
PRISMA flowchart of the selection process.

were searched from inception: Embase, Medline, Web of Science Core Collection, Cochrane Central Register of Controlled Trials, PsycInfo, and Google Scholar. The search included terms, both Mesh and free text, related to alopecia and the psychosocial impact, without restrictions on language or publication date. Only published, peer-reviewed papers were used. The full search is displayed in **Supplementary material**.

Eligibility criteria

Studies were included if they met the following eligibility criteria: (a) studied a sample with AA, AU, and/or AT, (b) reported quantitative data on anxiety, depression or QoL, and (c) the paper was an original research paper. Studies were excluded if they (a) reported no original data (e.g., case-reports, conference abstracts, and systematic reviews), (b) were not written in English, or (c) did not separate AA from other medical diagnoses. No criteria were set for the amount of timepoints in an article (i.e., the article being cross-sectional or longitudinal). In case of a longitudinal intervention study, only the baseline data were included.

Study selection

Studies were selected if they met the inclusion and exclusion criteria. Two reviewers (MD and KM) independently assessed the title and abstract. The interrater agreement was 81.55%. Discrepancies were resolved using consensus. Afterward, the

two reviewers independently assessed the full text for eligibility. Interrater agreement for this step was 87.46%. Discrepancies were again resolved using consensus. One of the reviewers (MD) checked the reference list of included articles for additional relevant references. Any references deemed relevant were first screened based on title and abstract. If still relevant, the full-text was read. When the article met the inclusion and exclusion criteria, it was included in the review. Endnote 20 was used to manage references.

Data extraction

Data collection was done by one researcher (MD) and checked by another researcher (KM) using a data extraction form. The following data were extracted: type of alopecia, sample size, percentage male, mean age (SD), age range, method involved (questionnaire or interview), main conclusions, mean score (when method is questionnaire), mean prevalence of symptoms/diagnosis, any relevant comparisons between groups (e.g., anxiety symptoms in AA vs. unaffected controls). Authors of papers were contacted when relevant data for meta-analyses was missing.

Quality and risk of bias

Quality and risk of bias were assessed using the relevant NIH quality assessment tool for controlled intervention studies, observational cohort and cross-sectional studies, case-control studies or before-after studies with no control group [National Heart, Lung, and Blood Institute (NIH), 2018] (25) or the QAVALS (26). Questions can be answered with "yes, no or cannot determine/not reported/not applicable responses." We rated >80% points as good, 60–80% points as fair and <60% as poor quality. Quality assessment was performed independently by two reviewers (MD and KM). Half of the articles were discussed in a consensus meeting, after which the remaining half of the papers was checked by one reviewer (MD).

Data synthesis and statistical analyses

All studies were included in the qualitative synthesis. Meta-analyses were conducted for five or more similar studies. As a high level of between-study heterogeneity was expected, a random-effects model was used to pool effect sizes. The Restricted Maximum Likelihood Estimator (REML) was used to calculate heterogeneity variance (27). Means and standard deviations (SDs) of samples were used to compute effect sizes, the standardized mean differences (SMDs), quantified in the form of Hedges' g (28). When means and SDs were not available, medians were transformed to means and SDs as described by Shi et al. (29). Publication bias was tested by visual inspection of a contour-enhanced funnel plot (30) and Egger's test in case of ≥10 studies. Exploratory meta-regressions were conducted. For each meta-analysis, one model was created with mean age, percentage male, and quality rating as independent variables. The significance level was set to $\alpha = 0.05$. Analyses were done using the meta package (31) in RStudio.

Results

Study selection

After removing duplicate records, a total of 1,249 records were retrieved for screening. After title and abstract screening, 280 records were assessed for eligibility. Finally, 93 articles were included for the qualitative synthesis of which 26 articles were also included in the quantitative synthesis. The full selection process is displayed in **Figure 1**. Overall, 74 papers were of poor quality, 16 papers were of fair quality and 4 papers were of good quality.

A total of 52 papers studied anxiety in children and/or adults with AA. Seven papers (32–38) had a combined research group with children and adults (n = 11,007, M_{age} = 41.78, 43.63% male), eight papers (39–46) studied children with AA (n = 398, M_{age} = 11.85, 47.00% male) and 37 papers (13, 14, 17, 19, 22, 37, 38, 47–77) studied adults with AA (n = 88,858, M_{age} = 40.03, 41.25% male).

For depression, 65 papers were included. Fourteen papers (32–36, 38, 78–84) looked at children and adults (n = 18.638, mean age = 36.26, 43.44% male), nine papers (39–46, 85) studied children (n = 3908, M_{age} = 11.85, 44.82% male) and 42 papers (13–17, 19, 22, 47–53, 55–66, 68–77, 86–90) studied adults with AA (n = 93,047, M_{age} = 41.69, 40.39% male).

A total of 40 studies investigated QoL in people with AA. Five studies (36, 78, 83, 91, 92), combined children and adults into one sample (n = 3611, M_{age} = 31.43, 60.09% male), three studies (41, 43, 93) investigated children (n = 258, M_{age} = 11.50, 47.45% male) and 32 studies (17, 19–22, 53, 61, 62, 67, 73, 75, 76, 94–113) investigated adults with AA (n = 5,373, M_{age} = 41.38, 42.83% male).

Anxiety

The results for anxiety are shown in **Table 1**.

Children and adults

Three studies with a total of 5,665 patients with AA, reported that people with AA experienced more symptoms of anxiety and were diagnosed with anxiety more often than healthy controls (32–34). One smaller study (n = 24) (35) did not find a difference

TABLE 1 Results for anxiety.

References	Country	Year	*N*	% male	Age (*M*, SD)	% AA, AT, AU	Controls	Measures	Conclusions	Quality score (%)
Pediatric and adult samples										
Ataseven et al. (32)	Turkey	NR	43	72.1	23.42 (11.41)	NR	30 healthy controls	HAM-A	AA more symptoms of anxiety than healthy controls	30[3]
Chu et al. (37)	Taiwan	2000–2009	5,117	49.2	NR	NR	20,468 healthy controls	ICD-9 codes	AA diagnosed with anxiety more often than controls	80[3]
Kökcam et al. (33)	Turkey	NR	17	NR	26.47 (12.2)	NR	11 vitiligo, 20 healthy controls	SCL-90-R	AA more symptoms of anxiety than healthy controls, no differences with vitiligo	20[3]
Marahatta et al. (38)	Nepal	August 2015–July 2016	75	53.3	29.40 (9.90)	NR	No	BAI	89.0% very low anxiety, 8.0% moderate anxiety, 0% severe anxiety	45.83[4]
Singam et al. (34)	USA	2002–2012	5,605 hospitalized patients	38.3	42.2 (NR)	NR	Hospitalized patients without AA (N unknown)	ICD-9 codes	AA diagnosed with anxiety more often than controls	45[3]
Talaei et al. (35)	Iran	April–July 2005	24	33.33	25.38 (8.32)	NR	24 healthy controls	SCL-90-R	No significant difference with controls	70[3]
Vélez-Muñiz et al. (36)	Mexico	March 2017–February 2018	32 child, 94 adults	41	NR	92.9% patchy AA, 3.2% AT, 1.6% ophiasis, 1.6% AU	No	HADS	For adults: 19.1% heightened anxiety/depression, 34.1% no anxiety/depression	50[4]
Pediatric samples										
Altunisik et al. (39)	Turkey	NR	27	29.6	11.9 (3.3)	85.19% AA, 14.81% AU	30 dermatology patients	K-SADS-PL; SCARED; STAI-C	No difference with controls on questionnaires or diagnoses. 51.8% of AA patients had at least 1 anxiety diagnosis	65[3]
Andreoli et al. (40)	Italy	1997–2000	176	NR	NR	NR	No	Diagnosis by psychologist	16% diagnosis generalized anxiety disorder, 8% social anxiety disorder	25[4]
Bilgiç et al. (41)	Turkey	NR	74	55.41	12.1 (2.8)	NR	65 healthy controls	STAI-C	AA more state anxiety than controls. Children, but not adolescents more trait anxiety than controls.	65[3]
Díaz-Atienza and Gurpegui (42)	Spain	NR	31	52	12.2 (3.8)	51.61% AA, 48.39% AU/AT	23 epilepsy, 25 siblings	STAI-C	No difference on symptoms of anxiety between AA and epilepsy or sibling group	65[3]
Erdoğan and Gür (43)	Turkey	October 2018–December 2019	31	54.83	12.54 (3.56)	100% AA	29 vitiligo, 30 healthy controls	RCADS-C; RCADS-P	More social anxiety and total anxiety in AA (child-reported) for HC. More panic disorder and total anxiety in AA (parent-reported) for HC. No differences with vitiligo.	60[3]
Ghanizadeh (44)	Iran	August 2004–November 2006	14	NR	11.66 (6.08)	NR	No	K-SADS-PL	7.1% diagnosis social anxiety SAS, 28.6% specific phobia, 7.1% generalized anxiety disorder	50[4]
Liakopoulou et al. (45)	Greece	NR	33	30.3	10.5 (0.3)	NR	30 patients from pediatrician	CMAS	AA higher scores on worry, oversensitivity and concentration	40[3]
Reeve et al. (46)	USA	NR	12	NR	11.5 (2.9)	NR	No	DICA-R; RCMAS	58.33% with any anxiety disorder diagnosis	37.5[4]

(continued)

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TABLE 1 (continued)

References	Country	Year	*N*	% male	Age (*M*, SD)	% AA, AT, AU	Controls	Measures	Conclusions	Quality score (%)
Adult samples										
Aghaei et al. (47)	Iran	NR	40	44.8	35.2 (9.2)	NR	40 healthy controls	BAI	More symptoms of anxiety in AA patients than controls	35[3]
Alfani et al. (48)	Italy	November 2009–October 2010	73	45.2	35.2 (9.2)	61.7% AA, 26.0% AT, 12.3% AU	73 healthy controls	Clinical interview; MMPI-2	More anxiety in AA patients than controls	35[3]
Altinöz et al. (49)	Turkey	September 2011–October 2012	30	50	33.3 (8.9)	NR	30 urticaria, 39 healthy controls	HADS	More anxiety in AA patients than healthy controls. No difference with urticarial.	40[3]
Annagur et al. (50)	Turkey	NR	73	65.75	27.66 (7.79)	100% AA	78 healthy controls	SCL-90	No difference in symptoms of anxiety	35[3]
Atış et al. (19)	Turkey	NR	39	59	33.5 (11.6)	NR	46 vitiligo, 46 healthy controls	HADS	AA more anxiety than healthy controls. No difference with vitiligo.	20[3]
Baghestani et al. (51)	Iran	NR	68	72	35.4 (7.6)	100% AA	68 healthy controls	HAM-A	AA more symptoms of anxiety than healthy controls	60[3]
Bain et al. (52)	UK	NR	39	23.07	43.15 (12.43)	NR	23 PsA; 26 healthy controls	HADS[2]	More anxiety in less severe AA and shorter disease duration	30[3]
Balieva et al. (53)	13 European countries	November 2011–February 2013	33	33.3	42.8 (14.1)	NR	1,359 healthy controls	EQ-5D-3L	AA 4 times higher chance of anxiety/depression than controls	65[3]
Brajac et al. (54)	Croatia	1995–1999	45	37.78	40.24 (13.01)	100% AA	45 benign scalp lesions	STAI	AA more symptoms of anxiety than healthy controls	60[3]
Bukharia et al. (55)	India	NR	100	48	54% 15–30 years, 46% 31–50 years	NR	100 TE, 100 healthy controls	HAM-A	36.84% of AA and 43.94% of TE heightened anxiety	45[3]
Cakirca et al. (56)	Turkey	March–December 2017	33	75.8	26.33 (6.08)	NR	33 healthy controls	HADS	AA more symptoms of anxiety than healthy controls	30[3]
Colon et al. (57)	USA	April 1985–October 1987	31	29	35.70 (10.23)	74% AA, 23% AT, 42% AU[1]	No	DIS	Lifetime prevalence generalized anxiety disorder 39%, specific phobia 23%, panic disorder 13%	33.33[4]
Conic et al. (58)	USA	2005–2014	584	31.5	35.54 (19.28)	94.7% AA, 2.05% AT, 3.25% AU	172 SD	Diagnoses in patient file	No difference with SD. 13.70% of AA has any diagnosis of anxiety	35[3]
Cordan Yazici et al. (59)	Turkey	NR	43	60.5	33.80 (10.02)	95.35% AA, 4.65% AT	53 healthy controls	HADS	No significant differences between AA and controls	25[3]
Devar (60)	India	NR	30	100	NR	NR	30 TV, 30 healthy controls	TMAS	AA more symptoms of anxiety than healthy controls, no difference with TV	50[3]
Endo et al. (61)	Japan	June 2009–August 2010	122	33.1	38.3 (16.5)	NR	No	STAI	Anxiety not related to disease severity and disease duration	56.25[5]
Gallo et al. (77)	Italy	NR	16	37.5	45.95 (13.25)	NR	No	BSI	AA more symptoms of anxiety than norm group	39.29[6]
Güleç et al. (62)	Turkey	March 2001–January 2002	52	65.38	31.53 (12.61)	94.23% AA, 3.65% AU, 1.92% AT	52 healthy controls	BAI	No differences AA and controls	25[3]

(continued)

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TABLE 1 (continued)

References	Country	Year	*N*	% male	Age (*M*, SD)	% AA, AT, AU	Controls	Measures	Conclusions	Quality score (%)
Karia et al. (17)	India	NR	50	60.0	27.76 (NR)	NR	50 psoriasis, 50 healthy controls	DSM-IV-TR diagnosis	4% of AA any anxiety disorder diagnoses. More often than healthy controls, less often than psoriasis.	60[3]
Kim et al. (13)	South Korea	2002–2013	7,706	51.9	54.6% 20–39, 39.4% 40–59, 6.1% 60+	NR	30,824 without AA	ICD-10 codes	AA higher risk of anxiety disorder diagnosis than controls	65[3]
Kose et al. (63)	Turkey	NR	18	100	21.3 (NR)	NR	No	STAI	Positive correlation between anxiety and depression or hopelessness	50.00[7]
Macbeth et al. (64)	UK	January 2009–December 2018	5,435	45.9	38.93 (14.35)	NR	21,470 healthy controls	Diagnoses in patient file	3.24% of AA and 0.24% of healthy controls had anxiety disorder diagnoses	80[3]
Rajoo et al. (65)	Australia	NR	83	NR	40.95 (13.24)	NR	No	DASS-21	66.3% reported extreme symptoms of anxiety	54.17[4]
Ruiz-Doblado et al. (66)	Spain	NR	32	15	NR	NR	No	SCAN	22.2% diagnosis generalized anxiety disorder, 7.4% social phobia	37.5[4]
Russo et al. (67)	Italy	September 2016–September 2017	27	33.3	37.55 (10.37)	NR	80 AGA, 36 TE	STAI; SPS	No differences in trait anxiety or social anxiety. AA less social phobias than AGA and TE	50[3]
Şahiner et al. (68)	Turkey	August 2009–July 2010	41	49	32.9 (10.5)	NR	30 psoriasis, 50 healthy controls	BAI	AA more symptoms of anxiety than healthy controls, no difference with psoriasis	20[3]
Sayar et al. (69)	Turkey	NR	31	100	23.8 (2.5)	NR	40 healthy controls	STAI	AA more state and trait anxiety	55[3]
Sellami et al. (70)	Tunisia	March–July 2010	50	48	32.92 (11.81)	NR	50 healthy controls	HADS	AA more symptoms of anxiety than healthy controls	45[3]
Senna et al. (71)	USA	January 2011–December 2018	68,121	39	40.3 (17.8)	98.1% AA, 1.3% AT, 0.6% AU	No	ICD-9 and ICD-10 codes	8.4% had an anxiety disorder	45.83[4]
Sorour et al. (14)	Egypt	NR	208	58.65	NR	NR	1,042 dermatology patients	DSM-5 interview	19.71% of AA had anxiety diagnosis, no effect of gender. No difference with psoriasis. Less symptoms than acne, vitiligo, urticaria, and atopic dermatitis.	55[3]
Tan et al. (72)	China	December 2012–August 2013	168	50	34.5 (11.5)	88.1% AA, 11.9% AT/AU	100 healthy controls	SCL-90-R	AA more symptoms of anxiety and phobic anxiety than controls	41.67[5]
Titeca et al. (22)	13 European countries	37	NR	NR	NR	NR	1,359 healthy controls, 20 AGA	HADS	AA more symptoms of anxiety than healthy controls and AGA	70[3]
Tzur Bitan et al. (15)	Israel	2018	41,055	62.9	39.97 (13.61)	NR	41,055 healthy controls	ICD-9 codes	AA higher risk of anxiety disorder than controls	80[3]
Willemsen et al. (73)	Belgium	September 2006–August 2009	21	24	41.95 (13.79)	33% patchy AA, 14% ophiasis, 29% AT, 24% AU	No	SCL-90	AA more symptoms of anxiety than norm group	54.17[7]

(continued)

10.3389/fmed.2022.1054898

TABLE 1 (continued)

References	Country	Year	*N*	% male	Age (*M*, SD)	% AA, AT, AU	Controls	Measures	Conclusions	Quality score (%)
Willemsen et al. (74)	Belgium	April 1999–April 2004	28	35.71	33.4	21.43% AA, 21.43% ophiasis, 28.57% AU, 3.57% AT	No	SCL-90	AA more symptoms of anxiety than norm group	50.00[7]
Yoon et al. (75)	South Korea	January 2015–February 2016	1,203	52.12	39.45 (12.21)	NR	No	BAI	10.1% symptoms of anxiety, 4.2% severe symptoms of anxiety	41.67[4]
Yu et al. (76)	China	October 2013–December 2014	130	41.5	31.78 (10.34)	NR	212 AGA	S-AS	No significant differences	70[3]

AA, alopecia areata; AGA, alopecia androgenetica; AU, alopecia universalis; AT, alopecia totalis; NR, not reported; PsA, psoriatic arthritis; SD, seborrheic dermatitis; TE, telogen effluvium; TV, tinea versicolor.
[1]Some patients had multiple episodes, with different forms of alopecia. Hence, the total is higher than 100%.
[2]This questionnaire was not administered to the control group.
[3]As measured by the NIH Quality Assessment of Case-Control studies.
[4]As measured by the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.
[5]As measured by the QAVALS (26).
[6]As measured by the NIH Quality Assessment of Controlled Intervention Studies.
[7]As measured by the NIH Quality Assessment Tool for Before-After (Pre-Post) Studies with no Control Group.

in the amount of symptoms of anxiety between people with AA and healthy controls.

When people with alopecia were compared to people with another (dermatological) condition, studies found that people with AA were diagnosed with an anxiety disorder more often than other hospitalized patients in general (34), but no differences were found for people with vitiligo (33).

One study without a control group (36) found that 19.1% of the adults with alopecia reported heightened symptoms of anxiety or depression. The same study also reported that 34.1% did not experience any symptoms of anxiety or depression. In the other study without a control group 89.0% of people with alopecia reported little to no symptoms of anxiety (38). Around 8% of people with AA reported moderate symptoms of anxiety.

Children

Of the papers investigating anxiety disorders, one study (46) reported that over half of the children had an anxiety disorder. However, this study included only 12 children and used the DSM-III-R, which was published in 1987. Two other studies reported that 7.1–16% had a generalized anxiety disorder, 7.1–8% had a separation anxiety disorder and 28.6% had a specific phobia (40, 44). However, none of the studies specified the number of patients with more than one anxiety disorder. It remains unclear from this data how many children with AA are diagnosed with an anxiety disorder. In a study by Altunisik et al. (39), 51.8% of the children was diagnosed with at least one anxiety disorder. This did not differ significantly from children with another dermatological condition.

When looking at symptoms of anxiety, studies comparing children with AA to healthy controls found mixed results. On the one hand, Bilgiç et al. (41) reported more state and trait anxiety in children aged 8–12 with AA. They did not find any differences for adolescents aged 12–18. On the other hand, Díaz-Atienza et al. (42) did not find significant differences when comparing children with AA to their siblings. Erdoğan et al. (43) found no difference on the Beck Anxiety Inventory (BAI), but found more child-reported separation anxiety and total anxiety and parent-reported panic disorder and total anxiety than healthy controls on the Revised Child Anxiety and Depression Scales (RCADS).

Studies comparing children with AA to children with other (dermatological) conditions found no differences in symptoms of anxiety when comparing to other dermatological conditions (39), epilepsy (42) and vitiligo (43). Liakopoulou et al. (45) found that children scored higher on worry, oversensitivity, and concentration than other patients.

Adults

Eight papers studied the prevalence of anxiety disorders in adults with AA (n = 86,014). These studies reported point prevalence rates of 3.24% (64), 4% (17), 8.4% (71), and 13.70% (58). Several papers also reported that people with AA have

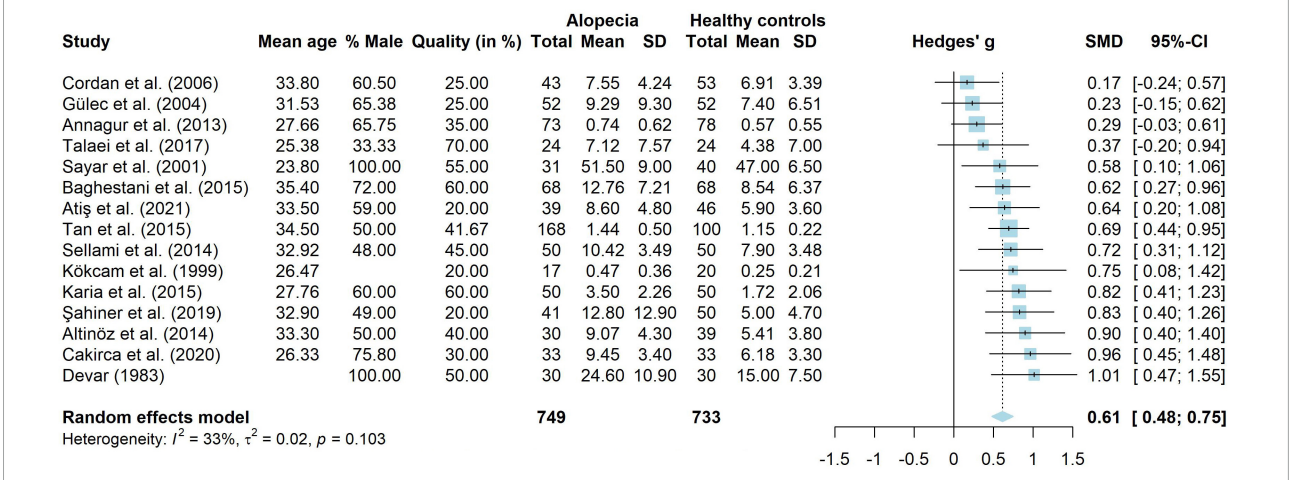

FIGURE 2
Forest plot for symptoms of anxiety in adults with alopecia compared to healthy controls.

a higher chance of being diagnosed with an anxiety disorder in comparison to healthy controls (13, 15, 17, 64). Prevalence rates of specific anxiety disorders in people with AA range from 7.4% for specific phobias and 22.2–39% for generalized anxiety disorders (57, 66). The lifetime prevalence of specific phobia and panic disorder was estimated at 23 and 13%, respectively (57).

When looking at symptoms of anxiety, 15 studies compared people with AA (n = 749) to healthy controls (n = 733). These results were combined in a meta-analysis, shown in **Figure 2**. The results showed that adults with AA reported significantly more symptoms of anxiety than people without AA (g = 0.61, 95% CI [0.48, 0.75], p < 0.001), with a medium to large effect. There was little heterogeneity (I^2 = 33.1%, 95% CI [<0.01, 64.0], τ^2 = 0.02, 95% CI [<0.01, 0.12]) and visual inspection of the funnel plot showed no indication for publication bias. Egger's test also did not show indications for a publication bias [$t(13)$ = 0.94, p = 0.363]. Thirteen studies without missing data were included in a meta-regression. The model did not explain any variance in the effect sizes (R^2 = <0.01%), with a residual heterogeneity of I^2 = 46.59%. Mean age (g = 0.01, p = 0.802, 95% CI [−0.04 to 0.05]), percentage male (g = <−0.01, p = 0.858, 95% CI [−0.01 to 0.01]) and quality score (g = <0.01, p = 0.583, 95% CI [<−0.01 to 0.01]) did not influence study effect sizes.

Studies comparing people with AA to people with other (dermatological) conditions showed mixed results. For the majority of studies, no significant differences were found. For instance, no differences were found when comparing to people with chronic urticaria (49), vitiligo (19, 17), seborrheic dermatitis (58), tinea versicolor (60), alopecia androgenetica and telogen effluvium (67), and psoriasis (68, 14). A smaller number of studies reported that adults with AA experienced more symptoms of anxiety than patients with benign skin lesions (54) and alopecia androgenetica (22, 76), but less than people with psoriasis (17), acne, vitiligo, chronic urticaria, and atopic dermatitis (14).

Three studies compared adults with AA (n = 61) to a norm group. These studies all reported more symptoms of anxiety in adults with AA (73, 74, 77).

Depression

The results for depression are shown in **Table 2**.

Children and adults

In terms of diagnoses of depression, 4.3% of the visits to a psychologist by people with AA were related to depression (79). The point prevalence varied from 2.9% (37) to 3.98% (81). Different studies reported that people with AA were diagnosed with depressive disorders (37, 84) and mood disorders in general (34) significantly more often than healthy controls.

When looking at depressive symptoms, results concerning comparisons to healthy controls are mixed. Two studies, with a combined sample size of 60, reported more depressive symptoms in people with AA (32, 33), while one study did not find any significant differences (n = 24) (35).

Two studies compared people with AA to people with another (dermatological) condition. They did not find significant differences concerning the amount of depressive symptoms when comparing to people with psoriasis or vitiligo (78) or people with acne vulgaris, psoriasis or vitiligo (80).

Four studies (n = 657) did not use a control group. They found little to no depressive symptoms in 31.5% (82), 33.3% (38), and 34.1% (36) of people with AA. According to these studies around 60–65% of people with AA experience at least moderate depressive symptoms.

TABLE 2 Results for depression.

References	Country	Year	*N*	% male	Age (*M*, SD)	% AA, AT, AU	Controls	Measures	Conclusions	Quality score (%)
Pediatric and adult samples										
Ataseven et al. (32)	Turkey	NR	43	72.1	23.42 (11.41)	NR	30 healthy controls	HAM-D; CDI	More symptoms of depression in AA compared to controls	30[1]
Chu et al. (37)	Taiwan	2000–2009	5,117	49.2	NR	NR	20,468 healthy controls	ICD-9 codes	2.9% AA has depression diagnosis, more often than controls	80[1]
Ghajarzadeh et al. (78)	Iran	January 2009–January 2010	100	69	23.02 (33.4)	NR	100 psoriasis, 100 vitiligo	BDI	No difference AA and psoriasis/vitiligo	55[1]
Gutierrez et al. (79)	USA	2006–2016	2,298,432 visits to dermatologist	35	37.8 (18.04)	NR	No	ICD-9 and ICD-10 codes	4.3% of the visits was related to depression	58.33[2]
Jagtiani et al. (80)	India	NR	38	65.8	25.79 (8.82)	NR	80 AV, 56 psoriasis	BDI	AA not significantly different from patients with acne vulgaris or psoriasis	55[1]
Kökcam et al. (33)	Turkey	NR	17	NR	26.47 (12.2)	NR	11 vitiligo, 20 healthy controls	SCL-90-R; ZSDS	AA more symptoms of depression than healthy controls, no difference with vitiligo	20[1]
Laitinen et al. (81)	Finland	1987–2016	176	25	29.7 (NR)	NR	No	ICD-9 and ICD-10 codes	3.98% was diagnosed with depression	54.17[2]
Layegh et al. (82)	Iran	October 2005–May 2006	73	NR	NR	NR	78 AV, 62 psoriasis, 87 vitiligo	BDI	31.51% minor depression, 23.29% mild depression, 24.66% moderate depression, 20.55% severe depression	55[1]
Liu et al. (83)	USA	NR	91 children, 292 adults	Child: 34.4%, adult: 27.9%	Child: 10 (2.92), adult: 41 (15.3)	NR	No	PHQ-9	On average mild symptoms of depression in children and adults	20.83[2]
Marahatta et al. (38)	Nepal	August 2015–July 2016	75	53.3	29.40 (9.90)	NR	No	BDI	66.7% depressive complaints. No relation to disease severity.	45.83[2]
Singam et al. (34)	USA	2002–2012	5,605 hospitalized patients	38.3	42.2 (NR)	NR	Hospitalized patients without AA (N unknown)	ICD-9 codes	AA more mood disorders than controls	45[1]
Talaei et al. (35)	Iran	April–July 2005	24	33.33	25.38 (8.32)	NR	24 healthy controls	SCL-90-R	No difference AA and controls	70[1]
Vallerand et al. (84)	GB	NR	6,861	43.9	32.20 (13.50)	NR	6,137,342 healthy controls	Read codes	AA higher chance of depression than controls	60[1]
Vélez-Muñiz et al. (36)	Mexico	March 2017–February 2018	32 children, 94 adults	41	NR	92.9% patchy AA, 3.2% AT, 1.6% ophiasis, 1.6% AU	No	DSRS-C; HADS	Children: 6.3% symptoms of depression. Adults: 19.1% subclinical depression or anxiety, 34.1% no symptoms of anxiety or depression.	50[2]
Pediatric samples										
Altunisik et al. (39)	Turkey	NR	27	29.6	11.9 (3.3)	85.19% AA, 14.81% AU	30 dermatology patients	K-SADS-PL; CDI	No difference AA and controls. 14.8% symptoms of depression.	65[1]
Andreoli et al. (40)	Italy	1997–2000	176	NR	NR	NR	No	Diagnosis by psychologist	10% dysthymia	25[2]

(continued)

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TABLE 2 (continued)

References	Country	Year	*N*	% male	Age (*M*, SD)	% AA, AT, AU	Controls	Measures	Conclusions	Quality score (%)
Bilgiç et al. (41)	Turkey	NR	74	55.41	12.1 (2.8)	NR	65 healthy controls	CDI	AA more symptoms of depression than controls	65[1]
Conic et al. (85)	USA	2019	3,510	44.7	26.2% <10 years, 73.8% 10–18 years	NR	8,310,710 patients without AA	Diagnoses in patient file	AA diagnosed with depression (2.6%) more often than controls (0.6%)	10[1]
Díaz-Atienza and Gurpegui (42)	Spain	NR	31	52	12.2 (3.8)	51.61% AA, 48.39% AU/AT	23 epilepsy, 25 siblings	CDI	No differences AA and epilepsy or siblings	65[1]
Erdoğan and Gür (43)	Turkey	October 2018–December 2019	31	54.83	12.54 (3.56)	100% AA	29 vitiligo, 30 healthy controls	RCADS-C; RCADS-P	AA more depression than healthy controls, no difference vitiligo	60[1]
Ghanizadeh (44)	Iran	August 2004–November 2006	14	NR	11.66 (6.08)	NR	No	K-SADS-PL	50% has diagnosis of depression	50[2]
Liakopoulou et al. (45)	Greece	NR	33	30.3	10.5 (0.3)	NR	30 patients from pediatrician	CDI	No difference AA and controls	40[1]
Reeve et al. (46)	USA	NR	12	NR	11.5 (2.9)	NR	No	DICA-R; CDS	No heightened group average	37.5[2]
Adult samples										
Aghaei et al. (47)	Iran	NR	40	44.8	35.2 (9.2)	NR	40 healthy controls	BDI	AA more symptoms of depression than controls	35[1]
Alfani et al. (48)	Italy	November 2009–October 2010	73	45.2	25.2 (9.2)	61.7% AA, 26.0% AT, 12.3% AU	73 healthy controls	MMPI-2	AA patients score above cut-off for depre ssion more often than controls	35[1]
Altinöz et al. (49)	Turkey	September 2011–October 2012	30	50	33.3 (8.9)	NR	30 urticaria, 39 healthy controls	HADS	AA more symptoms of depression than healthy controls. No difference with urticaria.	40[1]
Annagur et al. (50)	Turkey	NR	73	65.75	27.66 (7.79)	100% AA	78 healthy controls	SCL-90	AA more symptoms of depression than controls	35[1]
Atış et al. (19)	Turkey	NR	39	59	33.5 (11.6)	NR	46 vitiligo, 46 healthy controls	HADS	No differences between AA, vitiligo and healthy controls	20[1]
Baghestani et al. (51)	Iran	NR	68	72	35.4 (7.6)	100% AA	68 healthy controls	HAM-D	AA more symptoms of depression than controls (OR = 4.48)	60[1]
Bain et al. (52)	UK	NR	39	23.07	43.15 (12.43)	NR	23 PsA; 26 healthy controls	HADS*	Depressive symptoms in 18%. Less severe symptoms with higher SALT scores.	30[1]
Balieva et al. (53)	13 European countries	November 2011–February 2013	33	33.3	42.8 (14.1)	NR	1,359 healthy controls	EQ-5D-3L	AA 4 times higher chance of anxiety/depression than controls	65[1]
Bashir et al. (54)	Pakistan	January–March 2007	3	NR	NR	NR	No	GHQ-12; interview	1 person was diagnosed with depression	41.67[2]
Bukharia and Jain (55)	India	NR	100	48	54% 15–30 years, 46% 31–50 years	NR	100 TE, 100 healthy controls	HAM-D	23.68% AA and 33.33% TE with symptoms of depression	45[2]
Cakirca et al. (56)	Turkey	March–December 2017	33	75.8	26.33 (6.08)	NR	33 healthy controls	HADS	AA more depressive symptoms than controls	30[1]

(continued)

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TABLE 2 (continued)

References	Country	Year	*N*	% male	Age (*M*, SD)	% AA, AT, AU	Controls	Measures	Conclusions	Quality score (%)
Colon et al. (57)	USA	April 1985–October 1987	31	29	35.70 (10.23)	74% AA, 23% AT, 42% AU[3]	No	DIS	Lifetime prevalence depression 39%, dysthymia 16%	33.33[2]
Conic et al. (58)	USA	2005–2014	584	31.5	35.54 (19.28)	94.7% AA, 2.05% AT, 3.25% AU	172 SD	Diagnoses in patient file	No difference with control group	35[1]
Cordan Yazici et al. (59)	Turkey	NR	43	60.5	33.80 (10.02)	95.35% AA, 4.65% AT	53 healthy controls	HADS	No difference with controls	25[1]
Dai et al. (90)	Taiwan	NR	2,123	44.8	31.39 (9.02)	NR	2,298 siblings, 9,192 healthy controls	ICD-9 codes	7.87% of AA with MDD diagnoses, 8.22 times higher chance than healthy control. A total of 2.55 higher chance than siblings.	85[1]
Devar (60)	India	NR	30	100	NR	NR	30 TV, 30 healthy controls	BDI	AA more symptoms of depression than healthy controls, no difference with TV	50[1]
Endo et al. (61)	Japan	June 2009–August 2010	122	33.1	38.3 (16.5)	NR	No	CES-D	AA more symptoms of depression than norm group	56.25[4]
Gallo et al. (77)	Italy	NR	16	37.5	45.95 (13.25)	NR	No	BSI	AA more symptoms of depression than norm group	39.29[5]
Güleç et al. (62)	Turkey	March 2001–January 2002	52	65.38	31.53 (12.61)	94.23% AA, 3.65% AU, 1.92% AT	52 healthy controls	BDI	No differences between AA and controls	25[1]
Gupta and Gupta (16)	USA	NR	45	24.44	44.7 (11.6)	NR	72 AV, 146 AD, 217 psoriasis	CRSD	AA less depressive symptoms than AV and psoriasis, no difference with AD	15[1]
Karia et al. (17)	India	NR	50	66.00	27.76 (NR)	NR	50 psoriasis, 50 healthy controls	DSM-IV-TR diagnosis	18% AA depression diagnoses. More often than healthy controls, less often than psoriasis.	60[1]
Kim et al. (13)	South Korea	2002–2013	7,706	51.9	54.6% 20–39, 39.4% 40–59, 6.1% 60+	NR	30,824 people without AA	ICD-10 codes	AA higher chance of depression than controls	65[1]
Kose et al. (63)	Turkey	NR	18	100	21.3 (NR)	NR	No	BDI	On average subclinical depressive symptoms	50.00[6]
Macbeth et al. (64)	UK	January 2009–December 2018	5,435	45.9	38.93 (14.35)	NR	21,470 healthy controls	Diagnoses in patient file	AA higher chance of depression than controls	80[1]
Mirza et al. (87)	USA	2002–2012	138	0	NR	NR	No	Diagnoses in patient file	21.74% has depression diagnosis	58.33[2]
Pascual-Sánchez et al. (88)	Spain	NR	16	0	45.1 (NR)	100% AU	No	BDI	On average subclinical depressive symptoms	29.17[6]
Rajoo et al. (65)	Australia	NR	83	NR	40.95 (13.24)	NR	No	DASS-21	47.0% reported extreme depressive symptoms	54.17[2]
Ruiz-Doblado et al. (66)	Spain	NR	32	15	NR	NR	No	SCAN	7.4% depression diagnosis, 7.4% previously diagnosed, but currently free of symptoms	37.5[2]

(continued)

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TABLE 2 (continued)

References	Country	Year	*N*	% male	Age (*M*, SD)	% AA, AT, AU	Controls	Measures	Conclusions	Quality score (%)
Şahiner et al. (68)	Turkey	August 2009–July 2010	41	49	32.9 (10.5)	NR	30 psoriasis, 50 healthy controls	BDI	AA more depressive symptoms than healthy controls, no difference with psoriasis	20[1]
Sayar et al. (69)	Turkey	NR	31	100	23.8 (2.5)	NR	40 healthy controls	BDI	AA more symptoms of depression than controls	55[1]
Sellami et al. (70)	Tunisia	March–July 2010	50	48	32.92 (11.81)	NR	50 healthy controls	HADS	AA more symptoms of depression than controls	45[1]
Senna et al. (71)	USA	January 2011–December 2018	68,121	39	40.3 (17.8)	98.1% AA, 1.3% AT, 0.6% AU	No	ICD-9 and ICD-10 codes	9.5% had depression diagnosis	45.83[2]
Sorour et al. (14)	Egypt	NR	208	58.65	NR	NR	1,042 dermatology patients	DSM-5 interview	19.71% of AA had diagnosis of depression. 24.33% in psoriasis, 55.34% acne vulgaris, 31.47% vitiligo, 43.64% urticarial, and 43.63% in atopic dermatitis	55[1]
Tan et al. (72)	China	December 2012–August 2013	168	50	34.5 (11.5)	88.1% AA, 11.9% AT/AU	100 healthy controls	SCL-90-R	AA more symptoms of depression than controls	41.67[4]
Titeca et al. (22)	13 European countries	37	NR	NR	NR	NR	1,359 healthy controls, 20 AGA	HADS	AA more symptoms of depression than healthy controls	70[1]
Tzur Bitan et al. (15)	Israel	2018	41,055	62.9	39.97 (13.61)	NR	41,055 healthy controls	ICD-9 codes	AA diagnosed with depression more often than controls	80[1]
Willemsen et al. (73)	Belgium	September 2006–August 2009	21	24	41.95 (13.79)	33% patchy AA, 14% ophiasis, 29% AT, 24% AU	No	SCL-90	AA more symptoms of depression than norm group	54.17[6]
Willemsen et al. (74)	Belgium	April 1999–April 2004	28	35.71	33.4 (NR)	21.43% AA, 21.43% ophiasis, 28.57% AU, 3.57% AT	No	SCL-90	AA more symptoms of depression than norm group	50.00[6]
Yoon et al. (75)	South Korea	January 2015–February 2016	1,203	52.12	39.45 (12.21)	NR	No	BDI	40.9% depressive symptoms. Women more often than men, more symptoms with more severe AA.	41.67[2]
Yu et al. (76)	China	October 2013–December 2014	130	41.5	31.78 (10.34)	NR	212 AGA	ZSDS	No differences between AA and AGA	70[1]

*This questionnaire was not administered to the control group.
AD, atopic dermatitis; AGA, alopecia androgenetica; AV, acne vulgaris; PsA, psoriatic arthritis; SD, seborrheic dermatitis; TE, telogen effluvium; TV, tinea versicolor.
[1]As measured by the NIH Quality Assessment of Case-Control studies.
[2]As measured by the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.
[3]Some patients had multiple episodes, with different forms of alopecia. Hence, the total is higher than 100%.
[4]As measured by the QAVALS (26).
[5]As measured by the NIH Quality Assessment of Controlled Intervention Studies.
[6]As measured by the NIH Quality Assessment Tool for Before-After (Pre-Post) Studies with no Control Group.

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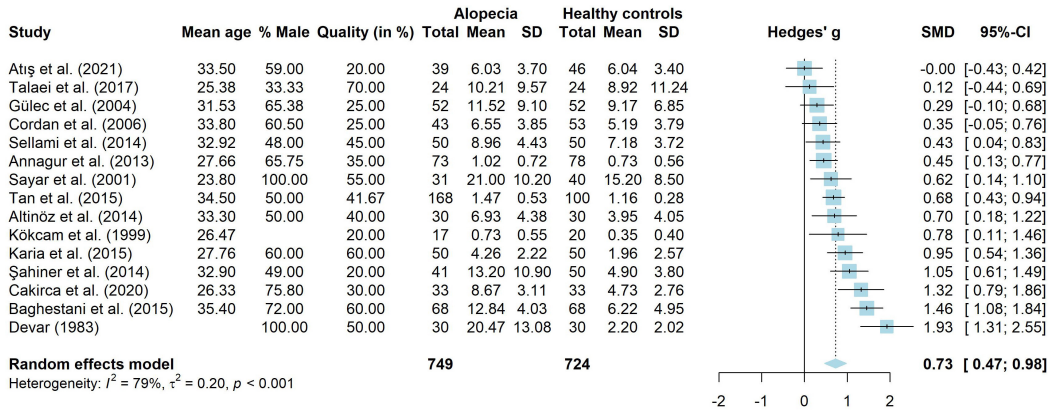

FIGURE 3
Forest plot for symptoms of depression in adults with alopecia compared to healthy controls.

Children

Three studies (n = 3,700) investigated depressive disorders. A small study of 14 children found 50% of the children to be eligible for a diagnosis of depressive disorder (44). Bigger studies reported that 10% of the children were diagnosed with dysthymia (40) and that children with AA were diagnosed with a depressive disorder more often than other patients (85).

Three studies (n = 136) investigated symptoms of depression in comparison to healthy controls. Two studies found more depressive symptoms in children with AA (41, 43), while one study did not find a significant difference when comparing to unaffected siblings (42).

Four studies compared children with AA to children with a different (dermatological) condition. They did not find a difference in depressive symptoms when comparing children with AA to children with other dermatological conditions (39), epilepsy (42), vitiligo (43), and pediatric patients in general (45).

One study with 14 children with AA did not use a control group. This study did not find a heightened group average for depressive symptoms (46).

Adults

Several studies investigated the prevalence of depressive disorders in adults with AA. One study, conducted in the late 1990s, found a lifetime prevalence of 39% for depression and 16% for dysthymia (57). Estimates for point prevalence range from 7.4% (66), 9.5% (71), 18% (17), 21.74% (87) to 55.29% (14). The largest and most recent study found a point prevalence of 9.5% (71). Furthermore, adults with AA have a higher chance of being diagnosed with a depressive disorder than healthy controls (13, 15, 17, 64). One study did not find any difference in the number of diagnoses (58). There were no differences in the number of diagnoses when comparing to adults with psoriasis or vitiligo (17) or seborrheic dermatitis (58).

Fifteen studies compared adults with AA to healthy controls on the amount of depressive symptoms. These studies were analyzed in a meta-analysis. The results are shown in **Figure 3**. A total of 749 adults with AA and 724 healthy controls were analyzed. Adults with AA reported significantly more depressive symptoms than the control group (g = 0.73, 95% CI [0.47, 0.98], p < 0.001), with a medium to large effect. There was considerable heterogeneity (I^2 = 78.5%, 95% CI [65.2, 86.8], τ^2 = 0.20, 95% CI [0.08, 0.62]). Visual inspection of the funnel plot showed no signs of publication bias and Egger's test was not significant [$t(13)$ = 0.80, p = 0.438]. Thirteen studies without missing data were included in a meta-regression. The model explained very little variance in the effect sizes (R^2 = 1.21%) and residual heterogeneity was high (I^2 = 77.27%). Mean age (g = 0.04, p = 0.289, 95% CI [−0.03 to 0.12]), percentage male (g = 0.01, p = 0.168, 95% CI [−0.01 to 0.03]) and quality score (g = 0.01, p = 0.265, 95% CI [−0.01 to 0.03]) did not influence study effect sizes.

Nine studies used a control group of adults with a different (dermatological) condition to assess the amount of depressive symptoms. The vast majority of the studies did not find any significant differences. For instance, no differences were found when comparing to chronic urticaria (49), vitiligo (19), telogen effluvium (55), tinea versicolor (60), atopic dermatitis (16), psoriasis (68), and alopecia androgenetica (22, 76). One study found that adults with AA reported less depressive symptoms than adults with acne vulgaris or psoriasis (16).

Studies without a control group found that people with AA (n = 183) reported more symptoms of depression than a norm group (61, 73, 74, 77). On average, they reported subclinical symptoms (63, 88). Estimates of the prevalence rates of people with depressive symptoms were 47.0% (65) and 40.9% (75).

Quality of life

The results for QoL are shown in **Table 3**.

TABLE 3 Results for quality of life.

References	Country	Year	*N*	% male	Age (*M*, SD)	% AA, AT, AU	Controls	Measures	Conclusions	Quality score (%)
Pediatric and adult samples										
Ghajarzadeh et al. (78)	Iran	January 2009–January 2010	100	69	23.02 (33.4)	NR	100 psoriasis, 100 vitiligo	DLQI; SF-36	AA better QoL than psoriasis. No difference with vitiligo. On average moderate effect on QoL.	55[1]
Liu et al. (83)	USA	NR	91 children, 292 adults	Child: 34.4%; adult: 27.9%	Child: 10 (2.92); adult: 41 (15.3)	NR	No	CDLQI; DLQI; FDLQI	Children, adults, and family members have moderate effect on QoL. Worse QoL related to more depressive symptoms.	20.83[2]
Park et al. (92)	South Korea	NR	40	27.5	30.0% 10–19 years, 17.5% 20–29, 17.5% 30–39, 17.5% 40–49, 17.5% 50+	NR	No	Skindex-29	Symptoms, emotions, and total score very little impairment. Functioning mild impairment	37.5[2]
Vélez-Muñiz et al. (36)	Mexico	March 2017–February 2018	32 children, 94 adults	41	NR	92.9% patchy AA, 3.2% AT, 1.6% ophiasis, 1.6% AU	No	CDLQI; DLQI	Children small impairment on QoL. Adults moderate effect. No differences for gender, disease duration, and disease severity.	50[2]
Pediatric samples										
Bilgiç et al. (41)	Turkey	NR	74	55.41	12.1 (2.8)	NR	65 healthy controls	PedsQL-P; PedsQL-C	Less QoL on child and parent reports. Less psychosocial QoL on parent reports.	65[1]
Erdoğan and Gür (43)	Turkey	October 2018–December 2019	31	54.83	12.54 (3.56)	100% AA	30 healthy controls; 29 vitiligo	CDLQI	AA worse QoL than vitiligo	60[1]
Putterman et al. (93)	USA	April 2017–July 2018	153	43.79	11.0 (4.8)	NR	No	CDLQI; FDLQI; QLCCDQ	On average small effect on child QoL, moderate effect for family members. Worse QoL for more disease severity and worse emotional QoL for higher age.	50[2]
Adult samples										
Abedini et al. (94)	Iran	October 2013–October 2014	176	64.23	31.39 (9.05)	NR	No	DLQI	Patients with mild AA moderate effect on QoL, patients with severe AA very large effect on QoL. Patients with more severe AA reported worse QoL on: symptoms and feelings, daily activities, leisure, personal relationships, work and school, treatment, and the total score.	50[2]
Abideen et al. (95)	India	NR	60	65	33.9 (9.3)	NR	No	DLQI	30% no effect on QoL, 55% small effect, 6.7% moderate effect, 8.3% very large effect	20.83[2]
Al-Mutairi and Eldin (91)	Kuwait	August 2002–July 2009	2,962 (300 for DLQI)	65.02	58.03% between 21 and 40 years	NR	300 healthy controls	DLQI	No difference between males and females or disease duration. Worse QOL for more severe alopecia	40[1]
Andersen et al. (20)	Denmark	NR	1,494	33	51.3 (16.0)	NR	No	DLQI; EQ-5D-5L	75% no effect on QoL. On average small effect.	41.67[2]

(continued)

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TABLE 3 (continued)

References	Country	Year	*N*	% male	Age (*M*, SD)	% AA, AT, AU	Controls	Measures	Conclusions	Quality score (%)
Atış et al. (19)	Turkey	NR	39	59	33.5 (11.6)	NR	46 healthy controls, 46 vitiligo	DLQI	On average moderate effect, no difference with vitiligo	20[1]
Balieva et al. (53)	13 European countries	November 2011–February 2013	33	33.3	42.8 (14.1)	NR	1,359 healthy controls	EQ-5D-3L	No significant difference for mobility, self-care, activity, and pain/discomfort	65[1]
de Hollanda et al. (96)	Brazil	January 2011–October 2012	37	37.84	35.89 (11.59)	NR	49 healthy controls	SF-36	AA score lower on mental health, role emotional and social functioning. No differences for vitality, bodily pain, general health, physical functioning, and role physical.	55[1]
Dubois et al. (97)	France	NR	60	35.00	40.1 (15.2)	NR	Dermatologic conditions and healthy controls from literature	SF-36; Skindex	Lower scores on role-physical, general health, vitality, social functioning, role-emotional, and mental health	41.67[2]
Endo et al. (61)	Japan	June 2009–August 2010	122	33.1	38.3 (16.5)	NR	No	SF-8	Average scores on physical and mental functioning	56.25[3]
Essa et al. (98)	Egypt	January–June 2015	17	NR	NR	NR	500 healthy controls	Skindex-16	No difference AA and dermatological conditions. AA worse QoL than healthy controls.	41.67[3]
Fayed et al. (99)	Egypt	February 2015–January 2016	41	78	26.68 (4.49)	NR	No	DLQI	0% no effect on QoL, 4.9% small effect, 29.3% mild effect, 29.3% moderate effect, 36.6% very large effect	50[4]
Gonul et al. (21)	Turkey	NR	56	55.4	29.34 (8.13)	92.86% AA, 7.14% AT	82 AGA	Hairdex; TQL	AA better QoL than AGA on total, emotions, functions, symptoms, and self-confidence. No difference on stigmatization and TQL.	60[1]
Güleç et al. (62)	Turkey	March 2001–January 2002	52	65.38	31.53 (12.61)	94.23% AA, 3.65% AU, 1.92% AT	52 healthy controls	SF-36	AA worse QoL on vitality and mental health than controls. AA higher QoL than healthy controls on social functioning.	25[1]
Han et al. (100)	USA	August 2018–November 2019	141	26.2	43.3 (15.6)	76.6% AA, 13.5% AU, 9.9% AT	No	AASIS	More stress is related to lower QoL	41.67[2]
Jankovic et al. (101)	Serbia	April 2012–June 2013	60	26.7	37.35 (14.26)	NR	110 psoriasis, 66 AD; 140 OM	DLQI; SF-36; Skindex-29	AA better QoL than psoriasis. Partially better QoL than AD and OM.	41.67[2]
Karia et al. (17)	India	NR	50	66	27.76 (NR)	NR	50 psoriasis, 50 healthy controls	WHOQOL-BREF	AA higher QoL than psoriasis and healthy controls	60[1]
Lai et al. (102)	Australia	NR	36	19.4	41 (14.5)	41.7% patchy, 25.0% AT, 33.3% AU	No	AASIS; aQoL-8D	No difference with norm group	75[5]
Liu et al. (103)	USA	NR	30	53.3	38.00 (21.80)	NR	No	Skindex-16	No difference between males and females	29.17[4]

(continued)

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TABLE 3 (continued)

References	Country	Year	*N*	% male	Age (*M*, SD)	% AA, AT, AU	Controls	Measures	Conclusions	Quality score (%)
Masmoudi et al. (104)	Tunisia	March–July 2010	50	48	32.92 (11.81)	NR	50 healthy controls	SF-36	AA worse scores on mental health, role emotional, social functioning, general health and total mean score. No significant differences for physical functioning, role physical and bodily pain. No relation QoL and disease severity.	55[1]
Nasimi et al. (105)	Iran	August 2017–August 2018	100	65	29.24 (8.31)	NR	No	AA-QLI; DLQI	On average very large effect. Males better QoL than females.	20.83[3]
Nijsten et al. (106)	Italy	NR	46	NR	NR	NR	151 AV; 76 psoriasis, 54 SD; 27 vitiligo; 100 nevi	Skindex-29	17.4% in worst category for total, 21.7% in worst category for emotions	55[1]
Öztürkcan et al. (107)	Turkey	January–February 2004	3	NR	NR	NR	16 CD, 6 psoriasis, 3 urticaria, 16 TP; 35 AV	DLQI	On average small effect	41.67[3]
Qi et al. (108)	China	January 2010–July 2012	698	50	38.8 (12.0)	82.5% patchy, 17.5% AT/AU	No	DLQI	On average moderate effect on QoL	54.17[2]
Reid et al. (109)	USA	March–November 2009	23	0	NR	NR	33 TE, 41 AGA, 7 unknown alopecia	Skindex-16	No differences on QoL for different alopecia types	55[1]
Russo et al. (67)	Italy	September 2016–September 2017	27	33.3	37.55 (10.37)	NR	80 AGA, 36 TE	DLQI	Females worse QoL than men. No differences with AGA or TE.	50[1]
Sampogna et al. (110)	Italy	NR	5	NR	NR	NR	Dermatological conditions	Scalpdex; Skindex-29	Average impact on symptoms, emotions, and functioning	55[1]
Sanclemente et al. (111)	Colombia	NR	11	NR	NR	NR	Dermatological conditions	Skindex-29	Median score indicates moderate effect on total score, symptoms, emotions, and functioning	60[1]
Senna et al. (71)	USA	2019	259	49.4	39.1 (13.6)	NR	No	Skindex-16	Worse QoL for longer disease duration, higher disease severity, and females	41.67[2]
Temel et al. (112)	Turkey	NR	50	46	30.92 (10.92)	84% AA, 6% AT, 10% AU	50 AV; 50 vitiligo	DLQI	On average moderate effect on QoL. No difference with AV or vitiligo.	40[1]
Titeca et al. (22)	13 European countries	37	NR	NR	NR	NR	1,359 healthy controls, 20 AGA	DLQI	Worse QoL than AGA	70[1]
Willemse et al. (113)	Multiple countries	NR	243	11	37.9 (13.0)	NR	No	DLQI	On average no effect on QoL. No differences for gender or disease severity. Worse QoL for shorter disease duration.	54.17[2]
Willemsen et al. (73)	Belgium	September 2006–August 2009	21	24	41.95 (13.79)	33% patchy, 14% ophiasis, 29% AT, 24% AU	No	SF-36; Skindex-17	SF-36: average physical functioning, below average mental functioning in comparison to norm group Skindex: moderate effect on psychosocial functioning, less physical symptoms in comparison to norm group	54.17[4]

(continued)

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TABLE 3 (continued)

References	Country	Year	*N*	% male	Age (*M*, SD)	% AA, AT, AU	Controls	Measures	Conclusions	Quality score (%)
Yoon et al. (75)	South Korea	January 2015–February 2016	1,203	52.12	39.45 (12.21)	NR	No	Skindex-29	30.3% impaired QoL, 9.9% severely impaired QoL. Females worse QoL than men.	41.67[2]
Yu et al. (76)	China	October 2013–December 2014	130	41.5	31.78 (10.34)	NR	212 AGA	DLQI	AA worse QoL than AGA on total, symptoms and feelings, daily activities, and leisure. AA scored higher on treatment. No differences for work and school and personal relationships.	70[1]
Unknown age										
Jun et al. (116)	South Korea	March 2012–February 2017	161	NR	NR	NR	380 AGA	Skindex-29	AA worse scores than AGA on functioning and better scores on symptoms. No differences for emotions and total score.	45[1]
Shi et al. (114)	USA	NR	532	27	50% older than 40	52% AU/AT, 46.6% with 100% hair loss	No	DLQI; Skindex-16	On average moderate effect on QoL. Moderate effect on emotions, symptoms, and functioning	20.83[2]

AD, atopic dermatitis; AGA, alopecia androgenetica; AV, acne vulgaris; CD, contact dermatitis; HS, hidradenitis suppurativa; NF1, neurofibromatosis, type 1; NR, not reported; OM, onychomycosis; SD, seborrheic dermatitis; TE, telogen effluvium; TP, tinea pedis.

[1]As measured by the NIH Quality Assessment of Case-Control studies.

[2]As measured by the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.

[3]As measured by the QAVALS.

[4]As measured by the NIH Quality Assessment Tool for Before-After (Pre-Post) Studies with no Control Group.

[5]As measured by the NIH Quality Assessment of Controlled Intervention Studies.

Children and adults

People with AA reported worse QoL than people with psoriasis, but there was no difference with vitiligo (78). On average, people reported a small (36, 92) or moderate (36, 78, 83) impact on their QoL.

Children

Children with AA reported more impaired QoL than healthy controls (41, 43). In a study without a control group children with AA reported a small effect on their QoL (93).

Adults

Fourteen studies used the Dermatology Life Quality Index (DLQI) to assess disease-specific QoL in 3,978 adults with AA (19, 20, 36, 67, 76, 78, 83, 94, 105, 107, 108, 112–114). These studies were included in a meta-analysis, shown in **Figure 4**. The total scores of the DLQI can be interpreted as follows: 0–1 = no effect on patient's life, 2–5 = small effect, 6–10 = moderate effect, 11–20 = very large effect, 21–30 extremely large effect (115). Results from the meta-analysis showed that people with AA reported a weighted average of 6.67 (95% CI [5.54, 7.81]), which is a moderate effect. However, there was very high heterogeneity amongst studies (I^2 = 98.9%, 95% CI [98.5, 99.0], τ^2 = 4.25, 95% CI [2.07, 12.29], $p < 0.001$). Results should thus be interpreted with extreme caution. Meta-regressions were run on 11 studies without missing data. The model explained 62.89% of the variance in the data, but still included a substantial amount of heterogeneity (I^2 = 89.56%). Mean age was negatively related to DLQI scores ($g = -0.28$, $p = < 0.001$, 95% CI [−0.44 to −0.12]). Studies with a higher mean age had lower DLQI scores and thus less impaired QoL. The same was true for the quality ratings of studies ($g = -0.08$, $p = 0.009$, 95% CI [−0.13 to −0.02]), where studies with a lower quality rating reported higher DLQI levels. The percentage male ($g = -0.04$, $p = 0.200$, 95% CI [−0.11 to 0.02]) was not significantly related to DLQI scores.

As two studies did not provide clear data on their sample and may have included children (78, 114), we conducted a sensitivity analysis to assess whether this influenced the results. Twelve studies (19, 20, 36, 67, 76, 83, 94, 105, 107, 108, 112, 113) with 3,346 people were included. The mean DLQI was unchanged (M = 6.68, 95% CI [5.33, 8.02]) and heterogeneity remained high (I^2 = 98.8%, 95% [98.4, 99.0], τ^2 = 5.14, 95% [2.38, 16.35]).

Five studies compared 188 adults with AA to healthy controls (53, 62, 96, 98, 104). There seemed to be no difference on physical functioning (53, 96, 104). However, adults with AA had more impaired mental (62, 96, 104) and overall (98) functioning.

Thirteen studies compared adults with AA to adults with another (dermatological) diagnosis (17, 20–22, 67, 76, 97, 101, 106, 109–112) and found very mixed results. On the one hand, no differences were found when comparing to adults with vitiligo (20, 112), alopecia androgenetica and telogen effluvium (67) and acne vulgaris (112). On the other hand, people with

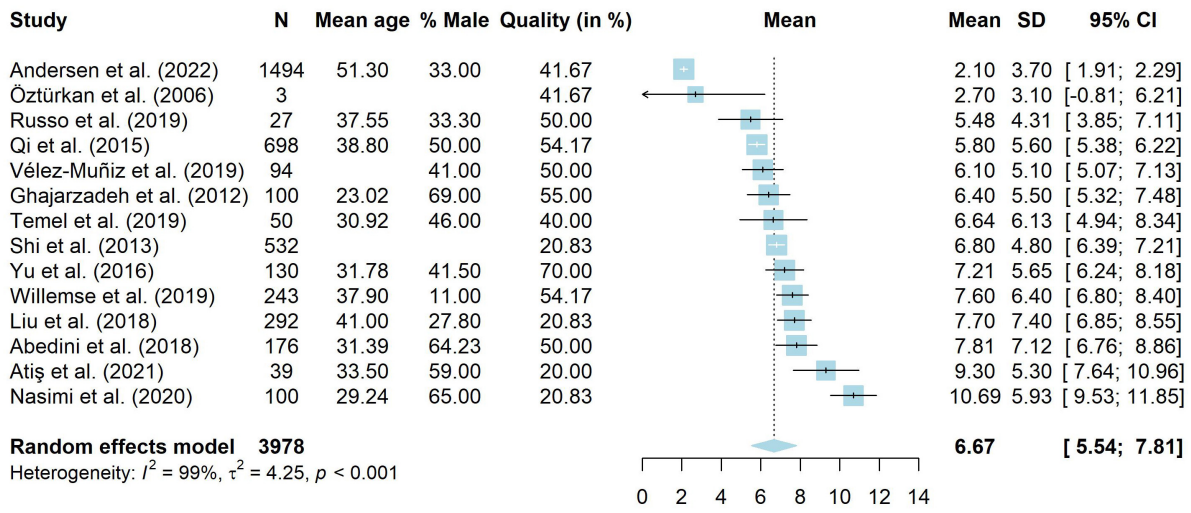

FIGURE 4
Forest plot for mean DLQI scores in adults with alopecia areata.

AA reported better QoL than people with psoriasis (101) or alopecia androgenetica (21). In yet other studies, people with AA reported worse QoL than people with alopecia androgenetica (22, 76).

Unknown samples

Two studies did not report whether they studied children or adults (114, 116). They found a moderate impact on QoL (114). When comparing to alopecia androgenetica, people with AA scored higher on subscales functioning and lower on symptoms (116). No differences were found for emotions and total score.

Discussion

In this systematic review and meta-analysis we aimed to provide an overview of the current literature on anxiety, depression and QoL in people with AA. Results showed that people with AA experienced adverse psychosocial consequences in all three domains. Results also point to more diagnoses of anxiety and depression, as well as more symptoms of anxiety and depression, compared to healthy controls.

Meta-analytic results showed that people with AA experience more symptoms of anxiety and depression than healthy controls. With a medium to large effect for both meta-analyses, we can conclude that this constitutes a clinically relevant effect. Our results were unable to shed light on which patients are at risk for experiencing symptoms of anxiety or depression as average age, percentage male and quality of the studies did not explain variance in the effect sizes. While the same studies were included in both meta-analyses, we found high heterogeneity for depression but not for anxiety. The range for effect sizes is much larger in depression than anxiety, however it is unclear where this originates from.

Meta-analytic results also showed that people with AA experience a moderate impact on their QoL. We were able to include around 3,800 patients in this meta-analysis, which makes it likely that our results generalize to other adults with AA. However, as we found very high heterogeneity, the moderate impact of AA on QoL is unlikely to be true for everyone with AA. Subgroups may exist based on variables that were not studied in the current meta-analysis, such as severity of disease, medication use, duration of disease or other variables.

Results concerning people with AA compared to people with other dermatological diagnoses were mixed for anxiety, depression, and QoL. However, the majority of the studies seems to point to people with AA experiencing the same amount of anxiety, depression, and impairment of QoL as people with other diagnoses. So, even though patients with AA do not experience physical symptoms that people with other dermatological diagnoses may experience, such as pain or itching (117), their QoL is comparable.

While we did not directly compare age groups, some observations can be noted. Firstly, for all three domains more studies were included for adults than for children. Hence, conclusions for adults can be made with more certainty. Both for anxiety and depression results of children with AA compared to healthy controls were mixed, while results for adults showed that adults with AA experienced more symptoms of anxiety and depression than healthy controls. As the mean age of the studies with children was 11.85, it is possible that symptoms of anxiety do not develop before puberty or adulthood, when appearance and peer relations become more important. This is corroborated by other studies showing more appearance-related

distress in puberty (118). For QoL only three studies were found for children, so direct comparisons are hard to make.

Overall, our results are in line with a previous meta-analysis finding positive associations between AA and experiencing (symptoms of) anxiety or depression (12). In addition, we have shown that adults with AA experience more symptoms of anxiety and depression than healthy controls. Our results concerning QoL are also in line with Toussi et al. (23), who found diminished QoL in children and adults with AA. More specifically, we found diminished QoL in mental wellbeing but not necessarily in physical wellbeing. This is slightly unsurprising, as AA is associated with little physical impairment. Despite this, qualitative studies have shown that losing one's hair has a considerable impact on mental health (7, 8).

It is also noteworthy that many studies included patients that were referred to a dermatologist. This could introduce a selection bias, where those who experience less psychological complaints are less likely to visit a dermatologist. However, large studies on primary care databases also reiterate that patients with alopecia are diagnosed with anxiety and depression more often than patients without alopecia (64, 84), with a diagnosis of depression preceding the diagnosis of AA for some patients (84).

This systematic review also has some strengths and limitations. A particular strength is the thorough literature search conducted. A formal search was created by a librarian, yielding 1,249 unique records. With this thorough search it is highly likely that no relevant articles were missed in the search process.

Despite the thorough literature search, we could only include a limited amount of studies in a quantitative analysis. For instance, we did not have enough data to disentangle psychological wellbeing in separate forms of AA (i.e., areata, universalis, or totalis) or how psychological wellbeing was related to disease severity or disease duration. Another limitation is that the included studies did not look at the remitting and relapsing course of AA specifically. Most studies were cross-sectional and longitudinal studies were often designed to look at a medical or psychological intervention. Qualitative research has highlighted that the unpredictable nature of AA can lead to feelings of anger or stress (119), but this has not been studied quantitatively. Hence, it remains unclear how the remitting and relapsing course of AA influences psychological wellbeing. A third limitation is that the included studies did not provide data on medication use. Inclusion criteria were often unclear when it came to participants' medication use and medication use was often omitted from reporting in the outcome data. We do know that medical treatments often fail to provide sustained hair regrowth and may lead to substantial side effects (3). Hence, it remains unclear whether the pros of medication use outweigh the cons.

Another limitation is that the goal of the included studies did not always line up with the goal of the current systematic review. For instance, this review also included questionnaire validation studies (107) and baseline data of randomized controlled trials (88). The data was therefore approached in a different manner than the original authors intended. This may impede the strength of the current conclusions. However, as the intention of this review was to provide a thorough overview of the current literature, minimal limitations were set for the inclusion of different types of papers.

Based on these limitations, future studies should aim to study AA longitudinally and investigate the influence of disease severity, disease duration, disease status (inactive, remission, or relapse) and medication use on psychological wellbeing. These results would provide useful insights on potential at-risk groups in need of referral to psychological care.

The results of the current study highlight the impact of AA on psychological wellbeing. Clinicians treating people with AA should therefore be aware of the impact and refer to psychological care if needed. This could be accomplished through regular screening, for instance as part of value-based healthcare (120), or through the physician checking in on people's mental health during outpatient clinic appointments.

Conclusion

In summary, we have shown that living with AA has important consequences for psychological wellbeing. People with AA experienced worse psychological outcomes than healthy controls and comparable psychological outcomes compared to people with other dermatological diagnoses. Important challenges lay ahead on how to treat AA, both psychologically as well as medically.

Data availability statement

The datasets analyzed as well as analysis scripts for this study can be found on the Open Science Framework (OSF): https://osf.io/fxt7p/.

Author contributions

MD: conceptualization, methodology, formal analysis, writing—original draft, visualization, and project administration. KM: formal analysis and writing—review and editing. JK-O, JO, and SP: writing—review and editing. All authors contributed to the article and approved the submitted version.

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Conflict of interest

Author JK-O is a board member of the Dutch Alopecia Association (volunteer position).

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.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2022.1054898/full#supplementary-material

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In or out?—Suggested criteria to systematically offer different treatment options to patients with body dysmorphic disorder

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body dysmorphic disorder, psychotherapy, inpatient treatment, outpatient treatment, differential indication

Introduction

Body dysmorphic disorder (BDD) is a highly complex mental disorder, which is characterized by preoccupation with one more perceived flaw in the individual's appearance. It often results in repetitive behavior strategies to hide, check, or alter these flaws causing massive distress and impairment as well as low quality of life (1). Recent studies confirm that prevalence among dermatological patients is higher than in the general public (2) with 10.5 vs. 2.1% (3), suggesting that especially patients suffering from hyperhidrosis, alopecia, and vitiligo are vulnerable to BDD. Patients often worry about facial issues such as skin and hair, which are omnipresent to others. It often goes along with high degrees of external shame as well as internal shame, fearing not to fulfill one's individual standards and ideals. BDD is often associated with a wide range of comorbidities such as depression, social anxiety, obsessive compulsive disorder (OCD), and substance use disorder. Besides these, there are comorbid personality disorders such as avoidant personality disorder (4). BDD results in poorer social adjustment, relationships, problems, and occupational functioning (5). Very concerning aspects of BDD are high rates of suicidality (6) and self-manipulation, such as skin-picking behavior and self-mutilation. These post a special challenge on treatment and patient and physician/therapist relationship.

Psychotherapeutic treatment

There is sound evidence that cognitive behavioral therapy (CBT), besides pharmacological therapy with high-dose selective serotonin reuptake inhibitors (SSRIs), is the first line of treatment showing good effects in symptom reduction (7). Besides these promising results, there is rather limited data on long-term therapy effects (8), suggesting that many patients stay symptomatic and still show risk factors. There has been little research so far on which treatment setting is most suitable and profitable

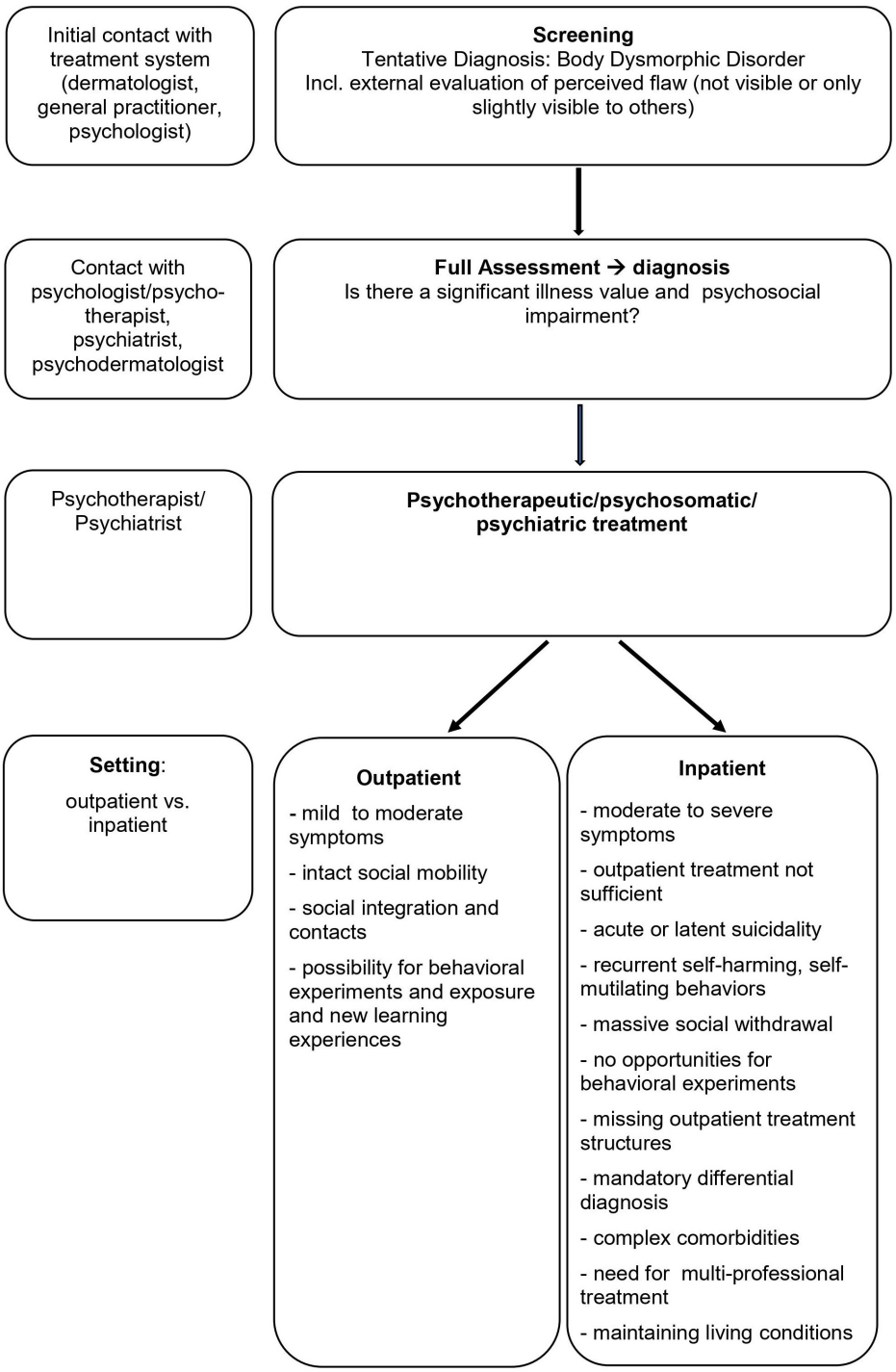

FIGURE 1
Criteria for outpatient vs. inpatient treatment.

for patients (9). This is partly due to a lack of specialized treatment options such as outpatient centers and specialized clinics. Nevertheless, many aspects of severe BDD symptoms suggest that solely outpatient counseling or therapy might sometimes not be enough to properly tackle BDD and that therapy requires a structured decision process. In addition to outpatient therapy, specialized inpatient therapy can provide a more intense and secure therapy process including group therapies together with other BDD patients, movement and art therapy as well as the possibility to incorporate further medical

investigations and pharmacological co-treatment. Furthermore, it can also provide a helpful therapeutic community helping to address shame and reduce social withdrawal. As many BDD patients see dermatologists first before possibly moving on to psychotherapy, dermatologists often obtain a special role and responsibility in evaluating which kind of treatment might be most suitable for their patients. Possible screening tools for the dermatological practice are the Body Dysmorphic Disorder Questionnaire (BDDQ) (2) or its dermatological version BDDQ-DV, as well as the Dysmorphic Concern Questionnaire (DCQ) (10).

Criteria for in- and outpatient treatment

The following model (**Figure 1**) incorporates the first criteria that could be helpful in making the decision and whether in- or outpatient psychotherapy would be preferable and describes a possible process of how to come to this decision.

Besides relying solely on symptom severity it might be helpful to take a closer look at aspects that facilitate or hinder therapy processes. Massive social avoidance and isolation may be a factor that enormously obstructs outpatient treatment, leading to a situation where core treatment elements such as behavioral experiments and exposure as well as mirror confrontations, etc., may not be possible. Furthermore, complex symptomatology and complex comorbidities (e.g., personality disorders) that require specific differential diagnosis or a multi-professional treatment approach (e.g., dermatological treatment next to psychotherapeutic) suggest an inpatient setting. In cases of frequent self-harm or suicidal ideation, a more secure and stabilizing therapy setting seems appropriate. Finally, living conditions that help to maintain BDD symptoms such as high family accommodation or ongoing bullying or criticism urge the removal of the patient from these surroundings and place them in a more constructive environment.

We highly recommend taking the inpatient setting into consideration, as it provides the chance for an intensive and multi-professional treatment approach and offers patients the chance to encounter other BDD patients which have proven to be very useful in our clinical experience. Specific and intensive therapy might help to save resources and lower treatment costs in the long run and prevent patients and healthcare professionals from recurring unsuccessful outpatient therapies.

Overall, this requires more specialized treatment settings with specialized centers, both out- and inpatient, which focus on body dysmorphic disorders, incorporating psychological, psychiatric, and psychodermatological competencies, as well as close cooperation between dermatologists, psychologists, and psychiatrists and a thorough screening and assessment process.

Author contributions

CS conceptualized and wrote the manuscript and developed the suggestions for differential criteria on in- and outpatient treatment. K-MT substantially contributed ideas and reflection on the manuscript and added ideas on clinical implications. Both authors contributed to the article and approved the submitted version.

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.

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A brief online writing intervention improves positive body image in adults living with dermatological conditions

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Introduction: Dermatological conditions can affect how individuals feel about their bodies. This research therefore seeks to evaluate the potential for a brief writing intervention, focused on body functionality, to improve body image in adults living with a range of dermatological conditions.

Methods: As part of a parallel Randomised Controlled Trial, 451 adults living with a dermatological condition were randomized to either three functionality-based writing tasks or three creative writing tasks (control). Of these, 155 participants completed pre- and post-intervention measures of body appreciation, functionality appreciation, appearance anxiety, skin-related shame, and skin-related quality-of-life.

Results: For participants with relatively low or mid-range scores on baseline body appreciation and functionality appreciation, there were medium-to-large positive effects of the intervention. Effects were smaller, with all but-one remaining significant, at 1-month follow up and in intention-to-treat analyses. No between-group effects of the intervention were found for measures of appearance anxiety, skin-related shame, and skin-related quality-of-life.

Discussion: These findings suggest that a 1-week writing intervention has the potential to improve positive aspects of body image, but not appearance- and skin-related distress in adults living with a dermatological condition.

Clinical trial registration: [https://clinicaltrials.gov/ct2/history/NCT04445974?V_3=View], identifier [NCT04445974].

KEYWORDS

psychodermatology, appearance anxiety, body appreciation, functionality appreciation, skin shame

Introduction

Dermatological conditions include a range of disorders and diseases that affect the functioning of the hair, skin, and/or nails. Existing research has identified the potential wide-ranging impact of skin conditions. In a global burden of disease study, skin diseases collectively accounted for the fourth greatest non-fatal burden of disease, with dermatitis, acne, urticarial, and psoriasis among the most burdensome (1). UK Population health surveys indicate approximately 54% of the adult population have a skin condition (2, 3).

Epidemiological studies report elevated levels of mental health difficulties, including depression, anxiety, and Body Dysmorphic Disorder (BDD) in populations with chronic skin conditions compared to the general population (2). For example, BDD, where individuals experience high levels of preoccupation and distress around a perceived flaw in their appearance, were estimated to have prevalence rates of 11.3% in dermatological populations as opposed to 1.9% in the general population (4).

Given skin is both visible and the body's largest organ, there is potential for skin conditions to lead to appearance concerns. Visible skin conditions are predominantly defined as conditions that affect the appearance of the skin in areas difficult to cover with clothing, such as the face, neck, and hands (5, 6) and are a leading cause of visible difference (7). It is therefore unsurprising dermatological conditions have the potential to influence how individuals relate to and evaluate their bodies. For example, qualitative and survey studies highlight the challenges skin conditions can pose to aspects of body and skin satisfaction, which are often associated with a desire to conceal the visible signs of the condition and avoid situations where the skin condition may be exposed (8–11). Furthermore, in the qualitative literature, appearance-related concerns have been consistently cited as a central aspect of living with a dermatological condition (10, 12, 13, 14).

Treatments for dermatological conditions primarily focus on physical signs and symptoms. Such treatments and advances play an important role in the management of dermatological conditions and in turn quality-of-life. However, clinician rated-severity correlates poorly with appearance-related distress (15). Instead, psychosocial variables including self-rated severity appear to be stronger predictors of distress (16). While effective medical treatments can improve psychosocial wellbeing, reports from the All Party Parliamentary Group on Skin [APPGS] (2, 17) emphasize the need to increase research and awareness of the impact of living with dermatological conditions and the need to improve both psychological and medical treatment.

Self-help interventions have the potential to provide flexible and discrete access to psychological interventions (18). However, existing evidence for specific self-help interventions targeting body image in adults living with a dermatological condition and/or visible differences is currently limited (19–21). Furthermore, a meta-analysis estimated medium-sized effects of psychological interventions on skin-disease severity, psychosocial measures, and itch-scratch cycles (20). However, reviews highlight limitations of the existing research, including a lack of randomised controlled trials (RCTs), lack of detail in reporting data analyses, and potential mechanisms of effects (19–21). Subsequently, there is a call for research using RCTs to evaluate the effectiveness of theory-driven interventions to improve psychosocial wellbeing (19–21).

One intervention with promising results in improving body image in female populations with high levels of body dissatisfaction and student samples, is the brief writing intervention "Expand Your Horizon" (EYH: 22, 23). Compared to controls, participants completing EYH reported increased levels of body satisfaction (22, 23), body appreciation (22, 23), body functionality (22, 23), body complexity (23), and lower levels of self-objectification (22). Effects were maintained at 1-week (22, 23) and 1-month follow up (23). Findings were replicated in an RCT evaluating the effectiveness of the intervention adapted for a clinical population with rheumatoid arthritis, with the additional finding that depression, but not anxiety, significantly improved in the intervention group (24). Evaluations around the importance of physical appearance are proposed to influence psychosocial adjustment in individuals with dermatological conditions (25, 26). EYH was therefore identified as a potential intervention to target the value placed on appearance and in-turn body image.

Expand Your Horizon can be delivered online and comprises of three writing exercises completed over the course of 1-week, encouraging participants to focus on their body-functionality instead of their physical appearance (22). EYH is based on principles of positive psychology whereby positive body image is not primarily the level of dissatisfaction and/or satisfaction, but is holistic and incorporates acceptance, appreciation of diversity and functionality (27). There is a growing area of research examining body functionality as a modifiable aspect of positive body image. Body functionality encompasses multiple domains, such as internal processes, health, self-care, senses, communication, creativity, and physical activities (28). Alleva et al. (28) argue that by training individuals to shift their focus from appearance to functionality, individuals can develop a more positive relationship with their body. This shift can also be understood with self-objectification theory, which posits that women, in particular, are socialized from an early age to view their bodies "from the outside," as objects to be looked at (29), and focusing on functionality allows women, including women with disabilities, to develop healthier relationships with their bodies (28, 30).

The primary aim of this study was to test whether, compared to a control condition, a brief functionality writing intervention could improve positive body image in individuals living with dermatological conditions, as measured by body and functionality appreciation. We hypothesized that participants completing the functionality intervention,

compared to participants completing a control writing task, would report significantly higher levels of positive body image on post-intervention and follow up measures of functionality and body appreciation.

A secondary aim was to test whether the writing intervention could improve levels of psychological wellbeing on measures of skin-related shame, appearance anxiety, and quality-of-life. We hypothesized that participants completing the functionality intervention, compared with participants completing the control tasks, would report lower levels of appearance anxiety, skin-related shame, and impaired quality-of-life.

Materials and methods

This study adopted a parallel RCT design to assess the effectiveness of an online brief writing intervention EYH, compared to a control condition, on body image in a population with dermatological conditions. The study protocol was pre-registered on ClinicalTrials.gov. Ethical approval was granted by the University of Sheffield ethics committee (reference number: 032128).

Participants

Eligible participants were age 18 or above, who self-reported having a dermatological condition that affects their body image. Dermatological conditions include health conditions that affect the hair, skin, and/or nails, but exclude dermatological changes due to traumatic injuries (e.g., burns). Participants were required to have sufficient English to complete the measures and writing exercises. Individuals were excluded if they did not consent to being randomly allocated to the intervention or control condition, completing three writing tasks or participating in the study.

A priori power analysis based on ANCOVA (for the primary outcome – body appreciation) was conducted using G*Power (31) to estimate the sample size required to achieve 80% power with a significance level of 0.05. Based on previous RCTs using EYH, a medium-sized effect was assumed [see (32) for a systematic review of positive body image interventions]. Assuming a medium effect size of $f = 0.25$, the total sample size required was 128.

Participants were recruited from a community sample. The study was advertised across various platforms including: University staff and student volunteers lists, social media/forums, charities (e.g., Alopecia UK; British Skin Foundation, Verity UK), and mailing lists of individuals who had previously participated in similar research. A total of 451 participants were randomized to the intervention ($n = 228$) and control ($n = 223$) conditions. Of these, 155 participants (34.4%) provided at least one follow up measure. In the intervention condition, 71 (31.1%) completed a follow up measure 1-month later, whereas within the control condition, 79 (35.4%) participants completed the post-intervention. Dropout was comparable across both conditions, and there were no significant differences in the number of non-completers between the intervention and control conditions [X^2 (1, N = 451) = 0.44, $p = 0.51$, $\varphi = 0.03$]. Characteristics of participants in the intervention and control conditions are presented in **Table 1** and **Supplementary Tables 1, 2**. Checks indicated that randomization was successful. Intervention and control groups did not significantly differ on key demographic and clinical variables or baseline measures.

Intervention

Participants allocated to the intervention received EYH (22). EYH consists of three writing exercises, typically completed over 6-days. Participants were asked to write for 15 mins each time, focusing on specific functions (e.g., functions related to communication and senses) that their body performs and why these functions are important (e.g., enjoyment from listening to music). The self-guided intervention is intended to help individuals practice thinking about what their body does for them, rather than what it looks like or cannot do. The wording of intervention materials, including the introduction and examples were adapted for a mixed-gender population with various dermatological conditions. Three experts-by-experience with different dermatological conditions and different backgrounds piloted the intervention. Their feedback was used to refine the intervention materials before being reviewed by the experts by experience and the author of the intervention.

Procedure

All components of the study were conducted online *via* Qualtrics (Qualtrics, Provo, UT, USA) to aid the blinding process.

At Timepoint 1 (T1), prospective participants self-identifying as having a dermatological condition that affects their body image were provided with information outlining the inclusion criteria, the broad purpose of the study, and what participation would involve. Participants were asked to confirm whether they had read the information and consented to: (1) participating in the study; (2) completing three 15 min writing tasks over 1-week; (3) being randomized to either the intervention or the control condition. Participants were then asked to complete the demographic measures (gender, age, ethnicity, educational level, and employment status) and provide information on their dermatological condition(s). This included duration, location, diagnosis, visibility and perceived

TABLE 1 Participant demographics.

Demographics	Participant characteristics	Intervention (n = 228)	Control (n = 223)	Statistics
Age (years)		M = 35.8, SD = 12.9, Range = 18–80	M = 34, SD = 11.1, Range = 18–76.	$t(441) = 1.54$, $p = 0.12$
Gender	Female	n = 198 (87.6%)	n = 195 (88.2%)	X^2 (2, N = 447) = 0.047, p = 0.98
	Male	n = 26 (11.5%)	n = 24 (10.9%)	
	Other	n = 2 (0.9%)	n = 2 (0.9)	
Ethnicity	White	n = 195 (85.5%)	n = 174 (76.3%)	X^2 (5, N = 450) = 7.9, p = 0.16
	Asian	n = 18 (7.9%)	n = 26 (11.7%)	
	Mixed	n = 10 (4.4%)	n = 10 (4.5%)	
	Black	n = 5 (2.2%)	n = 9 (4.1%)	
	Arab		n = 2 (0.9%)	
	Latin American		n = 1 (0.5%)	
Paid work?	Yes	n = 148 (64.9%)	n = 148 (67.9%)	X^2 (1, N = 446) = 0.044, p = 0.51
Higher education?	Yes	n = 156 (65.8%)	n = 148 (67.3%)	X^2 (1, N = 445) = 0.02, p = 0.64

severity. Participants were also asked if they had any other diagnosed health conditions, and whether they were receiving any psychological/pharmaceutical interventions.

Immediately after this, participants completed counterbalanced trait measures relating to body image (body functionality, body appreciation, and appearance anxiety), and skin-related shame and quality-of-life. The online system then randomly allocated participants, at a ratio of 1:1, to either EYH or a sham control (creative writing). Participants were asked to complete the first writing task, before rating their state appearance satisfaction, skin satisfaction, and functionality satisfaction, and providing an email to receive the links to the remaining exercises. Participants were not told whether they had been assigned to the intervention or control condition until the end of the 1-month follow up. Participants could unblind themselves by exiting the study and requesting the debrief information.

Two days later (Timepoint 2, [T2]), participants were sent an automated email with a link to the second writing exercise. Participants were asked to complete the writing exercise, before re-rating the state measures. A further 2 days later (Timepoint 3 [T3]), participants were asked to complete the final writing task and re-rate state measures, before repeating the counterbalanced trait measures given at baseline. One-month after completing the final writing task (Timepoint 4 [T4]), participants received a link to the final set of counterbalanced body image, and skin-related questionnaires, and again were asked to re-rate the state measures.

If participants did not complete part of the study, they received an additional reminder email. Following completion of the questionnaires, participants were shown the debrief information and unblinded. Most participants in the intervention and control groups fully adhered to the writing instructions. All participants regardless of condition were able to download a copy of the intervention materials at the end of the study.

Trait measures

Information on the measures presented to participants are provided below. Cronbach's alphas (α) were calculated using survey data to assess the internal consistencies of measures within this study. All scales showed good-to-excellent internal reliability ($\alpha \geq 0.85$).

Body appreciation

The Body Appreciation Scale-2 (BAS-2: 27) was used to measure trait levels of body appreciation. Each of the 10 items (e.g., "I appreciate the different and unique characteristics of my body") are rated on a scale of 1 (never) to 5 (always). Average score is calculated by adding each item and dividing by 10. Average scores range between 1 and 5, with higher numbers indicating higher levels of body appreciation. The scale had excellent internal reliability ($\alpha = 0.94$), and has established construct, concurrent validity, and 3-week test-retest reliability (27). In previous trials of EYH, the BAS-2 has been responsive to change (22, 23).

Functionality appreciation

The Functionality Appreciation Scale (FAS: 33), comprising of seven questions, was used to assess participants' trait levels of appreciation for their bodies' functionality. Each item (e.g., "I am grateful that my body enables me to engage in activities that I enjoy or find important.") is rated on a scale from 1 (strongly disagree) to 5 (strongly agree). Average score is calculated by adding each item and dividing by 7. Average scores range between 1 and 5, with higher numbers indicating higher levels of function appreciation. The scale had excellent internal reliability

within this study (α = 0.90), and has established construct, concurrent validity, and 3-week test-retest reliability (22). In previous trials of EYH, the FAS has been responsive to change (22, 23).

Appearance anxiety

The Appearance Anxiety Index (AAI: 34) was used to measure appearance anxiety. The AAI contains 10 questions (α = 0.86) focused on cognitive and behavioral components of appearance-related anxiety, including avoidance (e.g., "I try to camouflage or alter aspects of my appearance") and threat monitoring (e.g., "I check my appearance, e.g., in mirrors, by touching with my fingers, or by taking photos of myself"). Each item is scored on a five-point Likert scale from 0 (not at all) to 4 (all the time). Total scores can range from 0 to 40, with higher scores indicating greater levels of appearance-related anxiety. The AAI is responsive to change from interventions and scores of 20 or above indicate clinical levels of appearance anxiety (35).

Skin shame

The Skin Shame Scale (SSS: 36) was used to measure levels of skin-specific shame. The SSS contains 24 items (e.g., "I avoid intimate contact because of my skin"), which are rated on a scale from 1 (never) to 5 (always). Total scores can range from 24 to 120, with higher scores indicating greater levels of shame. The SSS had excellent internal consistency in this study (α = 0.90), and has good construct validity (36, 37).

Quality-of-life

The Dermatology Quality of Life Index (DLQI: 38) was used to measure the impact of skin-conditions on participants' quality-of-life. The DLQI contains 10 questions (e.g., "Over the last week how embarrassed or self-conscious have you been because of your skin") scored on a Likert scale from 0 (not at all/not relevant) to 3 (very much). Total scores range from 0 to 30, with lower scores indicating greater skin-specific quality-of-life. Scores are categorized into "no impact" (0–1), "small impact" (2–5), "moderate impact" (6–10), "very large" (11–20), "extremely large" (21–30) (39). Internal consistency in this study was good (α = *0.85*), and the scale is reported to have good test-retest reliability and construct validity (40). A change in score of 4 or more indicates clinical and reliable change (41).

State measures

After each writing exercise, participants were asked to rate their state appearance satisfaction, skin-appearance satisfaction and body-functionality satisfaction, on a 100-point visual analogue scale. Visual analogue scales are commonly used in experimental research to measure state changes in body image (42).

Analytic strategy

Data were analyzed using SPSS v.26 (IBM, Armonk, NY, USA: IBM Corp). Checks for normality using visual inspection (histograms) and absolute measures of skewness and kurtosis indicated outcome measures were approximately normally distributed. Outcome data from the DLQI were non-normally distributed, therefore, independent samples *t*-tests were used to test group differences post-intervention (T3–T1) and at follow up (T4–T1).

To assess whether randomization of allocation to groups (intervention vs. control) was effective, *t*-tests, chi-squared tests and ANOVAs were used, as appropriate, to compare participant characteristics, including demographics, dermatological history, and baseline scores on the outcome measures. To check whether the writing task manipulation was effective, *t*-tests were used to compare state functionality appreciation immediately after each writing task. Between group differences on state measures were compared for each timepoint.

Effectiveness of the intervention was tested in two ways. Firstly, for those participants who completed all stages of the procedure ("completers"), effectiveness was tested using a series of between-group ANCOVAs, with group (functionality vs. control) as the independent variable, post-intervention scores on the BAS-2, FAS, AAI, and SSS as the dependent variables, and baseline scores on the corresponding measure as the covariate. Secondly, for primary outcome measures (BAS-2 and FAS), ANCOVAs were rerun with intention-to-treat (ITT) analyses using the last-observation-carried-forward method for missing data. Initial assumption checks for the ANCOVAs indicated the assumptions of homogeneity of regression slopes may have been violated. Visual inspection of scatter plots indicated the strength of effects of the intervention and control at T3 and T4 may differ at different levels of the covariate (baseline scores). Consequently, interaction terms were included in ANCOVA models. ANCOVAs were run with the corresponding baseline (T1) score as the covariate at three levels: (1) one-standard deviation below the mean; (2) the mean; and (3) one-standard deviation above the mean, to differentiate effects for participants with relatively low, mid-range, and high baseline scores, respectively. Sidak's correction was used to correct for multiple comparisons.

The number of participants meeting the criteria for clinical change on measures of appearance anxiety and skin-specific quality-of-life were calculated for each group.

Results

Manipulation checks/state outcomes

A series of independent samples *t*-tests (**Table 2**) indicated the participants who completed the functionality tasks scored

TABLE 2 Mean (SD) scores on state measures immediately following each writing task for participants in the functionality and creative condition.

	Body functionality		Body satisfaction		Skin satisfaction	
	Functionality	Creativity	Functionality	Creativity	Functionality	Creativity
T1	69.4 (22.5)***	56.6 (24.9)	44.1 (27.1)	39.8 (25.7)	33.1 (24.4)	31.3 (23.6)
T2	71.3 (19.7)***	59.1 (22.9)	47.5 (22.9)	46.3 (23.6)	45.7 (23.8)	42.0 (23.5)
T3	73.5 (21.3)***	60.4 (22.8)	52.6 (23.7)	48.8 (24.6)	50.1 (24.1)	46.7 (25.9)
T4	72.9 (21.4)***	61.6 (24.9)	52.2 (22.8)	44.3 (25.0)	48.1 (24.4)*	39.4 (24.8)

*$p < 0.05$; ***$p < 0.005$.

TABLE 3 Summary of completer analysis for body appreciation (BAS-2), including estimated marginal means and effects of the intervention at baseline values of BAS-2 one-standard deviation below the mean, the mean, and one-standard deviation above the mean, as well as the interaction effect (baseline BAS-2 and study arm) on BAS-2 post-intervention (n = 151) and at 1-month follow up (n = 144).

Group	BAS-2 (pre)	BAS-2 (post-intervention)				Effect?		BAS-2 (follow up)				Effect?	
	M	*n*	*M*	*SE*	*CI*	*p*	ηp^2	*n*	*M*	*SE*	*CI*	*p*	ηp^2
Functionality	2.04	10	2.61	0.069	2.47–2.74	≤0.001	0.089	10	2.63	0.083	2.47–2.80	0.005	0.055
Creativity		14	2.25	0.063	2.13–2.38			13	2.31	0.079	2.15–2.46		
Functionality	2.78	52	3.19	0.048	3.10–3.28	≤0.001	0.11	51	3.18	0.058	3.07–3.30	0.007	0.051
Creativity		55	2.92	0.045	2.83–3.00			52	2.96	0.057	2.85–3.07		
Functionality	3.52	10	3.77	0.067	3.64–3.91	0.035	0.030	10	3.76	0.84	3.6–3.93	0.34	0.007
Creativity		10	3.58	0.065	3.45–3.70			8	3.65	0.083	3.49–3.81		
		Interaction: $F(1, 147) = 1.36$, $p = 0.25$, $\eta p^2 = 0.009$						Interaction: $F(1, 140) = 1.65$, $p = 0.20$, $\eta p^2 = 0.012$					

significantly higher than participants who completed the creativity tasks on state functionality appreciation at T1 [$t(259) = 4.35$, $p < 0.001$, $d = 0.54$], T2 [$t(164) = 3.77$, $p < 0.001$, $d = 0.59$], T3 [$t(149) = 3.65$, $p < 0.001$, $d = 0.59$], as well as at T4, [$t(142) = 2.91$, $p = 0.004$, $d = 0.49$]. There was a small marginally significant difference for skin satisfaction at 1 month follow up [$t(142) = 2.09$, $p = 0.038$, $d = 035$]. However, no other differences were statistically significant.

Body appreciation

Results of the ANCOVAs comparing completers post-intervention scores on the BAS-2, indicated there was a positive effect of the intervention on body appreciation (Table 3). Participants completing functionality exercises, as opposed to creativity exercises, reported significantly greater body appreciation post-intervention. Effect sizes were moderate for participants with relatively low [$F(1,147) = 14.36$, $p \leq 0.001$, $\eta p^2 = 0.089$]; and midrange [$F(1,147) = 17.55$, $p \leq 0.001$, $\eta p^2 = 0.11$], pre-intervention scores, and small for participants with relatively high initial scores [$F(1,147) = 4.54$, $p = 0.035$, $\eta p^2 = 0.030$]. At 1-month follow up, the effect of the intervention remained significant, but reduced to small for participants who initially had low [$F(1,147) = 8.09$, $p = 0.005$, $\eta p^2 = 0.055$], or mid-point [$F(1,147) = 7.47$, $p = 0.007$, $\eta p^2 = 0.051$], scores on the BAS-2, while between-group differences became non-significant for participants with relatively high initial scores [$F(1,147) = 0.92$, $p = 0.34$, $\eta p^2 = 0.007$]. However, there were no significant effects of the interaction between baseline BAS-2 score and study arm (intervention vs. control) on post-intervention and follow up BAS-2 scores.

In post-intervention ITT analyses (Table 4), participants randomized to functionality exercises, as opposed to creativity exercises, reported significantly greater body appreciation. Effect sizes were medium for participants with relatively low or midrange pre-intervention scores, and small for participants with relatively high scores [low [$F(1,447) = 5.92$, $p = 0.015$, $\eta p^2 = 0.013$]; mid-range [$F(1,447) = 11.32$, $p = 0.001$, $\eta p^2 = 0.025$], and high [$F(1,447) = 5.43$, $p = 0.020$, $\eta p^2 = 0.012$]. However, at 1-month follow up, between-group differences became non-significant for participants with relatively low [$F(1,147) = 3.27$, $p = 0.071$, $\eta p^2 = 0.007$], and high [$F(1,447) = 1.32$, $p = 0.252$, $\eta p^2 = 0.003$] pre-intervention scores, but remained significant for participants with midrange scores [$F(1,147) = 4.35$, $p = 0.038$, $\eta p^2 = 0.010$]. However, there were no significant effects of the interaction between baseline BAS-2 score and condition allocation (intervention versus control) on post-intervention and follow up BAS-2 scores.

Functionality appreciation

Results of the ANCOVAs comparing participant's post-intervention scores on the FAS (Table 5), indicated there was an effect of the intervention on functionality

TABLE 4 Summary of intention-to-treat (ITT) analysis for body appreciation (BAS-2), including estimated marginal means and effects of the intervention at baseline values of BAS-2 one-standard deviation below the mean, the mean, and one-standard deviation above the mean, as well as the interaction effect (baseline BAS-2 and study arm) on BAS-2 at post-intervention and 1-month follow up (N = 451).

Group	BAS-2 (pre)	BAS-2 (post-intervention)				Effect?		BAS-2 (follow up)				Effect?	
	M	*n*	*M*	*SE*	*CI*	*p*	ηp^2	*n*	*M*	*SE*	*CI*	*p*	ηp^2
Functionality	1.84	41	2.00	0.27	1.95–2.05	0.015	0.13	41	2.00	0.031	1.94–2.06	0.071	0.007
Creativity		36	1.91	0.27	1.85–1.96			36	1.92	0.031	1.86–1.98		
Functionality	2.63	155	2.77	0.019	2.73–2.81	0.001	0.025	155	2.76	0.022	2.72–2.81	0.038	0.010
Creativity		157	2.68	0.019	2.64–2.72			157	2.70	0.022	2.66–2.74		
Functionality	3.42	32	3.54	0.026	3.48–3.59	0.020	0.012	32	3.52	0.030	3.46–3.58	0.252	0.003
Creativity		30	3.48	0.27	3.39–3.50			30	3.47	0.031	3.41–3.53		
		Interaction: $F(1, 447) = 0.006$, $p = 0.94$, $\eta p^2 \leq 0.001$						Interaction: $F(1, 447) = 0.22$, $p = 0.64$, $\eta p^2 \leq 0.001$					

TABLE 5 Summary of completer analysis for functionality appreciation (FAS), including estimated marginal means and effects of the intervention at baseline values of FAS one-standard deviation below the mean, the mean, and one-standard deviation above the mean, as well as the interaction effect (baseline FAS and study arm) on FAS at post-intervention (n = 151) and 1-month follow up (n = 143).

Group	FAS (pre)		FAS (post-intervention)			Effect?			FAS (follow up)			Effect?	
	M	*n*	*M*	*SE*	*CI*	*p*	ηp^2	*n*	*M*	*SE*	*CI*	*p*	ηp^2
Functionality	2.93	9	3.77	0.091	3.59–3.95	≤0.001	0.16	8	3.82	0.100	3.62–4.02	≤0.001	0.085
Creativity		13	3.14	0.078	2.98–3.29			11	3.34	0.091	3.16–3.15		
Functionality	3.70	52	4.24	0.55	4.13–4.35	≤0.001	0.14	52	4.16	0.067	4.03–4.30	0.002	0.067
Creativity		51	3.87	0.53	3.77–3.97			47	3.86	0.067	3.74–3.99		
Functionality	4.47	11	4.60	0.074	4.45–4.74	0.10	0.018	11	4.51	0.095	4.32–4.69	0.39	0.005
Creativity		15	4.43	0.072	4.28–4.57			14	4.39	0.095	4.2–4.58		
		Interaction: $F(1, 147) = 7.94$, $p = 0.006$, $\eta p^2 = 0.051$						Interaction: $F(1, 139) = 3.75$, $p = 0.055$, $\eta p^2 = 0.026$					

TABLE 6 Summary of intention-to-treat (ITT) analysis for functionality appreciation (FAS), including estimated marginal means and effects of the intervention at baseline values of FAS: one-standard deviation below the mean, the mean, and one-standard deviation above the mean, as well as the interaction effect (baseline FAS and study arm) on FAS at post-intervention and 1-month follow up (N = 451).

Group	FAS (pre)		FAS (post-intervention)			Effect?		FAS (follow up)				Effect?	
	M	*n*	*M*	*SE*	*CI*	*p*	ηp^2	*n*	*M*	*SE*	*CI*	*p*	ηp^2
Functionality	2.76	34	3.02	0.035	2.95–3.09	0.003	0.020	34	3.00	0.038	2.92–3.07	0.043	0.009
Creativity		41	2.86	0.033	2.81–2.94			41	2.89	0.36	2.82–2.96		
Functionality	3.58	157	3.76	0.024	3.71–3.80	0.001	0.025	157	3.72	0.026	3.67–3.77	0.021	0.012
Creativity		144	3.64	0.024	3.59–3.69			144	3.64	0.026	3.58–3.69		
Functionality	4.40	37	4.50	0.043	4.43–4.56	0.074	0.007	37	4.45	0.037	4.38–4.52	0.214	0.003
Creativity		38	4.41	0.035	4.34–4.48			38	4.38	0.038	4.31–4.46		
		Interaction: $F(1, 447) = 0.78$, $p = 0.38$, $\eta p^2 = 0.002$						Interaction: $F(1, 447) = 0.31$, $p = 0.58$, $\eta p^2 = 0.001$					

appreciation, moderated by completers' baseline FAS scores. Post-intervention, participants in the intervention condition who started with low [$F(1,147) = 27.3$, $p < 0.001$, $\eta p^2 = 0.16$] or mid-range [$F(1,147) = 23.44$, $p < 0.001$], $\eta p^2 = 0.14$] scores on the FAS scored significantly higher than participants with similar scores within the control group. However, for participants with initially high scores, between-group differences were non-significant [$F(1,147) = 2.74$, $p = 0.10$, $\eta p^2 = 0.018$]. At 1-month follow up, between-group differences for initially low [$F(1,139) = 12.9$, $p < 0.001$, $\eta p^2 = 0.085$], and mid-range [$F(1,139) = 10.0$, $p = 0.002$, $\eta p^2 = 0.067$] scorers remained significant, but effect sizes reduced from large to medium. Differences remained non-significant for relatively high scorers [$F(1,139) = 0.74$, $p = 0.39$, $\eta p^2 = 0.005$]. There was a small but significant interaction of baseline FAS scores and condition (intervention vs. control) on post-intervention FAS scores. However, the interaction between baseline FAS score and study arm (intervention vs.

control) on follow up FAS score was small and marginally non-significant.

Within ITT analyses (Table 6), effects of the intervention on functionality appreciation were significant, but small for participants with low baseline scores at T3 [$F(1,447) = 9.22$, $p = 0.003$, $\eta p^2 = 0.020$], and at follow up (T4) [$F(1,447) = 4.12$, $p = 0.043$, $\eta p^2 = 0.009$], and participants with mid-range baseline scores at T3 [$F(1,447) = 11.62$, $p = 0.001$, $\eta p^2 = 0.025$] and at follow up (T4) [$F(1,447) = 5.35$, $p = 0.021$, $\eta p^2 = 0.012$]. For relatively high baseline scorers on the FAS, there were no significant effects of intervention allocation on functionality appreciation at T3 [$F(1,447) = 3.22$, $p = 0.074$, $\eta p^2 = 0.007$], or at follow up (T4) [$F(1,447) = 1.55$, $p = 0.214$, $\eta p^2 = 0.003$]. In ITT analyses, there were no significant effects of the interaction between baseline FAS score and condition (intervention versus control) on post-intervention and follow up FAS scores.

Skin shame and appearance anxiety

Results of the ANCOVAs (Table 7) comparing completers' post-intervention scores on the AAI indicated there were no significant effects of the intervention regardless of whether participants had low [$F(1,147) = 0.86$, $p = 0.36$, $\eta p^2 = 0.006$]; mid-range, [$F(1,147) = 1.76$, $p = 0.19$, $\eta p^2 = 0.012$]; or high [$F(1,147) = 0.88$, $p = 0.35$, $\eta p^2 = 0.006$], baseline scores at T3. Similarly, at follow up (T4) there were no significant effects for participants with low, [$F(1,140) = 4.12$, $p = 0.054$, $\eta p^2 = 0.029$]; mid-range [$F(1,140) = 3.11$, $p = 0.080$, $\eta p^2 = 0.022$]; and high [$F(1,140) = 0.88$, $p = 0.35$, $\eta p^2 = 0.006$], scores on the AAI. Furthermore, there were no significant effects of the interaction between baseline AAI score and condition (intervention vs. control) on post-intervention and follow up AAI scores.

Similarly, results of the ANCOVA (Table 8) comparing completers' post-intervention scores on the SSS indicated there were no significant effects of the intervention regardless of whether participants had low [$F(1,147) = 1.50$, $p = 0.22$, $\eta p^2 = 0.010$]; mid-range, [$F(1,147) = 2.83$, $p = 0.095$, $\eta p^2 = 0.019$]; or high [$F(1,147) = 1.29$, $p = 0.26$, $\eta p^2 = 0.009$], baseline scores at T3. Furthermore, at follow up (T4) there were no significant effects for participants with low, [$F(1,139) = 0.59$, $p = 0.45$, $\eta p^2 = 0.004$]; mid-range [$F(1,139) = 3.13$, $p = 0.079$, $\eta p^2 = 0.022$]; and high [$F(1,139) = 2.96$, $p = 0.087$, $\eta p^2 = 0.021$], scores on the SSS. Furthermore, there were no significant effects of the interaction between baseline SSS score and condition (intervention versus control) on post-intervention and follow up SSS scores.

TABLE 7 Summary of completer analysis for appearance anxiety (AAI), including estimated marginal means and effects of the intervention at baseline values of AAI one-standard deviation below the mean, the mean, and one-standard deviation above the mean, as well as the interaction effect (baseline AAI and study arm) on AAI at post-intervention ($n = 151$) and 1-month follow up ($n = 144$).

Group	AAI (pre)		AAI (post-intervention)			Effect?			AAI (follow up)			Effect?	
	M	*n*	*M*	*SE*	*CI*	*p*	ηp^2	*n*	*M*	*SE*	*CI*	*p*	ηp^2
Functionality	11.9	11	10.0	0.96	8.1–11.9	0.36	0.006	10	9.1	1.09	7.0–11.3	0.054	0.029
Creativity		11	11.8	0.89	9.4–12.9			10	12.2	1.03	10.1–14.2		
Functionality	20.2	52	15.5	0.67	14.2–16.8	0.19	0.012	52	14.9	0.76	13.4–15.3	0.080	0.022
Creativity		52	16.7	0.64	15.5–18.0			50	16.8	0.75	15.3–18.3		
Functionality	28.5	9	21.1	1.92	19.1–23.2	0.35	0.006	9	21.1	1.15	18.8–23.4	0.68	0.001
Creativity		16	22.4	0.87	20.7–24.1			13	21.7	1.05	16.7–23.8		
		Interaction: $F(1, 147) < 0.001$, $p = 0.99$, $\eta p^2 < 0.001$						Interaction: $F(1, 140) = 1.21$, $p = 0.27$, $\eta p^2 = 0.009$					

TABLE 8 Summary of completer analysis for skin shame (SSS), including estimated marginal means and effects of the intervention at baseline values of SSS one-standard deviation below the mean, the mean, and one-standard deviation above the mean, as well as the interaction effect (baseline SSS and study arm) on SSS at post-intervention ($n = 151$) and 1-month follow up ($n = 143$).

Group	SSS (pre)	SSS (post-intervention)			Effect?		SSS (follow up)				Effect?	
	M	*n*	*M*	*SE*	*CI*	*p*	ηp^2	*n*	*M*	*SE*	*CI*	*p*	ηp^2
Functionality	66.5	11	61.8	1.54	58.8–64.9	0.22	0.01	11	60.97	1.80	57.4–64.5	0.45	0.004
Creativity		13	64.3	1.35	61.6–66.9			10	62.87	1.70	59.5–66.2		
Functionality	80.3	50	73.4	1.03	71.3–75.4	0.095	0.019	48	72.0	1.22	69.6–74.4	0.079	0.022
Creativity		50	75.8	0.99	73.8–77.7			47	75.1	1.21	72.7–77.5		
Functionality	94.1	11	84.9	1.48	82.0–87.8	0.26	0.009	11	82.5	1.74	79.0–85.9	0.087	0.021
Creativity		16	87.2	1.39	84.5–89.9			16	86.6	1.66	83.3–89.9		
		Interaction: $F(1, 147) = 0.005$, $p = 0.95$, $\eta p^2 < 0.001$						Interaction: $F(1, 139) = 0.42$, $p = 0.52$, $\eta p^2 = 0.003$					

Clinical change

Among completers, 67.7% of participants scored above the threshold (39) for moderately impaired dermatology-related quality-of-life, measured with the DLQI, and 91.6% reported at least some impairment to their quality-of-life. Participants' changes in DLQI scores post-intervention (T3–T1) ranged between −7 and 12 (M = 2.17, SD = 4.15) for participants completing functionality exercises and −10 and 10 (M = 1.38, SD = 3.68) for participants completing creativity tasks, and did not significantly differ between groups [$t(149) = 1.24$, $p = 0.22$, $d = 0.20$]. Similarly, at follow up (T4-T1), changes in DLQI ranged from −8 to 21 (M = 2.42, SD = 4.15) and −11 to 14 (M = 1.23, SD = 4.71), and did not significantly differ between groups [$t(149) = 1.51$, $p = 0.13$, $d = 0.25$]. A change of 4 or more indicates clinical and reliable change (41), and at T3, 24 (33.3%) participants in the intervention condition and 20 (25.3%) participants in the control condition showed clinical and reliable improvement, and 7 (9.72%) and 7 (8.86%) showed clinical and reliable deterioration, which did not differ significantly between groups [X^2 (2, N = 151) = 1.34, $p = 0.51$, $V = 0.094$]. At 1-month follow up (T4), 27 (38.0%) participants in the intervention condition and 21 (28.4%) participants in the control condition showed clinical and reliable improvement, and 6 (8.45%) and 10 (13.5%) showed clinical and reliable deterioration, respectively, which did not differ significantly between groups [X^2 ($2, N = 145$) = $1.34, p = 0.51, V = 0.094$].

The clinical threshold for AAI is 20 or above (35). Among completers, 58.1% of participants met the clinical threshold for appearance anxiety. At T3 similar numbers of participants exhibited clinical change in the intervention condition (n = 20, 28.2%) and control condition (n = 21, 26.6%), with one (1.4%) and two (2.5%) participants exhibiting clinical deterioration, respectively [X^2 ($2, N = 150$) = $0.27, p = 0.87, V = 0.043$]. At follow up (T4), differences between-groups remained non-significant [X^2 ($2, N = 144$) = $0.78, p = 0.68, V = 0.074$] with 21 (29.6%) and two (2.81%) participants in the intervention condition and 19 (25.6%) and 4 (5.41) in the control condition meeting the criteria for clinical improvement and deterioration, respectively.

Clinical cut-offs are not available for the BAS-2, FAS, and SSS, therefore clinical change was not calculated on these measures.

Discussion

This study examined whether a 1-week body functionality writing intervention could improve body image and reduce appearance/skin-related distress in adults living with a range of dermatological conditions. For this purpose, the potential effectiveness of an adapted version of EYH was examined in a parallel RCT. In line with the primary hypothesis, participants in the intervention condition, as opposed to the control condition, with lower or mid-range baseline levels of body appreciation and functionality appreciation, reported significantly higher levels of positive body image after completing the final exercise and 1-month later. However, effect sizes reduced from medium to small for body appreciation, and large to medium for functionality appreciation. Outcomes remained fairly similar in ITT analyses, although effects of the intervention on body appreciation were small regardless of baseline score, and at follow up the effect only remained significant for participants with mid-range baseline scores. Similarly, ITT analysis indicated that the effect of the intervention on functionality appreciation dropped from large to small at post-intervention, and medium to small at follow up. There remained no effect of the intervention on functionality appreciation for relatively high baseline scorers.

There was evidence that baseline scores on the FAS and the BAS-2 moderated the effect of the intervention on post-intervention functionality appreciation and body appreciation. The moderation indicated that the intervention may be less relevant for individuals with already high levels of functionality appreciation and body appreciation. This may have been a result of a ceiling effect, and the measures were not sensitive enough to detect change in individuals with higher baseline levels of positive body image. That may in fact be the case for functionality appreciation, where the mean pre-intervention score in the high group was 4.47 (for completers)/4.40 (for the ITT analysis) (**Tables 5**, **6**), close to the maximum mean score of 5 on the FAS. However, mean pre-intervention body appreciation scores in the high group – 3.52 for completers and 3.42 for the ITT analysis – were some distance away from the maximum mean score of 5 on the BAS-2. Indeed, in our study, overall completers reported lower levels of baseline body appreciation (intervention: M = 2.65, SD = 0.79; control: M = 2.62, SD = 0.80; **Supplementary Table 2**) compared to participants included in the development of the BAS-2, which used student (M = 3.47–3.97, SD = 0.73) and community samples (M = 3.22–3.47, SD = 0.86–0.96: 27).

Another possibility is that the moderation effect reflects the recruitment of participants with higher levels of distress. In a meta-analysis of standalone body image interventions, selection of participants with elevated appearance distress was identified as a moderator (43). In our sample, there appeared to be elevated levels of skin shame, given that the mean baseline score on the SSS (intervention: M = 83.2, SD = 0.14; control: M = 83.0, SD = 13.5; **Supplementary Table 2**) was higher than that reported in the community dermatology sample (M = 66.9, SD = 17.8) included in the development of the SSS (36). Likewise, in our sample, there appeared to be elevated levels of appearance anxiety, given that the mean baseline score in the AAI (intervention; M = 22.0, SD = 8.1; control: M = 22.0, SD = 8.0) was higher than that previously reported elsewhere (M = 12.49, SD = 8.46; 44), including a community sample with

high levels of appearance concern (Median = 13.0, Inter quartile range = 13.5; 34).

Over a third of participants completing the intervention met the criteria for clinical change (39) on the DLQI and close to 30% met the threshold for clinical change (35) on appearance anxiety. However, differences between groups were non-significant. Comparisons of participants' scores on secondary measures of distress did not support the hypothesis that participants in the intervention would report lower levels of skin shame, appearance anxiety and impaired quality-of-life compared to participants in the control condition. It is unclear why participants did not exhibit improvements on negative aspects of body image and dermatology-related impairments, especially given the high level of impairment found in our sample (see above). It is possible that participants' scores were influenced by the Coronavirus pandemic. For example, some participants fed back that they felt less self-conscious of their skin due to leaving the house less and face masks concealing their skin. It is also possible that some participants may have felt more self-conscious given facemasks have been known to exacerbate skin conditions (45). Another potential explanation for the difference is that negative and positive body image are separate constructs (46), therefore it is possible that aspects of positive body image are more responsive to change. Consequently, the short nature of the intervention may have been insufficient to reduce feelings of shame or improve quality-of-life, particularly where individuals have experienced intrusive reactions from others. Additionally, the absence of components directly addressing shame and other maintaining factors in appearance and health-related distress may explain the lack of effect, which warrants further investigation. For example, compassion-focused and societal-level approaches have some evidence for reducing shame (47, 48). Whilst our findings do not support the use of EYH to specifically reduce distress associated with living with a dermatological condition, our findings suggest that in a community sample, completion of the intervention does enhance positive body image.

A major limitation of this study is the high rate of attrition (>65%). Attrition is often high in studies testing self-help interventions within populations with visible differences (49–51), as well as in the wider literature on self-help (52, 53), with pure self-help interventions typically reporting lower rates of attrition when compared to wait-list controls and facilitated interventions (50, 54). However, attrition in our study was higher than attrition reported in previous trials of EYH. It is likely aspects of recruitment partly explained this difference. For example, financial incentives and human facilitated enrollment, as used in previous trials, are linked to higher levels of attrition (52). In addition, technical issues in the study likely contributed to the high attrition (e.g., some participants had difficulty loading the writing task, and there were problems with downloading the functions list). In future it may be helpful to offer individuals the option to download the full intervention materials or receive a print copy of the intervention.

In previous research, authors have emphasized the likelihood that participants completing trials of non-facilitated psychosocial interventions are likely to be non-random (55). For instance, participants experiencing positive outcomes and participants higher in motivation are more likely to complete the intervention (55). In order to address high attrition, we employed a conservative method of last-observation-carried-forward to examine the effect of participant assignment on potential outcomes. However, last-observation-carried-forward is associated with increased risk of type two errors (56). Nonetheless, the effect of the intervention remained predominantly significant, though smaller, in conservative ITT analysis, indicating that effects of the intervention on positive body image were relatively robust. Furthermore, high dropout is likely a naturalistic reflection of who will use and potentially benefit from self-help interventions. Future research using writing interventions would benefit from further investigating the reasons for discontinuation as well as examining techniques to retain engagement.

Another important limitation of this study was the relatively short (1 month) follow up period following completion of the intervention. Whilst the follow up provided evidence that there were continued, yet smaller, effects of the intervention on positive body image, it is not possible to conclude whether an effect would be maintained over a longer period. Therefore, future research would benefit from a longer follow up period, such as 6–12 months, with consideration for monitoring and controlling for the effect of changes in severity and/flare ups.

A strength of this study was the use of a "sham" control to differentiate the effect of the functionality writing intervention, beyond writing more generally. Studies using active controls arguably have more robust findings (43). Although not a focus of this study, it is possible that the process of writing creatively had a therapeutic benefit for some participants, given the clinical change detected in the control condition. As with previous studies comparing EYH to matched creative writing tasks (22), there were effects over time for participants allocated to both conditions. This effect may reflect natural changes over time, or active components of the control condition, like distraction and enjoyment. It is possible participants' emotional responses to the writing tasks may have influenced participants' subsequent scores on outcome measures.

The findings from this study add further support to the growing evidence that completing a 1-week functionality intervention has the potential to improve functionality appreciation and body appreciation for a range of groups including adults with dermatological conditions, women with rheumatoid arthritis (24), student populations (28, 57), and women with high levels of body dissatisfaction (22). Furthermore, given the brief and low-cost nature of the intervention, it is promising that the effect of the intervention

remained at 1-month post-intervention. However, no existing studies have examined the longevity of the intervention beyond 1-month and subsequently further research including longer follow up periods is required.

Conclusion

This research adopted a RCT design to examine the effectiveness of a 1-week writing intervention on positive body image and skin/appearance-related distress, in a community sample of adults living with a range of dermatological conditions. For participants who did not start the study with relatively high levels of positive body image, there were medium-to-large effects of completing the functionality tasks on body and functionality appreciation, which were generally maintained at 1-month follow up, with small-to-medium effects. However, attrition was high and there were no effects of the intervention, compared to a control, on measures of appearance anxiety, skin-related shame, or quality-of-life.

Data availability statement

All relevant data is contained within the article. Further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by Department of Psychology, University of Sheffield. The patients/participants provided their written informed consent to participate in this study.

Author contributions

KA conducted this study as part of completion of a doctorate in clinical psychology, collected all the data, conducted the analysis, and prepared the first draft of the manuscript. AT and PO supervised the dissertation project at every stage and contributed to revising the manuscript for publication. All authors contributed to the article and approved the submitted version.

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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.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2022.1064012/full#supplementary-material

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Factors associated with worsened clinical symptoms of psoriasis and disease-related quality of life during the COVID-19 lockdown: A cross-sectional study

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Objective: In this cross-sectional study, we aimed to evaluate the factors associated with psoriasis symptom worsening and impaired quality of life (QoL) in individuals with psoriasis during the COVID-19 pandemic lockdown.

Methods: During the second COVID-19 national lockdown (January–April 2021) in Lithuania, individuals diagnosed with psoriasis were invited to fill in an anonymous online survey including sociodemographic and life-style factors, psoriasis-related clinical symptoms, the Dermatology Life Quality Index (DLQI) and the Patients' Health Questionnaire (PHQ).

Results: A total of 297 respondents completed the survey. The majority of them (52.5%) reported worsened clinical symptoms of psoriasis during the COVID-19 lockdown period. In total, 43.1% of responders reported significant depressive symptoms (PHQ-9 $\geq$ 10) and 23.6% reported impaired disease-related QoL (DLQI $>$ 10). The strongest predictor of psoriasis symptoms worsening was the need for changes in psoriasis treatment, with an odds ratio (OR) of 2.73 (95% CI 1.37–5.44, $p = 0.004$) and decreased income (OR = 2.33, 95% CI 1.30–4.17, $p = 0.004$). The strongest predictor of impaired QoL was male sex (OR = 3.35, 95% CI 1.70–6.59, $p < 0.001$). Contribution of specific depressive symptoms was evident for both models.

Conclusion: Worsening of psoriasis symptoms during the COVID-19 lockdown was associated with decreased income, psoriasis treatment changes and depression symptoms. Impaired QoL was associated with male sex, symptom worsening and depression. Specific depression symptoms may have contributed to more symptom worsening and impaired QoL than the depressive symptomatology as a whole.

KEYWORDS

COVID-19, depression, psoriasis, quality of life, stress psychological

Introduction

Coronavirus disease 2019 (COVID-19) outbreak, with lockdown periods and strict quarantine requirements, and the fear of being infected and transmitting the disease, led to significant life style changes, that were associated with psychological distress and the risk of deterioration of mental health (1, 2). During the COVID-19 lockdowns, a considerable number of subjects with somatic illnesses may have found it more difficult to access health care services and receive their usual treatment, leading to deterioration of clinical symptoms (3–5). Overall, the COVID-19 pandemic lockdown has affected many people with somatic conditions, as well as patients' psychological wellbeing and quality of life (QoL) (6); individuals with psoriasis were no exception (7).

Psoriasis is a chronic, papulosquamous, multisystem inflammatory skin disease (8) with a prevalence varying globally from 0.5 to 11.4% and affecting over 125 million people worldwide (9, 10). Psoriasis is known to be associated with multiple metabolic, arthritic and cardiovascular comorbidities (11), seriously diminishes patients' QoL (12), and might be regarded as life-altering and stigmatizing (13). There are significant correlations between psychological distress and clinical severity of psoriasis symptoms (14, 15). Risk factors, such as stress, lifestyle changes, smoking, alcohol use and mental distress symptoms such as depression and anxiety could trigger psoriasis onset and also contribute to the need for prolonged treatment, or even cause treatment resistance (16–19).

Psoriasis is a benign disease, and as such does not affect patients' survival; however, it has a profound impact on individuals' disease-related QoL (20). Previous studies have shown that factors associated with impaired psoriasis-related QoL are longer duration of the disease, specific somatic symptoms such as itch and pain, which lead to worse physical functioning. However, in some studies, QoL was unrelated to disease severity; the strongest relationships with QoL were found for disease perception and stress coping habits (21–24). However, it is still unclear how these factors might have contributed to disease symptom worsening and impaired QoL during the COVID-19 pandemic.

The COVID-19 pandemic posed as an additional stressor for individuals with psoriasis, and a number of factors associated with the burden of the pandemic may have contributed to the worsening of disease symptoms and impaired QoL. For example, changes in family status during the COVID-19 pandemic may have affected individuals' ability to cope with stress, as having a significant other may have acted as a form of support during difficult times, thus preventing disease symptoms from worsening or QoL impairment. Education has been shown to be a protective factor for impaired QoL; however, it is unlikely that this factor directly contributed to disease symptom worsening. Specific factors associated with COVID-19 posed changes such as physical isolation, higher intensity of work load, and reduced income may have contributed to symptom worsening and impaired QoL. These factors have been shown to greatly contribute to mental distress, mainly depression, associated with the COVID-19 pandemic (25). Furthermore, due to increased mental distress during COVID-19, many have sought psychological/psychotherapeutic help and started the use of psychotropic medications (26, 27). Disease-specific factors, such as the duration of illness and available treatment options, were considered as factors that might have contributed to disease symptom worsening and impaired QoL during the COVID-19 pandemic. We also expected that previously-identified risk factors, such as greater age, female sex (28), and depression symptoms would be associated with greater psoriasis symptom worsening and impaired QoL.

We designed a study that allowed us to investigate the factors contributing to disease symptom worsening and impaired QoL in individuals with psoriasis during the COVID-19 pandemic lockdown. We expected that younger age and female sex would be associated with both disease symptom severity and impaired QoL. However, we expected that various aspects of patients' lives, including lower education levels, decreased income, relationships and other previously-identified risk factors (29) would be significantly associated with impaired individuals' psoriasis-related QoL, but not with worsened psoriasis symptoms (30). We expected that clinical markers such as psychotropic medication usage or change in psoriasis treatment regime would be significantly associated with worsening psoriasis condition. Taking into account results from previous studies (31), we also hypothesized that individuals' depression symptom severity would be associated with both worsened clinical symptoms of psoriasis and impaired health-related QoL. Our exploratory aim was to investigate the association of specific depression symptoms with worsened clinical symptoms of psoriasis and impaired disease-related QoL.

Materials and methods

Procedure

Adult (over 18 years) subjects with a psoriasis diagnosis were invited to participate in this study and fill in an anonymous online survey. Information about the study and an invitation for participation was provided by the study researchers, sharing information about the study and the link to the online survey to primary care physicians and to a number of psoriasis patient social media groups. Inclusion criteria for the study were: adult (over 18 years old) subjects with a diagnosis of any type of psoriasis at any time during their life. This cross-sectional study was conducted between January and April 2021, during the second COVID-19 lockdown period in Lithuania. The study procedures were approved by the Bioethics Center

of the of Lithuanian University of Health Sciences (Approval no. BEC-LSMU (R)-19, January 21, 2021). Before starting the survey, participants had to provide online informed consent to participate in the study by ticking the appropriate answer "agree/disagree." Of the 306 respondents who accepted the invitation and completed the survey, data from nine surveys were excluded from the final analysis due to not having a confirmed clinical diagnosis of psoriasis. There were no significant differences among the included and excluded subjects in terms of age or sex ($p > 0.05$). Otherwise, there were no missing data in our dataset and the remaining sample of 297 was comprised of the individuals who fully completed the questionnaire. However, the engagement rate for accessing the questionnaire was not monitored.

The minimal study sample size needed to detect a significant difference between the means of two groups of subjects with psoriasis with different disease-related QoL, with 80% power at the 5% level of significance, was calculated to be 186 participants (32).

Methods

The survey was composed of three parts. The first part of the survey asked individuals for sociodemographic and life-style factor information, evaluating possible triggers and risk factors for exacerbation of psoriasis symptoms. This included respondents' age, marital status, education, work and leisure activities, income and income change during the COVID-19 lockdown. Also included was information about clinical manifestations of psoriasis (confirmation of psoriasis diagnosis, psoriasis-related clinical symptoms, duration of the disease, and treatment methods) and changes in mental health symptoms, and initiation or change in psychotropic medications and/or psychotherapeutic interventions during the COVID-19 lockdown period. The psoriasis symptom worsening was assessed using a single question "During the COVID-19 pandemic (since approximately March 2020), have the symptoms caused by psoriasis changed" with possible answer ranging from "0" "symptoms got better" to "5" "significantly worsened symptoms". More information about questions provided for the study participants can be found in the Supplementary material.

In the next two parts of the evaluation, two standardized questionnaires were used: the Dermatology Life Quality Index (DLQI) (33) and the Patients' Health Questionnaire-9 (PHQ-9) (34, 35).

DLQI

The DLQI questionnaire is the first dermatological QoL questionnaire, published in 1994 (33). This questionnaire is used to measure the impact of most dermatological diseases on the health-related QoL of an affected person. The aim of the use of this questionnaire in the current study was to assess the effect of the severity of psoriasis on the patient's disease-related QoL over the past week. This is a self-reported questionnaire, which consists of 10 short questions that assess the following areas of the patient's life due to their skin condition during the last week: physical symptoms and feelings; daily activity; leisure time; work/school/studies; personal relationships with friends/relatives/partners; and treatment. Each question of the DLQI questionnaire was scored on a four-point Likert scale: very much/yes-3, a lot-2, a little-1, and not at all/not relevant/question unanswered/no-0. The final score of the questionnaire is the sum of the scores of all questions, with a maximum score of 30 points. Over a threshold score of DLQI > 10, individuals are considered to have moderately-to-severely impaired QoL. The higher the final score, the lower the patient's disease-related QoL. The internal consistency of the questionnaire in this sample is considered to be good (Cronbach's alpha 0.895).

PHQ-9

The PHQ-9 is a brief self-rated questionnaire, which is part of the PHQ for the assessment of the severity of depressive symptoms during the past 2 weeks. The questionnaire consists of nine items that fit the Diagnostic and Statistical Manual-IV diagnostic criteria for major depressive disorder (34, 35). For each question, one of the four responses should be marked to describe how often the symptom in question has occurred in the last 2 weeks, with each of the nine items scored according to a Likert scale from 0 ("not at all") to 3 ("nearly every day"). The severity of depressive symptoms was assessed by the sum of the scores of the nine items, and ranges from 0 to 27, where higher scores indicate more severe depressive symptoms. A threshold of $\geq$10 for the PHQ-9 was considered to indicate an increased risk for depression (35). There was an additional question that asked the respondent to assess how the depressive symptoms were affecting their everyday life, work activities or communication with other people, with self-ratings of: "not difficult at all", "somewhat difficult", "very difficult", and "extremely difficult". The internal consistency of the scale in this study sample is considered to be good (Cronbach's α 0.901).

Statistical analysis

The data were analyzed with SPSS Version 27.0.0 (IBM, USA). Mann-Whitney *U* test were used to examine the continuous variables, and chi-square tests were used to test the categorical variables.

The differences in sociodemographic, clinical and life-style factors, and mental distress symptoms reported by individuals who experienced worsened psoriasis symptoms

and those who did not experience any change in symptoms were assessed. Mann-Whitney U test were applied to compare PHQ-9 and DLQI scores, and chi-square tests were used for comparisons in terms of sex, family status, education, activity in relation to the COVID-19 lockdown, intensity of workload, income, duration of psoriasis, treatment of psoriasis, the need for changes in psoriasis treatment during the COVID-19 lockdown, and whether they had to seek psychological/psychotherapeutic help. The same comparisons were later performed in individuals who reported impaired disease-related QoL (threshold score of DLQI $>$ 10) vs. individuals with psoriasis who experienced only mild impairment in their health-related QoL (DLQI $\leq$ 10) during the COVID-19 pandemic. This comparative analysis was conducted in order to investigate possible significant differences between the two groups and identify those variables that might play a role in psoriasis symptom worsening and impaired QoL during the COVID-19 pandemic.

Two separate logistic regression analyses were then performed to investigate associations between sociodemographic factors, life-style factors and mental distress symptoms, and worsened psoriasis symptoms and impaired health-related QoL. The response variable for the first regression model was worsened psoriasis symptoms (classified as 0, "no change or better" or 1, "worsened"), whereas, for the second regression model, the response variable was health-related QoL (classified as 0, "satisfactory QoL (DLQI $\leq$ 10)" or 1, "moderate-to-severe impairment of QoL (DLQI $>$ 10)".

At the final stage, we performed logistic regression analyses (stepwise method) to determine whether specific PHQ-9 items predicted psoriasis symptom worsening and impaired QoL more precisely compared to the total score of the scale.

Results

Sociodemographic and clinical characteristics

The final sample comprised 297 individuals with psoriasis who completed the survey. Table 1 shows the sociodemographic, clinical and life-style factors, and mental distress characteristics of the individuals overall and by group. The age of the individuals ranged from 18 to 69 years old (M = 34; SD = 10), and the majority were female (n = 232; 78.1%). Most of the sample were highly educated, with at least a bachelor's degree ($>$15 years of studies) (n = 173; 58.6%), and with stable or increased income during the pandemic (n = 211; 71.1%). A considerable number of individuals reported over 5 years of history of psoriasis (n = 239; 80.5%), and most of the participants were receiving topical treatment (n = 213; 71.7%) including direct application of topical drugs onto skin rashes (including emollients, moisturizers, vitamin D3 derivatives, retinoids, glucocorticoids, calcineurin inhibitors, anti-interleukin 8 [IL-8] monoclonal antibodies, and coal tar preparations).

A total of 52 (17.5%) individuals reported starting use of psychotropic medications or increasing their dosage and 31 (10.4%) individuals reported seeking psychological/psychotherapeutic help during the COVID-19 pandemic. Almost half of the individuals responding to the survey reported significant depression symptoms (PHQ-9 $\geq$ 10, n = 128; 43.1%). Impaired disease-related QoL was reported by a smaller number of individuals (DLQI $>$ 10, n = 70; 23.6%).

Worsening of psoriasis symptoms

Decreased activity in relation to the COVID-19 lockdown was found among those who reported worsened psoriasis symptoms [$\chi^2(1, N = 297) = 8.84$, $p = 0.003$; $N = 156$], with a greater proportion of respondents with limited activity or self-isolation (n = 104, 66.7%) reporting worsened symptoms compared to those with unlimited activity (n = 52; 33.3%).

Decreased income was also among the factors related to worsened psoriasis symptoms [$\chi^2(1, N = 297) = 14.43$, $p = 0.001$], together with the need for changes in psoriasis treatment during the COVID-19 lockdown [$\chi^2(1, N = 297) = 12.23$, $p < 0.001$], and starting the use of psychotropic medications or increasing their dosage [$\chi^2(1, N = 297) = 7.06$, $p = 0.009$].

The median score on the PHQ-9 was 9.0 (range: 4.0–14.0), with individuals with worsened psoriasis symptoms (median 11.5; range: 7.0–16.0 showing significantly higher values than those who experienced no change in their symptoms (median 5; range: 2.0–10.5), [$z(295) = -6.10$, $p < 0.001$, $d = 0.76$].

The DLQI scores were also significantly higher in individuals with worsened psoriasis symptoms (median 7.5; range: 3.0–13.0) in comparison to individuals who reported no such changes (median 2.0; range 1.0–6.5), [$z(295) = -3.95$, $p < 0.001$, $d = 0.42$].

Impaired health-related QoL

A sex difference was found among those who reported impaired QoL [$\chi 2(1, N = 297) = 8.24$, $p < 0.004$; $N = 70$], with a greater proportion of female (n = 46; 65.7%) than male (n = 24, 34.3%) participants reporting QoL impairment.

The group with impaired disease-related QoL (based on the DLQI threshold score of $>$10) comprised a higher number of individuals who needed to change psoriasis treatment during the COVID-19 lockdown [$\chi^2(1, N = 297) = 5.91$, $p < 0.015$], needed to seek psychological/psychotherapeutic help [17.1 vs. 8.4%, $\chi^2(1, N = 297) = 4.41$, $p = 0.036$], and who had a higher severity of depressive symptoms [PHQ-9 total score (median 12.0; range 8.0–17.0) vs. (median 7.0; range: 3.0–13.0), $z(295) = -4.21$, $p < 0.001$, $d = 0.50$].

TABLE 1 Changes in clinical symptoms of psoriasis and disease-related quality of life during the COVID-19 lockdown in relation to sociodemographic and life-style factors, and mental symptoms.

	All, $n = 297$ (100%)	Psoriasis symptoms improved/ not changed $n = 141$ (47.5%)	Psoriasis symptoms worsened $n = 156$ (52.5%)	z/χ^2	p	DLQI ≤ 10, $n = 227$ (76.4%)	DLQI > 10, $n = 70$ (23.6%)	z/χ^2	p
Age, years; median (IQR)	33.0 (27.0–40.0)	33.0 (28.0–39.0)	32.0 (25.3–40.0)	−0.82	0.23	33.0 (27.0–40.0)	31.0 (27.0–40.0)	−0.37	0.71
Sex, n (%)				2.09	0.1672			8.24	0.004
Male	65 (21.9)	36 (25.5)	29 (18.6)			41 (18.1)	24 (34.3)		
Female	232 (78.1)	105 (74.5)	127 (81.4)			186 (81.9)	46 (65.7)		
Family status, n (%)				2.47	0.2971			2.33	0.36
Lives as a couple	230 (77.4)	111 (78.7)	119 (76.3)			177 (78.0)	53 (75.7)		
Single	38 (12.8)	14 (9.9)	24 (15.4)			26 (11.5)	12 (17.1)		
Lives with family members	29 (9.8)	16 (11.3)	13 (8.3)			24 (10.6)	5 (7.1)		
Education, n (%)				3.67	0.4572			3.58	0.47
≤ 10 years	26 (8.8)	8 (5.7)	18 (11.5)			17 (7.5)	9 (12.9)		
11–12 years	35 (11.8)	16 (11.3)	19 (12.2)			26 (11.50)	9 (12.9)		
13–14 years	63 (21.2)	31 (22.0)	32 (20.5)			46 (20.3)	17 (24.3)		
15–16 years	97 (32.7)	50 (35.5)	47 (30.1)			76 (33.5)	21 (30.0)		
$>$ 16 years	76 (25.6)	36 (25.5)	40 (25.6)			62 (27.3)	14 (20.0)		
Activity in relation to the COVID-19 lockdown, n (%)				8.84	0.003			0.69	0.41
Unlimited	123 (41.4)	71 (50.4)	52 (33.3)			97 (42.7)	26 (37.1)		
Limited/self-isolation	174 (59.2)	70 (49.6)	104 (66.7)			130 (57.3)	44 (62.9)		
Intensity of workload, n (%)				1.18	0.29			0.94	0.33
Increased	76 (25.6)	32 (22.7)	44 (28.2)			55 (24.2)	21 (30.0)		
Decreased/not changed	221 (74.4)	109 (77.3)	112 (71.8)			172 (75.8)	49 (70.0)		
Income, n (%)				14.43	0.001			2.98	0.08
Decreased/no income	86 (29.0)	26 (18.4)	60 (38.5)			60 (26.4)	26 (37.1)		
Increased/not changed	211 (71.0)	115 (81.6)	96 (61.5)			167 (73.6)	44 (62.9)		
Duration of psoriasis, n (%)				0.59	0.75			3.88	0.14
$<$ 1 year	17 (5.7)	7 (5.0)	10 (6.4)			15 (6.6)	2 (2.9)		
1–5 years	41 (13.8)	18 (12.8)	23 (14.7)			35 (15.4)	6 (8.6)		

(Continued)

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TABLE 1 (Continued)

	All, $n = 297$ (100%)	Psoriasis symptoms improved/ not changed $n = 141$ (47.5%)	Psoriasis symptoms worsened $n = 156$ (52.5%)	z/χ^2	p	DLQI ≤ 10, $n = 227$ (76.4%)	DLQI > 10, $n = 70$ (23.6%)	z/χ^2	p
> 5 years	239 (80.5)	116 (82.3)	123 (78.8)			177 (78.0)	62 (88.6)		
Treatment of psoriasis, n (%)				13.34	0.02			2.13	0.83
Combination therapy[a]	15 (5.1)	6 (4.3)	9 (5.8)			11 (4.8)	4 (5.7)		
Topical therapy[b]	213 (71.7)	91 (64.5)	122 (78.2)			165 (72.7)	48 (68.6)		
Systemic therapy[c]	23 (7.7)	12 (8.5)	11 (7.1)			18 (7.9)	5 (7.1)		
Biologic therapy[d]	9 (3.0)	8 (5.7)	1 (0.6)			7 (3.1)	2 (2.9)		
Phototherapy[e]	18 (6.1)	11 (7.8)	7 (4.5)			14 (6.2)	4 (5.7)		
Do not use any treatment	19 (6.4)	13 (9.2)	6 (3.8)			12 (5.3)	7 (10.0)		
Need for changes in psoriasis treatment during the COVID-19 lockdown, n (%)				12.23	<0.001			5.91	0.02
Yes	59 (19.9)	16 (11.3)	43 (27.6)			38 (16.7)	21 (30.0)		
No	238 (80.1)	125 (88.7)	113 (72.4)			189 (83.3)	49 (70.0)		
Started use of psychotropic medications or increased their doses, n (%)	52 (17.5)	16 (11.3)	36 (23.1)	7.06	0.009	36 (15.9)	16 (22.9)	1.81	0.18
Need to seek psychological/psychotherapeutic help, n (%)	31 (10.4)	10 (7.1)	21 (13.5)	3.21	0.09	19 (8.4)	12 (17.1)	4.41	0.04
DLQI									
DLQI, total score; median (IQR)	5.0 (2.0–10.0)	2.0 (1.0–6.5)	7.5 (3.0–13.0)	−3.95	<0.001	3.0 (1.0–6.0)	15.0 (12.8–19.0)	−8.93	<0.001
PHQ-9									
PHQ-9, total score; median (IQR)	9.0 (4.0–14.0)	5.0 (2.0–10.5)	11.5 (7.0–16.0)	−6.10	<0.001	7.0 (3.0–13.0)	12.0 (8.0–17.0)	−4.21	<0.001
PHQ-9 total score ≥ 10	128 (43.1)	38 (27.0)	90 (57.7)	28.54	<0.001	86 (37.9)	42 (60.0)	10.67	0.001

SD, Standard deviation; z, Mann-Whitney U test; χ^2, chi-squared test; DLQI, Dermatology Life Quality Index; PHQ-9, Patient Health Questionnaire-9.

[a]Combination therapy, more than one agent is prescribed; [b]Topical therapy, the direct application of topical drugs onto skin rashes (including emollients, moisturizers, vitamin D3 derivatives, retinoids, glucocorticoids, calcineurin inhibitors, anti-interleukin 8 [IL-8] monoclonal antibodies, and coal tar preparations); [c]Systemic therapy, oral and injected medications that work throughout the entire body (including methotrexate, cyclosporine, acitretin, mycophenolic acid, hydroxyurea, 6-thioguanine, and other *systemic* agents); [d]Biologic therapy, biologic drugs designed to act on specific immune system targets, as TNFα (including etanercept, infliximab, adalimumab and certolizumab), IL-12/IL-23 (including ustekinumab), IL-17 (including secukinumab, ixekizumab and brodalumab) and IL-23 (including guselkumab, tildrakizumab and risankizumab); [e]Phototherapy, *treatment* that *uses ultraviolet rays* with in the *UVA* and *UVB* spectrum.

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TABLE 2 Multivariate regression analysis of factors associated with subjectively worsened psoriasis symptoms, including both sociodemographic factors and severity of depressive symptoms (PHQ-9 total score).

Factors	$R^2 = 0.241$	OR	95% CI	*p*
Sex		1.24	0.66–2.30	0.50
Age		0.99	0.97–1.02	0.76
Activity in relation to the COVID-19 lockdown		1.43	0.85–2.40	0.181
Income		2.33	1.30–4.17	0.004
Treatment of psoriasis		0.87	0.74–1.03	0.12
Need for changes in psoriasis treatment during the COVID-19 lockdown		2.73	1.37–5.44	0.004
Started use of psychotropic medications or increased their doses		1.25	0.60–2.60	0.55
PHQ-9		1.10	1.05–1.14	<0.001

95% CI, confidence interval; OR, odds ratio; PHQ-9, Patient Health Questionnaire-9; Sex (male, 1/female, 2); Age (years); Activity in relation to the COVID-19 lockdown (Unlimited, 0/ Limited/self-isolation, 1); Income (Increased/not changed, 0/ Decreased/no income, 1); Need for changes in psoriasis treatment during the COVID-19 lockdown (No, 0/ Yes, 1); Started use of psychotropic medications or increased their doses (No, 0/ Yes, 1).

Predictors of worsened psoriasis symptoms

Logistic regression to identify predictors of worsened psoriasis symptoms (classified as 0, "no change" or 1, "worsened") included sex (1, "male"; 2, "female"), age, activity in relation to the COVID-19 lockdown, income, treatment of psoriasis, need for changes to psoriasis treatment during the COVID-19 lockdown, starting use of psychotropic medications or increasing their doses, and PHQ-9 (Table 2). The strongest predictor of worsened symptoms was the need for changes in psoriasis treatment during the COVID-19 lockdown, with an odds ratio (OR) of 2.73 (95% CI 1.37–5.44, $p = 0.004$). The probability of symptom worsening doubled with decreased income in comparison to stable or increased income during the COVID-19 pandemic (OR = 2.33, 95% CI 1.30–4.17, $p = 0.004$). Depression symptoms were also significantly associated with worsening of psoriasis symptoms during the COVID-19 lockdown (OR = 1.10, 95% CI 1.05–1.14, $p < 0.001$).

A stepwise logistic regression model for specific depression items showed that the PHQ-9 item 2 "feeling down, depressed, or hopeless" predicted symptom worsening even better than the sum score of the PHQ-9, increasing the R2 by 0.282 (OR = 2.22, 95% CI 1.65–2.99, $p < 0.001$) (Supplementary Table 1S).

TABLE 3 Multivariate regression analysis of factors associated with impaired disease-related quality of life (DLQI > 10) in patients with psoriasis, including both sociodemographic factors and severity of depressive symptoms (PHQ-9 total score).

Factors	$R^2 = 0.203$	OR	95% CI	*p*
Sex		3.35	1.70–6.59	<0.001
Age		0.99	0.97–1.03	0.90
Need for changes in psoriasis treatment during the COVID-19 lockdown		1.53	0.78–2.99	0.22
Need to seek psychological/ psychotherapeutic help		1.58	0.67–3.73	0.30
Psoriasis symptoms worsened		3.22	1.66–6.24	<0.001
PHQ-9		1.07	1.02–1.16	0.008

95% CI, confidence interval; OR, odds ratio; PHQ-9, Patient Health Questionnaire-9; Sex (female, 1/male, 2); Age (years); Need for changes in psoriasis treatment during the COVID-19 lockdown (No, 0/ Yes, 1); Need to seek psychological/psychotherapeutic help (No, 0/ Yes, 1); Psoriasis symptoms worsened (no change or better, 0/ worsened, 1).

Predictors of impaired QoL

Logistic regression on disease-related QoL (classified as 0 "DLQI $\leq$ 10" or 1, "DLQI > 10") included sex (2, "male"; 1 "female"), age, the need for changes in psoriasis treatment during the COVID-19 lockdown, need to seek psychological/psychotherapeutic help, psoriasis symptoms worsening, and PHQ-9 (Table 3). The strongest predictor was male sex, which improved the chances of impaired QoL during the COVID-19 lockdown in comparison to female sex (OR = 3.35, 95% CI 1.70–6.59, $p < 0.001$). The probability of being attributed to the group with impaired QoL was also tripled if the individual experienced worsened psoriasis symptoms during the COVID-19 lockdown (OR = 3.22, 95% CI 1.66–6.24, $p < 0.001$). Depression also contributed to the probability of impaired QoL (OR = 1.07, 95% CI 1.02–1.16, $p = 0.008$).

A stepwise logistic regression model for specific depression items showed that the PHQ-9 item 9 "Thoughts that you would be better off dead, or of hurting yourself in some way" predicted impaired QoL better than the sum score of the PHQ-9, increasing the R2 by 0.231 (OR = 1.58, 95% CI 1.12–2.24, $p = 0.010$) (Supplementary Table 2S).

Discussion

In the current study, we aimed to investigate whether sociodemographic and COVID-19 lockdown lifestyle factors affected changes in clinical symptoms of psoriasis and psoriasis-related QoL, and to evaluate the contribution of specific

mental symptoms, such as depressive symptoms, in this process. We found that the need for changes in psoriasis treatment during the COVID-19 lockdown, decreased income, and depression symptoms were the strongest predictors of psoriasis symptom worsening. Psoriasis-related QoL during the COVID-19 lockdown was associated with male sex, psoriasis symptoms worsening, and depression symptoms. Specific symptoms of depression, such as thoughts of feeling down, depressed or hopeless, were associated with psoriasis symptom worsening, while suicidal thoughts were associated with impaired psoriasis-related QoL.

The main finding in this study was that the predictors for worsened psoriasis symptoms during the COVID-19 lockdown were limited to decreased income and the need for changes in psoriasis treatment, starting use of psychotropic medications or changing their doses, and higher severity of depressive symptoms (36, 37). A similar web-based survey conducted in China confirms our findings, revealing a similar conclusion; as in this study, exacerbation of psoriasis was associated with outdoor activity restriction and income loss (38). Some people with psoriasis had stopped or changed their treatment of psoriasis during the COVID-19 lockdown. The leading reasons were perceived stress, fear, worry, depression, and anxiety about the risk of being infected with COVID-19. These data indicate a burden due to the COVID-19 pandemic in people with psoriasis; worsening psoriasis is common and is associated with poor mental health (39). Furthermore, studies show that, in individuals with psoriasis, depression is associated with increased risk of myocardial infarction, stroke and cardiovascular death, especially during acute depression (40).

Overall, the strongest predictor of worsened psoriasis symptoms during the COVID-19 lockdown was limited access to health care (38), which caused difficulties in continuous treatment for patients with chronic diseases, non-adherence to treatment and adverse health outcomes. We observed a consequent need to change psoriasis treatment in the current study sample. Only 8% of individuals in our study sample were receiving systemic psoriasis treatment during COVID-19 period. However, it is estimated that around 17% of individuals experiencing psoriasis symptoms ranging from moderate to severe, require systemic treatment (41). No possibilities to initiate such treatment due to lockdown might have fueled individuals' with psoriasis symptoms of depression and impaired QoL.

Next, we tested factors associated with psoriasis-related QoL. Our findings showed that predictors for impaired psoriasis-related QoL were male sex, worsened psoriasis symptoms, and higher severity of depressive symptoms.

A similar self-administered web-based questionnaire was distributed through social media by Yeye Guo et al. (7). Authors found that isolation, income loss and unemployment were associated with impaired health-related QoL in patients with skin diseases during the COVID-19 pandemic (7). Also, outdoor activity restriction was significantly associated with anxiety, depression and impaired QoL (7). Besides depression being one of the strongest predictors of impaired QoL, our study does not confirm the findings of Guo et al. (7). This discrepancy may be explained by the fact that Guo et al. (7) did not use psoriasis symptom worsening in their prediction models. It is possible that the pathway between impaired psoriasis-related QoL and reduced income and isolation is mediated *via* symptom worsening. Thus, symptom worsening might be a mediating factor in this process; however, investigation of a mediation model was beyond the scope of our study.

Contrary to our hypothesis, male, but not female, sex contributed to impaired psoriasis-related QoL. Results in the scientific literature on the role of sex differences in psoriasis-related QoL are somewhat contradictory, with some studies showing no sex differences (21, 42), some reporting lower QoL for females in comparison to males (43, 44), and some suggesting the opposite (45). However, in our study sample, we had more males than females (21.5 vs. 10.3%) who were not receiving treatment for psoriasis, and more males than females (13.8 vs. 4.3%) who were living alone during the COVID-19 pandemic. These factors may have influenced the relationship between sex and psoriasis-related QoL.

Besides well spotted factors in prediction modeling for both psoriasis symptom worsening and impaired QoL, several other characteristics should be considered in future studies investigating aforementioned associations. COVID-19 period was marked not only with increased numbers of depression but also with anxiety disorders (46, 47) accompanied with certain cognitive difficulties attributed to the COVID-19 infection (48) or, such as inflexible thinking style, to personality features (49). Several other characteristics, such as stigmatization (50, 51) and alexithymia (52–57) have been shown to predict psoriasis symptom worsening as well as impaired OoL. Unfortunately, due to the brevity of our survey, we have not included these factors which might have also contributed to the prediction of symptom worsening and impaired QoL in our study design.

Lastly, we observed that some of the individual questions of the PHQ-9 were even better than the whole questionnaire in prediction modeling for both psoriasis symptom worsening and impaired psoriasis-related QoL. The question about "Feeling down, depressed, or hopeless" was associated with psoriasis symptom worsening, while "Thoughts that you would be better off dead, or of hurting yourself in some way" was associated with impaired psoriasis-related QoL. The question on being depressed summarizes a cardinal feature of the mental disorder, which other studies have also shown to have good psychometric characteristics in its prediction (58). As expected, psoriasis symptom worsening was greatly affected by depression symptoms, and thus the question on the particular experience of being depressed predicted the probability of symptom worsening. On the other hand, the question regarding suicidal thoughts contributed most to impaired psoriasis-related

QoL, besides male sex and psoriasis symptom worsening. This symptom is common in depression, with a higher prevalence in male than in female. Since male sex was one of the main contributors to impaired psoriasis-related QoL, and more males than female experienced suicidal ideation (12.3 vs. 3.4%, based on the PHQ-9 question) more than half of the days, we believe that question on suicidal ideation added more to the model than indicating a general feeling of depression, which was common in both males and females.

The limitations of the study included the selection bias associated with online surveys and recall bias of patient-reported outcomes. Thus the reader has to take into account that we assessed subjectively experienced symptom worsening rather than the objective clinical documentation of psoriasis exacerbation. Furthermore, to identify any treatment changes we used generally phrased item "Did you have your medical treatment of psoriasis changed during the COVID-19 pandemic". This phrasing precludes identifying whether treatment change was related to the pandemic (e.g., restricted access to care) or a result of symptom changes. We acknowledge, that in general there is a large association between symptom worsening and the need to change the treatment. If symptoms worsen then dermatologist might prescribe different medication that might work better. Existing restriction in accessing such care might have contributed to the need for psoriasis treatment change. Since "change in psoriasis treatment" is one of the main predictors in the model, careful understanding of our item phrasing is important not to overstate our study results.

It might be also relevant to consider the effect of vaccination on psoriasis symptom worsening. Vaccination is not common trigger for psoriasis symptoms exacerbation (59), but there are some reports of psoriasis symptoms worsening after vaccination for influenza, pneumococcal pneumonia, and yellow fever (60). New onset and exacerbation of psoriasis were reported in the systemic review and case series documenting new diagnosis of psoriasis or psoriasis exacerbation after at least one dose of any COVID-19 vaccine (61, 62). However, COVID-19 vaccination in Lithuania has actively started in Jan 2021 and lasted until the end of this study (Apr 2021) with 24.7% of Lithuanian population receiving the first dose of the vaccine. By the end of the study data collection only 10.8 % of Lithuanian were fully vaccinated (63). Unfortunately, our study has no data on vaccination during the period of data collection.

Furthermore, our study sample was relatively small and consisted of individuals in their early thirties. Thus, the results may not represent geriatric patients, who were less accessible *via* the internet or social media or those with more severe psoriasis conditions (72 % of individuals in our study were using topical agents). The engagement rate was not monitored precluding information on actual interest in participating in the study.

Hopefully, taking our research into consideration, several health and research practices could be implemented. In our study were able to identify specific modifiable and non-modifiable factors related with both psoriasis symptom worsening and impaired QoL in individuals with psoriasis during COVID-19 pandemic. Along with other well-known risk factors (such as alcohol use, smoking, anxiety and alexithymia), the factors we identified could be used for targeted prevention and intervention. Furthermore, based on our analysis on specific depression symptoms, spotting these, could also be used for future practices to detect individuals vulnerable to symptom worsening and impaired QoL.

Conclusion

More than half of psoriasis patients reported subjectively worsened psoriasis symptoms during the COVID-19 lockdown period, and one quarter were evaluated as having impaired psoriasis-related QoL.

Worsened psoriasis symptoms during the COVID-19 lockdown are associated with decreased income, psoriasis treatment changes and depression symptoms. QoL impairment is associated with male sex, psoriasis symptom worsening and depression. Specific depression symptoms may have contributed more to symptom worsening and impaired QoL than the depressive symptomatology as a whole.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The study and it's consent procedures were approved by Bioethics Center of Lithuanian University of Health Sciences [Approval no. BEC-LSMU (R)-19, January 21, 2021]. The patients/participants provided their written informed consent to participate in this study.

Author contributions

JB and VS: designed the study. MS: collected and analyzed the data. AP: statistical analyses. JB, MS, AP, and VS: drafted and edited the manuscript. All authors contributed to the manuscript and approved the final version.

Conflict of interest

JB works as a consultant to Cronos. VS reported being a consultant to SignantHealth and received personal fees from

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Supplementary material

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The relationship between atopic dermatitis and atopic itch in children and the psychosocial functioning of their mothers: A cross-sectional study

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Atopic dermatitis is a chronic inflammatory skin disease significantly affecting patients' and their parents' lives. Mothers are mostly responsible for the long-term treatment and their wellbeing is essential. The major objective of this cross-sectional study was to investigate the relationship between atopic dermatitis in children, especially concomitant itch, and the quality of life, stress, sleep quality, anxiety, and depression of their mothers. The study included 88 mothers of children with atopic dermatitis and 52 mothers of children without atopic dermatitis. All mothers completed sociodemographic questionnaire, the Perceived Stress Scale, the Athens Insomnia Scale and the Hospital Anxiety and Depression Scale. Additionally, mothers of children with atopic dermatitis filled in the Family Dermatology Life Quality Index. The severity of atopic dermatitis and pruritus intensity were evaluated by the Scoring Atopic Dermatitis Index and the Numerical Rating Scale, respectively. The severity of atopic dermatitis and itch significantly correlated with the quality of life, insomnia, and perceived stress of the mothers. Mothers whose children had had atopic dermatitis for more than 6 months had significantly higher scores of anxiety and depression. The results highlight the importance of screening mothers for functional impairment to provide adequate support. More attention should be directed to the standardization of stepped care interventions addressing factors resulting in the impaired functioning of mothers.

KEYWORDS

atopic dermatitis, itch, mothers, quality of life, sleep, stress

1. Introduction

Atopic dermatitis (AD) is the most common chronic, pruritic, inflammatory skin disease in pediatric patients and often presents as ill-defined, erythematous weeping or crusted papules and plaques. It affects up to 20% of preschool children, with increasing prevalence in developed countries (1). AD in children has been extensively investigated, especially regarding its influence

on the functioning of the patients and their parents, and found to be a debilitating disease due to its highly negative physical and mental consequences (2).

Out of all of the symptoms of AD, itch is reported as the most burdensome, affecting almost 91% of patients on a daily basis (3). Sleep disturbance is an important consequence of itch in children. It has been associated with daytime fatigue, irritation, loss of concentration, headaches and increased rates of attention deficit hyperactivity disorder (4). In adults, the "itch that rashes" is believed to drive much of the impact on the quality of life (QoL) and to increase mental distress, leading to a higher risk of suicidal ideation, anxiety, and depression (5). Sleep disturbance in the course of AD begins early in infancy and often leads parents to co-sleep with their infants to prevent them from constantly scratching themselves (6). Managing night-time pruritus results in regular sleep loss for parents and leads to tiredness, increased marital tension, impaired occupational functioning, and a higher rate of anxiety and depression (7). Reducing itch has been found to be the most important treatment goal (8).

Moderate to severe forms of AD in children negatively influence the emotional life of their caregivers. Parents of children with AD report feeling helpless and distressed about caring for them (9). They tend to become overprotective and develop more empathy toward their children, often feeling guilty and blaming themselves for the child's disease and related suffering (10). Furthermore, parents of children with AD report inadequate social support or even receiving criticism for their parenting from relatives and society (10, 11).

Although the AD of a child influences the psychosocial functioning of both parents, it has a greater impact on the mother's QoL than on the father's (12). Current knowledge supports interdisciplinary approach to improve the wellbeing of patients and their caregivers based on the "greater patient" concept (13). Applied from the onset of AD, it could prevent patients and their caregivers from experiencing the considerable burden of AD. It is known that genetic, personal, and environmental variables (e.g., locus of control, coping stress strategies, social support, and various psychological traits) may predict, protect against, and either maintain or counteract anxiety, depression, and perceived level of stress amongst parents of children with AD. Therefore, it is important to investigate which factors impact wellbeing of primary caregivers and how they do so, to better tailor programs supportive to their needs.

The aim of this cross-sectional study was to compare perceived stress levels, sleep patterns, depression, and anxiety in mothers of children with and without AD. Moreover, the major objective of this study was to investigate the relationship between AD, with particular emphasis on pruritus, and the psychosocial functioning of the mothers of affected children.

2. Materials and methods

The study included mothers of children with AD and mothers of children without AD for comparison. Children with AD were hospitalized due to AD exacerbation in the Department of Dermatology, Pediatric Dermatology, and Oncology of the Medical University of Lodz, Poland. Children without AD visited the same Department of Dermatology on an outpatient basis or attended a preschool located in Lodz.

Inclusion criteria were the following: Age of the child from 3 months to 18 years, age of the mother of at least 18 years, and agreement to participate in the study. AD was diagnosed according to Hanifin and Rajka. Exclusion criteria included additional chronic diseases in children and psychiatric or other chronic disorders in mothers.

The study was approved by the Bioethics Committee of the Medical University of Lodz (RNN/296/17/KE) and was performed according to the principles of the Helsinki Declaration. All participants provided written informed consent.

The severity of AD in the children was evaluated with the Scoring Atopic Dermatitis (SCORAD) index by an experienced dermatologist (AKK) (14). Mothers of children with AD were asked to rate their child's itch intensity from the past 3 days on a numerical rating scale (NRS) and to complete a questionnaire with sociodemographic data and questions about the onset and duration of AD, and the Polish-language versions of the Family Dermatology Life Quality Index (FDLQI), the Perceived Stress Scale (PSS 10), Athens Insomnia Scale (AIS), and Hospital Anxiety and Depression Scale (HADS). Mothers of children without AD were asked to fill in the sociodemographic questionnaire, PSS 10, AIS, and HADS.

The modified NRS used in the study is a 10-cm long horizontal line with numbers from 0 to 10 on which participants indicate the intensity of pruritus, with 0 being no pruritus and 10 being the worst itch. Itch NRS scoring was categorized as mild (>0–3 points), moderate (≥3–7 points), and severe or very severe itch (≥7–10 points) (15–17).

The FDLQI measures the impact of the children's skin disease on the caregivers' QoL in the past month (18). The questionnaire consists of 10 questions concerning the influence of the patient's skin disease on different aspects of family life. Each question can be answered by choosing 1 out of 4 answers scored 0–3. Higher scores indicate poorer QoL (19).

The PSS 10 measures perceived level of stress in the participant's life during the past month (20). It is a 10-item questionnaire that participants answer on a 5-point scale ranging from 0 (never) to 4 (very often). The higher the score, the greater the perceived stress. The Polish version scale has a Cronbach's α of 0.86 (20).

The AIS is a self-rated psychometric questionnaire measuring sleep disturbances over the past month, based on the criteria of the International Classification of Diseases—10th edition (ICD-10). Each of the eight questions can be scored on a 0–3 scale, in which three designates negative outcomes. Scores ≥6 points reflect a diagnosis of insomnia (16, 21).

The HADS is used to identify anxiety and depression symptoms during last week (22). It consists of 14 questions divided in two subscales for anxiety (HADS-A) and depression (HADS-D). Each question can be answered on a scale ranging from 0 (never) to 3 (very often). The maximum score for each subscale is 21. Scores indicating probable anxiety/depression were both defined as ≥8.

2.1. Statistical analysis

The results are presented as means ± standard deviations (SDs). The data were analyzed with descriptive statistics, using non-parametric tests because the data did not meet the assumptions about normal distribution and equality of variances. Correlations were determined using Spearman's rho. Groups that differed in disease duration where analyzed using the Mann–Whitney *U*-test. The level of significance was set at $\alpha = 0.05$. Statistical analyses were performed using Jasp ver.0.12.1/774.

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TABLE 1 Characteristics of the study group.

	Mothers of children with AD, *n* = 88	Mothers of children without AD, *n* = 52	*P*-value	Children with AD, *n* = 88	Children without AD, *n* = 52	*P*-value
Age of mother, years, mean ± SD	35.05 ± 6.56	34.81 ± 3.88	0.795	N/A	N/A	
Range	19–52	27–42				
Age of children, months, mean ± SD	N/A	N/A		60.16 ± 56.60	60.25 ± 37.71	0.227
Range				1–216	5–132	
Sex of child	N/A	N/A				0.006
Male, *n* (%)				59 (67.05)	29 (55.77)	
Female, *n* (%)				29 (32.95)	23 (44.23)	
Education			0.051	N/A	N/A	
<9 years of education, *n* (%)	1 (1.14)	2 (3.85)				
High school, *n* (%)	27 (30.68)	7 (13.46)				
Vocational school, *n* (%)	10 (11.36)	3 (5.77)				
University degree, *n* (%)	50 (56.82)	40 (76.92)				
Employment				N/A	N/A	
Employed, *n* (%)	66 (75)	44 (84.62)	0.355			
Unemployed, *n* (%)	22 (25)	8 (15.38)				
Marital status				N/A	N/A	
Single, *n* (%)	2 (2.27)	1 (1.92)	0.809			
Married, *n* (%)	61 (69.32)	38 (73.08)				
Partnership, *n* (%)	16 (18.18)	8 (15.38)				
Divorced, *n* (%)	7 (7.96)	3 (5.77)				
Widowed, *n* (%)	2 (2.27)	0 (0.00)				
Unknown, *n (%)*	0 (0.00)	2 (3.85)				
Average number of children, mean ± SD	1.55 ± 0.71	1.58 ± 0.70	0.706	N/A	N/A	
Range	1–4	1–3				
AD in the family	N/A	N/A				
Mothers, *n* (%)				3 (3.40)	3 (5.77)	
Fathers, *n* (%)				3 (3.40)	1 (1.92)	
Siblings, *n* (%)				7 (7.95)	0 (0.00)	
No, *n* (%)				78 (88.64)	48 (92.31)	
Duration of AD, months, mean ± SD	N/A	N/A		43.68 ± 51.19	N/A	
Range				1–216		
<6 months, *n* (%)				27 (30.68)		
≥6 months, *n* (%)				61 (69.32)		
SCORAD (points), mean ± SD	N/A	N/A		46.64 ± 15.17	N/A	
Range				13–84		
Mild, <25, *n* (%)				11 (12.50)		
Moderate, 25–50, *n* (%)				46 (52.27)		
Severe, >50, *n* (%)				31 (35.23)		
Itch NRS (points), mean ± SD	N/A	N/A		6.14 ± 3.03	N/A	
Range				0–10		
Mild, <3, *n* (%)				11 (12.50)		
Moderate, 3–6, *n* (%)				29 (32.96)		

(Continued)

TABLE 1 (Continued)

	Mothers of children with AD, *n* = 88	Mothers of children without AD, *n* = 52	*P*-value	Children with AD, *n* = 88	Children without AD, *n* = 52	*P*-value
Severe, 7–10, *n* (%)				48 (54.54)		
FDLQI, (points), mean ± SD	16.45 ± 6.56	N/A		N/A	N/A	
Range	0–30					
PSS-10, (points), mean ± SD	21.66 ± 6.81	16.90 ± 5.83	<0.001	N/A	N/A	
Range	1–35	2–29				
AIS, (points), mean ± SD	9.20 ± 5.46	6.00 ± 3.92	<0.001	N/A	N/A	
Range	0–20	1–16				
Insomnia, ≥6, *n* (%)	59 (67.05)	23 (44.23)				
HADS A, (points), mean ± SD	9.12 ± 4.63	4.63 ± 3.38	<0.001	N/A	N/A	
Range	0–18	0–16				
Anxiety, >8, *n* (%)	51 (57.96)	6 (11.54)				
HADS D, (points), mean ± SD	7.34 ± 4.13	3.40 ± 3.10	<0.001	N/A	N/A	
Range	0–15	0–14				
Depression, >8, *n* (%)	44 (50.00)	4 (7.69)				

AD, atopic dermatitis; N/A, not applicable; SD, standard deviation; SCORAD, scoring of AD; NRS, numerical rating scale; FDLQI, Family Dermatology Life Quality Index; PSS-10, Perceived Stress Scale; AIS, Athens Insomnia Scale; HADS A, Hospital Anxiety and Depression Scale, Subscale Anxiety; HADS D, Hospital Anxiety and Depression Scale, Subscale Depression.

The sample size of the study cohort was determined by sample size calculation using the principle of the anticipated response distribution of 50%, with 95% confidence interval (CI), and 10% precision.

3. Results

A total of 120 mothers of children with AD and 70 mothers of children without AD were found to be eligible for the study. However, 10 mothers of children with AD and 12 mothers of children without AD refused consent due to lack of time. In addition, 22 and 6 mothers, respectively, did not return the completed tests. Thus, the study group consisted of 88 mothers of children with AD (response rate 73.33%), whereas the control group comprised 52 mothers of children without AD (response rate 74.29%). The characteristics of the study and control groups, including sociodemographic data, AD disease parameters, and overall psychosocial health status are summarized in Table 1.

The mean age of mothers of children with and without AD was 35.05 ± 6.56 years (range 19–52 years) and 34.81 ± 3.88 (range 27–42 years), respectively. In the group of children with AD, the mean age was 60.43 ± 56.60 months (range 1–216 months) and about 67% were boys. Children without AD were age-matched, with the mean age of 60.25 ± 37.71 months (range 5–132 months).

Three mothers in each group reported having had AD in the past. The mean duration of AD in children was 43.68 months, with large differences in the duration of the disease. According to the SCORAD index, most of the children had moderate AD (52%), followed by severe (35%). Itch was permanently present in every child with AD, with most of the children (54%) experiencing severe itch according to the NRS assessment.

The children's AD had a negative impact on various aspects of their mothers' wellbeing and QoL. Mothers of children with AD reported higher levels of perceived stress compared to the control group ($p < 0.001$). Sixty-seven percent of mothers in the study group and 44% in the control group had co-existing insomnia. Also, 58 and 50% of mothers of children with AD reported symptoms of anxiety and depression, respectively (HADS A and HADS $D \geq 8$), whereas among controls, the proportions were 11.5% and almost 8%, respectively. Between-group differences in HADS scores are statistically significant ($p < 0.001$).

The correlations between the severity of the children's AD, the duration of the disease, the intensity of itch and the psychosocial functioning of their mothers are presented in Table 2. The severity of AD in children (SCORAD) correlated significantly with the mothers' FDLQI ($\rho_s = 0.38$, $p < 0.001$), PSS-10 ($\rho_s = 0.26$, $p = 0.02$), and AIS ($\rho_s = 0.27$, $p = 0.017$) scores but not with their HADS A and HADS D scores. Similarly, statistically significant correlations were found between the severity of itch (NRS) and the FDLQI ($\rho_s = 0.43$, $p < 0.001$), AIS ($\rho_s = 0.33$, $p = 0.002$), and PSS 10 ($\rho_s = 0.32$, $p = 0.003$) scores but not with symptoms of anxiety (HADS A) and depression (HADS D).

Although the duration of the disease did not correlate with the HADS scores, we found that mothers of children with AD presented significantly higher HADS scores when the duration of the disease was longer than 6 months. The scores are presented in Table 3.

4. Discussion

Our results indicate that the severity of AD and pruritus in children affects various aspects of the psychosocial functioning of their mothers. AD is a burdensome disease for the families of the affected children, and caregivers, in particular, report higher levels of stress than those of children not affected by this disease (23, 24). Mothers are most often the primary caregivers of children with AD (25), and the severity of the illness has a greater impact on the QoL of mothers than of fathers (12, 25). The QoL impairment of the mothers in our study was similar to that reported by others (12, 25),

TABLE 2 Correlation between the parameters of the children's atopic dermatitis and the psychosocial functioning of their mothers.

	SCORAD ρ_s (p-value)	Itch NRS ρ_s (p-value)	Disease duration ρ_s (p-value)
FDLQI	0.38 (<0.001*)	0.43 (<0.001*)	0.33 (0.002*)
PSS 10	0.26 (0.021*)	0.32 (0.003*)	0.11 (0.293)
AIS	0.38 (0.017*)	0.33 (0.002*)	0.10 (0.377)
HADS A	0.11 (0.32)	0.17 (0.131)	0.20 (0.072)
HADS D	0.13 (0.24)	−0.03 (0.796)	0.17 (0.130)

ρ_s: Spearman's rho; *$p < 0.05$; SCORAD, scoring of atopic dermatitis; NRS, numerical rating scale; FDLQI, Family Dermatology Life Quality Index; PSS-10, Perceived Stress Scale; AIS, Athens Insomnia Scale; HADS A, Hospital Anxiety and Depression Scale, Subscale Anxiety; HADS D, Hospital Anxiety and Depression Scale, Subscale Depression.

TABLE 3 Results from the Mann–Whitney U-test comparing the HADS scores of mothers whose children had had atopic dermatitis for less than 6 months vs. longer than 6 months.

	Group	N	Mean	SD	U	P-value
HADS A	<6 months	30	7.80	4.23		
	>6 months	56	9.82	4.71	622.00	0.024*
HADS D	<6 months	29	6.17	3.78		
	>6 months	56	7.95	4.21	604.50	0.027*

HADS A, Hospital Anxiety and Depression Scale, Subscale Anxiety; HADS D, Hospital Anxiety and Depression Scale, Subscale Depression, N, number of mothers, SD, standard deviation, U, Mann–Whitney U-test value; *$p < 0.05$.

as was their level of perceived stress (25). Our results suggest that the mothers of children with AD have a lower QoL than the caregivers of children with other pediatric dermatoses, including epidermolysis bullosa (26), psoriasis (27), vitiligo (28), and alopecia areata (29).

The mothers' QoL impairment and level of perceived stress had a significant positive correlation with the severity of AD in their children, which is in agreement with data reported by other authors (25, 30–32). In our study, the QoL was the only psychosocial parameter of the mothers that was correlated with disease duration, suggesting a cumulative negative effect. Interestingly, some have reported that the higher stress in the mother is related to coping mechanisms and family structure rather than to the severity of the disease (24, 33).

In our study insomnia affected a significant percentage of mothers in both the study and the control groups. Several studies documented that sleep in women may be negatively affected by biological, personal and environmental variables (e.g., hormonal changes in female reproductive cycle, life stressors, use of stimulant medications) (34). In women who are mothers insomnia may be also associated with post-partum period, breastfeeding, child sleep patterns and disturbances, and maternal distress of caring for a child (35). Additionally having a child with disease is another important factor of sleep problems (35). We observed a positive correlation between the severity of AD and sleep disturbances in the mothers, similar to what has been reported by others (6, 36). The severity of AD is associated with poor quality of sleep in both the parents and the affected children (6). One reason for this is that the more severe AD, the more severe itch is reported. Itch is the most prominent symptom of AD and has a significant detrimental effect on the patient's QoL. It generally worsens at night and is responsible for a diminished quality of sleep in patients. In our study, itch was universally present, and most of the children experienced severe itch. Scratching or rubbing the skin indicates the child's suffering. This may evoke helplessness, distress and irritation in the mothers, who try to prevent the child from scratching eczema (24).

Indeed, we observed that the more severe the itch, the greater the QoL impairment, severity of insomnia, and perceived stress of the mothers. To the best of our knowledge, this is the first study that comprehensively presents the relationship between atopic itch in children and functional impairment of their mothers. Loss of sleep is particularly troublesome in the mothers, since they are also in charge of many other normal parenting activities besides taking care of their child's AD treatment. To cope with the increased level of itch at night, parents of children with AD often develop shift-sleeping or co-sleeping strategies (2, 6). However, both of these strategies are doubtful. Shift-sleeping is associated with numerous health risks, including diabetes, cardiovascular disease (2), and motor and executive function deterioration. Co-sleeping, on the other hand, leads to unhappiness and increased level of stress in the parents (6).

Others, however, have found that the loss of sleep in the mothers of children with AD is not associated with the child's sleep disturbances (34). Research in other pediatric chronic illnesses suggest that the sleep disturbances in the caregivers may be related to their stress and anxiety about their child's illness (36). Moore et al. found that parents of children with AD lost more sleep than parents of children with asthma, and the severity of sleep disturbance was directly correlated with anxiety and depression in the mothers (7). In our study, half of the mothers had symptoms of anxiety and depression, and mothers with children that had had AD for longer than 6 months reported more severe symptoms, which might arise from feelings of guilt or pressure put upon the mothers (32).

Many studies have shown that structured educational programs reduce the severity of AD, parental stress and anxiety, as well as improve the quality of family life and parental disease management (37–39). Although educational programs are recommended in recent guidelines, no consensus has been reached on the form and content (40). Educational strategies and psychological support programs should be developed and used along with conventional therapy (41). Stepped care model that monitors and delivers interventions depending on the level of parental distress or needs could also be beneficial for both parents and patients (42). In some countries, e.g., Germany and the United Kingdom, "atopic schools" with multi-disciplinary teams (including clinicians and psychologists) that offer patient education are becoming increasingly popular (41). In Poland, such centers are still lacking, which might have influenced the mothers' psychological status.

Our study has a few limitations. It was conducted at a single center in Poland, which limits the generalization of the results to other populations, including those receiving better education about AD. Mothers were recruited from a hospital-based dermatology ward where more severe cases of eczema are more prevalent, and this may also limit the generalization of our findings. Furthermore, children without AD were not sex-matched to those with AD. Additionally, we measured the intensity of itch with the NRS scale, which may not accurately detect the children's pruritus because their mothers filled in the questionnaire on their behalf. Although it is a valid and widely used instrument to asses pruritus in children, results are subjective and dependent on personal interpretation. However, no single method has been recognized as a gold standard to objectively assess itch intensity in the pediatric population in clinical trials (16).

To summarize, QoL impairment, sleep disturbances, and the perceived level of stress in the mothers of children with AD are correlated with the severity of AD and atopic itch. Furthermore, a prolonged illness can aggravate symptoms of anxiety and depression in the mothers. Mothers are often responsible for the successful treatment of AD in their children by ensuring adherence to medical recommendations and supervising children unable to independently implement a multi-element therapeutic process. The management of children with AD should include effective reduction of pruritus in children, screening for functional impairment of their mothers and the provision of psychological support for them to ensure long-term treatment adherence and prevent further consequences of the disease. More attention should be directed to the standardization of stepped care interventions addressing factors resulting in the impaired functioning of mothers. These interventions should consist of education, training in stress-coping strategies, pharmacological and psychological itch management techniques, supportive groups, and regular mental health support to prevent anxiety and depression.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by the Bioethics Committee of the Medical University of Łódź. Written informed consent to participate in this study was provided by the participants or their legal guardian/next of kin.

Author contributions

AKK and AZ-J: conceptualization, methodology, and funding acquisition. AKK: validation, investigation, writing—original draft preparation, visualization, and project administration. BT and AKK: formal analysis. AKK, AK, JN, and AL: resources. AKK and BT: data curation. BT, AZ-J, AL, JN, and AK: writing—review and editing. AZ-J: supervision. All authors have read and approved the published version of the manuscript, guarantee the integrity, and accuracy of this study.

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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.

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Reducing scratching behavior in atopic dermatitis patients using the EMDR treatment protocol for urge: A pilot study

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Background: Itch, and thereby the scratching behavior, is a common complaint in atopic dermatitis. Scratching damages the skin, which in turn worsens the itch. This itch-scratch cycle perpetuates the skin condition and has a major impact on the patient's quality of life. In addition to pharmacological treatment, psychological interventions show promising results in reducing scratching behavior.

Objectives: To investigate the effect of treatment according the EMDR treatment protocol for urge on scratching behavior of atopic dermatitis patients in a controlled study.

Methods: This study applies a multiple baseline across subjects design. Six patients were randomly allocated to different baseline lengths and all of them started registration of scratching behavior at the same day, using a mobile phone application. Nocturnal scratching was registered by a smart watch application. The total study duration was 46 days and was equal for all patients. Treatment consisted of two sessions using the EMDR treatment protocol for urge. Furthermore, standardized measures were used to assess disease activity, quality of life, and self-control. The nonoverlap of all pairs effect size was calculated for the daily measure data.

Results: One patient dropped out. Visual inspection suggests that the scratching behavior decreased over time in all patients. Furthermore, a moderate effect size of the treatment is found. During the baseline phase, scratching behavior fluctuated considerably and showed a slight negative trend. Outcomes of disease activity decreased over time and patients' self-control and quality of life improved after treatment. Nocturnal scratching behavior did not change after the intervention.

Conclusion: The results of the visual analysis of day time scratching behavior, disease activity, quality of life, and self-control seem promising. These findings pave the way for future research into the effect of the new intervention on other skin conditions suffering from scratching behavior, such as prurigo nodularis.

KEYWORDS

atopic dermatitis, itch, scratching, Eye Movement Desensitization and Reprocessing (EMDR), urge, DEP

Introduction

Atopic dermatitis (AD) occurs in ∼1 to 10 % of all adults (1, 2) and is characterized by chronic inflammation of the skin. Skin inflammation results in itch, which results in scratching, and a negative feedback loop causing worsening of the skin condition. Itch has been found to drive the burden of AD, as it causes sleeping problems and is related to reports of pain, anxiety and depression (3). Mental health scores for AD patients were described lower than those of patients with other chronic health conditions such as diabetes and heart diseases (4). The disease and the more or less continuous itch severely impact patients' daily and working lives, and their health-related quality of life (3, 5), and asks for a multidisciplinary approach (6).

Besides pharmacological treatment, psychological interventions that target scratching behavior show significant ameliorating effects on itching intensity and scratching (7, 8). Psychological treatments for scratching behavior are based on 'self-control procedures' and 'habit reversal'. More recent, novel types of treatment to reduce scratching behavior in AD patients appear to be effective, such as internet-delivered and exposure-based cognitive behavioral therapy (9, 10) and a self-care intervention without therapist support (11).

The psychological intervention to be investigated in this study is the EMDR treatment protocol for urge (*Drang EMDR Protocol*, DEP; Doeksen, 2018) (12), which draws on elements of Eye Movement Desensitization and Reprocessing (EMDR) therapy, cognitive behavioral therapy, and hypnotherapy. In the current treatment, not the full EMDR procedure is applied, but only the EMD-part—that is the desensitization part. Desensitization aims at the "fading out" or "losing urge" for the behavior that is longed for, in this case the scratching (13). Patients are allowed to perform the scratching in imagination, while at the same time the working memory is being taxed. The use of EMDR to alter addictive behavior has been previously studied by Popky (14). In 2005, Popky introduced an Urge Reduction Protocol for Addictions and Dysfunctional Behaviors (DeTUR). DeTUR consists of multiple steps, including positive goal setting, and the identification and desensitization of triggers of the unwanted behavior. Moreover, clients learn to use the technique at home. DeTUR was shown to be effective in reducing unwanted behavior in multiple case studies in clients with substance use disorders, eating disorders and trichotillomania. Furthermore, the DEP treatment protocol draws on elements of cognitive behavior therapy, as self-registration of behavior and homework assignments are core elements of treatment. Finally, elements of hypnotherapy are incorporated in this treatment, with respect to the interpretation to perceive the treated skin spots—that does (no longer) evokes the urge to scratch—as "calm and white." This protocol turned out to be successful in a number of individual treatments (12), but the intervention has not been subject of scientific research yet. Therefore, we aim to investigate the effects of this intervention in a controlled study.

Materials and methods

Participants

Patients with a confirmed diagnosis of AD and systemic immunosuppressive treatment were included. Only patients with stable disease activity, suffering from persistent and frequent scratching behavior, no successful response to care as usual, and sufficiently motivated to take part in a new intervention aimed at behavior change, were eligible for study participation. Patients were invited to participate in the study by their treating dermatologist. All patients signed informed consent. The study was approved by the medical scientific research Ethical Committee of the Erasmus University Medical Center (reference number MEC-2020-0127).

Study design and intervention

This pilot study applies a multiple baseline across subjects design, consisting of three phases: baseline, intervention and follow-up (see Figure 1, and the paragraph below). The total study duration was 46 days and was equal for all patients. All of them started registration of scratching behavior at the same day. Six participants were randomly allocated to different baseline lengths, to determine whether any observed changes in scratching behavior are due to the intervention or simply the passage of time. This randomization was not blinded, as patients and researchers knew when the treatment started. Pairs of two patients were randomly selected and were assigned to one of three possible starting weeks, with a randomly selected weekday for each patient to start treatment. Randomization was performed with a randomization application, in which the possible starting points for all six patients were entered (15). The intervention phase duration was 10 days for all patients, and consisted of two treatment sessions in the setting of the psychiatry outpatient clinic of the Erasmus University Medical Center and two additional phone calls. The intervention phase was followed by a follow-up phase.

Baseline phase: Patients were invited for a first meeting after signing informed consent. During this appointment they were instructed regarding the daily registration, the T0 questionnaires were administered, and the disease activity was evaluated by a dermatologist. The mobile phone application for daily registration of scratching behavior was installed on patients' mobile phone and explained. A smartwatch and mobile phone to pair the watch for night-registrations were handed out. During baseline, patients registered scratching behavior, but did not receive treatment yet.

Intervention phase: The EMDR treatment protocol for urge (*Drang EMDR Protocol*, DEP; Supplementary material S1) was performed by a trained EMDR Europe Accredited Practitioner supervised by a EMDR Europe Accredited Consultant, who is also the developer of the protocol (12). The intervention consisted of two DEP treatment sessions of maximum 90 min, which took place in two consecutive weeks (one session per week). Within 3 days after each session, participants were called by the therapist to discuss potential difficulties in applying the intervention at

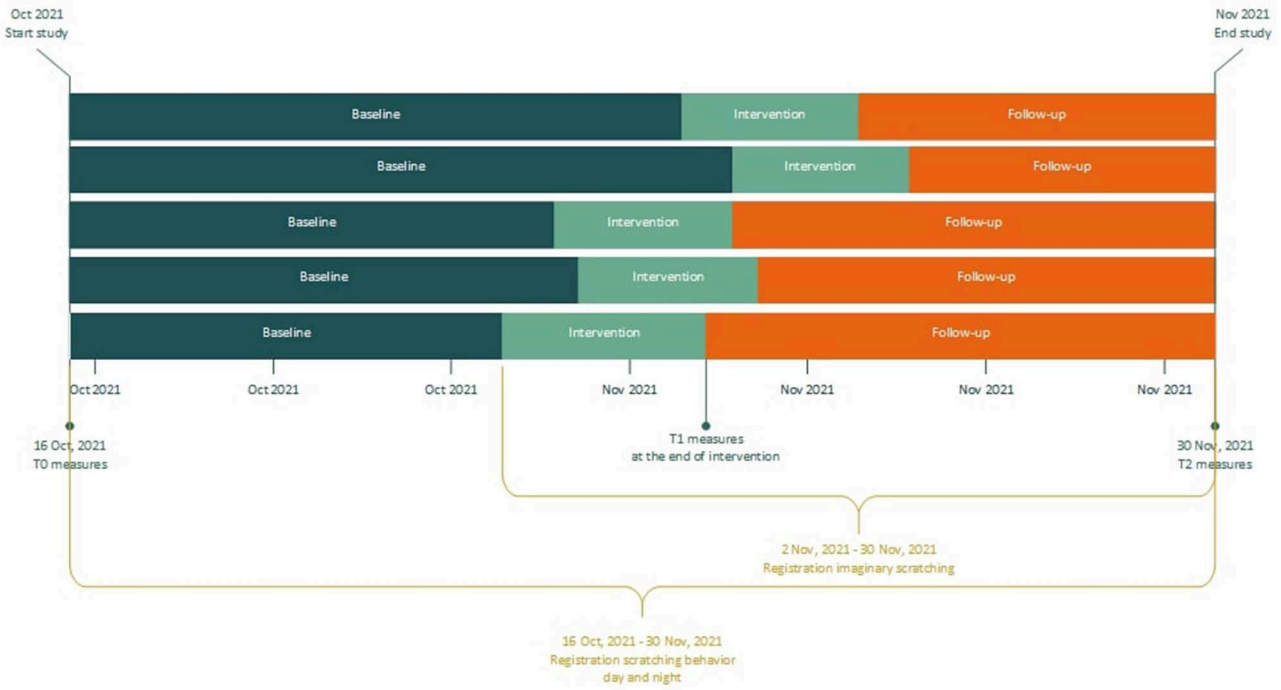

FIGURE 1
Flowchart of study design.

home. At the end of the intervention phase, questionnaires were administered again for T1.

Follow-up phase: The follow-up phase commenced after the intervention phase, and consisted of at home practice of the techniques acquired during the intervention phase. At the end of the follow-up phase, patients filled out the questionnaires for the third and last time. This last measurement took place in the hospital, as their skin was evaluated again by the dermatologist. In addition, the course of the study and the intervention were evaluated together with the research assistant, and the smartwatch and mobile phone were handed in.

During the study, patients were occasionally called by the research assistant to check if technical problems occurred, and to resolve registration issues early. The contact details of this researcher were given to the patients, so that patients had the opportunity to easily contact the researcher themselves in case of technical problems.

Measures

In multiple baseline designs it is common to work with "target measures" and "standardized measures". Target measures are aimed at frequent (often daily) measuring of the complaints or behavior that is to be altered ("targeted") by the intervention under study. Standardized measures are well- validated outcome measures, that are applied at set times during the study. The aim of applying standardized measures is to get an overall idea of respondents' outcomes on well-known measures.

Target measures

Day time scratching

Frequency and duration of actual scratching behavior were measured on a daily basis. A mobile telephone application was designed for this study to register the actual scratching behavior. Each time a patient had scratched, he had to record the duration of scratching in a "hit list." Duration was classified into seven categories (<1 min; 1–3 min; 4–5 min; 6–10 min; 11–15 min; 16–30 min; >30 min). During data analysis this was reduced to 3 categories (<1 min "short"; 1–3 min "medium"; >3 min "long"). The "day time scratching" outcome was calculated by multiplying the number of scratching episodes with duration (1 = short, 2 = medium, and 3 = long). For example, if a patient had eight short, three medium and two long scratching episodes during a day, the sum score was 20 (8 + 6 + 6).

Imaginary scratching

Each time a patient applied the learned intervention at home, he had to record the duration of the imaginary scratching. The number of these episodes and their duration were also registered with the mobile phone app.

Nocturnal scratching

Duration and intensity of scratching behavior during the night was registered by a smart watch application, developed by the Center for Human Drug Research (CHDR) (16). The outcome was the sum of the episodes of scratching, which were described as the intensity multiplied with the duration of the episode.

Standardized measures

Disease activity, measure to be filled out by dermatologist at T0 and T2: Eczema Area and Severity Index (EASI) (17). A validated scoring system that grades the physical signs of atopic dermatitis/eczema.

Three Quality of Life measures, at T0, T1 and T2: (1) the Patient-Oriented Eczema Measure (POEM) is a self-report questionnaire consisting of 7 items to be scored on a 4-point Likert scale (18); (2) The SKINDEX-17 is a dermatology-specific health-related quality of life (HRQOL) instrument. It consists of 17 items to be scored on a 5-point Likert scale. The instrument has two subscales: psychosocial impact and impact of symptoms (19); (3) The EQ-5D-5L measures health-related quality of life. It is a generic instrument that can be used in a wide range of health conditions and treatments. The EQ-5D-5L consists of a descriptive system and the EQ VAS. The descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The EQ VAS records the patient's self-rated health on a vertical visual analog scale (20).

Self-Control, at T0, T1 and T2: The Self-Control Cognition Questionnaire, Dutch: Zelfcontrole Cognitie Vragenlijst (ZCCL). The ZCCL is an 11-item self-report questionnaire measuring perceived self-control. There are two subscales: 'positive reward' (of the unwanted behavior) and 'difficulty resisting'. Each item is scored on a 5-point Likert scale (21).

Statistical analysis

Day time scratching data is analyzed by visual inspection. Moreover, the nonoverlap of all pairs (NAP) effect size is calculated, using the computer program Shiny SCDA (Single-Case Data Analysis) (15, 22). NAP, which is an index of data overlap between phases in single-case research, depends on the expected direction of the treatment effect, in this case a reduction of the scratching behavior (23). NAP is defined in terms of all pair-wise comparisons between the data points in different phases. The Shiny application can compare only two phases. We therefore combined the intervention and follow-up phase and compared those combined phases with the baseline phase.

Standardized measures were analyzed using IBM SPSS Statistics for Windows, Version 28.0 was used (Armonk, NY: IBM Corp) and are presented as descriptives, as no statistical test can be performed to produce a reasonable estimation of any effect, give the low number of patients typical for this design.

Results

Participants

Six AD patients completed the baseline phase. One patient dropped out during the intervention phase for motivational reasons. Three males and two females successfully completed all three phases (mean age 39.3 years (*SD 11.5*) (Table 1). One patient experienced technical problems with the smart watch application. As a result, no data is available on this persons nocturnal scratching behavior.

TABLE 1 Patient characteristics.

Participant	Gender	Age (years)	EASI score at T0 (interpretation)
1	Male	41	34.8 (Severe)
2	Female	25	34.2 (Severe)
3	Male	39	22.2 (Severe)
4	Male	37	Drop out
5	Male	33	19.3 (Moderate)
6	Female	56	6.5 (Mild)

Target measures

Visual analysis of day time scratching

Figure 2 shows the plots of the individual patients. The vertical dotted lines represent the end of the baseline (A) and the start of the intervention phase (B). The horizontal lines represent the mean of scratching behavior for both phases. The visual inspection of the individual patterns in Figure 2 shows a decrease in the scratching behavior for all patients after starting with the intervention. In most patients the scratching behavior fluctuated heavily and a negative trend is already visible during the baseline phase. Please note that patient 5 underwent a change of medication during the intervention phase.

Effect size

A non-overlap of all pairs (NAP) effect size of 0.74 is found, which indicates a moderate effect of the treatment for this type of study design.

Nocturnal scratching

Figure 3 shows the sum of the duration and intensity of nocturnal scratching behavior for all patients, measured with the smart watch application. Due to technical problems with the smart watch application, the nocturnal scratching data of patient 3 is excluded from the figure. There appears to be no effect of the intervention on the nocturnal scratching behavior. There is a large spread, and no clear trend is visible over time.

Standardized measures

Table 2 shows the explorative analysis of the disease activity, quality of life and self-control measures of the five patients. The results indicate that the disease activity as determined by the dermatologist (EASI) decreased between T0 and T2. Quality of life measured with the POEM questionnaire shows a large decrease between T0 and T1, with a slight increase at T2. Dermatology-specific health-related quality of life measured with the SKINDEX-17 shows a U-curve for both subscales. Furthermore, the EQ-5D-5L index and VAS scores show an increase of quality of life over time. Both factors of self-control in scratching ("positive reward" and "difficulty resisting") decreased from T0 to T2.

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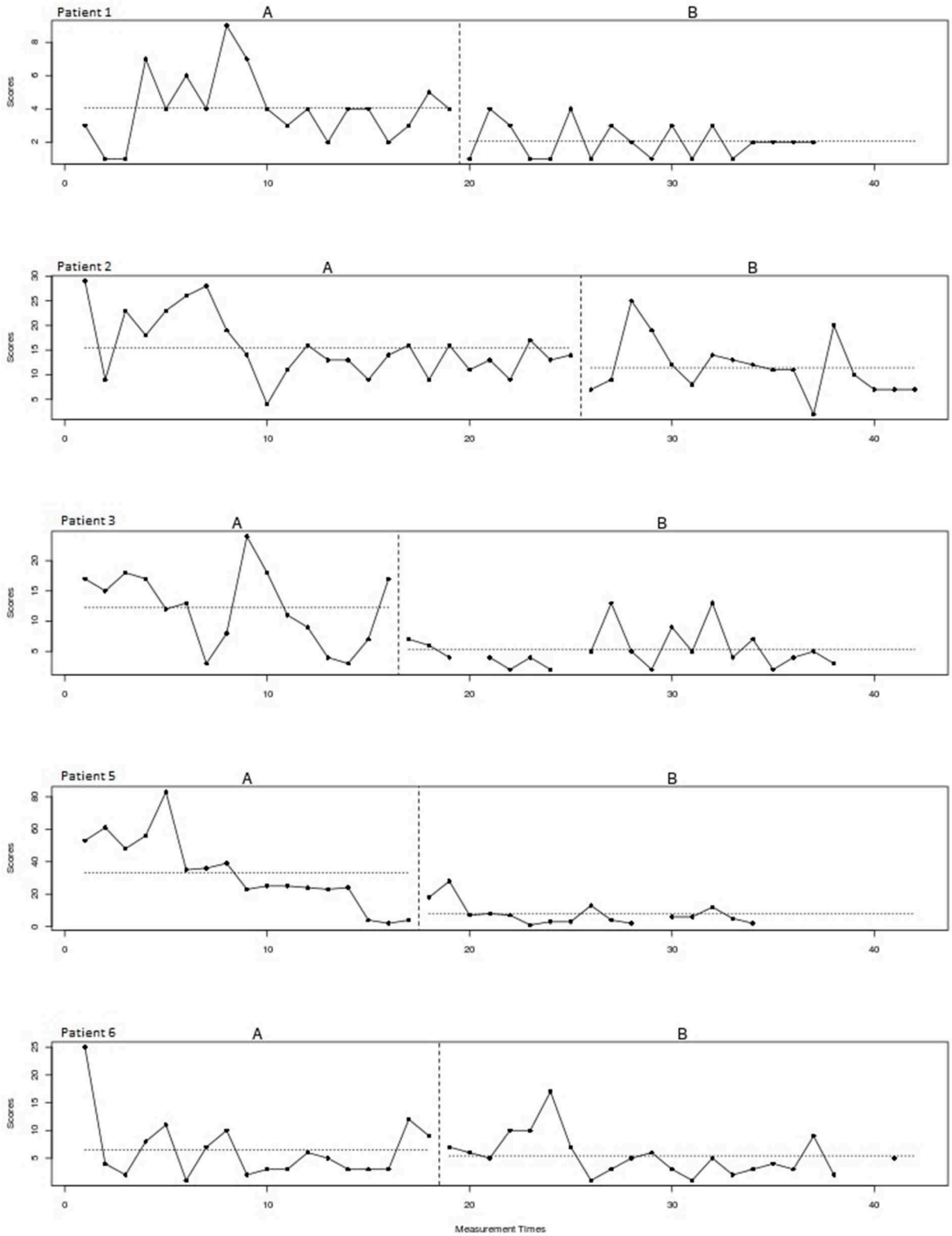

FIGURE 2
Scratching behavior of individual patients over time for the baseline **(A)** and intervention **(B)** phase.

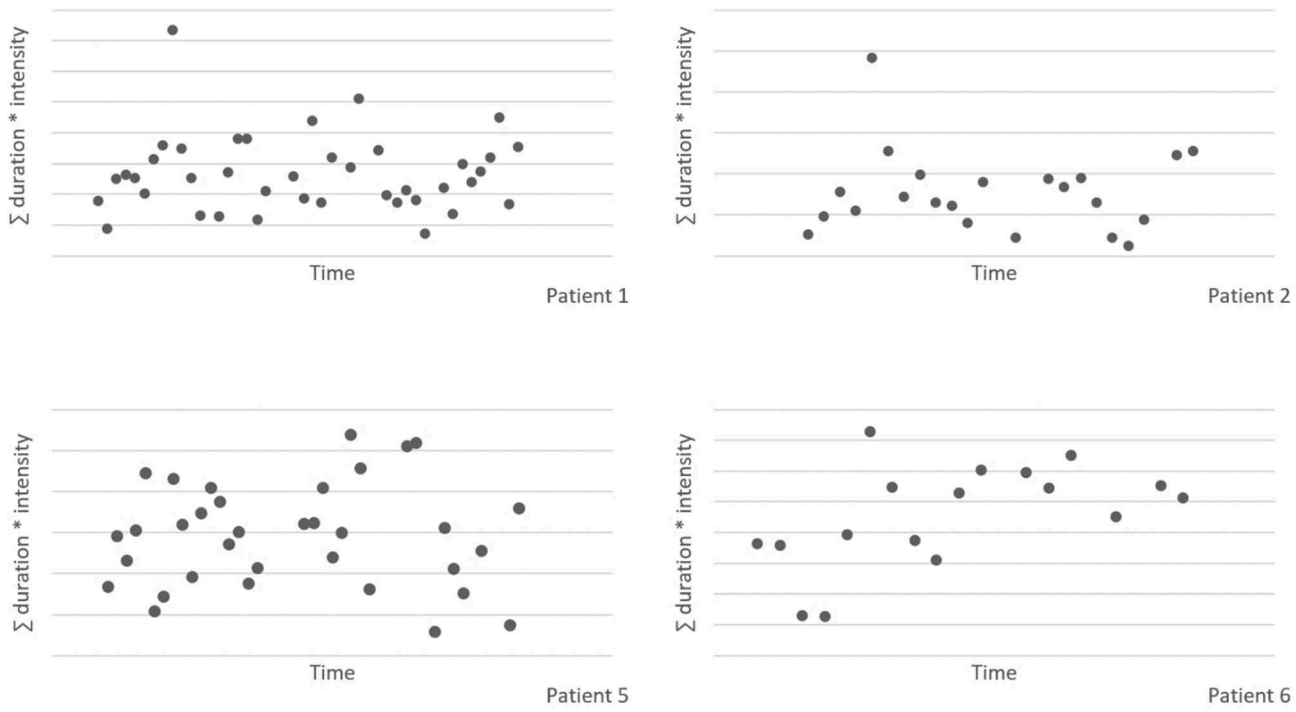

FIGURE 3
Nocturnal scratching behavior, measured with the smart watch application.

TABLE 2 Explorative analysis decease activity, quality of life and self-control.

Questionnaire*	Median (IQR)		
	T0	T1	T2
EASI	26.75 (24.95)		11.30 (8.35)
POEM	21.00 (9.25)	15.50 (9.25)	17.50 (11.50)
ZCCL "Positive reward"	8.00 (15.5)	7.50 (9.00)	6.00 (2.25)
ZCCL "Difficulty resisting"	16.00 (8.50)	12.50 (7.00)	10.00 (8.75)
Skindex-17 psychosocial	9.00 (5.50)	1.50 (1.75)	7.00 (7.00)
Skindex-17 symptoms	5.00 (1.50)	3.50 (3.25)	4.50 (1.00)
EQ-5D-5L index	0.82 (0.21)	0.83 (0.19)	0.91 (0.21)
EQ-5D-5L VAS	69.00 (17.00)	82.50 (9.00)	77.50 (20.00)

*Cut-off scores: EASI: 0 (clear); 0.1–1.0 (almost clear); 1.1-7.0 (mild); 7.1–21.0 (moderate); 21.1–50.0 (severe); 50.1–72.0 (very severe) POEM: 0–2 (clear/almost clear); 3-7 (mild); 8–16 (moderate); 17–24 (severe); 25–28 (very severe) ZCCL "Positive reward": range from 6 to 30 ZCCL "Difficulty resisting": range from 5 to 25 Skindex-17 Psychosocial: 0–4 (little impairment); 5–9 (moderate impairment); 10–24 (high impairment) Skindex-17 Symptoms: 0–4 (few); 5-10 (a lot) EQ-5D-5L index: range from 0 to 1 EQ-5D-5L VAS: range from 0 to 100.

Evaluation by the patients

During the evaluation of the course of the study and the intervention, all patients indicated that they planned to continue with the learned technique in the future. Registration of the scratching did elevate the awareness of this habitual behavior and was perceived to be helpful in reducing scratching behavior. A frequently mentioned limitation of the newly learned technique is that it is difficult to apply it during daily activities. While driving a car or attending a meeting, taxing the working memory is impossible or even dangerous. Moreover, the technique was perceived to be time consuming by some of the patients. Furthermore, patients tended to "re-design" the treatment following their own preferences: some focused more on the imaginary part, and others seemed to profit more from the taxing of working memory-part of the treatment.

Discussion

This pilot is the first study to investigate the use of the EMDR treatment protocol for urge for scratching behavior in patients with AD. Visual analysis of the data showed a decrease of scratching behavior over time in all patients. During the baseline phase, scratching behavior fluctuated heavily and already showed a slight negative trend. After receiving treatment and during follow-up, all patients showed less scratching behavior compared to the baseline registration. The NAP effect size indicated a moderate effect of the intervention. Outcomes of disease activity decreased over time and patients' self-control and quality of life improved after treatment. Furthermore, nocturnal scratching behavior did not differ after the intervention, compared to the baseline phase.

So far, little is known about the working mechanisms of the EMDR treatment protocol for urge. Initially, the effectiveness of this method in reducing scratching behavior was found by chance (12). After additional single case successes, the curiosity about the effect further rose. To learn more about possible working

mechanisms, it may be useful to draw parallels with other types of unwanted behavior. For example, the use of EMDR in addictive behavior has been subject of studies in the past two decades, in smaller and larger studies, with varying results (24–26). Scratching behavior and addiction share the same sensory mechanisms and neurobiological foundations (27, 28), which makes addiction an interesting starting point in the search for explanations. Scratching is often experienced as pleasurable and can have a rewarding effect (29, 30). However, when the itch is chronic, for example in the case of AD, an itch-scratch cycle can develop: scratching provides relief in the short term, but the damage done by scratching can aggravate the itching in the long term. Also, the wounds created by scratching cause itch. This vicious circle, driven by the urge to scratch, resembles with drug addiction and share the same basic principles (31). First, scratching/intoxication serves as a positive reinforcement (high/itch relief). Second, itch returns when the scratching stops. This corresponds to withdrawal symptoms when the drug is not administered. In the third and final stage, the person gets preoccupied with the itch/drug, which results in more scratching/drug use (32). In addition to similar fundamentals, the treatments of these disorders may also show similarities (33). Most addiction-focused EMDR approaches focus on mitigating craving. Since craving in addiction shows much resemblance with the urge to scratch, the crux for successful treatment may lie in that the treatment explicitly addresses the physical component of the (addictive) behavior, for instance, reaching for a beer/cigarette or moving the scratching hand toward the skin. In this respect, the imaginary scratching shows similarities with the EMDR-technique of "cognitive interweaves," as patients are allowed to perform the scratching in imagination, while at the same time working memory is being taxed.

A notable observation of the results is that the downward trend of the registered scratching behavior already started during the baseline phase. In other words, even before patients started with the intervention, scratching behavior already decreased. This can possibly be explained by the effect of the registration and the associated openness to change. Previous research has shown that simply registering unwanted behavior can result in a decrease in the frequency of this behavior (34, 35).

Another remarkable finding is that the smartwatch measurements show no change in nocturnal scratching behavior, while the measurements during the day showed a decrease. A conceivable explanation for this is that the intervention targets the conscious scratching behavior, but that the unconscious—and therefore automatic—scratching during the night remains the same.

Furthermore, without knowledge of the study results, most patients indicated during the evaluation that they would continue to use the learned technique in the future. Despite the mentioned limitations in using imaginary scratching, patients are willing to invest time to focus on the intervention.

Strengths and limitations

This study is the first to investigate the effect of EMDR treatment protocol for urge on scratching behavior of AD patients in a controlled trial. To investigate this effect, high-tech methods are used to measure scratching behavior. This strength to use innovative techniques makes it possible to study all scratching episodes during day and night. However, using new high-tech measurements also entails risks. In practice, the use of the watch measurement did not always work properly.

An important limitation lies in the methodology, in particular the design of the multiple baseline. First, the Shiny application can compare only two phases. We therefore had to combine the intervention and follow-up phase. As a result, possible short-term and long-term effects of the intervention cannot be compared. Second, during the baseline, registered scratching behavior fluctuated heavily in all patients. By extending the baseline, patients are given more time to get used to the registration, which may result in a more stable course. This may result in a more reliable statements about whether the decrease of scratching behavior is attributable to the treatment. Furthermore, one patient underwent a change of medication during the intervention phase, which may have affected the results.

Conclusion

Possible effects of treatment according to the EMDR treatment protocol for urge most likely present themselves in daily scratching, and not nocturnal scratching. The results of the visual analysis of day time scratching behavior, disease activity, quality of life, and self-control seem promising. These findings pave the way for future research into the effect of the new intervention on atopic dermatitis and other skin conditions suffering from scratching behavior, such as prurigo nodularis.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Medical Scientific Research Ethical Committee of the Erasmus University Medical Center (reference number MEC-2020-0127). The patients/participants provided their written informed consent to participate in this study.

Author contributions

RW-S, DD, and LK conceived and designed the study. RW-S and DH selected possible patients. MV and LK acquired, analyzed, interpreted the data, and wrote the draft. JB supervised the project. All authors critically read, reviewed and revised the manuscript, and approved the final manuscript before submission.

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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.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2023.1101935/full#supplementary-material

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Is stress related to itch in German students? Results of an online survey

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Introduction: German students report to be more stressed than the general population. Highly stressed students from other countries (United States, Australia, Saudi-Arabia) were found to have more skin symptoms, including itch, than lowly stressed students. The current study aimed to assess whether itch is associated with stress in a larger sample of German students.

Methods: 838 students (3.2% of all invited students) took part in the questionnaire based study and filled in the Perceived Stress Questionnaire as well as a modified version of the Self-Reported Skin Questionnaire. Students were categorized into highly (HSS) and lowly stressed students (LSS) by determination of the 25th and 75th percentile.

Results: Itch occurred significantly more often in HSS compared to LSS (OR=3.41 (2.17–5.35)). In addition, itch intensity was significantly related to perceived stress.

Discussion: These findings not only highlight the importance of offering stress management trainings also to students in Germany in order to minimize itch, but also encourage future research on stress and itch in certain student subgroups.

KEYWORDS

pruritus, skin symptoms, perceived stress, students, self report

Background

Studying often implies having to cope with a variety of stressors. One year after having started university, students report a decline in physical and psychological well-being, especially due to high study demands, difficult time management or low social support (1). Moreover, students name relationship stressors, trying to fulfill expectations from self and others or lack of resources (e.g., lack of time, money or support) as stressors they have to face (2).

Perceived stress differs in students from different countries. In one study, a greater proportion of medical students from a Middle Eastern country (not named) reported stress compared to US medical students (75% vs. 58%) (3). Eventhough in Germany studying is less expensive than in other countries like the US, German students (in this case first year medical students) still report high amounts of stress compared to a reference sample of the general population (4). Studies showed that 21–36% of German students suffer from high or very high levels of stress (5, 6). 25% of the students feel clearly overstrained (6). Kötter and Voltmer (7) assessed medical students' stress levels and their physical and psychological health status. The study showed that highly stressed students in comparison to lowly stressed students had

significantly worse physical and psychological health, characterized, e.g., by lower physical or social functioning.

Thus, an association between health and stress has been shown for students. Regarding dermatological conditions, relationships between stress and the intensity of various skin diseases have already been reported (8–10). An association between stress and itch has been shown in patients with skin diseases like psoriasis (11, 12) and atopic dermatitis (13, 14), but also in the general population (15).

So far, three studies, conducted in the US (16), Australia (17) and Saudi Arabia (18), investigated the relationship between stress and skin symptoms in student populations. The Saudi-Arabian study (18) included medical students only. These studies found that students with high perceived stress levels reported to have itch significantly more often than students with low perceived stress levels.

The present study aims to replicate these findings in a sample of German students. We hypothesize that also in German students we will find a positive relationship between reported stress levels and the occurrence of itch. A second aim of the study is to investigate whether stress is also related to other skin symptoms in German students.

Materials and methods

All persons studying at the Justus-Liebig University Gießen in the summer semester of 2015 ($n = 26{,}060$) were made aware of this questionnaire study *via* three circular emails. The first email was sent around in mid May, while the second and third emails were sent around three and 6 days later, respectively. Thus, data collection was finished within 7 days. Students were instructed to only participate once. They were informed that the aim of this study was to investigate the relationship between stress and skin symptoms in German students and further that it would take approximately 10 min to participate. Moreover, they were told that they had the chance to win one of three vouchers after participation. Participation in the raffle was voluntary. The email contained a link to the questionnaire.

Of all contacted students, 838 (3,2%) agreed to participate. 44 students were excluded due to incomplete responses, unspecified gender or being younger than 18 or older than 30 years. Electronic informed consent was obtained from all participants. Before the beginning of the study it was approved by the Ethics committee of the Medical Faculty of the Justus-Liebig-University Giessen.

Measures

Stress

To assess the students' perceived stress levels we used the German version of the Perceived Stress Questionnaire (PSQ) (19). The PSQ consists of 30 items, which need to be answered on a scale from 1–4 (1: almost never, 2: sometimes, 3: often, and 4: usually). This instrument measures self-reported psychological stress within the last 4 weeks. It comprises seven subscales, namely harassment (example item: "You are under pressure from other people"), overload ("You have too many things to do"), irritability ("You are irritable or grouchy"), lack of joy ("You feel lonely or isolated"), fatigue (example item: "You feel tired"), worries (example item: "You are afraid for the future ") and tension (example item: "You have trouble relaxing"). A PSQ-raw score can be calculated by inverting the items 1,7,10,13,17,21,25,29 and summing up the values for all 30 items afterwards. This raw score is then inserted in the formula: (raw score – 30)/90 in order to receive the PSQ index. This can range from 0–1 with 0 indicating no stress and 1 indicating highest levels of stress. In the validation sample, persons scoring ≤0.3 fell into the lowest quartile, while persons with scores ≥0.52 fell into the highest quartile (19). We decided not to use these cut-off-values, but to calculate the 25th and 75th percentile for our sample instead, because this approach has also been chosen in the former US-, Australian and Saudi-Arabian studies. In our sample, students scoring ≤0.3 were classified as lowly stressed students and students scoring ≥0.57 were regarded as highly stressed students.

Itch and other skin symptoms

To assess itch and other skin symptoms, we applied a modified version of the Self-Reported Skin Questionnaire (SRSQ) (20). The SRSQ measures the occurrence and extent of different skin symptoms during the last 7 days. In this study we extended this time period to 4 weeks in order to align it with the time period of the PSQ. The SRSQ items were answered on a 4-point scale with 1 representing "no complaints," 2 "a little," 3 "quite a lot" and 4 "very much." For further analyses we dichotomized these answers as to whether itch and other skin complaints did or did not occur in the students. This gave us the opportunity of comparing students stating they had "no complaints" to students who fell into the other three answer categories.

Itch intensity

In addition, we asked the students to rate their itch intensity during the last 4 weeks on a Visual Analog Scale (VAS), ranging from 0 ("no itch at all") to 10 ("worst itch ever").

Statistics

Data analyses were conducted using SPSS 24. For the main analysis participants were grouped into lowly stressed students (LSS) and highly stressed students (HSS) by determination of the 25th and 75th percentile of the PSQ index. Students in between, who were neither categorized as lowly nor highly stressed, were regarded as moderately stressed. These were not included in the analysis. In order to compare LSS and HSS regarding sociodemographic variables and itch intensity we computed t-tests for independent groups in case of continuous variables and chi square-tests in case of nominal variables. Odds ratios and 95% confidence intervals were calculated in order to investigate whether skin symptoms, including itch, were more prevalent in HSS than in LSS. For further analysis of the relationship between itch and stress we determined the 25th and 75th percentile for all PSQ-subscales separately as well. Again, we calculated odds ratios and 95% confidence intervals.

Results

Sample characteristics

The final sample size comprised $n = 794$ students, of whom 659 (83%) were female. The mean age ± SD of the subjects was 23.1 ± 2.7 years. Of the total sample, 207 students were classified as LSS and 201 as HSS (one person with non-specified gender was excluded from this group). Gender distribution and age did not differ between HSS and LSS ($p > 0.05$).

Relationship between stress and itch

HSS significantly more often reported to have itch compared to LSS ($p < 0.001$, OR 3.41 (95% CI 2.17–5.35)). In addition, itch intensity in HSS was significantly higher than in LSS ($p < 0.05$; 3.02 ± 2.46 vs. 1.51 ± 1.79). Further analyses revealed that students with high scores on the PSQ-subscales more often reported itch than students with low scores on the subscales (all $p < 0.05$). The results are shown in Table 1.

Relationship between stress and skin complaints

HSS reported oily, waxy or flaky patches on the scalp, scaly skin, nail-biting (onychophagia), itchy rashes on hands, hair pulling (trichotillomania), other rashes on face, dry/sore rashes, pimples and warts more often than LSS (all $p < 0.05$). For more details see Table 2.

Discussion

The aim of the present study was to analyze whether self-rated stress and itch are related in a sample of German university students. The study revealed that HSS more often reported to have itch compared to LSS. It is striking that in this study, the prevalence of itch was very high with 81.6% in HSS and 56.5% in LSS. Other studies found a prevalence of 8.4% or 25.4% in the general population (21, 22). The major difference between these studies and the current study can possibly be explained by the different time intervals for which itch was assessed. In our study, we asked students whether they had itch during the last month, while the time intervals in the other studies were one week (21) or current moment (22).

Similar results were noted for the PSQ-subscales: Students with high scores regarding harassment, overload, irritability, lack of joy, fatigue, worries and tension more often had itch than students with low scores on these subscales. In addition, itch intensity, measured *via* VAS, was related to self-rated stress with significantly higher scores in the group of HSS compared to LSS.

Our results regarding the relationship between stress and itch are not only in line with the results of previous studies from the United States (16), Australia (17) and Saudi Arabia (18), but also with several former investigations which found relationships between stress and itch in people with skin diseases (e.g. 8) and the general population (15). Besides the connection between stress and itch, we also found that HSS compared to LSS more often reported a variety of other skin complaints of which the majority is itchy, such as oily, waxy or flaky patches on the scalp. These symptoms are suggestive of seborrheic dermatitis that is often itchy and associated with stress (23). Also scaly skin, itchy rashes

TABLE 1 Percentage of persons who reported itch in the group of highly stressed students (HSS) and lowly stressed students (LSS).

Scale that was used to determine whether a person was highly or lowly stressed	% of HSS reporting itch	% of LSS reporting itch	OR (95 % CI)
PSQ-total score	81.6 %	56.5 %	3.41 (2.17–5.35)
Harrassment (S1)	76.9 %	56.3 %	2.57 (1.71–2.93)
Overload (S2)	74.8 %	63.3 %	1.73 (1.20–2.48)
Irritability (S3)	78.3 %	61.6 %	2.25 (1.52–3.33)
Lack of joy (S4)	81.8 %	56.8 %	3.41 (2.02–5.77)
Fatigue (S5)	80.4 %	55.4 %	3.31 (2.21–4.97)
Worries (S6)	80.4 %	59 %	2.85 (1.85–4.39)
Tension (S7)	78.2 %	56.9 %	2.72 (1.83–4.04)

OR, odds ratios; CI, confidence interval; S, subscale. Participants were grouped into LSS and HSS by determination of the 25th and 75th percentiles of the total PSQ-index as well as by determination of the 25th and 75th percentiles of the seven PSQ-subscales (S1-7).The third column represents corresponding OR for HSS vs LSS (95% confidence interval).

TABLE 2 Percentage of students who reported to have specific skin symptoms in the group of highly stressed students (HSS) and lowly stressed students (LSS).

Skin symptoms	% of HSS reporting to have specific symptoms	% of LSS reporting to have specific symptoms	OR (95 % CI)
Flaky patches on the scalp	54.2 %	30.0 %	2.90 (1.93 – 4.37)
Scaly skin	65.7 %	44.4 %	2.39 (1.60 – 3.57)
Nail-biting (Onychophagia)	36.8 %	26.6 %	1.61 (1.06 – 2.45)
Itchy rash on hands	38.3 %	15.9 %	3.27 (2.05 – 5.23)
Hair pulling (trichotillomania)	11.4 %	3.9 %	3.21 (1.40 – 7.37)
Other rashes on face	28.4 %	11.1 %	3.17 (1.86 – 5.39)
Dry/sore rash	43.3 %	26.1 %	2.16 (1.43 – 3.28)
Pimples	85.6 %	77.3 %	1.74 (1.05 – 5.56)
Warts	15.9 %	6.3 %	2.83 (1.44 – 5.56)

OR, odds ratios; CI, confidence interval. Students were regarded as HSS in case they had a PSQ total score falling into the highest quartile of the sample; students were regarded as LSS in case they had a PSQ total score falling into the lowest quartile of the sample. Illustrated are also corresponding OR for HSS vs LSS in PSQ total score (95% confidence interval).

on hands, hair pulling, other rashes on face and dry/ sore rashes were associated with stress. These findings are similar to reported associations between stress and the occurrence of different skin symptoms (24–27). Furthermore, it is important to note, that an exacerbation of itch can further worsen stress, leading to a vicious cycle of itching and scratching that significantly impairs patients' quality of life (28).

There are some limitations that need to be mentioned. A limitation of this study is the low response rate of only 3.2% which occurred eventhough many efforts (e.g., raffle of vouchers, short duration of the questionnaire) were made to increase it. A second limitation lies in the gender distribution as 83% of the participants were female. Thus, future studies should especially try to recruit non-female persons in order to receive a better picture of the relationship between stress and skin symptoms in males and persons with non-binary gender also. Moreover there may be some selection biases as it is possible that those students who pay more attention to their skin due to more itch and skin complaints as well as more students with high amounts of perceived stress particularly agreed to participate in the online survey. Another shortcoming is the time period to which the itch assessment as well as the assessment of the other skin symptoms refers. As we asked about the occurrence of itch and itch intensity within the last 4 weeks, we cannot control for a possible memory bias. It is possible that the reported itch differed from the itch that actually occurred during that time period. In line with this thought, a review (29) about memory for pain revealed quite an inconsistent picture regarding the comparison of patients' actual pain sensation and their reports on remembered pain sensation afterwards.

Nevertheless, our findings encourage the implementation of interventions that aim to lower students' stress levels and through that possibly the occurrence of itch and other skin symptoms. Previous studies demonstrated benefits of psychological interventions in people suffering from itch (30, 31) or the itchy skin disease psoriasis (32). Furthermore, studies investigating stress reducing interventions in university students particularly found reduced anxiety and psychological distress (33–35), mood disturbances (36) or better emotional adjustment (37) among students.

An interesting next step could be to examine whether a relationship between itch and stress occurs more often in certain study disciplines. According to a study by a German insurance company (38), veterinary medicine, agricultural sciences, nutritional sciences and computer sciences students seem to exhibit the highest stress levels, while students studying cultural sciences, linguistic, arts, teaching and sport sciences display the lowest stress levels. Future studies should also compare the relationship between students' stress levels and their skin symptoms in different countries as the relationships may differ in different environments and cultures.

Data availability statement

Data will be made available by the corresponding author upon reasonable request.

Ethics statement

The studies involving human participants were reviewed and approved by Ethics committee of the Medical Faculty of the Justus-Liebig-University Giessen. The ethics committee waived the requirement of written informed consent for participation.

Author contributions

StK: formal analysis (lead), investigation (equal), methodology (equal), project administration (support), visualization (lead), and writing – original draft (equal). JK: conceptualization (support), investigation (equal), methodology (support), project administration (support), and writing – review and editing (equal). SoK: conceptualization (support), investigation (lead), data acquisition (lead), and writing – review and editing (equal). UG and GY: conceptualization (support), methodology (support), and writing – review and editing (equal). CS: conceptualization (lead), formal analysis (support), methodology (equal), project administration (lead), supervision (lead), visualization (support), and writing – original draft (equal). All authors contributed to the article and approved the submitted version.

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.

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Appearance-related concerns in individuals with pathological skin picking—a comparison with individuals with dermatological conditions and skin-healthy controls

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Introduction: Pathological skin picking (PSP) is an excessive behavior which characterizes Skin Picking Disorder. Individuals repeatedly pick their skin and cause skin lesions, but are unable to control the behavior, which can cause severe distress. Visible self-inflicted skin lesions can additionally affect individuals with PSP due to emerging appearance-related concerns. However, these concerns and their role in PSP have hardly been studied, especially not in comparison with individuals with dermatological conditions and skin-healthy controls.

Methods: The present cross-sectional study (n=453, 83.9% female, 15.9% male, 0.2% diverse) aimed at analyzing appearance-related concerns and mental health outcomes between four groups: Individuals with PSP and dermatological conditions (SP/DC; n=83), PSP without dermatological conditions (SP; n=56), dermatological conditions without PSP (DC; n=176) and skin-healthy controls (SH, n=138). We compared questionnaire data on dysmorphic concerns, appearance-based rejection sensitivity, and body dysmorphic symptoms, as well as PSP-symptoms and mental health outcomes (depression, anxiety, and self-esteem) between groups.

Results: The analyses showed a significant multivariate group effect in the appearance-related variables, $F(6, 896)=19.92$, Wilks' $\Lambda=0.78$, $p<0.001$, and mental health outcomes, $F(6, 896)=16.24$, Wilks' $\Lambda=0.81$, $p<0.001$. The SP/DC group had the strongest appearance-related concerns and mental health impairments, followed by the SP group, the DC group and the SH group. The SP/DC group and SP group only differed significantly with regard to dysmorphic concerns, but not in other variables. The DC group was less affected but still showed higher dysmorphic concerns and mental health impairments than skin-healthy controls. In contrast to the PSP groups, the other two groups did not exceed clinically relevant cut-off scores.

Discussion: The present study shows that individuals with PSP exhibit strong appearance-related concerns, regardless of the presence or absence of underlying or comorbid dermatological conditions. These findings shed new light on the importance of appearance-related concerns in Skin Picking Disorder and the role of PSP as a potentially overlooked risk factor in dermatological patients. Therefore, appearance-related concerns should be explicitly addressed in dermatological and psychotherapeutic settings. Future studies should also include longitudinal and experimental analyses to more clearly classify the role of appearance-related concerns in the etiology of PSP and Skin Picking Disorder.

KEYWORDS

pathological skin picking, skin picking disorder, excoriation disorder, body dysmorphic disorders, body image, body dissatisfaction, mental health, skin diseases

1. Introduction

With regard to pimples, crusts or other skin imperfections, it is a common cosmetic routine for most people to remove these imperfections by picking, squeezing, or scratching. A large proportion of the population generally reports engaging in this skin picking behavior on an occasional or regular basis, for example, 46.1% in a Polish sample of young adults (1), 62.7% in a US community sample (2), and 91.7% in a German student sample (3).

However, for some people the extent of skin picking clearly exceeds cosmetic routine and becomes a clinically relevant behavior referred to as pathological skin picking (PSP). PSP represents the core symptom of a mental disorder, which was first included as a separate diagnosis in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) in 2013. Excoriation (Skin Picking) Disorder (SPD) is a mental disorder in which individuals repeatedly and pathologically pick their skin (i.e., PSP), resulting in skin lesions and tissue damage. Despite frequent intentions to reduce or stop the behavior, affected individuals do not manage to refrain from PSP and clearly experience distress and social impairments. These impairments arise from the feeling of loss of control but also from the frequently visible consequences of skin picking, like wounds, inflammations and scars. PSP in the context of SPD must not be explained by substance influences, medical conditions or other psychological disorders [e.g., body dysmorphic disorder (BDD)] (4).

While the DSM-5 classifies SPD as a disorder within the obsessive–compulsive spectrum, the current International Classification of Diseases-11 further highlights its character in a subcategory of body-focused repetitive behavior disorders, together with other related disorders, such as pathological hair pulling (trichotillomania) or a residual category including nail biting (onychophagia) or cheek biting [e.g., (5–7)].

The reported prevalence rates of SPD vary depending on the respective diagnostic assessment and sample. A recent study by Grant and Chamberlain (8) reported a current prevalence of 2.1% with SPD and a lifetime prevalence of 3.8% in a large community sample, while the DSM-5 reports a lifetime prevalence of 1.4% (4). Most studies find a higher prevalence of SPD among women compared to men [e.g., (9, 10)], and current comorbidities include generalized anxiety disorder (63.4%), depression (53.1%), panic disorder (27.7%), post-traumatic stress disorder (27.2%), obsessive–compulsive disorder (26.3%), attention-deficit hyperactivity disorder (23.5%), eating disorders (19.3%), drug or alcohol abuse (16.0%), trichotillomania (12.7%), bipolar disorder (12.2%), and tic disorder (7.0%) (8).

Frequently mentioned triggers of PSP in SPD, are confrontations with skin imperfections, like pimples, blackheads, scabs, pustules, or crusts. Many affected individuals report having difficulties suppressing the behavior when confronted with these skin imperfections (11). Therefore, transient or persistent skin conditions may increase the risk for PSP (12–14). Subsequently, PSP may occur in individuals with transient (e.g., pubertal) skin conditions and persist as a behavior even after the skin conditions have vanished in adulthood. Similarly, PSP may develop in individuals with long-standing dermatological conditions (e.g., acne, atopic dermatitis, and psoriasis) and persist in a distressing manner over time. Especially in these groups of persons the additional problem of PSP besides the actual dermatological diagnosis can easily be overlooked (13).

Furthermore, distress and states of emotional tension and insufficient abilities in emotion regulation often lead to skin picking to relieve internal stress (15, 16). Those affected often report a trance-like state for the duration of the skin manipulations, in which time is sometimes forgotten and dissociative states occur (17). While PSP often leads to short-term relaxation and stress reduction, the repeated episodes elicit feelings of shame and guilt in the long term (16–18). In addition to the stressful experience that it is difficult to stop skin picking and to experience a lack of understanding from their social environment as well as from health care professionals [e.g., dermatologists; (18–20)], those affected often also suffer from the visible consequences of the behavior, for example scabs or scars. To avoid skin blemishes or to cover or treat skin picking wounds, many affected people undergo various cosmetic procedures (e.g., dermabrasion, laser therapy) and use camouflaging make-up (21, 22).

These treatments and camouflaging procedures can, in turn, compromise wound healing or cause further skin blemishes, which may then trigger further skin picking episodes. This often results in significant scarring, which is often distressing to those affected. As reported in clinical reports and in the general literature on SPD, many individuals with SPD therefore suffer from the self-perceived disfigurement caused by their own behavior (21). However, the actual empirical data on this relationship is still scarce. Still, a recent study by Gallinat et al. (23) showed specific evidence that SPD is associated with a negative body image.

Reports of cooccurring skin picking behaviors and BDD (24, 25) further illustrate possible relations of dysmorphic concerns and PSP. Fear of being rejected by others because of one's appearance due to the clearly visible skin imperfections [i.e., appearance-based rejection sensitivity (ARS); (26)] may increase over the course of the mental illness and additionally contribute to avoidance behaviors, social withdrawal, decreased self-esteem, and comorbid anxiety and depression (27–29). In line with this assumption, Tucker et al. reported that a large proportion of individuals with PSP show social withdrawal, or avoid social events and going into public (18). However, to date there are only few empirical reports on the relation of these avoidance behaviors with appearance concerns and its role in individuals with PSP has not been examined.

The study on body image and PSP by Gallinat et al. (23) reported mainly correlative associations between PSP and body image disturbances. In addition, the study did not include comparisons with skin-healthy controls or other control groups that might be affected by a similar skin appearance. Here, potential groups of interest include individuals with (visible) dermatological conditions (e.g., acne, atopic

dermatitis or psoriasis) that might also promote skin picking behavior, PSP and/or body image concerns (12, 14, 30–32).

The present study is therefore addressing the research question to what extent individuals with PSP with (SP/DC) and without (SP) dermatological conditions differ from individuals with dermatological conditions only (DC) and skin-healthy controls (SH) regarding the degree of their dysmorphic concerns, ARS, and BDD-symptoms. Here, we focus on PSP as a pathological behavior rather than the full syndrome of SPD, which would require a clinical diagnosis and exclusion of differential diagnoses. As further variables, we will also examine group differences in general mental health outcomes (i.e., depression, anxiety, and self-esteem). We hypothesize that individuals with PSP (with or without dermatologic conditions: SP/DC and SP) have more pronounced appearance concerns than both participant groups without PSP (DC and SH).

2. Materials and methods

2.1. Study design

The study had a cross-sectional design and was conducted as an online survey using SoSci-Survey software (33). Data collection took place in a German convenience sample in spring to summer 2018. All participants provided active informed consent via the online form of the questionnaire. The study was approved by the Ethics Committee of the University of Wuppertal and adhered to the Helsinki Declaration. In addition to answering the research questions presented here, the study also pursued the purpose of validating newly developed translated measurement instruments from the field of skin picking research. Therefore, the number of measurement instruments used in the study was greater than the number of measures presented here and study participation took approximately 30 min. Participants could be notified of study results via email upon request. Students at the University of Wuppertal were able to receive course credit for participation. For participants outside of the university, the allowance consisted of the opportunity to win a gift certificate worth 10 Euros.

2.2. Participants

We recruited participants via newsletter announcements and flyers at the University of Wuppertal, websites of psychological journals, flyers in dermatological practices and via various social media platforms. Individuals with PSP were recruited specifically via the newsletter and the internet-forum of the German Self-Help Network for Skin Picking, as well as via Facebook groups on the topic of skin picking. Overall inclusion criteria were legal age in Germany (18 years or above) and sufficient German language skills to understand the questionnaire. There were no general exclusion criteria for the study participation.

However, additional criteria were established for grouping the four groups of interest: (1) skin-healthy individuals without skin picking or dermatological conditions (SH), (2) dermatological conditions without PSP (DC), (3) PSP without skin conditions (SP), and (4) individuals with dermatological conditions and PSP (SP/DC).

For the definition of dermatological conditions to be considered, we decided to focus on three common dermatological conditions that are usually associated with visible skin irregularities and for which previous studies have already demonstrated possible impairments in mental health and psychosocial impairments (34–38). These included acne, atopic dermatitis, and psoriasis. To be included under the dermatological condition subgroups, participants had to indicate that they had ever received a medical diagnosis (lifetime diagnosis) of one of these three dermatological conditions. Individuals who reported other dermatological conditions (e.g., vitiligo, urticaria, rosacea, warts, and alopecia etc.) were excluded from this analysis.

With regard to the PSP subgroups, participants had to be recruited via calls in the German Self-Help Network for Skin Picking and Facebook groups via a separate recruitment link and had to report values >7 on the German version of the Skin Picking Impact Scale [SPIS-D; (39)] to indicate PSP instead of subclinical skin picking. This cut-off corresponds to the original English SPIS (40) and was applied to assure a clinically relevant severity of the PSP at the time of the study. Here, subgrouping into the SP/DC and SP groups was dependent on the presence or absence of a diagnosis of one of the aforementioned skin conditions.

To be classified in the groups without dermatological conditions (SH or SP), participants had to indicate that they have never received a medical diagnosis of any dermatological condition. For the skin-healthy group, participants further had to indicate that they are currently not affected by any skin condition and have a score ≤7 on the SPIS-D.

After exclusion of unsuitable datasets that met exclusion criteria or did not fulfil quality or classification requirements (see Section 2.3.6.1), $n = 453$ participants remained, leading to $n = 138$ participants for the SH group, $n = 176$ for the DC group, $n = 56$ for the SP group, and $n = 83$ for the SP/DC group.

An *a priori* power analysis with G*Power 3.1.9.7 (41) indicated that a sample of 336 participants would be sufficient to detect medium effects between the four groups on eight response variables in a multivariate analysis of variance (MANOVA) with a conservative α error of 0.0001 due to multiple comparisons and a statistical power 1-β of 0.95. Thus, the present sample size was determined to be sufficient for the planned analyses.

2.3. Assessment instruments

2.3.1. Sociodemographic data

To describe the sociodemographic characteristics of the sample, we recorded age, gender (male/female/other), highest school degree, highest professional degree, and current employment (yes/no).

2.3.2. Dermatological conditions

Dermatological conditions were assessed via self-report. First, we asked participants if they had ever been diagnosed with a skin condition (yes/no). Afterwards, the participants had the opportunity to select from a list of different skin conditions those which they had been medically diagnosed with [e.g., allergies, fungal infections, atopic dermatitis, seborrheic eschar, rosacea, psoriasis, (stages of) skin cancer, alopecia areata, herpes zoster, other herpes diseases of the skin, warts, pruritus, eczema, contact allergies, chafing skin or others with a free entry option].

2.3.3. Assessment of skin picking

Skin picking behavior, severity, and corresponding impairments were assessed using the modified German translation of the Skin Picking Scale-revised (mSPS-D) and the German Skin Picking Impact Scale (SPIS-D) (38). The latter tool was used as a screening instrument for group assignments.

The mSPS-D assesses the frequency, intensity, and ability to control skin picking urges on nine items with five-point Likert scales (e.g., 0 = no urge, 4 = ongoing urge [>8 h per day]). The wording of the answer options is adapted to the wording of the items and therefore varies (38). Compared to the original Skin Picking Scale-Revised (42), the mSPS-D includes one more item because the original item „How much control do you have over your skin picking? To what degree can you stop yourself from picking? "was divided in two items in line with other instruments to assess BFRBs, such as the Massachusetts General Hospital Hairpulling Scale (43). In addition, the wording of items and answer options has been shortened to make the instrument more time economic (39). Higher sum scores indicate greater symptom severity and impairment from skin picking. The mSPS-D has demonstrated good psychometric properties in a validation study (39). The internal consistency in the present sample was excellent ($\alpha = 0.95$).

The SPIS-D (39) is based on the English Skin Picking Impact Scale (40) and captures impairments due to skin picking in various life domains (e.g., relationships, shame, daily routines) on 10 items. Answers are provided on five-point-Likert scales (0 = not at all; 4 = severe). The SPIS served as a screening instrument to classify PSP, using the cut-off score >7 suggested by Keuthen et al. (40). The answer format of the German adaptation differs slightly from the original scale which is rated on 6-point-Likert scales. Although this lowers the total achievable score of the German version, we assume that the screening cut-off value proposed by Keuthen et al. (40, see also: 44) is still sufficiently sensitive as a conservative measure to identify individuals with PSP. The internal consistency in the present sample was excellent ($\alpha = 0.97$).

2.3.4. Appearance concerns

As primary outcomes, appearance-related concerns were assessed using three different measurement instruments in German to capture different relevant facets of appearance-related concern: The Dysmorphic Concerns Questionnaire (DCQ), the Appearance-based Rejection Sensitivity Scale (ARS-D), and a brief screening for symptoms of BDD, based on the DSM-5 diagnostic criteria (BDD-screen).

2.3.4.1. Dysmorphic Concerns Questionnaire

Dysmorphic concerns were assessed using the German translation of the DCQ (45) as an economic and widely used screening instrument in clinical settings. It consists of seven items by which respondents report their appearance-related worries and behaviors compared to the scale of most other people (e.g., "Have you ever worried about a particular aspect of your appearance?") with a four-point Likert-scale to provide answers from 0 = not at all to 3 = much more than other people. The sum score ranges from 0 to 21 with higher overall scores indicating stronger dysmorphic concerns. The unidimensional scale has been shown to have good psychometric properties (46), and its sum score is frequently used for identification of cases with clinically relevant dysmorphic concerns, for example, using a cut-off of ≥9 in community samples (47), or a more conservative score of ≥11 in samples with dermatological conditions (45). The internal consistency in the present sample was good ($\alpha = 0.86$).

2.3.4.2. Appearance-based Rejection Sensitivity Scale

As an interpersonal aspect of appearance-based concerns, ARS (26) was assessed using the German ARS-D (48). The questionnaire (short-version) consists of 12 items assessing specific appearance-related scenarios in terms of the extent to which these scenarios generate worry about being rejected on the basis of appearance (a): affective component; response format ranging from 1 = very unconcerned to 6 = very concerned and how likely rejection experiences are rated in these scenarios (b): cognitive component; response format ranging from 1 = very unlikely to 6 = very likely. An example scenario would be "You are at a dance and all your friends have been asked to dance, except you".

Answer scores for affective and cognitive components of each item are first multiplied and then summed up for an overall score. Higher values indicate higher ARS. The instrument has shown good psychometric properties and discriminative validity to differentiate between groups with and without clinically relevant appearance concerns (48). The internal consistency in the present sample was excellent ($\alpha = 0.94$).

2.3.4.3. Screening for body dysmorphic disorder

The adapted short version of the BDD screening (49) consists of four items that assess core criteria of BDD according to the DSM. Item 1 assesses the belief of having ugly or disfiguring body features "Do you think you have one or more ugly or disfigured body parts although other people do not share this opinion or believe your concern to be markedly exaggerated?" (yes/no); Item 2 assesses the individual suffering due to the preoccupation with these body features "Is the preoccupation about the ugly or disfigured body parts very distressing to you?" (yes/no); Item 3 assesses impairments due to the preoccupation with these body features "Are you so affected by concerns about your own physical disfigurement that it impacts your daily life (e.g., at work, in relationships with others)?" (yes/no); and item 4 asks about the duration (years) since when the worries and preoccupation about the respective body features occur. With confirmation of items 1– 3 participants were classified as *BDD positive* cases. Otherwise, they were classified as *BDD negative* for the present analyses. Here, we aimed at comparing the proportions of positive screenings between the groups.

2.3.5. Assessment of mental health variables and self-esteem

As secondary outcomes, we assessed mental health variables to compare additional possible mental health impairments that might result from or be associated with dermatological conditions and/or skin picking. Here, we focused on symptoms of depression and of anxiety, and general self-esteem.

2.3.5.1. Patient Health Questionnaire-9 for depression

Depressive symptoms were assessed with the German version of the Patient Health Questionnaire-9 (PHQ-9) (50), a frequently used screener for symptoms of major depression according to the DSM-5 criteria. The questionnaire assesses the frequency of depressive symptoms within the last 2 weeks on nine items with 4-point

Likert-scales ranging from 0 = not at all to 3 = nearly every day. Higher sum scores (range 0–27) indicate more severe depressive symptoms. Good psychometric properties have been reported for the German version (51). For the present study, internal consistency was good ($\alpha = 0.89$).

2.3.5.2. General Anxiety Disorder Scale-7

We assessed symptoms of anxiety with the German General Anxiety Disorder Scale-7 (GAD-7), the anxiety form of the Patient Health Questionnaire (52). The scale consists of seven items that assess the presence of anxiety symptoms within the last 2 weeks on 4-point Likert scales, ranging from 0 = not at all to 3 = nearly every day. The symptoms include for example, worries, nervousness/tension, difficulties to relax etc. Higher sum scores indicate more severe anxiety symptoms. For the present study, internal consistency was excellent ($\alpha = 0.90$).

2.3.5.3. Rosenberg Self-Esteem Scale

We measured participants' general self-esteem with the German Rosenberg Self Esteem Scale (RSES) (53). The self-report scale captures self-esteem as a trait on 10 statement-items with four-point Likert scales (0 = strongly disagree; 3 = strongly agree). Inverted items have to be recoded before an overall sum score is calculated. Higher values in this sum score indicate stronger self-esteem. Good psychometric properties have been reported for the RSES (53), and the internal consistency in the present study was excellent ($\alpha = 0.92$).

2.3.6. Procedure

For participation, the online questionnaire was accessible via a hyperlink sent with the study calls. Participants thus reached the study's information page, on which participation requirements, the topic and duration of the survey, as well as the research ethics aspects of voluntary participation, the possibility of withdrawal without disadvantages, and the anonymization of the data were explained. In addition, the contact details of the researchers for queries were listed on the page.

Then, the interested respondents were directed to the consent form page and indicated that they had read, understood, and agreed with the terms and conditions of participation and were at least 18 years old. If respondents did not consent here, the survey was automatically terminated.

The survey began with questions about sociodemographic data. Subsequently, questions were asked about the dermatological diagnoses and current impairments, followed by the questionnaires on skin picking. Afterwards, participants filled in the ARS-D, RSES, DCQ, GAD-7, and PHQ-9, as well as additional questionnaires that were target variables for another research question (e.g., on former teasing experiences, eating behavior).

The progress of the survey was displayed with a visual progress bar on every page. In general, except for the informed consent, participants were able to skip single questions or pages in case they did not want to answer them. However, in case of blank answers, a warning pop-up asked the participants, whether they want to add answers for the missing items. Upon completion of the survey, participants were thanked and given information on how to enter the raffle or receive course credit.

2.3.6.1. Data analysis

Overall, a total of $N = 765$ individuals completed the questionnaire, whereof $n = 11$ participants had to be excluded due to an age <18 and $n = 24$ participants had to be excluded for insufficient data quality, because they showed conspicuously fast completion behavior indicated by quality indicators of the questionnaire software (DEG_TIME values >100) (54). Participants who could not be assigned to any of the four groups of interest (DC/SP, SP, DC, and SH), were excluded from the analyses ($n = 300$) and one person had to be excluded after the grouping process because she indicated both, to have never been diagnosed with a skin condition and to have been diagnosed with acne ($n = 1$), leading to a final analysis sample of $n = 453$. Single missing values in questionnaires were replaced by means of multiple imputation technique ($m = 20$), selecting the imputation with the least deviations from the mean values in the original dataset, which showed only a very small deviation of 0.02 points at maximum.

We calculated descriptive statistics for the sociodemographic characteristics and skin conditions, frequencies and proportions of positive BDD screenings as well as means and standard deviations for the scales on appearance-concerns, skin picking, and mental health. After checking for violations of relevant assumptions, we used three multivariate analyses of variance (MANOVAs) with Wilks Tests to assess appearance concerns (DCQ, ARS-D), and mental health impairments (PHQ-9, GAD-7). Significant multivariate effects were followed up by analyses of variance (ANOVAs) with *post hoc*-comparisons to assess significant differences between the four groups. Additional ANOVAs were conducted for the assessments of differences in skin picking symptoms (mSPS-D) and self-esteem (RSES).

In case of violations of the normality assumption, the results of the ANOVAs were compared to those of a Kruskal-Wallis-test but there were no deviations in results. Thus, ANOVA results are reported throughout the manuscript. In case of violations of the assumption of homogeneity of variances, the results of Welch-ANOVA and of the Games-Howell *post-hoc* tests are reported. Finally, we conducted a χ^2-test with exact Fisher-test to assess different proportions of positive BDD screening between the groups.

The significance level for the analyses was set to $p < 0.05$. All statistical analyses were performed using IBM SPSS 28 and JASP (55).

3. Results

3.1. Sample characteristics

The analysis sample consisted primarily of women (83.9%) in middle adulthood (M = 30.20 years, SD = 10.54 years) with participants' ages ranging between 18 and 68 years. The level of education can generally be described as high, as the majority (74.0%) of the sample had a high school diploma as their highest school qualification. Just under one-third of the sample was currently in a degree program or vocational training, while over 40% had already attained at least a bachelor's degree or higher. Two-thirds of the participants were currently employed (full- or part-time). Among the groups with diagnosed dermatological conditions, the majority (56.0%) reported diagnosed acne, while 46.4% were affected by atopic dermatitis. Psoriasis was the least common diagnosed dermatological condition, accounting for only 8.1% (multiple answers were possible).

Overall, the groups differed significantly in age and sex, with *post hoc* tests showing that the difference was only notable between the DC group and the SP group. The latter was younger, but the group

difference was no longer significant in the Bonferroni-corrected *post hoc* test ($p = 0.059$). With regard to gender differences, the proportion of female participants was significantly higher in the two groups with PSP (SP/DC and SP). Therefore, all ANOVAs were repeated with age and gender as covariates in additional analyses. Detailed information on the sample characteristics are displayed in Table 1.

3.2. Group comparisons in outcome variables

The two MANOVAs indicated significant group differences for appearance concerns [$F(6, 896) = 19.92$, Wilks' $\Lambda = 0.78$, $p < 0.001$] and mental health variables [$F(6, 896) = 16.24$, Wilks' $\Lambda = 0.81$, $p < 0.001$]. The following ANOVAs showed highly significant group differences (all ps < 0.001) with large effect sizes ($\eta^2 > 0.14$) for all variables except ARS-D ($\eta^2 = 0.08$, medium effect size). In all variables, the SH group had the lowest values (respectively the highest for self-esteem), followed by the DC group. The SP/DC group had the highest values for all variables (and the lowest values for self-esteem), except for anxiety, for which the SP group reported minimally higher values (see Table 2).

Post hoc group comparisons showed that the subgroups differed significantly in most of the variables. Regarding appearance concerns, the SH group differed significantly from the DC, SP, and SP/DC groups (ps < 0.001). However, regarding ARS, there was no significant difference between the SH and DC groups regarding their concerns on appearance-based rejection ($p > 0.999$). In addition, the DC and SP group did not differ significantly in their DCQ-scores indicating comparable dysmorphic concerns ($p = 0.431$). Overall the results of the appearance concerns indicated that the SH group had the lowest concerns, followed by the DC group, the SP group, and the SP/DC group, which differed significantly from the SP group in DCQ-values, but not in the ARS-D score (see Figures 1, 2).

With regard to skin picking assessments, almost all groups differed highly significantly in their skin picking symptoms (mSPS-D), with the SH group showing the lowest scores and significantly lower scores than all other groups (ps < 0.001), followed by the DC group. The scores of both of these groups were significantly exceeded by the two skin picking groups (SP and SP/DC). However, these two groups did not differ significantly among themselves in the assessed skin picking symptoms ($p = 0.516$).

A similar pattern of results was seen in the mental health variables, with smaller differences between groups. With regard to depression, the DC, SP and SP/DC groups all had higher depression scores than the SH group (ps <0.001). The SP group and the DC group did not differ significantly from each other ($p = 0.060$). Further, there were no significant differences between the SP group and the SP/DC group (ps > 0.242). In general, however, the SP/DC group was found to be the most impaired in almost all mental health variables (except GAD-7, where it was nearly equal to the SP group), followed by the SP group, the DC group, and the SH group, which was the least impaired. The results of all *post hoc* comparisons are displayed in Table 3.

Screening for possible symptoms of BDD showed that the proportion of cases with positive screening was lowest in the SH group at 10 of 138 participants. In the DC group, the proportion of individuals with BDD symptoms was three times higher (38 of 176 participants). Over 40% of individuals in the SP group (25 of 56 participants) showed indications for a positive BDD screening and in the SP/DC group, the proportion of individuals with positive screenings (53 of 83 participants) was almost 64%. Thus, comparable to the other variables for appearance-related concerns, individuals with skin picking are significantly more likely to be affected by BDD symptoms, with individuals with dermatological conditions also showing an increased prevalence. Accordingly, the group difference was highly significant, $\chi^2(3) = 94.07$, $p < 0.001$, $C = 0.42$.

3.3. Additional analyses

Given the significant group differences in age and gender, all ANOVAs were repeated as analyses of covariance (ANCOVAs), using age and gender as covariates. Overall, the results did not differ from the reported pattern, except for a nonsignificant difference in self-esteem between the SH and DC group ($p = 0.076$).

4. Discussion

The aim of the present study was to investigate the extent to which individuals with PSP differ from control groups with and without dermatological conditions with respect to their appearance-related concerns. Thus, the study intended to extend the evidence on the role of appearance-related aspects in PSP that might contribute to the phenomenology and maintenance of this mental disorder. While earlier research has already shown that body image concerns may play a role in PSP (23) as well as in dermatological conditions [e.g., (30, 31)], specific differences between individuals with PSP, those with dermatological conditions and skin-healthy controls have so far not been analyzed. The present study therefore examined possible group differences in appearance concerns and mental health outcomes between four groups with different skin related impairments [skin-healthy (SH), dermatological conditions only (DC), skin picking only (SP), and a combination of skin picking and dermatological conditions (SP/DC)].

Throughout all variables, appearance concerns, skin picking assessments, and mental health outcomes, we found that individuals with PSP were significantly more affected than individuals with dermatological conditions only or skin-healthy controls. Except for dysmorphic concerns, the PSP groups with and without any diagnosed skin conditions did not differ significantly from each other. Compared to suggested cut-off scores to assess clinically relevant dysmorphic concerns (45, 47), on average both PSP groups exceed the respective cut-off scores and are therefore subjects to a high body image impairment.

Still, the SP/DC group showed the strongest impairments in almost all variables and the highest proportion of possibly clinically relevant symptoms of BDD. Thus, appearance concerns might arise from or be aggravated by existing skin conditions in individuals with PSP. Further, skin conditions can trigger the development and single episodes of PSP (12–14). However, PSP alone seems to account for a marked impairment regarding appearance concerns, such as dysmorphic concerns or appearance-based rejection sensitivity. This result is in line with a recent study by Gallinat et al. (23), who found that skin picking severity was positively and significantly correlated with appearance variables such as body image disturbances and

TABLE 1 Sample characteristics of the subgroups and the overall sample.

Variable	SH	DC	SP	SP/DC	Total	Test statistics
n	138	176	56	83		
Age *M* (SD) [Range]	29.49 (11.11) [18–68]	31.85 (10.98) [19–66]	27.60 (9.42) [18-61]	29.12 (8.78) [18-62]	30.10 (10.54) [18–68]	**$F(3,449) = 3.04$, $p = 0.029$, $\eta^2 = 0.020$**
Gender *n* (%)						**$X^2(6) = 30.58$, $p < 0.001$, $C = 0.25$**
Female	99 (71.7)	148 (84.1)	53 (94.6)	80 (96.4)	380 (83.9)	
Male	38 (27.5)	28 (15.9)	3 (5.4)	3 (3.6)	72 (15.9)	
Other	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	
School degree *n* (%)						**$X^2(12) = 25.24$, $p = 0.014$, $C = 0.23$**
Secondary/elementary school diploma	2 (1.4)	4 (2.3)	1 (1.8)	3 (3.6)	10 (2.2)	
Secondary school leaving certificate/ equivalent	11 (8.0)	14 (8.0)	14 (25.0)	15 (18.1)	54 (11.9)	
Specified A-levels	18 (13.0)	17 (9.7)	4 (7.1)	14 (16.9)	53 (11.7)	
A-levels	106 (76.8)	141 (80.1)	37 (66.1)	51 (61.4)	335 (74.0)	
Other	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	
Professional degree *n* (%)						X^2 (21) = 29.82, $p = 0.096$, $C = 0.25$
Currently studying/in vocational training	43 (31.2)	46 (26.1)	20 (35.7)	21 (25.3)	130 (28.7)	
Working without a training degree	1 (0.7)	1 (0.6)	1 (1.8)	5 (6.0)	8 (1.8)	
Vocational training degree	26 (18.8)	34 (19.3)	15 (26.8)	20 (24.1)	95 (21.0)	
Master craftsman/ technician/equivalent technical college degree	4 (2.9)	3 (1.7)	1 (1.8)	4 (4.8)	12 (2.6)	
Bachelor's degree	32 (23.2)	37 (21.0)	7 (12.5)	11 (13.3)	87 (19.2)	
Master's degree (or equivalent)	28 (20.3)	51 (29.0)	9 (16.1)	21 (25.3)	109 (24.1)	
PhD	3 (2.2)	2 (1.1)	1 (1.8)	0 (0.0)	9 (1.3)	
Other	1 (0.7)	2 (1.1)	2 (3.6)	1 (1.2)	6 (1.3)	
Current employment						X^2 (3) = 2.99, $p = 0.394$, $C = 0.08$
Yes	96 (69.6)	119 (67.6)	33 (58.9)	60 (72.3)	308 (68.0)	
No	42 (30.4)	57 (32.4)	23 (41.1)	23 (27.7)	145 (32.0)	
Dermatological diagnoses *n* (%)						
Acne (yes/no)	0/138 (0/100)	90/86 (51/49)	0/56 (0/100)	55/28 (66/34)	145/308 (32/68)	**$X^2(3) = 165.67$, $p < 0.001$, $C = 0.52$**
Atopic dermatitis (yes/ no)	0/138 (0/100)	88/88 (50/50)	0/56 (0/100)	33/50 (40/60)	121/332 (27/73)	**$X^2(3) = 126.69$, $p < 0.001$, $C = 0.47$**
Psoriasis (yes/no)	0/138 (0/100)	13/163 (7/93)	0/56 (0/100)	8/75 (10/90)	21/432 (5/95)	**$X^2(3) = 17.14$, $p < 0.001$, $C = 0.19$**

SH, skin-healthy; DC, dermatological condition only; SP, skin picking only; SP/DC, skin picking and dermatological condition; significant group differences are indicated in bold print.

appearance orientation even after controlling for depressive symptoms. In the present study, we were able to replicate this finding. Moreover, we used a broad range of measures to capture different facets of appearance concerns, such as dysmorphic concerns, BDD symptoms and the interpersonal construct of ARS, which has not been investigated in PSP so far. Last, this study adds new knowledge on the

TABLE 2 Descriptive statistics and ANOVA-results for the outcome variables.

Variable	SH	DC	SP	SP/DC	Test statistics (ANOVA)
n	138	176	56	83	
	***M* (SD)**	***M* (SD)**	***M* (SD)**	***M* (SD)**	
Appearance concerns					
Dysmorphic concerns (DCQ)	6.06 (4.05)	9.06 (4.79)	10.18 (4.79)	12.42 (4.06)	$F(3, 180.1) = 44.49$, $p < 0.001$, $\eta^2 = 0.20$
Appearance-based rejection sensitivity (ARS-D)	11.25 (7.41)	12.40 (7.93)	16.78 (8.66)	17.03 (8.31)	$F(3, 449) = 13.49$, $p < 0.001$, $\eta^2 = 0.08$
Mental health					
Depression (PHQ-9)	5.69 (4.50)	8.35 (6.25)	10.70 (5.96)	12.27 (5.51)	$F(3, 177.2) = 32.42$, $p < 0.001$, $\eta^2 = 0.15$
Anxiety (GAD-7)	5.76 (4.36)	7.72 (5.18)	11.09 (5.02)	11.05 (4.76)	$F(3, 449) = 28.44$, $p < 0.001$, $\eta^2 = 0.16$
Self-esteem					
Self-esteem (RSES)	22.68 (5.75)	20.76 (6.93)	17.25 (6.87)	15.01 (6.90)	$F(3, 177.4) = 27.81$, $p < 0.001$, $\eta^2 = 0.16$
Skin picking					
Skin picking symptoms (mSPS-D)	4.61 (4.09)	10.47 (6.85)	19.63 (5.41)	20.84 (4.63)	$F(3, 181.1) = 283.21$, $p < 0.001$, $\eta^2 = 0.56$

SH, Skin-healthy; DC, Dermatological condition only; SP, Skin picking only; SP/DC, Skin picking and dermatological condition; DCQ, Dysmorphic Concerns Questionnaire; ARS-D, Appearance based Rejection Sensitivity Scale; mSPS-D, modified Skin Picking Scale; PHQ-9, Patient Health Questionnaire-9 for depression; GAD-7, General Anxiety Disorder Scale-7; RSES, Rosenberg Self-Esteem Scale. ANOVAs with corrected degrees of freedom indicate Welch-ANOVAs with homogeneity corrections. Significant test statistics are indicated in bold print.

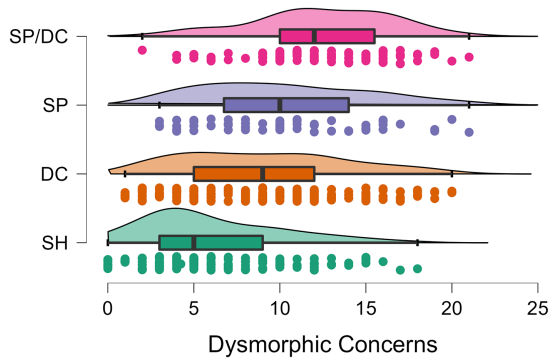

FIGURE 1
Boxplots of the four subgroups with datapoints and distributions of dysmorphic concerns. SH, skin-healthy; DC, dermatological condition only; SP, skin picking only; SP/DC, skin picking and dermatological condition; scale range of the Dysmorphic Concerns Questionnaire: 0–21.

potential even aggravating role of dermatological conditions regarding these appearance concerns in individuals with and without PSP.

With regard to dermatological conditions only, we found individuals in the DC group (including participants with diagnosed acne, atopic dermatitis or psoriasis) to be still significantly more affected than skin-healthy controls, regarding their appearance concerns, but not the fear of being rejected due to their appearance. Thus, while possible visible differences might lead to more cognitive concerns, they do not seem to impair the respective individuals that much in their interpersonal relationships. With regard to mental health, slight impairments were visible but the differences to skin-healthy controls were less pronounced than those to the PSP groups. In addition, according to the cut-off scores for the PHQ-9 suggested by Kroenke et al. (56), both, skin-healthy participants and those with dermatological conditions would be classified as reporting mild depressive symptoms (values of 5 to 9), while the PSP groups scored in the range of moderate depressive symptoms (values of 10 to 14). This underlines the distressing nature of PSP which can impair other mental health outcomes.

While this finding is in line with results from previous studies on body image and mental health impairment in dermatological patients (e.g., 30–38), the results of the present study also indicate that skin picking, as a common behavioral pattern in dermatological patients (12, 14), should be given particular sensitive attention. Skin picking can lead to additional appearance-related impairments as well as negatively affect mental health of individuals with skin conditions and should therefore be assessed and addressed by dermatological professionals and, if present, be treated in cooperation with specialists for psychodermatological conditions with primary psychopathology [see, e.g., (57)].

The present study also highlights that, while previous research has mainly focused on skin picking as a behavioral symptom of BDD (24, 25), the co occurrence of both phenomena should be considered in clinical settings. To date, the possible comorbid diagnosis of SPD is often overlooked in patients with BDD who might not exclusively pick their skin to remove blemishes or change their appearance, but also show automatic forms of PSP. Further, the fact that BDD can arise secondarily from the possible visible consequences of skin picking—since the focus is very strongly placed on the skin appearance—has hardly been investigated so far. This cooccurrence of symptoms offers important impulses for practice, especially when it comes to treating SPD in psychological therapies.

While the current evidence-based therapies for SPD rely on cognitive behavioral therapy—mainly cognitive behavior therapy incorporating habit reversal techniques [i.e., (58)]—body image and appearance concerns are still very rarely considered in the treatment approaches for SPD. However, these concerns may be a major contributor to the observed social withdrawal and everyday impairments in SPD (18). The specific approach of addressing appearance-related concerns and body image aspects in therapy, as it is used for example in the therapy of BDD or eating disorders, could

therefore significantly enrich the therapy for SPD and reduce psychosocial impairments in this group.

The present study has the strength of comparing groups with and without PSP and dermatological conditions, including a relatively large sample of individuals with PSP via the recruitment support of the large German Self-Help Network for Skin Picking. Further, the results of the group comparisons remain stable even in additional analyses that control for possible influences of gender and age. However, the study is also subject to several limitations.

First, this is an online study in which only psychometrically valid screening instruments for PSP, appearance concerns and for mental health variables were used. However, this cannot replace clinical diagnostics by appropriately trained experts. Therefore, it is important to conduct corresponding studies also in face-to-face settings in mental health and dermatological settings in order to be able to distinguish the groups based on clinical diagnoses by medical experts. This would further allow for more objective assessments of the exaggerated nature of an individual's appearance-related concerns which are a prerequisite for the clinical diagnosis of BDD. With regard to the inclusion criteria of dermatological conditions, it should additionally be noted that the selection of subjects was based on lifetime diagnoses and not on current complaints. Since even past skin diseases without acute impairment can result in visible and permanent skin changes (e.g., acne scars), we did not exclusively include currently acute complaints. At the same time, however, the screening question targeted existing medical diagnoses. Thus, there is the possibility that persons were excluded from the analysis who suffer from acute skin complaints but do not have a medical diagnosis. Since we limited ourselves to three disorders (acne, atomic dermatitis and psoriasis), which in many cases are frequently medically examined in Germany, we nevertheless assume a good representation of the sample. However, it must be emphasized that some persons were certainly excluded despite existing current skin conditions without medical diagnoses.

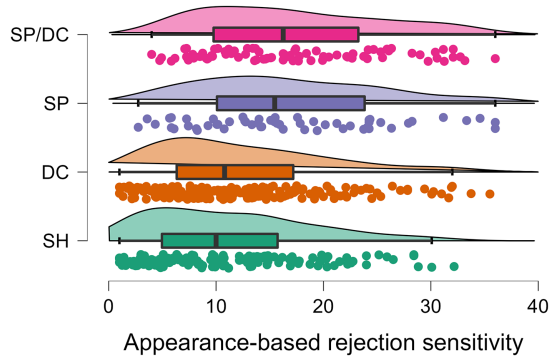

FIGURE 2
Boxplots of the four subgroups with datapoints and distributions of appearance-based rejection sensitivity. SH, skin-healthy; DC, dermatological condition only; SP, skin picking only; SP/DC, skin picking and dermatological condition; scale range of the Appearance-based Rejection Sensitivity Scale: 0–36.

Second, the proportion of women in the analysis sample is disproportionately high, especially in the PSP groups. Even though the gender ratio in older studies is very high with a share of 75–94% women in PSP and SPD (59), the percentage of women in our study even exceeds this upper limit. In addition, more recent studies using diagnostic screenings based on DSM-5 criteria have found a more balanced gender ratio in SPD [e.g., (8, 11)]. Furthermore, the gender distribution in the DC groups does not correspond to the usual, more gender-balanced ratios, in larger epidemiological studies on the prevalence of skin conditions [e.g., (60)]. In future studies, more attention should be paid to the recruitment of male patients. In addition, it should be noted that for the present study, participants were in part specifically recruited from corresponding topic forums, Facebook groups and dermatological practices. Therefore, this is not a representative sample and the prevalence found here, both for PSP and for clinically relevant mental health impairments, deviate significantly from the general population, which may also correspond to the proportion of persons with BDD symptoms.

Third, we did not assess appearance concerns specifically targeting aspects of the skin. The DCQ as well as the ARS-D and the BDD screening also assess concerns about other aspects of the body, such as weight or height. Given that there is for example, according to a recent study by Grant and Chamberlain (11) a relatively high comorbidity of SPD and eating disorders, we cannot disentangle, whether the worries of the participants in our study result from their skin conditions (only) or other aspects related to their external appearance. Using additional measures that specifically address concerns and dissatisfaction regarding the skin [e.g., cutaneous body image scales, see (31)] instead of more general appearance-related screening instruments as well as additional questions to rule out possible weight concerns might provide deeper insights and unveil more relevant differences between individuals with PSP compared to dermatological patients.

TABLE 3 Pairwise group comparisons (*post hoc* tests) in all relevant outcome variables.

Group comparison (*post hoc* test)	SH vs. DC	SH vs. SP	SH vs. SP/DC	DC vs. SP	DC vs. SP/DC	SP vs. SP/DC
DCQ	**<0.001**	**<0.001**	**<0.001**	0.431	**<0.001**	**0.025**
ARS-D	>0.999	**<0.001**	**<0.001**	**0.002**	**<0.001**	>0.999
mSPS-D	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	0.516
PHQ-9	**<0.001**	**<0.001**	**<0.001**	0.060	**<0.001**	0.400
GAD-7	**0.003**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	>0.999
RSES	**0.038**	**<0.001**	**<0.001**	**0.007**	**<0.001**	0.242

SH, skin-healthy; DC, dermatological condition only; SP, skin picking only; SP/DC, skin picking and dermatological condition; DCQ, Dysmorphic Concerns Questionnaire; ARS-D, Appearance Based Rejection Sensitivity Scale; mSPS-D, modified Skin Picking Scale; PHQ-9, Patient Health Questionnaire-9 for depression; GAD-7, General anxiety scale-7; RSES, Rosenberg Self-Esteem Scale. *p*-values for *post hoc* tests are Bonferroni-corrected for simple ANOVAs and Games-Howell *post hoc* comparison are reported for Welch ANOVAs. Significant values are indicated in bold print.

To shed more light on the potential role of appearance-related concerns in the etiology of PSP and SPD, future studies should implement longitudinal designs to disentangle psychopathological mechanisms. Due to the cross-sectional design, we cannot deduce, whether PSP is the cause or a symptom of appearance-related concerns.

Future research could also include additional experimental studies regarding possible differences in the (tactile or visual) perception of their own body and elicited urges in patients with SPD compared to control groups. For example, in the study of Mehrmann et al. (44) individuals with SPD showed a higher urge to pick their own skin in response to the presentation of visual skin-picking-related stimuli, compared with skin-healthy controls and patients with atopic dermatitis. In an experimental study with functional Magnetic Resonance Imaging, Schienle et al. (61) further demonstrated that patients with SPD, who were confronted with visual images of skin irregularities, reported higher levels of disgust and corresponding specific neural responses (greater activation of the amygdala and insula). Based on the tactile sensory modality, Houghton et al. (62) showed that a mixed group with SPD and Hair Pulling Disorder had a low tactile sensory threshold (i.e., increased tactile sensitivity) compared to a healthy control group, which could account for a different response to skin irregularities.

Such differences in the perception of visual and tactile cues may on the one hand promote PSP symptoms, but on the other hand also cause a different perception of one's own body and thus also account for appearance-related concerns. However, to date, there are still no distinct comparisons of individuals with PSP to those with different skin conditions regarding self-referential perceptive processes that could further illuminate processes in the formation of appearance concerns and possible treatment approaches.

In addition, intervention studies on cognitive-behavioral therapies or self-help interventions for individuals with PSP should explicitly examine therapeutic components that address body image and appearance-related concerns. This is also especially important for patients with dermatological conditions and PSP, in whom the factor of appearance-related concerns is seldom addressed in health care. Those interventions could aim at changing the importance of appearance for the individual via cognitive restructuring or enable patients to discover new sources of their self-esteem in therapy [e.g., (63)]. This could alleviate the distress and suffering of individuals with PSP and SPD and potentially promote long-term treatment success.

5. Conclusion

Overall, we found that appearance concerns constitute an important phenomenological aspect of PSP that has long been neglected and should be further examined and addressed in interventions for individuals with SPD as well as for dermatological patients who exhibit skin picking as a behavioral pattern that could aggravate their skin conditions and cause additional mental health impairments.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Ethics Committee of the University of Wuppertal. The patients/participants provided their written informed consent to participate in this study.

Author contributions

JS and AM: conception and design of the study. JS, CG, and AM: interpretation of the data, drafted the work, and revised the paper. All authors contributed to the article and approved the submitted version.

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Conflict of interest

JS declares that she has received a financial compensation by the German Self-Help Network for Skin Picking to present the findings of the study on the German Self-Help Meeting "BFRB Tage 2021" to present the results of this study.

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.

Publisher's note

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Evidence of the content validity, acceptability, and feasibility of a new Patient-Reported Impact of Dermatological Diseases measure

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Background: The Global Research on the Impact of Dermatological Diseases (GRIDD) team is developing the new Patient-Reported Impact of Dermatological Diseases (PRIDD) measure of the impact of dermatological conditions on the patient's life, in partnership with patients. To develop PRIDD, we conducted a systematic review, followed by a qualitative interview study with 68 patients worldwide and subsequently a global Delphi survey of 1,154 patients to ensure PRIDD items were meaningful and important to patients.

Objective: To pilot test PRIDD with patients with dermatological conditions, focusing on its content validity (comprehensiveness, comprehensibility, and relevance), acceptability, and feasibility.

Methods: We conducted a theory-led qualitative study using the Three-Step Test-Interview method of cognitive interviewing. Three rounds of semi-structured interviews were conducted online. Adults (≥ 18years) living with a dermatological condition and who spoke English sufficiently to take part in the interview were recruited through the International Alliance of Dermatology Patient Organizations' (GlobalSkin) global membership network. The topic guide met the gold-standard COSMIN (Consensus-based Standards for the Selection of Health Measurement Instruments) standards for cognitive interviewing. Analysis followed the thematic analytical model of cognitive interviewing.

Results: Twelve people (58% male) representing six dermatological conditions from four countries participated. Overall, patients found PRIDD to be comprehensible, comprehensive, relevant, acceptable, and feasible. Participants were able to discern the conceptual framework domains from the items. Feedback resulted in: the recall period being extended from 1 week to 1 month; removal of the 'not relevant' response option; and changes to the instructions and item ordering and wording to improve clarity and increase respondents' confidence in their ability to respond. These evidence-based adjustments resulted in a 26-item version of PRIDD.

Conclusion: This study met the gold-standard COSMIN criteria for the pilot testing of health measurement instruments. The data triangulated our previous findings, in particular the conceptual framework of impact. Our findings illuminate

how patients understand and respond to PRIDD and other patient-reported measurement instruments. The results of comprehensibility, comprehensiveness, relevance, acceptability, and feasibility of PRIDD provide evidence of content validity from the target population. The next step in the development and validation of PRIDD is psychometric testing.

KEYWORDS

patient-reported outcome measure, dermatology, pilot test, cognitive interview, content validity (MeSH), patient-centered, quality of life, burden of disease

1. Introduction

Dermatological conditions carry a substantial physical, psychological, and social burden for patients (1, 2). The stigma of living with a visible condition (3), symptoms including pain and itch (4, 5), and financial cost (6) partially explain this burden (7). Many dermatological conditions have associated comorbidities (8), further increasing the disease burden (9).

The Global Burden of Disease (GBD) project (10, 11) is the most comprehensive worldwide epidemiological study to date, providing burden and mortality estimates for health problems at global, national, and regional levels. These estimates are exceptionally influential as they provide the evidence-base for identifying patient need, determining resource allocation and research priorities globally. We, along with others in the dermatology community [e.g., (12)], maintain that the GBD studies systematically underestimate the burden of dermatological conditions as they are evaluated according to symptoms that affect only the skin (itch, disfigurement) and do not include the broader psychological and social aspects such as depression, anxiety, stigma, and social isolation in their measure of impact (13–16).

The Global Research on the Impact of Dermatological Diseases (GRIDD) project, the first patient-initiated and led impact research project in dermatology, is collecting global data on the impact of living with dermatological conditions. These data will support local, national, and international advocacy work to prioritize dermatological conditions more accurately in the global health debate.

To address GRIDD's aim, a comprehensive measure of the impact of dermatological conditions on the patient's life is required. Our systematic review (17) evaluated the quality of existing dermatology-specific (can be used across conditions) patient-reported outcome measures (PROMs) against the gold-standard Consensus-based Standards for the Selection of Health Measurement Instruments (COSMIN) criteria (18). PROMS, like all measurement instruments (e.g., thermometers, sphygmomanometers), must meet predefined criteria for measurement properties—validity, reliability, and responsiveness—to have confidence that the data they produce are accurate (19–21). None of the 36 existing dermatology PROMs identified in our review, including widely used measures such as Dermatology Life Quality Index (DLQI) (22) and Skindex (23–25), met the standards to be recommended for use according to their known measurement properties and could not capture the full impact of the dermatological condition on the patient's life according to our conceptual framework of impact (26). The single most common reason for poor quality assessment was insufficient patient involvement during PROM development. This included, for example, inadequate sample sizes and inappropriate data collection methods (27, 28). Other systematic reviews of existing quality of life PROMs in the context of psoriasis (29), eczema (30), and acne (31) have found a similar lack of adequate dermatology-specific PROMs.

We are developing the Patient-Reported Impact of Dermatological Diseases (PRIDD) measure in close collaboration with patients and according to best practices in PROM development (Supplementary material 1) (18, 19, 32–34). PRIDD is designed for use with adults (≥18 years) with a dermatological condition worldwide and for use in research and clinical practice. Congruent with best practice in cross-cultural translation of PROMs, PRIDD is initially being developed and validated in English before being translated into other languages.

Content validity, "the degree to which the content of an instrument is an adequate reflection of the construct to be measured" (35), is considered the most important measurement property (28, 36). We began the content validity phase of PRIDD development by conducting a qualitative interview study with 65 patients from 29 countries representing 29 dermatological conditions (26) and identified 263 areas of impact that cut across conditions and global regions. This work formed, to our knowledge, the first conceptual framework of the impact of dermatological conditions on patients' lives. In the second phase of PRIDD development, 1,154 patients from 65 countries representing 90 dermatological conditions participated in a global Delphi survey to prioritize the 263 items for inclusion in PRIDD (37). While existing dermatology PROMs have included a range of domains relevant to the construct of impact (17), no single PROM has unified all relevant domains outlined in the conceptual framework of impact. This demonstrates that, as the first measure to capture all aspects of the conceptual framework as a unified construct, PRIDD advances knowledge in and makes a unique contribution to dermatology.

Following best practice, the next phase in PRIDD development is to pilot test the measure with dermatology patients and make any necessary adjustments (38, 39). The purpose of the pilot is to rigorously test three aspects of content validity: comprehensiveness (all key aspects of impact are present), comprehensibility (items are understood by respondents as intended) and relevance (all items are relevant to the impact of dermatological conditions from the patients' perspective) (39). The acceptability (whether patients are willing to complete the instrument) and feasibility (whether patients are able to complete the instrument) can also be tested.

Cognitive interviewing is a pilot testing method that use a semi-structured topic guide to direct the interview according to Tourangeau's four-stage model of question response (40, 41) to obtain

information about how participants interpret questions and choose their answers. The COSMIN group recommend the Three-Step Test-Interview (TSTI) (42, 43) method of cognitive interviewing as this combines the "think-aloud" (44) and "probing" techniques (36, 38), thereby offsetting the weaknesses of each and providing a deeper understanding of how questions are interpreted and answered (38).

The aim of the current study was to pilot-test PRIDD by qualitatively exploring whether the measure (items, structure, response options and recall period) is comprehensive, comprehensible, relevant, feasible, and acceptable to people with dermatological conditions through cognitive interviews.

2. Materials and methods

2.1. Design

We conducted a theory-led, qualitative study using the TSTI method of cognitive interviewing to pilot test PRIDD. This study was tested against the latest COSMIN guidance on the pilot testing of PROMs (27, 33, 45) and is reported according to the Cognitive Interviewing Reporting Framework (46). Ethical approval was obtained from Cardiff University School of Healthcare Sciences Ethics Committee (SREC:637).

2.2. Participants

Participants met the inclusion criteria if they were an adult (≥18 years) with a dermatological condition from anywhere in the world and spoke English sufficiently to take part in the interview and complete PRIDD independently (without a translator). Those who required translation to complete PRIDD were excluded as construct equivalence, the assumption that items in the translation measure the same construct in the same way as in the original language (47–49), could not be determined and, therefore, confidence in the evidence of content validity would be lacking. Children and proxies, such as family members or carers, were also excluded as they are not PRIDD's target population.

Participants were drawn from PRIDD's target population via the International Alliance of Dermatology Patient Organizations' (GlobalSkin) global membership network using purposive sampling to achieve maximum variation according to dermatological condition and demographic factors: age, gender, and country of residence. Participants were directed to a secure online platform which included the participant information sheet (PIS), electronic consent form, and interview booking information. Twelve patient organizations were invited to recruit to the interviews; 8 (66.7%) agreed to participate. Reasons for non-participation included lack of staff capacity, scheduling conflicts, and non-response. Recruitment ceased at the point of data saturation; when there was sufficient evidence that most problems had been detected and/or resolved (46, 50).

2.3. Materials

We tested the first draft of PRIDD (Supplementary material 2), a 27-item, English language measure of the impact of a dermatological condition on the patient's life over the last week. The conceptual framework of impact (26) depicts a reflective measurement model (Supplementary material 3). The first draft of PRIDD has five subscales: physical impact, psychological impact, social impact, daily life and responsibilities impact, and financial impact. All items are rated on a 5-point scale with scores of 0 ("never"), 1 ("rarely"), 2 ("sometimes"), 3 ("often"), and 4 ("always"), each with an additional "not relevant" option.

A topic guide was developed detailing the interview procedures, instructions, and questions (Supplementary material 4). Two versions of PRIDD were used during the interviews: one with the original item order and one with items in reverse order. This enabled us to test item order effects (i.e., whether the order in which the items are presented affects people's responses) and establish whether items were understood independently of each other. An online platform was created to enroll potential participants in the study using the PIS and consent form and included a demographic questionnaire.

2.4. Procedure

Twelve interviews were conducted via Zoom video conferencing software across three rounds from 2 August to 1 September 2021 with one of four researchers (RP, RH, MVL, and NTG), at a mutually convenient time. All interviewers were trained in cognitive interviewing by the study co-investigator (CB) and had backgrounds in healthcare practice and/or research.

Interviews were approximately 1 h long and followed the three steps of the TSTI method (see Supplementary material 5). They were audio-recorded using a high-quality audio recorder (OLYMPUS WS-833) and transcribed verbatim. Transcripts were checked and anonymized by RP by being allocated participant identifiers (PIDs).

2.5. Analysis

Data collection and analysis were interrelated and concurrent, with analysis beginning after the completion of the first interview. Accordingly, generated themes and edits made to PRIDD were incorporated into subsequent interviews.

Quantitative data were uploaded to SPSS version 26 and sample characteristics were summarized for clinical and demographic variables. Qualitative data were exported to NVivo 12 qualitative data software package. RP independently analyzed the data. NTS reviewed the coding and results reporting for accuracy. Analysis followed the thematic analytical model of cognitive interviewing (51) (see Supplementary material 6). This produced a summary of each item's performance that established the comprehensiveness, comprehensibility, and relevance of the items, providing evidence of content validity and informing evidence-based improvements.

3. Results

Eighteen people completed the online consent form and demographics questionnaire. Of these, three people were excluded because they were not sufficiently proficient in English to complete PRIDD independently and three did not respond to invitations to schedule an interview. In total, 12 people (response rate = 67%) across

TABLE 1 Participant characteristics.

	n (%)
Total	12
Age	*M* = 53.42 (SD = 15.87, range = 29–75)
Gender	
Male	7 (58.3)
Female	5 (41.7)
Dermatological condition	
Common[a]	7 (58.3)
Rare[b]	5 (41.7)
Duration (years)	*M* = 31.39 (SD = 20.59, range = 3–60)
Country	
UK	7
Ireland	3
Canada	1
USA	1

[a]Psoriasis (*n* = 5); Alopecia (*n* = 2).
[b]Discoid Lupus, Hidradenitis Suppurativa, Extensive Linear Porokeratosis (*n* = 1); Pityriasis Rubra Pilaris (*n* = 2).

six dermatological conditions (Table 1) and four countries participated in an interview.

Supplementary material 7 outlines the changes made to PRIDD between the three rounds of cognitive interviews. Evidence-based adjustments resulted in a 26-item version of PRIDD (Supplementary material 8).

3.1. General feedback

Participants praised the comprehensiveness, comprehensibility, and relevance of PRIDD to their lived experiences:

> I've completed a lot of dermatological questionnaires, but I don't think I've ever seen them all integrated like this in such a questionnaire … I'm very, very happy with this. It has stirred my heart … There are things here that I wanted to discuss with my dermatologist. PID5, Patient with hidradenitis suppurativa, Ireland

> They were short questions, and they were quite easily answered. PID15, Patient with alopecia, UK

PRIDD also appeared to be acceptable and feasible for patients. The average time taken to complete the questionnaire was 4.11 min (SD = 1.35, range = 2.62–7).

> The questions are so concise. You can quickly fill that in, in the waiting room. PID12, Patient with extensive linear porokeratosis, Ireland

While no participants found any of the items offensive or objectionable, they felt that others might be "uncomfortable" (PID9, Patient with psoriasis, UK) with item 26 ("it has been difficult to be intimate with a partner") as it referred to intimacy, but stressed it was important to include. Instead, participants felt that completing PRIDD initiated a process of reflection on their experiences with their condition:

> I wasn't offended by any of them [items] … It actually made me aware of how much this is actually controlling my life again. PID11, Patient with discoid lupus, Ireland

A minority of participants, most with alopecia, questioned the focus on the negative impacts of dermatological conditions and felt that positive impacts should be included too.

> I think it's sometimes nice to balance the negatives out with positives … in the past week, I've felt a lot of empowerment, I've felt a lot of like confidence, I've felt a lot of people praising me for something I've tried to hide away for so long, so it's not just negatives that you could capture as well, having a separate question saying I've felt confident, or I've felt empowered or something. PID15, Patient with alopecia, UK

Some participants wanted to further elaborate on items with qualitative data.

> You could even go deeper than that … you could even have … a box to maybe put is there anything you'd like to add … that [you] feel is relevant … because everybody isn't the same PID16, Patient with Pityriasis Rubra Pilaris (PRP), UK

3.2. Feedback on instructions

Overall, the instructions appeared easy to comprehend as participants were able to summarize them accurately and succinctly.

> It was asking me to answer the below questions based on my condition, how it's affected me in the last week, and answer them with what's relevant to me and my experience. … I felt the instructions were really clear … it's a fairly straightforward questionnaire PID15, Patient with alopecia, UK

However, some "did not read that part [instructions]" (PID11, Patient with discoid lupus, Ireland), which affected the validity of their answers, particularly in relation to the recall period. On this basis, several sections of the instructions were emboldened to draw respondents' attention to the instructions and their most important aspects.

Some suggestions to improve clarity were provided. First, participants felt that the example "because you do not work" created confusion as it led participants to believe that the items should be answered in relation to both their dermatological condition and employment. As a result, this example was removed from the instructions.

> Going through the questions in my head, I don't know how work would have anything to do with the questions that were asked … I don't even really think you need it all. PID14, Patient with psoriasis, Canada

Second, some participants suggested alternatives to the term "dermatological conditions," feeling it was wordy. A minority of participants with conditions primarily affecting the skin suggested using 'a simple word like skin' (PID9, Patient with psoriasis, UK) instead. Others with conditions that did not primarily affect the skin such as alopecia felt that dermatology implied a focus on the skin and would prefer another word, but could not provide a suitable alternative:

> Is there another word to say skin, which includes hair, nails, whatever, you know? I don't think there is, but that's the only thing that I would maybe look into, but I don't think there is a synonym. PID18, Patient with alopecia, UK

Because most participants found it acceptable and it is more inclusive than "skin," the term 'dermatological conditions' was retained.

> You need it to be applicable to several different conditions, not just one and … there is the difficulty. So with that in mind, your questions are brilliant. PID18, Patient with alopecia, UK

> I am sure phrases like dermatological, I mean will be familiar to anyone with any sort of conditions PID13, Patient with psoriasis, UK

3.3. Feedback on the recall period

Participants were almost unanimous in their criticism of the one-week recall period. Many felt that a longer recall period was required to accurately reflect the impact that their dermatological condition has had on their lives, largely due to the relapse and remitting nature of many of these conditions:

> Seven days isn't long enough for someone with … [a] condition that they've no control over, and people can see it. Because that's another thing like, lupus can flare, and it'll go back down, and I can have three good weeks and then one really crap week where it's just blown up on my face. So, I still think that the past week is too short a term to ask someone how it is. PID11, Patient with discoid lupus, Ireland

Participants also explained that many people do not engage in some of the experiences captured by the items (e.g., intimacy, life decisions and social activities) on a weekly basis and so expanding the recall period would likely increase item relevance to a higher proportion of patients and consequently more accurately capture disease burden:

> If the timeframe had been three months, six months, a year, or your lifetime … the feedback would be very different. So, you talk about relationships, intimate with [a] partner, all of these kinds of things, you know, social interactions, if somebody hasn't had a social interaction in the last week they're going to say never, whereas if the timeframe is much larger, you're going to get a more realistic feedback. PID12, Patient with extensive linear porokeratosis, Ireland

A 2-week and 1-month recall period were tested. These were generally more acceptable to participants than the 1-week recall. A 1-month recall period was adopted, having been suggested as an alternative to the 1-week recall period by multiple participants.

3.4. Feedback on the items

A summary of the evidence of comprehensibility, relevance, and problems detected for each item is presented in Supplementary material 9. Nine of the 27 items remained unchanged because they were easily understood, relevant to participants and distinct from other items.

Sixteen items were modified to align them more closely with the intended concept of interest outlined in the item definition list or to reduce conceptual overlap with other items.

One item, "I have felt dismissed or abandoned by others," was deleted because it was not easily understood by participants and was felt to be highly similar to "I have been excluded, bullied or discriminated against."

Overall, participants found the item ordering acceptable. The five domains of the conceptual framework were evident in the items, as participants correctly recognized categories of items, providing evidence in support of the suitability of the item ordering as well as the conceptual framework.

> They seemed to be grouped together quite well and I think the order of them was fine. PID15, Patient with alopecia, UK

The order of seven items was changed to enhance understanding. For example, the item "my everyday choices have been affected (for example, choice of clothes, hairstyle or products)" was listed before the item "my life goals and choices have been affected (for example, career choice or having children)" to highlight that the latter does not include everyday choices, which some participants subsumed under life goals and choices.

Subgroup differences were found on four items. People with alopecia felt that the item "my treatment has caused practical problems (for example, by taking up time or being messy)" was not relevant to them as they had no treatments. They also differed from people with other conditions on three items as alopecia appeared to have a positive impact in terms of timesaving, reduced financial costs and feelings of attractiveness.

> It positively impacted it [daily routine], because I don't have to mess about with my hair as much in the morning… it's a bit of a blessing. PID15, Patient with alopecia, UK

3.5. Feedback on the response options

Participants found the response options ("never," "rarely," "sometimes," "often," and "always") to be appropriate, cover the full range of experience, and comprehensible.

> I found it quite easy, I think it gives a good range of options. Obviously always and never are complete extreme [s] and then a couple of the intermediates of different intensity, is fine. I think it

> is a really good way of asking questionnaires and usually makes it quite easy to answer. PID13, Patient with psoriasis, UK

Some participants had difficulty interpreting the "not relevant" response (NRR) option. NRRs caused confusion, especially for items where the condition had been an obstruction to engaging in the relevant life area. This was most clearly discussed in relation to the item on intimacy, for example:

> 'It's been difficult to be intimate with a partner' … this is the question that I always struggle with. [I chose] not relevant because I've not got a partner, but that can also be always, because I haven't got a partner, it can be both … the reason why I've not got a partner is because it's been difficult … I think it's an important question … I think [psoriasis is] … probably the reason why I'm single. In my formative years between when I started getting psoriasis and in hospital, was years when all my mates were getting wives and babies and all that. All of a sudden it had just passed me by, it had gone, you know. And it's like all of a sudden, I'm 40 odd and I'm like all my mates are married and having kids and I seem to have missed that bit. PID1, Patient with psoriasis, UK

Others could not distinguish the NRR option from the 'never' response option.

> There were some questions where it was never or … not relevant and I'm thinking … what did not relevant mean? … you might think not relevant is fairly self-explanatory but it's not in my case … what's not relevant? … I've ticked it and it's not relevant because it never occurred … [so] you'd say never, wouldn't you? PID9, Patient with psoriasis, UK

The edits to items 12 ("I have struggled to concentrate") and 26 ("I have been prevented from or found it difficult to be intimate with another person") reduced the need for the not relevant option as these items could now apply to all respondents, regardless of employment or relationship status. This option was no longer necessary and was therefore removed to simplify.

4. Discussion

This study tested the content validity, acceptability, and feasibility of PRIDD. It met the highest standards for cognitive interviews outlined by COSMIN (Supplementary material 10) (19, 27), providing high-quality evidence of the comprehensibility, comprehensiveness, and relevance of PRIDD from the target population. The study findings and resultant adjustments produced a 26-item version of PRIDD, ready for field testing, and psychometric testing.

4.1. Implications for measuring the impact of dermatological conditions on the patient's life

4.1.1. The challenge of dermatology-specific PROMs

With the International Classification of Disease (ICD)-10 (52) classifying over 1,000 dermatological conditions, dermatology patients are a particularly heterogeneous group in relation to age and condition type, relative to other medical specialties. Unsurprisingly then, participants differed in their relation to the term "dermatological condition" but understood the rationale behind this and no alternate sufficiently inclusive terms were suggested.

While PRIDD appears to be relevant to people with dermatological conditions overall, some sub-group differences were found. The physical, psychological, and social impacts were generally consistent across conditions but practical impacts such as time and financial resources differed for people with alopecia. They emphasized the positive impacts of their condition, for example, regaining time lost to styling hair. Nevertheless, the feedback indicated a consensus that PRIDD was relevant and accepted across conditions. We believe this shows that, despite their inherent challenges, dermatology-specific PROMs are appropriate but need to be developed carefully with high levels of patient involvement throughout.

4.1.2. The conceptual framework of impact

The findings of this cognitive interview study support our conceptual framework of the impact of dermatological conditions (26). First, participants' lived experiences encompassed the biopsychosocial nature of their conditions. Second, no new items or domains were added to PRIDD, and participants could identify which items corresponded to the underlying domains. Third, the data support our previous decision to remove an "impact of healthcare" domain from the original conceptual framework (37). One participant, for example, summarized this decision while reflecting on being dismissed by healthcare professionals saying, "that could be a whole … paper all by itself … that's a whole different ball game if you get involved in that" PID14. Future work should quantitatively hypothesis test the conceptual framework to complete the evaluation of content validity.

Given the importance patients placed on the influence of healthcare in determining the impact of their condition in our previous work (26, 37), we suggest that these data could form the basis of a separate 'quality of dermatological care' measure.

4.1.3. Patient perspectives on issues with response options

We pilot tested a 5-point rating scale with an additional NRR option for each item. NRR options are common in dermatology. The DLQI, the most widely used PROM in dermatology (53), for example, uses a sum score of its 10 items, eight of which have a NRR option that is given the same zero score as "not at all" responses (22). This scoring method assumes that NRRs are due to a lack of disease burden and therefore have no impact on overall quality of life scores. However, recently several independent studies have shown that this interpretation is problematic (54–56) and revised scoring methods have subsequently been proposed (54, 57). Concurrent with these findings, we found the NRR to be problematic as participants differed in their interpretation of this option with consequences for the accuracy of their scores.

This calls into question the current use and scoring of NRRs in dermatology PROMs. Indeed, the emerging body of research on NRRs has shown that approximately 20%–76% of patients provide at least one NRR on the DQLI (54, 56, 58–60). The frequency of NRRs differs across socio-demographic groups with the elderly, females, those not working full time, and less educated patients reporting higher rates of NRRs than others (54). This is may be related to the consistent finding that the DQLI items with the highest rates of NRRs are those on

impairment in work and school, sport, sexual relationships, and social activities (54–56, 61, 62), areas of life that may be less applicable to these particular subgroups. Content validity requires that the PROM is comprehensive, comprehensible, and relevant *across* the target population. Such high frequency and differing rates of NRRs suggest content validity issues with the DLQI as certain items are not relevant to a significant proportion of patients and subgroups groups (31). Indeed, since relevance is a central parameter of content validity (19, 27), the inclusion of items with NRRs, regardless of their rates, could be viewed as a fundamental threat to content validity.

Because NRRs are scored as 0, a higher yield of NRRs should be associated with a lower DLQI score. However, Rencz et al. (54) found the inverse; a greater number of NRRs was associated with a higher DQLI score, indicating poor construct validity. Researchers and clinicians have hypothesized that NRRs do not reflect actual lower quality of life burden but rather the opposite.

To our knowledge, this is the first study to provide the patient perspective on NRRs and clarify the above findings. First, we provide qualitative data to show that socio-demographic factors do play a role in the use of NRRs. For example, the item on work and study was not relevant to people who were retired. Second, our data suggest that low disease burden is not the only reason patients chose an NRR option. As hypothesized previously, NRRs can indicate a high disease burden. This is most clearly seen in items relating to romantic relationships and intimacy. Some participants felt that these items were not relevant to them as they were not in a relationship but explained that their condition was the cause of this. These findings challenge the use of NRRs in dermatology PROMs as they show that the assumption of low disease burden is not always correct.

We overcame the issues inherent in NRRs by following our participants' recommendation to remove this option. As all the items pilot tested here had been prioritized for inclusion in PRIDD, it was clear that these were important impact concepts to patients and therefore we did not remove items to remove the NRR. Instead, we maximized the applicability of each item across the target population. For example, the item "It has been hard to work or study" was changed to "I have struggled to concentrate" as this tapped the underlying concept while being applicable regardless of employment status or age. We were also careful not to link items too closely to specific examples. To illustrate, the DLQI item on leisure and daily activities asks "how much has your skin interfered with you going shopping or looking after your home or garden?." The true impact of the condition on the patient's leisure and daily activities may be hidden by this question if shopping, housework, or gardening are not relevant to them. We used neutral wording, e.g., "my leisure time/activities have been negatively affected" to overcome this. We also reworded the item "It has been difficult to be intimate with a partner" to "I have been prevented from or found it difficult to be intimate with another person" to increase its relevance in light of the finding that NRRs to this item may be due to high disease burden. We believe that by removing the NRR option and rewording items to maximize their applicability across the target population, we have overcome the scoring limitations of the existing dermatology PROMs by using a more valid and reliable method.

4.1.4. Determining the recall period

Choice of recall period is an aspect of internal validity as a suboptimal recall period can introduce measurement error. There is no "gold standard" recall period for PROMs as "one size does not fit all" (63). The FDA guidance (64) on PROM development states a preference for items with short recall periods or those that ask patients to describe their current or recent state. Their rationale is twofold. First, longer recall periods are thought to undermine content validity because they rely on memory and therefore may introduce recall bias. Second, longer recall periods may be impractical in research or clinical practice with frequent data collection points or clinic visits due to overlapping periods. Hence, we initially assumed that a one-week recall period would be the most appropriate for PRIDD.

Study participants almost unanimously criticized the one- and two-week recall periods and proposed longer recall periods (e.g., 1–6 months, years, or lifetime), supporting the concept of Cumulative Life Course Impairment in dermatology (65–68). Participant's views strengthen previous work suggesting that a shorter recall period likely underestimates the burden of long-term conditions (69), particularly those with a relapsing-and-remitting course (70), results in loss of information (71) and that patients can accurately recall over a longer period of time than the FDA guidance suggests (36), particularly when their issues are bothersome and memorable (69, 72). In response, we changed the recall period to 1 month, which is within the recommended range for PROMs of phenomena such as quality of life and is likely to reduce the risk of recall bias (63).

4.1.5. Acceptability and feasibility of PRIDD

During PROM development, a balance is evident between maximizing the information gained about the construct of interest and reducing respondent burden, meaning that every item in a PROM must earn its place (21). Where participant interviews demonstrated that items were not easily interpreted or clearly aligned with their underlying concept of interest, they were removed or edited during the interview rounds. In this way, this study provides evidence of the value of each of the 26 items.

PRIDD appears to be feasible for use, with participants taking an average of approximately 4 min to complete. The average time to complete PRIDD in research and clinical practice is likely to be lower because, in most cases, participants were thinking and responding aloud while completing PRIDD and edits were consequently made to improve the comprehensibility of the measure.

4.2. Strengths and limitations

Though it is an important step in the development and validation of new PROMs (27), the pilot testing of dermatology-specific PROMs is rare and, when conducted, is often of poor methodological quality (17). This is the first pilot study of a dermatology-specific PROM to both (a) be of high methodological quality and (b) show evidence sufficient content validity, acceptability, and feasibility, according to the COSMIN criteria (27).

The main strength of this pilot test is the use of qualitative methods. The interviews followed the COSMIN-recommended TSTI method of cognitive interviewing (38), eliciting data from a range of sources (i.e., observational, think aloud, and probing techniques). Our approach of asking participants to elaborate in detail regarding their understanding of each aspect of and item in PRIDD provided manifold definitions and examples of impact as well as identifying how participants understood each item. From these data, we could

detect and resolve problems with item wording, ordering, and redundancies. Notably, we followed the COSMIN guidance by testing each aspect of PRIDD separately and in its final form, except for a minor adjustment to the instructions (27). PRIDD, therefore, is the first dermatology-specific PROM to meet the COSMIN standards for cognitive interviews (17).

Participants were sampled purposively through GlobalSkin's unique global network to achieve diversity in terms of clinical (e.g., common and uncommon, inflammatory and non-inflammatory dermatological conditions) and demographic variables (e.g., age and gender). This strengthens the content validity of PRIDD for global use across dermatological conditions. However, our participants were mainly patient organization members and therefore may not represent the experiences or views of non-members. With a sample size of 12, we were able to demonstrate data saturation as no major problems that could be resolved were identified in the final round of interviews. Still, rarer problems or those pertaining to conditions not represented may have gone undetected. Five of the 12 participants had psoriasis and we were unable to recruit participants with other common conditions such as acne, eczema, and vitiligo or those who do not speak British, American, or Canadian English, reducing the transferability of PRIDD. The next stage of development is psychometric testing. Here, we will be able to further test PRIDD with a larger sample of patients representing a wider array of dermatological conditions and global regions and who speak other variations of English.

4.3. Implications for clinical practice

A PROM's potential to advance person-centered care is contingent upon its applicability, comprehensiveness, and relevance to patients. PRIDD should not *replace* the discussion of the wider impact of the disease during the clinical consultation, but *facilitate* and frame patient-centered discussions (73). Indeed, participants in the current study and previous dermatology PROM development work [e.g., (74)] expressed a desire to provide qualitative information alongside their response options to afford clinicians a deeper understanding of their lived experiences.

As Tourangeau's (40, 41) cognitive theory demonstrates, the completion of a PROM requires cognitive processing. Clinicians should be aware that a patient's literacy level, among other factors, may facilitate or create barriers to PROM completion. Consequently, patient-centeredness in the administration of PROMs should be paramount to avoid perpetuating health inequalities.

Consistent with the literature (75, 76), while developing PRIDD, participants have consistently expressed that the psychological aspects of dermatological conditions require more attention (26, 37). There is a need to establish effective psychological interventions and pathways to psychological support, improve clinicians' skills and confidence to address psychological and social issues (77) and develop effective collaboration between dermatologists and mental health professionals including psychologists.

4.4. Implications for research

Some participants reported positive impacts of their dermatological conditions and expressed a desire for these to be measured as well as the negative impacts. The positive impacts reported—e.g. empowerment, confidence, and gratitude—are congruent with Tedeschi and Calhoun's (78) work on post-traumatic growth and validate the analysis of our concept elicitation study which also discerned positive impacts (26). Because PRIDD focuses on the burden of dermatological conditions, positive impacts were not incorporated as this would violate the unidimensionality required of the measure. Given the importance of the various positive impacts to patients, the data gathered throughout the development of PRIDD could serve as the basis of a new, separate measure of the positive impact of dermatological conditions. Qualitative research to inform the development of psychological interventions typically focuses on the negative aspects of long-term health conditions, but it can be worthwhile to consult with people with positive experiences as they are well placed to provide input that may lead to effective interventions.

Researchers, clinicians, and regulatory agencies should choose measurement instruments based on their quality. Before PRIDD can be recommended for use in research and clinical practice, validation of the measurement properties (validity, reliability, and responsiveness) and interpretability information (i.e., Minimally Important Change) is required (36). While cognitive interviews allow patients to have greater input into the item refinement process than purely statistical methods allow, ideally, they would not be the sole method of item refinement. Several items were identified as having conceptual overlap in the current study. It will be important to test for item redundancy and data structure in the psychometric testing phase.

5. Conclusion

In this final step in the content validity phase of development, PRIDD was pilot tested through cognitive interviews with the target population. The data triangulated previous findings, recommendations, and the conceptual framework of impact. The results provide insight into how patients understood the items in PRIDD and shed light on the patient perspective on current debates regarding PROMs in dermatology. The resultant confirmation of the comprehensibility, comprehensiveness, relevance, acceptability, and feasibility of PRIDD provides evidence of content validity from the target population. The next step in the development of PRIDD is the psychometric testing phase.

Data availability statement

The datasets presented in this article are not readily available because, due to the nature of this research, participants of this study did not agree for their data to be shared publicly. Requests to access the datasets should be directed to RP, pattinsonr@cardiff.ac.uk.

Ethics statement

This study involves human participants was reviewed and approved by Cardiff University School of Healthcare Sciences Ethics Committee. The patients/participants provided their written informed consent to participate in this study.

Author contributions

RP: conceptualization, methodology, validation, formal analysis, investigation, resources, data curation, writing—original draft, writing—review and editing, visualization, supervision, and project administration. NT-S: methodology, validation, and writing—review and editing. RH, MV, and NT: investigation and writing—review and editing. JA: conceptualization, resources, writing—review and editing, project administration, and funding acquisition. AF: resources, writing—review and editing, and project administration. NC: methodology, writing—review and editing, and supervision. MA: conceptualization, methodology, writing—review and editing, and supervision. CB: conceptualization, methodology, validation, resources, writing—review and editing, and supervision. All authors contributed to the article and approved the submitted version.

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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.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2023.1020523/full#supplementary-material

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A network analysis of psychological flexibility, coping, and stigma in dermatology patients

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Introduction: Despite the negative effects of stigma in individuals with skin conditions, interventions to address its effects are rare. This might be in part due to a continued lack of understanding as to how individuals respond to stigma.

Methods: In this study, we employed a step-case analytic method, using traditional regression, moderation, and network analyses, to examine the role of psychological flexibility (PF) with stigmatized experiences, and stigma-related outcomes. We run a cross-sectional study (n = 105 individuals with various skin conditions) and analyzed stigma-related variables. We included variables examining perceived stigmatization (PSQ), anxiety (GAD-7), depression (PHQ-9), well-being (EQ5D5L), and variables stemming from the PF model (CompACT), presented as three coping with stigma responses, namely "open," "aware," and "active.".

Results: Using network analysis, the most influential or central variables that contributed to stigma were generalized anxiety, perceived stigmatization, and valued actions. In relation to PF, being open to the experience of stigma (as opposed to avoidance), keeping a distance from stigmatized thoughts (as opposed to self-stigmatizing), and bringing attention to value-based committed actions (as opposed to passivity) were all found to contribute to less stigmatized experiences.

Discussion: The results indicate that two of the three skills of the PF model ("open" and "active") may be important targets for interventions targeting stigma in people living with skin conditions.

KEYWORDS

stigma, psychodermatology, process-based therapy, psychological flexibility, coping

1. Introduction

Stigma is characterized by a proneness to either devaluate and discredit a person/group considered to possess a negative attribute (1), or an individual's/group's tendency to come to believe what others attribute to them (2, 3). Given the highly visible nature of skin conditions, it is unsurprising that stigma is commonly experienced (4–7). The visible marks on the skin can

be perceived as "deviant" from what is considered the norm in appearance, making it easier for people in society to stigmatize individuals with skin conditions, compared to other conditions that show no visible differences in appearance (e.g., individuals with diabetes) (8, 9).

Existing research shows that stigma in various skin conditions, including acne, atopic dermatitis, vitiligo, and psoriasis, is associated with poorer quality of life and increased distress (7, 10–18). For example, individuals with psoriasis often feel "different" from others. This increases stigma-related stress, consequently, impacting individuals' daily functioning (19). Further, studies in patients living with acne show that stigma is the largest contributor in predicting poorer quality of life, over and above disease and demographic variables (11). These findings are concerning, highlighting that individuals with skin conditions have to deal with the diagnosis/management of the condition in addition to the potential negative effects of feeling stigmatized. Promoting approaches that focus on managing stigma and distress, is required, yet, this has proven to be difficult thus far to achieve (20, 21).

One approach that helps researchers and clinicians to identify effective responses to stigma is the process-based approach (22–25). This approach attempts to identify common responses to stigma that can be flexible enough so that they can concurrently target the contextual (e.g., stigmatization) and psychological (e.g., how individuals cope with thoughts and emotions) elements of stigma (20). A therapeutic approach that can target both the context of stigma and the way individuals respond to it is psychological flexibility (PF) (26–28). PF includes three trainable psychological skills, named "openness to experience" (defusion and acceptance), "behavioral awareness" (contacting the present moment and self-as-context), and "valued action" (values and committed action) that can be presented as "coping with stigma" responses. Research examining these PF-related skills on other conditions, such as stigma in relation to chronic pain or weight self stigma shows that the PF skills can buffer the effects of stigma (29–32). These sets of psychological skills are amenable to interventions (e.g., can be employed as coping with stigma responses outside of a therapy room) and can be delivered in different forms (e.g., digitally, in-group, one-to-one, etc.) (33–35). Yet, no research so far has examined how these skills can help individuals with skin conditions, experiencing stigma.

To date, the existing studies attempting to identify parameters of coping with stigma in this population are rare (6, 20). Further, existing studies have employed traditional methods to examine variables, such as mediation and moderation analyses that only present a static picture of how stigma, coping with stigma, and stigma-related outcomes interact. For example, McCleary-Gaddy and James (36) found mediating effects of stigma consciousness between skin tone, life satisfaction, and psychological distress among African Americans, highlighting the potential role of increased awareness of stigmatization in reducing distress. Further, Bohm et al. (37), and Schmid-Ott et al. (38) both found mediating effects of reduced self-esteem and rejection as stigmatization parameters in skin condition severity and quality of life, indicating the potential role of defusion from stigma related experiences as a coping response. Likewise, Krüger and Schallreuter (39) found behavioral avoidance as the main coping with stigma response in patients with vitiligo, and Lu et al. (40) found helplessness as an illness cognition response to stigmatization in patients with psoriasis and atopic dermatitis.

Overall, traditional moderation and mediation methods limit practical applications for intervention development targeting stigma (41, 42). This is because they may generate a wide range of skills (20), potentially increasing uncertainty about which skills to select and target (20, 43). Further, these approaches do not allow the dynamic and simultaneous bi-directional interaction of stigma-related thoughts, emotions, and behaviors (responses to stigma) to be studied. Given that stigma is a multi-dimensional construct (41, 42), new innovative data-driven methods that can address these complexities, such as network analyses, are needed.

Unlike traditional mediation and moderation analyses, network analysis explores relations between variables through partial correlations, which are visually illustrated with links (e.g., lines connecting different variables) that show the connection between the variables. Adopting such an approach would allow the conceptualization of stigma as a network of interactional patterns, centred around defining variables of interest, such as coping with stigma responses, and stigma-related outcomes, rather than artificially assigning variables into static dependent and independent variables (24).

A network analytic approach was taken in this study that tested the importance of variables and identified an empirically dynamic network of skills focusing on stigma alleviation. Stigma-related variables, including perceived stigmatization, anxiety, depression, well-being, and psychological variables, such as PF, were examined. In short, this study aimed to identify the most influential or central parameters contributing to stigma alleviation by attempting to determine (a) the relationships among all variables of interest, (b) the variance of stigma and PF skills in explaining individuals' well-being; (c) the potential role of certain or all the three PF skills in buffering the effects of stigma; and (d) the bidirectional relations among the PF processes, stigma, and stigma related outcomes.

2. Methods

2.1. Design

The study was nested in a multi-center European study conducted by the European Society for Dermatology and Psychiatry (ESDaP)[1]. The ESDaP multi-country study collected data on the association between stigmatization and the psychosocial burden of individuals living with a skin condition in 17 European countries (ESDaP, 2016). In addition to the variables examined across all countries, some countries also investigated other variables. In the UK, the survey was expanded to include variables related to psychological flexibility so that the aims of this study could be addressed. The study had ethical approval from the NHS Health Research Authority (18/LO/0639).

2.2. Inclusion and exclusion criteria

Eligible participants were recruited from patients attending outpatient appointments with a dermatology department within a large teaching hospital in the UK. Inclusion criteria consisted of individuals

1 https://www.psychodermatology.net/

over 18 years of age with a sufficient English capacity to complete questionnaires and provide consent, and a diagnosis of a chronic skin condition. The exclusion criteria consisted of a non-primary diagnosis of chronic skin conditions, the presence of a primary psychiatric condition relevant to skin distress (e.g., trichotillomania, delusional parasitosis etc.), a benign skin lesion (e.g., a noncancerous related skin lesion), and/or a suspected/diagnosed skin cancer.

2.3. Recruitment and study procedures

Eligible participants were recruited using convenience and purposive approaches. During clinic appointments, Dermatologists invited consecutive patients who met the study criteria to participate. Upon consent, participants completed the package of questionnaires with the assistance of a research team member, and study Dermatologists recorded their skin condition and severity. Dermatologists used the International Classification of Diseases (ICD-10) criteria to rate the participating individuals' severity of their skin disease as mild, moderate or severe. Data collection occurred between July and September 2018. Figure 1 presents the flow chart with all the study procedures.

2.4. Measures

Participants completed a series of measures, including demographics, such as age, gender, education level, and employment status, clinically relevant questions about their skin conditions (disease severity and intensity), and a set of five standardized self-reported questionnaires, measuring stigma, depression, anxiety, quality of life, and a measure assessing the skills stemming from the PF, presented as three dyads or coping responses: "open," "aware," and "active." In sum, the following measures were completed by the participants.

2.4.1. Stigma-related variables

Perceived Stigmatization Questionnaire (PSQ) (44) consists of 21 items, assessing perceived stigmatization in social experiences (e.g., people avoid looking at me or people do not know how to act around me) in individuals with visible differences in appearance. Higher scores indicate a greater perception of stigmatized behaviors. The measure assesses stigmatized behaviors on a 5-point Likert scale (never, almost never, sometimes, often, always) and has good internal consistency and criterion validity with other related psychosocial constructs (e.g., good convergent and discriminant validity within a sample of adult burn survivors) (44). The Cronbach's alpha for this study was a = 0.90.

2.4.2. Psychosocial-related outcome variables

The Patient Health Questionnaire (PHQ-9) (45) is a self-administered questionnaire with 9 items, measuring the presence and severity of depressive symptoms (e.g., feeling down, depressed, hopeless or having little interest or pleasure in doing things). Participants are required to rate the frequency of nine symptoms of depression on a scale from "not at all (0)" to "nearly every day (3)" for the past 2 weeks. Total scores can range from 0 to 27. Depression is indicative of "mild" (scores 5–9), "moderate" (scores 10–14), "moderately severe" (scores 15–19), or "severe" depression (>20). The measure presents excellent internal reliability (Cronbach's alpha = 0.89) and test–retest reliability ($r = 0.84$) (46), as well as an acceptance construct validity, as assessed by functional status (46). The Cronbach's alpha for this study was a = 0.98.

The Generalized Anxiety Disorder Assessment (GAD-7) (47) is a self-administered 7 items measure of symptoms of a generalized anxiety disorder (GAD). The questionnaire asks participants to rate the frequency of nine symptoms of GAD within the last 2 weeks on a scale from "not at all" to "nearly every day" (scored 0–3 with a total score ranging from 0 to 21). Total scores can be interpreted of "minimal" (0–4), "mild" (5–9), "moderate" (10–14), or "severe" (15–21) anxiety. Research shows that the GAD-7 has excellent reliability (test–retest correlation of 0.83) and construct validity, as presented with correlations measuring functional impairment (47). The Cronbach's alpha for this study was a = 0.98.

The EuroQOL 5-Dimensions (EQ5D5L) (48) is a visual analog scale (VAS) assessing self-reported health. Participants are asked to rate their health on the day of reporting ("today"), using a zero ("the worst health you can imagine") to 100 ("the best health you can imagine") metric. The validity of the EQ5D5L in skin populations shows good psychometric characteristics (49), showing moderate-to-strong correlations with other health-related quality-of-life measures (e.g., SF-12) and can detect significant changes in health status over time. The VAS is a subtest within this measure, and validation is not available for this subscale alone. Thus, the psychometric assessments refer to the whole EQ5D5L.

2.4.3. PF related variables

The Comprehensive Assessment of Acceptance and Commitment Therapy Processes (*CompACT*) (50) is a 23-item measure of psychological flexibility with three subscales: openness to experience, behavioral awareness, and valued actions. The three factors represent latent constructs of PF skills, merged as dyads, reflecting acceptance and defusion ("open" being present; CompOE), present moment awareness and self-as-context ("aware" behavioral awareness; CompBA), and values and committed actions ("active"; doing what matters"; CompVA) (51). Participants respond to a series of items (e.g., I behave in line with my personal values) on a 7-point Likert scale from "strongly disagree" to "strongly agree." Higher scores in each subscale or the total score indicate greater psychological flexibility (e.g., greater openness to experience, mindful attention to current activities and engagement in valued actions). The measure demonstrates excellent internal consistency in its subscales ($\alpha = 0.90$, 0.87, and 0.90, respectively) and acceptable criterion validity with existing ACT measures, such as the Acceptance and Action Questionnaire (50). The Cronbach's alpha for this study was for the CompOE $a = 0.88$, for the CompBA $a = 0.91$, and for the CompVA $a = 0.93$, correspondingly.

2.5. Statistical analyses

As part of the preliminary analysis, we examined the parametric assumptions and tested the normality of distribution by visually inspecting the histograms, P–P residual plots, and missing cases. We did not detect a serious violation of the normality assumptions (linearity, homoscedasticity, collinearity, and multicollinearity). Also, univariate and multivariate outliers and missing cases were negligible. We examined the histograms and plots for any issues with the skewness and kurtosis. There were no values below or above the −/+3.

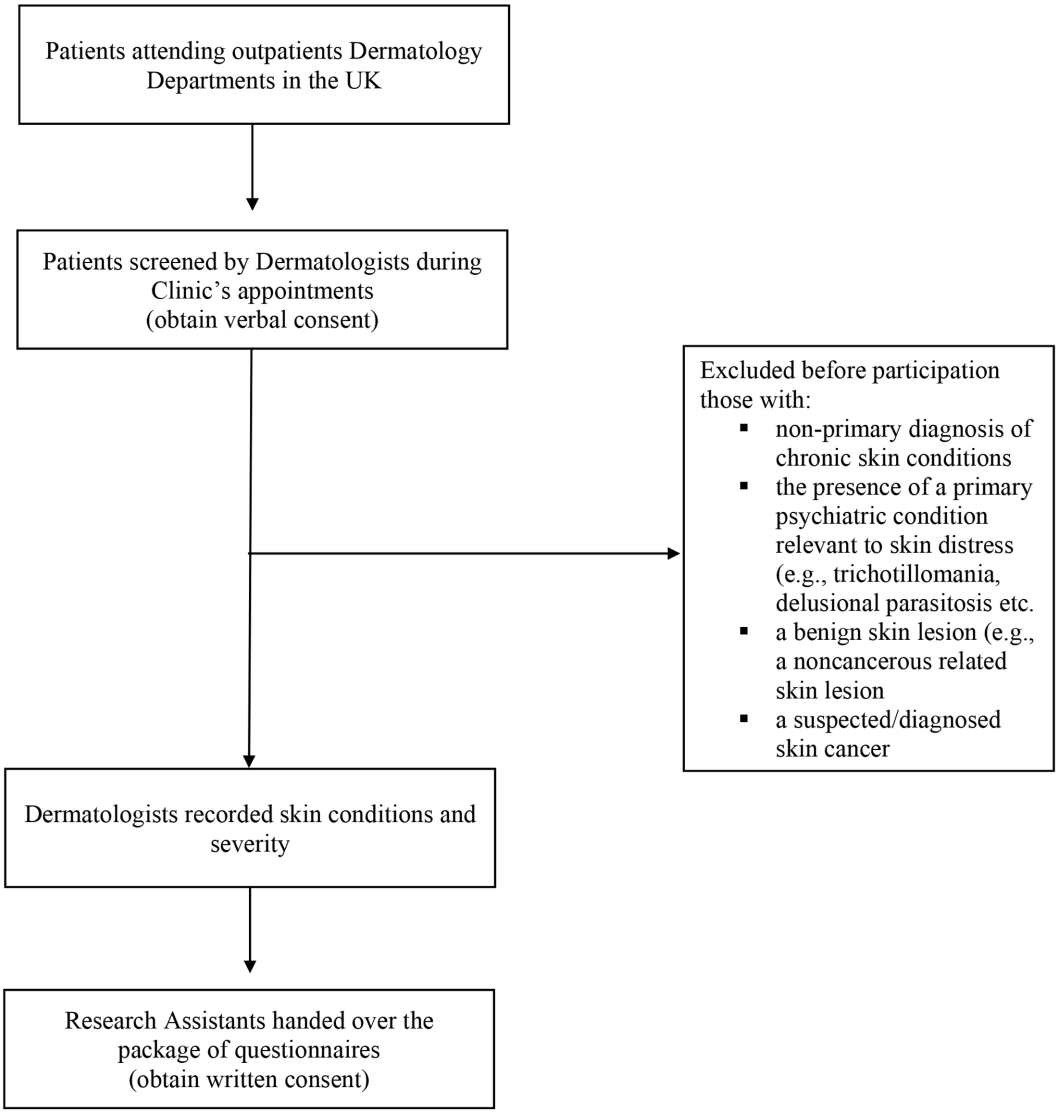

FIGURE 1
Flow chart with study procedures.

The measures of psychological distress (anxiety and depression) were positively skewed. Ratings of self-reported health were negatively skewed. There was a notable outlier in the stigma data, with one participant scoring very high on the Perceived Stigmatisation Questionnaire (49, $z = 3.15$). We rerun all the reported analyses without the outlier and conclusions drawn were the same. Therefore, the reported results include the outlier as it was deemed a genuine, although extreme score. Hence we left the data intact. To corroborate with the visual inspection of the dataset, we run a missing data analysis to assess any pattern of non-identifiable missingness (52). Little's MCAR test indicated that the data were missing completely at random.

The main analytic plan followed an exploratory step-wise approach. We first explored a "static" or pre-defined model of variables, using traditional regression and moderation regression analyses, to examine predictive relationships among the variables (e.g., stigmatized experiences as predictors of distress and low perceived health). We then examined "dynamic" and "bidirectional" relationships of the variables using network analyses. We used IBM SPSS Statistics 27 to test and compare the variables' importance. We then used the packages of JASP[2] and R studio (53) to run the network analysis.

Firstly, we run a series of Pearson's correlation coefficient analyses (54) and a series of hierarchical multiple linear regression analyses (simultaneous forced entry method using R^2 and adjusted R^2), to examine the prediction of stigma on well-being, controlling for any effects of age, gender, and clinician-rated severity of the skin condition. Then, we performed a series of moderation analyses, to test whether PF moderated the relationship between feelings of stigma and well-being. We then run a network analysis to simulate a hypothesized stigma model and identify the most central, therefore, most influential, PF skills that correlated with stigmatization and stigma-related

2 https://jasp-stats.org/

outcomes. We examined the partial correlations network (total scale/subscale scores, rather than individual items) of the PSQ (stigma), GAD (generalized anxiety), PHQ9 (depression), EQ5D5L (perceived health), and the three sub-scales of the *CompACT*, CompOE (open to experience), CompVA (values), and CompBA (Behavioral awareness). Using the glasso R package (55) embedded in the JASP, we depicted graphically the edge weights connecting the nodes (e.g., the variables included in the model) and examined the nodes' strengths. We also used the Fruchterman-Reingold positioning algorithm (56)- a forced-directed method- to visualize the network model variables and examine which variables are posed in the center of the graph.

For the interpretation of the outcomes, we applied the graphic LASSO [Least Absolute Shrinkage and Selection Operator (57)] estimator [a stunning parameter set to 0.5-using the EBIC; Extended Bayesian Information Criterium (58)], to counterbalance the relevant small sample size of the study (model regularization) (59). The technique estimates the variance–covariance matrix and removes less relevant edges from the model, returning a parsimonious network of partial correlation coefficient which is more conservative and easily interpretable (e.g., only a reasonably small number of edges are used to explain the covariation structure of the model). We also examined the stability of centrality indices using a parametrization technique called *bootent* (59) in the *R* software (53). We estimated the Coefficient Intervals (CIs), to examine if the order of centrality indices remains the same after bootstrapping (re-estimating) the network with fewer cases (e.g., dropping cases from the original dataset) and without replacing them. To assess this stability, we used the correlation stability coefficient, or CS-coefficient (quantification of stability). CS-coefficient defines the percentage of cases that can be dropped, with a 95% probability of maintaining ~0.70 correlation, compared to the completed data (59). The edge-weight accuracy is estimated when values are over 0.50 but not lower than 0.25. Finally, we examined the edge weights CIs to assess the precision with which PF processes are strongly interconnected within the network. Narrower CIs indicate better accuracy (59).

2.6. Statistical power and sample size

The proposed analysis included a maximum of seven variables to detect medium effect sizes in the first round of analyses which included multiple regression and moderation analyses. Following suggestions from Cohen and Field (60, 61) a G* power analysis (62) suggested a sample size of 105 participants, for $p < 0.05$. For the second round of network analysis, the number of observations in our tested model (e.g., $n \sim 100$) seemed appropriate for estimating the partial correlation network analysis. That is, we expect 20 nodes to occur on the network model, allowing us to examine the validation and robustness of the model even when the highly conservative Lasso penalty estimator is applied (59).

3. Results

3.1. Sample and descriptive characteristics

One hundred five participants filled out the questionnaires, and 57% ($n = 59$) were women, with a mean age of 54 (ranging from 19 to 90). Most of the participants had completed the highest level of education (GCSE equivalent or below; 63%, $n = 66$), with more females ($n = 46$) than males ($n = 20$), achieving the highest level of education. Most of the participants were, at the time of the study, employed (41%, $n = 43$) or retired (40%, $n = 42$). As for the participants clinical characteristics, among the 29 reported primary skin conditions, the most common diagnoses were: psoriasis ($n = 23$), eczema ($n = 16$), and alopecia ($n = 11$). Other skin diseases diagnoses that occurred in >3% of the sample, included acne ($n = 7$), rosacea ($n = 3$), and urticaria ($n = 2$). Skin disease diagnoses given in >1% are presented in the Supplementary material S4 where we also present the comprehensive list of participants' skin diagnoses. Clinicians' ratings of the severity of participants' skin disease were most commonly moderate (45%, $n = 44$) or severe (34%, $n = 36$). There were no differences between males and females in the employment status and clinicians' rated severity of skin diseases (both $ps < 0.05$). Table 1 presents more detailed characteristics of participants' demographic information.

3.2. Correlation analyses

The stigma experience scale (PSQ) score demonstrated medium negative correlations with the openness to experience subscale score (CompACT_OE, $r > -0.33$), the behavioral awareness (CompACT_BA, $r > -0.27$) scores of the PF processes, and the perceived health (VAS, $r > -0.24$) scores. Further, stigma showed a positive correlation with the study outcomes, such as higher levels of stigma experiences being associated with higher levels of depression (PHQ-9, $r > 0.34$) and generalized anxiety (GAD-7; $r > 0.29$). As Table 2 shows, these findings support the first study hypothesis, indicating a significant relationship between stigma, PF processes, and stigma-related outcomes, consequently, allowing us to build the predictive models.

3.3. Multivariate analyses

The hierarchical multiple regression models consisted of seven predictors. We firstly entered (forced entry) demographics and clinical characteristics (step 1), followed by stigma (step 2), and finally, the three PF dyads of response processes (step 3). Before running the models, we log-transformed anxiety, depression, and self-reported health variables as they did not meet the criteria for normality due to skewness. Screening criteria showed no multicollinearity or the presence of multivariate outliers, and the variables met the criteria for normality, linearity, and homoscedasticity. For all the models, the variance inflation factor (VIF) was less than 3.3, and tolerance statistics were all 0.296 or above.

As Table 3 shows, the seven predictors, after controlling for demographics and clinical characteristics accounted for 57% of the variance explained in generalized anxiety (adj. $R^2 = 0.53$). The equation was highly significant [F (7,95) = 16.53, $p < 0.001$], representing a large effect size, $f^2 = 1.14$. Age, skin condition severity, stigma, and the three PF response styles were all significant predictors in the final model, with behavioral awareness (CompACT_BA) showing the highest contribution ($b = -0.451$) when compared with the other six predictors. In predicting depression, the seven predictors accounted for 38% of the variance (Adj. $R^2 = 0.379$). The equation was highly significant [F

TABLE 1 Participants characteristics.

Characteristic[1]	Sex			Total
	Male (n=44) (Mean, N or %)	Female (n=59)	T r x^2 (p/df)* n=105	n=105 (Mean, N or %)
Age	52.50 (16.96)	54.88 (18.71)	0.26	53.86 (17.94)
Educational level (% years completed)			0.002 (*2*)	
GCSE or below	20	46		62.9% (n = 66)
A Level or equivalent	7	3		9.5% (n = 10)
Degree or above	18	11		27.6% (n = 29)
Employment Status			0.11 (*5*)	
Unemployed	6	9		14.3% (n = 15)
Retired	13	29		40% (n = 42)
Sick leave	1	0		1% (n = 1)
In education	1	1		1.9% (n = 2)
Employed	24	19		41% (n = 43)
Clinician rated severity of skin disease			0.21 (*3*)	
Mild	7	13		19% (n = 20)
Moderate	15	32		44.8% (n = 47)
Severe	21	15		34.3% (n = 36)
Descriptive Characteristics[2]				
Stigma (PSQ score range 0–27)	16.64 (*11.18*)	12.61 (*10.68*)	0.99 (*100*)	14.42 (*11.04*)
Anxiety (GAD 7 score range: 0–21)	6.31 (*6.04*)	6.95 (*6.23*)	0.37 (*100*)	6.67 (*6.12*)
Depression (PHQ 9 score range: 5–27)	7.43 (*6.96*)	8.03 (*7.85*)	0.20 (*100*)	7.77 (*7.45*)
Self-rated health (EQ5D5L score range, 0–100)	67.45 (*17.73*)	66.04 (*22.92*)	0.06 (*99*)	66.65 (*20.73*)
CompOE (Open; open to experience)	31.02 (*9.40*)	30.75 (*9.89*)	0.53 (*97*)	30.87 (*9.63*)
CompBA (Aware; Behavioral awareness)	16.64 (*6.49*)	17.04 (*7.49*)	0.22 (*97*)	16.86 (*7.03*)
CompVA (Active; Doing what matters)	35.11 (*9.16*)	34.38 (*9.95*)	0.61 (*97*)	34.71 (*9.57*)

[1]Mean comparisons between groups were executed with independent t-tests for continuous variables and ×2 fisher tests for categorical variables. Due to missing, the overall sum up does not equate n = 105 in all variables examined.
[2]Descriptive characteristics present means and standard deviation of the total scores for the study variables, split into males and females.

(7,95) = 9.28, $p < 0.001$], representing a large effect size $f^2 = 0.85$. Examining the individual prediction (criterion) of the seven variables, one can see that stigma and valued-based actions approached significance ($p = 0.07$). In contrast, the two other PF dyads, openness to experience and behavioral awareness were significant. The variable with the highest prediction was behavioral awareness ($b = -0.34$, $p < 0.01$) compared to the other six variables. Finally, as for the perceived health, the overall model accounted for 22% of the variance explained (Adj. $R^2 = 0.218$). This finding was also highly significant [F (7,95) = 1.69, $p < 0.01$], representing a large effect size $f^2 = 0.52$. Behavioral awareness and value-based actions were the only significant predictors in the final model, with an almost equal prediction of perceived health ($b = -0.281$ and $b = -0.241$). The regression analyses supported the second study hypotheses, where perceived stigmatization predicts higher anxiety, depression, and lower self-reported health. Notably, PF processes might revert the negative effects of stigma on individuals' well-being, particularly the process of behavioral awareness (being present). We tested which PF processes of change exert effects in the following analyses.

3.4. Moderation mediation analysis

We conducted a moderated regression analysis to assess whether PF (total score on the CompACT questionnaire) moderates the relationship between stigma and well-being. We hypothesized that higher levels of PF would indirectly buffer the negative effects of stigma and stigma-related outcomes. To test for moderation, stigma, PF, and their interaction was entered together in a single block to three models, predicting generalized anxiety, depression, and perceived health. Variables were mean-centered prior to computing the interaction terms to minimize multicollinearity problems. A significant interaction term would indicate the presence of moderating effects.

As Supplementary material S1 shows, none of the moderation analyses were significant. For example, when stigma and PF were entered together, they explained 50% of the variance in log anxiety $R^2 = 0.50$, F (3, 91) = 28.92, $p < 0.001$, but the interaction term was not a significant predictor of anxiety. For depression, when the same variables were entered together (stigma and PF), they explained 38% of variance in log depression scores $R^2 = 0.38$, F (3,93) = 20.63,

TABLE 2 Correlations between predictor variables (stigma), mediators (PF processes), and outcome variables (stigma-related impact).

	1	2	3	4	5	6	7
1. PSQ		−0.33**	−0.27**	−0.15	0.34**	0.29**	−0.24*
2. CompACT_OE	−0.33**		0.68**	0.08	0.58**	−0.65**	0.34**
3. CompACT_BA	−0.27**	0.68**		0.22	−0.58**	−0.63**	0.41**
4. CompACT_VA	−0.15	0.08	0.02		−0.23*	−0.28**	0.30**
5. PHQ-9	0.34**	−0.58**	−0.58**	−0.23*		0.84**	−0.62**
6. GAD-7	0.29**	−0.64**	−0.63**	−0.28**	0.84**		−0.61**
7. VAS	−0.24*	0.34**	0.41**	0.30**	−0.62**	−61**	

All correlations are Pearson's r; $n = 107$; PSQ, perceived stigmatization questionnaire; CompACT_OE, openness to experience; CompACT_BA, behavioral awareness; CompACT_VA, valued actions; PHQ-9, patient health questionnaire; GAD-7, generalised anxiety disorder; VAS, EQ5D5L.
**$p < 0.01$.
*$p < 0.05$.

$p < 0.001$, but again the interaction was not significant. Finally, the same results were observed for perceived health where stigma and PF explained 16% of the variance in log self-reported health $R^2 = 0.16$, $F(3,94) = 7.2$, $p < 0.001$, yet the interaction was not significant. In sum, the third aim was not supported, indicating that the relationship between stigma, PF processes, and stigma-related outcomes appears to be more complex and dynamic than static, as these predictive models indicate. To examine the dynamic role of the PF processes, we finally run a network analysis.

3.5. Network analysis

The final network is illustrated in Figure 2. Based on the strength centrality indices, the node with the highest centrality, and therefore the most influential within the model, was generalized anxiety (GAD-7), followed by perceived stigmatization (PSQ), valued actions (CompACT_VA), and depression (PHQ-9). As expected, the model's strongest (more meaningful) positive relations, excluding the PF, were observed between depression and anxiety, and stigma and depression (see Supplementary Table S2 for all the variables examined weights partial correlations). The strongest negative relationships were observed between anxiety and perceived health, and depression and perceived health.

We found strong positive relationships between open and aware, and active and perceived health. The strongest negative relationships of PF with stigma were observed between open and anxiety, aware and anxiety, and open and stigma. Table 4 presents the edge weights partial network correlations of PF processes when LASSO regularization was applied. Stigma had the strongest negative relationships (edge) with openness to experience (weight matrix), followed by valued actions and behavioral awareness. Further, generalized anxiety was also found to exert a large negative relationship with openness to experience, followed by behavioral awareness, and valued actions. Depression was only found to be negatively related to behavioral awareness and positively to stigma. The Supplementary Table S2 presents all the relevant partial correlations among the examined variables. When percentages of cases were dropped off, stability assessment showed that the order of node strength was interpretable with some care. The edge weight accuracy (CIs) was found narrow for most PF processes when interconnecting with other nodes (see Supplementary material S3).

4. Discussion

Stigmatization is a common problem associated with living with a skin condition, yet relatively little is known about how this is influenced by psychological variables associated with distress. Network analysis has the potential to examine the multifaceted and bidirectional interactions associated with several variables potentially relevant to stigmatization in skin conditions (1, 59). In this study we specifically examined the relationship between psychological flexibility (PF), quality of life, stigmatization, and distress.

Findings showed that stigma was negatively related to the three skills PF associated with depression and anxiety. Behavioral awareness accounted for the largest portion of variance explained among the three skills of PF response styles (open, aware, and active), predicting lower anxiety, depression, and higher perceived health. Moderation analyses showed no effect of the three PF response styles between stigma and outcomes. This finding suggests that PF responses may not be considered as static-not amenable to direct change variables, but as dynamic, sharing some potentially therapeutic role in buffering the effects of stigma in individuals with skin conditions. To further examine our hypothesis, we run a network analysis. Findings indicated generalized anxiety, depression, perceived stigmatization, and value-based actions as the most highly interconnected variables within the network. Stigma was most strongly negatively associated with avoidance (as opposed to being open) and value-based actions (as opposed to being active), and positively with anxiety and depression. These findings are congruent with existing research demonstrating the negative role of stigma in increasing psychological distress to individuals with skin conditions. However, our study provides support for the role of the PF responses as trainable skills that may play central role in tackling stigma. As such, these responses may be foci for interventions, designed that can lower stigma-related distress.

The role of depression and anxiety is consistent with studies on stigma (7, 63, 64). In our study, we observed depression as the only variable associated with stigma in the network model. Concerning stigma, depression in individuals with skin conditions might be seen as a form of avoidance and passivity behaviors (39). These behaviors can lead individuals with skin conditions to avoid seeking support as a result of of stigma and shame (65). On the other hand, anxiety can be seen as a form of social anxiety related to the visible difference in appearance, further supporting some studies, showing that social anxiety is the most common form of distress for this

TABLE 3 Linear regression for the prediction of anxiety, depression, and perceived health.

Independent variables (Predictors)	Steps (blocks)[1]	B^2	*t*	*p*	R^2	Adj. R^2	*F (Df)*	*p*
Dependent variable: anxiety								
Age	1	−0.151	−2.210	0.030	0.051	0.020	1.66 (3,95)	0.18
Gender		0.036	0.417	0.677				
Severity		−0.024	−0.024	−0.024				
Stigma (PSQ)	2	0.005	2.48	0.015	0.11	0.072	2.85 (4,95)	0.03*
Openness to experience (CompACT_OE)	3	−300	−3.07	0.003	0.57	0.534	16.53 (7,95)	<0.001
Behaviorsal Awareness (CompACT_BA)		−0.451	−4.71	<0.001				
Valued-based actions (CompACT_VA		−0.180	−2.52	0.013				
Dependent variable: depression								
Age	1	0.027	0.326	0.745	0.004	−0.028	0.13 (3,95)	0.93
Gender		0.018	0.209	0.835				
Severity		−0.012	−0.148	0.883				
Stigma (PSQ)	2	0.196	1.885	0.063	0.132	0.094	3.46 (4,95)	0.011
Openness to experience (CompACT_OE)	3	−0.258	−2.285	0.025	0.425	0.379	9.28 (7,95)	<0.001
Behaviorsal Awareness (CompACT_BA)		−0.343	−3.107	0.003				
Valued-based actions (CompACT_VA)		−0.149	−1.816	0.073				
Dependent variable: perceived health								
Age	1	0.085	0.881	0.381	0.013	−0.019	0.41 (3,95)	0.742
Gender		0.021	0.213	0.832				
Severity		0.105	1.075	0.285				
Stigma (PSQ)	2	0.140	1.338	0.184	0.079	0.038	1.95 (4,95)	0.109
Openness to experience (CompACT_OE)	3	−0.032	−0.243	0.808	0.218	0.156	1.69 (7,95)	0.002
Behaviorsal Awareness (CompACT_BA)		−0.281	−2.185	0.032				
Valued-based actions (CompACT_VA		−0.241	−2.520	0.014				

[1]Variables were entered simultaneously in blocks (steps) and each independent variable was assessed in terms of what it adds to the prediction of the dependent, when the previous variables were controlled for.

[2]Beta represents standardized coefficients to the equation to allow for comparisons.

population (66, 67). In this case, a measure assessing generalized anxiety disorder (GAD-7) might not entirely capture the distress individuals with skin problems experience.

The findings in this study point towards the role of PF skills as effective responses to stigmatization. More specifically, findings from the network analysis indicated the influential central role of the "*open*" response style (comprising the PF skills of acceptance and defusion) as a promising intervention target, to reduce the effects of stigmatized behaviors in people with skin conditions. Existing research shows that being willing to experience both internalized stigma (e.g., when individuals come to believe the stigmatized thoughts) and enacted stigma (e.g., when others impose stigmatized attitudes) can reduce stigma-related distress and improves daily functioning (34, 51, 68). In our case, such finding suggests that being more open and engaged allows individuals with skin conditions first to acknowledge more willingly that their visible difference in appearance may trigger stigmatized reactions and correspondingly respond to stigma more openly by minimizing avoidance (e.g., attempting to control one's stigmatized behaviors) and by abstaining from attaching rigidly to stigmatized thoughts (e.g., seen stigmatized thoughts as true literal entities that can define behaviors) (29, 30, 69). Findings from research in the area of social psychology resonate with this approach of

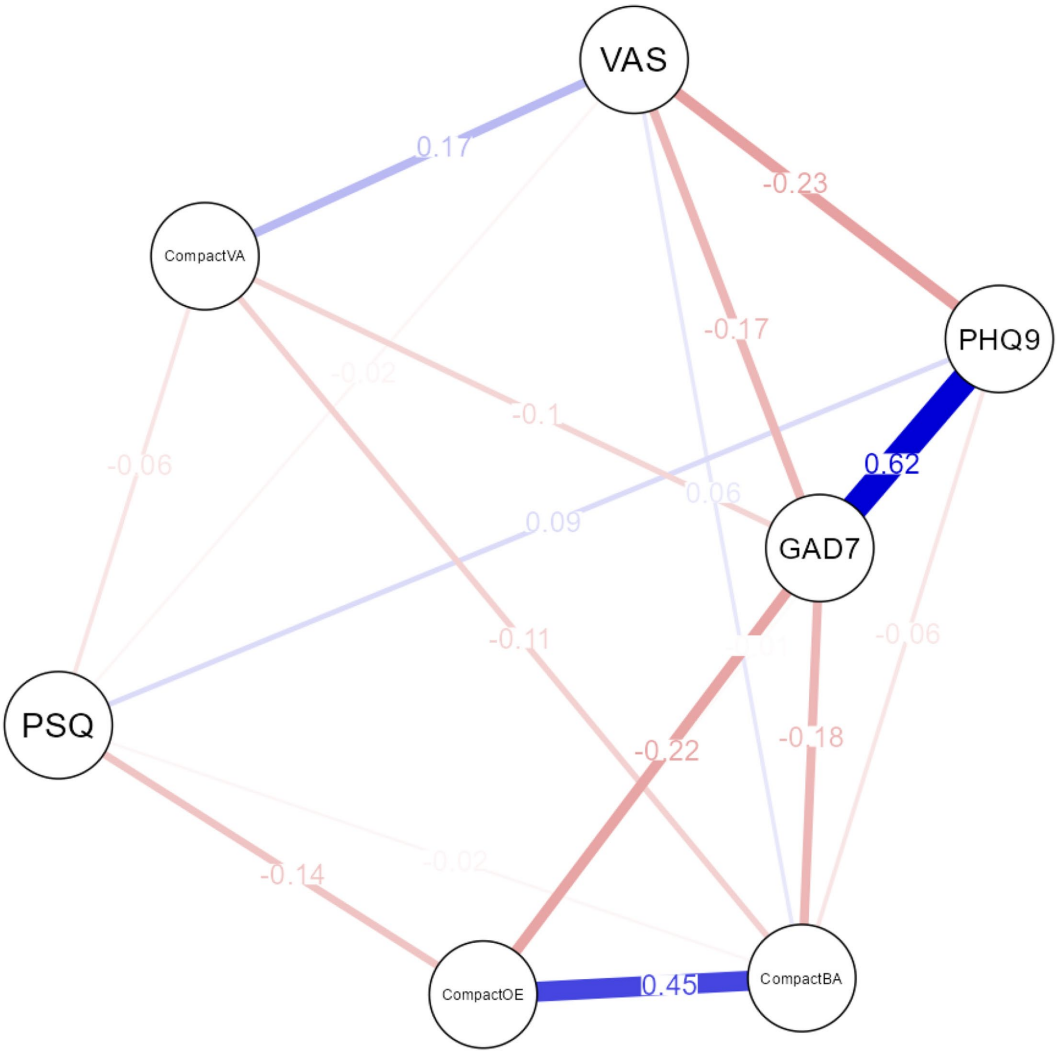

FIGURE 2
Network model of Stigma, PF responses skills (dyads), and stigma-related outcomes. Red edges indicate negative partial correlations; blue edges indicate positive partial correlations; PSQ: Perceived Stigmatisation Questionnaire; PHQ9: Patient Health Questionnaire; GAD7: Generalised Anxiety Disorder Assessment; VAS: EuroQOL 5- Dimensions- EQ5D5L Visual Analogue Scale; CompactOE: openness to experience; CompactBA: behavioral awareness; CompactVA; valued actions.

TABLE 4 LASSO regularized partial correlation coefficients for PF processes.

Psychological flexibility processes	Stigma	Emotional functioning		Daily functioning
		Anxiety	Depression	Perceived healthy (QoL)
Openness (Compact OE)	−0.142	−0.218	−0.010	0.000
Awareness (Compact BA)	−0.022	−0.177	−0.060	0.170
Active (Compact VA)	−0.062	−0.102	0.000	0.055

LASSO estimator was applied to controls for spurious (non-reliable) relations and to return a sparse (conservative) network model where only a relatively small number of edges are used to explain the covariation structure in the data. Therefore, edge (nodes) relations estimated as 0.00 reflect negligible relations within the model.

awareness vs. control of stigmatized behaviors (70, 71) or changing self-stigmatized thoughts (72), yet further research is warranted, especially, to indicate how being open to stigmatized experiences, is an effective practice for individuals with skin problems.

Additionally, the study showed the important role of the "*active*" response style (comprising of the PF skills of values and committed actions), indicating foci for intervention development. Findings showed value-based actions as one of the most influential nodes in the

network, exerting a negative association with stigma, anxiety, and a positive one with perceived health. Other studies indicates that values can lower distress and increase daily functioning (73–75). Value-based interventions help individuals identify and clarify their values, shift attention toward value-based actions in moments of distress, and guide them to resonate with those choices (76). Because stigma can promote a disconnect and a dissonance from one's values (77, 78), the process of increased attention to value-based actions may not directly impact the cognitive or emotional content related to stigma but cultivate engagement of individuals' to more healthy behaviors, such as adhering to medical prescription or taking care of ongoing flares due to the disease's progress (79). Consequently, this can increase the frequency where healthy behaviors are chosen in different contexts where stigma occurs (e.g., "*I can see others frown their eyes when they spot my pale white patches on my face, but this does not stop me from enjoying shopping in the mall or attending a social event").* Research indicates values as the process that increases motivation towards health behavioral changes (31, 80), yet, future research will shed more light on how individuals with skin conditions, in particular, can use values in this way, even in the presence of stigma.

The present study findings are noteworthy, suggesting both theoretical and clinical implications. From a theoretical point of view, our findings indicate two of the three PF response of psychological flexibility as being essential to tackle the effects of stigma and related psychological distress. This contains a set of trainable behavioral responses that allow individuals to address concurrently core psychological, behavioral, and contextual parameters of perceived stress (27, 81), such as stigma. Because these skills reflect common responses to perceived threats (e.g., stigmatized behaviors), we can more directly specify what are the core functionally important pathways that we can focus on and change. Theoretically, for this to occur, we first need to link how individuals respond to stigma. Findings from this study indicated the use of the "*open*" and "*active*" response styles of the PF as skills that hold the potential to reduce the effects of stigma. Secondly, we need to find approaches that incorporate all the relevant past, present and contextual factors (e.g., demographic, disease severity, health care professionals' behaviors) that seem to contribute to the psychological reaction involved in stigma (e.g., social anxiety and avoidance). Notably, we can achieve this level of analysis by employing methods, such as momentary ecological assessments that can collect high temporal personalized density data at the context of individuals' lives (82). As a first step towards this approach, our findings indicated foundational knowledge about the nuances of unidirectional and bidirectional relationships of stigma-related associations within a nomological network that goes beyond static correlational, regression, and moderation analyses. Such a level of analysis can propose future directions and indicates clinical progress (83).

From a clinical perspective, focusing on functionally important skills, clinicians can develop scalable interventions for stigma that can meet the needs of a heterogeneous group of individuals with skin conditions (21). For example, the open response style should be employed when the problem is a narrow response to self-stigmatization where individuals attempt to reduce the stigmatized thoughts or replace them with more neutral or informative ones. On the contrary, when individuals respond to stigma with avoidance or passivity, values and commitment to health behaviors (as opposed to avoidance) should be employed. As stigma is a multidimensional phenomenon, focusing solely on individuals' responses as the main intervention to tackle the effects of stigma, is likely to be suboptimal. One should move beyond skills and attempt to understand stigma as a context-specific problem, including biophysiological and sociocultural levels of stigma. Consistent with the network intervention approach, these skills should not be seen as snapshots that can be delivered across skin conditions. Rather, they ought to be seen as dynamic and interconnected systems of an intervention that are likely to modify person-specific coping with stigma responses, including broader sociocultural parameters that feed into the stigma. This requires a deliberate shift to models that organize different intervention strategies into a more coherent network (25). Such a model is the new Extended Evolutionary Meta-Model [see further here (81)]. It is based on evolutionary science and allows interventions to expand targeted PF skills, including conceptions about adaptation and resilience (84–86).

The present study had several limitations. First, the study used self-reported subjective measures known for their source bias and shared method variance. Secondly, the study was part of a larger cross-sectional epidemiological study that employed only a few psychosocial parameters involved in stigma. While we present new knowledge using variables that indicated the "central" role of PF, other variables that were not included, should be measured for a more integrated interpretation of stigma, such as contextual, interpersonal, and functional (6). Likewise, we made use of the UK-only self-selected sample, and this narrows the interpretation of the findings to predominantly white Caucasian populations. Equally, the sub-sample that measured stigma and PF parameters was underpowered for network analysis. Although the network model stability was found to be within acceptable ranges, interpretation should be cautious as the interpretation of CIs in analyses such as LASSO regularization is problematic because the initial estimates of network analyses are biased towards zero (59). Therefore, further replication of the study findings is warranted.

Future research should attempt to collect multiple and large-scale data, using measures that examine the experience of stigma holistically, with samples from different countries and with more heterogeneous skin conditions. This will allow researchers to use network comparison analyses and explore coping with stigma-related outcomes interconnections, including several contextual characteristics (e.g., demographics, race/ethnicity, disease onset or progress, etc.). Further, as the affective component of body image (e.g., anxiety, distress, shame, etc.) may be related to specific aspects of physical appearance (21), future studies should use disease-specific measures to assess affection. Likewise, future studies should attempt to examine stigma and coping responses, employing more idiographic and personalized methods, such as ecological momentary assessments (EMA). These methods can longitudinally collect behavioral and self-reported highly temporal data to assess the impact of targeted skills on stigma in the context of within-person variability, indicating personalized interventions.

This study applied step-wise analytic approaches to individuals with skin problems. Among the examined variables, stigma, depression, and two of the three response styles of the PF model, namely "*open*" and "*active*" skills, appeared important. The role of PF in the network analyses indicate certain functionally important pathways that may have clinical utility in psychosocial programs, attempting to reduce the effects of stigma in skin populations. Tailoring personalized approaches may increase the likelihood of a truly good outcome for individuals with skin

problems, experiencing stigma. For this to occur, researchers and implementation scientists should employ newest approaches, such as the process-based intervention approach (25) and the Extended Evolutionary Meta-Model (EEMM) (81) as guides to develop a coherent network of intervention strategies that will tap across the multiple nature of stigma.

Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: data are part of a larger European epidemiological research and can be available upon request. Requests to access these datasets should be directed to AT, thompsona18@cardiff.ac.uk.

Ethics statement

The studies involving human participants were reviewed and approved by NHS Health Research Authority (18/LO/0639). The patients/participants provided their written informed consent to participate in this study.

Author contributions

VV: writing – original draft (lead), methodology (equal), formal analyses (equal), and writing – review & editing (equal). HR: conceptualization (equal), formal analysis (equal), project administration (lead), and resources (equal). SC: investigation (lead) and resources (equal) GC: software (lead). AT: methodology (equal), conceptualization (equal), writing – review & editing (equal), and supervision (lead). All authors contributed to the article and approved the submitted version.

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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.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2023.1075672/full#supplementary-material

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Subliminal attentional bias modification training for itch

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Introduction: Itch is unpleasant and induces the urge to scratch. This is adaptive to remove the itch-inducing stimulus from the skin. Accordingly, itch draws attention to protect our bodily integrity. Recent studies investigated whether attention is preferentially drawn towards its location, i.e., attentional bias (AB), and also whether this bias could be changed in healthy individuals. So far, results are mixed concerning the existance of an attentional bias towards itch stimuli in healthy individuals as well as the impact of modifications. However, available studies have typically focused on conscious processing and might miss preconscious aspects of attention and potential biases at these stages.

Methods: This study included 117 healthy individuals who underwent a subliminal Attentional Bias Modification (ABM)- training for itch based on a dot-probe paradigm with itch- related pictures. Participants were randomly assigned to a training towards itch group, a training away from itch group and a control group. This was done by manipulating the itch-target congruency of the dot-probe task during a training block. Pre- and post-training assessments were regular dot-probe tasks. Exploratorily, also attentional inhibition, cognitive flexibility and itch-related cognitions were assessed. Lastly, participants received an itchy stimulus on the inner forearm before and after the ABM-training to assess potential effects on itch sensitivity.

Results: Results showed no AB towards itch across groups at baseline, i.e., pre-training, but an AB away from itch, hence, avoidance of itch, post-training. Further analyses showed that this effect was driven by an attentional bias away from itch in the control group, while there were no significant effects in the experimental groups. There was no effect on itch sensitivity.

Conclusion: These findings are in line with recent studies on conscious ABM-training for itch and pain that also did not find significant training effects. Therefore, it is suggested that the field of AB might need to reconsider the current assessment of AB. Moreover, AB is probably a dynamic process that is highly dependent on current itch-related goals and relevance of itch in a specific situation. This suggests that processes probably differ in patients with chronic itch and that also ABM-training might work differently in these populations.

Clinical trial registration: https://trialsearch.who.int/Trial2.aspx?TrialID=NTR7561, identifier NTR7561.

KEYWORDS

itch, pruritus, attention, cognitive bias, unconscious processing, experimental psychology, psychodermatology

1. Introduction

Itch is an unpleasant sensation which induces the urge to scratch and can lower individual's quality of life if it is present for a prolonged time (1–4). Recent studies have highlighted the importance of psychological mechanisms in the experience of itch, such as attention (5–7). Specifically, it has been suggested that the experience of itch is impacted by attentional processing (8–10). Although attention allocation towards itch-related stimuli may be helpful in adapting our behavior to protect bodily integrity, it can also interfere with the execution of other tasks in daily life. This is especially true if itch can no longer be adaptively controlled, e.g., chronic itch; no concrete action allows to alleviate the itch.

Overall, research on attention to itch showed that, in healthy individuals, itch interferes with the execution of other tasks, i.e., itch is distracting (9, 11, 12). Furthermore, it has been researched whether visual itch-related stimuli draw attention towards their location, i.e., an attentional bias towards itch, which resulted in mixed findings so far (9–11). These studies have shown that attention for itch might differ between conscious and preconscious processing stages: while some studies found heightened conscious attention towards itch (9), others could not replicate this finding (10, 11) and a recent finding suggests preconscious avoidance of itch-related stimuli (13). The importance of fast processing of itch is also supported by contagious itch which suggests very fast and maybe unconscious processing of itch-related gestures, e.g., scratching, which then induces itchiness in the observer (14, 15).

A possible intervention for biases for itch-related information is Attentional Bias Modification (ABM) training for itch. These kind of trainings use itch-related stimuli, like words or pictures to manipulate individuals' attention away from (or towards) these stimuli. As yet, only one study employed an ABM-training for itch in healthy individuals which investigated conscious processing of itch-related visual stimuli (16). This study investigated whether attention could be either trained towards visual itch stimuli or away from these stimuli. Results of this study could, however, not support the effectiveness of an ABM-training, neither by affecting attention directly, nor by influencing individuals' sensitivity to a light cutaneous itch stimulus on the skin (16).

Nevertheless, there is some evidence that ABM-training for other somatic complaints such as pain can be effective (17–20), although this could not be supported by all studies (21, 22). Interesting to note here is that in most cases there was no direct effect on attentional bias towards pain stimuli after the training but effects on for example pain intensity or tolerance (17–19). This suggests that ABM-training might show effects on symptom perception, for instance itch tolerance or sensitivity, which could be especially valuable for clinical practice. After all, the lack of significant effects on attentional bias measures themselves leaves open questions about the working mechanism of ABM-training.

Because attention is a continuum, including first orienting towards a stimulus, actual selective attention to a stimulus and eventual disengagement (23–25), attention can be biased at different stages of attentional processing (26) which is suggested by the inconsistend findings on attentional bias towards itch so far at different processing stages, e.g., conscious engagement and disengagement vs. preconscious orienting (9–11, 13). However, preconscious ABM-trainings are scarce and actually lacking in itch. To our knowledge, there is only one study which investigated preconscious ABM training. This study used an ABM training for threat-related stimuli in socially anxious individuals (27) which, while not finding an effect on attentional bias, did find a positive effect on anxiety during a stressful task. This finding indicates that training attention away from itch-related information very early in the attention process may prove helpful in reducing negative outcomes.

With the very limited knowledge on preconscious ABM-training and attention towards itch in general, the current study investigated the effect of preconscious ABM-training for itch in healthy individuals in a proof-of-principle approach. More specifically, the effects on attentional measures and on sensitivity to a somatosensory itch stimulus were investigated. Participants were either trained towards or away from visual itch stimuli or received a sham (control) training by means of computerized, single-session ABM-training. We expected an effect on attentional bias post-training compared to pre-training in both training groups, i.e., more attention towards itch in the towards group vs. less attention towards itch in the away group, compared to the control group. In line with this, we expect higher itch sensitivity after the training in the towards group, and lower itch sensitivity in the away group, compared to the control group. In addition, a possible role of general attentional abilities, namely attentional inhibition and cognitive flexibility, as well as on self-reported itch-related cognitions was explored to shed more light on individual differences that might be related to the effectiveness of the ABM-training and could potentially explain mixed-findings in this field.

2. Materials and methods

2.1. Participants

The study sample consisted of 117 healthy individuals. This sample size was calculated in line with an earlier study with a comparable design (16). Participants were included if aged between 18 and 35 years, fluent in either Dutch or English, and with normal vision (corrected with contact lenses if needed). Participants were excluded if they had a (history) of psychological disorder (e.g., depression or anxiety), had a medical diagnosis (e.g., atopic dermatitis or heart disease), used recreative drugs on a regular basis (e.g., MDMA or cannabis) or suffered from color blindness or dyslexia. All participants gave written informed consent before the experiment. Data collection took place between October 2018 and July 2019. The study was approved by the Psychology Research Ethics Committee of Leiden University (CEP19-0703/376) and registered in the Nederlands Trial Register (Dutch Trial Register; NTR7561).

2.2. General procedure

Participants were recruited via the Online Research Participation system of the university (SONA Systems Ltd., Tallinn, Estonia) and via advertisement at the faculty. The experiment took place at the Faculty of Social and Behavioral Science of Leiden University and took about 1.5 h. See Figure 1 for an overview. Information about the study was given upon sign-up and repeated at the start of the study, after which participants signed the informed consent form. The procedure started with a short questionnaire about current levels of depression, anxiety and stress and demographic information. Thereafter, two general attention tasks (order counterbalanced) were completed, measuring attentional inhibition and cognitive flexibility. Next, an itchy stimulus was applied to the forearm of the participant to assess their itch sensitivity at baseline (randomized either the dominant or non-dominant arm). The actual subliminal attention bias modification (ABM) training was completely automatized with a pre-training, i.e., baseline-attentional bias block, and a post-training block and the training block in between. Group allocation was based on participant number and the experimenter and the participants were unaware of the corresponding group, i.e., a blinded design. A second itch sensitivity assessment followed by applying the same itch stimulus on the other forearm of the participant (e.g., dominant arm if first application was on the non-dominant arm). Lastly, participants filled out several questionnaires, assessing itch-related cognitions, e.g., catastrophizing and body vigilance. All participants were debriefed and received either monetary reimbursement or course credits for their time investment.

2.3. Technical set-up

All computer tasks, including the ABM-training, were programmed with E-Prime 2.0 (Psychology Software Tools, Inc., Sharpsburg, United States) and self-report questionnaires were presented with Qualtrics (Provo, Utah, United States) on an Iiyama HM703UT A Vision Master Pro 413 CRT monitor (17 inch; refresh rate 100 Hz; resolution 1,024 × 768px). Participants used a chin rest to keep a constant distance of 78 cm to the screen. Responses were collected with a Serial Response Box (Psychology Software Tools, Inc., Sharpsburg, United States) with two custom-made buttons for the left and right index fingers. A Tobii Pro X3-120 Eye Tracker (Tobii AB, Danderyd, Sweden) was also installed to measure eye-movements during the ABM-training. Unfortunately, data quality of eye-movement data appeared to be insufficient for further analyses.

2.4. Attention tasks

2.4.1. Subliminal attentional bias assessment and training

Attentional bias towards itch was measured with a dot-probe paradigm (9–11). Forty pairs of two pictures were used, one being itch-related and one being neutral (i.e., 20 stimuli presenting neutral skin and 20 presenting a neutral object), validated and used in earlier studies (10, 13). An itch-related picture showed someone scratching their own body. Neutral skin pictures displayed the same body parts, but without a scratching gesture.

Each trial began with a fixation cross (500 ms) followed by a picture pair (20 ms). The picture pair was thereafter masked with corresponding scrambled versions of the same pictures (480 ms). The pictures were presented at the 80 and 20% height position of the screen. Lastly, a target appeared which consisted of two dots, either horizontally or vertically oriented. If the target appeared in the same location as the itch-picture, this was a congruent trial, while if the target appeared in the opposite location, this was an incongruent trial. Participants had to respond to the orientation of the dots by pressing a left button with their left index finger to indicate vertical dots or a right button with their right index finger to indicate horizontal dots or vice versa (counterbalanced). Accuracy and reaction times were assessed as outcome measures. Attentional bias towards itch is inferred if congruent trials have a shorter reaction time (RT) than incongruent trials, while attentional bias away from itch (i.e., avoidance) is inferred if incongruent trials have a shorter RT than congruent trials. The resulting difference score is called the AB-index. The whole ABM-training, including pre- and post-training assessment, took about 30 min to complete.

In line with an earlier study for itch (16), participants were distributed across three groups: one trained towards itch (towards-group), one trained away from itch (away-group) and one control-group (sham training). For each participant, the picture pairs were randomly distributed to the pre-training, training and post-training block.

2.4.1.1. Pre- and post-training attentional bias

For the pre-training, i.e., baseline, assessment of attentional bias towards itch, and the post-training attentional bias towards itch assessment, 10 picture pairs (different picture pairs: for baseline and post-training assessment) were used. All pairs appeared two times: with the itch picture in the upper and lower part of the screen, as a congruent and incongruent trial, and with horizontal and vertical dots, resulting in 160 trials. A break of 10 s was inserted after every 40 trials.

2.4.1.2. Training

For the training, 20 picture pairs (different from baseline and post-training assessment) were presented two times in both locations and with

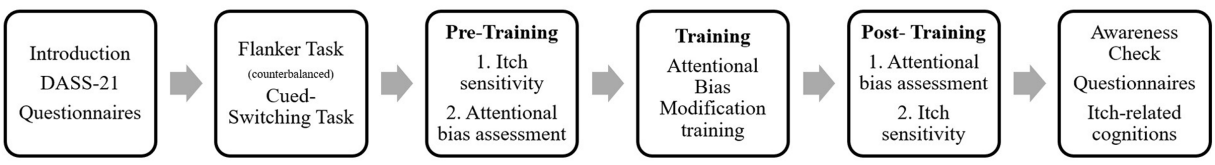

FIGURE 1
Overview of the general procedure.

both targets types. The task was manipulated for the towards-group by only consisting of itch-congruent trials and for the away-group by only consisting of itch-incongruent trials. The control-group received evenly distributed congruent and incongruent trials, alike the pre- and the post-training. The whole training block consisted of 320 trials, also interrupted with 10 s breaks after every 40 trials.

2.4.1.3. Awareness check

Awareness of the subliminally presented pictures during the ABM-training, was checked by two subjective awareness questions and an objective awareness check in line with an earlier study (13). Subjective awareness was assessed by directly asking whether participants noticed something special during the task (question 1) and if this was answered with yes, whether they noticed any pictures (question 2). For the objective awareness check, a forced-choice paradigm was used. Participants were presented with 20 picture pairs that consisted of one picture shown during the ABM-training and one new picture from the same validated stimulus set (10). For each pair, they had to indicate which of the two pictures they had seen earlier during the ABM-training. There was no time pressure, but participants were asked to answer as intuitively as possible. Accuracy was measured and if this was at chance level (ca. 50%), the subliminal design was assumed to be successful.

2.4.2. Flanker task

General attentional inhibition, unrelated to itch, was measured with a Flanker paradigm (28, 29) to assess any individual differences in attentional inhibition that might influence an AB towards itch. During each trial within this task, a target number appeared in the middle of the screen, flanked by either two target-identical flanking numbers on each side (i.e., congruent trial) or two different flanking numbers on each side (i.e., incongruent trial). Stimuli were twos and fours, e.g., "22222" or "22422". Numbers were shown until a response was given, with a maximum of 1,500 ms. After eight practice trials, 120 trials were presented (50% congruent and 50% incongruent) with a short break in the middle. Accuracy and reaction times to respond to the target (middle) number were measured. Attentional inhibition is inferred if incongruent trials have a longer RT than congruent trials, that is, more time is needed to inhibit the incongruent flanking numbers. This is called a Flanker effect (Flanker Index = $RT_{incongruent}$ – $RT_{congruent}$). The Flanker task took about 5 min to complete.

2.4.3. Cued-switching task

General attentional switching, unrelated to itch, was measured with a cued-switching paradigm (28). On each trial of the cued-switching paradigm, a target number between one and nine appeared on the screen. Before the target number appeared, one of two instructions were given for 500 ms: either to indicate by button press whether the target is odd or even ("odd/even") or whether the target is above or below five ("high/low"). Target numbers were shown until a response was given, with a maximum of 1,500 ms. After 16 practice trials, 200 experimental trials were administered (50% odd/even, 50% high/low) with a short break after 100 trials. Trials could be either repeat-trials (same instruction as preceding trial, 50% of trials) or change-trials (other instruction than preceding trial, 50% of trials). A switching cost is inferred if change trials have longer reaction times than repeat trials, that is, switching from one instructions to another instructions costs time. This is called switching cost (RT_{change} – RT_{repeat}). Accuracy and reaction times to respond to the targets was assessed as outcome measure. The cued-switching paradigm took about 10 min to complete.

2.5. Itch sensitivity

General itch sensitivity was assessed by applying cowhage spicules (hairs of the tropical *mucuna pruriens* plant) on the inner forearm of the participants. Forty to forty-five spicules were taken with negative grip tweezers (Dumont Tweezers Negative Action Style NS, Electron Microscopy Sciences, Switzerland), counted with the aid of a Bresser microscope Advance ICD 10x-160x (Meade Instruments Europe GmbH & Co. KG, Rhede, Westfalen, Germany). The spicules were applied to a 1.5 cm by 1.5 cm area on the inner forearm, 1 cm above the wrist. The area was demarcated with 1.25 cm surgical tape (3 M Transpore White, St. Paul, MN, United States). The experimenter gently rubbed the spicules, with the index finger, onto the skin for 45 s. Thereafter, participants rated their itch level continuously for 3 min on a digital Visual Analogue Scale (VAS) ranging from zero ("not at all") to ten ("worst imaginable itch") on a Lenovo Tab 4 10 Plus (Lenovo Group Limited, Beijing, China). The VAS was displayed with the APK Pure VAS App 1.3 (30). After 3 min, the spicules were removed by rapidly attaching and removing a 2.5 cm surgical tape (3 M Transpore White, St. Paul, MN, United States) to the demarcated area for five times. After another 3 min, participants rated their current itch once orally on a numeric rating scale from zero to ten. If the answer was above one, participants indicated their current level of itch again after another 2 min to make sure that the itch had passed before continuing the session.

2.6. Self-report questionnaires

Besides general demographic information and information about in- and exclusion criteria, several questionnaires were administered. The Depression, Anxiety and Stress Scale- short version (DASS-21) (31, 32); the Pain Vigilance and Awareness Questionnaire- adjusted for itch (10, 33, 34); the Experience of Cognitive Intrusion of Pain scale- adjusted for itch to assess cognitive intrusions about itch (10, 35); and the Pain Catastrophizing Scale- adjusted for itch (10, 36). These questionnaires were used to assess emotional distress, vigilance to itch, intrusive cognitions about itch and catastrophizing about itch, respectively. Lastly, one item about disengagement from itch (12) was measured, as well as current level of itch and fatigue with two VAS scales ranging from zero ("not at all") to ten ("worst imaginable"). These questionnaires were administrered to explore the effect of itch-related cognitions on an AB towards itch.

2.7. Statistical analyses

Data of the computer tasks was extracted with E-Prime Data Aid 3.0 (Psychology Software Tools, Inc., Sharpsburg, United States). For the dot-probe pre-training and post-training task the following data was extracted for all experimental trials: reaction times (RT, ms), accuracy, congruency, group and trial number. In addition, mean accuracy levels per participant were extracted for the training itself. For the Flanker task, mean RT, separately for congruent and incongruent trials, and accuracy

TABLE 1 Descriptive statistics (mean (*M*) and standard deviation (SD)) for all background variables.

	Total sample *N*=117		Control group *N*=42		Towards group *N*=38		Away group *N*=37		*p*-value
	M (SD)	Range	*M* (SD)	Range	*M* (SD)	Range	*M* (SD)	Range	
Age[a]	21.0 (2.3)	18–29	21.0 (2.3)	18–26	21.2 (2.6)	18–29	20.8 (2.1)	18–25	0.807
PVAQ-I	41.3 (14.7)	5–74	40.0 (12.4)	9–67	42.7 (15.2)	5–74	41.3 (16.4)	10–74	0.650
PCS-I	23.0 (9.0)	0–45	21.8 (9.0)	0–45	24.0 (8.9)	0–43	23.3 (9.0)	2–43	0.412
ECIP-I	11.1 (9.0)	0–48	10.7 (10.1)	0–48	13.2 (11.4)	0–39	9.9 (11.6)	0–45	0.758
DASS-Depression[b]	7.2 (4.6)	0–19	7.4 (4.2)	0–16	7.3 (4.9)	0–17	6.8 (4.9)	0–19	0.592
DASS-Anxiety[b]	7.1 (4.1)	0–17	7.1 (3.9)	0–17	7.4 (4.3)	0–14	6.7 (4.1)	0–14	0.748
DASS-Stress[b]	9.5 (4.8)	0–18	9.4 (4.0)	0–17	9.7 (5.0)	0–18	9.2 (5.4)	0–17	0.889
Diseng-I	3.7 (1.0)	1–5	3.9 (1.0)	2–5	3.4 (0.9)	1–5	3.7 (1.1)	1–5	0.297
Flanker Index (ms)	46.7 (27.3)	−25.5 to 141.2	44.0 (25.0)	−0.1 to 123.7	50.5 (27.2)	6.49–133.0	44.7 (29.5)	−25.7 to 141.2	0.991
Switching cost (ms)	133.7 (118.4)	−41.5 to 551.9	153.9 (130.6)	−21.1 to 551.9	112.6 (90.0)	−6.9 to 319.1	132.5 (125.5)	−41.5 to 481.8	0.422

p-values with bootstrapped residuals are reported to indicate significant group differences due to skewed distributions.
[a]Total sample $n = 116$; Control group $n = 41$, due to one missing value.
[b]Total sample $n = 113$; Control group $n = 38$, due to four missing values.
PVAQ-I = Pain Vigilance and Awareness Questionnaire -adjusted for itch (0–80); Cronbach's alpha = 0.91.
PCS-I = Pain Catastrophizing Scale -adjusted for itch (0–52); Cronbach's alpha = 0.91.
ECIP-I = Experience of Cognitive Intrusions of Pain Scale -adjusted for itch (0–60); Cronbach's alpha = 0.97.
DASS = Depression, Anxiety, and Stress Scale- short form (0–21 for each subscale).
Cronbach's alpha $_{Depression} = 0.94$; Cronbach's alpha $_{Anxiety} = 0.88$; Cronbach's alpha $_{Stress} = 0.91$.
Diseng-I = One item on ability to disengagement from itch (1–5).

were extracted for each participant. Likewise, for the cued-switching task mean RT for the change-trials and for the repeat-trials were extracted, as well as mean accuracy. In both tasks, only trials that were responded to correctly and with RT > 150 ms were included for the mean calculations. As explained in Sections 2.4.2 and 2.4.3, respectively, a Flanker index (attentional inhibition) and switching costs (cognitive flexivility) were calculated to use as predictors during statistical analyses. For the questionnaires, data was extracted from Qualtrics (Provo, Utah, United States) and total scores and reliability scores were calculated with SPSS (IBM Statistics for Windows, Armonk, NY, United States). Itch sensitivity data was operationalized as Area Under the Curve (AUC) during the 180 s that were rated on the digital Visual Analogue Scale. AUC was calculated for each participant's pre- and post-training itch induction.

All subsequent analyses, as described below, were done with R Version 4.0.4 (37) with a significance level of 0.05. Descriptive statistics are given as mean (*M*) and standard deviation (*SD*) if not stated otherwise. Reliability of the dot-probe pre- and post-training was calculated with the package "splithalfr" (38) in line with earlier studies (13, 16).

2.7.1. Manipulation and baseline checks

The objective awareness measure was analyzed with a single proportion test to check if accuracy to detect the picture that was shown during the subliminal pre-training dot-probe task was at chance level (0.5). Subjective awareness (i.e., aware of something and aware of pictures) was investigated with frequency tables.

Baseline between-group differences were checked with bootstrapped (1,000 samples) analyses of variance (ANOVA) with group (control vs. towards vs. away group) as between-subjects effect. This was done for age, the Flanker index, switching costs, self-report questionnaire scores and the pre-training itch-sensitivity AUC score. Gender distribution across groups was assessed with a chi-square test.

2.7.2. Attentional bias pre- and post-training

For the pre- and post-training analyses, only trials with RTs > 150 ms were included. Furthermore, all variables were checked visually for extreme values. For the post-training, only participants who had an accuracy level of at least 0.70 during the training were included (16).

Pre-training attentional bias was analyzed with a mixed-model analysis with RT as dependent variable and random effects for participant and trial number. Model 1 included fixed effects for accuracy, congruency (congruent vs. incongruent) and group (away vs. towards vs. control) as well as the interaction between congruency and group. In Model 2, the Flanker index (and its interaction with congruency), switching costs (and its interaction with congruency) and self-report scores were added as covariates. Post-training attentional bias was analyzed with the same mixed- models (Model 3 and 4, respectively) but added pre-training AB index ($RT_{congruent} - RT_{incongruent}$) as a covariate to control for baseline attentional bias effects. A negative AB index indicates that attention is biased towards itch (see Section 2.4.1).

2.7.3. Itch sensitivity pre- and post-training

Itch sensitivity was analyzed with bootstrapped (1,000 samples) ANOVA on cowhage evoked itch scores (AUC) with group as between-subject effect. Again, pre-training itch scores (AUC) were added as a covariate in the post-training analysis to control for any baseline effects.

3. Results

3.1. Participants and baseline characteristics

The final sample of 117 participants was mostly female (86% female and 14% male) with a mean age of 21.0 years (SD = 2.3). Table 1 shows descriptive statistics for all self-report questionnaires and the flanker and cued-switching paradigm. As expected,

TABLE 2 Mixed-model analyses of the pre-training attentional bias measurement: estimates of the effect of the predictors in the outcome (*ES, in ms*) with standard errors (*SE*), significance level (*p*-value) and 95% confidence intervals of the estimates (95% *CI*) (*n*=114).

		ES	SE	*p*-value	95% CI
Model 1	(Intercept)	478.60	18.62	<0.001	[442.14; 515.07]
	Accuracy	21.69	3.40	<0.001	[14.26; 29.12]
	Congruency	−4.15	4.68	0.375	[−13.33; 5.02]
	Group	0.11	8.62	0.990	[−16.78; 17.00]
	Group × congruency	0.22	2.22	0.922	[−4.13; 4.57]
Model 2	(Intercept)	513.10	42.77	<0.001	[431.55; 594.66]
	Accuracy	21.71	3.79	<0.001	[14.30; 29.16]
	Congruency	−11.34	6.22	0.069	[−23.53; 0.86]
	Group	0.07	8.32	0.993	[−15.79; 15.94]
	Flanker index	−0.73	0.25	0.005	[−1.210; −0.25]
	Switch cost	0.14	6.88	0.028	[0.020; 0.27]
	Diseng-I	−11.14	6.88	0.108	[−24.24; 1.97]
	PVAQ-I	0.001	0.97	0.999	[−1.14; 1.14]
	PCS-I	1.75	1.19	0.146	[−0.52; 4.02]
	ECIP-I	−1.58	0.96	0.104	[−3.41; 0.26]
	Group × congruency	0.10	1.23	0.966	[−4.28; 4.47]
	Flanker index × congruency	0.15	0.07	0.032	[0.01; 0.28]
	Switching costs × congruency	0.01	0.02	0.768	[−0.03; 0.04]

Model fit statistics; Model 1: AIC = 226,245; Model 2: AIC = 226,233.

participants showed a significant Flanker index, $t(231.98) = -4.99$, $p < 0.001$, and a significant switching cost, $t(223.33) = -3.55$, $p < 0.001$. Overall, scores on self-reported itch-related cognitions were low to moderate in the current sample with a high dispersion of individual scores. There were no significant differences between all three groups on any background variables (all $p > 0.05$).

3.2. Pre-training

During the pre-training attentional bias measurement, 3% of the data had to be excluded due to trials with RT < 150 ms, data due to an extreme value of two participants' switching costs, and data due to one participant's low accuracy during the task. Reliability analyses showed high reliability for congruent trials, with a mean Spearman-Brown coefficient of 0.97 [Interquartile Range (IQR) = 0.96; 0.97]. Likewise, for incongruent trials, the mean Spearman-Brown coefficient was 0.96 (IQR = 0.96; 0.97). AB index reliability had a mean Spearman-Brown coefficient of 0.43 (IQR = 0.36; 0.52).

Mixed model analyses of the pre-training attentional bias measurement showed no significant effect of congruency, group or congruency by group interaction, see Model 1 in Table 2A and Figure 2A for visualisation of the data. Therefore, there was no significant attentional bias towards itch in the three groups.

After adding the Flanker index, switching costs and self-report questionnaires as covariates (Model 2), results show a significant effect of Flanker index and switching costs on RT during the pre-training block, as well as a significant interaction between Flanker index and congruency. This means that overall RT during the attentional bias measurement was

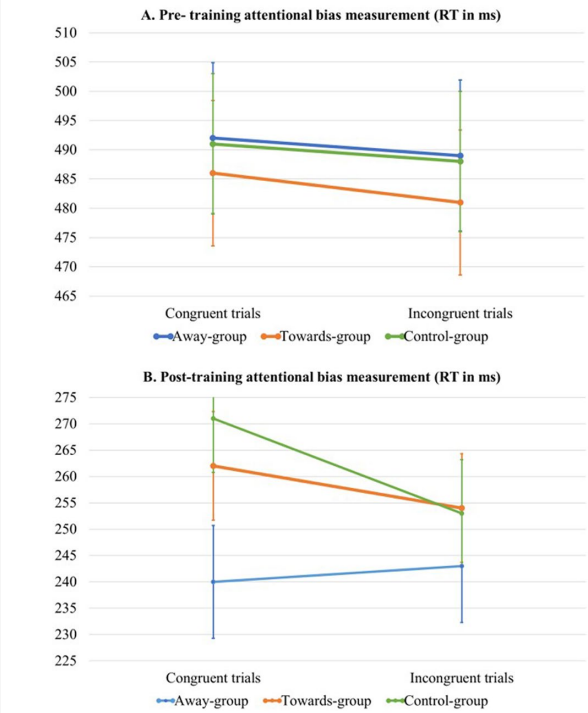

FIGURE 2
Estimated marginal means per trial type (congruent vs. incongruent) and group (away- vs. towards- vs. control-group) during the pre-training **(A)** attentional bias measurement and the post-training **(B)** attentional bias measurement.

TABLE 3 Mixed-model analyses of the post-training attentional bias measurement: estimates of the effects of the predictors on the outcome (*ES in ms*) with standard errors (*SE*), significance level (*p*-value) and 95% confidence intervals of the estimates (95% *CI*) (*n*=114).

		ES	SE	*p*-value	95% CI
Model 3	(Intercept)	226.68	14.99	<0.001	[197.44; 256.01]
	Accuracy	120.87	6.42	<0.001	[108.09; 133.51]
	Congruency	−28.97	8.86	0.001	[−46.24; −11.51]
	Group	−15.60	5.90	0.009	[−27.13; −4.08]
	Pre – AB index	0.52	0.24	0.032	[0.05; 0.99]
	Group × congruency	10.73	2.07	<0.001	[6.67; 14.79]
Model 4	(Intercept)	205.60	32.17	<0.001	[144.50; 266.82]
	Accuracy	120.90	6.42	<0.001	[108.16; 133.57]
	Congruency	−36.38	9.70	<0.001	[−55.38; −17.37]
	Group	−14.78	6.03	0.016	[−26.22; −3.33]
	Pre – AB index	0.42	0.24	0.089	[−0.04; 0.87]
	Flanker index	−0.23	0.18	0.212	[−0.58; 0.12]
	Switch cost	0.04	0.05	0.383	[−0.05; 0.13]
	Diseng-I	0.45	4.94	0.927	[−8.92; 9.83]
	PVAQ-I	−0.09	0.42	0.919	[−0.89; 0.70]
	PCS-I	1.29	0.86	0.137	[−0.34; 2.91]
	ECIP-I	−0.23	0.69	0.738	[−1.54; 1.08]
	Group × congruency	11.98	2.11	<0.001	[7.85; 16.10]
	Flanker index × congruency	−0.04	0.06	0.559	[−0.16; 0.09]
	Switching costs × congruency	0.05	0.02	0.001	[0.02; 0.09]

Model fit statistics; Model 3: AIC = 195,003; Model 4: AIC = 194,996.

influenced by participants' attentional inhibition (Flanker index) and their cognitive flexibility (switching costs). More attentional inhibition led to overall faster RT and more switching costs led to overall slower RT. Moreover, the effect of congruency (congruent vs. incongruent) interacted with someone's ability to inhibit irrelevant information (Flanker index). Specifically, participants with a higher Flanker index showed slower RT during incongruent trials compared to congruent trials during the attentional bias measurement, see Table 2.

Pre-training itch sensitivity AUC scores did not differ significantly between groups before the training, $p_{boot} = 0.609$.

3.2.1. Post-training

Post-training attentional bias measurement data was filtered based on trials with RT < 150 ms, extreme values for the switching costs ($n = 2$), and due to very low accuracy (<0.70) during the training block ($n = 1$). This resulted in a data loss of 16.9%. Again, reliability analyses showed a high mean Spearman-Brown coefficient for congruent trials (0.94; IQR = 0.93; 0.95) and incongruent trials (0.92; IQR = 0.91; 0.93), but the mean Spearman-Brown coefficient for the AB index was lower (0.70; IQR = 0.65; 0.75), indicating lower reliability.

For the post-training measurement of attentional bias, mixed model analyses revealed a significant main effect of congruency, in which RT on incongruent trials was lower compared to congruent trials. This could be interpreted as an attentional bias away from itch stimuli. The analyses also revealed a significant difference between groups. Pairwise comparisons for the main effect of group showed no significant results (all $p > 0.05$). Even though this seems counterintuitive based on the main effect, this can happen because the main effect takes into account all possible comparisons. However, only the pairwise comparisons relevant to the hypotheses were inspected and appeared to be not significant. Furthermore, we found a significant association between pre-training AB-index and RT. This means that a higher AB-index during the pre-training is associated with slightly higher RT during the overall RT during the post-training. Lastly, there was a significant group by congruency interaction effect, see Model 3 in Table 3 and Figure 2B for visualisation of the data. Pairwise comparisons showed a significant effect for congruency in the control group only ($p = 0.028$), with slower RTs for incongruent trials [Estimated Marginal Mean (EMM) = 253.0] compared to congruent trials (EMM = 271.0). Therefore, it can be concluded that the interaction effect between congruency and group is driven by this single comparison within the control group.

Model 4, with Flanker index, switching costs and self-report questionnaires as covariates (see Table 3), shows significant main effects for congruency and group, as well as a significant interaction effect for group by congruency and a significant interaction effect for congruency by switching costs. This means that after controlling for all these covariates, it can be seen that congruent trials are significantly slower than incongruent trials, which is interpreted as an attentional bias away from itch for all participants. Pairwise comparisons to investigate the main effect of group did not yield significant differences (all $p > 0.05$), but pairwise comparisons of the

interaction effect of congruency by group, showed a significant congruency effect for the control group ($p = 0.017$). Lastly, the significant interaction effect between switching costs and congruency showed that higher switching costs, which means less cognitive flexibility, are related to slightly slower RT on incongruent trials. However, the estimate is too low to be interpreted as a meaningful effect (ES = 0.05 ms).

Lastly, itch sensitivity AUC scores post-training did not differ significantly between groups, while controlling for pre-training AUC scores, $p_{boot} = 0.412$.

4. Discussion

Results of this study indicated that healthy individuals did not show an attentional bias (AB) towards visual itch-related stimuli. Next, it was found that a single-session attentional bias modification training (ABM) could influence attention towards visual itch-related stimuli in healthy individuals. Across all training groups, participants showed an AB away from itch after the training, i.e., avoidance of itch. However, when looking into the AB effect for specific groups, i.e., the interaction between group and AB, only the sham- training (control) group showed avoidance of visual itch-related stimuli after the training while there was no effect in the experimental groups. Finally, and in contrast with our hypotheses, the ABM-training did not impact upon itch-sensitivity.

While we indeed found an effect of ABM-training on attention to itch, this effect was not as intended, because the experimental groups that were either trained towards or away from itch showed no significant effect. Therefore, we cannot conclude that the ABM-training worked as we assume. This is in line with the most recent findings on ABM-training for itch (16) and also pain (39, 40), as well as the limited findings on preconscious ABM-training for threat (27). In addition to the fact that the current ABM-training had not the expected effect on the AB assessment measures, it also did not show effects on itch sensitivity, although this appeared to be more promising according to earlier findings in pain (17–19). Lastly, the current findings also add to the mixed findings on baseline AB towards visual itch-related stimuli in healthy individuals (9–11, 13). The absence of an AB towards itch at baseline might therefore explain why we did not find specific effects of the current training. Patients with chronic itch, in line with previous research showing a small AB towards pain in patients with chronic pain (41, 42), are expected to display a baseline attentional bias. For patients with chronic itch, the experience of itch is highly relevant and acting upon this experience is probably a relevant goal for patients. However, current ABM trainings in patients with chronic pain are thus far also not very successful (17–19), so it remains unknown how patients with chronic itch would respond to an ABM training for itch.

Recent developments in the field of pain have suggested that AB might be more dynamic, i.e., changes from moment to moment, than current AB assessment paradigms can capture and this might explain why attention bias modification training effects are often not found (43–45). In light of this, we might miss other, probably interrelated, aspects of cognitive bias, such as interpretation and memory biases towards itch (46). Especially interpretation of stimuli might be highly important, because at this moment, we are unaware of the specific interpretation that individuals give to used stimulus materials. To our knowledge only one study asked participants to rate the stimulus material that was used during AB assessment which actually showed that material was not rated very high on its intended dimension (i.e., itchiness or painful in this study) and results indeed showed no AB towards itch or pain in heathy individuals (10). Because the same stimulus material was used in the current study, this might also be true for the current study. In addition, especially for healthy individuals like in the current study, the ABM paradigm lacks personal significance because it is not related to an individual's goal to relieve an itch. Although participants received an itchy stimulus before the ABM-training, the actual experience of itch had already vanished during ABM, as intended in our case. It is assumed that AB in its original evolutionary function informs us about potential harm to our bodies and to induce adaptive behaviours, but this was not the case in the current study. The idea that individuals only show AB towards itch while experiencing itch is supported by the recent finding that only participants who received a histamine-induced itch stimulus on their skin, showed avoidance of itch-representing stimuli (47). Although the itch-stimulus was not even goal-related in this study, it might at least set a context that was related to itch and hence, increase personal relevance.

The finding that the control-group in the current study actually showed avoidance after the sham-training is surprising. For this group, the training did not differ to the pre-training and post-training assessment, which would not suggest any changes during the post-training. There are no clear explanations for this, but one could speculate about an effect of prolonged exposure and learning which might enhance attentional control, and therefore distraction by the pictures from the actual task. Still, these same effects would have been true for the experimental groups. Interestingly, the current result in the control group is in line with a recent study on preconscious AB towards itch which also showed avoidance in healthy individuals (13). This would suggest that this effect is not yet visible with less exposure and an extensive number of trials is needed to evoke avoidance of itch-related stimuli (13). In the current study, the control-group actually did one long AB assessment without any manipulations which in this sense is comparable to regular AB assessments, in line with earlier findings of preconscious avoidance (13).

In conclusion, the current study suggests that common ABM-training paradigms for itch are not working for healthy individuals as we assume. Development of theories on how cognitive biases in itch, and more specifically attentional biases, work are needed and these should guide the development of new paradigms and research designs. In a second step, the possibility to modify these biases can be investigated, because as long as we do not know how these biases operate we do not know where, when and how we should intervene. This is of course even more important if we consider bias modification trainings in the clinical context where patients with chronic itch are included. All in all, assessment of AB and application of ABM trainings in the clinical setting needs to be investigated in more detail, e.g., by taking the dynamics and context relevant to the individual into account, in the future before any conclusions can be drawn.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Psychology Research Ethics Committee, Leiden University. The patients/participants provided their written informed consent to participate in this study.

Author contributions

AL, JB, DR, SD, GC, and RW designed the study. JB led the data acquisition with substantial support by YS, wrote the initial draft of the manuscript, with help of YS, and revised the manuscript according to the critical feedback of AL, DR, RR, SD, GC, YS, and RW. JB and RR analyzed the data. All authors contributed to the article and approved the submitted version.

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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.

Publisher's note

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Interest in a short psychological intervention in patients with psoriasis: a cross-sectional observational study at a German clinic

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Introduction: Utilization of health services is not only associated with the kind of illness one has, but also with patient characteristics like age, sex or psychological variables. Psoriasis (PS) is a chronic inflammatory skin condition, in which psychological interventions were shown to be beneficial regarding not only psychological variables, but also regarding the skin status. The present study investigated with regard to which patient characteristics PS-patients with interest in participation in a short psychological intervention differ from PS-patients without interest.

Methods: This cross-sectional questionnaire study was conducted at a German rehabilitation clinic. At the beginning of their stay at the clinic, 127 PS-patients filled in questionnaires to assess the severity of their PS, stress, illness perceptions, mindfulness, anxiety, and depression. Interest in taking part in a short psychological intervention was assessed using a dichotomous item. The statistical analysis comprised group comparisons using *t*-tests of patients with and without interest to take part in a short psychological intervention.

Results: Sixty-four of the participants were male (50.4%). Participants were 50.7±10 years on average (range: 25–65). 50.4% of them had a mild, 37.0% a moderate, and 12.6% a severe PS. Results indicated that patients with interest in a short psychological intervention were younger, reported to have more skin symptoms due to their PS (higher skin-related illness identity), were more anxious and depressed, but less stressed and less mindful than patients without interest.

Conclusion: This study shows that in PS-patients with certain characteristics, it might help to raise awareness on the relationship between psychological factors and symptoms of the skin disease in order to motivate this group of patients to take part in psychological interventions to improve their skin condition. Further studies are needed to investigate whether patients who show interest in a psychological intervention also actually take part in the intervention and profit from it.

Clinical Trial Registration: DRKS00017426.

KEYWORDS

psoriasis, anxiety, depression, illness perception, psychological intervention

Introduction

The utilization of health services is related not only to disease-related factors [e.g., self-rated health, multimorbidity (1, 2)], but also to sociodemographic variables such as age, sex and socioeconomic status (2, 3). Having a psychological disease like an anxiety disorder, depression, panic disorder, somatoform disorder, or affective disorder as comorbidity is associated with higher use of health-related services (4, 5).

Psychological interventions, which can be a useful add-on in the treatment of different conditions, are more often used by women, persons without a partner or job, and patients with chronic diseases compared to persons with the opposite characteristics (3, 6, 7). Also, complementary and alternative medicine are used more often by women (8).

Psoriasis (PS) is a chronic, inflammatory disease with a 1-year-prevalence of about 2.5% in the German population (9). In other studies prevelance rates between 0.9 % and 8.5% were found (10). It is a multifactorial condition in which psychological factors such as stress (11), anxiety (12), and depression (13, 14) play a role.

In PS patients, psychological interventions such as meditation or cognitive behavior therapy were shown to have effects on the severity of PS symptoms (15). Also, mindfulness-based cognitive interventions often, but not always led to a significant improvement in the severity of the skin condition and a better quality of life (16–19).

Thus, psychological interventions seem to be beneficial in patients with PS and especially in those who experience psychological stress in daily life (20). However, in this patient group demographic, skin-related and psychological variables associated with interest in such a psychological intervention have not been identified, although interventions should be adapted to the needs of the patients (21). The aim of the study therefore was to examine if patients with and without interest in a short psychological intervention differ regarding demographic, psychological, and skin-related factors.

Methods

Study design and setting

This observational study took place at the rehabilitation clinic Borkum Riff, a clinic for patients with skin conditions and pneumological diseases. In Germany, a stay at a rehabilitation aims to reduce the severity of a disability or prevent its aggravation in order to reduce days of absence from work. Usually, patients stay there for 4 to 6 weeks. Data collection started in August 2019 and ended in September 2020. There were three data collection periods: August–September 2019; March 2020; and July–August 2020. Patients were recruited during their first week at the clinic by two of the authors (LS; ME) and a psychology student (see Acknowledgements). The study protocol was published before the recruitment of the participants was completed [for further details see Stadtmüller et al., (22)].

Participants

Patients were included consecutively. They were eligible to take part, if they fulfilled the following inclusion criteria: age between 18 and 65 years, clinical diagnosis of PS according to the International Classification of Diseases ICD-10 (23) for at least 6 months as well as the occurrence of symptoms during the last 6 months and sufficient knowledge of the German language in order to be able to fill in the questionnaires. They were excluded in case they were cognitively impaired. We originally planned to exclude patients with concomitant other skin conditions (especially itchy ones) than PS, but during the process of the study decided to include them. However, we conducted separate analyses for the group of patients with and without another skin condition.

Variables

Quasi-dependent variables

Demographic variables (age and sex), severity of PS, perceived stress, illness perception, anxiety, depression, and mindfulness were assessed as variables possibly distinguishing between patients with and without interest in a short psychological intervention.

The severity of PS was measured by the Self-Administered Psoriasis Area and Severity Index (SAPASI), which is a validated instrument that records the severity of PS by assessing the intensity of redness, thickness, and scaliness of the skin as well as the extent of affected areas (24).

The perceived stress level was measured by the Perceived Stress Scale [PSS; (25, 26)] which comprises 10 items (e.g., "How often have you been feeling nervous and stressed during the last week") that need to be answered on a 5-point scale. In this study, we were interested in the stress level during the last week instead of during the last month and therefore modified the wording in the instruction accordingly [also see Stadtmüller et al. (22)].

Furthermore, patients' illness perceptions were assessed with the German version of the Illness Perception Questionnaire (IPQ) capturing the five dimensions disease illness identity (e.g., "How frequently have you experienced pain as part of your illness"; divided into skin related and general illness identity), experienced causes of the disease (e.g., "A germ or virus caused my illness"), time-line of the disease (e.g., "My illness will last a short time"), consequences of the disease (e.g., "My illness is a serious condition"), and cure control (e.g., "My illness will improve in time"; 27).

Anxiety and depression were measured by means of the Patient Health Questionnaire (PHQ), which includes four items, two measuring the cardinal symptoms of anxiety disorders and two measuring the cardinal symptoms of depression (28).

After internal discussion within the working group, the Comprehensive Inventory of Mindfulness Experience (CHIME; 29) was additionally used to assess current levels mindfulness as a variable potentially differing between patients with and without interest in a short psychological intervention.

Quasi-independent variable

Interest in a short psychological intervention was assessed by the dichotomous item "Are you interested in participation in a short psychological intervention during your stay at the rehabilitation clinic?" The explanation that the intervention would be a mindfulness-based training at the clinic was orally added as the word psychological intervention led to resistance at the beginning of the study.

Further variables

Further sociodemographic variables such as education level, family status, and itch (average and maximal itch intensity during the

last 24 h) were assessed in order to describe the sample. For more information, see Stadtmüller et al. (22).

Statistical analysis

As mentioned before, we conducted two analyses, one including only patients without any other itchy skin disease than PS ($n = 111$) and another one including all patients ($n = 127$), also the ones who had another itchy skin condition besides PS ($n = 16$). Because the results of the two analyses did not differ significantly, we will only present the results of the analyses including all patients in this manuscript. The statistical analysis was done using SPSS version 28 (30). To investigate whether patients with and without interest in a short psychological intervention differed, *t*-tests for independent groups were conducted.

Ethics

The study was conducted in concordance with the declaration of Helsinki. The local ethics committee of the Faculty of Medicine at the Justus-Liebig-University approved the study (date of IRB approval: March 21st, 2019; AZ 19/19). In addition, the Federation of German Pension Insurance Institutions (Deutsche Rentenversicherung Bund, DRV-Bund) approved the study before recruiting the first study participant. All eligible patients were informed about the purpose and procedure of the study. Subjects participated in the study on a voluntary basis and were free to withdraw from the study at any time. They received a monetary allowance of 15 € for participation. The data were collected pseudonymously and kept locked separately from the consent forms.

Results

Participants

One hundred and fifty-nine PS-patients were treated at the rehabilitation clinic the during data collection periods. One hundred and fifty-seven persons could be reached, 149 patients took part in the study. 127 patients could be included in the analyses, while 22 had to be excluded *post hoc* because of not fulfilling the inclusion criteria (see Figure 1).

Sample characteristics

Sex was equally distributed in the sample: $n = 64$ of the participants were male (50.4%), $n = 63$ were female (49.6%). Participants were 50.7 ± 10 years on average (range: 25–65). 99.2% were German. More than half of the participants were married (53.5%) and living with their husband/ wife (55.1%). 60.6% had no possibility to go to college, 9.4% had this possibility, and 29.9% had a university diploma. The mean duration of PS was 20.8 ± 13.5 years (range: 0.5–54 years) with an average SAPASI of 7.3 ± 4.1 (range: 0.7–19.4) at the time of assessment. According to the SAPASI-classification (24), 64 (50.4%) had a mild PS, 47 (37.0%) a moderate and 16 (12.6%) a severe PS. Forty-seven participants did not have interest in a short psychological intervention, while 80 had interest. For further sample characteristics, see Table 1. A more detailed description of the sample will be given in the doctoral thesis by the first author of this article.

Differences between patients with and without interest

T-Tests for independent groups showed significant differences between patients with and without interest in a short psychological intervention regarding age, illness identity, stress, anxiety, depression, and the belief that nutrition and virus/bacteria cause the disease as well as mindfulness [$p < 0.05$]: Patients with interest in a short psychological intervention were younger [$p = 0.031$], reported to have more skin symptoms due to their PS [IPQ-scale skin-related illness-identity; $p = 0.041$], reported to be more anxious [$p = 0.005$], more depressed [$p = 0.01$], less stressed [$p = 0.006$], and less mindful [$p = 0.008$] than patients who were not interested in the intervention. In addition, patients with interest in a short psychological intervention

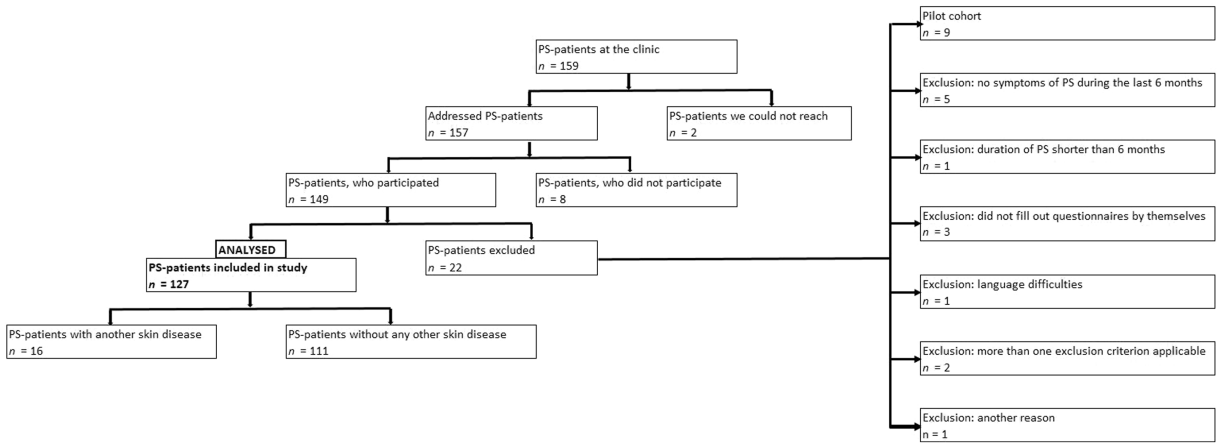

FIGURE 1
Overview of included and excluded patients and exclusion criteria.

TABLE 1 Sample characteristics.

Variable	Subscale	$\bar{x}$	SD	Range
Illness perception	IPQ_A_illness_identity_general	5.5	2.8	0–10
Illness perception	IPQ_D_illness_identity_skin	3.8	3.0	0–11
Illness perception	IPQ_cause_stress	3.7	1.1	1–5
Illness perception	IPQ_cause_nutrition	3.2	1.1	1–5
Illness perception	IPQ_cause_mental_state	3.1	1.3	1–5
Illness perception	IPQ_cause_timeline	4.1	0.8	1–5
Illness perception	IPQ_cause_consequenses	2.9	0.7	1–5
Illness perception	IPQ_cause_control/cure	3.2	0.6	1–5
Stress	PSS _total	2.3	0.7	0–4
Anxiety	PHQ_Anxiety	0.9	0.8	0–3
Depression	PHQ _Depression	0.9	0.7	0–3
Mindfulness	CHIME_total	3.9	0.5	2.8–5.1

SD, Standard deviation; $\bar{x}$, mean; IPQ, Illness perception questionnaire; PSS, Perceived Stress Scale; PHQ, Patient Health Questionnaire; CHIME, Comprehensive Inventory of Mindfulness Experiences.

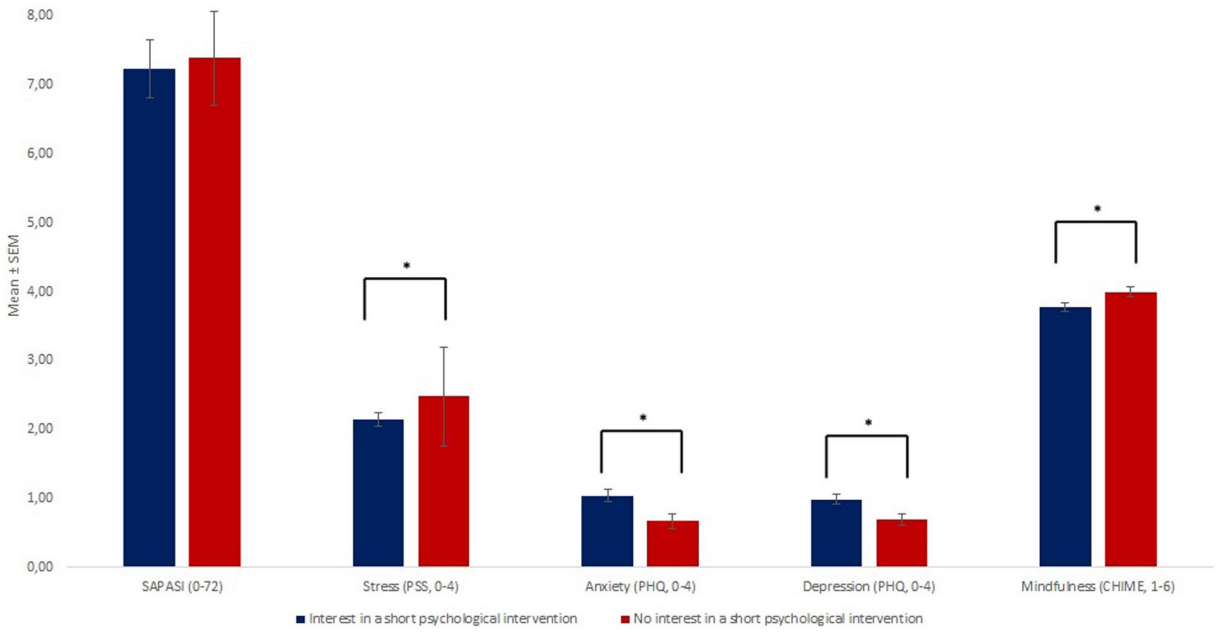

FIGURE 2
There were no group differences regarding the skin status, but regarding stress, anxiety, depression and mindfulness between patients with and without interest in a psychological intervention. * Illustrates a significant group difference (p<0.05).

more often believed that nutrition and virus/bacteria are an important cause of the disease than patients without interest [nutrition: $p < 0.001$; virus/bacteria: $p = 0.034$]. For further details, see Figures 2, 3.

Discussion

The aim of this study was to analyze how PS-patients with and without interest in participation in a short psychological intervention differ regarding demographic variables, the severity of PS, illness perception, anxiety, depression, stress and mindfulness. Knowledge regarding factors contributing to interest in participation in a short psychological intervention is necessary in order to offer patients individual information about the advantages and disadvantages of psychological interventions and their effects.

The study revealed that interested patients were younger, reported to have more skin symptoms due to their PS, be more anxious, more depressed, but less stressed and less mindful than patients without interest in a short psychological intervention. Interested persons also more often regarded nutrition and a virus/bacteria as cause of their disease than non-interested persons.

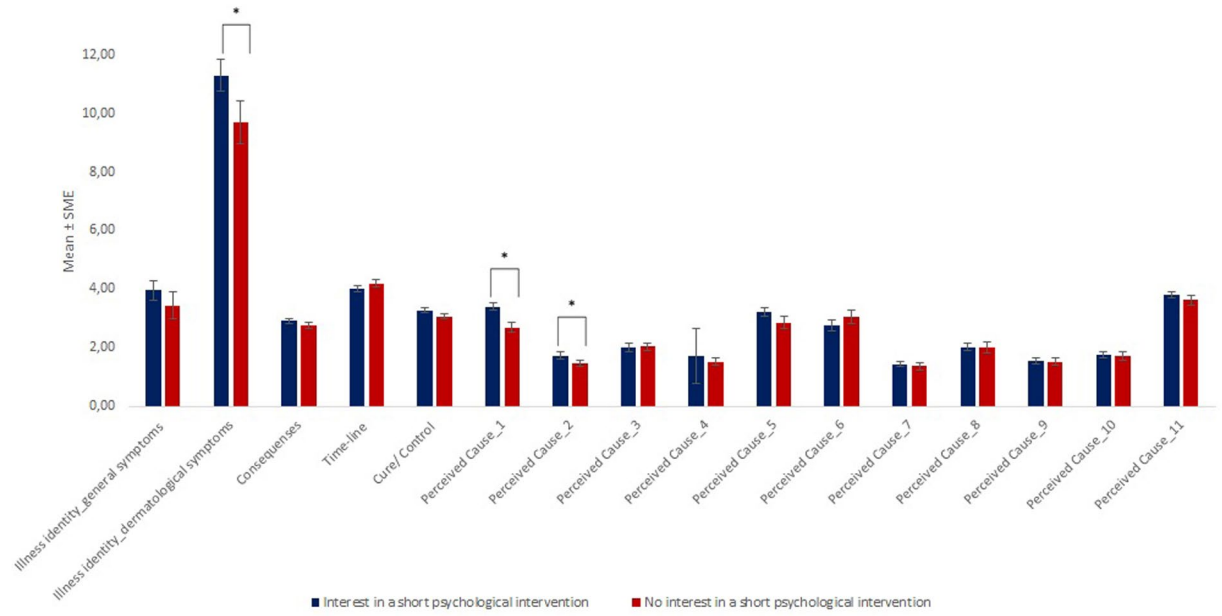

FIGURE 3
Group differences regarding illness perception. Explanations: Perceived Cause_1: Nutrition played a major role in causing my illness; Perceived Cause_2: A germ or virus caused my illness; Perceived Cause_3: It was just by chance that I became ill; Perceived Cause_4: Pollution of the environment caused my illness; Perceived Cause_5: My state of mind played a major part in causing my illness; Perceived Cause_6: My illness is hereditary—it runs in my family; Perceived Cause_7: Allergy causes my illness; Perceived Cause_8: Other people played a large role in causing my illness; Perceived Cause_9: My illness was caused by poor medical care in the past; Perceived Cause_10: My illness is largely due to my own behavior; Perceived_Cause_11: Stress was a major factor in causing my illness. * Illustrates a significant group difference ($p<0.05$).

These findings are partly in congruence with other studies, in which more anxious and depressed patients also had more interest in (additional) care services than less anxious and depressed persons (4, 6). This could result from the fact that anxious and depressed people have a greater interest in managing their psychological burden associated with PS and also experience a lower threshold for accessing services because they might have already received psychological help.

The finding that people with higher skin-related illness identity were more interested could maybe be explained by a greater interest in managing their illness in this group.

In this context, however, it is interesting to note that less stressed PS-patients were more interested in participation in a short psychological intervention than more stressed PS-patients. This is in contradiction with studies showing that emotionally burdened individuals usually use more clinical help (31, 32). However, in our study, these results might be explained by the fact that people who are busy participating in other programs during their stay at the rehabilitation clinic do not want to additionally take part in a psychological intervention that after all included 8 sessions of about 45 min plus homework (22).

Patients, who reported to be less mindful, were also more interested in participation than patients with higher scores regarding mindfulness. This result can possibly be explained by the fact that patients scoring low on mindfulness hoped for an increase of their mindfulness by participation in the intervention and regarded this as necessary to manage their disease.

Interestingly, also the belief that nutrition contributed to the disease differed between patients with and without interest in a short psychological intervention: Patients, who were interested in participation in the intervention, more often believed that their nutrition impacted their skin disease. With this regard, it is possible that patients who believe that they have aggravated their skin disease by an unhealthy lifestyle would now like to change this by participating in any additional program offered at the clinic (e.g., nutrition counseling/stress management/sport activities).

The result that rather younger patients were interested in a short psychological intervention fits to the result of a former study including patients with breast cancer. Here, also younger persons were more likely to participate in a psychological intervention than older persons (33). However, it has to be stated that interest in and actual participation are two different things (also see below).

Contrary to our expectation, patients with and without interest in a short psychological intervention did not differ regarding the severity of PS. This finding is in line with the results of a former study, in which interest in participation in a patient education program for parents of children with atopic dermatitis was also not related to the skin status of the children (34). When interpreting this result, it has to be kept in mind that psychological burden is not linear to the severity of the skin condition in PS-patients (35). This could also be shown in this study as the severity of the PS neither significantly correlated with anxiety nor with depression ($p > 0.05$).

Dermatologists working at a rehabilitation clinic can profit from knowing which patient characteristics contribute to interest in (further) psychological treatment during the stay at the clinic as this can lead to especially addressing patients without interest in order to raise their motivation. According to the transtheoretical model of health behavior (36) patients in different stages of behavior change profit from different information. It can thus, e.g., be helpful to

provide empirical data on the relationship between psychological factors and PS as well as on the effects of psychological interventions in dermatological patients to a certain group of PS-patients in order to improve the decision making of patients who are not interested in psychological interventions in the first place.

However, before clear recommendations can be given from the results, they should be replicated in a larger sample, also comprising outpatients. Moreover, future prospective studies should investigate whether there are certain characteristics, which differentiate between patients who actually take part in a psychological intervention and those who only pretend to be interested, but at the end drop out during the course of the intervention or do not participate at all.

Data availability statement

Data will be made available by the corresponding author upon reasonable request.

Ethics statement

The studies involving human participants were reviewed and approved by Ethics Committee at the Faculty of Medicine at the Justus-Liebig-University Gießen, Germany. The patients provided their written informed consent to participate in this study.

Author contributions

LS: conceptualization (support), investigation (equal), methodology (support), project administration (support), formal analysis (support), visualization (lead) and writing—original (equal). ME: conceptualization (support), data curation (equal), investigation (equal), methodology (equal), project administration (support), and writing—review and editing (equal). CZ: conceptualization (support), investigation (support), project administration (support), resources (support), and writing—review and editing (equal). JK: conceptualization (lead), methodology (equal), project administration (support), resources (equal), supervision (support), and writing—review and editing (equal). CS: conceptualization (lead), data curation (equal), formal analysis (lead), methodology (equal), project administration (lead), resources (equal), supervision (lead), visualization (support), and writing—original draft (equal). All authors contributed to the article and approved the submitted version.

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Conflict of interest

CS has received speakers honoraria by Novartis in 2020 and is a consultant for Mahana Therapeutics, United States.

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.

Publisher's note

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