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Digital health technologies (DHT) support patient-centered care by delivering behavioral, educational, self-efficacy and self-management interventions. Yet, multifactorial chronic diseases are shaped by complex interactions between genetics, environment and behavior, embodied in social and commercial determinants of health. Given that people in the United States spend on average 18 h per day at home, the impact of home environment on a person's health is underutilized in medicine. Herein, we discuss opportunities to improve therapy outcomes through bridging digital interventions with intentionallydesigned restorative and multisensory environments that simultaneously foster physiological and emotional homeostasis. Harnessing positive effects of biophilic design, neuroarchitecture and therapeutic home environments can enhance the effectiveness of digital interventions, including digital therapeutics (DTx), wearables and drug + digital combination therapies that utilize "prescription drug use-related software" (PDURS) framework. Real-world barriers to advance these solutions include a lack of public awareness about connections between the built environment, health and wellbeing, the knowledge gap in longterm clinical outcomes of biophilic interventions, and a limited funding for advancing "biophilic design as an adjunctive therapy" applications. In conclusion, creating digital health ecosystems that favor symbiosis between digital health interventions and enriched environments can promote sustained behavior change, elevate precision care and improve value-based healthcare outcomes.

KEYWORDS

prescription digital therapeutics, mobile medical app, virtual reality, built environment, household, housing, salutogenic, biophilia

1 Introduction

DHT belong to a broad category of mobile devices and software that deliver clinical benefits through mobile and virtual reality (VR) apps, video games, digital health platforms, wearables and medical devices. A rapid growth of DHT includes an emergence of digital therapeutics (DTx), or Software as a Medical Device products, intended to diagnose and treat medical conditions (1, 2). An example of DHT supporting patient care are digital health platforms that provide medication management, monitoring symptoms and other disease management services (3). Digital interventions and pharmacotherapies can be integrated using "prescription drug use-related software" (PDURS) framework or as adjunctive DTx in combination with drugs intended to treat specific conditions (4). Adoption of DHT in medicine is limited by reimbursement rates, regulatory policies, and concerns from diverse healthcare stakeholders (5-8). Challenges for DHT include patient engagement and attrition that can impact long-term therapy outcomes (9-11). Many mobile apps for chronic diseases that are available in Google Play Store and Apple App Store lack the acceptable standards for the quality and content, undermining their effectiveness (12).

A majority of chronic conditions are multifactorial diseases where both the gene-environment interactions and a patient's behavior play important roles in their etiology and treatment outcomes (13). Environmental exposure has a significantly greater influence on non-communicable chronic diseases than genetic predisposition (14). For example, the presence of natural environments, e.g., neighborhood green spaces, can positively impact mental and physical health through physical and social activities (15–17). The intersection of housing and health is recognized as a means for public health interventions (18, 19), as well as to improve patient outcomes (20–22).

The concept of intentionally-designed environments that promote health is embodied in biophilic design, salutogenic architecture and neuroarchitecture. Biophilic design is an approach to improve health and wellbeing by incorporating natural elements into the built environment (23). Salutogenic architecture aims to create health-promoting spaces by supporting a person's "sense of coherence" (24), while neuroarchitecture is focused on how architectural features influence the human brain, cognitive functions, emotions and behavior (25). Grounded in biophilic design and the self-care model, we recently described the therapeutic home environments intended to provide clinical benefits for people with chronic conditions (20, 26). In this work, we discuss a confluence of design and digital health, as we highlight an opportunity to bridge behavior change interventions with living spaces that support homeostasis and lifestyle medicine. The thesis of this perspective article is that the effectiveness of DHT can be improved when a patient lives in an intentionally-designed home environment that fosters health and wellbeing.

2 Digital health offers multimodal therapies plus at-home convenience

DHT aim to improve health outcomes by delivering diverse therapeutic modalities, including behavioral and cognitive

therapies (e.g., cognitive behavioral therapy, CBT, or acceptance and commitment therapy), mindfulness, health education, physical therapy, disease self-management, remote patient monitoring, coaching, relaxation techniques and biofeedback, among many others (27). These interventions are provided with at home convenience, as exemplified by digital health platforms for chronic disease management, such as Welldoc and Dawn Health, or a prescription digital therapeutic, RelieVRx, an FDA-authorized VR technology for patients with a moderate to severe chronic low back pain (28, 29). Clinical benefits of digital interventions span a wide range of chronic conditions, e.g., cancer (30), neurological (31), neurodegenerative (32), mental (33), metabolic (34), cardiovascular, and autoimmune disorders (35). The breadth, depth, flexibility, accessibility and scalability of multimodal DHT to treat chronic diseases make digital interventions an attractive value proposition for healthcare stakeholders.

DHT are also gaining popularity through fitness trackers and other consumer health wearables that enable monitoring vital signs and disease symptoms (36, 37). Wearables such as Apple Watch, Oura Ring, FitBit, Garmin Health, Samsung Galaxy watch are merging with medical device functionalities, based on receiving the FDA authorization or clearance for specific applications. These aforementioned wearables and their associated apps promote lifestyle medicine (e.g., physical activities, sleep hygiene, stress management), while ongoing research points toward their applications in the prevention of chronic conditions, such as irritable bowel syndrome or mild cognitive impairment (38, 39). An apparent advantage of wearables coupled with mobile apps is their ability to bridge daily activities with biofeedback and health outcomes (40).

Innovation of medical treatments includes integration of DHT with pharmacotherapies, leading toward drug + digital combination therapies (41-43). The indication-specific Rx+DTx combinations are illustrated by adjunctive DTx such as reSET-O app (in combination with buprenorphine for opioid use disorder), and Rejoyn app (in combination with antidepressant drugs for the treatment of major depressive disorder). The FDA's guidelines on prescription drug use-related software represent a paradigm shift in evolving medical treatments by enabling integration of Rx and DTx through drug labeling (44). Currently, companies like Click Therapeutics (USA), Remepy (Israel) and Closed Loop Medicine (UK), advance the development of personalized drug + digital combination therapies (aka "software-enhanced drugs," or "hybrid drugs") for migraine, Parkinson's disease, cancer and other indications. As discussed below, DHT are positioned to integrate pharmacological and behavioral interventions with a patient's home environment that promotes healing and the tertiary prevention.

3 Health behavior is a function of a person and environment

Grounded in diverse theories, health behavior includes beliefs, motivation, abilities and daily actions that support health and prevent diseases (45). Most digital interventions targeting health behavior change utilize goal setting and self-management (46). However, the impact of housing environment on health behavior has been largely overlooked, perhaps with an exception for trauma-informed care. For people experiencing post-traumatic stress disorder, trauma-informed design creates spaces intended to promote relaxation and feeling safe, while removing adverse environmental stressors (47). On the other hand, extensive research on migraine triggers, such as stress, disrupted sleep, lighting and air pollution, has not translated to studying migraine-informed home spaces that support lifestyle modifications and prevent headaches (20, 26, 48–50). Among general population, housing conditions that lead to sleep disruption can negatively impact mental health (51).

The built environment that promotes health behavior is likely to prevent chronic diseases (52, 53). Based on the Kurt Lewin's theory that behavior is a function of a person and environment, Brug and colleagues studied associations between homes, schools and workplaces (defined as micro-environment) and behaviors leading to obesity and cardiometabolic conditions (54). In another study, the relationships between the exposome and risks for developing diabetes revealed that neighborhood walkability and greenspaces can reduce the risk for type 2 diabetes (55).

Figure 1 summarizes the complex interplay between health, individual behavior and environmental exposure. The exposome and a person's behavior are affected by both social and commercial determinants of health (56–58). Poor housing and nutrition, especially when coupled with environmental pollution, elevate the risk for a broad range of chronic conditions (59, 60). Furthermore, exposure to trauma and chronic stress significantly influence the onset and progression of chronic disease, as well as treatment outcomes (61-63). Based on research studies, we hypothesize that the built environment that fosters positive affect

and self-management can influence health behavior, and thus health outcomes (64-66).

4 How can the built environment impact health outcomes?

The built environment (housing, workplaces, schools, healthcare facilities, neighborhoods etc) can have either negative or positive effects on individual and public health. Most people are aware of the environmental impact on health, as exemplified by air pollution, including indoor air quality (60, 67). Harvard's Healthy Buildings program offers educational information on optimizing housing and workplaces for health focused mostly on mitigating the negative effects of the built environment (68, 69). The expert tips on creating healthier homes include recommendations to reduce the exposure to unhealthy and toxic chemicals and to "(re)connect with nature and natural light indoors" (68). However, despite available information about toxic hazards associated with household products, consumer's willingness to pay for safer alternatives is low (70). For people living with conditions related to the nervous, neuroendocrine or immune systems, it is important to reduce the exposure to unhealthy household goods that may disrupt their functions (20).

In the book "Constructing Health," Tye Farrow bridges translational research on enriched environment with designing spaces that can actively promote healing and health (71). The author describes examples of salutogenic architecture in order to create the built environment that provides



theory, B = f(P,E), states that behavior (B) is a function of a person (P) and environment (E). The Lewin's Force Field approach to health behavior change shows competition between the health-harming exposome and therapeutic interventions that encompass a patient and the environment.

neurological, psychological and emotional benefits. Grounded in the salutogenesis framework, salutogenic design aims to actively promote health by supporting an individual's "sense of coherence" through comprehensibility (easy navigation of spaces), manageability (providing a sense of control), and meaningfulness (spaces fostering a sense of purpose), collectively known as generalized resistance resources (24, 72). The patient-centered applications of salutogenic design include healthcare environments that support recovery and healing through connection with nature, provide social support, and offer opportunities for both relaxation and physical activity (73). Salutogenic spaces contribute to self-efficacy through cues that nurture confidence and relaxation (74).

The main objective of neuroarchitecture is to integrate neuroscience, environmental psychology and architecture in order to optimize design features, spatial arrangements, lighting, colors and acoustics for better health and wellbeing (25). A person's experience of neuroarchitecture-based environments modulates the activity of specific brain structures, such as amygdala, the prefrontal cortex, the anterior cingulate cortex, as well as the hypothalamic-pituitary-adrenal axis (75–78). Neuroarchitecture and neuroaesthetics research shows that intentionally-designed built environment can provide personal comfort, fascination and coherence, while yielding physiological, neurocognitive, behavioral and emotional responses (79–83). Physiological stress is also affected by architectural and nature-inspired interior features (81, 84–86).

Biophilic design is an approach to architecture and interior design that incorporates natural materials, patterns and elements into the built environment in order to reconnect humans with nature (23). Grounded in the biophilia and attention-restoration theories, biophilic design creates enriched environments that evoke multisensory experiences leading to restorative states and diverse physiological responses (87). Based on research studies, examples of the health-related benefits of biophilic design elements include: (*a*) stress reduction and improved recovery from stress, (b) improved positive emotions and mood, (c) reduced anxiety and depressive symptoms, (d) lowering blood pressure and heart rate, (e) improved pain management and cognitive functions, and (f) improved immune functions (87-90). Investigating biophilic intervention for cognitive functions in diabetic patients highlights the knowledge gap on long-term effects of biophilic design for chronically-ill patients (91).

Research on healthcare outcomes of biophilic design shows that the presence of biophilic features in hospitals can: (*a*) shorten the postsurgical recovery and hospitalization time, (*b*) reduce mortality and healthcare utilization (*c*) improve pain management, and (*e*) reduce stress for patients and healthcare professionals (92–94). Similarly, nature-enriched neighborhoods were shown to reduce healthcare utilization for mental and cardiovascular diseases (95–97). Based on emerging evidence and the ongoing research, biophilic design can be harnessed together with disease selfmanagement to create therapeutic home environments for people living with chronic pain, migraine, depression, anxiety, cancer and other chronic conditions (20, 26).

Biophilic design is also recognized as a strategy to create therapeutic spaces for people living with dementia (98), Parkinson's disease (99), diabetes (91), and cancer survivors (100, 101). Medical applications of biophilic design can be illustrated by a "refuge and prospect" space intended to reduce stress, mitigate allostatic load and support cognitive reserve through rebalancing the autonomic nervous system and nurturing neuroplasticity. Biophilic attributes and neuroarchitecture can enhance response to analgesic, anxiolytic and antidepressant drugs, further supporting the relationships between intentionally-designed built environment and therapy outcomes (102). In conclusion, biophilic design offers unique prospects to transform the built environment into a therapeutic modality.

5 Integrating digital health and biophilic design

From translational point of view, the pleiotropic effects of biophilic design and the enriched environment can deliver broadspectrum therapeutic effects, just like physical exercise, patient education and cognitive behavioral therapies (4, 20, 71). Therefore, transforming biophilic design into adjunctive therapies creates a novel value proposition for digital and pharma companies innovating medical treatments for chronic conditions. As detailed below, DHT are uniquely positioned to integrate biophilic design with behavioral, physical, and pharmacological interventions enabling "enriched environment-enhanced" multimodal therapies.

Figure 2A shows the evolving role of DHT in chronic disease management. The emergence of DTx opened several strategies for the delivery of non-pharmacological therapies and their subsequent integration with prescription medications (41–43). In our earlier work, we advocated for leveraging digital technologies to amplify the therapeutic effects of music, physical activity, sleep hygiene, breathing exercises, mindfulness meditation, yoga, and other selfcare practices with pharmacotherapies for depression, epilepsy, chronic pain, and cancer (103–105). More recently, we provided a rationale for developing multimodal interventions that combine DHT, prescription drugs and the therapeutic home environment (20).

One approach to integrate biophilic design and digital interventions is by delivering patient education focused on how natural environments provide health benefits and offering biophilic design DIY (do-it-yourself) actionable insights (20). This notion is further supported by biophilic VR interventions that showed positive effects such as stress reduction, alleviating anxiety and pain, and behavior change in oncology patients (106-109). Biophilic design is well positioned to enhance health outcomes of the smart home technologies that employ consumer electronics, wearables and mobile apps delivering health information (e.g., Samsung's "Home for Wellness" ecosystem), as previously suggested for the aging population (110-112). Emergence of AI-powered mobile apps and extended reality (XR) technologies for interior designers also illustrates opportunities to provide ideas for health-centric optimization of a patient's home environment (113). Another strategy to bridge the health benefits of biophilic design and digital health is through health-centric, household goods e-commerce as a digital health platform that enables creating the therapeutic home environment (20).



self-efficacy.

Promoting biophilic design through DHT can benefit pharma and biotech companies. For example, PDURS-based drug + digital combination therapy is an innovative approach to simultaneously treat chronic conditions at the molecular and behavioral levels. As illustrated in Figure 2B, once reaching remission, continuum of care through digital interventions reinforces the tertiary prevention. The therapeutic home environment may further improve the effectiveness of Rx+DTx combinations by accelerating remission of chronic pain, migraine, depression, anxiety or cancer (20). This aspect is illustrated in Figure 2C highlighting how living spaces that provide more natural light and other biophilic elements can integrate drug + digital + biophilic interventions. Once a patient reaches remission, deprescribing medications can be mitigated by a continuous use of DTx. In such cases, the therapeutic home environment that comprises biophilic spaces fostering self-care can support the prevention of relapses through

restorative effects. For people living with epilepsy, such approach can improve the effectiveness of drug + digital combination therapy in controlling epileptic seizures (43).

6 Indications and future directions

Digital and pharmacological interventions for chronic diseases can be enhanced by biophilic, enriched environments intended to reduce stress, improve positive affect, rebalance the autonomic nervous system and promote neuroplasticity (20). For example, DTx-delivered Rhythmic Auditory Stimulation therapy for Parkinson's disease (PD) can be enhanced through multisensory home environment designed for PD patients (32, 99, 114, 115). To ameliorate the prognosis for mild cognitive impairment and dementia, DHT and biophilic design can simultaneously deliver multisensory experiences intended to improve patient care, including management of comorbidities, e.g., depression (98, 116-119). Such integrative approach also applies to enhancing outcomes of non-invasive sensory stimulation technologies and music-based interventions for the Alzheimer's disease (119-121). For chronic pain and migraine, outcomes of DTx and drug + digital combination therapies can be further improved in the presence of intentionallydesigned biophilic home environment that fosters self-care practices (20, 26, 31, 122, 123). As emphasized in Figure 2C, drug + digital combination therapies for chronic pain or depression can be further optimized by the therapeutic home environment that offers multisensory stimulation through natural light and greenery, haptic feedback from natural materials, and personalized soundscapes that support positive emotions (124). Based on aforementioned examples, we conclude that home ecosystem can be embodied in AI-powered digital interventions to enhance overall patient experience, engagement and, ultimately, outcomes.

DHT are uniquely positioned to validate a patient's home environment as a therapeutic target for chronic disease prevention and treatment (20). Furthermore, incorporating biophilic design, as an "active non-pharmacological ingredient," into digital therapies can improve their effectiveness, hence creating a new value proposition for digital health companies, healthcare systems and payers, to name a few examples of stakeholders. In our previous work, we described household goods e-commerce as a digital health platform delivering biophilic design and therapeutic home environment for specific chronic conditions (20), illustrating one possible research and development (R&D) strategy to integrate biophilic design and DHT. Another opportunity for advancing "enriched environment-enhanced" DTx solutions is expanding content by adding biophilic e-design functionality, biophilic design education focused on the health benefits, and incorporation of fractal designs into visuals to enhance user experience via relaxation (125, 126). For XR-based DHT, incorporating health-centric e-design features can integrate behavioral and environmental interventions. Given the growing interest in longevity and healthy aging, creating biophilic housing communities that prioritize connection with nature, social interactions and physical activities may also positively impact the effectiveness of digital interventions (127, 128).

7 Limitations

While this perspective article highlights opportunities to pivot DHT toward harnessing medicinal properties of biophilic design, we acknowledge real-world barriers for such approach. For example, the knowledge gap on long-term effects of biophilic interventions for chronic conditions, when combined with the knowledge-practice gap can delay a broader adoption of biophilic design into healthcare by many years. We suggest that the real-world pathway to validate biophilic design as a long-term therapeutic modality is through pragmatic clinical trials in hospitals, hospital at home programs, neurorehabilitation facilities, senior at-home care and assisted-living care settings (26, 92, 98, 129, 130). Testing the effects of biophilic design in improving patient's outcomes is feasible through remote patient monitoring employed in hospital at home programs (130, 131).

Additionally, a lack of awareness among general public and healthcare professionals about the impact of home environment on health outcomes poses a challenge to accelerate R&D activities to optimize health-centric solutions for a patient's living spaces. While limited return on investment (ROI) analysis for biophilic design are related to workplaces, education, hospitality and healthcare (132, 133), to the best of our knowledge, there are no health economics and outcomes research (HEOR) data on the use of biophilic design and a patient's home environment-based interventions for chronic diseases.

The commercial success of integrating digital health with biophilic design hinges on more than just innovation; it requires a nuanced understanding of market dynamics and user adoption. While the potential for improved health outcomes is promising, the real challenge lies in creating scalable, economically viable solutions that meet both consumer demand and organizational goals. DHT must not only complement natural environments and improve human health but be designed in ways that drive measurable ROI for companies—whether through improved outcomes, enhanced user engagement, productivity or reduced healthcare costs. Bridging the gap between these disciplines isn't just about technology or design; it's about creating sustainable business models that align with the evolving needs of consumers and the healthcare industry.

8 Conclusions

There are needs to improve the prevention and treatment outcomes for people living with chronic disorders, in particular for those who struggle with refractory conditions. Software-based health technologies have unique abilities to deliver multimodal therapies comprising cognitive and behavioral interventions, physical activities, patient education, disease self-management and self-efficacy. Given growing research evidence on medicinal properties of biophilic design and enriched environments, DHT are uniquely positioned to bridge interior design and health outcomes by delivering biophilic interventions, as well as integrating home environment with pharmacotherapies using the PDURS framework or adjunctive DTx strategy.

Digital technologies that transform the built environment into therapeutic spaces can benefit diverse stakeholders, including

patients, healthcare professionals, value-based healthcare systems, payers, digital health and pharma companies, architects, interior designers, social impact and real estate investors. We hope that our perspective article will encourage DHT innovations to target chronic diseases at the combined person + behavior + environment levels. Our call to action is to initiate a dialogue on how to harness the medicinal properties of intentionally-designed spaces to enhance patient-centered care through digital health interventions.

Data availability statement

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

Author contributions

GB: Writing – original draft, Conceptualization, Writing – review & editing. MF: Writing – original draft, Writing – review & editing. DH: Conceptualization, Writing – review & editing, Writing – original draft.

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Conflict of interest

GB is a founder and owner of OMNI Self-care, LLC, a health promotion and consulting company supporting evidence-based self-care and e-commerce solutions to improve health outcomes. OMNI Self-care has a contract agreement with Dayhouse Studio. GB is a co-inventor on two issued US patents related to digital health technologies 9,569,562 and 9,747,423 "Disease Therapy Game Technology" and patent-pending application "Multimodal Platform for Treating Epilepsy". These patents are owned by the University of Utah. GB and DH are co-inventors on a patent-pending technology "System and method for improving therapeutic interventions using household goods e-commerce platform." DH is the founder and owner of Dayhouse Studio, a health-centric biophilic interior design firm, and the Dayhouse Living magazine. MF is a VC investor, board member and strategic advisor to healthcare startups in areas of digital health, precision medicine and women's health. She is the Founder of MF7 Ventures, Senior Advisor for Accelmed Partners and Seed Healthcare, and board director of Click Therapeutics among many other portfolio companies.

Generative AI statement

The author(s) declare that no Gen AI was used in the creation of this manuscript.

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