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SPECIAL ARTICLE

Leveraging the Metaverse for Enhanced Longevity as a Component of Health 4.0

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Abstract

In this review, we describe evidence that supports building a metaverse to promote healthy longevity. We propose that the metaverse offers several physical advantages (architecture, music, and nature), social (accessibility, affordability, community-building, and relief of social anxiety), and therapeutic (immersive, anti-inflammatory, and adjunctive use in complementary and integrative medicine). Lifelogging by patients may help clinicians personalize interventions by matching data to therapeutic outcomes. Although the metaverse cannot entirely replace our current model of care, a strategic approach will ensure adequate resource allocation and value assessment. In a collaborative effort between Reulay, Inc and Mayo Clinic, we are building a platform for the delivery of personalized and idiographic interventions to promote healthy longevity. To this end, we are using specific science-informed art design to reduce stress and anxiety for patients, with the progressive addition of integrated care elements that connect to this framework and connect treatment response to biomarkers that are relevant to healthy longevity. This review is a commentary on the thought process behind this effort.

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According to the World Health Organization, "health is a state of complete physical, mental, and social well-being." Health care is compromised by lack of access, high costs of care, poor quality of care, lack of safety, and a low degree of satisfaction. Persistent inflation continues to challenge all of these elements. The metaverse, or immersive internet, maybe a potential solution to these challenges.

Health 4.0 is a concept that originated in Industry 4.0 and aims to offer instant personalized medical services for patients and sophisticated virtual tools for health care stakeholders.[1] The goal of Health 4.0 is to eliminate barriers to health care and provide high-quality health care services that are efficient, effective, and cost-effective, with appropriate resource use. A recent review emphasized that therapy aided by virtual reality (VR) is an essential component of the health 4.0 infrastructure.[2] We extend this concept by proposing that the metaverse is a potential delivery mechanism for transforming health care and increasing healthy longevity.

The metaverse is an immersive internet environment in which physicians and patients can perform daily activities by using avatars that symbolize their real or imaginary selves. The World Economic Forum anticipates that digital services will be one of the most revolutionary paths to transforming health care,[3] and we anticipate that the metaverse offers several powerful alternatives to the way medicine is practiced today.

In this review, we outline the strengths of the metaverse as a complementary model of health care, specifically for enhancing healthy longevity and also consider some limitations that will result from poor integration. We outline our proposed initial steps for leveraging the metaverse for healthy longevity and focus on strategic connections between mental health and integrative medicine. Our primary objective is to review previously published evidence that supports the metaverse as a venue for longevity interventions. Specifically, we focus on the physical and social aspects of the metaverse that relate to longevity, and the metaverse in the context of achieving nonordinary

ARTICLE HIGHLIGHTS

- As spatial computing gathers momentum, science-based and practical strategies are needed to build an immersive internet for healthy longevity.
- Although virtual reality has been associated with nonordinary consciousness, we extend this association to a novel point of view about how the metaverse as an exposome can be modified to promote changes central to healthy longevity. We highlight how principles of geometry can be incorporated into metaverse-based art to enhance mental and physical health. We also describe an alternative viewpoint based on neuroscientific hypotheses that fractal art has therapeutic potential for mental and physical illnesses by reducing inflammation and rewiring the default mode network.
- Although others have highlighted the urgent need for business innovation and scientific research to address early death for patients with mental illness, we describe a potential framework for realizing business-science partnerships to enhance healthy longevity by using principles of technology, mental health, physical health, and art.

consciousness to positively influence health and longevity. We also describe how we at Mayo Clinic are designing a metaverse to improve healthy longevity for our patients.

Determinants of Longevity

Healthy longevity refers to successful aging, which is defined as living longer than 90 years (ie, long-living people) but maintaining optimal physical, psychological, and social functioning, with delayed onset of aging-associated diseases.[4] The Blue Zones project identified 9 factors that are associated with longevity,[5] such as: moving naturally, having a sense of purpose, downshifting regularly, eating to 80% satiety, having a vegetarian-leaning diet, consuming alcohol moderately, having a sense of belonging, putting loved ones first, and belonging to social circles that support good health. In the world at large, these factors are difficult to operationalize and scale, but the metaverse provides a controllable environment in which this may be possible.

Longevity may be associated with other factors, such as education, the timing of commencing or ending employment, occupation and income, physical activity, and personal hobbies.[4] These factors may be captured through a database in the metaverse and then matched to how they factor into the success of metaverse-based interventions. Plasma levels of total protein, albumin, α_1-globulins, high-density lipoprotein, free triiodothyronine, and 25-hydroxyvitamin D are also associated with health and longevity[4]; therefore, these intrinsic physiologic markers may interact with environmental and relational factors to affect health outcomes and can be similarly associated with metaverse-based interventions.[6]

Others have reported that a healthy diet, moderate food consumption, and physical and social activity all contribute to healthy longevity.[7] Although exceptional longevity is widely accepted to result from a combination of genetic predisposition, various environmental factors, resiliency, and chance, all of which are influenced by culture and geography. The metaverse provides a context to investigate healthy longevity factors because it provides a specific physical context and relational environment that researchers and clinicians can study and provide interventions in a relatively controlled manner.

Traditional Health Care Models Versus State-of-the-Art Digital Health Care Technologies and the Metaverse

Globally, most people who require mental health care do not have access to such care. Approximately 1 billion people in the world have mental health disorders,[8,9] but only 200,000 psychiatrists[10] and 1 million psychologists[11] are currently practicing. With this tremendous mismatch between patient needs and available services, software is the only mechanism through which mental health care needs can be addressed at scale. Worldwide, 6.4 billion people own a smartphone[12]; therefore, digital therapies that leverage this device are plausible. The metaverse is a venue in which mental health care can be provided on a smartphone.

Digital health care technologies offer the potential to ensure that health care services are cost-effective, coordinated, and accessible.[13,14] The metaverse is a digital health care technology that has the potential to create a community of people whose data can be leveraged via machine learning for personalized representations through the use of digital twins (or avatars) that represent various domains relevant to the patient (eg, genetics, overall biology, and medical status).[15] This technology may revolutionize health care because a lifetime of data can be stored online to strengthen the quality of personalized interventions. Indeed, testing has already begun in the context of breast cancer,[16] and behavioral, microbial, multiomic, metabolic, immune, genetic, and epigenetic variables may be included in predictive or therapeutic models for any disease. The technology has also been tested in the context of cervical vertebral maturation (for dental health and orthodontics) with blockchain technology, which provides the additional advantage of patient ownership of their own data.[17]

The metaverse may also offer additional insights into the behavior and clinical importance of microorganisms, such as viruses, fungi, algae, bacteria, protozoa, archaea, and multicellular animal parasites. Through digital twinning of bacteria, for example, we may be able to more clearly distinguish between harmful and helpful bacteria and thereby refine treatment recommendations. Deep-learning methods in the context of health care have been reported to reduce diagnostic errors.[18] The metaverse also poses opportunities for drug discovery. By combining the internet of medical things, edge computing, and deep-learning techniques, real-time medical data from medical sensors on smartphones can be integrated into predictive and therapeutic models. Blockchain technology may also be used to enhance the security of data transmission.[19]

The metaverse offers a novel, yet promising, opportunity for a decentralized system of aggregating data that patients own and clinicians can leverage to personalize interventions and augment in-person clinical care.

Physical Components of the Metaverse

Architecture. The collective environmental factors that affect longevity are referred to as the exposome. The metaverse—an environment in which people can exist, interact, and receive care—is now an additional factor to consider in the exposome. The extent to which its structure and function can be built to simulate an ideal exposome or to improve an undesirable exposome should be leveraged in health care.

Architecture is an important factor for healthy aging and longevity.[20] The Salutogenic Model of Health proposed by Aaron Antonovsky posits that a key factor in health promotion is a *sense of coherence*. This model spurred salutogenic design in health care environments, such that health care buildings are considered supportive environments rather than sterile facilities for the provision of services.[6] Others have reported how architectural design principles can inform building facilities for psychiatric care.[20] Three design principles are key for salutogenic designs in health care: comprehensibility, manageability, and meaningfulness. Referred to as therapeutic architecture,[21] these principles can be extrapolated to design principles for the metaverse without the materials or labor necessary for physical structures.

Current research indicates that incorporating principles of Maharishi Vastu architecture (MVA) into buildings may be helpful for healthy longevity.[22] Maharishi Vastu architecture principles include development of architect consciousness and consideration of building orientation and site. In addition, the dimensions of the building and how key functions are placed or situated, as well as the direction of the occupant's head when sleeping, all contribute to MVA design. The physical and mental health and quality of life of occupants in such structures increases as more MVA principles are incorporated. In addition to sleeping more restfully, children are happier and feel more secure and less stressed.[23] Fewer burglaries also occur in buildings with MVA design principles, and this leads to overall better health.[23] Optimal sleep[24] and stress[25] levels are recognized determinants of healthy longevity. Happiness[26] and social determinants of health also positively affect longevity.[27]

The field of neuroaesthetics studied at the International Arts + Mind Lab (Johns Hopkins University School of Medicine)[28] addresses intractable health problems through the integration of architecture, art, and music. Other principles, such as holistic housing, integrated design processes, and integrated building envelopes, can also be applied in the metaverse. The Mayo Clinic Well Living Lab is currently researching this topic, and the Massachusetts Institute of Technology offers courses on the subject. In the metaverse, various principles of architecture and design can be used to build and study their effect on health and longevity.

Music. Music confers a large number of positive effects on physical and mental health. Indeed, when people engage in music (ie, passive listening, singing, or playing music) during the middle to late life, this alone may enhance healthy longevity.[29] Music can also benefit mental health and immunity, both of which affect longevity. Listening to relaxing music is strongly associated with decreased cortisol levels,[30] and music has positive effects on components of the immune system, such as leukocytes, cytokines, immunoglobulins, hormones, and neurotransmitters.[30] In the metaverse, music can be used as an environmental stimulus to benefit healthy longevity. In addition, music in the metaverse can be studied and personalized.

Nature. Music,[31] video, and VR experiences of nature have been reported by Mayo Clinic[32] and several other institutions to reduce stress and anxiety. The metaverse can be populated with various calming aspects of nature, which thereby affects longevity through stress reduction. Because life stresses are known to affect activity of the hypothalamic-pituitary-adrenal axis, hypothalamic-pituitary-gonadal axis, sympathetic-adrenal-medullary axis, and immune system (with a considerable effect on the human brain and genome), nature-based video and VR experiences in the metaverse may be protective of health.[33]

Social Aspects of the Metaverse

Access. Globally, nearly 400 million people do not have adequate access to health care, and 8 million people die due to potentially treatable health problems.[34,35] This results in a loss of ∼US $6 trillion in low-income and middle-income countries.[36] Because 70% of people with mental illnesses have no access to care,[37] mortality rates are further increased in this population because serious mental illnesses are associated with excess deaths.[38]

In 2017, 5.8 million people in the United States (1.8%) received medical care too late because they lacked access to transportation, and the number of people who reported barriers to transportation increased between 2003 and 2009.[39] Patients with transportation barriers also have a greater burden of disease, ostensibly because of their socioeconomic circumstances.[40] Studies have reported that the global rates of transportation barriers affecting health care access are between 3% and 67%, depending on the population sampled.[41,42]

The metaverse is a potential solution to lack of health care access, which considerably affects quality of life for patients with illnesses. Because the metaverse can be accessed on a mobile device and without a VR headset, the metaverse may circumvent transportation barriers to health care access.

Affordability. The Ayushman Bharat Digital Mission is building digital highways in the metaverse to provide effective, affordable, safe, and inclusive medical care.[43] In addition to eliminating the costs of transportation, the metaverse may provide a first point of care by providing carefully researched self-help rooms. This would also mitigate random internet searches for self-help remedies and may prevent premature emergency department or tertiary care visits, which inevitably lead to increased costs.

Studies suggest that when people support themselves, use of health care services can be reduced without compromising patient health outcomes. This is especially helpful for patients with diabetes or respiratory, cardiovascular, or mental health conditions.[44] However, implementation of metaverse-based care cannot simply follow the principles of telehealth. Indeed, some studies have indicated that telehealth models do not provide cost savings.[45]

Relationships, Community, and Loneliness. Many factors that affect healthy longevity may be accentuated in the metaverse. These factors include reflecting on having a sense of purpose, consuming alcohol moderately, having a sense of belonging, and belonging to social groups that support good health. Being a member of a community with a shared sense of purpose, socially drinking alcohol, feeling affiliated with a metaverse group, and interacting in a nurturing environment can all improve healthy longevity.

Social relationships affect the risk of death in a way that is comparable with other known risk factors for death. When 148 studies including 308,849 participants were analyzed, participants with stronger social relationships had a 50% increased likelihood of survival.[46] Moreover, older adults who have poor relationship quality, especially those critiqued by their spouse or partner, have an increased risk of death.[47] Loneliness is also a risk factor for death from all causes.[31] The metaverse can offer multiple relational options or group therapy to counteract these effects. Overall, the metaverse can be used for social support or enriching interpersonal interactions, which thereby increases the chances of living longer and living well. Notably, social isolation may be associated with neuroinflammation, and the metaverse may be helpful for patients with long coronavirus disease (COVID) who frequently have brain fog and neuroinflammation.[48]

Social Anxiety Disorder. Anxiety disorders are associated with increased mortality rates.[49] The ability to socialize as an avatar in the metaverse may be helpful for people with social anxiety who do not wish to be seen, although negative online phenomena (eg, cyberbullying) should be considered.

Immersive Therapies and Nonordinary Consciousness Interventions in the Metaverse

The convergence of telepresence, digital twinning, and blockchain have the potential to considerably influence health care.[43] The therapies and medical applications of the metaverse to healthy longevity may be grouped into 4 categories: augmented reality, lifelogging, mirror worlds, and VR.

Immersive Therapies. Augmented reality places a digital overlay on our perceptible reality. This can be used in medical education so that patients learn more about their bodies through a digital overlay of anatomic or physiologic interactions. Such overlays can be performed in a physician's office or the metaverse.[50]

Virtual Reality can immerse patients in an alternate 3-dimensional reality through telepresence. The immersive space can be designed to reduce anxiety, pain, or the need for sedatives. These indications may apply to intensive care units, emergency departments, and inpatient or outpatient settings.[50] Some indications include distraction from uncomfortable medical procedures, use in chemotherapy settings, anxiety reduction (through exposure or calming scenes), rehabilitation (eg, fall prevention education),[51] treatment of diseases of the nervous system (eg, stroke), and pain management.[2]

Inflammation Reduction Through Nonordinary Consciousness. Inflammation reduction associated with nonordinary consciousness states has been reported for mindfulness,[52] transcendental meditation,[53] psychedelic drugs,[54] and hypnosis.[55] Because inflammation is the basis of many psychiatric[56] and physical diseases,[57] using the metaverse to induce nonordinary states of consciousness through unusual movement experiences (eg, floating or levitation) and mind-altering art could considerably affect longevity.

Complementary and Integrative Medicine. Virtual Reality is a potentially useful adjunctive tool for meditation, hypnosis, palliative care, tai chi, qigong, acupoint sticking therapy, aromatherapy, and yoga.[58]

Data Collection and Monitoring. Lifelogging—self-documentation of personal data—may be an important component of providing personalized or idiographic health care solutions in the metaverse. A digital twin refers to a virtual representation of a physical entity, with interactive, bidirectional links between the physical entity and the digital twin. Digital twinning may allow for capturing patient data and using these data to predict outcomes of interventions in the metaverse. Blockchain offers the promise of secure data storage, personalization, and unique nonfungible tokens (NFTs) that may be used to anchor health state data and track progress. Using idiographic interventions that are customized and dynamically delivered to patients as their personal biometrics or physiologic characteristics change is an exciting application of the metaverse.

An Innovative Approach to Building a Metaverse for Longevity

To adapt the metaverse for healthy longevity, using lessons learned from longevity studies is important. To this end, partnering with world-class pioneers in longevity, science-based art designers, architects, blockchain experts, and artists who create NFTs may be helpful for building such a world. The Blue Zones project's Power 9 principles are a useful guide,[59] and an N-of-1 laboratory will be instrumental to provide personalized and idiographic[60] solutions based on a multiomics approach by associating outcomes with the microbiome, proteome, metabolome, genome, and epigenome and using these findings to further refine the metaverse.

Starting With Mental Health. Focusing first on mental health applications of the metaverse for longevity has a strong rationale. Poor mental health is intimately connected to longevity. Indeed, patients with serious mental illness have increased excess mortality rates,[61] and stress-induced epigenetic changes may reduce longevity.[62] Furthermore, crosstalk between inflammatory pathways and neural circuits in the brain may be a driver of depression,[63] anxiety,[64] posttraumatic stress disorder,[65] bipolar disorder,[66] and schizophrenia.[67] Suicide and its association with psychiatric disorders also affects longevity.[68] Inflammation is also hypothesized to be the common pathway for all stress-related diseases.[57] The microbiome, proteome, genome, and metabolome are known contributors to aging and mental illness.[69,70] Mental illness is, therefore, a construct that allows for integrated studies to better understand how the determinants of longevity interact to enhance or reduce the overall health of patients.

Providing Regular Downshifting at Scale as a Mental Health Intervention. Virtual Reality may be effective at improving anxiety, emotional distress, and focus by providing an environment for regular downshifting (ie, mitigating stress by reducing known stressors).[32] Further studies are needed to elucidate personalized and idiographic determinants of therapeutic outcomes. An initial focus on healthy longevity may help to build on-demand downshifting for all patients and to measure the most efficacious types of downshifting.

How Downshifting May Affect Longevity. An 18-year follow-up study of 1.5 million people in Denmark reported that people who worked in high-stress occupations had a higher incidence of chronic disease than those with minimal-stress occupations.[71] Others have reported that chronic stress is associated with accelerated aging.[72] Many mechanisms appear to underlie the stress-induced aging process, and associations between stress and aging include hastened shortening of telomeres, inflammation, oxidative stress, changes in tissue protein composition, and disrupted immunity.[72-75] In addition, genetic, epigenetic, environmental, and stochastic stresses have complex interactions.[75]

Downshifting as a form of relaxation and disconnecting from daily stressors may increase healthy longevity. Several forms of downshifting are linked to decelerating the aging process.[76-79] Indeed, certain meditation practices may help maintain telomere length by decreasing cognitive stress and stress arousal and by increasing positive states of mind and hormonal variables that promote telomere maintenance.[76] Many studies have reported a beneficial effect of mindfulness meditation, Zen meditation, transcendental meditation, and yoga-related practices on telomere length and healthy longevity.[77-79]

Meditative practices not only affect telomere length but also reduce excessive inflammatory responses[69] and enhance immunity.[80] Indeed, a study of long-term transcendental meditators reported that all 49 genes associated with severe inflammatory responses were downregulated, whereas genes associated with improved immunity and the oxygen-carrying capacity of erythrocytes were upregulated.[53] In addition, a recent study indicated that meditative monks in Tibet have a protective plasma proteome.[81] The proteome of these monks was associated with a decreased incidence of atherosclerosis, enhanced glycolysis, and oxygen release, all of which protect against cardiovascular disease. Clinical risk factors for cardiovascular disease, including total cholesterol, low-density lipoprotein cholesterol, apolipoprotein B, and lipoprotein(a) levels, were also markedly lower in the meditative monks than in a control population. Meditative practices also have a beneficial effect on the gut microbiome.[82] Overarchingly, meditation practices affect the microbiomes,[83] genomes,[84] epigenomes,[85] transcriptomes,[53] and proteomes.[81] Aside from meditation, rest-break interventions such as active rest or physical exercise during breaks have been reported to be beneficial for physical and mental health.[86,87]

VR for Downshifting. At its most basic level, 5-10 minutes of exposure to nature-based VR during the day is an active form of disconnecting that is equivalent to downshifting. Many studies have indicated that VR is beneficial for emotional distress, anxiety, and even focus.[32] Thus, VR is promising for mental health applications because of the beneficial effects of downshifting and rest-break interventions on physical and mental health through stress reduction.

In addition to the potentially relaxing effects of imagery through VR, VR also has the potential to immerse the user in a state of consciousness that is meditative or meditation like. A report by Montes[88] stated that most creators of VR experiences use the trick aspect of VR (ie, that the sensation of being somewhere else is an illusion that the brain believes) to design experiences. Therefore, the malleability of how the body feels with VR may be used to cultivate nonordinary states of consciousness.[88]

In meditative states, practitioners experience nonchanging pure consciousness, which has the quality of unity with one's surroundings or imparts feelings of being a witness of the activity by a deeper inner faculty.[89] This confers a feeling of peace or bliss. Maslow[90] described a similar state of peak consciousness, referred to as self-transcendence, in which a person experiences the highest levels of human consciousness. In this state, physical and psychological boundaries are dissolved,[91] and a nondual awareness that precedes intention or awareness of context eliminates the boundary between intrinsic processes and action in the world.[92,93] This state is reportedly associated with activation of the central precuneus network[92] and a network in the prefrontal cortex responsible for adaptive coding, especially in the anterior prefrontal cortex, which thereby enhances connections between these networks and other parts of the brain. Awareness is augmented through enhanced flexible connections between different brain regions with changes in perspective that result in a deeply held belief that change in any domain of life is possible.[94] This phenomenon is associated with sustained prefrontal α-band coherence.[94,95]

With VR, many phenomena described in these meditative states can be instigated. Rapid movement through dark space, levitation, and a feeling of unity with one's surroundings are all experiences that VR can simulate. Creating and measuring an emotional presence through deep immersion in the VR environment is also possible.[96]

A recent study of VR rehabilitation for posttraumatic osteoarthritis reported that training in the VR environment may induce more changes in inflammatory biomarkers (ie, C-reactive protein and several interleukins) than sensory-motor training alone.[97] Some psychological constructs that can be used to inform science-based design include nature-based art, geometric art, and fractal art.

Nature-Based Art in VR. According to the biophilia hypothesis, the evolution of humans is closely connected to our affinity for nature. Indeed, experimental studies have reported that people who spend longer times in natural environments have better mental health outcomes and cognition than do those with limited exposure to nature.[98] Some cross-sectional observational studies also reported that a longer duration of exposure to nature is associated with increased levels of physical activity and decreased risk of cardiovascular disease.[98] The long-term effects of natural exposure on depression, anxiety, cognitive function, and chronic disease will be clarified by studies with longer observational periods.

The connections between positive health outcomes and nature may be explained by 2 theories: attention restoration theory and stress reduction theory.[99,100] According to attention restoration theory, mental fatigue associated with modern life leads to depleted attentional resources, and exposure to nature

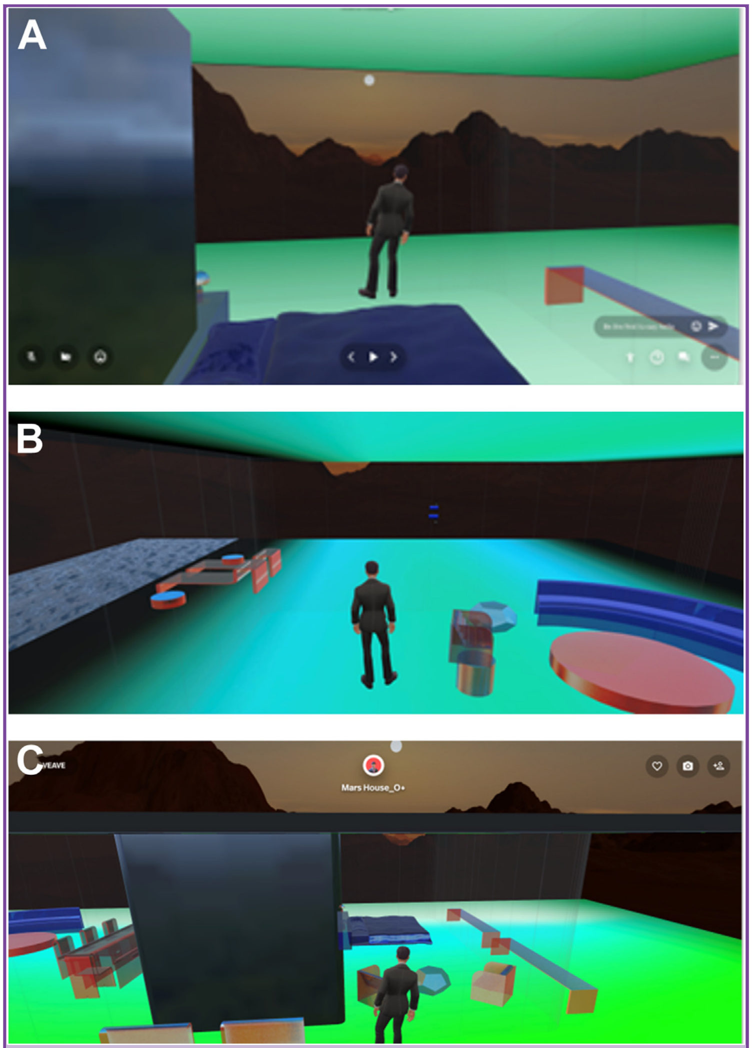

FIGURE 1. Representative images of the Mars House NFT metaverse environment. Images depict different viewpoints of the Mars House NFT with an avatar of 1 author (SSP) observing the mountains in a relaxing setting. A, View of outside landscape. B, View of interior room. C, Broad view of Mars House NFT. The NFT indicates nonfungible token. (Courtesy of Krista Kim Studio Inc; used with permission).

helps to restore these attentional resources.[99] According to stress reduction theory, exposure to nature reduces stress and autonomic arousal because of an innate connection of humans to the natural world that activates the parasympathetic nervous system.[100] Although exposure to nature in VR is not to actual nature, potentially beneficial effects of attention restoration and stress reduction may also benefit health outcomes. In addition, VR offers the opportunity for social engagement, which may further affect health outcomes because loneliness can increase the risk of cardiovascular disease,[101] immune dysfunction, and inflammation.[102]

Geometric-Based Art in VR. Simple geometric shapes have emotional consequences. For example, when people are exposed to downward-pointing V-shapes, they perceive them as threatening, whereas they unconsciously perceive curvilinear forms as pleasant.[103] Although many studies have reported that people prefer curved contours to straight lines,[104] more recent studies have reported that some people prefer curves, but others prefer angles. Therefore, contours elicit a psychological response in people.[105] Indeed, the aesthetic attributes of architecture have an effect on mood, cognitive functioning, actions, and mental well-being.[106] Thus, the order and shapes in structures and buildings represent an aspect of the exposome.[107] Because geometry can also affect cognition and mental health, it most likely affects longevity, as well.

Fractal Art in VR. The default mode network is a neural network in the brain that is activated during daydreaming and mind-wandering.[108] Reduced connectivity on the default mode network may be a hallmark of aging,[109] and neurodegenerative diseases such as Alzheimer disease have decreased brain entropy.[110] By contrast, psychedelic drugs, which are considered useful for the modulation of neuroinflammation, hippocampal neurogenesis, neuroplasticity, and brain complexity,[111] increase default mode network entropy.[112] A report by Keshmiri[113] stated that the brain is highly dependent on complexity and entropy for adaptability, and when this complexity is lost with aging, the risk of disease is increased because the body's adaptive functions are lost.

Mimicking the effect of psychedelic drugs on the brain would involve creating a state of ego dissolution and oceanic boundlessness,[114] along with an authoritative sense of unity or connectedness that is accompanied by feelings of reverence, positive valence emotions (eg, love or peace), altered sense of time and space, and difficulty putting the experience into words.[115] Achieving this state may be possible with the use of fractal-based art, which may be both engaging and relaxing.[116] Activation

FIGURE 2. Representative image of a metaverse environment during a demonstration at the 2023 World Economic Forum meeting in Davos, Switzerland. Representative avatars of some of the more than 1000 audience members who registered to watch the event asynchronously are reported.[123] (Courtesy of Krista Kim Studio Inc; used with permission).

of the default mode network may also be achieved by using art created with generative artificial intelligence[117] or by artwork with a high level of entropy.[118]

Extending Immersive Art Into the Metaverse. The metaverse provides a context for health or hospital-at-home models of care in a digitally constructed environment. Mars House NFT is a metaverse-based environment currently housed on the Spatial platform (Spatial Systems, Inc) that may be used for such models of care (Figure 1). A pilot program for social gatherings could be launched in such an environment to determine whether relevant longevity factors (eg, quality of relationships, purpose, and belonging) can be enhanced in the metaverse. In addition to immersive VR, augmented reality, and lifelogging of digital data, other elements of health care for longevity may be added (eg, virtual nurse avatars).[119] Customized environments can address various mental health needs. For example, a recent randomized controlled trial reported that when people living in Montreal, Québec, toured a virtual museum weekly for 3 months, social inclusion and physical and mental health improved.[120] These environments and experiences may also be used in other health care contexts, such as preoperative and postoperative cardiac procedures, which have a large effect on morbidity and mortality rates.[121] Patients may also be able to transition to a metaverse facility for rehabilitation before discharge.

How mental health is defined is radically changing; however, treatment paradigms for mental health disorders have not changed. For example, crosstalk between inflammatory pathways and neural circuits in the brain is well known,[53,63,67] but no treatments targeting inflammation are available in the context of mental health. The metaverse may provide a solution to this shortcoming. Stress can cause negative epigenetic changes that drive chronic diseases, such as cancer, heart disease, stroke, and neurodegenerative disease.[122] Preventing such epigenetic changes would most likely reduce the development of these diseases.

The metaverse is a context in which interactions relevant to mental health can be studied and delivered and treatments for mental illness can be considerably advanced. A recent study highlighted the urgent need for business innovation and scientific exploration to address early death for patients with mental illness.[38] An integrative approach using a multidisciplinary foundation and machine learning to guide data collection and interventions may provide a novel approach to this challenge. A discussion on this topic was recently conducted at the 2023 World Economic Forum meeting, which highlighted the importance of the metaverse for mental health.[123] This discussion was attended by various people who appeared in the metaverse as avatars (Figure 2).

Potential Pitfalls of the Metaverse

Quality control will be essential for using the metaverse for health care applications. The ability to deliver quality architectural, environmental, science-informed, and tested art and personalized interventions will rely heavily on the quality of the data collection, science, and machine learning.

As we are learning more about blockchain and secure patient-owned data, security issues about data collection will be of the utmost importance in the metaverse.[43] Cybersecurity and prevention of hacking of expensive digital architecture is also critical. In addition, the high initial production costs associated with building health care environments in the metaverse may be prohibitive without sequential development of the various components. To determine this sequence, a clear strategy is essential. A clear connection to a current procedural terminology code for digital therapeutics must be established, and payor systems must decide on criteria and payment plans for the authorization of visits.

To date, many health care organizations are using immersive internet environments for interventions.[43] For example, iMining Technologies Inc established the first hospital in the metaverse. Since then, UK-based occupational health company Latus Health created a virtual hospital, and Apollo Hospitals launched a novel partnership with 8chili, Inc (an organization that delivers immersive skills training). In addition, All India Institute of Medical Sciences in New Delhi instituted new digital surgical technology from ImmersiveTouch Inc on January 13, 2022.[43] Learning from the successes of such pioneers and not replicating their errors will be important for future metaverse-based health care companies.

Of importance, the metaverse should not be considered an alternative to our world but rather as an addition to it. The metaverse is a controllable exposome. It should not replace medical care but augment it. Although the metaverse aids knowledge acquisition, some aspects of in-person learning are superior to virtual learning. For example, VR can effectively improve knowledge retention in nursing education but is comparable with other education methods for skill development, and students report similar levels of satisfaction, confidence, and performance time in many domains of skills training with any of these methods.[124]

CONCLUSION

The metaverse is an important component of Health 4.0, but metaverse environments for health care must be strategically built with an aim to provide services that advance those that are currently available and are also cost-effective for both metaverse creators and patients. As previous publications have emphasized, opportunities in the metaverse are extensive, especially those about digital twinning, data capture, and enhanced privacy, all of which may enhance predictive and therapeutic models of care.

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Abbreviations and Acronyms: **MVA,** Maharishi vastu architecture; **NFT,** nonfungible token; **VR,** virtual reality

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