

Promoting Tech Transfer Between Space and Global Mental Health

Donald D. Chang; Eric A. Storch; Lance Black; Michael Berk; Neal Pellis; Helen Lavretsky; Jeffrey Sutton; Kylie Ternes; Marc Shepanek; Erin Smith; Ryan Abbott; Harris A. Eyre

- INTRODUCTION:** Numerous issues in mental health benefit from technological innovation. An example involves the mental health challenges of long-duration spaceflight (such as a Mars mission), including prolonged confinement, microgravity, and different sunlight exposure lengths. Persisting on Earth are global mental health challenges stemming from disease burdens, limited interview-based diagnostic systems, trial-and-error treatment approaches, and suboptimal access. There is potential for cross-pollinating solutions between these seemingly disparate challenges using a range of emerging technologies such as sensors, 'omics', and big data. In this review, we highlight the bidirectional value of mental health technology transfer aimed to address issues both on Earth and in space.
- METHODS:** We prepared a systematic review of studies pertaining to mental health technological innovation and space medicine.
- RESULTS:** For Earth mental health technologies translatable to long-duration space missions, we cite several example technologies, including device-based psychotherapy and social support, conversational agents 'aka chatbots', and nutritional and physical activity focused mental health. Space technologies translatable to Earth mental health include remote sensing devices, global navigation satellite systems, satellite communications, chronotherapies, and nutritional advances.
- DISCUSSION:** There is a rich history of space technologies informing Earth technological trends, including general health care on Earth, and vice versa. To avoid the traditional happenstance approach that results in delays, missed opportunities, and increased cost, and to improve outcomes for both Earth and space utilization of these technologies, we propose increased dialogue and training opportunities to enhance innovation and outcomes.
- KEYWORDS:** mental health, astronautics, space medicine, technology, psychology, psychiatry.

Chang DD, Storch EA, Black L, Berk M, Pellis N, Lavretsky H, Sutton J, Ternes K, Shepanek M, Smith E, Abbott R, Eyre HA. *Promoting tech transfer between space and global mental health. Aerosp Med Hum Perform.* 2020; 91(9):737–745.

The first human interplanetary mission to Mars is anticipated to take place this century. One analysis of space travel modeling and propulsion calculations suggests a time frame of ~930 d as a standard time frame for round trip travel to Mars (including ~180 d to Mars, ~570 d on Mars, and ~180 d to return). This timeframe is more than ~500 d beyond the duration that humans have remained confined in a space mission to date.

The results from a 520-d simulated interplanetary mission to Mars (i.e., a ground-based analog isolation study) suggest significant psychological challenges and demands during prolonged confinement even without the physiological challenges of space missions such as extended exposure to radiation and microgravity.^{3,7,32} Indeed, existing space missions have already reported a number of psychiatric problems that occur.^{32,58} The most common are adaptation reactions that generally present

From the School of Medicine, University of Queensland-Ochsner Clinical School, Brisbane, Queensland, Australia; the Department of Psychiatry and Behavioral Sciences, the Translational Research Institute for Space Health, the Center for Space Medicine, and the School of Medicine, Baylor College of Medicine, Houston, TX, USA; Innovation Institute, Texas Medical Center, Houston, TX, USA; Deakin University, IMPACT, the Institute for Mental and Physical Health and Clinical Translation, School of Medicine, Geelong, Victoria, Australia; the Department of Psychiatry, University of Melbourne, Melbourne, Victoria, Australia; Orygen, the National Centre of Excellence in Youth Mental Health, Melbourne, Victoria, Australia; the Florey Institute for Neuroscience and Mental Health, Parkville, Victoria, Australia; the Department of BioSciences, Rice University, Houston, TX, USA; the David Geffen School of Medicine, UCLA, Los Angeles, CA, USA; the Office of the Chief Health and Medical Officer, NASA, Washington, DC, USA; the School of Medicine, Brainstorm Laboratory for Mental Health Innovation, and the Department of Psychiatry, Stanford University, Palo Alto, CA, USA; the School of Health Law, Surrey University, Surrey, United Kingdom; the Discipline of Psychiatry, University of Adelaide, Adelaide, South Australia, Australia; and the Global Brain Health Institute, University of California, San Francisco, and Trinity College Dublin.

This manuscript was received for review in January 2020. It was accepted for publication in July 2020.

Address correspondence to: Harris Eyre, M.B.B.S., Ph.D., Brainstorm Lab for Mental Health Innovation, Stanford University, Palo Alto, CA, USA; harris.eyre@gmail.com.

Reprint & Copyright © by the Aerospace Medical Association, Alexandria, VA.

DOI: <https://doi.org/10.3357/AMHP:5589.2020>

with symptoms of anxiety or depression.^{57,59} Key challenges in space include isolation from friends and family, confinement, conflict among flight participants, pervasive danger, circadian disruption secondary to shifting light exposure, spaceflight-associated stressors (e.g., microgravity, radiation, and noise), boredom, monotony, and an unusual environment. Due to communication delays and limited medical support, a Mars mission will also require substantially more crew autonomy than prior space missions.⁶⁰ Current knowledge, practice, and preparations are not equipped or situated to support the unique circumstances these astronaut pioneers will face. Clearly, innovation is required to mitigate these major concerns for a Mars mission.¹⁰⁹

While certain technological innovations have been postulated to add value in long-term space missions, clinical trials assessing the value of these tools are challenging due to the cost and operational constraints of testing for or during a long-duration spaceflight. Furthermore, the biological changes associated with prolonged microgravity during a spaceflight make Earth trials limited in applicability. Yet, there are notable examples taking this challenge head-on, including MyCompass, an online cognitive behavioral therapy platform currently being tested for its relevance and value for long-term spaceflight.¹⁰⁶ This ground-based clinical trial will involve 135 participants who are demographically similar to astronauts: well-educated individuals who are relatively healthy and have high stress occupations, e.g., physicians, residents, and graduate students. Participants will be randomly assigned to one of three groups: 1) MyCompass intervention in isolation; 2) MyCompass intervention supported by delayed therapist contact via text messages; or 3) or MyCompass intervention supported by delayed therapist contact via recorded video messages. The asymmetric time lapse in delivery of therapist support is designed to mimic the real-life delay of up to 44 min that would be encountered in long-duration space missions. The treatment will occur over 7 wk (49 d), followed by assessments 4 wk later to evaluate progress and the participant's experience of the treatment package. This clinical trial will be the first time this technology will be tested among 'astronaut-like' adults. The research will assess how effective such programs are with and without video or text-based messaging, when real-time and face-to-face psychological assistance is unavailable, mimicking constraints of long-term spaceflight.

Concurrent with overcoming the mental health challenges of long-duration spaceflight, extensive innovation is also required to overcome existing mental health challenges on Earth. Indeed, the prolonged confinement of long-duration spaceflight is akin to the COVID-19 pandemic social and physical distancing. Disability and lost productivity secondary to mental illness are a significant global burden in developing and developed countries alike.¹¹⁸ Conditions include depression, anxiety disorders, schizophrenia, bipolar disorder, alcohol and drug use disorders, eating disorders, personality disorders, attention deficit hyperactivity disorder, autism spectrum disorder, and health conditions with strong linkages with psychiatric copresentations such as migraines, dementias, and epilepsy. Moreover, these conditions

are expected to cost the world \$16 trillion USD by 2030.⁷⁵ Individuals with these disorders additionally face increased rates of morbidity and mortality from general medical conditions (e.g., heart disease) as well as illness-related functional disability.⁶⁴ There are currently significant limitations with interview-based diagnostic systems, trial-and-error treatment approaches, and limited evidence-based preventive strategies. In addition, mental health care often suffers from the challenges of stigma and discrimination, limited access due to poor funding, hard to access service delivery models, and inadequate numbers of licensed mental health providers.^{2,36,75} Many organizations and groups have concluded that these issues are unsustainable, including the U.S. National Council for Behavioral Health Medication Director Institute and the Lancet Commission for Global Mental Health.^{36,75,89} Fortunately, however, there are promising developments with technological innovations in digital, personalized, and convergence science-based tools (for reviews see Bousman *et al.*¹⁷ and Eyre *et al.*^{36,38}).

The concurrent issues of mental health care and support needed for long-duration spaceflights and global mental health lead us to speculate: Is there value in cross-pollination of technological innovations for mental health between Earth and space applications?

To begin with, there is a rich history of space technologies informing Earth technological trends, including general health care on Earth. For example, there are now movements to explore the role of space technologies in global health with frameworks such as the United Nations' Sustainable Development Goals.³¹ A scoping review outlined key examples already in use and ready for optimization for global health, such as global navigation satellite systems (GNSS) and geographic information systems used for the study and forecasting of communicable and noncommunicable diseases. The review also outlined satellite communication and global navigation satellite systems for disaster response; satellite communication for telemedicine and tele-education; and global navigation satellite systems to improve autonomy for disabled individuals using geolocation, access to health care, and for safe and efficient transportation.³¹

Conversely, Earth-based tools such as telemedicine are already used in spaceflight medical care.⁵ Further, there are a number of potential Earth-based tools which may be effectively used in space mental health, such as chat bots, telemedicine platforms, and app-based support tools; however, there is no systematic model exploring these tools and innovations. We are not aware of any systematic literature exploring the potential value of space technologies in Earth mental health. In this review, we highlight the bidirectional value of mental health technology transfer between Earth and space.

METHODS

Studies were identified for inclusion in this review by searching PubMed, Google Scholar, PsychINFO, and Ovid Medicine from inception through December 2019. Articles were limited

to those published in English. The literature search strategy used combinations of the following keywords: mental health, technological innovation, space medicine, Mars mission, brain health, and cross-pollination.

Role of Technology in Clinical Mental Health Innovation

In recent years, technology has emerged as an important clinical tool in mental health therapy.⁷⁵ Perhaps the best developed is the area of internet and app-based therapies for mental health disorders. A plethora of evidence-based interventions (some for independent use and some for use in conjunction with mental health professionals) are being studied for conditions including insomnia, depression, bipolar disorder, and anxiety disorders.¹²⁶

A review of 49 studies of digital technology interventions from over 20 low- and middle-income countries and the literature on their use in high-income settings reveals 4 distinct roles of these technologies: technology for supporting clinical care and educating health workers; mobile tools for facilitating diagnosis and detection of mental disorders, including substance use disorders; technologies for promoting treatment adherence and supporting recovery; and online self-help programs for individuals with mental disorders.⁸⁶ Lifestyle has become a very active area of investigation and implementation, focusing on diet and physical activity.

Pharmacogenetic-based clinical decision support tools show promise to improve outcomes for medication-based treatment. Several companies have developed pharmacogenetic-based decision support tools, marketed to prescribers to inform the process of medication treatment and dose selection for individual patients.¹⁸ These decision support tools characterize a patient's genetic profile based on a select number of genes.

Driving Mental Health Innovation Through Entrepreneurship

Parallel to advances in mental health technology is the emergence and contribution of the entrepreneurial sector in mental health innovation. This trend is encouraging and exemplified by the number of start-up and investments focused on mental health. One report examining venture capital-backed deals into mental health and wellness start-ups since 2012 shows funding to mental health tech start-ups has increased every year since 2013, nearly reaching USD \$200M in 2016.²⁶ Many mental health tech start-ups raising funds today are purportedly working to increase access to mental healthcare. Such strategies include telemedicine platforms that enable remote access to care, interactive apps that track fluctuations in emotional states, daily motivational text messaging services, chat bots, and augmented/virtual reality tools. Another report details how major hospital systems (e.g., Cedars-Sinai), technology companies (e.g., Google), and health insurers (e.g., Aetna and BlueCross BlueShield) are now partnering and participating in agreements with mental health start-ups, underscoring the growing recognition and importance of entrepreneurship in mental health innovation.²⁵

We suggest the importance of the field of Responsible Innovation to guide and monitor the implementation of new products and services in mental health care.³⁵ Responsible innovation

entails a set of principles and practices in the development of technical solutions for complex problems. It encapsulates collaborative endeavors, wherein stakeholders commit to identifying and meeting a set of ethical and social principles by designing products and services to identify and manage risks in order to sustainably address the needs and challenges of users. Responsible innovation is an increasingly prominent initiative. A recent Organizations for Economic Co-operation and Development Recommendation on Responsible Innovation in Neurotechnology⁹² proposed the first international standard in this domain. It 'aims to guide governments and innovators to anticipate and address the ethical, legal, and social challenges raised by novel neurotechnologies while promoting innovation in the field.' It articulates 'the importance of 1) high-level values such as stewardship, trust, safety, and privacy in this technological context, 2) building the capacity of key institutions like foresight, oversight, and advice bodies, and 3) processes of societal deliberation, inclusive innovation, and collaboration.' These principles can be usefully adapted to guide the development and implementation of novel technologies for dementia care problems. Altogether, technology innovation and multinet network collaborations are, therefore, critical components for advancing mental health therapies and improving outcomes.

Mental Health-Related Biological Changes Induced by Prolonged Spaceflight

Understanding the biological mechanisms of the brain that create mental illness is challenging both on Earth and in space. If we could study the brain's physiological changes on orbit, it might enable technological advances to develop targeted therapies and personalized care for astronauts. Perhaps the tools developed to study those on-orbit changes could then make the terrestrial brain's physiological changes in mental illness more accessible, as well.

A recent study explored the effects of spaceflight on anatomical configuration of the brain and on cerebrospinal fluid spaces.⁹⁸ In this study, researchers used magnetic resonance imaging to compare images of 18 astronauts' brains before and after missions of long duration, involving stays on the International Space Station (ISS), and of 16 astronauts' brains before and after missions of short duration, involving participation in the Space Shuttle program. Narrowing of the central sulcus, upward shift of the brain, and narrowing of cerebrospinal fluid spaces at the vertex occurred frequently and predominantly in astronauts after long-duration flights, an interesting observation as this goes against the natural progression of aging, which entails enlargement of cerebrospinal fluid spaces. Postflight astronauts are at risk of "visual impairment and intracranial pressure" (VIIP) syndrome, recently renamed Spaceflight Associated Neuro-ocular Syndrome (SANS). Studies to date have offered interesting physiological observations; the clinical significance of these changes and its relationship to the brain, including the ocular system, is a subject of current analysis and research. A recent study explored multiple biomarkers from a pair of male monozygotic twins, one of whom spent 340 d aboard the ISS (flight subject), while his identical twin remained

on Earth (ground subject).⁴³ The subjects were 50 yr of age at onset. Physiological, telomeric, transcriptomic, epigenetic, proteomic, metabolomic, immune, microbiomic, cardiovascular, vision-related, and cognitive data were collected over 25 mo. The results demonstrated both transient and persistent changes associated with long-duration spaceflight across multiple cell types, tissues, genotypes, and phenotypes. These specific data, as well as the broader biomedical measures and sample collection methods, can now serve as a foundation for scientific and medical assessments of future astronauts, especially for those on prolonged, exploration-class missions.

Earth Technologies Translatable to Mental Health in Long-Duration Space Missions

In this section, we outline several fields of mental health technology and review their potential space mental health significance, current limitations of knowledge, and potential innovations and opportunities. Supplementary **Table A** (online, <https://doi.org/10.3357/AMHP.5589sd.2020>) outlines these technologies, their significance in long-duration space missions, and potential for insights to be transferred to space. We note the critical role of the crew medical officer in the safe and efficacious use of these tools.

Space Technologies Translatable to Mental Health on Earth

We broadly consider there to be two types of space technologies translatable to Earth mental health: 1) those arising from fundamental engineering and physics advances (i.e., GNSS, satellite communications, noninvasive and remote sensing devices); and 2) those arising from space medicine advances (e.g., nutritional advances, chronotherapies, conflict resolution, and group stress). Supplementary **Table B** and **Table C** (online, <https://doi.org/10.3357/AMHP.5589sd.2020>) provide overviews of these areas.

The Mars Mental Health Model: Innovation and Bidirectional Technology Transfer at the Intersection of the Mars Mission and Global Mental Health

We hereby postulate a comprehensive model of ‘Innovation and Bidirectional Technology Transfer at the Intersection of the Mars Mission and Global Mental Health’ (**Fig. 1**). The aim is to create a bidirectional model for effective cross-pollination between space technologies in long-duration spaceflight environments with Earth mental health. By facilitating exchanges of ideas and technology, the hope is to improve mental health outcomes both during long-duration spaceflight environments and on Earth.

Recommendations

Accelerate Earth mental health technologies into the space market. Given the complexities of fitting Earth technologies into the space market, novel mechanisms and processes are required to support companies and entrepreneurs. There are a number of examples of these types of organizations and events. Established in 1997, the National Space Biomedical Research Institute (NSBRI) was a unique nonprofit research

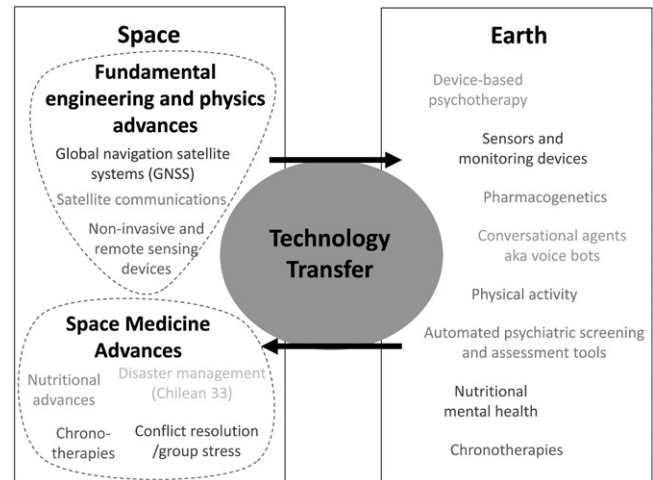


Fig. 1. The Mars Mental Health Model: innovation and bidirectional technology transfer at the intersection of the Mars mission and global mental health.

consortium in partnership with NASA and over 70 other agencies, universities, and institutions. Their objective was to work on countermeasures to address the health-related problems as well as the physical and psychological challenges astronauts will face on long-duration missions.⁸⁵ Research addressed key technologies required to enable and enhance exploration. In particular, NSBRI scientists and physicians developed technologies to provide medical monitoring, diagnosis, and treatment in the extreme environments that will be faced during exploration missions. Examples of technologies that NSBRI accelerated from human health care into the space environment include: lower back pain therapy with ultrasound¹³ and a novel brain monitoring device (leveraging magnetic induction phase-shift spectroscopy to monitor CSF pressure).¹² The Translational Research Institute for Space Health (TRISH; <https://www.bcm.edu/centers/space-medicine/translational-research-institute>), supported by the NASA Human Research Program and based at the Baylor College of Medicine, provides a useful example of a strategy ‘Launch Pad.’¹¹⁴ The TRISH Launch Pad aims to prepare early-stage companies and precompanies to meet the needs of the space medicine industry. Launch Pad provides a 10-wk intensive program. Sessions are led by industry veterans who help teams create a viable commercialization pathway to Earth’s health technology market and a secondary space market. Launch Pad provides companies and precompanies with: 1) access to experts working in space health care and at NASA, 2) rapid technology maturation and de-risking, 3) preparation for commercial success in U.S. healthcare markets, and 4) pathways to government sales in the emerging space market. TRISH has also announced an ‘Industry Program 2020’¹¹⁵ grant call for industry and academic behavioral health experts to contribute toward the development of specific key areas of interest, including the optimization of communications which have inherent delays (modeling the real-life delay in transmissions), novel anxiety and stress monitoring techniques, and unobtrusive monitoring technologies.

Accelerate space technologies into the Earth mental health market. There are a number of examples of mechanisms to accelerate space technologies into the Earth health care market. NASA's Spinoff provides extensive cataloguing of technologies that are benefitting life on Earth (see <https://spinoff.nasa.gov>). The aforementioned NSBRI generated a number of technologies which were applied to the Earth health care market, namely a noninvasive ultrasound method to expel kidney stones.¹⁴

Bidirectional training programs. As the field of space medicine and mental health simultaneously develop, there will be a need for a targeted training program focused on merging the two fields. Examples can include conferences such as one offered earlier this year by TRISH and the MIT Media Lab Space Exploration Initiative, which focused on “optimizing behavioural health and cognitive performance in confined environments.”¹¹³ Further, we recently proposed that the new field of innovation diplomacy can be adapted to promote responsible innovation in mental health.^{37,111} This could be useful in merging these two fields. To this end, we articulated a model of Mental Health Innovation Diplomacy^{37,111} which aims to strengthen the positive role of novel solutions and recognize and work to manage both real and potential risks of digital platforms. It recognizes that mental health technological innovation can have political, ethical, cultural, and economic influences. Adapted from the NESTA Innovation Policy Toolkit,¹⁶ we elucidated roles relevant to Mental Health Innovation diplomats.¹¹¹

As of now, there is no formal training program with this particular focus and training modules are limited to conferences such as the aforementioned. Developing a focused training program that aims to train individuals well-versed in both space medicine and clinical mental health may accelerate the discovery process of mental health technologies in space. Graduates of such a program would not only be able to identify the unmet needs in both arenas, but also be able to recognize and identify technologies that have the potential to cross over and be applied.

Enriched dialogue between mental health technology innovators and space medicine experts. Key to any technological development across two fields is a productive cross-collaboration. To that end, key opinion leaders in mental health and space medicine experts will need to establish an open channel of communication, share skillsets, and discuss ideas in order to foster important foundations to advance the development of mental health applications in long manned spaceflight missions. One example forum is the 2019 Space Health Innovation Conference in San Francisco cohosted by the University of California, San Francisco and TRISH.¹¹⁶ Their aim was to “convene a diverse audience of Space experts and Health Tech Innovation stakeholders with a goal to inform, inspire, and invite participation in the exciting challenge of optimizing health and medical management in Space environments.” Future development and production of similar forums will be critical in facilitating a productive cross-collaboration.

Ethical and legal considerations with the global nature of the Mars mission. With the multicountry nature of the Mars mission, it is important to consider legal and regulatory perspectives through a global lens. Critical questions include: what regulatory framework will be used for medical devices, digital health solutions, and genetic-based clinical tools? How do health care ethics from different countries reconcile in space? What legal framework applies on Mars?

The World Health Organization (WHO) has recently released guidelines for digital health tools where they pay particular attention to data privacy issues.¹²² Furthermore, the WHO has also developed guidelines for quality and safety in clinical genetic testing.¹²⁰ There is also work from the WHO to create guidelines and standardization for medical device regulation.¹²¹ As technological acceleration continues in the coming years, careful and diligent work is required to ensure regulations keep up with innovation.

Track outcomes of this bidirectional model. The success of any model is measured by the outcomes of the effort itself so it is important to define the deliverables of this model. However, a challenge unique to space medicine that can hamper outcome measurement are the infrequent space missions as compared to the rapid pace of study outcomes done on Earth. Whereas a mental health research study could potentially be completed within months, a space mission is on the scale of at least years. Thus, outcomes reports should be cognizant of space mission deadlines and special attention devoted to ensure all relevant data are collected from each space mission from which to compare with Earth studies, given the infrequency. More discernible outcomes from the model include results from the application of technologies in simulated labs, multicenter trial outcomes, and publications. With regards to clinical outcomes, this is more difficult, but the most direct approach is large randomized control trials of the technological tools. A pragmatic approach would likely be to first assess clinical outcomes on Earth sample populations before trialing it on space missions. Outcome assessment should be tracked and staged in increments, including: 1) number of interactions between space and Earth experts, 2) forms of collaboration, 3) potential developments, 4) intellectual property developed, 5) translation, and 6) implementation.

Conclusion

Both long-distance space missions and global society do and will continue to experience mental health issues. With the advent of new technologies, it is critical we leverage these to invent and innovate to optimize mental health and wellbeing. While space and Earth represent seemingly disparate environments, they nevertheless require overlapping solutions. Our research suggests there are likely benefits to cross-pollinating between space technology and Earth mental health and we hope to further promote bidirectional sharing of innovations.

ACKNOWLEDGMENTS

All authors were responsible for substantial contributions to conception and design of the paper, acquisition of data, analysis and interpretation of results. All authors revised the paper carefully for important intellectual content. All authors reviewed the final version for publication.

Financial Disclosure Statement: Michael Berk is supported by a NHMRC Senior Principal Research Fellowship (1059660 and APP1156072). Harris Eyre received payment from CNSdose LLC, CNSdose Pty Ltd, Altoida LLC, Prodeo LLC, Scioto Biosciences LLC, and PreActive Technologies LLC. Ryan Abbott has consulted for CNSdose Pty Ltd. Eric Storch owns shares in Prodrome Labs Inc. No other authors note conflicts of interest.

Authors and affiliations: Donald D. Chang, Ph.D., School of Medicine, University of Queensland-Ochsner Clinical School, Brisbane, Queensland, Australia; Eric A. Storch, Ph.D., Department of Psychiatry and Behavioral Sciences, Lance Black, M.D., Translational Research Institute for Space Health, Neal Pellis and Jeffrey Sutton, M.D., Ph.D., Center for Space Medicine, and Jeffrey Sutton and Kylie Ternes, M.D., School of Medicine, Baylor College of Medicine, Houston, TX, USA; Lance Black and Harris A. Eyre, M.B.B.S., Ph.D., Innovation Institute, Texas Medical Center, Houston, TX, USA; Michael Berk, M.D., Ph.D., and Harris Eyre, Deakin University, IMPACT, the Institute for Mental and Physical Health and Clinical Translation, School of Medicine, Geelong, Victoria, Australia; Michael Berk and Harris Eyre, Department of Psychiatry, University of Melbourne, Melbourne, Victoria, Australia; Michael Berk, Orygen, the National Centre of Excellence in Youth Mental Health, Melbourne, Victoria, Australia; Michael Berk, Florey Institute for Neuroscience and Mental Health, Parkville, Victoria, Australia; Neal Pellis, Ph.D., Department of Biosciences, Rice University, Houston, TX, USA; Helen Lavretsky, M.D., and Ryan Abbott, M.D., J.D., David Geffen School of Medicine, UCLA, Los Angeles, CA, USA; Marc Shepanek, Ph.D., Office of the Chief Health and Medical Officer, NASA, Washington, DC, USA; Erin Smith, School of Medicine, and Harris Eyre, Brainstorm Laboratory for Mental Health Innovation, Department of Psychiatry, School of Medicine, Stanford University, Palo Alto, CA, USA; Ryan Abbott, School of Health Law, Surrey University, Surrey, United Kingdom; and Harris Eyre, Discipline of Psychiatry, University of Adelaide, Adelaide, South Australia, Australia, and Global Brain Health Institute, University of California, San Francisco, CA, USA, and Trinity College Dublin.

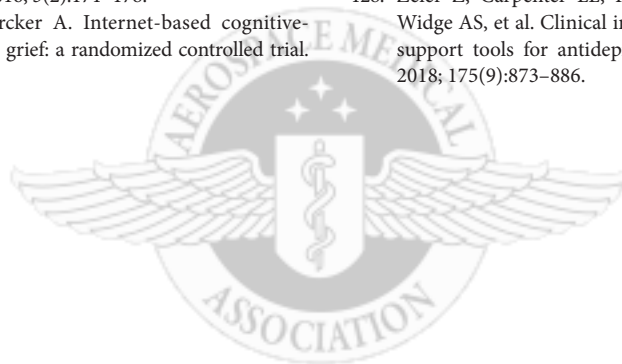
REFERENCES

- Aleksandrovskiy Y, Novikov M. Psychological prophylaxis and treatments for space crews. In: Nicogossian A, Mohler S, Gazenko O, Grigoriev A, editors. *Space Biology and Medicine III: Humans in Spaceflight Book 2*. Reston (VA): American Institute of Aeronautics and Astronautics; 1996: 443–444.
- Andrilla CHA, Patterson DG, Garberson LA, Coulthard C, Larson EH. Geographic variation in the supply of selected behavioral health providers. *Am J Prev Med*. 2018; 54(6S3):S199–S207.
- Ball JR, Evans CH. Safe passage: astronaut care for exploration missions. Washington (DC, USA): NASA; 2001.
- Barger LK, Flynn-Evans EE, Kubey A, Walsh L, Ronda JM, et al. Prevalence of sleep deficiency and use of hypnotic drugs in astronauts before, during, and after spaceflight: an observational study. *Lancet Neurol*. 2014; 13(9):904–912.
- Barratt MR, Pool SL, editors. *Principles of clinical medicine for space flight*. New York: Springer; 2008.
- Basner M, Dinges DF, Mollicone D, Ecker A, Jones CW, et al. Mars 520-d mission simulation reveals protracted crew hypokinesia and alterations of sleep duration and timing. *Proc Natl Acad Sci U S A*. 2013; 110(7):2635–2640. Erratum in: *Proc Natl Acad Sci U S A*. 2013; 110(7):2676.
- Basner M, Dinges DF, Mollicone DJ, Savelev I, Ecker AJ, et al. Psychological and behavioral changes during confinement in a 520-day simulated interplanetary mission to mars. *PLoS One*. 2014; 9(3):e93298.
- Ben-Zeev D, Scherer EA, Wang R, Xie H, Campbell AT. Next-generation psychiatric assessment: using smartphone sensors to monitor behavior and mental health. *Psychiatr Rehabil J*. 2015; 38(3):218–226.
- Bergouignan A, Stein TP, Habold C, Coxam V, O’Gorman D, Blanc S. Towards human exploration of space: The THESEUS review series on nutrition and metabolism research priorities. *NPJ Microgravity*. 2016; 2(1):16029.
- Berk M, Turner A, Malhi GS, Ng CH, Cotton SM, et al. A randomised controlled trial of a mitochondrial therapeutic target for bipolar depression: mitochondrial agents, N-acetylcysteine, and placebo. *BMC Med*. 2019; 17(1):18. Erratum in: *BMC Med*. 2019;17(1):35.
- Bilello JA, Thurmond LM, Smith KM, Pi B, Rubin R, et al. MDDScore: confirmation of a blood test to aid in the diagnosis of major depressive disorder. *J Clin Psychiatry*. 2015; 76(2):e199–e206.
- BioSpace.com. National Space Biomedical Research Institute (NSBRI) Funds Cerebrotech to Accelerate Development of Brain Monitoring Device. 2013. [Accessed 14/12/19]. Available from: <https://www.biospace.com/article/releases/national-space-biomedical-research-institute-nsbri-funds-b-cerebrotech-b-to-accelerate-development-of-brain-monitoring-device/>.
- BioSpace.com. National Space Biomedical Research Institute (NSBRI) Release: Clinical Study To Treat Lower Back Pain On Earth May Help Astronauts In Space. 2014. [Accessed 14/12/19]. Available from: <https://www.biospace.com/article/releases/national-space-biomedical-research-institute-nsbri-release-clinical-study-to-treat-lower-back-pain-on-earth-may-help-astronauts-in-space/>.
- BioSpace.com. National Space Biomedical Research Institute (NSBRI) Release: “First In Humans” Clinical Trial Demonstrates Non-Invasive Expulsion Of Kidney Stones. 2015. [Accessed 14/12/19]. Available from: <https://www.biospace.com/article/releases/national-space-biomedical-research-institute-nsbri-release-first-in-humans-clinical-trial-demonstrates-non-invasive-expulsion-of-kidney-stones/>.
- Blazer DG, Kessler RC, Swartz MS. Epidemiology of recurrent major and minor depression with a seasonal pattern: The National Comorbidity Survey. *Br J Psychiatry*. 1998; 172(2):164–167.
- Bound K, Saunders T. Innovation Policy Toolkit: introduction to innovation policy and collaboration. 2015. [Accessed 04/15/20]. Available from: <https://www.nesta.org.uk/toolkit/innovation-policy-toolkit-introduction-to-innovation-policy-and-collaboration/>.
- Bousman CA, Arandjelovic K, Mancuso SG, Eyre HA, Dunlop BW. Pharmacogenetic tests and depressive symptom remission: a meta-analysis of randomized controlled trials. *Pharmacogenomics*. 2019; 20(1):37–47.
- Bousman CA, Hopwood M. Commercial pharmacogenetic-based decision-support tools in psychiatry. *Lancet Psychiatry*. 2016; 3(6):585–590.
- Bousman CA, Jaksa P, Pantelis C. Systematic evaluation of commercial pharmacogenetic testing in psychiatry: a focus on CYP2D6 and CYP2C19 allele coverage and results reporting. *Pharmacogenet Genomics*. 2017; 27(11):387–393.
- Bradley P, Shiekh M, Mehra V, Vrbicky K, Layle S, et al. Improved efficacy with targeted pharmacogenetic-guided treatment of patients with depression and anxiety: a randomized clinical trial demonstrating clinical utility. *J Psychiatr Res*. 2018; 96:100–107.
- Breitenstein B, Scheuer S, Pfister H, Uhr M, Lucae S, et al. The clinical application of ABCB1 genotyping in antidepressant treatment: a pilot study. *CNS Spectr*. 2014; 19(2):165–175.
- Carter JA, Buckley JC, Greenhalgh L, Holland AW, Hegel MT. An interactive media program for managing psychosocial problems on long-duration spaceflights. *Aviat Space Environ Med*. 2005; 76(6, Suppl.):B213–B223.
- Cartreine JA, Chang TE, Seville JL, Sandoval L, Moore JB, et al. Using self-guided treatment software (ePST) to teach clinicians how to deliver problem-solving treatment for depression. *Depress Res Treat*. 2012; 2012:309094.
- Caudle KE, Klein TE, Hoffman JM, Muller DJ, Whirl-Carrillo M, et al. Incorporation of pharmacogenomics into routine clinical practice: the Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline development process. *Curr Drug Metab*. 2014; 15(2):209–217.

25. CBInsights. Psych 101: the most active investors in mental health tech. CBInsights; 2017. [Accessed 7/9/2020]. Available from <https://www.cbinsights.com/research/active-investors-mental-health-tech-startups/>.
26. CBInsights. Timeline: VC investment in mental health & wellness tech on the rise. CBInsights; 2017. [Accessed 7/9/2020]. Available from <https://www.cbinsights.com/research/mental-health-startups-vc-investment/>.
27. Chang DD, Eyreuro HA, Abbott R, Coudreaut M, Baune BT, et al. Pharmacogenetic guidelines and decision support tools for depression treatment: application to late-life. *Pharmacogenomics*. 2018; 19(16):1269–1284.
28. Choi KW, Chen CY, Stein MB, Klimentidis YC, Wang MJ, et al. Assessment of Bidirectional Relationships Between Physical Activity and Depression Among Adults: A 2-Sample Mendelian Randomization Study. *JAMA Psychiatry*. 2019; 76(4):399–408. Comment in: *JAMA Psychiatry*. 2019; 76(4):361–362 and *Nat Hum Behav*. 2019; 3(4):320.
29. Czeisler CA, Richardson GS, Coleman RM, Zimmerman JC, Moore-Ede MC, et al. Chronotherapy: resetting the circadian clocks of patients with delayed sleep phase insomnia. *Sleep*. 1981; 4(1):1–21.
30. Davcheva E, Adam M, Benlian A. User dynamics in mental health forums—a sentiment analysis perspective. In: *Proceedings of WI 2019*. Atlanta (GA, USA): Association for Information Systems; 2019.
31. Dietrich D, Dekova R, Davy S, Fahrni G, Geissbuhler A. Applications of space technologies to global health: scoping review. *J Med Internet Res*. 2018; 20(6):e230.
32. Doarn CR, Polk JD, Shepanek M. Health challenges including behavioral problems in long-duration spaceflight. *Neurol India*. 2019; 67(Suppl. S2):190–195.
33. Engemann K, Pedersen CB, Arge L, Tsirogiannis C, Mortensen PB, Svenning JC. Residential green space in childhood is associated with lower risk of psychiatric disorders from adolescence into adulthood. *Proc Natl Acad Sci USA*. 2019; 116(11):5188–5193.
34. Espadaler J, Tuson M, Lopez-Ibor JM, Lopez-Ibor F, Lopez-Ibor MI. Pharmacogenetic testing for the guidance of psychiatric treatment: a multicenter retrospective analysis. *CNS Spectr*. 2017; 22(4):315–324.
35. Eyre HA, Ellsworth W, Fu E, Manji H, Berk M. Leveraging responsible innovation to steward mental health technology development. *Lancet Psychiatry*. 2020; (In Press).
36. Eyre HA, Lavretsky H, Forbes M, Raji C, Small G, et al. Convergence science arrives: how does it relate to psychiatry? *Acad Psychiatry*. 2017; 41(1):91–99.
37. Eyre HA, Robb A, Abbott R, Hopwood M. Mental health innovation diplomacy: an under-recognised soft power. *Aust N Z J Psychiatry*. 2019; 53(5):474–475.
38. Eyre HA, Vahabzadeh A, Abbott R, Cook IA, Berk M. The future of psychiatry commission. *Lancet Psychiatry*. 2018; 5(1):13.
39. Fabbri C, Zohar J, Serretti A. Pharmacogenetic tests to guide drug treatment in depression: Comparison of the available testing kits and clinical trials. *Prog Neuropsychopharmacol Biol Psychiatry*. 2018; 86:36–44.
40. Fagerness J, Fonseca E, Hess GP, Scott R, Gardner KR, et al. Pharmacogenetic-guided psychiatric intervention associated with increased adherence and cost savings. *Am J Manag Care*. 2014; 20(5):e146–e156.
41. Firth J, Marx W, Dash S, Carney R, Teasdale SB, et al. The effects of dietary improvement on symptoms of depression and anxiety: a meta-analysis of randomized controlled trials. *Psychosom Med*. 2019; 81(3):265–280.
42. Fitzpatrick KK, Darcy A, Vierhile M. Delivering cognitive behavior therapy to young adults with symptoms of depression and anxiety using a fully automated conversational agent (Woebot): a randomized controlled trial. *JMIR Ment Health*. 2017; 4(2):e19.
43. Garrett-Bakelman FE, Darshi M, Green SJ, Gur RC, Lin L, et al. The NASA Twins Study: a multidimensional analysis of a year-long human spaceflight. *Science*. 2019; 364(6436):eaau8650.
44. Girard JM, Cohn JF. Automated audiovisual depression analysis. *Curr Opin Psychol*. 2015; 4:75–79.
45. Golden RN, Gaynes BN, Ekstrom RD, Hamer RM, Jacobsen FM, et al. The efficacy of light therapy in the treatment of mood disorders: a review and meta-analysis of the evidence. *Am J Psychiatry*. 2005; 162(4):656–662.
46. Gottlieb JD, Gidugu V, Maru M, Tepper MC, Davis MJ, et al. Randomized controlled trial of an internet cognitive behavioral skills-based program for auditory hallucinations in persons with psychosis. *Psychiatr Rehabil J*. 2017; 40(3):283–292.
47. Gratch J, Morency LP, Scherer S, Stratou G, Boberg J, et al. User-state sensing for virtual health agents and telehealth applications. *Stud Health Technol Inform*. 2013; 184:151–157.
48. Gruebner O, Rapp MA, Adli M, Kluge U, Galea S, Heinz A. Cities and mental health. *Dtsch Arztebl Int*. 2017; 114(8):121–127.
49. Hafner M, Stepanek M, Taylor J, Troxel WM, van Stolk C. Why sleep matters—the economic costs of insufficient sleep: a cross-country comparative analysis. *Rand Health Q*. 2017; 6(4):11.
50. Hall-Flavin DK, Winner JG, Allen JD, Carhart JM, Proctor B, et al. Utility of integrated pharmacogenomic testing to support the treatment of major depressive disorder in a psychiatric outpatient setting. *Pharmacogenet Genomics*. 2013; 23(10):535–548.
51. Hall-Flavin DK, Winner JG, Allen JD, Jordan JJ, Nesheim RS, et al. Using a pharmacogenomic algorithm to guide the treatment of depression. *Transl Psychiatry*. 2012; 2(10):e172.
52. Hicks JK, Bishop JR, Sangkuhl K, Müller DJ, Ji Y, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and CYP2C19 genotypes and dosing of selective serotonin reuptake inhibitors. *Clin Pharmacol Ther*. 2015; 98(2):127–134.
53. Hicks JK, Sangkuhl K, Swen JJ, Ellingrod VL, Müller DJ, et al. Clinical Pharmacogenetics Implementation Consortium Guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. *Clin Pharmacol Ther*. 2017; 102(1):37–44.
54. Hilty DM, Sunderji N, Suo S, Chan S, McCarron RM. Telepsychiatry and other technologies for integrated care: evidence base, best practice models and competencies. *Int Rev Psychiatry*. 2018; 30(6):292–309.
55. Ikegame M, Hattori A, Tabata MJ, Kitamura KI, Tabuchi Y, et al. Melatonin is a potential drug for the prevention of bone loss during space flight. *J Pineal Res*. 2019; 67(3):e12594.
56. Jacka FN. Nutritional psychiatry: where to next? *EBioMedicine*. 2017; 17:24–29.
57. Kanas N. *Humans in space: the psychological hurdles*. Switzerland: Springer International Publishing; 2015.
58. Kanas N. Psychiatric issues in space. *Psychiatr Times*. 2016; 33(6). [Accessed 7/9/2020]. Available at <https://www.psychiatrictimes.com/view/psychiatric-issues-space>.
59. Kanas N, Manzev D. *Space psychology and psychiatry*. El Segundo (CA, USA): Springer; 2008.
60. Kanas N, Sandal G, Boyd JE, Gushin VI, Manzey D, et al. Psychology and culture during long-duration space missions. *Acta Astronaut*. 2009; 64(7–8):659–677.
61. Kane RL, Short P, Sipes W, Flynn CF. Development and validation of the spaceflight cognitive assessment tool for windows (WinSCAT). *Aviat Space Environ Med*. 2005; 76(6, Suppl.):B183–B191.
62. Kawada T. Applicability of the actigraphy for astronauts in spaceflight. *Sleep Sci*. 2016; 9(2):59.
63. Khan M, Beg S. Transference and retrieval of voice message over low signal strength in satellite communication. *Innov Syst Softw Eng*. 2012; 8(4):293–299.
64. Kilbourne AM, Beck K, Spaeth-Ruble B, Ramanuj P, O'Brien RW, et al. Measuring and improving the quality of mental health care: a global perspective. *World Psychiatry*. 2018; 17(1):30–38.
65. Kumar V, Sattar Y, Bseiso A, Khan S, Rutkofsky IH. The effectiveness of internet-based cognitive behavioral therapy in treatment of psychiatric disorders. *Cureus*. 2017; 9(8):e1626.
66. Laranjo L, Dunn AG, Tong HL, Kocaballi AB, Chen J, et al. Conversational agents in healthcare: a systematic review. *J Am Med Inform Assoc*. 2018; 25(9):1248–1258.
67. Lavoie MP, Lam RW, Bouchard G, Sasseville A, Charron MC, et al. Evidence of a biological effect of light therapy on the retina of patients with seasonal affective disorder. *Biol Psychiatry*. 2009; 66(3):253–258.

68. Lavretsky H. Eco-psychiatry: air pollution is associated with depression in older adults. *Am J Geriatr Psychiatry*. 2019; 27(10):1097–1098.
69. Levitt AJ, Boyle MH, Joffe RT, Bauml Z. Estimated prevalence of the seasonal subtype of major depression in a Canadian community sample. *Can J Psychiatry*. 2000; 45(7):650–654.
70. Lewy AJ, Ahmed S, Jackson JM, Sack RL. Melatonin shifts human circadian rhythms according to a phase-response curve. *Chronobiol Int*. 1992; 9(5):380–392.
71. Lockley SW, Brainard GC. Lighting effects. Joint CSA/ESA/JAXA/NASA Increments 49 and 50 Science Symposium 2016. Washington (DC, USA): NASA; 2016. Report No.: JSC-CN-36456.
72. Lockley SW, Brainard GC, Czeisler CA. High sensitivity of the human circadian melatonin rhythm to resetting by short wavelength light. *J Clin Endocrinol Metab*. 2003; 88(9):4502–4505.
73. Lucas GM, Gratch J, King A, Louis-Philippe M. It's only a computer: virtual humans increase willingness to disclose. *Comput Human Behav*. 2014; 37:94–100.
74. Luger E, Sellen A. Like having a really bad PA: the gulf between user expectation and experience of conversational agents. ACM SIGCHI Conference on Human Factors in Computing Systems; May 7–12, 2016; San Jose, CA, USA. New York: Association for Computing Machinery; 2016:5286–5297.
75. Lund C, Brooke-Sumner C, Baingana F, Baron EC, Breuer E, et al. Social determinants of mental disorders and the Sustainable Development Goals: a systematic review of reviews. *Lancet Psychiatry*. 2018; 5(4): 357–369.
76. Ma J, Rosas LG, Lv N, Xiao L, Snowden MB, et al. Effect of integrated behavioral weight loss treatment and problem-solving therapy on Body Mass Index and depressive symptoms among patients with obesity and depression: the RAINBOW randomized clinical trial. *JAMA*. 2019; 321(9):869–879.
77. Magnusson A. An overview of epidemiological studies on seasonal affective disorder. *Acta Psychiatr Scand*. 2000; 101(3):176–184.
78. Maples-Keller JL, Bunnell BE, Kim SJ, Rothbaum BO. The use of virtual reality technology in the treatment of anxiety and other psychiatric disorders. *Harv Rev Psychiatry*. 2017; 25(3):103–113.
79. Martin CR, Osadchiv V, Kalani A, Mayer EA. The brain-gut-microbiome axis. *Cell Mol Gastroenterol Hepatol*. 2018; 6(2):133–148.
80. McPhee JC, Charles JB. Human health and performance risks of space exploration missions. 2009. [Accessed 1/7/20]. Available from: <https://ntrs.nasa.gov/archive/nasa/casi.ntrs.nasa.gov/20160004365.pdf>.
81. Mikkelsen K, Stojanovska L, Polenakovic M, Bosevski M, Apostolopoulos V. Exercise and mental health. *Maturitas*. 2017; 106:48–56.
82. Morris RR, Kouddous K, Kshirsagar R, Schueller SM. Towards an artificially empathic conversational agent for mental health applications: system design and user perceptions. *J Med Internet Res*. 2018; 20(6): e10148.
83. NASA. How NASA helped the 33 Chilean miners. 2015. [Accessed 28/8/19]. Available from: <https://www.nasa.gov/feature/how-nasa-helped-the-33-chilean-miners>.
84. NASA. Paired sleep tracker, light therapy tools retrain circadian rhythms. 2018. [Accessed 13/12/19]. Available from: https://spinoff.nasa.gov/Spinoff2018/cg_8.html.
85. NASA. National Space Biomedical Research Institute. 2019. [Accessed 14/12/19]. Available from: https://www.nasa.gov/exploration/humanresearch/HRP_NASA/research_at_nasa_NSBR.html.
86. Naslund JA, Aschbrenner KA, Araya R, Marsch LA, Unutzer J, et al. Digital technology for treating and preventing mental disorders in low-income and middle-income countries: a narrative review of the literature. *Lancet Psychiatry*. 2017; 4(6):486–500.
87. National Sleep Foundation. Sleep Health Index Quarterly Report. Q4 2016. 2016. [Accessed 13/12/19]. Available from: https://www.sleepfoundation.org/sites/default/files/2019-02/NSF_SHI2016Report.pdf.
88. NCCAM. National Center for Complementary and Alternative Medicine. 2014. [Accessed 10/28/14]. Available from: <http://nccam.nih.gov/>.
89. NCFBH. The psychiatric shortage: causes and solutions. Washington (DC, USA): National Council for Behavioral Health; 2017.
90. Nguyen T, Phung D, Dao B, Venkatesh S, Berk M. Affective and content analysis of online depression communities. *IEEE Trans Affect Comput*. 2014; 5(3):217–226.
91. Odeh R, Guy CL. Gardening for therapeutic people-plant interactions during long-duration space missions. *Open Agric*. 2017; 2(1):1–13.
92. OECD. OECD recommendation on Responsible Innovation in Neurotechnology. Paris (France): Organisation for Economic Co-operation and Development; 2020.
93. Paluska SA, Schwenk TL. Physical activity and mental health: current concepts. *Sports Med*. 2000; 29(3):167–180.
94. Pandi-Perumal SR, Gonfalone AA. Sleep in space as a new medical frontier: the challenge of preserving normal sleep in the abnormal environment of space missions. *Sleep Sci*. 2016; 9(1):1–4.
95. Parletta N, Zarnowiecki D, Cho J, Wilson A, Bogomolova S, et al. A Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: a randomized controlled trial (HELFIMED). *Nutr Neurosci*. 2019; 22(7):474–487.
96. Pavy-Le TA, Saivin S, Soulez-LaRivière C, Pujos M, Güell A, Houin G. Pharmacology in space: pharmacotherapy. In: Bonting SL, editor. *Advances in space biology and medicine*. Greenwich (CT): JAI Press; 1997.
97. Putchá L, Marshburn TH. Fatigue, sleep, and chronotherapy. In: Barratt MR, Pool SL, editors. *Principles of clinical medicine for space flight*. New York: Springer; 2008.
98. Roberts DR, Albrecht MH, Collins HR, Asemanni D, Chatterjee AR, et al. Effects of spaceflight on astronaut brain structure as indicated on MRI. *N Engl J Med*. 2017; 377(18):1746–1753.
99. Roekklein KA, Wong PM, Miller MA, Donofry SD, Kamarck ML, Brainard GC. Melanopsin, photosensitive ganglion cells, and seasonal affective disorder. *Neurosci Biobehav Rev*. 2013; 37(3):229–239.
100. Rosenblat JD, Lee Y, McIntyre RS. The effect of pharmacogenomic testing on response and remission rates in the acute treatment of major depressive disorder: a meta-analysis. *J Affect Disord*. 2018; 241:484–491.
101. Sakai T, Moteki Y, Takahashi T, Shida K, Kiwaki M, et al. Probiotics into outer space: feasibility assessments of encapsulated freeze-dried probiotics during 1 month's storage on the International Space Station. *Sci Rep*. 2018; 8(1):10687.
102. Salamon N, Grimm JM, Horack JM, Newton EK. Application of virtual reality for crew mental health in extended-duration space missions. Proceedings of the 68th International Astronautical Congress (IAC); 25–29 Sept. 2017; Adelaide, Australia. Paris (France): International Astronautical Federation; 2017:29–36.
103. Salazar J. James Cartraine is working to treat depression with Virtual Space Station. 2010. [Accessed 13/12/19]. Available from: <https://earthsky.org/human-world/james-cartraine-is-working-to-treat-depression-with-virtual-space-station>.
104. Sandoval LR, Buckley JC, Ainslie R, Tombari M, Stone W, Hegel MT. Randomized controlled trial of a computerized interactive media-based problem solving treatment for depression. *Behav Ther*. 2017; 48(3):413–425.
105. Sarkar C, Webster C, Gallacher J. Residential greenness and prevalence of major depressive disorders: a cross-sectional, observational, associational study of 94,879 adult UK Biobank participants. *Lancet Planet Health*. 2018; 2(4):e162–e173.
106. SBU. E-Mental Health Tool May Be Key for Astronauts to Cope with Anxiety, Depression in Space. 2017. [Accessed 26/05/19]. Available from: <https://news.stonybrook.edu/news/general/mental-health-tool-may-be-key-stony-brook>.
107. Singh AB. Improved antidepressant remission in major depression via a pharmacokinetic pathway polygene pharmacogenetic report. *Clin Psychopharmacol Neurosci*. 2015; 13(2):150–156.
108. Stein TP. The relationship between dietary intake, exercise, energy balance and the space craft environment. *Pflugers Arch*. 2000; 441(2–3 Suppl.):R21–R31.
109. Stepanek J, Blue RS, Parazyński S. Space medicine in the era of civilian spaceflight. *N Engl J Med*. 2019; 380(11):1053–1060.

110. Taylor JL, O'Hara R, Mumenthaler MS, Yesavage JA. Relationship of CogScreen-AE to flight simulator performance and pilot age. *Aviat Space Environ Med.* 2000; 71(4):373–380.
111. Ternes K, Iyengar V, Lavretsky H, Dawson WD, Booi L, et al. Brain health INnovation Diplomacy: a model binding diverse disciplines to manage the promise and perils of technological innovation. *Int Psychogeriatr.* 2020; 2020:1–25.
112. Tonozzi TR, Braunstein GD, Kammesheidt A, Curran C, Golshan S, Kelsoe J. Pharmacogenetic profile and major depressive and/or bipolar disorder treatment: a retrospective, cross-sectional study. *Pharmacogenomics.* 2018; 19(15):1169–1179.
113. TRISH. Spaces in Space: Optimizing Behavioral Health & Cognitive Performance in Confined Environments. 2019. [Accessed 27/8/19]. Available from: <https://stonewaterproductions.swoogo.com/trish/244637>.
114. TRISH. TRISH Launch Pad. 2019. [Accessed 27/8/19]. Available from: <https://colab.secure-platform.com/a/page/TRISH-home>.
115. TRISH. Industry Program 2020. 2020. [Accessed 5/10/20]. Available from: https://spacehealth.bcm.edu/prog/industry_program_2020/.
116. UCSE. Space Health Innovation Conference 2019. [Accessed 27/8/19]. Available from: <https://shic.swoogo.com/shic19/248306>.
117. Vernikos J, Deepak A, Sarkar DK, Rickards CA, Convertino VA. Yoga therapy as a complement to astronaut health and emotional fitness stress reduction and countermeasure effectiveness before, during, and in post-flight rehabilitation: a hypothesis. *Gravit Space Biol.* 2012; 26(1):65–76.
118. Vigo D, Thornicroft G, Atun R. Estimating the true global burden of mental illness. *Lancet Psychiatry.* 2016; 3(2):171–178.
119. Wagner B, Knaevelsrud C, Maercker A. Internet-based cognitive-behavioral therapy for complicated grief: a randomized controlled trial. *Death Stud.* 2006; 30(5):429–453.
120. WHO. Human Genomics in Global Health: Quality & Safety in Genetic Testing: An Emerging Concern. 2019. [Accessed 14/12/19]. Available from: https://www.who.int/genomics/policy/quality_safety/en/.
121. WHO. Medical Devices: Regulations. 2019. [Accessed 14/12/19]. Available from: https://www.who.int/medical_devices/safety/en/.
122. WHO. WHO guideline: recommendations on digital interventions for health system strengthening. Geneva: World Health Organization; 2019.
123. Winner JG, Carhart JM, Altar CA, Allen JD, Dechairo BM. A prospective, randomized, double-blind study assessing the clinical impact of integrated pharmacogenomic testing for major depressive disorder. *Discov Med.* 2013; 16(89):219–227.
124. Winner JG, Carhart JM, Altar CA, Goldfarb S, Allen JD, et al. Combinatorial pharmacogenomic guidance for psychiatric medications reduces overall pharmacy costs in a 1 year prospective evaluation. *Curr Med Res Opin.* 2015; 31(9):1633–1643.
125. Yang Y, Fairbairn C, Cohn JF. Detecting depression severity from vocal prosody. *IEEE Trans Affect Comput.* 2013; 4(2):142–150.
126. Ybarra ML, Eaton WW. Internet-based mental health interventions. *Ment Health Serv Res.* 2005; 7(2):75–87.
127. Yeung KS, Hernandez M, Mao JJ, Haviland I, Gubili J. Herbal medicine for depression and anxiety: a systematic review with assessment of potential psycho-oncologic relevance. *Phytother Res.* 2018; 32(5):865–891.
128. Zeier Z, Carpenter LL, Kalin NH, Rodriguez CI, McDonald WM, Widge AS, et al. Clinical implementation of pharmacogenetic decision support tools for antidepressant drug prescribing. *Am J Psychiatry.* 2018; 175(9):873–886.



IP: 182.239.161.159 On: Tue, 01 Sep 2020 22:39:10
 Copyright: Aerospace Medical Association
 Delivered by Ingenta