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Possible therapeutic approaches of health hazards of astronauts in microgravity: A review

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Abstract
This review examines the potential therapeutic approaches to mitigate the health hazards faced by astronauts during extended exposure to microgravity. Prolonged spaceflight leads to a range of physiological challenges, including musculoskeletal atrophy, cardiovascular deconditioning, neurovestibular disturbances, immune dysregulation, and visual impairment. The review explores various strategies to counteract these effects, including pharmacological interventions, nutritional support, physical exercise regimens, and emerging biotechnologies such as artificial gravity and neuromuscular electrical stimulation. Additionally, psychological stress and sleep disorders, which are exacerbated by the isolating and confined environment of space, are also addressed through behavioral health support and sleep management techniques. By evaluating the efficacy of these therapeutic measures, the review highlights the importance of integrated, multi-faceted approaches to enhance astronaut health, performance, and safety during long-duration missions, ultimately ensuring mission success and safe return to Earth.

Keywords: Space, astronauts, therapeutic approaches, neuromuscular electrical stimulation, neurovestibular disturbances, nutritional support

1. Introduction
Astronauts face a distinct set of physiological difficulties when exploring space, especially when exposed to microgravity conditions for extended periods of time (West, 2000) [62]. Numerous health risks, including as musculoskeletal deterioration, cardiovascular deconditioning, fluid redistribution, neurovestibular disorders, and immune system malfunction, arise when gravity forces are absent (Bottomley and Lewis, 2024) [7]. These modifications may have a negative effect on the health and performance of astronauts while on missions and present hazards when they return to Earth's gravity (January, 2008) [27]. Effective treatment approaches are becoming more and more important as space organisations prepare for lengthier missions to the Moon and Mars (Nair *et al.*, 2008) [43]. The purpose of this review is to investigate and assess potential therapeutic strategies that can lessen the negative health effects of microgravity on humans, improving mission safety and success (Dobney *et al.*, 2023) [14]. These strategies range from physical countermeasures and emerging biotechnologies to pharmacological interventions and nutritional support.

2. Health Hazards Associated with Microgravity
During space missions, astronauts face a distinct set of physiological problems brought on by microgravity, which have a substantial impact on several body systems (Blaber *et al.*, 2010) [5]. Long-term exposure causes cardiovascular deconditioning, fluid redistribution, muscular atrophy, bone demineralisation, and weakened immunological responses (Carrothers, 2024) [8]. Additionally, crew members frequently experience psychological stress, visual impairment, and neurovestibular dysfunction. In addition to endangering astronaut health, these health risks significantly reduce mission efficacy and duration (Mohammad, 2024) [40]. To preserve physiological homeostasis, improve recovery, and guarantee astronauts' long-term health and performance during and after spaceflight, it is essential to comprehend these negative impacts in order to create complete therapeutic techniques (Winkler, 2023) [63].

2.1 Musculoskeletal Atrophy
One of the biggest physiological problems astronauts have during prolonged microgravity exposure is musculoskeletal atrophy, which is defined by the loss of skeletal muscle mass and bone mineral density, especially in the spine and lower limbs (Bonanni *et al*., 2023) [6]. The lack of gravity loading significantly reduces the mechanical stimuli necessary to preserve musculoskeletal health, which in turn lowers muscle protein synthesis and osteoblast activity (Kohrt *et al*., 2009) [30]. Pharmaceutical interventions such as bisphosphonates and selective androgen receptor modulators (SARMs), nutritional supplements with sufficient protein, vitamin D, and calcium, and resistive exercise regimens utilising cutting-edge equipment like the Advanced Resistive Exercise Device (ARED) are some therapeutic strategies to counteract these effects (Xie *et al*., 2022) [64]. Recent studies also investigate the possibilities of electrical muscle stimulation and short-radius centrifugation as adjuvant therapies to create artificial gravity (Frett, 2023) [18]. The best method for preventing musculoskeletal degradation in space conditions is still an integrated approach that include medication, food, and exercise (Lewis *et al*., 2019) [35].

2.2 Cardiovascular Deconditioning
For astronauts who spend extended periods of time in microgravity, cardiovascular deconditioning—which manifests as decreased cardiac output, decreased plasma volume, orthostatic intolerance, and altered baroreflex sensitivity—is a major health risk (Aubert *et al*., 2005) [3]. Blood and other body fluids migrate towards the upper body when gravity is absent, which lowers central venous pressure and causes changes in cardiovascular homeostasis (Furst and Furst, 2020) [20]. The use of lower body negative pressure (LBNP) devices to mimic gravitational stress, structured aerobic and resistive exercise programmes, and pharmaceutical therapies including volume expanders and vasoconstrictors are some of the therapeutic strategies used to combat this problem (Goswami *et al*., 2019) [21]. Furthermore, short-radius centrifugation is being investigated as a possible countermeasure to preserve cardiovascular function by creating artificial gravity (Frett *et al*., 2014) [19]. To maintain astronaut health throughout extended space flights and guarantee a safe return to Earth's gravity, these tactics—either separately or in combination—are crucial.

2.3 Neurovestibular Disturbances
One of the most noticeable and immediate impacts astronauts encounter when exposed to microgravity is neurovestibular disruptions, which frequently show up as space motion sickness, disorientation, and poor balance and coordination (Kourtidou-Papadeli, 2022) [31]. The changed input to the inner ear's vestibular system, which depends on gravity to deliver indications about spatial direction, causes these disruptions (Jamon, 2014) [26]. There is sensory conflict between visual, proprioceptive, and vestibular inputs in microgravity because the otolith organs, which typically sense linear acceleration and head position relative to gravity, do not work as they do on Earth (Hilbig *et al*., 2017) [24]. Preflight adaptation training with motion simulators and virtual reality, pharmacological treatments like scopolamine and promethazine to control symptoms, and post-flight rehabilitation to aid in readjusting to Earth's gravity are some of the therapeutic approaches being studied (Reschke, 2016) [50]. In order to preserve motor control and spatial orientation during extended space missions, emerging strategies also emphasise vestibular stimulation technology and neurosensory retraining.

2.4 Immune Dysregulation
A major worry for astronauts on space missions is immunological dysregulation, especially in microgravity settings where the immune system is both suppressed and activated abnormally (Crucian *et al*., 2018) [11]. According to studies, extended exposure to microgravity increases vulnerability to infections and inflammatory reactions by changing the distribution of leukocytes, impairing the activity of natural killer cells, and reactivating dormant viruses (Mann *et al*., 2019) [38]. Other spaceflight-related stresses like radiation, irregular circadian cycles, and psychological stress may exacerbate this dysregulation (Afshinnekoo *et al*., 2020) [1]. The use of immunomodulatory drugs, customised diets high in antioxidants and omega-3 fatty acids, probiotics to promote gut-immune interaction, and pre-mission immunisation programmes are among therapeutic options to lessen immunological dysfunction in space (Napiórkowska-Baran *et al*., 2025) [44]. Furthermore, to protect astronauts' health during prolonged space travel, research is still needed to monitor biomarkers of immune function and create countermeasures like artificial gravity or pharmaceutical therapies.

2.5 Visual Impairment Intracranial Pressure (VIIP) Syndrome
Impairment of Vision A major health risk for astronauts on extended space flights is Intracranial Pressure (VIIP) Syndrome, which is now more often known as Spaceflight-Associated Neuro-ocular Syndrome (SANS) (Lee *et al*., 2020) [34]. The syndrome is characterized by structural changes in the eye, such as optic disc edema, globe flattening, choroidal folds, and a hyperopic shift in vision, which are believed to result from fluid redistribution and elevated intracranial pressure in microgravity (Scheie and Grayson, 1971) [54]. Potential treatment strategies being researched include the creation of artificial gravity environments, pharmacological interventions like carbonic anhydrase inhibitors to decrease the production of cerebrospinal fluid, and lower-body negative pressure (LBNP) devices to reverse cephalad fluid shifts. To lessen VIIP symptoms and maintain eye health during prolonged spaceflight, customised countermeasures are also being investigated. These include non-invasive intracranial pressure monitoring and customisable visual correction (Otto, 2021) [47].

2.6 Psychological Stress and Sleep Disorders
Astronauts in microgravity face serious health risks from psychological stress and sleep disorders as a result of extended confinement, isolation, disruption of their circadian cycle, and demanding missions (Arone *et al*., 2021) [2]. These stressors have the potential to compromise crew safety and mission success by affecting cognitive function, mood stability, and decision-making (Klein, 2013) [29]. Reduced sleep duration and quality are common symptoms of sleep disruptions that are frequently observed in space. In addition to non-pharmacological techniques like

light therapy, cognitive-behavioral therapy (CBT), and structured regimens to strengthen circadian alignment, therapeutic approaches also include pharmaceutical interventions like melatonin and hypnotic drugs to encourage sleep. Additionally, using virtual reality relaxation settings, mindfulness exercises, and consistent psychological support might help reduce stress and improve mental toughness in general when in space (O'Caoimh *et al*., 2019) [45].

3. Therapeutic Approaches
A mix of pharmaceutical, dietary, physical, and technological interventions are used in therapeutic techniques to reduce the health risks astronauts encounter in microgravity situations (Pal *et al*., 2021) [48]. While pharmaceutical medicines like bisphosphonates and antioxidants are being investigated to maintain skeletal and cardiovascular health, countermeasures like resistance and aerobic exercise regimes are essential in preventing muscle atrophy and bone demineralisation (Marcucci *et al*., 2023) [39]. Nutritional tactics that improve metabolic balance and lower inflammation include vitamin D, calcium, and omega-3 fatty acid supplements (Ticinesi *et al*., 2016) [60]. Furthermore, cutting-edge technology like wearable health monitoring devices and artificial gravity systems present intriguing ways to replicate Earth-like settings and quickly treat physiological abnormalities. Together, these multidisciplinary therapeutic strategies are essential for ensuring astronaut health, performance, and mission success during prolonged space travel (Mohammad, 2024) [40].

3.1 Physical Exercise Regimens
Because physical activity helps preserve muscle mass, bone density, and cardiovascular health, it is essential for reducing the health risks astronauts encounter in microgravity (Riski, 2024) [52]. Because there are no gravitational pulls in microgravity situations, astronauts suffer from bone loss and muscle atrophy, which can cause long-term health problems when they return to Earth. Exercise regimens are specifically created to target the important bone and muscle regions that are most impacted by microgravity in order to mitigate these effects (Bonanni *et al*., 2023) [6].
Aerobic workouts, resistance training, and weight-bearing exercises like cycling, treadmill walking with harnesses, and the use of specialised exercise equipment like the Advanced Resistive Exercise Device (ARED) are commonly included in these regimens (Donaghe, 2011) [15]. Frequent exercise also improves blood circulation, preserves cardiovascular health (Myers, 2003) [42], and enhances mental and physical well-being—all of which are critical for astronauts' performance on long-duration space missions. When strictly adhered to, these routines are thought to be essential for maintaining astronaut health while they are in orbit and facilitating their safe and healthy return to Earth (Shah *et al*., 2024) [55].

3.2 Pharmacological Interventions
The main goal of pharmacological therapies to reduce the health risks astronauts encounter in microgravity is to reverse the physiological changes brought on by the space environment, such as cardiovascular abnormalities, muscle atrophy, and bone density loss (Pal *et al*., 2021) [48]. The ability of a number of pharmaceutical substances, such as myostatin inhibitors, bisphosphonates, and selective androgen receptor modulators (SARMs), to maintain bone strength and muscle mass is being studied. Furthermore, drugs that target oxidative stress, such antioxidants (like vitamin E and ascorbic acid), are being examined to shield cells from harm brought on by the increased creation of free radicals in space. By encouraging the synthesis of red blood cells, erythropoiesis-stimulating agents (ESAs) may also lessen the symptoms of anaemia brought on by microgravity. In order to promote astronaut health during extended missions, pharmaceutical strategies to regulate neurocognitive impacts and sleep disturbances—such as melatonin and cognitive enhancers—are also being investigated. By reducing the health hazards connected to extended space travel, these therapeutic approaches hope to improve astronaut performance and wellbeing (Arone *et al*., 2021) [2].
Various drugs are being tested or used:

- **Bisphosphonates**: To mitigate bone loss.
- **Midodrine**: For orthostatic hypotension.
- **Melatonin or Zolpidem**: For sleep regulation.
- **Antioxidants and anti-inflammatory agents**: To address oxidative stress and immune imbalance.

3.3 Nutritional Strategies
Maintaining general health during extended space flights requires nutritional solutions for reducing health risks for astronauts exposed to microgravity (Dakkumadugula *et al*., 2023) [12]. To combat oxidative stress and boost immunological function, these tactics include incorporating nutrient-dense diets high in vitamins, minerals, and antioxidants (Obeagu *et al*., 2024) [46]. While specific supplements like calcium, vitamin D, and omega-3 fatty acids aid in preventing bone density loss and inflammation brought on by the changed gravitational environment, maintaining muscle mass and preventing muscle atrophy requires ensuring enough protein consumption (Cretoiu and Zugravu, 2018) [10]. Furthermore, the creation of functional meals and probiotics, as well as customised hydration techniques, may improve gut health and lessen digestive problems in space. In order to protect astronauts' health in microgravity and eventually improve their performance and resilience during space missions (Montesinos *et al*., 2021) [41], advanced nutritional formulations that take into account both physiological and psychological variables can be extremely important (Benton, 2013) [4].

3.4 Artificial Gravity
A possible treatment strategy to lessen the health risks astronauts face in microgravity is artificial gravity, which is produced by rotating a spacecraft or habitat to mimic the effects of gravity (Clément *et al*., 2015) [9]. Among other physiological problems, prolonged exposure to microgravity causes muscular atrophy, bone loss, cardiovascular deconditioning, and abnormal fluid distribution (Iwase *et al*., 2020) [25]. Astronauts can experience the mechanical loads required to preserve cardiovascular and musculoskeletal health by harnessing centrifugal forces to generate an artificial gravity environment. According to research, the use of artificial gravity—such as rotating centrifuges or rotating space habitats—may help avoid or lessen fluid changes, bone density loss, and muscle weakening, all of which could improve long-term health during prolonged space travel. To guarantee their efficacy

and viability in upcoming space exploration, more research is necessary to determine the design, viability, and ideal parameters of artificial gravity systems (Young, 1999) [65].

3.5 Neuromuscular Electrical Stimulation (NMES)

A promising treatment strategy to reverse the muscle atrophy and strength loss astronauts endure from extended microgravity exposure is neuromuscular electrical stimulation, or NMES (Maffiuletti *et al*., 2019) [37]. The pressure on skeletal muscles is much lessened in space due to the lack of gravity, which results in a loss of muscle mass and function (Stein, 2013) [59]. In order to simulate the effects of physical exercise on the muscles, NMES applies electrical impulses to induce muscular contractions. NMES can lessen the negative consequences of muscular disuse in microgravity by increasing muscle activation and encouraging the recruitment of muscle fibres. Additionally, it has the potential to shorten the recuperation period needed following extended space missions by enhancing astronauts' muscle strength, endurance, and general rehabilitation upon their return to Earth (Hackney *et al*., 2015) [22].

3.6 Behavioral Health Support

Support for behavioural health in microgravity is crucial for resolving the emotional and psychological difficulties that astronauts encounter during long space flights (Mohammad, 2024) [40]. Increased stress, anxiety, and even depression can result from microgravity's physical stresses, confinement, and isolation. Maintaining mental health through practices like mindfulness and relaxation techniques must be the major goal of therapeutic approaches (Smith, 2005) [57]. Important emotional relief can also be obtained through virtual support networks, which include peer, family, and mental health professional communication. Supporting astronauts' mental health also requires customised interventions, such as stress-reduction and mood-enhancing exercise programmes and good sleep hygiene habits. By incorporating behavioural health care into mission planning and astronaut training, psychological problems can be reduced, improving crew cohesiveness and performance in the demanding microgravity environment (Landon, 2022) [32].

3.7 Radiation Shielding

A vital component of reducing the health risks astronauts encounter on prolonged trips in microgravity settings is radiation shielding (Dobney *et al*., 2023) [14]. Galactic cosmic rays (GCRs) and solar particle events (SPEs) are examples of space radiation, which carries a number of serious dangers, such as an elevated chance of cancer, heart problems, and neurological disorders (Reitz and Hellweg, 2018) [49]. To shelter astronauts from these negative effects, effective radiation shielding techniques are crucial. Present methods combine sophisticated active shielding technologies, like magnetic fields or electrostatic shields, with passive shielding materials, like polythene. To increase radiation shielding, research is being done on new materials and technologies like as hydrogen-rich materials, high-density composites, and creative spacecraft architecture (Shahzad *et al*., 2022) [55]. Furthermore, in order to supplement physical shielding and lower the long-term health hazards connected with space travel, therapeutic interventions—such as the use of medications to lessen radiation-induced damage—are being investigated.

Table 1: Therapeutic Approaches to Health Hazards in Microgravity

Health Hazard	Therapeutic Approach	Mechanism/Effect	Reference
Muscle atrophy	Resistance exercise, Protein supplementation	Maintains muscle mass and function	(Fitts *et al*., 2001) [17]
Bone demineralization	Bisphosphonates, Vibration therapy	Inhibits bone resorption, stimulates osteogenesis	(LeBlanc *et al*., 2002; Rittweger, 2010) [33, 53]
Cardiovascular deconditioning	Lower body negative pressure (LBNP), Exercise	Maintains blood volume, orthostatic tolerance	(Hargens & Watenpaugh, 1996) [23]
Immune system dysregulation	Probiotics, Antioxidant-rich diet	Supports gut microbiota, reduces oxidative stress	(Sonnenfeld, 2002; Turroni *et al*., 2020) [58, 61]
Neurovestibular dysfunction	Adaptation training, Pharmacological agents	Enhances vestibular compensation	(Reschke *et al*., 1998) [51]
Space radiation exposure	Antioxidants, Shielding technologies	Scavenges free radicals, protects DNA	(Durante & Cucinotta, 2008) [16]
Psychological stress and isolation	Digital cognitive behavioral therapy, Social support	Improves coping mechanisms, mental well-being	(Kanas & Manzey, 2008) [28]
Sleep disturbances	Melatonin, Controlled lighting	Regulates circadian rhythm and improves sleep quality	(Dijk *et al*., 2001) [13]
Altered gut microbiota	Prebiotics and probiotics	Modulates microbiota composition, supports gut-brain axis	(Turroni *et al*., 2020) [61]
Visual impairment (VIIP syndrome)	Lower-body negative pressure, Fluid redistribution	Prevents fluid shift to head, relieves intracranial pressure	(Mader *et al*., 2011) [36]

5. Conclusion

The success and safety of long-duration space missions, such as those headed for Mars and permanent lunar colonisation, depend on tackling the health risks that humans encounter in microgravity. In order to mitigate the negative effects of microgravity on astronauts' musculoskeletal, cardiovascular, neurovestibular, immune, and psychological health, a variety of therapeutic approaches are presented, ranging from physical exercise regimens and pharmaceutical interventions to nutritional strategies and cutting-edge technologies like artificial gravity and neuromuscular electrical stimulation. Maintaining astronaut performance and well-being while also strengthening their resilience to the difficulties of space travel requires the integration of these interdisciplinary approaches. The development of cutting-edge technology and continued research into these defences will be essential to prepare astronauts for upcoming deep space exploration missions and, eventually, allowing humanity to flourish beyond Earth.

6. References

1. Afshinnekoo E, Scott RT, MacKay MJ, Pariset E, Cekanaviciute E, Barker R, *et al*. Fundamental biological features of spaceflight: advancing the field to enable deep-space exploration. Cell. 2020;183(5):1162-1184.
2. Arone A, Ivaldi T, Loganovsky K, Palermo S, Parra E, Flamini W, *et al*. The burden of space exploration on the mental health of astronauts: a narrative review. Clinical Neuropsychiatry. 2021;18(5):237.
3. Aubert AE, Beckers F, Verheyden B. Cardiovascular function and basics of physiology in microgravity. Acta Cardiologica. 2005;60(2):129-151.
4. Benton D. To establish the parameters of optimal nutrition do we need to consider psychological in addition to physiological parameters?. Molecular Nutrition & Food Research. 2013;57(1):6-19.
5. Blaber E, Marçal H, Burns BP. Bioastronautics: the influence of microgravity on astronaut health. Astrobiology. 2010;10(5):463-473.
6. Bonanni R, Cariati I, Marini M, Tarantino U, Tancredi V. Microgravity and musculoskeletal health: what strategies should be used for a great challenge?. Life. 2023;13(7):1423.
7. Bottomley JM, Lewis CB. Pathological manifestations of aging. In: A Clinical Approach to Geriatric Rehabilitation. 4th ed. New York: Routledge; 2024. p. 74-108.
8. Carrothers L. Fatigue and deconditioning. In: Clinical Exercise Pathophysiology for Physical Therapy. New York: Routledge; 2024. p. 137-154.
9. Clément GR, Bukley AP, Paloski WH. Artificial gravity as a countermeasure for mitigating physiological deconditioning during long-duration space missions. Frontiers in Systems Neuroscience. 2015;9:92.
10. Cretoiu SM, Zugravu CA. Nutritional considerations in preventing muscle atrophy. In: Muscle Atrophy. 2018. p. 497-528.
11. Crucian BE, Choukèr A, Simpson RJ, Mehta S, Marshall G, Smith SM, *et al*. Immune system dysregulation during spaceflight: potential countermeasures for deep space exploration missions. Frontiers in Immunology. 2018;9:1437.
12. Dakkumadugula A, Pankaj L, Alqahtani AS, Ullah R, Ercisli S, Murugan R. Space nutrition and the biochemical changes caused in astronauts' health due to space flight: A review. Food Chemistry: X. 2023;20:100875.
13. Dijk DJ, Neri DF, Wyatt JK, Ronda JM, Riel E, Ritz-De Cecco A, *et al*. Sleep, performance, circadian rhythms, and light-dark cycles during two space shuttle flights. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology. 2001;281(5):R1647-R1666.
14. Dobney W, Mols L, Mistry D, Tabury K, Baselet B, Baatout S. Evaluation of deep space exploration risks and mitigations against radiation and microgravity. Frontiers in Nuclear Medicine. 2023;3:1225034.
15. Donaghe HE. Physiological response to body weight-supported treadmill exercise in healthy adults [dissertation]. Davis (CA): University of California, Davis; 2011.
16. Durante M, Cucinotta FA. Physical basis of radiation protection in space travel. Reviews of Modern Physics. 2008;80(3):1021.
17. Fitts RH, Riley DR, Widrick JJ. Functional and structural adaptations of skeletal muscle to microgravity. Journal of Experimental Biology. 2001;204(18):3201-3208.
18. Frett T. Artificial gravity through short-arm centrifugation as potential countermeasure for human spaceflight: feasibility, safety and neuromuscular response [dissertation]. Hannover: Medizinische Hochschule Hannover; 2023.
19. Frett T, Mayrhofer M, Schwandtner J, Anken R, Petrat G. An innovative short arm centrifuge for future studies on the effects of artificial gravity on the human body. Microgravity Science and Technology. 2014;26:249-255.
20. Furst B, Furst B. The effect of gravity and upright posture on circulation. In: The Heart and Circulation: An Integrative Model. Cham: Springer; 2020. p. 319-341.
21. Goswami N, Blaber AP, Hinghofer-Szalkay H, Convertino VA. Lower body negative pressure: physiological effects, applications, and implementation. Physiological Reviews. 2019;99(1):807-851.
22. Hackney KJ, Scott JM, Hanson AM, English KL, Downs ME, Ploutz-Snyder LL. The astronaut-athlete: optimizing human performance in space. The Journal of Strength & Conditioning Research. 2015;29(12):3531-3545.
23. Hargens AR, Watenpaugh DE. Cardiovascular adaptation to spaceflight. Medicine and Science in Sports and Exercise. 1996;28(8):977-982.
24. Hilbig R, Gollhofer A, Bock O, Manzey D, Hilbig RW, Anken RH. Impact of micro- and hypergravity on neurovestibular issues of fish. In: Sensory Motor and Behavioral Research in Space. 2017. p. 59-86.
25. Iwase S, Nishimura N, Tanaka K, Mano T. Effects of microgravity on human physiology. In: Beyond LEO - Human Health Issues for Deep Space Exploration. London: IntechOpen; 2020.
26. Jamon M. The development of vestibular system and related functions in mammals: impact of gravity. Frontiers in Integrative Neuroscience. 2014;8:11.
27. January O. Human health and performance for long-duration spaceflight. Future. 2008;79:629-635.
28. Kanas N, Manzey D. Space Psychology and Psychiatry. Berlin: Springer Science & Business Media; 2008.
29. Klein G. The effect of acute stressors on decision making. In: Stress and Human Performance. New York: Psychology Press; 2013. p. 49-88.
30. Kohrt WM, Barry DW, Schwartz RS. Muscle forces or gravity: what predominates mechanical loading on bone?. Medicine and Science in Sports and Exercise. 2009;41(11):2050.
31. Kourtidou-Papadeli C. Effects of spaceflight on the nervous system. In: Handbook of space pharmaceuticals. Cham: Springer International Publishing; 2022. p. 521-553.
32. Landon LB. Risk of performance and behavioral health decrements due to inadequate cooperation, coordination, and psychosocial adaptations within a team. 2022.

33. LeBlanc A, Matsumoto T, Jones J, Shapiro J, Lang T, Shackelford L, *et al*. Bisphosphonates as a supplement to exercise to protect bone during long-duration spaceflight. Osteoporosis International. 2002;13(11):884-890.
34. Lee AG, Mader TH, Gibson CR, Tarver W, Rabiei P, Riascos RF, *et al*. Spaceflight associated neuro-ocular syndrome (SANS) and the neuro-ophthalmologic effects of microgravity: a review and an update. npj Microgravity. 2020;6(1):7.
35. Lewis R, Gómez Álvarez CB, Rayman M, Lanham-New S, Woolf A, Mobasheri A. Strategies for optimising musculoskeletal health in the 21st century. BMC Musculoskeletal Disorders. 2019;20:1-15.
36. Mader TH, Gibson CR, Pass AF, Kramer LA, Lee AG, Fogarty J, *et al*. Optic disc edema, globe flattening, choroidal folds, and hyperopic shifts observed in astronauts after long-duration space flight. Ophthalmology. 2011;118(10):2058-2069.
37. Maffiuletti NA, Green DA, Vaz MA, Dirks ML. Neuromuscular electrical stimulation as a potential countermeasure for skeletal muscle atrophy and weakness during human spaceflight. Frontiers in Physiology. 2019;10:1031.
38. Mann V, Sundaresan A, Mehta SK, Crucian B, Doursout MF, Devakottai S. Effects of microgravity and other space stressors in immunosuppression and viral reactivation with potential nervous system involvement. Neurology India. 2019;67(Suppl 2):S198-203.
39. Marcucci G, Domazetovic V, Nediani C, Ruzzolini J, Favre C, Brandi ML. Oxidative stress and natural antioxidants in osteoporosis: novel preventive and therapeutic approaches. Antioxidants. 2023;12(2):373.
40. Mohammad K. Navigating the challenges and opportunities of human spaceflight: health, psychology, and preparation for long-duration missions. In: AIAA Aviation Forum and Ascend 2024. 2024. p. 4817.
41. Montesinos CA, Khalid R, Cristea O, Greenberger JS, Epperly MW, Lemon JA, *et al*. Space radiation protection countermeasures in microgravity and planetary exploration. Life. 2021;11(8):829.
42. Myers J. Exercise and cardiovascular health. Circulation. 2003;107(1):e2-e5.
43. Nair GM, Murthi KS, Prasad MYS. Strategic, technological and ethical aspects of establishing colonies on Moon and Mars. Acta Astronautica. 2008;63(11-12):1337-1342.
44. Napiórkowska-Baran K, Treichel P, Dardzińska A, Majcherczak A, Pilichowicz A, Szota M, *et al*. Immunomodulatory effects of selected non-nutritive bioactive compounds and their role in optimal nutrition. Current Issues in Molecular Biology. 2025;47(2):89.
45. O'Caoimh R, Mannion H, Sezgin D, O'Donovan MR, Liew A, Molloy DW. Non-pharmacological treatments for sleep disturbance in mild cognitive impairment and dementia: a systematic review and meta-analysis. Maturitas. 2019;127:82-94.
46. Obeagu EI, Ubosi NI, Obeagu GU, Obeagu AA. Nutritional strategies for enhancing immune resilience in HIV: a review. International Journal of Current Research in Chemistry and Pharmaceutical Sciences. 2024;11(2):41-51.
47. Otto C. The visual impairment intracranial pressure (VIIP) risk in spaceflight. In: Handbook of Bioastronautics. Cham: Springer International Publishing; 2021. p. 641-673.
48. Pal N, Goswami S, Singh R, Yadav T, Singh RP. Precautions & possible therapeutic approaches of health hazards of astronauts in microgravity. The International Journal of Aerospace Psychology. 2021;31(2):149-161.
49. Reitz G, Hellweg CE. Space radiation and its biological effects. In: Applications of Laser-Driven Particle Acceleration. CRC Press; 2018. p. 217-236.
50. Reschke MF, Clément G, Thorson SL, Harm DL, Mader TH, Dudley AM, *et al*. Space Physiology and Medicine: From Evidence to Practice. 2016. p. 245.
51. Reschke MF, Bloomberg JJ, Harm DL, Paloski WH, Layne C, McDonald V. Posture, locomotion, spatial orientation, and motion sickness as a function of space flight. Brain Research Reviews. 1998;28(1-2):102-117.
52. Riski AD. Effects of microgravity on muscle and bone health in astronauts during space missions: preventive procedures and medical interventions. The Korean Journal of Aerospace and Environmental Medicine. 2024;34(3):89-95.
53. Rittweger J. Vibration as an exercise modality: how it may work, and what its potential might be. European Journal of Applied Physiology. 2010;108(5):877-904.
54. Scheie HG, Grayson MC. Ocular manifestations of systemic diseases. Disease-a-Month. 1971;17(2):1-51.
55. Shah SA, Karim S, Kumar R, Bhatti AL. Beyond the gravity: exploring legal position of astronauts' well-being in space. Journal of Social Sciences Review. 2024;4(4):154-168.
56. Shahzad K, Kausar A, Manzoor S, Rakha SA, Uzair A, Sajid M, *et al*. Views on radiation shielding efficiency of polymeric composites/nanocomposites and multi-layered materials: current state and advancements. Radiation. 2022;3(1):1-20.
57. Smith JC. Relaxation, meditation, & mindfulness: a mental health practitioner's guide to new and traditional approaches. New York: Springer Publishing Company; 2005.
58. Sonnenfeld G. The immune system in space and microgravity. Medicine and Science in Sports and Exercise. 2002;34(12):2021-2027.
59. Stein TP. Weight, muscle and bone loss during space flight: another perspective. European Journal of Applied Physiology. 2013;113:2171-2181.
60. Ticinesi A, Meschi T, Lauretani F, Felis G, Franchi F, Pedrolli C, *et al*. Nutrition and inflammation in older individuals: focus on vitamin D, n-3 polyunsaturated fatty acids and whey proteins. Nutrients. 2016;8(4):186.
61. Turroni S, Magnani M, Kc P, Lesnik P, Vidal H, Heer M, *et al*. Gut microbiome and space travelers' health: state of the art and possible pro/prebiotic strategies for long-term space missions. Frontiers in Physiology. 2020;11:553929.
62. West JB. Historical perspectives: physiology in microgravity. Journal of Applied Physiology. 2000;89(1):379-384.
63. Winkler LH. Human physiological limitations to long-term spaceflight and living in space. Aerospace Medicine and Human Performance. 2023;94(6):444-456.

64. Xie Y, Tian Y, Zhang Y, Zhang Z, Chen R, Li M, *et al*. Overview of the development of selective androgen receptor modulators (SARMs) as pharmacological treatment for osteoporosis (1998-2021). European Journal of Medicinal Chemistry. 2022;230:114119.
65. Young LR. Artificial gravity considerations for a Mars exploration mission. Annals of the New York Academy of Sciences. 1999;871(1):367-378.