Artificial Intelligence Applications in Space Medicine

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INTRODUCTION: During future interplanetary space missions, a number of health conditions may arise, owing to the hostile environment of space and the myriad of stressors experienced by the crew. When managing these conditions, crews will be required to make accurate, timely clinical decisions at a high level of autonomy, as telecommunication delays and increasing distances restrict real-time support from the ground. On Earth, artificial intelligence (AI) has proven successful in healthcare, augmenting expert clinical decision-making or enhancing medical knowledge where it is lacking. Similarly, deploying AI tools in the context of a space mission could improve crew self-reliance and healthcare delivery.

METHODS: We conducted a narrative review to discuss existing AI applications that could improve the prevention, recognition, evaluation, and management of the most mission-critical conditions, including psychological and mental health, acute radiation sickness, surgical emergencies, spaceflight-associated neuro-ocular syndrome, infections, and cardiovascular deconditioning.

RESULTS: Some examples of the applications we identified include AI chatbots designed to prevent and mitigate psychological and mental health conditions, automated medical imaging analysis, and closed-loop systems for hemodynamic optimization. We also discuss at length gaps in current technologies, as well as the key challenges and limitations of developing and deploying AI for space medicine to inform future research and innovation. Indeed, shifts in patient cohorts, space-induced physiological changes, limited size and breadth of space biomedical datasets, and changes in disease characteristics may render the models invalid when transferred from ground settings into space.

KEYWORDS: space medicine, space exploration, artificial intelligence, machine learning, decision support.

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Providing medical care during future exploration-class missions to Mars will be highly challenging. Space health hazards, including altered gravity fields, isolation and confinement, hostile and closed environments, space radiation, and extreme distance from Earth (**Fig. 1**), give rise to several space-specific medical conditions and limit evacuation opportunities and telemedical support from the ground.[53,96] To complicate the problem, space medical conditions could be associated with emergencies that require immediate medical attention, such as septic shock, fractures secondary to bone demineralization,[113] or postflight orthostatic intolerance.[24] The crew must be capable of making accurate, timely clinical decisions at a high level of independence from Earth, as real-time communication is virtually impossible due to signal transmission delays.

On Earth, artificial intelligence (AI) encompasses knowledge and/or data-intensive computer-based solutions that have proven useful to support and improve the decision-making of human healthcare providers.[117] For example, mortality prediction models in intensive care,[95] diabetic retinopathy automated classification,[29] or acute kidney injury prediction tools[40] all support decision-making by clinicians.

These AI algorithms belong to one of the three categories of machine learning algorithms: supervised, unsupervised, or reinforcement learning. Supervised learning is interested in learning the mathematical function linking input data (e.g., patient characteristics and severity at the time of hospital admission) and a label (e.g., presence of sepsis or mortality at day 28).[11] As such, supervised learning is applied to prediction tasks, where a model is built on training data and applied

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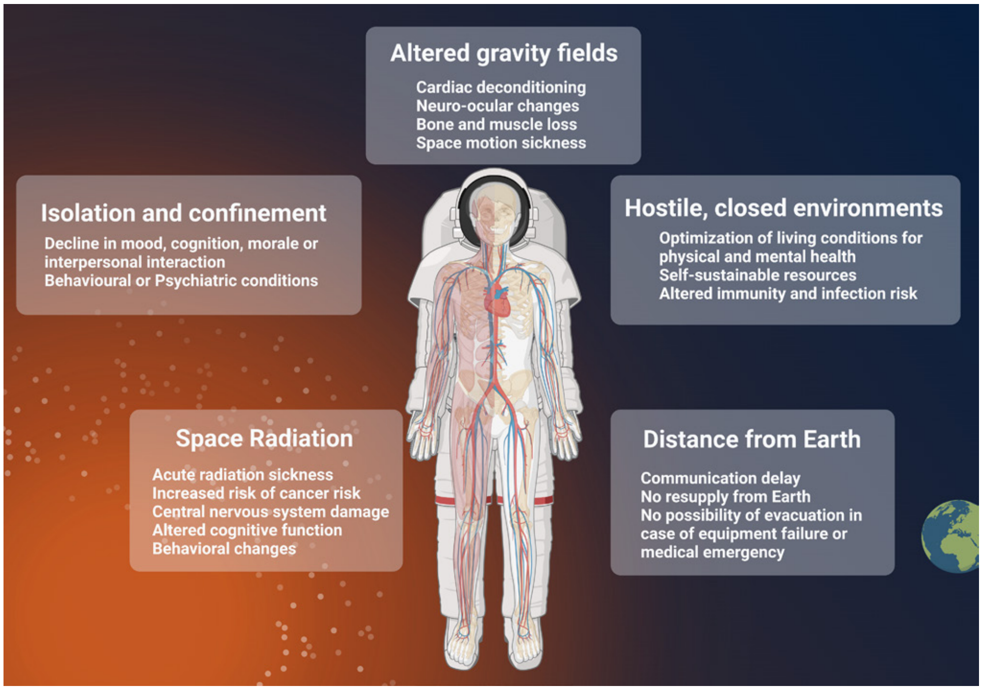

Fig. 1. NASA: The Five Hazards of Spaceflight of Human Spaceflight.[31] Reproduced from Patel et al.,[91] with modifications (Creative Commons Attribution license, permission to reuse not required; Created with BioRender.com).

prospectively to new, previously unseen data points.[11] There is a wide range of supervised techniques available to researchers, the most common being logistic regression, decision trees, neural networks (and their "deep" version in deep learning), or gradient boosting.[52] Another field of machine learning is represented by unsupervised learning, where an algorithm aims to establish the underlying structure or hidden patterns in a high-dimensional dataset.[11] Identifying homogeneous phenotypes in heterogeneous syndromes such as sepsis or acute respiratory distress syndrome may allow for more targeted therapy and/or inform the inclusion of patients in clinical trials.[65,101] Here again, various methods are available to researchers, each with advantages and limitations. Some popular algorithms in this category are represented by Principal Component Analysis, k-means clustering, and hierarchical clustering.[17] Finally, reinforcement learning is interested in optimizing a sequential decision process to maximize some form of predefined outcome.[112] For example, it has been applied to the questions of sepsis resuscitation,[63] glycemic control,[126] or the control of mechanical ventilation.[93]

All these algorithms can form the basis of decision support tools for complex clinical pictures or enhance medical expertise where it is lacking. In space, AI technology has the potential to augment the capabilities, autonomy, and self-reliance of the crew.[99] However, many uncertainties and limitations remain when applying AI to medicine on Earth, and many more are to be expected if we were to deploy such technologies in space. Most importantly, shifts in patient cohorts, space-induced physiological changes, and disease characteristics may render AI models invalid when transferred from ground settings into space. Keeping in mind this important caveat, the objective of this review is to highlight the potential for AI technologies to assist with the prediction, identification, assessment, and/or management of serious or frequent medical and surgical conditions during long-duration interplanetary spaceflight to Mars. We also discuss the most pressing challenges and limitations when considering deploying these technologies in space.

METHODS

Due to the wide variety of conditions in space medicine and the high heterogeneity of potential sources, this topic was unsuitable for a systematic review. Instead, we conducted a narrative review, which is suitable in situations when there are disparate interventions or when there is a dissimilarity of outcome measures and follow-up times in the analyzed material.[79]

First, we created an initial inclusive list of medical and surgical conditions and syndromes of interest to the topic, focusing on the conditions of highest impact on the mission based on their severity and likelihood. The list of conditions of interest was collated using several sources: the NASA Human Research Program list of accepted medical conditions;[15] the NASA Human Research Roadmap (HRR) risks[86] and evidence report[77]; space medicine reference textbooks[10,43,46]; a European Space Agency commissioned report on health control during long-duration interplanetary missions[22]; and relevant publications.[53,91,96] Based on the NASA Human System Risk Management Plan,[4] which provides an evidence-based rating system of likelihood and impact on crew health and/or mission objective (termed "consequence") (**Table I**), we

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Table I. A) Likelihood and B) Consequence Rating System for In-Mission Events, Reproduced from the NASA Human Risk Management Plan Report.[4]

A: RATING	1 / VERY LOW	2 / LOW	3 / MODERATE	4 / HIGH	5 / VERY HIGH
In-Mission Likelihood	Nearly certain not to occur in-mission ($P^* \leq 0.01\%$)	Unlikely to happen during the mission ($0.01\% \leq P \leq 0.1\%$)	May happen during the mission ($0.1\% \leq P \leq 1\%$)	Likelihood is high during the mission ($1\% \leq P \leq 10\%$)	More likely to happen than not during the mission ($P > 10\%$)

	B: RATING	1	2	3	4	5
In-Mission Consequences	Crew Health Impact	Temporary discomfort	Minor injury/illness that can be dealt with by crew without ground support, minor crew discomfort	Significant injury/ illness or incapacitations that requires diagnosis and/or treatment support from ground, may affect personal safety	Critical injury/illness of one crewmember requiring extended medical intervention and support, may results in temporary disability	Death or permanently disabling injury/illness affecting one or more crewmember
	Mission Objectives Impact	Insignificant impact to crew performance and operations – no additional resources required	Minor impact to crew performance and operations – requires additional resources (time, consumables)	Significant reduction in crew performance, threatens loss of a mission objective	Severe reduction of crew performance results in loss of multiple mission objectives	Loss of mission due to crew performance reduction or loss of crew

In "In-Mission Consequences", we only considered crew (short term) health and mission objectives impact and ignored flight recertification and long-term health impact.
**P* = Probability (NASA Scientific Technical Information Program document; public use permitted).

created a "Likelihood x Consequence" risk matrix for the space medicine conditions in consideration (see **Fig. 2** in Results section).

Then, we conducted a literature search on PubMed, Medline, and Google Scholar from 1 January 2000 to 31 July 2022 for each condition to summarize their clinical presentation, likelihood, estimated incidence or prevalence during spaceflight, severity and mission impact, current prevention, countermeasures, detection or diagnosis, and treatment on Earth and in space.

Next, we conducted another literature search for potential AI applications that could help crews with prevention/countermeasures, detection/diagnosis, and/or treatment of the conditions. For example, we used the following search terms for the condition of postflight orthostatic intolerance: ("space orthostatic intolerance" OR "postflight orthostatic hypotension") AND ("artificial intelligence" OR "closed loop" OR "machine learning"). These include mostly AI applications that have been developed (and sometimes validated) on Earth and could theoretically be transferred to space and have applications specifically developed for the space environment.

All authors reviewed the final list of included articles and extracted knowledge relevant to addressing the research question for each identified medical condition.

RESULTS

Choice of the Conditions of Interest

As shown in Fig. 2, the space medical conditions in consideration have been categorized based on their likelihood of occurrence and consequences on crew health and mission objectives. "Red" risks are given the highest research priority due to their significant impact on crew health and performance. "Yellow" risk can be those: i) accepted due to a very low probability of occurrence, ii) that require in-mission monitoring to be accepted, or iii) that require refinement of standards or mitigation strategies to be accepted. "Green" risks are considered sufficiently controlled either due to low likelihood and consequence or because sufficient mitigation strategies are available to manage the risk to an acceptable level.

In this article, given their need for further research, we have only included "red" and "yellow" risks and the final list of conditions is shown here:

- Psychological and Mental Health includes HRR risks:
  - Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders
  - Performance Decrements and Adverse Health Outcomes Resulting from Sleep Loss, Circadian Desynchronization, and Work Overload
- Acute Radiation Sickness
- Surgical Emergencies and Anesthesia includes HRR risks:
  - Renal Stone Formation
  - Bone Fracture due to Spaceflight-induced Changes to Bone
  - Injury and Compromised Performance Due to Extra-Vehicular Activities
  - Injury from Dynamic Loads
- Cardiovascular Deconditioning including Post-Flight Orthostatic Intolerance
- Altered Sensorimotor/Vestibular Function Impacting Critical Mission Tasks

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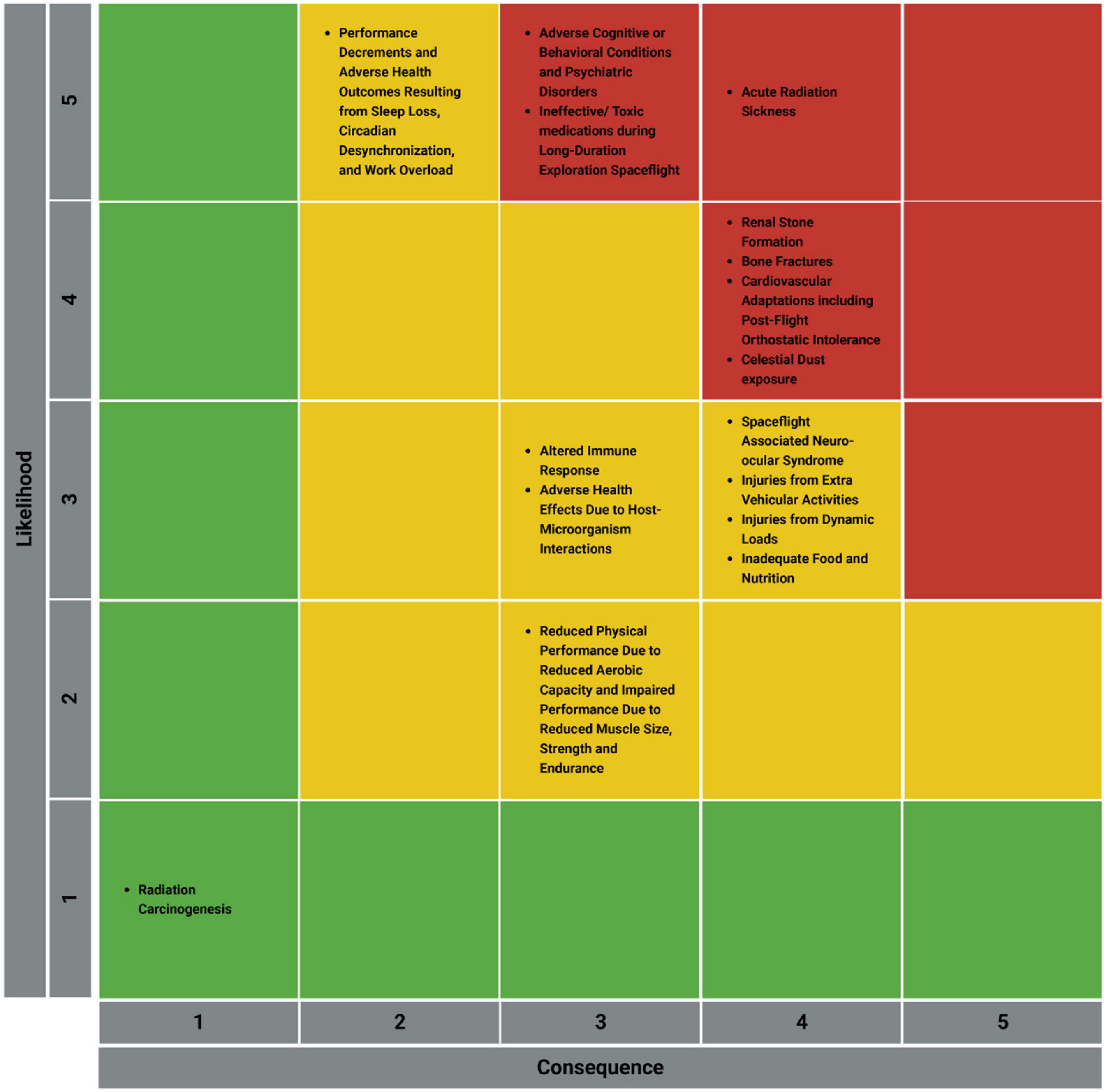

Fig. 2. Likelihood-consequence risk matrix of medical conditions during deep space exploration missions, developed from combining multiple sources as described in the methods. This review focused on the conditions of highest likelihood and/or consequences. (Created with BioRender.com).

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- Infections and Sepsis includes HRR risks:
    - Adverse Health Effects Due to Host-Microorganism Interactions
    - Adverse Health Event Due to Altered Immune Response
- Spaceflight Associated Neuro-ocular Syndrome Performance Decrement
- Crew Illness Due to Inadequate Food and Nutrition
- Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity
- Impaired Performance Due to Reduced Muscle Size, Strength and Endurance
- Adverse Health and Performance Effects of Celestial Dust Exposure
- Ineffective or Toxic Medications During Long-Duration Exploration Spaceflight

Psychological and Mental Health

A journey into deep space places exceptional challenges on the psychological health of the crew. A 2001 National Academy of Sciences commissioned report named psychological health among the most significant risks for crewmembers during a Mars mission.[9] During such missions, crewmembers will be exposed to many stressors, including extended periods of social isolation and close-quarter confinement, chronic stress from carrying out high-caliber work, solving unexpected emergencies with little help from the ground,[58] and structural brain changes due to microgravity and ionizing radiation.[54] As such, conditions such as depression and anxiety disorders are likely to arise, as shown from previous long-duration missions on Mir and similar ground analog studies.[77] Fortunately, more acute conditions such as delirium have only been described on rare occasions.[77]

Without appropriate and effective mitigation, such conditions could derail a mission and even threaten crewmembers' lives. Most countermeasures developed for short-duration and International Space Station (ISS) missions involve keeping crews connected to home, such as video conferences with family members, mission control and healthcare professionals, and resupplying cargos of letters, food, and surprises.[77] Unfortunately, these will be restricted, or indeed wholly unavailable, as crews journey toward Mars and communication latency increases up to 22 min.[57]

Various AI systems are being developed to combat this unusual form of "homesickness"; for instance, closed loop communication systems that integrate behavioral monitoring and real-time feedback. The Crew Interactive Mobile Companion system has been deployed on the ISS since 2018 to provide artificial companionship and work assistance.[21] It is equipped with natural language processing and computer vision capabilities to interpret speech and facial expressions. Therefore, it can carry out simple mission tasks and converse empathetically based on the derived emotional state of astronauts.[106] NASA and Ejenta have also collaborated recently to develop a conversational AI that provides emotional support for mission crews.[106]

On Earth, there is unprecedented attention in developing AI chatbots for mental health conditions. In their systematic review, Abd-Alrazap and colleagues identified 41 unique mental health chatbots and 14 randomized controlled trials that assessed the effectiveness of chatbots in mental health.[1] A number of chatbots relevant to spaceflight-induced psychological stressors have also been validated in clinical trials. They include *Woebot*, which delivers personalized psychotherapy for depression and anxiety,[38] *Tess*, which teaches coping skills and provides support for social isolation,[30] and an interview-style conversational system developed by Welch et al. to cope with the psychological and health stress due to the COVID-19 pandemic.[125] To better emulate the patient-clinician experience, these trials drew similar conclusions on the importance of appropriately expressed empathy; assigned human traits (e.g., being helpful, caring, open to listening, and nonjudgmental); minimization of speech interpretation errors; closer simulation of natural conversation; and involvement of trained and experienced clinicians in the design process.[30,38,125] To adapt these systems for aerospace research, tests designed specifically for the high-performing astronaut population against long-duration mission stressors should be adopted, such as the Cognition Test Battery that has been tested in NASA's ground-based Human Exploration Analog project.[85]

Acute Radiation Sickness

As Mars crews leave Earth's magnetosphere and venture into deep space, they will be exposed to space radiation originating from background galactic cosmic radiation and highly energetic solar particle events.[91] Both induce high levels of oxidative stress on the human body.[91] Among the associated health effects, the most serious and unpredictable is acute radiation sickness related to solar particle events.[34] Chronic exposure to space radiation also exposes the crew to long-term risks, including cardiovascular diseases,[16] cataracts,[13] cognitive dysfunction,[88] and carcinogenesis;[124] however, these are beyond the scope of this review article. The combined risk of radiation-induced mortality for a Mars mission was estimated to be around 5%, with an upper 95% confidence interval near 10%.[27] Morbidity is dependent on the level of radiation exposure, and early mortality is often due to gastrointestinal mucosa destruction leading to fluid loss via extensive vomiting and diarrhea, and bone marrow depletion leading to significant anemia, thrombocytopenia, and immunosuppression.[74] Acute physiological support entails aggressive control of vomiting, fluid and electrolyte replacement, antibiotics, and transfusion of blood products.[87] Adequate treatment can only be achieved through accurate quantification of exposure levels and clinical markers, such as the rate of decline of absolute lymphocyte count and the time to onset of emesis and chromosomal changes, to discern disease severity and anticipate future complications.[87]

Although in-flight radiation dosimeters and radiation sensors are commonplace on the ISS, quantifying changes in chromosomal structures and molecular signatures offers a more accurate estimation of the radiation dose absorbed by the body. However, these techniques are often laborious and require dedicated expertise. Considerable success has been achieved in automating and streamlining the dicentric assay, the current gold standard of radiation dosimetry.[55,70,104] For example, Jang et al.[55] proposed a new deep learning system, and doses ranging from 1–4 Gray agreed well within a 99% confidence interval of gold-standard measurement methods. In their recent review, Ainsbury et al.[2] have also highlighted the potential for AI to predict personalized risks and responses toward radiation exposure and the significance of translating such technology to aerospace research. A note of caution for translation toward space application is that the dose–effect correlation is different between terrestrial ionizing radiation and space radiation.[69]

Point-of-care automated quantification of full blood count is limited on both the ISS[56] and Earth,[7] likely due to poor extrapolation from small volume samples. To overcome this, new systems incorporating AI have been developed and validated. For example, the Sight OLO system, a cubic-foot-sized device developed by Bachar et al., was shown to achieve accuracy comparable to clinical hematology analysers[7]; the Hilab system developed by Gasparin et al. also provides low-cost and accurate analysis of full blood count parameters.[41]

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Despite all preventative and protection measures, crews may still be affected by acute radiation sickness. In this situation, it may be necessary to provide the affected individuals with supportive treatment, including hemodynamic resuscitation, intravenous (IV) fluid restoration, and bone marrow transplant.[34] AI tools could assist in this task, with systems dedicated to hemodynamic optimization, for example, in the perioperative context or in sepsis (see following sections).

Surgical Emergencies and Anesthesia

Conditions requiring surgical intervention are expected to have one of the highest impacts on a potential Mars mission. Within the NASA HRR, three standalone "red" risks have been identified for surgery-related conditions (renal stones, bone fractures, and injuries during extravehicular activities).[86] Additionally, data from analog populations and previous spaceflight estimated that the risk of conditions potentially requiring general anesthesia to be around 2.56% on a 950-d mission to Mars with six crewmembers.[22] Some of the risks are directly increased by exposure to the space environment. For instance, significant bone mass loss in microgravity could increase the risk of fractures during extravehicular activities.[48] Managing surgical complications will pose major challenges due to equipment and manpower constraints, such as limited perioperative imaging capabilities and lack of both surgical equipment and on-board surgical expertise.[8]

Realistically, nonoperative options should be attempted first, with surgery reserved to conditions that threaten the loss of limb or life.[66] Open surgery in weightlessness may be restricted as body fluids become hard to control in microgavity.[48] For example, in the case of a femur fracture, temporary stabilization such as long leg plastering or external fixation may be considered. Regional anesthesia should also take preference over general anesthesia in the spaceflight setting, because of their lower risks and requirement for preoperative, intraoperative, and postoperative resources.[66] If general anesthesia were necessary, adapted approaches such as the use of IV ketamine, which is commonly used in austere settings, and the use of video laryngoscopes for airway management could increase safety and likelihood of success.[66,108] These techniques could be carried out by the crew under the guidance of validated instructional videos, as real-time telecommunication and remote control of equipment will be precluded by transmission delays.[57]

Despite the enormous challenges involved, we anticipate that several AI applications could assist remote crewmembers in caring for a surgical patient. Preoperative imaging is a crucial step in surgical planning. Among the different imaging modalities, ultrasonography is currently and will likely remain the leading imaging modality for human spaceflight.[61,97] Among the high risk surgical conditions listed in the NASA HRR, ultrasonography-based AI tools have proven useful in the detection of renal stones[82,90] and soft-tissue injuries.[28,103] For bone fractures, AI has only been developed for the pediatric population,[131] in whom radiation exposure from plain radiographs or computed tomography is a significant concern.[119] However, given the increasing interest in implementing ultrasonography for point-of-care diagnosis of bone fractures,[18,89] it is reasonable to expect future AI research to extend its application to adults.

The correct identification of anatomical landmarks is also crucial to ensure safety and success during surgery, especially if emergency procedures were to be carried out by nonexpert crewmembers. Semantic segmentation, i.e., partitioning an image to locate underlying structures and boundaries,[114] has been applied to medical imaging to provide intraoperative guidance, such as avoiding biliary tract injury during laparoscopic cholecystectomy[76] and ureteric injury during rectal cancer resection.[62] Although autonomous surgical robots are a long way away, some exciting progress has been made. For example, the Smart Tissue Autonomous Robot developed by Johns Hopkins University matched or outperformed human surgeons in autonomous bowel anastomosis in animal models.[102] However, researchers must develop ways to minimize the mass and volume of these advanced hardware until they can be carried on board.

The use of AI in anesthesia has been reviewed in several articles.[49,51,105] One of the most useful areas for translation into spaceflight is closed-loop systems designed for automated anesthesia delivery.[71,83] They are usually based on real-time measurement of electroencephalogram data and vital signs, which are surrogate markers for the depth of sedation. Perioperative hemodynamic optimization has also been developed to decrease postoperative morbidity and reduce both hospital length of stay and hospital costs in studies involving major surgery.[64,92,111] Most of these systems work by administering IV fluids and vasopressors at a rate guided by an AI controller, informed by physiological parameters which can be invasive or noninvasive, and include blood pressure, cardiac output, and/or estimators of fluid responsiveness.[64]

Finally, AI has seen its application for postoperative care to predict complications such as surgical site infections,[44] bleeding,[19] intensive care unit admission, and mortality.[20] This might have important implications for accurate planning and allocation of the limited resources, as well as optimization of the recovery process for crewmembers who require surgery in future spaceflight.

Spaceflight-Associated Neuro-ocular Syndrome

Spaceflight-associated neuro-ocular syndrome (SANS) is a constellation of structural and functional changes to astronauts' vision after prolonged exposure to the space environment.[3] This syndrome was observed in around 23% of short-duration Shuttle crewmembers and 48% of long-duration ISS astronauts.[130] Affected individuals presented with one or more of the following clinical signs: refractive error, optic disc edema, choroidal folds, cotton wool spots, and optic nerve thickening.[67] The main contributor of SANS is thought to be microgravity-induced cephalad shift and the associated increase in intracranial pressure, venous congestion, and changes in intraocular pressure; however, its exact etiology remains unknown.[67] This has prevented the development of effective countermeasures other than symptomatic

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relief, such as prescription glasses to adapt to refractive changes.[3] A few risk factors for SANS have been identified, including duration of spaceflight, high salt diets, intensive resistive exercise, increased ambient carbon dioxide concentrations, and nutritional deficits.[3]

Although intracranial pressure changes underlie much of the pathology of SANS, it has never been measured during spaceflight. This is because the process is invasive, requiring insertion of a needle through the vertebral discs into the cerebrospinal space, and risks bleeding, infection, and injury to local structures such as the spinal cord. Novel AI tools or models that rely on surrogate markers for intracranial pressure have emerged in recent years, with the potential of accurate noninvasive estimation.[35,37,60]

Currently, SANS diagnosis relies on manual interpretation of in-flight ocular ultrasound, fundoscopy, and optical coherence tomography scans, which astronauts must collect with real-time remote guidance by ground experts.[3] However, this privilege will soon be lost with deep space missions. Proof of concept AI applications to automatically interpret these imaging modalities have been proposed.[116] The European Space Agency recently carried out the "Retinal Diagnostics" research project on the ISS, which made use of a portable retinal imaging device linked to an iPad, where images taken were fed into an AI model for rapid identification and monitoring of ocular abnormalities.[110] NASA has also announced plans to develop a multimodal visual assessment system, creating a "pooled" diagnosis from multiple diagnostic tests as they have different sensitivities and specificity at picking up the ocular signs associated with SANS.[72]

AI solutions could address the different shortcomings of SANS research and incorporate greater automation in the prediction, early diagnosis, and monitoring of SANS. However, no potential AI application dedicated to SANS treatment could be identified.

Infections and Sepsis

On Earth, sepsis, which refers to severe infection with organ failure, is a primary cause of mortality and the most expensive condition treated in hospitals.[39,42,118] Among the medical conditions that threaten astronauts, sepsis and infections are estimated to have the highest negative impact on mission success (ranked 1st out of 30 conditions).[96] The estimated incidence of infection during a 950-d Mars mission with 6 crewmembers (with 4 on the Mars surface) is a staggering 90.49 events.[22] The most likely sources of infections are acute respiratory infection and skin and subcutaneous tissue infection.[9]

Evidence from spaceflight shows that the risk and severity of infections, both newly acquired and reactivated, are increased due to physiological changes in space. First, the immune system is downregulated by microgravity, radiation, and chronic stress.[115] This is due to significant changes such as lymphoid hypoplasia,[107] decreased phagocytic activity,[94] and decreased T cell activity.[75] Second, the virulence of microbial pathogens, which is the ability to manifest and cause severe disease, is increased in microgravity. Microgravity allows aerosolized pathogen-containing particles to persist, increasing their likelihood of inoculating the human body.[80] Once inside the host, microgravity-induced phenotypic changes, such as more extensive biofilm structures and enhanced antibiotic resistance, complicates effective pathogen clearance.[45,80]

On Earth, sepsis has received considerable attention in AI research. Various systems have been developed and tested in almost every aspect of sepsis management, including early diagnosis, phenotyping, and sepsis treatment. *InSight*, a prediction tool built upon six vital signs, used data from a multicenter cohort of more than 684,000 patients to predict which patients would develop sepsis and whether they would proceed into severe sepsis or septic shock.[73] It achieved an area under the curve of 0.85–0.96 and outperformed traditional sepsis scoring systems.[73] To guide fluid and vasopressor therapy, the cornerstone of sepsis treatment,[68] AI algorithms have been developed to provide treatment guidance and retrospective data show that treatment regimens close to the AI recommendations resulted in the lowest patient mortality.[63]

A final issue with treating infections, as well as other conditions, is that drugs degrade faster in space.[32] A possible solution would be to generate medicines and antibiotics in situ at a Mars/Moon outpost, a concept that has been proven feasible in principle.[33]

Cardiovascular Deconditioning and Postflight Orthostatic Intolerance

Exposure to weightlessness alters blood volume, blood flow, and pressure distribution, which manifests in structural and functional changes in the cardiovascular system,[6] contributing to orthostatic intolerance and decreased exercise capacity.[10,24,50] Postflight orthostatic intolerance (PFOI), the inability to maintain blood pressure while in an upright position after re-exposure to gravity,[109] is one of the most well-documented symptoms in astronauts[12] and was described as "the most significant operational risk associated with the cardiovascular system of astronauts."[24] The etiology of PFOI is complex and includes a hypoadrenergic response to the orthostatic position, alongside plasma volume losses and fluid shifts.[109] These lead to an excessive fall in cardiac output and/or inadequate vasoconstriction to maintain cerebral blood supply,[123] leading to symptoms of light-headedness, dizziness, presyncope, and syncope.[24] This problem affects about 20–30% of crewmembers who fly short-duration missions and 83% of astronauts following long-duration missions.[128] Symptom manifestation could prohibit an astronaut from standing and performing emergency egress from a spacecraft after landing.[24] Identified risk factors for PFOI include: 1) being female; 2) lower norepinephrine response upon standing and subsequently insufficient increase in peripheral vascular resistance; 3) lower diastolic and supine systolic blood pressure; 4) duration of the orthostatic and heat stress; 5) length of the mission; and 6) participation in in-flight exercise countermeasures.[109]

Conventionally, during the prelanding phase, prevention of PFOI is done through oral fluid-loading, oral midodrine (an alpha-adrenergic agonist), and/or subcutaneous octreotide

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(a somatostatin analog which is currently the preferred option).[109] The treatment regime is based on individual risk factors and determined by flight surgeons on the ground. To provide objective and more quantifiable guidance, an AI-based risk stratification score could prove useful. This could consider firstly, the vast number of risk factors identified in previous research, and secondly, the success of similar scores developed for related Earth-based diseases.[26,59,121] For instance, Costantino et al.[26] tested artificial neural networks in the risk stratification of patients evaluated in the emergency department for syncope. It was based on ten variables, including sex, age, syncope during exertion, trauma following syncope, and presence of abnormal electrocardiogram, and was effective in predicting the short-term risk of patients with syncope.

After landing, a combination of IV fluids and vasopressors are administered by flight surgeons to treat hypotension, and rehabilitation is carried out in comprehensive medical facilities on Earth.[10] To guide hemodynamic optimization of crewmembers during re-entry and in the postlanding phase, inspiration can be taken from closed-loop systems developed for the hemodynamic management of surgical patients.[92,111] These systems require a controller that administers the drugs to maintain hemodynamic parameters (blood pressure, cardiac output) within a target range. Ideally, these closed-loop systems require continuous blood pressure monitoring, which is generally invasive. However, potential noninvasive or minimally invasive solutions exist, e.g., the *Finapres* system.[36] Convertino[25] also described a wearable finger photo-plethysmographic device with integrated AI, which could collect and perform real-time feature extraction of arterial waveforms for the early detection of central hypovolemia and circulatory collapse. In particular, the author described its potential use in PFOI for guiding the administration of IV fluids before the onset of a syncopal episode during re-entry and landing. These technologies still require future validation in operational missions and partial gravity. Finally, to guide postlanding hemodynamic optimization, the crew could also rely on ultrasound-based echocardiographic assessment, whose interpretation could be automated by an AI.[5]

Medical Conditions of Interest with No Identified AI Applications

There are many medical conditions for which we could not identify relevant existing or potential AI applications, or that AI would not serve as the best mitigation technique. These include the issues of muscle and bone loss, nutritional aspects of spaceflights, exposure to toxic environments (including fire and pollution of the cabin atmosphere by lunar or Mars dust, irritants, or chemicals), space motion sickness, and decompression sickness during extravehicular activities.

A potential explanation is that conditions such as muscle and bone loss and the nutritional aspects of spaceflight do not necessitate immediate, critical decisions by a medical expert, unlike shock or induction of general anesthesia.[77] Mitigation strategies could be planned well before commencing the mission. Prevention, diagnosis, and mitigation for other conditions, such as space motion sickness and decompression sickness during extravehicular activities, are relatively well understood and controlled,[14,23] even in the absence of dedicated medical expertise. In terms of exposure to toxic environments (including fire and pollution of the cabin atmosphere by lunar or Mars dust, irritants, or chemicals), the main focus of mitigation should be centered on preventative hardware and crew training.[77] Taken together, AI technology would most likely not be very beneficial in the conditions listed above and will not be discussed in this paper.

DISCUSSION

This review has identified many AI applications that target the medical conditions of the highest concern identified by the space medicine community for long-duration space missions beyond low Earth orbit. We summarized our main findings in **Table II**. Broadly, they may: 1) reduce the incidence of the conditions through screening and prevention, 2) improve the timeliness and accuracy of their diagnosis, and 3) support crews in managing these conditions. As such, the AI applications identified here have the potential to improve crew self-reliance when dealing with serious medical conditions in a context where evacuation will be impossible and telemedical support will be drastically limited.

Among the research we identified, we can highlight several core applications that have the greatest potential for translation into space and impact for future crews. AI chatbots designed to prevent and mitigate behavioral and mental health conditions have demonstrated their benefit on Earth and have been validated in different clinical trials.[1] Similarly, AI-based analysis of ultrasound, optical imaging, and retinal photographs are now widely used on Earth[122] and have been researched and tested on the ISS.[110] Intelligent closed-loop systems capable of restoring hemodynamic stability with noninvasive or minimally invasive sensors[36,111] would find a wide range of applications: for example, in acute radiation sickness, PFOI, severe trauma, and sepsis.

In contrast, nascent technologies such as space radiation risk prediction and protection, or autonomous surgical robots, cannot be safely deployed for use in human spaceflight until better evidence is available. Also, a number of conditions, such as space motion sickness and bone and muscle loss, represent poor targets for AI technology because alternative mitigation strategies already exist or real-time decision-making is not required.

Although the future for adopting AI systems in space medicine is promising, we must acknowledge several barriers and limitations associated with deploying these technologies in space. One of the main limitations is the availability of data for training and prospective validation of AI models in real-world clinical environments. Historically, only around 600 people have traveled to space.[120] Data collection has been limited by the equipment available on board the spacecraft, and much of the data has remained confidential as test subjects can easily be identifiable.[9] This could prove a problem for model training because the

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Table II. Summary of the Main Findings: Most Promising AI Applications That Could Improve the Prevention, Assessment or Management of the Conditions of Interest.

CONDITION	PREVENTION	ASSESSMENT	TREATMENT
Psychological and Mental Health	Artificial companionship and work assistance	AI chatbots for psychotherapy, coping skills, social support, and expressive interviewing	
Acute Radiation Sickness	Personalized risk and response prediction from radiation exposure	Biological radiation dosimetry	Closed-loop hemodynamic optimization
Surgical Emergencies and Anesthesia	Prediction of postoperative complications	Automated image analysis of ultrasound imaging	Semantic segmentation of anatomical structures Autonomous surgical robot Closed-loop anesthesia delivery Closed-loop hemodynamic optimization
Spaceflight Associated Neuro-ocular Syndrome	/	Noninvasive intracranial pressure measurement Automated image analysis for fundus images, ultrasound, Optical Coherence Tomography	/
Infections and Sepsis	Sepsis prediction	Early sepsis detection	Sepsis resuscitation In-situ antibiotic generation
Cardiovascular Deconditioning (Postflight Orthostatic Intolerance)	Risk stratification tool for syncope	Early detection of central hypovolemia and circulatory collapse Automated echocardiographic assessment	Closed-loop hemodynamic optimization

best AI performance is typically achieved with large to very large datasets. For instance, the seminal work on deep learning diabetic retinopathy classification used over 128,000 images for training,[47] while outcome prediction models from hospitalized patients used over 46 billion data points.[95] The same problem could also impact prospective model validation, which is already a significant barrier to the safe deployment of medical AI on Earth. A recent meta-analysis on AI for medical imaging, one of the most active areas of medical AI research, identified only nine prospective studies and ten randomized control trials.[84] Medical AIs that have not undergone rigorous validation are at high risk of bias[84] and unsafe to be used during spaceflight, when clinical decisions could have significant implications on crew survival and mission success. Fortunately, the recent push by NASA and the Translation Research Institute for Space Health to create an open biomedical dataset could pave the way for greater involvement of the research community in developing AI systems for space medicine.[120] Opportunities will also open up with the boom in space tourism that is expected to see a drastic increase in the number of spacefarers.[120]

Another limitation is related to the quality of data used by the AI models for space medicine, which can be influenced by several factors. Most AI models discussed in this paper have been developed using data collected from the ground and from subjects who could have significantly different physiological profiles compared to spacefarers. Space-induced physiological drifts, changes in disease characteristics, and shifts in patient cohorts may render the models invalid when transferred from ground settings into space. For example, the optimal blood pressure target in shock states might need to be recalibrated for the Martian gravity, which is only 38% of the Earth's.[98,127] Historical spaceflight data could be used, but its quality is impacted by operational factors and underreporting of symptoms of astronauts, which are well-recognized problems in space medicine. For example, in PFOI, severely affected crewmembers are either not tested or tested at a later time when they are sufficiently well to participate in testing[109]; in decompression sickness, symptoms are often not reported due to concerns about losing the license for further spaceflight.[23]

Hardware constraint is also an important limitation to the successful deployment of AI technology in space medicine. Unlike psychological and mental health, where support could be delivered completely virtually, medical conditions might require a much greater payload than what could be available in future space vehicles for accurate diagnoses and effective countermeasures. For instance, exploration vehicles might not have the capability to carry medicines and blood products with limited storage life and additional refrigeration requirements.[81] Undoubtedly, medical payload must be meticulously prioritized for conditions with the greatest expected mission impact, and any equipment required on planetary habitats should be pre-deployed separately. Sustainable solutions such as on-site fabrication of medications[100] and IV fluids,[78] as well as three-dimensional printing of surgical equipment,[129] should receive extensive research focus and comprehensive validation on Earth before deployment in future space missions.

Finally, many space medicine conditions cannot be matched to existing or prospective AI applications, such as demineralization, muscle loss, exposure to planetary dust, or decompression sickness. We argue that AI technology would most likely not be instrumental in preventing, detecting, or mitigating these conditions, which can already be managed with existing knowledge or do not require real-time urgent decision-making.

AI technology has significant potential to support crew health and improve crew autonomy during future long-duration interplanetary spaceflights. However, we must address numerous challenges and limitations such as data poverty, data underrepresentation and biases, and underlying differences between terrestrial and spaceflight physiology and disease before the potential of AI technologies can be realized.

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