Managing Select Medical Emergencies During Long-Duration Space Missions

Kim-Anh Tran; Neal W. Pollock; Pierre-Marc Dion; Marjorie Lapierre; Sophie Tremblay; William Witteman; Caroline Rhéaume; Daniel Lafond; Félix-Antoine Fortier; Andréanne Marion; Lara Dutil-Fafard; Camille Morin; Geneviève LePabic; David P. M. Monnot; Patrick M. Archambault

INTRODUCTION: Space agencies and private industries worldwide are planning long-duration missions, which come with complex medical challenges. Crews must be prepared for medical emergencies due to longer mission durations, increased travel distance, communication delays, and higher levels of isolation. This study aimed to systematically review the existing literature and knowledge gaps that could be related to the management of medical emergencies during long-duration space missions.

METHODS: A scoping review was conducted following the PRISMA extension for scoping reviews. Electronic databases, including ARC, Embase, IEEE Xplore, Medline Ovid, PsycINFO, and Web of Science, were searched from inception to June 1, 2023. Empirical study designs published in English or French were eligible for inclusion provided they described the management of at least 1 of 10 prioritized potentially mission-critical medical conditions.

RESULTS: A total of 484 full-text studies were assessed for eligibility, with 99 included in this review. Conditions with the highest representation were spaceflight-associated neuro-ocular syndrome ($N = 23$), herniated disk ($N = 22$), and nephrolithiasis ($N = 22$). Conditions with the least representation were cerebrovascular accidents ($N = 4$), eye penetration ($N = 3$), and retinal detachment ($N = 2$). The duration of missions varied between 5 and 438 d for studies conducted in space. The data reflected the scarcity of evidence concerning prolonged deep-space exposure beyond the Earth's magnetosphere.

DISCUSSION: Substantial medical autonomy is essential for the success of long-duration space missions, when medical support and even communication will be limited. Future research should prioritize knowledge gaps to improve preparedness and medical autonomy for space exploration activities.

KEYWORDS: astronaut health, exploration, medical autonomy, spaceflight, space medicine.

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Complex medical challenges must be considered as space agencies and private industries prepare for long-duration space missions to the Moon, Mars, and beyond.[1–3] Exploratory missions will require crews to endure longer durations, increased travel distance, communication delays, and higher levels of confinement and isolation.[4] Distance and logistical challenges will make it increasingly difficult to return to Earth in a timely manner, necessitating higher levels of medical autonomy.[5] It is crucial that crewmembers are prepared to handle medical emergencies, even when they may have limited medical training.[5,6] Resources that include diagnostic and decision-aid systems will be important to support astronaut teams to manage mission-critical events. Effective tools will help manage crewmember health during missions and will also aid in planning, medical technology development, and critical resource availability.

From Université Laval, Quebec City, Quebec, Canada; McGill University, Montreal, Quebec, Canada; Centre de recherche intégrée pour un système apprenant en santé et services sociaux de Chaudière-Appalaches, Lévis, Quebec, Canada; University of Ottawa, Ottawa, Canada; Thales Research and Technology Canada, Quebec City, Quebec, Canada; and Université de Montréal, Montreal, Quebec, Canada

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Address correspondence to: Patrick M. Archambault, M.D., M.Sc., FRCPC, Department of Family Medicine and Emergency Medicine, Université Laval, 1050 Avenue de la Medecine, Québec G1V 0A6, Canada; patrick.archambault@fmed.ulaval.ca.

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Crew selection is crucial in mitigating medical risks during space missions. To aid the medical preparedness and autonomy of crewmembers during exploration-class missions, it is imperative to implement robust and adaptable systems that support medical diagnosis, treatment, and clinical skill maintenance.[7] Recent efforts in this field have focused on developing clinical decision rules,[8,9] trend analysis for prognostic and health management,[10] and data architecture for clinical decision support systems.[11] To support the creation of decision support systems, the Canadian Space Agency (CSA) sponsored a team of scientists from Thales Research and Technology Canada (Québec, Canada) and Université Laval (Québec, Canada) to develop an evidence-based database for managing medical conditions in space. The evolving database will contain relevant information on human medical conditions, including hazard, diagnostic and management tools, and prognostic information.[12] To begin to develop this database, a comprehensive review was necessary to highlight the existing literature and identify knowledge gaps related to managing select space-related medical emergencies.

This study aimed to systematically review the existing literature related to 10 prioritized medical conditions that could foreseeably arise with a high likelihood of mission-critical impact during long-duration space missions.

METHODS

This scoping review was conducted based on existing methodology[13,14] and a prospectively published protocol.[15] The review was reported based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR).[16] The design of this study did not require the approval of an ethics committee.

The focus of this effort was on 10 medical conditions previously prioritized by this group[12] drawn from the 100 priority conditions included in the National Aeronautics and Space Administration (NASA) integrated medical model medical conditions list[17]: acute coronary syndrome, atrial fibrillation and arrhythmia, eye penetration, herniated disk, nephrolithiasis, pulmonary embolism, retinal detachment, sepsis, cerebrovascular accident, and spaceflight associated neuro-ocular syndrome (SANS), formerly known as visual impairment and intracranial pressure syndrome.[18]

Procedure

In collaboration with an information specialist, we developed a comprehensive search strategy to address our research question.[12] The specialist identified relevant sources of evidence, and we used combinations of specific medical conditions and space-related terms to ensure a thorough search. We used terms such as "myocardial infarction," "acute coronary syndrome," "atrial fibrillation," "cardiogenic shock," "pulmonary embolism," "stroke," "cerebrovascular disorders," "intracranial pressure," "vision disorders," "retinal detachment," "sepsis," "septic shock," "neurogenic shock," "spinal cord injury," "intervertebral disc," "urolithiasis," and "renal colic" to identify publications about the prioritized medical conditions. Each of these terms was paired with space-related terms such as "astronauts," "space shuttles," "space exploration," "planets," "space flight," "deep space," "long-duration space exploration missions," and "NASA." This strategy was designed to capture literature at the intersection of these medical conditions and space exploration. We searched several scientific databases, including Aerospace Research Central, Embase, IEEE Xplore, Medline Ovid, PsycINFO, and Web of Science, for publications from inception to June 1, 2023. Additionally, we reviewed the reference lists of included studies and previously published systematic reviews, as well as reports available from the CSA and NASA.

We employed a three-step iterative process for literature selection. Studies were screened by six pairs of independent reviewers using Covidence (version 2.0, Veritas Health Innovation, Melbourne, Australia), a web-based systematic review software. A screening tool featuring questions based on predefined eligibility criteria[15] was developed, piloted, and refined. Reviewer calibration occurred during this process, whereby screeners clarified questions and reasons for decision-making. Pairs of independent reviewers conducted eligibility screening of titles and abstracts in duplicate. Studies were excluded at this stage if the two independent reviewers determined they did not meet eligibility criteria. Otherwise, studies proceeded to full-text screening. Disagreements about inclusion or exclusion at each stage were resolved by consensus or through a third member of the research team as needed. The final list of included articles was reviewed by the investigator team to determine if any known additional articles should have been captured.

During the first step of literature selection, studies were retained if they met the following criteria: focused on disease events in space or analogous environments, addressed the incidence or prevalence of diseases in space or among astronauts (from 1990 onward), dealt with equipment or protocols developed for space application (from 1985 onward), or evaluated diagnostic tests or devices in space. Studies were excluded based on language constraints (not written in English or French), irrelevant content, not addressing the target medical conditions, being editorials or letters to the editor, abstract only, conceptual, nonscientific, representing outdated studies on disease incidence or prevalence in space or astronaut cohorts, focusing on inappropriate cohorts, inadequately described methods, clearly flawed methodology, or duplication.

After narrowing the scope of the review, each reviewer independently conducted a second round of screening on the title and abstract. The exclusion criteria were further refined to exclude studies that were not clinically relevant for the 10 target medical conditions. During this step, studies were excluded if they were not directly related to spaceflight exposure, such as high G-force aviation, civilian air travel, helicopter vibration, or unrelated injury. Basic science studies and studies that were not relevant to the 10 target medical conditions (such as orthostatic intolerance and decompression sickness) were excluded. Studies presenting data from human spaceflight missions of any duration were included. Studies were excluded if the reports were inaccessible, if they focused on preflight screening, or they did not pertain to a long-duration spaceflight timeline, such as head-down tilt analog experiments of less than 14 d.

During the third round of screening, full-text studies were excluded if the methodology was not described, if they were review articles or textbook chapters, and if they only contained basic science with no immediate clinical relevance for space missions.

Data Analysis

Individual reviewers extracted the data after a full-text review of studies included in the third phase. A data-charting table was developed using Google Sheets (Google, Mountain View, CA, United States) for the extraction of quantitative and qualitative variables of the included studies. These data fields were based on parameters required by the CSA for its medical conditions parameter database.[15] Accuracy was compared and verified by the reviewer pairs upon completion of data extraction. Critical appraisal is not required for scoping reviews and was therefore not conducted.[14,19]

Included studies were collated and coded by study design, subjects, and settings. The synthesis of results was presented as descriptive narrative summaries of the data on the other parameters for each medical condition. We also reported the included studies' country of origin, agency funding the research, study design, subjects, and context for objective interpretation. Specific recommendations on treatment plans were included when warranted by existing data, but not in cases where evidence was lacking. Knowledge and research gaps were described where appropriate.

RESULTS

The number of studies included at each step of the screening and assessment process is described in **Fig. 1**. The initial search through all databases resulted in 13,295 studies after duplicates were removed. A review of titles and abstracts left 484 manuscripts remaining. The full text review led to the

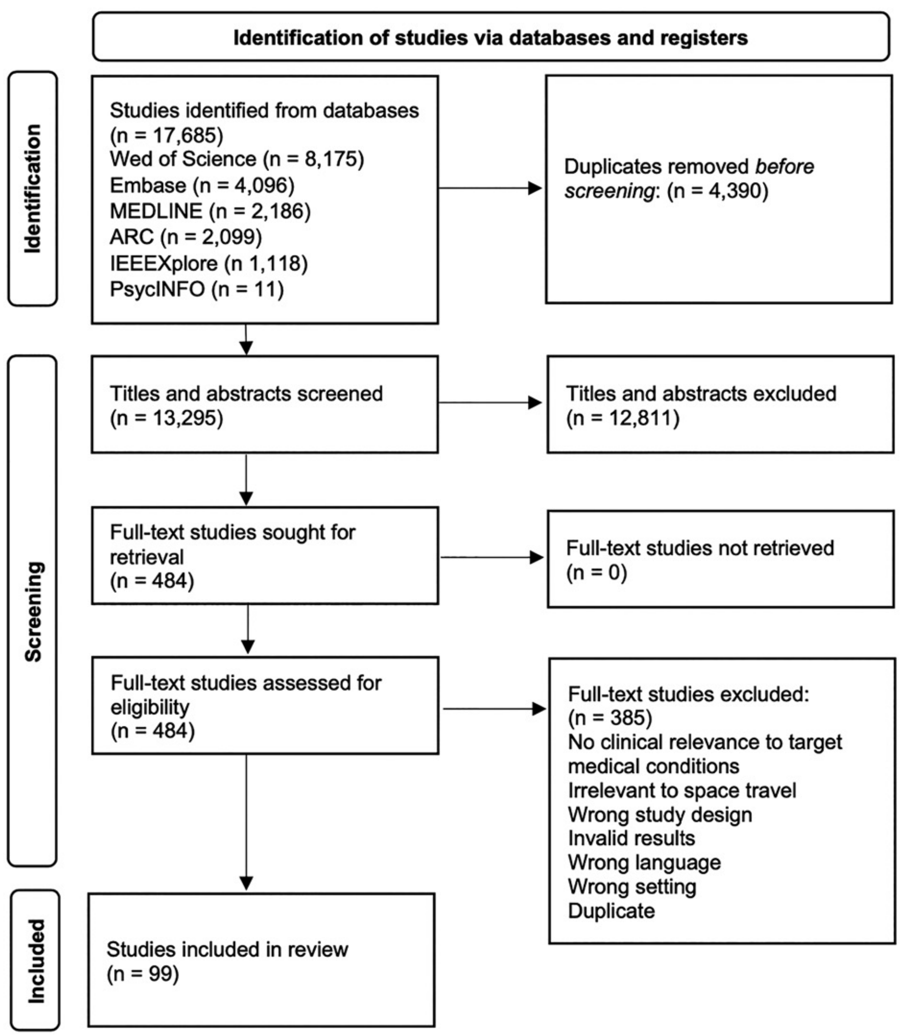

Fig. 1. PRISMA scoping review flow chart.

Table I. Number of Included Studies by Country of Corresponding Author.

	CONDITION									
COUNTRY	**ACS ($N = 7$)**	**AF ($N = 7$)**	**CVA ($N = 4$)**	**EP ($N = 3$)**	**HD ($N = 22$)**	**NL ($N = 22$)**	**PE ($N = 7$)**	**RD ($N = 2$)**	**SEP ($N = 12$)**	**SANS ($N = 23$)**
United States	6	6	3	2	13	20	5	2	12	22
Germany					6					
Russia		1	1	1						
Canada					1	1				
Sweden	1						1			
United Kingdom					2					
France										1
Japan						1				
Netherlands							1			

ACS = acute coronary syndrome, AF = atrial fibrillation and arrhythmia, CVA = cerebrovascular accident, EP = eye penetration, HD = herniated disk, NL = nephrolithiasis, PE = pulmonary embolism, RD = retinal detachment, SEP = sepsis, SANS = spaceflight associated neuro-ocular syndrome.

removal of 385 studies. A total of 99 studies were included in this scoping review.

The characteristics of the included studies are presented in **Table I**, **Table II**, and **Table III**. The conditions with the highest representation were spaceflight-associated neuro-ocular syndrome ($N = 23$), herniated disk ($N = 22$), nephrolithiasis ($N = 22$), sepsis ($N = 12$), acute coronary syndrome ($N = 7$), atrial fibrillation and arrhythmia ($N = 7$), and pulmonary embolism ($N = 7$). Conditions with the least representation were cerebrovascular accidents ($N = 4$), eye penetration ($N = 3$), and retinal detachment ($N = 2$).

Among the included studies, the most frequent type of study design was observational ($N = 69$), with 19 experimental studies, 8 quasi-experimental studies, and 3 qualitative studies. Humans (astronauts or analog civilian cohorts) were the most studied subjects compared with animals and other models (e.g., virtual/theoretical, cadaver, cell culture, infectious pathogen) for all medical conditions. Sepsis-related studies had a similar number of studies on animals and other models ($N = 6$) compared to studies on human subjects ($N = 6$). The included manuscripts investigated various analog environments: head-down tilt ($N = 28$), hindlimb suspension ($N = 3$), low-shear modeled microgravity ($N = 1$), and ionizing radiation generation on Earth ($N = 2$). In the studies conducted in space ($N = 67$), the total mission duration varied between 5 and 438 d. There were no existing data for deep space exposure beyond the Moon and extremely limited data for exposures beyond the Earth's magnetosphere.

The following sections present our narrative summary of the evidence identified for the 10 selected medical conditions presented in descending order by condition severity and threat on mission success and crew health: acute coronary syndrome, pulmonary embolism, cerebrovascular accident, sepsis, atrial fibrillation and arrythmia, spaceflight-associated neuro-ocular syndrome, eye penetration, retinal detachment, nephrolithiasis, and herniated disk.

Acute coronary syndrome is a condition that could have serious consequences on long-duration space missions.[20] However, its pathophysiology in space was not detailed in the included studies. A ground-based head-down tilt position immobilization study showed that platelet activation markers (P-selectin and platelet-derived growth factor) were downregulated after long-term immobilization.[21] The ground-based incidence of acute myocardial infarction-induced sudden cardiac arrest has been estimated to be 1:33,000 person-years.[20] There was no evidence that being an astronaut is a risk factor for cardiovascular disease for exposures to date.[22] However, researchers suggest that prolonged radiation during missions may increase this risk.[23,24] The diagnosis and treatment of acute coronary syndrome in space were not documented in the included studies. Still, an event sequence diagram for acute myocardial

Table II. Number of Included Studies by Organization Funding the Study.

	CONDITION									
ORGANIZATION	**ACS ($N = 7$)**	**AF ($N = 7$)**	**CVA ($N = 4$)**	**EP ($N = 3$)**	**HD ($N = 22$)**	**NL ($N = 22$)**	**PE ($N = 7$)**	**RD ($N = 2$)**	**SEP ($N = 12$)**	**SANS ($N = 23$)**
National Aeronautics & Space Administration	6	6	3	2	10	18	5	2	11	18
European Space Agency	1				6		2			
National Institutes of Health					3	2			1	
Multiple agency international collaborations			1		3	1				
Local funding						1				4
Russian Space Agency		1		1						
Centre national d'études spatiales										1

ACS = acute coronary syndrome, AF = atrial fibrillation and arrhythmia, CVA = cerebrovascular accident, EP = eye penetration, HD = herniated disk, NL = nephrolithiasis, PE = pulmonary embolism, RD = retinal detachment, SEP = sepsis, SANS = spaceflight associated neuro-ocular syndrome.

Table III. Number of Included Studies by Study Characteristics and Dates of Publication.

STUDY CHARACTERISTIC	CONDITION AND DATE OF PUBLICATION (MEDIAN, IQR 25–75%)									
	ACS (*N* = 7) 2015 (2012-2017)	**AF (*N* = 7) 2004 (1999-2012)**	**CVA (*N* = 4) 2016 (2016-2017)**	**EP (*N* = 3) 2006 (2005-2011)**	**HD (*N* = 22) 2013 (2010-2016)**	**NL (*N* = 22) 2007 (1999-2009)**	**PE (*N* = 7) 2013 (2011-2019)**	**RD (*N* = 2) 2008 (2006-2009)**	**SEP (*N* = 12) 2007 (2003-2014)**	**SANS (*N* = 23) 2017 (2013-2021)**
Study Design (n)										
Observational	6	5	4	2	17	16	5	2	8	14
Experimental	1				5	4	1			8
Quasi-experimental		1				2			4	1
Qualitative		1		1			1			
Study Subjects (n)										
Human	6	7	3	3	17	20	7	2	6	21
Animal	1		1		4	2			4	1
Modeling/Microbiological					1				2	1
Study Context (n)										
Space	4	5	3	2	11	14	5	2	8	15
Analog	2	2			11	6	2		4	7
Earth	1		1	1		2				1

ACS = acute coronary syndrome, AF = atrial fibrillation and arrhythmia, CVA = cerebrovascular accident, EP = eye penetration, HD = herniated disk, NL = nephrolithiasis, PE = pulmonary embolism, RD = retinal detachment, SEP = sepsis, SANS = spaceflight associated neuro-ocular syndrome.

infarction management and possible outcomes has been described.[20] Investigation and management of an acute coronary syndrome could include electrocardiography,[25] echocardiography,[26] defibrillation,[20] and cardiopulmonary resuscitation.[27] None have been studied in the real context of an in-flight acute coronary syndrome. More experience is needed to specify the risk of in-flight acute coronary syndrome and more research to determine potential treatment options such as thrombolysis since an acute coronary syndrome could cause cardiogenic shock and a sudden cardiac arrest, two conditions with low survivability and a high negative impact on missions.[28]

Pulmonary embolism is another condition that could have important consequences if left undiagnosed and untreated for future exploration-class missions.[29] The risk of pulmonary embolism may be increased during spaceflight by microgravity, oral contraceptives, and blood stasis, as supported by the Virchow triad.[29–31] However, other studies have found conflicting results showing an absence of activation of coagulation markers in ground-based long-term immobilization head-down tilt position studies.[21,32] Most of the risk factors associated with phlebitis and pulmonary thromboembolism are likely to be minimized by the selection of healthy candidates as astronauts.[29] For air embolism, one study did not show any ventilation-perfusion change during forced spirometry associated with extravehicular activity denitrogenation protocols.[33] Doppler ultrasound appears to be the optimal imaging modality in microgravity for the diagnosis of thrombosis since it is likely to be accessible and can be performed by astronauts.[29] In a recent cohort study, two astronauts were diagnosed with asymptomatic intrajugular thrombosis[29]: one thrombus diagnosed prospectively was occlusive[30] while the other thrombus was partial and diagnosed retrospectively.[29] For the astronaut whose thrombus was diagnosed prospectively, therapeutic anticoagulation with low-molecular-weight heparin was started initially, followed by direct oral anticoagulation for a 3-mo total regimen while aboard the International Space Station, and then thromboprophylaxis until return to Earth. Both astronauts reported favorable outcomes.[29] Further investigation is required regarding the diagnostic algorithm for pulmonary embolism in space.[30] This will involve the need for better understanding of the impact of long-duration spaceflight on lung physiology[34] and exploring the use in space of diagnostic tools such as transthoracic echocardiography to look for indirect signs,[26] biomarkers like D-dimers, and the use of lower body negative pressure devices as a preventive measure.[29]

Cerebrovascular accidents can also have serious negative impacts on long-term space missions.[28] To our knowledge, in-flight diagnosis and treatment of a cerebrovascular accident has not been described. While the microgravity environment has not been identified as a risk factor, the potential effects of space radiation on vascular endothelium could heighten the risk for vascular disease, potentially leading to cerebral arterial occlusive disease.[23] Decreased cerebrovascular autoregulation in prolonged exposure to microgravity could also increase the infarct size of a cerebrovascular accident.[35] Although the incidence rate of cerebrovascular accidents among astronauts is not statistically different from nonastronauts,[22] the potential negative impact of such an event on mission success has been estimated as high.[28] Although the development of portable computed tomography and magnetic resonance technology for long-duration space missions is ongoing,[36,37] routine imaging like computed tomography and magnetic resonance performed in space for investigation of stroke have not been documented. Transthoracic echocardiography has been performed in flight by crewmembers to detect cardiac abnormalities.[26] Even though cardiovascular diseases or defects can be the etiological basis of stroke, the clinical value of echocardiography in the investigation of stroke occurring in space remains unknown. Research efforts should focus on establishing a comprehensive cerebrovascular accident contingency plan. In particular, research is needed to develop evidence-based protocols to support rapid diagnosis using validated clinical decision rules and in-flight portable imaging tools, such as computed tomography, magnetic resonance, and ultrasonography, combined with pharmacological interventions like thrombolytics. Additionally, rehabilitation strategies and ongoing monitoring would be essential components of the treatment plan, depending on the mission context and distance from Earth.

Sepsis due to bacterial[38,39] or viral[40–42] infections in mice[38] and in astronauts[43] have been documented in microgravity settings. Infections seem to increase with the duration of microgravity exposure, which appears to activate latent pathogens[40,43,44] and disturb the immune system.[44–46] Low-dose radiation exposure over long periods of time can also damage immune hematopoietic cell lines.[47] Moreover, genes linked to multidrug resistance and pathogenicity were found on the International Space Station, which constitutes a potential threat to future missions.[48] Research is needed to establish the influence of microgravity and radiation exposure on microbial resistance and pathogenicity. Diagnosis and treatment of sepsis or infection during missions were not addressed in the included studies. Saliva, blood, and urine sampling in flight is possible[40,41,43] and could be useful in investigating these conditions, but the capacity for crewmembers to analyze samples in flight remains unknown. Vaccination before launch[41] and antibiotic therapy[49] have been proposed as countermeasures to infection. Sepsis is considered a medical condition that could significantly reduce survivability and negatively impact long-duration missions.[28] Research on preventing, diagnosing, and treating infections and sepsis in space is needed.

Atrial fibrillation was initially selected as one of the 10 prioritized medical conditions, but we broadened our review to include studies about arrhythmia in general due to lack of evidence. The incidence of arrhythmia in astronauts is unclear, with some researchers finding a higher incidence in astronauts[50] and others not.[51] The prevalence appears to mirror that of the general population.[52] The risk of arrhythmia seems to be dependent on the duration of a space mission.[25,50] Researchers have reported that increased atrial size and high heart rate during training may heighten the risk of atrial fibrillation among astronauts.[52] Increased beta-adrenoreceptor responsiveness after exposure to prolonged microgravity may also be involved in generating junctional rhythms with premature atrial and ventricular contractions.[53] Since electrocardiograms (ECG) are likely to be available during long-duration space missions,[25,51,52] atrial fibrillation can be diagnosed, and crewmembers should be trained to interpret ECGs. Imaging, such as echocardiography, is also possible.[26] One study described a cosmonaut with arrhythmia related to psycho-physiological stress who required treatment with a mix of medications: beta-blockers, a phenothiazine-derived antiarrhythmic (Aetmozin), cardiotropics (potassium and magnesium asparaginate, and riboxin), and benzodiazepines.[54] Further investigations are needed to develop contingency plans and treatment options for arrhythmias in space.

SANS causes vision impairment that affects 15 to 20% of astronauts exposed to long-duration missions.[55] SANS is believed to be a consequence of microgravity-induced vascular fluid shifts[56] and subsequent changes in ocular structure.[57] It has been suggested that SANS may be due to altered cerebrospinal fluid dynamics,[58,59] altered intraocular pressure,[60] vascular congestion,[61–63] and clearance of toxins.[64] Altered connectivity within visual and vestibular-related brain networks has also been observed.[65] Genetic predispositions[66] and altered metabolic pathways[67–69] are believed to have a role in the pathophysiology of this syndrome. One factor that impairs the understanding of SANS is a lack of quantitative, continuous, and reproducible measures of SANS severity.[58,61,64] The most frequently observed manifestations attributed to SANS are hyperopic shift, varying degrees of optic nerve protrusion, optic disk edema,[70–72] posterior scleral flattening, retrobulbar expansion of the optic nerve sheath, and choroidal folds. Following return to Earth, these changes have been partially or totally reversed in some astronauts, but persistent in others.[58,61] There are currently no medications commonly prescribed as in-flight treatment of SANS. Some studies suggested some pharmacological options, including diuretics. Further investigation is required regarding the dose, duration, and effectiveness of pharmacological approaches.[73] Other physical countermeasures such as short-radius centrifuge artificial gravity,[74] impedance threshold breathing,[75] venoconstrictive thigh cuffs,[76] integrated resistance and aerobic exercise,[77] and lower body negative pressure[55,78] also need further research.

Eye penetration is a serious concern for astronauts due to floating debris in microgravity.[28,79] Only one article addressing traumatic ocular injury occurring in space was captured[54] and no specific studies on eye penetration in space were found. Despite the known risk of eye penetration for astronauts,[28,79] data on the incidence rate of this medical condition were not found. Aside from ultrasound, which can be used to diagnose eye pathologies,[80] it is unclear what equipment will be available to assess and manage this condition. Ultrasound is relatively contraindicated for suspected open globe injuries due to the pressure it places on the eye.[81,82] Since eye penetration has a high likelihood of impacting the mission,[28] establishing in-flight treatment options is warranted. Research is needed on the safety of using ultrasound in the context of potential extrusion of ocular content, the prevention of further damage to the eye, including posttraumatic endophthalmitis, and the use of temporary surgical procedures to prevent further deterioration while planning for definitive surgical treatment.

Retinal detachment is a serious vision-threatening condition that could also be a potential threat to long-duration missions, but no studies specifically focused on retinal detachment in space were found. Only two relevant studies were included.[61,80] There was no literature found regarding the occurrence of retinal detachment during or after spaceflight, including its incidence in astronauts and space-related risk factors. Since ultrasound devices are likely to be available on long-duration mission spacecraft, diagnosing retinal detachment through ocular ultrasound examination may be possible with appropriate training.[80] Research is needed to ascertain the likelihood of occurrence to determine the potential threat to long-duration space missions.

Nephrolithiasis is a common problem for astronauts with a higher risk of developing symptomatic nephrolithiasis during and following spaceflight.[83–85] Both short[86] and long-duration[87] missions increase this risk. Several factors contribute to the formation of renal stones in space, including dehydration, dietary changes,[87–89] bone metabolism,[90–92] calcifying nanoparticles,[93] and decreased urine output volume.[84,85,94] Although male sex is a risk factor on Earth, it was not found to be a risk factor in spaceflight.[91,95] Ultrasound diagnosis,[96] nutritional,[86,88,90] pharmaceutical,[97–99] and physical preventive measures,[100,101] and surgical treatments[102,103] have been outlined for the medical management of nephrolithiasis in space.[104] The feasibility of urologic surgical procedures during long-duration space missions has not been described, and restrictions in cargo capacity may limit the applicability of certain preventive measures.

Herniated disk has been described in postflight astronauts,[105] but there is a lack of in-flight data on disk herniation. Even though many bed rest studies exist,[106–108] no record of disk herniation diagnosed and treated during spaceflight was found. Although disk herniation has not been described in space, space adaptation back pain is frequently reported by astronauts.[109,110] Several factors contribute to back pain and the increased risk of herniated disk in space, including intervertebral disc swelling,[111–113] biomechanical changes,[114,115] vertebral bone loss,[116] biochemical alterations to the intervertebral disc,[117–119] and paraspinal muscle atrophy.[120,121] Targeting the main cause of injury will likely help researchers develop the most effective countermeasures.[122] Medical management of disk herniation in space may be possible as ultrasound is available as an imaging modality to assess back pain, spine, and intervertebral disk injuries,[111,123] and, as physical therapeutic measures,[124–126] can help limit the effects of microgravity on the morphology of the spine, its disks, and the surrounding muscles.[106,127] Contingency plans are needed to address disk herniation complicated by severe neurological symptoms.

DISCUSSION

The primary challenge in planning deep-space medical support is the lack of experience with deep-space exposures and the inevitable lessons that will come with them. It is necessary to use ground-based and low-Earth orbital data to gain insights into medical concerns believed to have the potential for major disruption of deep space missions. There are vast knowledge gaps that need to be addressed. Through this scoping review, we synthesized the current knowledge concerning 10 prioritized medical conditions. Our intent was to provide insight into the pathophysiology, diagnosis, and treatment for these conditions with potential relevance to long-term space missions.

We identified multiple studies exploring the pathophysiology of selected medical conditions in space or under simulated microgravity conditions, as well as the use of portable diagnostic modalities. We found many scientific articles on back pain and herniated disks, nephrolithiasis, and SANS, which could reflect the availability of tools or testing capabilities, but the risk and prevalence of most conditions can currently only be speculated upon. Herniated disk and retinal detachment were included in the top 10 priority list of the NASA integrated medical model due to their potential to significantly impact mission success and crew health.[12] Although current research on these conditions in the context of space missions is sparse, their inclusion highlights the need for preventive measures and contingency plans for these potentially debilitating conditions.

This study adds to existing knowledge syntheses[128–130] by employing a robust and systematic methodology in the identification and selection of studies. The use of a structured approach enabled us to systematically review a large number of studies. The medical summaries that were produced informed the creation of a decision support system and system requirements analysis tool that integrated the summaries, diagnostic modalities, potential treatments, and required medical skills into event sequence diagrams with resulting logic models that were used to perform scenario-based queries.[12] Further research needs to expand these summaries to improve the knowledge basis and capabilities of decision algorithms and resource planning tools.

The most important knowledge gap concerns the lack of deep space-based evidence. This was to be expected considering that the first manned long-duration foray into deep space will likely be achieved through the Artemis missions in the coming years.[131] While the available manned space data has relevance, it represents exposures primarily of relatively short duration and almost all within the Earth's protective magnetic field. Deep space missions will be outside the magnetic field and with distances allowing no option for immediate return. The available literature is insufficient to assess the expected risk, but it does serve as an important starting point. Most of the included studies focused on preventative countermeasures against probable pathophysiological mechanisms rather than treatments. Even though potential outcomes for mission success and crewmembers' survivability have been explored,[20,28] no studies have assessed the occurrence and management of a specific pathology throughout the entire course of spaceflight from initial investigation to final outcome. This knowledge gap prevented us from producing evidence-based contingency plans for diagnosis and treatment. While certain diagnostic tools such as ultrasound, biologic fluid analysis, and ECG have been used in flight, we did not find clear evidence that they have been validated to effectively monitor and manage medical conditions in future long-duration missions.

Health risks have been identified and, in some cases, prioritized, but the development of these and other conditions and their incidence in space largely remain to be established. Human experience with prolonged spaceflight outside of near-Earth orbit missions, of multiyear exposure to space, and on the psychological, physical, and physiological responses and complications associated with the combination of extended space travel and extraplanetary activity will undoubtedly provide both confirmation and surprises regarding astronaut health. Even though analog data can provide some insights, the complexity of actual experience cannot be paralleled. The last manned mission outside of the Earth's orbit was 1972 during the Apollo space program, making the recent data on possible outcomes more theoretical than evidence based.

Many published studies are at the level of basic science with yet-to-be-proven clinical significance for long-duration exploration missions. The small number of astronauts and selection bias are likely to remain limitations in data collection for the foreseeable future. Unknowns concerning equipment and skill sets during long-term missions are a challenge in planning for adverse events. The results regarding equipment and necessary crewmembers' medical skills echo recent work[28] reporting that there is no consensus on the medical equipment and supplies that will be available to crew during a long-duration exploration mission, making it difficult to determine if a given medical condition can be diagnosed or treated onboard.

The current state of knowledge provides insight into the needs of extended deep space exploration, but the most important findings will come through actual experience. The collection of research quality data during missions will be critical in furthering our understanding. Astronaut crews should be selected with research drive as an important criterion. As experience grows, insights will improve mission planning, readiness, medical decision-making, and management of medical conditions that may threaten the safety of astronauts and mission performance during long-duration spaceflight. Establishing a living systematic review methodology[132] could increase efficiency in identifying and resolving knowledge gaps and keeping information resources current as new evidence emerges.

This study has several limitations. We did not consider studies written in languages other than English and French. We also excluded studies that focused only on environmental factors such as radiation, even though these may be relevant to developing engineering solutions for the future. It is also possible that some work was misclassified despite our best efforts. Articles on nonspecific medical procedures in flight were not included, such as general imaging,[133] airway management,[134–136] and general surgery,[137] as they remained too broad. Finally, since this effort was a scoping review, we did not conduct an in-depth critical appraisal of the included studies.

Our limited experience in space and with analog studies create substantial challenges in planning for long-duration missions. Integration of the best research data related to space activity is an important step in assessing risk and developing mitigation strategies. We have summarized the literature evidence related to 10 prioritized medical conditions, but the knowledge gaps are extreme regarding both these conditions and the host of others that could play an important role in astronaut health and mission effectiveness. Substantial research effort is needed, with the experience gained in progressive future missions most critical in building readiness. Research should be prioritized to advance tools and to ensure readiness for conditions demanding increasing degrees of medical autonomy.

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Authors and Affiliations: Kim-Anh Tran, M.D., Neal W. Pollock, Ph.D., Caroline Rhéaume, M.D., Ph.D., Félix-Antoine Fortier, M.D., Lara Dutil-Fafard, M.D., Camille Morin, M.D., Geneviève LePabic, M.D., David P. M. Monnot, Ph.D., and Patrick M. Archambault, M.D., M.Sc., Université Laval, Quebec City, Quebec, Canada; Kim-Anh Tran, McGill University, Montreal, Quebec, Canada; Kim-Anh Tran, Neal W. Pollock, William Witteman, MI, Félix-Antoine Fortier, Camille Morin, Geneviève LePabic, and Patrick M. Archambault, Centre de la recherche pour un système de santé apprenant en santé et services sociaux de Chaudière-Appalaches, Lévis, Quebec, Canada; Pierre-Marc Dion, Marjorie Lapierre, and Sophie Tremblay, University of Ottawa, Ottawa, Canada; Daniel Lafond, Ph.D., Thales Research and Technology Canada, Quebec City, Quebec, Canada; and Andréanne Marion, M.D., Université de Montréal, Montreal, Quebec, Canada.

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