Clinical Finding Form (CliFF)

Branch Baseline

ICL95_Space Adaptation - Insomnia

Insomnia is a sleep disorder resulting in a lack of adequate, restful sleep. It is usually characterized by complaints of difficulty sleeping, such as difficulty initiating sleep, difficulty maintaining sleep, early morning awakening, and nonrestorative sleep. A specific form of this condition, Early Insomnia due to Space Adaptation Syndrome, usually occurs in the first 3-5 days of a space mission during the adaptation to microgravity, multiple short light-dark cycles per work day, abnormally long work periods, variations in sleep-wake schedules, shift work, temperature, humidity, medication, and noise. It is distinct from late insomnia which occurs after adapting to spaceflight. General efforts used to partially mitigate this specific condition fall in line with good sleep hygiene measures and include private sleep quarters, noise-reducing ear plugs, window covers, blindfolds and adhering to a consistent schedule if possible. Treatment includes short acting hypnotics. (Putcha, 2008) Of note, use of sleep medications in flight has increased from reported 15% in 1990 to 45% in 2008. (Slack, 2009)

INCIDENCE DATA INCLUDED IN THE MODEL

The model imports the following incidence information from the MEDPRAT Evidence Library Database: incidence data category, space adaption status, EVA status, incidence data type, incidence and occurrence distribution data and incidence data characteristics. Data category defines the type of data available for incidence calculations (i.e. raw data vs. adjusted data). Space adaptation identifies medical events that where onset occurs in the first 5-7 days of flight and does not reoccur. EVA-related incidence values identify medical events that occur only during an EVA. Incidence values types vary by data category and define the number of medical events per person-year (rates) or medical events per person at-risk (proportion) for each medical condition. Incidence values can be modified by crew characteristics such as gender sex and certain crew medical history characteristics. Modifying characteristics are noted below and incidence values are listed individually for each characteristic. Distributions are assigned to medical events incidence values and occurrences in the model. For each crewmember in a given trial, the incidence and number of occurrences of each medical condition are randomly selected from these probability distributions. Detailed descriptions of the distributions are included in the MEDPRAT Technical Description Document.

INCIDENCE DATA

SPACEFLIGHT LITERATURE

Space adaptation insomnia is a common occurrence during the early phase of spaceflight. The incidence of space adaptation insomnia (specifically occurring within the first 5 days of spaceflight) has been estimated based on LSAH inflight data.

ANALOG LITERATURE

Not applicable. No analog literature search completed due to this being a space adaptation condition.

TERRESTRIAL LITERATURE

Not applicable. No terrestrial literature search completed due to this being a space adaptation condition.

OVERALL INCIDENCE SUMMARY

INCIDENCE

mean: 0.472 and SD: 0.01754

INCIDENCE SUMMARY

Bayesian posterior distribution for the incidence proportion given the inflight experience (381 events over 807 person-missions) under a uniform(0,1) is represented by a Beta(shape1=381.9, shape2=427.2) which has mean: 0.472 and SD: 0.01754.

TABLE 1. INCIDENCE MODEL

Incidence Details

Incidence Type
SAS

Segment
Space Adaptation
Env. Exposure
NA

Sex
Any
Crowns
Any
Contacts
Any

Pregnancy
Any

Incidence Distribution

Occurrence Dist
Binomial
Incidence Dist.
Beta
Mean
0.472006
SD
0.0175396

Beta
(Alpha): 381.9
(Beta): 427.2
Onset Timing (Hours)
(Min): 1
(Max): 120
(Most Likely): 12

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
LSAH Data (Walton, 2010)	Spaceflight	4
LSAH Data (Saile, 2017a)	Spaceflight	4

Incidence is given an LOC = 4 (confident) since the incidence is based on astronaut inflight data.

CREWMEMBER SELECTION/PREVENTION

DISQUALIFYING CONDITIONS

Refer to Medical Evaluation Documents (MED) Volume A, Medical Standards for ISS Crewmembers, International Space Station Program, Rev 3.4 (2016).

PREFLIGHT PREVENTATIVE MEASURES

There are no specific preflight preventive measures for this condition. General preventive and management measures used for sleep/circadian rhythm adjustment and late insomnia also apply to Space Adaptation Insomnia. However, the novelty of the space environment cannot be adjusted for.

BEST CASE SCENARIO DEFINITION

Insomnia occurring within the first 5 days of spaceflight that is mild and is effectively treated with appropriate crew scheduling/sleep-shifting and sleep-aids.

WORSE CASE SCENARIO DEFINITION

Insomnia within the first 5 days of spaceflight that is severe or refractory to treatment with appropriate crew scheduling/sleep-shifting and sleep-aids.

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

None

BEST CASE/WORST CASE PROBABILITY COMMENTS

Based on LSAH inflight data, there were 15 worst case scenario space adaptation insomnia events among a total of 381 events. This results in an estimated worst case percentage of 4% (15/381) and an estimated best case percentage of 96% (366/381).

TABLE 3.BEST/WORST CASE PROBABILITY LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
LSAH (Walton, 2010)	Spaceflight	4
LSAH (Saile, 2017a)	Spaceflight	4

Incidence is given an LOC = 4 (confident) since the incidence is based on astronaut inflight data.

TABLE 4. CLIFF TREATMENT & OUTCOME TABLE BY CLINICAL PHASE

Case Scenario	Composite Incidence	Condition Probability %	CP1: Diagnosis		CP2: Treatment			CP3: Condition End State				
			TI%	Duration	TI%	Duration		TI%	RTDC		LOCL	
			Preset	Preset	Preset	Min	Max	Preset	Min%	Max%	Min%	Max%
Treated Best Case (TBC)	mean: 0.472 and SD: 0.01754	96 - 96	100	0.65	13.3803	0	72	0	0	0	0	0
Treated Worst Case (TWC)		4 - 4	100	0.64996	14.5628	72	120	0	0	0	0	0
Untreated Best Case (UTBC)	N/A	N/A	N/A	0.65	14.5628	0	72	0	0	0	0	0
Untreated Worst Case (UTWC)	N/A	N/A	N/A	0.64996	17.5259	72	120	0	0	0	0	0

TABLE 4 KEY

Composite Incidence: The same composite incidence will be used for both TBC and TWC. For EVA conditions: events per EVA (events/EVA). For space adaptation conditions: events per person (events/person). For non-spaceflight conditions: events per person year (events/py).

Condition Probability: The probability that CLiFF condition progresses to a worst case scenario. Best case scenario: 100%-Worst Case.

Clinical Phase General Comments:

- TI% = Task Impairment %. Task Impairment is the % of tasks that the crewmember is incapable of performing without impairment secondary to the medical condition.
- Durations are defined in hours.
- Removal to Definitive Care (RTDC): The probability the entire crew aborts the mission and returns to earth. This is considered as a condition end state result if any of the following criteria are met: 1) the potential for LOCL, 2) potential for significant permanent task impairment, or 3) potential for intractable pain.
- Loss of Crew Life (LOCL): The probability of death of affected crewmember due to medical condition.

Clinical Phase 1: Initial Assessment and Diagnosis:

- Covers only the initial assessment and diagnosis of the affected crewmember to define his or her medical condition. While the affected crewmember is being assessed, he or she is not able to perform any assigned tasks, thus Task Impairment (TI) during this phase is considered 100%. In the untreated case, there is no diagnosis performed, therefore Task Impairment and Duration will always be " not applicable."

Clinical Phase 2: Stabilization, Treatment, and Convalescence:

- The affected crewmember is receiving any appropriate initial or follow-on treatment for his or her medical condition to allow the crewmember to recover as much as he or she is able to recover in the spaceflight environment. Clinical phase 2 also encompasses relapses or recurrences of the same original medical condition in Clinical Phase 1. The duration of Clinical Phase 2 is expressed as minimum and maximum hours.

Clinical Phase 3: Condition End State:

- Reached once the affected crewmember has recovered from the medical condition as much as he or she is able to recover in the spaceflight environment amongst treated and untreated best and worst case scenarios. This may or may not be recovery from the given medical condition to the full extent possible. If this “recovered” state results in Removal to Definitive Care (RTDC) or Loss of Crew Life (LOCL) this will be noted in the condition end state results.

SCENARIO OVERVIEW COMMENTS

This condition falls within space adaptation syndrome phase specifically. The countermeasures and treatments do not differ significantly to that of Late Insomnia or terrestrial equivalents. The definitional constraints and limited course of the condition presents mild impairment overall, treated or untreated, and are not expected to have a RTDC or LOCL impact based on LSAH data.

TREATED BEST CASE (TBC) SCENARIO COMMENTS

Occurrence and duration data comes directly from spaceflight data (LSAH) in the prior IMM CLiFF. By definition, these best case scenarios are mild and are effectively treated with appropriate crew scheduling/sleep-shifting and sleep-aids and/or spontaneously resolve. These represent the vast majority of cases (96%) causing little to mild impairment for a short duration until resolution within an assigned 0 to 72 hours (Clinical Phase II durations) once treatment has been started and adaptation to the environment has been made. As a result, RTDC and LOCL probability are deemed 0%. No literature searches were performed for RTDC or LOCL.

TREATED WORST CASE SCENARIO (TWC) COMMENTS

Occurrence and duration data comes directly from spaceflight data (LSAH) in the prior IMM CLiFF. By definition, these worst case scenarios are severe or refractory to treatment with appropriate crew scheduling/sleep-shifting and sleep-aids and don't easily resolve during adaptation to the new environment. These represent a small fraction of cases (4%) causing mild impairment for the assigned 72 to 120 hours duration during the space adaptation phase. As a result, RTDC and LOCL probabilities are deemed 0%. No literature searches were performed for RTDC and LOCL.

UNTREATED BEST CASE (UTBC) SCENARIO COMMENTS

Occurrence and duration data comes directly from spaceflight data (LSAH) from the prior IMM CLiFF. By definition, these best case scenarios are mild and spontaneously resolve with adaptation. These represent the vast majority of cases (96%) causing little impairment for a short duration until resolution within the assigned 0 to 72 hours (Clinical Phase II duration) once adaptation to the environment has been made. As a result, RTDC and LOCL probabilities are deemed 0%. No literature searches were performed for RTDC and LOCL.

UNTREATED WORST CASE (UTWC) SCENARIO COMMENTS

Occurrence and duration data comes directly from spaceflight data (LSAH) from the prior IMM CLiFF. By definition, these worst case scenarios are severe or refractory to treatment with appropriate crew scheduling/sleep-shifting and sleep-aids and don't easily resolve during adaptation to the new environment. These represent a small fraction of cases (4%) causing some mild for the assigned 72 to 120 hours duration during the space adaptation phase. As a result, RTDC and LOCL risks are deemed 0%. No literature searches were performed.

TABLE 5. CLINICAL PHASE II DURATION LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
LSAH (Walton, 2010)	Spaceflight	3
LSAH (Saile, 2017a)	Spaceflight	

LOC = 3 (somewhat confident) based on limited spaceflight data.

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
LSAH (Walton, 2010)	Spaceflight	

Citation	Source	LOC Value
LSAH (Saile, 2017a)	Spaceflight	4

LOC = 4 (confident) based on spaceflight data and due to the fact that the condition tends to be self-limited.

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
LSAH (Walton, 2010)	Spaceflight	4
LSAH (Saile, 2017a)	Spaceflight	

LOC = 4 (confident) based on spaceflight data and since there is no expectation that LOCL would occur directly as a result of space flight insomnia.

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

Capabilities and Resourcing Scope

Overview

Worst Case Definition: Insomnia within the first 5 days of spaceflight that is severe or refractory to treatment with appropriate crew scheduling/sleep-shifting and sleep-aids.

Best Case Definition: Insomnia occurring within the first 5 days of spaceflight that is mild and is effectively treated with appropriate crew scheduling/sleep-shifting and sleep-aids.

Diagnostic Scope and Resourcing

In the best-case scenario, diagnosis is based on a focused psychiatric history, psychiatric review of systems, mental status exam and assessment and plan. Additionally, vital signs and a cardiopulmonary exam should be conducted
For behavioral health conditions ground communication and further higher-level psychiatric consultation should occur for diagnostic clarification.

In the worst-case scenario, diagnosis is based on a focused psychiatric history, psychiatric review of systems, mental status exam and assessment and plan. Additionally, vital signs and a cardiopulmonary exam should be conducted
For behavioral health conditions ground communication and further higher-level psychiatric consultation should occur for diagnostic clarification.

Clinical Phase 1 Duration and Rationale
This version of IMPACT presumes physician level knowledge, skill, and ability will be present on the mission. The CRT working group SME consensus duration is as follows:

CP1 BC (Treated or Untreated): 0.65 (39 min).
1. Obtain Vital Signs
2. Take a proper history of the patient and psychiatric ROS
3. Perform a cardiopulmonary exam
4. Perform a mental status exam
5. Interpret the history, physical exam and MSE
6. Obtain a psychiatry consult
7. Establish ground communication

CP1 WC (Treated or Untreated): 0.64996 (39 min)
1. Obtain Vital Signs
2. Take a proper history of the patient and psychiatric ROS
3. Perform a cardiopulmonary exam
4. Perform a mental status exam
5. Interpret the history, physical exam and MSE
6. Obtain a psychiatry consult
7. Establish ground communication

The highest scope of practice code used in this CRT which includes interpretation of diagnosis, performing diagnostic tests and performing treatment would be a four, or an intern level.

Treatment Scope and Resourcing
Most best-case terrestrial populations resolve before day five and are effectively treated with effectively treated with appropriate crew scheduling sleep shifting and sleep aids. Cognitive behavioral therapy for insomnia is an effective psychotherapeutic treatment modality for sleep disturbances on orbit and in the BC should be provided on a weekly basis for one month and be continued bi-weekly thereafter for the duration of the mission. Furthermore, considering the austere environment and communication barriers that exist on long duration missions it is recommended that there be on board private psychological conferences for the direct administration of psychotherapeutic treatment.

Chronobiologic and antihistaminic agents can be helpful for circadian desynchrony. Antihistaminic agents such as diphenhydramine are second line

agents for insomnia should be included for their positive soporific effects for sleep initiation. The cognitive effects of fatigue related to chronic insomnia would outweigh the cognitive effects related to temporary use of diphenhydramine from a risk benefit perspective and would justify its inclusion.

Promethazine is an agent that has been utilized on orbit for relief of physical discomfort related to adapting to the microgravity environment. Promethazine has been administered on the first day of flight before sleep and is the agent of choice for space motion sickness. Physician/Astronauts have reported that promethazine increases physical comfort which allows them to fall asleep more easily and rest.

As with any of the sleep medications performance vigilance testing would be performed to assess for any impairments in performance caused by medication side effects.

For critical mission events stimulants can be employed as effective fatigue countermeasures.
Other measures such as crew rest/day off should be implemented as necessary.

Additionally, non-pharmacologic sleep aids which are part of fatigue management services include: Blue Light Blocking Glasses, Adjustments of the solid state lighting system, sleep masks, ear plugs (when appropriate), Oura Ring (wearable device that provides objective sleep data), performance vigilance testing, sleep hygiene, naps, sleep shift schedule.

The CES devices can be helpful for symptom reduction, are safe, require a minimal footprint and can be self-administered. However, justification as a primary treatment modality over psychotherapy remains controversial. However, they should be considered as an adjunct treatment modality along with therapy.
Terrestrially, worst case conditions generally require a combination of medications, fatigue management countermeasures and psychotherapy. Cognitive behavioral therapy for insomnia has demonstrated to be an effective psychotherapeutic treatment modality for insomnia and in the WC should be provided on a weekly basis for three months and be continued bi-weekly thereafter for the duration of the mission. Furthermore, considering the austere environment and communication barriers that exist on long duration missions it is recommended that there be on board private psychological conferences for the direct administration of psychotherapeutic treatment.

As above chronobiologic and antihistaminic agents can be helpful for circadian desynchrony. Antihistaminic agents such as diphenhydramine are second line agents for insomnia should be included for their positive soporific effects. The cognitive effects of fatigue related to chronic insomnia would outweigh the cognitive effects related to temporary use of diphenhydramine from a risk benefit perspective and would justify its inclusion. Promethazine is an agent that has been utilized on orbit for relief of physical discomfort related to adapting to the microgravity environment. Promethazine has been administered on the first day of flight before sleep and is the agent of choice for space motion sickness. Physician/Astronauts have reported that promethazine increases physical comfort which allows them to fall asleep more easily and rest.

As with any of the sleep medications performance vigilance testing would be performed to assess for any impairments in performance caused by medication.

In WC sleep disturbances other pharmacologic agents such as ground tested hypnotic agents as well as tetracyclic antidepressants with antihistaminic effects have shown to be effective and should be utilized when necessary.

Other measures such as crew rest/day off should be implemented as necessary.
Additionally, non-pharmacologic sleep aids which are part of fatigue management services include: Blue Light Blocking Glasses, Adjustments of the solid state lighting system, sleep masks, ear plugs (when appropriate), Oura Ring (wearable device that provides objective sleep data), performance vigilance testing, sleep hygiene, naps, sleep shift schedule.

As above the CES devices can be helpful for symptom reduction, are safe, require a minimal footprint and can be self-administered. However, justification as a primary treatment modality over psychotherapy remains controversial. However, they should be considered as an adjunct treatment modality along with therapy.

Communications and Support Needs

Sleep disturbances related to space adaptation are common in spaceflight and can be managed with coordination between ground and the CMO. In the BC it is recommended that ground communication and a psychiatric consult be established for diagnostic clarification and medication/psychotherapeutic treatment guidance. Further support would include ongoing onboard private psychological conferences to provide direct psychotherapeutic care for the duration of the mission.
Following suit, for WC, ground communication and a psychiatric consult should be established for diagnosis, medication management and psychotherapeutic treatment guidance. Further support would include ongoing onboard private psychological conferences to provide direct psychotherapeutic care for the duration of the mission.
Additionally, increased fatigue management countermeasures though the BHP fatigue management services are part of the overall supportive care for this condition.

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Validity and Sensitivity of a Brief Psychomotor Vigilance Test (PVT-B) to Total and Partial Sleep Deprivation Mathias Basner, MD, PhD, MSc,1 Daniel Mollicone, PhD,1,2 and David F. Dinges, PhD1 Acta Astronaut. 2011 Dec 1; 69(11-12): 949–959. doi: 10.1016/j.actaastro.2011.07.015

JAMA, June 28, 2006-Vol 295, No 24, Table 1 Principles in treatment modules included cognitive behavioral therapy condition
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IMM CLIFF RECONCILATION COMMENTS

Updated CLiFF is based on the prior IMM CLiFF documentation and largely unchanged. The only changes relate to switching from Functional Impairment to Task Impairment and changing from resource tables to CRTs.

LIMITATIONS SUMMARY

The primary limitations of the data retrieved consist of a limited number of subjects/sample size, specific vehicle and mission profiles. Future missions may differ in terms of vehicles and mission profiles. The clinical phase II durations for this CLiFF were all taken from the prior IMM CLiFF which are based on LSAH data. The ExMC composer/editor of this CLiFF does not have access to that primary source, but felt after looking through multiple other sources that these estimates for duration were reasonable given they are spaceflight specific.

TABLE 8. TASK IMPAIRMENT CALCULATION BASED ON AFFECTED HUMAN SYSTEMS TASK CATEGORIES (HSTC)

Clinical Phase 2: Treatment												
	Affected HSTCs											
	Cognitive - Simple	Cognitive - Complex	Communications	Inter-personal Skills	Vision	Hearing	Cardio-pulmonary	Dentition	GI	GU		
Treated Best Case (TBC)		664										
Untreated Best Case (UTBC)		664		89								
Treated Worst Case (TWC)		664		89								
Untreated Worst Case (UTWC)	223	664		89								
	Affected HSTCs (Continued)								TI Calculation			TI Score
	Hand (Dom)	Hand (Any)	Upper Extremity	Lower Extremity	Ambul & Standing (g)	Translation & Stabilization (microgravity)	Don/Doff Equipment	Pressure Ops	Total Tasks Impaired By Condition	Total Human System Category Tasks Full Mission	TI Decimal	TI %
Treated Best Case (TBC)	132							211	1007	3763	0.267606	26.7606
Untreated Best Case (UTBC)	132							211	1096	3763	0.291257	29.1257
Treated Worst Case (TWC)	132							211	1096	3763	0.291257	29.1257
Untreated Worst Case (UTWC)	132							211	1319	3763	0.350518	35.0518

Clinical Phase 3: Condition End State												
	Affected HSTCs											
	Cognitive - Simple	Cognitive - Complex	Communications	Inter-personal Skills	Vision	Hearing	Cardio-pulmonary	Dentition	GI	GU		
Treated Best Case (TBC)												
Untreated Best Case (UTBC)												
Treated Worst Case (TWC)												
Untreated Worst Case (UTWC)												
	Affected HSTCs (Continued)								TI Calculation			TI Score

	Hand (Dom)	Hand (Any)	Upper Extremity	Lower Extremity	Ambul & Standing (g)	Translation & Stabilization (microgravity)	Don/Doff Equipment	Pressure Ops	Total Tasks Impaired By Condition	Total Human System Category Tasks Full Mission	TI Decimal	TI %
Treated Best Case (TBC)									0	3763	0	0
Untreated Best Case (UTBC)									0	3763	0	0
Treated Worst Case (TWC)									0	3763	0	0
Untreated Worst Case (UTWC)									0	3763	0	0

TABLE 8 KEY
Human System Task Category (HSTC) Definitions: Cognitive-Simple: Tasks requiring simple cognitive involvement (low levels of attention, following simple checklists, and not requiring extensive decision making) in conjunction with inputs from other systems. Cognitive-Complex: Tasks requiring complex cognitive involvement (requiring constant attention, frequent interpretation of outside stimuli to inform real-time situations) in conjunction with inputs from other systems. Communication: Tasks requiring primarily communication, via hearing and speaking. Interpersonal Skills: Tasks requiring interpersonal, social interaction between crew including complex technical tasks that require extended crew interaction. Vision: Tasks in which visual information is required. Hearing: Tasks in which primarily auditory information is required, excluding communication, e.g. hearing alarms, medical auscultation, OOHAs. Cardiopulmonary: Tasks requiring greater-than-baseline cardiopulmonary effort, e.g. physically strenuous activities. Dentition: Tasks requiring use of teeth for mastication. GI (Gastrointestinal): Tasks requring use of the alimentary sytem, e.g. solids/liquids consumption and solids excretion. GU (Genitourinary): Tasks requiring use of the male/female genitourinary systems. Hand (Dominant): Tasks performed using primarily the hand, requiring use of the dominant hand (piloting, medical procedures, dental procedures). Hand (Any): Tasks performed using primarily the hand(s), with no preference for dominance, with equivalent bilateral effectiveness. Upper Extremity: Tasks requiring specific use of the upper extremities, excluding hands. Lower Extremity: Tasks requiring specific use of the lower extremities (excluding ambulation and standing in the presence of gravity), e.g. using exercise equipment. Ambulation and Standing (g): Tasks requiring use of both lower extremities to accomplish ambulation or standing in the presence of gravity. Translation and Stabilization (microgravity): Tasks requiring use of either the upper or lower extremities to accomplish translational movement and stabilization (securing oneself to remain stationary) in the setting of microgravity. Don/Doff Equipment: Tasks requiring the donning of personal equipment (including pressure suit, exercise harness, EVA equipment, etc). Pressure Ops: EVA/contingency tasks performed while pressurized in a suit.

Criteria for Assignment of Conditions to HSTCs (any of the following):
1) Is affected crew member physically incapable of performing the human system task category, without impairment, with the condition?
2) Would the treatment (e.g. medications) impair the crewmember's ability to perform the human system task category? (Does not apply to UTx)
3) Does the condition have a high likelihood of causing a significant aeromedical contraindication with an associated human system task category
4) Would performing tasks in an associated task category worsen the condition? (If so, it is affected).
5) Does pain associated with the condition impair any further human system categories?

TASK IMPAIRMENT COMMENTS

CP2: No comment. CP3: No comment.

EVIDENCE COLLECTION PROCESS

Mesh terms that most closely resembled the best-case and worst-case scenarios, and associated Conditions Included but Not Explicitly Stated (CNES), were utilized to build incidence, duration, RTDC, and LOCL searches by best- and worst-case.

Incidence:
Databases searched for spaceflight and analog incidence data included: PubMed, Google Scholar, NASA Technical Reports Server (NTRS) public search, Defense Technical Information Center (DTIC), and Barratt MR, Baker E, Pool SL. Principles of Clinical Medicine for Space Flight. New York, NY: Springer; 2019. 2nd Edition. Databases searched for terrestrial incidence included: DynaMed, PubMed, and Google Scholar.

Duration, RTDC, LOCL:
Databases searched for duration, RTDC, and LOCL included: Dynamed, Cochrane, PubMed, and Google Scholar. Note, that if duration, RTDC, or LOCL data was found in a DynaMed search, the other search engines were not included. Relevant articles were selected and reviewed. If applicable, the article was included in the CLiFF.

LEVEL OF CONFIDENCE (LOC) SCORING

Articles obtained to update the evidence behind this CLiFF were scored by ExMC editors, based on their applicability to the Exploration Spaceflight environment using the following grading scale:

4 – Confident
3 – Somewhat confident
2 – Neutral
1 – Somewhat unconfident
0 – Not confident

The following considerations factor into the grading scale above:

• How closely does the paper describe the medical condition as defined by the IMPACT 1.0 Condiltion List (relevance)?
• How closely does the population included resemble the astronaut population?
• Quality of the paper (number of subjects, methods, etc.)
• How much does the editor trust the source of the evidence?
• How closely does the editor think that the data represents the exploration spaceflight environment?
• Other considerations, at the discretion of the editor, supported in the comments for LOE scoring.

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ACRONYMS

ACRONYM	PHRASE
AAOMS	American Association of Oral and Maxillofacial Surgeons
AMA	American Medical Association
ARCL	All Remaining Conditions List
ARS	Acute Radiation Sickness
BHP	Behavioral Health and Performance
CAC	Coronary Artery Calcium
CHS	Crew Health and Safety
CL	Condition List
CliFF	Clinical Finding Form
CMO	Crew Medical Officer
COMFORT	Clinical Outcome Metrics for Optimization of Robust Training
CP1	Clinical Phase 1
CP2	Clinical Phase 2
CP3	Clinical Phase 3
CRL	Clinical Resource Level
CRT	Capability Resource Table
CST	Clinical Science Team
DCS	Decompression Syndrome
DRM	Design Reference Mission
ED	Emergency Medicine Doctor
EL	Evidence Library
EMCL	Exploration Medical Condition List
EMT	Emergency Medical Technician
EVA	Extravehicular Activity

EXMC	Exploration Medical Capability
HRP	Human Research Program
ICD	International Classification of Disease
ICL 1.0	IMPACT 1.0 Medical Conditions List
ICU	Intensive Care Unit
IMCL	iMED Condition List
iMED	Integrated Medical Evidence Database
IMM	Integrated Medical Model
IMPACT-MD	Impact Medical Database
IP	Incidence Proportion
IR	Incidence Rate
ISS	International Space Station
IV	Intravenous
JSC	Johnson Space Center
LEO	Low-Earth orbit
LEVA	Lunar Extravehicular Activity
LOCL	Loss of Crew Life
LOM	Loss of Mission
LSAH	Lifetime Surveillance of Astronaut Health
LSO	Lunar Surface Operations
MCL	Master Condition List
MEVA	Medical Extravehicular Activity
NASA	National Aeronautics and Space Administration
N/A	Not Applicable
NP	Nurse Practitioner
OBGYN	Obstetrics and Gynecology
OR	Occurrence Rate
PA	Physician Assistant
PDQ	Pain Disability Questionnaire
PFCL	Proposed Future Conditions List
PPE	Personal Protective Equipment
PTRS	Project Technical Requirements Specification
PRL	Pharmaceutical Resource Level
QTL	Quality Time Lost
RCL	Removed Conditions List
REP	Rochester Epidemiology Study
RTDC	Removal to Definitive Care
SANS	Spaceflight-Associated Neuro-ocular Syndrome
SAS	Space Adaptation Syndrome
SEVA	Spaceflight Extravehicular Activity
SME	Subject Matter Expert
SoP	Standard Operating Procedure
SPE	Solar Particle Event

TBD	To Be Determined
TI	Task Impairment