Clinical Finding Form (CliFF)

Branch: Baseline

ICL5_Allergic Reaction (Mild To Moderate)

Allergic reactions are sensitivities to a specific substance, known as an allergen that occur after the substance comes in contact with the skin, the lungs, the gastrointestinal tract, or is injected. In mild and moderate forms, these reactions can be treated with oral medications such as antihistamines and steroids. These allergic reactions can present as skin rashes, nasal congestions, conjunctivitis, asthma, GI symptoms such as vomiting, abdominal cramping, etc. In contrast, in severe forms such as anaphylaxis, intravenous medications and more advanced procedures such as airway management might be required to treat potentially life-threatening symptoms. This CLiFF focuses on the mild to moderate forms of acute allergic reaction that are generally not fatal. Countless objects can potentially cause an allergic reaction, including food, medications, materials, pollen, fungi, animals, and mites. It is known that immune dysregulation occurs during spaceflight, thus increasing the risk of an allergic reaction (Crucian 2016). During spaceflight, common potential allergens would be food and medications.

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

Acute allergic reactions in space appear to be exceptionally rare. (Crucian 2016) evaluated the medical records of astronauts who flew up through Expedition 38/39 and found two total "allergic reaction/hypersensitivity" events over 20.57 flight years (incidence rate of 0.1 events per flight year). They did not specify the severity of these reactions, but it can be assumed that most were mild to moderate and not life-threatening. (Saile, 2017) from previous IMM CLiFF was able to calculate incidence rate through existing data set. Current literature search did not reveal any new relevant spaceflight data.

ANALOG LITERATURE

(Gaudio 2008) published their recommendations at the Wilderness Medical Society's roundtable discussion regarding acute allergic reactions and anaphylaxis in the wild. The National Outdoor Leadership School, which we send our Astronaut Candidates to, has maintained records of incidents throughout its history. In 20 years and over 2.5 million participants, only 149 participants had an acute allergic reaction. All of them were given antihistamines and none of them died. These numbers also exclude the handful of anaphylaxis cases.

TERRESTRIAL LITERATURE

The terrestrial literature shows that about 1% of all ED visits in the United States are for acute allergic reactions. Depending on the severity, they are generally treated with antihistamines +/- steroids. (Gaeta 2007) is a national study conducted between 1993 and 2004 looking at ED visits due to allergic reactions. They estimated an annual allergic reaction ED visit rate of 3.8 visits/1000 people. (Lee 2000) found, depending on the medication, an incidence anywhere between 0.1 - 15% for acute allergic reactions to medications in hospitalized patients. (Apter 2006) is a retrospective cohort of over 500,000 patients exposed to penicillin found only 0.7% of them had an acute, allergic reaction within 30 days. (Macy 2012) records review of over 2 million patients found an incidence of new drug allergic reactions in 6.6% of men and 10.2% of women. However, novel medication administration in spaceflight will be much lower than in patients therefore the likelihood of unknown allergies resulting in allergic reactions would be much lower.

OVERALL INCIDENCE SUMMARY

INCIDENCE

Mean of 0.3293 SD 0.08532

INCIDENCE SUMMARY

The Bayesian posterior distribution for the incidence rate given the spaceflight evidence (15 events over 45.49 person-years (Saile,2017)) is Gamma(shape=14.896, rate=45.237) with mean 0.3293 and SD 0.08532.

TABLE 1. INCIDENCE MODEL

Incidence Details

Incidence Type
General

Segment
All

Env. Exposure
NA

Sex
Any

Crowns
Any

Contacts
Any

Pregnancy
Any

Incidence Distribution

Occurrence Dist
Poisson

Incidence Dist.
Gamma

Mean
0.329288

SD
0.0853181

Gamma
(Shape): 14.896
(Rate): 45.237

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Saile, 2017	Space	4
Crucian, 2016	Space	4
Gaudio, 2008	Analog	3
Lee, 2000	Terrestrial	2
Macy, 2012	Terrestrial	2
Deacock, 2008	Terrestrial	2
Apter, 2006	Terrestrial	2

Overall, we know there is a very low incidence of acute allergic reactions in a space or analog environment based on the current literature. The terrestrial literature, particularly with respect to medication reactions, appears to be somewhere between 2-10% incidence. (Crucian, 2016) and (Saile, 2017) provide incidence data from previous spaceflight missions, receiving a LOC of 4. (Crucian, 2016) found two total "allergic reaction/hypersensitivity" events over 20.57 flight years (incidence rate of 0.1 events per flight year). (Saile, 2017) reported 15 events over 45.49 person-years. (Gaudio, 2008) provides good analog incidence data in the wild but does not really reflect the environment in space, receiving a LOC of 3. Terrestrial incidence data provided by (Lee, 2000) (Macy, 2012) (Deacock, 2008) (Apter, 2006) are either partial to specific medications or incompatible with the reality and environment during spaceflight, all receiving LOC of 2.

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

Photodocumentation of allergic reactions of the skin

BEST CASE SCENARIO DEFINITION

A crewmember with an allergic reaction that is quickly relieved by one dose of oral medication.

WORSE CASE SCENARIO DEFINITION

A crewmember with a more severe allergic reaction; able to be treated with oral medication, but requires multiple doses and a longer duration of treatment.

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

None

BEST CASE/WORST CASE PROBABILITY COMMENTS

(Saile, 2017) is likely still the benchmark to use for astronaut-based data and what we could expect for best/worst case probability. (Saile 2017) from IMM CLiFF found that 93% of allergic reactions from current available spaceflight data would fall into the BC scenario category. No better data specific to WC/BC scenario probability could be found in the terrestrial literature.

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

Citation	Source	LOC Value
Saile, 2017	Spaceflight	4

Though the number of subjects is low, the confidence is high. This data was calculated by data from acute allergic reactions in space and how our astronaut population has generally responded to therapy. Many potential triggers can be identified (and potentially desensitized) on the ground prior to flight. Overall, it makes sense that the majority of cases within the scope of this ICL should be best case.

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 0.3293	93 - 93	100	0.83	13.4	0.25	24	0	0	0	0	0
Treated Worst Case (TWC)		7 - 7	100	0.83	13.4	48	240	0	0	0	0	0
Untreated Best Case (UTBC)	N/A	N/A	N/A	0.83	2.80361	24	48	0	0	0	0	0
Untreated Worst Case (UTWC)	N/A	N/A	N/A	0.83	15.75	72	240	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

Many different entities can trigger an acute allergic reaction, but by far the most relevant to the astronaut population are going to be first-and-foremost due to medications, followed by foods. Within the scope of this ICL, we only considered type I (IgE-mediated) acute allergic reactions. Other subtypes, like serum sickness or delayed hypersensitivity, were felt to be outside the scope of this ICL and would likely occur even less commonly in a space environment. Seasonal allergies were also excluded from literature searches and analysis, as typical triggers are less likely to be found on-board and their management is more chronic in nature. Anaphylaxis, which is on the most extreme end of the acute allergic spectrum, will be covered in a different ICL. Ultimately, the risk of acute allergic reactions from medications or foods could be mitigated with pre-flight allergy testing (and subsequent desensitization). No RTDC or LOCL is expected under any circumstances within the scope of this ICL.

TREATED BEST CASE (TBC) SCENARIO COMMENTS

Ultimately, we could reasonably expect a treated best case scenario to be resolved with a single dose of an antihistamine somewhere between 15 minutes to as much as 24 hours after taking the medication. Mild symptoms of an acute allergic reaction are generally urticaria and/or skin erythema. (Frossard, 2008) specifically tracked improvement of histamine-induced wheals over 24 hours, and though the wheals were present a day later, they were significantly decreased compared to the placebo group. (Banerji, 2007) brings up an excellent point regarding the sedating quality of second generation antihistamines (such as diphenhydramine). In flight or on a space mission, we recommend the affected individual should take and respond well to a second generation, non-sedating medication such as cetirizine in the best case scenario. No RTDC or LOCL is expected.

TREATED WORST CASE SCENARIO (TWC) COMMENTS

Treated worst case scenarios require multiple days of therapy and possibly multiple medications. Though the symptoms may be uncomfortable or unpleasant (e.g. persistent pruritis), it is important to note that within the scope of this ICL that no RTDC or LOCL would be expected. In the (Pollack, 1995) study, patients were drastically improved by day 2 following therapy with antihistamines and steroids, with complete resolution by day 5. (Schaefer, 2017) provided general treatment windows of 3-10 days for those who progress to the point of requiring steroids, giving us a reasonable worst case range for this scenario.

UNTREATED BEST CASE (UTBC) SCENARIO COMMENTS

Defining which cases should still fall into the best case, and yet untreated, category from a time perspective is a little more challenging. Anything lasting 24-48 hours could potentially be argued that it was a mild enough case that had an antihistamine been available, it would have resolved within 1 day rather than up to 2. The (Pollack, 1995) study, though small, did show on average that the placebo arm was significantly improved 2 days later (while some fared better than others). We would infer that some folks in the placebo arm of the Pollack study would fall into the "best case untreated" and some into the "worst case untreated" for the purposes of this ICL. (Schaefer, 2017) review article broadly cites each individual wheal may self-resolve within 24 hours, but no papers were found providing a concrete minimum time inside of 24 hours (or that the entirety of the patient's condition would be gone). (Frossard, 2008) followed patients for 24 hours following a histamine-induced wheal and flare reaction, with the placebo arm showing minimal improvement compared to those taking a single, oral dose of a newer generation antihistamine. Frossard's study helps confirm a minimum duration of 24 hours in the UTWC scenario. No RTDC or LOCL is expected.

UNTREATED WORST CASE (UTWC) SCENARIO COMMENTS

The untreated, worst case scenario is a little bit harder to pinpoint from the duration perspective. The (Pollack, 1995) study followed up on patients at Day 2 and Day 5 in the action and placebo arms of the study. Those that had significant improvement at day 2 in the placebo arm, for the sake of this ICL, would fall more into the "UTBC" category. Those who carried on to Day 5 are better considered in the "UTWC" category. By Day 5, they were all nearly resolved, giving us a 3-5 day range in this study. Schaefer's 2017 review article generically discusses a 3-10 day steroid treatment period, implying that those in the UTWC category would likely continue to suffer symptoms during this time period. Finally, the (Lin, 2000) ED study should make us consider an alternative process in play (such as chronic urticaria rather than an acute allergic reaction) if symptoms persist. No RTDC or LOCL is expected for this ICL.

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

Citation	Source	LOC Value
Church, 2011	Terrestrial	3
Lin, 2000	Terrestrial	
Frossard, 2008	Terrestrial	
Banjeri, 2007	Terrestrial	
Schaefer, 2017	Terrestrial	
Pollack, 1995	Terrestrial	

Acute, allergic reactions are overall a well known and well described entity. Regardless of whether they occur in space, analog environments, or in everyday life, we can safely say a treated best case can be resolved within 24 hours. Despite the unknown effect of spaceflight environment to the human immune system, terrestrial data was able to provide ample treatment duration information, receiving a collective LOC of 3. It is more difficult to bracket how long the worst case scenario will last, as this could be anywhere from 3-10 days depending on how the astronaut responds to steroids (or if there are no medications whatsoever).

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
N/A	N/A	3

RTDC is not expected within the scope of this ICL

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
N/A	N/A	3

LOCL is not expected within the scope of this ICL

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

Capabilities and Resourcing Scope Overview Allergic Reaction in this definition refers to non life threatening reactions that cause manifestations including rashes, rhinorrhea, and/or mild bronchospasms. Anaphylaxis is covered in a separate condition, as is eye irritation. CNES: NONE Diagnostic Scope and Resourcing Diagnostics are limited to history and physical exam since allergic reaction does not require biomarkers, imaging, or instrumentation. This is true for both the best case and worst case of this definition 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): 0.83 hours for history, cardiopulmonary exam, skin exam, and an oropharyngeal exam. CP1 WC (Treated or Untreated): 0.83 hours for history, cardiopulmonary exam, skin exam, and an oropharyngeal exam. This condition requires a Scope of Practice 4 corresponding to the training and skill level of a high functioning first year resident (Intern). Treatment Scope and Resourcing For the best case treatment resources include topical antihistamines, oral antihistamines with priority given to non drowsy histamine blockers, and topical corticosteroids. For the worst case treatment, oral corticosteroids, and a short and long acting inhaled bronchodilators are added to the resourcing. The bronchodilators will be delivered by way of a metered dose inhaler and a spacer chamber to limit the medication spread caused by a nebulizer while providing adequate medication delivery to the patient. Communications and Support Needs No additional communications resources are expected to be necessary for diagnosis and treatment of this condition in both best and worst case.

IMM CLIFF RECONCILATION COMMENTS

Since there are no additional spaceflight data found on this topic, we report similar incidence rate to the IMM CLiFF. BC and WC scenario definitions are the same for both CLiFFs. No additional available spaceflight data for incidence and BC/WC scenario were found. Therefore, we report identical probabilities. However, for phase II treatment duration, with evidence from terrestrial studies, we report a slightly different range. Overall, there are few dissimilarities between these two CLiFFs.

LIMITATIONS SUMMARY

A wider range of medications will be carried on exploration missions in the future, making incidence data calculated from past shuttle missions (with very limited formulary) likely an underestimation of potential future adverse drug reactions in space. This CLiFF also only considered IgE mediated reactions, excluding potential type II to Type IV reactions. Additionally, the best case scenario definition of "allergic reaction quickly relieved by one dose of oral medication" is less ideal for calculation WC/BC probability since symptoms of allergic reactions such as rashes would rarely disappear within a couple hours. In reality, these mild to moderate allergic reactions would be treated with more than one dose of medication while pending recovery. Therefore, there is no terrestrial data found on WC/BC probability. As for treatment duration, estimations can be made with reasonable assumptions from currently available terrestrial data.

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)												
Treated Worst Case (TWC)		664										
Untreated Worst Case (UTWC)		664					145					

	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)								211	211	3763	0.0560723	5.60723
Treated Worst Case (TWC)	132							211	1007	3763	0.267606	26.7606
Untreated Worst Case (UTWC)	132						34	211	1186	3763	0.315174	31.5174

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: Certain anti-allergy medications are aeromedically contraindicated, hence a higher TI in the treated version of BC. 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