

Clinical Finding Form (ClIFF)

Branch

Baseline

ICL63_Headache

Terrestrially tension headaches are the most frequent cause of headaches in general and the high workload of crewmembers during a mission makes tension headache a likely diagnosis for in-flight headaches after the first 5 days on orbit. (Marshburn, 2008) There have been several headache events in this category reported on orbit. Most have resolved within a couple hours, and were readily treatable with available medication. (Walton, 2010)

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

First 2 articles evaluate astronauts specifically. They are survey articles that look at the incidence of headache in astronauts during spaceflight. Tend to look more at males than females.

ANALOG LITERATURE

Potasman (2008) conducted a questionnaire-based study among consecutive travelers to determine the rate, severity and duration of flight-associated headaches (FAHA). Of the 906 eligible travelers (mean age 33.3 +/- 13.8 years), 22.3% reported headaches at least once per month. FAHA occurred in 52 travelers (5.7%), of whom 34 were women (P = 0.0023 vs. none FAHA). The duration of pain was 4.0 +/- 10.2 h after takeoff and continued for 5.7 +/- 14.2 h after landing. Migraine was diagnosed in 19.2% of those with FAHA. The magnitude of headache was 6 +/- 2 (on a scale of 1-10). Among those who suffer from FAHA, 45.4% reported that their pain was unilateral, in contrast to 72.7% among those with 'non-flight' headaches (P = 0.019). Davis et al (2016) took a cross-sectional convenience sample of hikers. Sixty percent of hikers were male with an age range of 17-62 years. Eighty percent reached the summit of Mount Grays/Torrey's (4349 m). Seventy-nine percent of participants resided in Colorado; the median elevation of residence for subjects was 1697 m (interquartile range 1557-1765 m). HAH occurred in 39% of hikers, while AMS occurred in 26% of hikers. A history of migraine was associated with increased risk of any headache at altitude (OR: 2.49, 95% CI: 1.62-3.65) and was strongly associated with the development of migrainous headache while at altitude (OR: 14.05, 95% CI: 5.49-35.93).

TERRESTRIAL LITERATURE

One paper looks at headache in more typical aircraft flight on earth and incidence of people reporting headache. Interesting in that they have recorded if participants gets headaches regularly, which is important to look at for cause and effect. The other paper is looking at people who have migraine and if this predicts migraine at high altitudes. Of course, space is the ultimate altitude, so knowing this it may be helpful to predict if migraines will be a problem.

OVERALL INCIDENCE SUMMARY

INCIDENCE

mean 2.56 and SD 0.7432

INCIDENCE SUMMARY

The Bayesian posterior distribution for the incidence rate given the reference data under an uninformative prior is Gamma(shape=11.865, rate=4.6348) with mean 2.56 and SD 0.7432. The ESA headache study showed 12 events outside launch over 4.69 person-years of flight – IR: 2.561

(95%CI: 1.387, 4.353). Initially this distribution used data from a bedrest study but was revised to exclude that study.

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
2.55998
SD
0.743195
Gamma
(Shape): 11.865
(Rate): 4.6348

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Vein AA, et al. 2009	Spaceflight	4
van Oosterhout WP, et al. 2015	Spaceflight	4
Potasma I, et al. 2008	Analog	3
Davis C, et al. 2016	Analog	3
Santy PA, et al. 1991	Terrestrial	2

Majority of these articles are surveys so they are not case-controlled. However, they are in a specific population (i.e. flight, astronauts) so this makes the reported data relevant.

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

General disqualifying conditions: In general, any medical condition that, in the judgment of the Multilateral Space Medicine Board, may compromise mission operations or crew safety, or require urgent medical treatment while during a space mission.

BEST CASE SCENARIO DEFINITION

An uncomplicated headache (unrelated to space adaptation), which resolves spontaneously or with first line medications or non-pharmacologic treatment. (Note this is exclusive of headaches secondary to CO2, which is covered by "Headache - CO2" condition).

WORSE CASE SCENARIO DEFINITION

A headache refractory to second line medications and non-pharmacologic treatments, requiring additional interventions. (Note this is exclusive of headaches secondary to CO2, which is covered by "Headache - CO2" condition).

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

None

BEST CASE/WORST CASE PROBABILITY COMMENTS

A worst case scenario has not been observed on orbit and is fairly unlikely. A best/worst case split following roughly that of the original CLiFF data is appropriate and likely reflects mission realities

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

Citation	Source	LOC Value
Vein AA, et al. 2009	Space	4

Vein AA, et al. (2009) used a specifically designed questionnaire based on the criteria of the International Classification of Headache Disorders, 2nd edn (ICHD-II). Of the 16 male and one female astronauts who participated in the survey, 12 (71%) reported having experienced at least one headache episode while in space, whereas they had not suffered from headache when on earth.

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 2.56 and SD 0.7432	99 - 99	100	0.53	0	0	2	0	0	0	0	0
Treated Worst Case (TWC)		1 - 1	100	1	16.4895	2	72	0	0	1.2	0	0
Untreated Best Case (UTBC)	N/A	N/A	N/A	0.53	15.3069	0.5	168	0	0	0	0	0
Untreated Worst Case (UTWC)	N/A	N/A	N/A	1	28.6208	4	773	0	0	1.2	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

Primary headaches include tension-type, cluster, and migraines. Generally speaking, tension and cluster headaches last on the order of 0.5-8 hours, whereas migraines generally range from 4-72 hours. Treatment is generally effective in all categories, though 1-2% of cluster headaches may require hospitalization. Based on epidemiology data, less than 1% of migraines will need hospitalization. There is no LOCL expected for this ICL, as more life-threatening/secondary causes of headaches (e.g. intracranial bleed) is outside the scope of this ICL.

TREATED BEST CASE (TBC) SCENARIO COMMENTS

By definition, TBC scenarios either rapidly resolve within a couple of hours and/or are easily treated with oral medications. No RTDC or LOCL is expected.

TREATED WORST CASE SCENARIO (TWC) COMMENTS

Charles (NEJM 2017) great review article on migraines. Generally expect them to last 2 hours (with triptan therapy some respond that quickly) and upwards of 72 hours in duration. Any longer is suggestive of a secondary cause, and is outside the scope of this ICL. A small percentage (~1-2%) may require hospitalization for status migrainosus

UNTREATED BEST CASE (UTBC) SCENARIO COMMENTS

Untreated best case headaches will generally resolve on their own; however, there is a possibility (albeit unlikely) of them lasting up to a week. Clinical practice is more consistent with tension-type headaches lasting on the order of 0.5-8 hours at most. RTDC and LOCL is not expected.

UNTREATED WORST CASE (UTWC) SCENARIO COMMENTS

Migraines classically last 4-72 hours; however, there is discussion in the medical literature of them lasting up to 4.6 weeks (though this is going to be very uncommon). Data regarding RTDC for untreated cases is difficult to obtain, so best surrogate will still be in the 1-2% range. LOCL not expected.

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

Citation	Source	LOC Value
Levin M., 2015	Terrestrial	3
Lipton RB, et al. 1998	Terrestrial	
Lee, M. J., et al. 2018	Terrestrial	
Chua AL, et al. 2019	Terrestrial	

Cross-sectional review of annual data from 2011, in particular older population experienced more headache. Report of primary headache typically lasting up to 2 hours; important to rule out secondary headache causes. Adults visiting US emergency rooms with main complaint of headache 2015. Need to count headache with treatment as individual event, as 24hr after treatment up to 64% patients had return of severe headache. Charles (NEJM 2017) great review article on migraines. Generally expect them to last 2 hours (with triptan therapy some respond that quickly) and upwards of 72 hours in duration. Lipton et al (1998): 1357 enrolled patients (1250 study and 1220 placebo) with history of migraines or severe headache that met the International Headache Society diagnostic criteria. By 6 hours post-intervention (drug administration vs placebo), 50.8% of the drug-treated patients were pain free compared with 23.5% of the placebo-treated patients. Lee et al (2018) Patients diagnosed at Samsung Medical Center with headache and lost to follow-up for over 5 years. All were CLUSTER (not tension) primary headaches, and longest duration was 2 hours. Dynamed discusses that tension-type headaches can last up to 7 days Chua AL, Grosberg BM, Evans RW. Status Migrainosus in Children and Adults. Headache. 2019;59(9):1611-1623. doi:10.1111/head.13676

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Jensen RM, et al. 2007	Terrestrial	3
Diener, H. et al. 2008	Terrestrial	

By definition, a best case scenario primary headache will resolve either on its own or with basic medication treatment Jensen et al (2007): 78 consecutive patients from The Danish Headache Center and compared with the use of health-care services in the general population. All patients had consulted their GP; 43.5% had seen specialists; 10.6% had required emergency services; and 1.2% had been admitted to hospitals. A small percentage of folks will ultimately need to be hospitalized for conditions like status migrainosus, which reflects clinical experience. Insinga et al (2011) found for migraines in the U.S in 2007 that there were 680,946 outpatient visits for migraines, 88,128 going to emergency departments, and only 5516 requiring hospital admission Those with life-threatening, secondary causes (e.g. subarachnoid) is outside the scope of this ICL Linde et al (2012) Review of adults aged 18-65 from general population in Austria, France, Germany, Italy, Lithuania, Luxembourg, Netherlands, Spain, UK, Ireland. Even with placebo, primary headache would resolve in specified duration (2 hours on the upper end of time). Best case primary headaches resolve on their own, and therefore would not require RTDC Difficult to find papers where individuals are hospitalized and do not receive any treatment whatsoever. Best surrogate for this is the paper citing 1.2% hospitalized for headaches.

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Lyngberg, A.C. 2005. Prognosis of migraine and tension-type headache A population-based follow-up study	Terrestrial	3

Comprehensive literature searches were run and there is no evidence of loss of crew life from a headache with the parameters listed. Therefore with known clinical knowledge, LOCL is not expected. Study of Note: 740 persons (aged 25 to 64 years) examined in a 1989 Danish cross-sectional headache study, 673 were eligible for follow-up in 2001. Deaths were not from headache. By the definition of this ICL, a primary headache (even worst case) would not result in death. A headache causing death would be suggestive of a secondary cause which is outside the scope of this ICL Comprehensive literature searches were run and there is no evidence of loss of crew life from a headache with the parameters listed. Therefore with known clinical knowledge, LOCL is not expected. Comprehensive literature searches were run and there is no evidence of loss of crew life from a headache with the parameters listed. Therefore with known clinical knowledge, LOCL is not expected.

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

Capabilities and Resourcing Scope

Overview

Worst Case Definition: An uncomplicated headache (unrelated to space adaptation), which resolves spontaneously or with first line medications or non- pharmacologic treatment. (Note this is exclusive of headaches secondary to CO2, which is covered by "Headache - CO2" condition).
Best Case Definition: A headache refractory to second line medications and non-pharmacologic treatments, requiring additional interventions. (Note this is exclusive of headaches secondary to CO2, which is covered by "Headache - CO2" condition).

Essentially this is a headache that cannot be attributed to another cause, such as spaceflight adaptation, or high CO2 levels. This condition is terrestrially known as a "Tension type headache." Generally this condition is one of discomfort rather than a medical emergency.

The CRT condition focuses solely on the relief of this discomfort whether that requires pain or moderate pain management, or not. The extent to which relief is achieved is simply crew preference and there is no medical assessment necessary.

Diagnostic Scope and Resourcing

In the best-case scenario, diagnosis is based on history and physical examination.

In the worst-case scenario, diagnosis is based on history and physical examination.

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): 0.53 hours

This is the longest reasonable time to complete this task for an experienced clinician adjusted for being in the spaceflight environment to do the following:

- 1 - Take a proper history of the patient
- 2 - Perform a physical on the patient

CP1 WC (Treated or Untreated): 1.0 hours

This is the longest reasonable time to complete this task for an experienced clinician adjusted for being in the spaceflight environment to do the following:

- 1 - Take a proper history of the patient
- 2 - Perform a physical on the patient

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

Treatment Scope and Resourcing

In the best-case scenario, treatment is limited to mild pain medications as this was specifically in the definition of the best case for this condition.

The worst case scenario, where the pain is refractory to mild medications results in an escalation of therapy options including: metoclopramide (i.e. Benadryl), promethazine, ketorolac, Sumatriptan, etc. that are generally used for refractory therapy options.

Most headache in terrestrial populations (best or worst case) are resolved with medication without need for surgical or psychiatric intervention.

Communications and Support Needs

In the best-case and worst-case scenario, diagnosis and course of treatment is uncomplicated and likely within the scope of care of onboard crew members.

IMM CLIFF RECONCILIATION COMMENTS

Headache is not included as a condition in the American Medical Association guides to the Evaluation of Medical Impairment. The calculation of functional impairments (FI) follows the IMM standard template for mild non-space adaptation conditions; we combined two tables: Migraine and Complex Regional Pain Syndrome - Upper Extremity (CRPS-UE). Migraine ratings are based on Table 13-18, p.342 (American Medical Association, 2008). The ratings for Whole Person Impairment are in the same table. Complex Regional Pain Syndrome (CRPS-UE) ratings are based on Table 15-16, p. 454 (American Medical Association, 2008). The CRPS is converted to Whole Person Impairment based on table 15-1, page 385 (American Medical Association, 2008). Final FI ratings are calculated using the Combined Values Chart as indicated in Appendix A, pp604-606 (American Medical Association, 2008). For further information refer to the Cliff Appendix. For Clinical Phase I, by definition FI is 100%. Duration is estimated in 15 minutes to evaluate headache as described in the ISS medical checklist for sick call. Mission Operations Directorate (MOD), 2011) During Clinical Phase II, FI is estimated at 0 to 10%, and duration is estimated at 1.5 to 24 hours based on Vein's and Ashina's studies. (Vein, 2009); (Ashina, 2010) During Clinical Phase III, headache (late) by definition is expected to resolve and FI is 0%. Based in space flight data EVAC and LOCL are not expected. (Walton, 2010)(In-flight Compilation Lockdown revised, 2010)

LIMITATIONS SUMMARY

There was little data to support the worst case untreated clinical phase durations or RTDC probabilities. Under-reporting for this condition could have been significant during past space missions due to mild cases that were treated symptomatically without being reported. It is unclear whether successive headaches were reported as separate events or a single, continuing event. Some spaceflight data is not clearly delineated into mission phase and makes interpretation difficult. The main paper used to compute incidence was based on astronaut recall.

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)												
Untreated Best Case (UTBC)		664					145					
Treated Worst Case (TWC)		664		89			145					
Untreated Worst Case (UTWC)	223	664	113	89			145		13			
	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)	132							211	1152	3763	0.306139	30.6139
Treated Worst Case (TWC)	132							211	1241	3763	0.32979	32.979
Untreated Worst Case (UTWC)	132	564						211	2154	3763	0.572416	57.2416
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	T1 Decimal	T1 %
Treated Best Case (TBC)									0	0	0	0
Untreated Best Case (UTBC)									0	0	0	0
Treated Worst Case (TWC)									0	0	0	0
Untreated Worst Case (UTWC)									0	0	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 requiring use of the alimentary system, 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 Condition 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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15 -

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