Clinical Finding Form (CliFF)

Branch Baseline

ICL78_Rash, Spaceflight Associated

Skin rashes or skin eruptions are a relative common occurrence during spaceflight (Barratt et al., 2019). In a review of medication records from 24 crewmembers on 20 long-duration missions over a 10-year period, “skin rash” was the fourth most frequent indication listed for medication use (Wotring, 2015). Skin eruptions can be secondary to many different etiologies including dermatitis (contact (irritant or allergic) or atopic), infection, systemic allergic reactions, or drug eruptions. This CLiFF condition only covers the former. This distinction is important as many studies in spaceflight, including the Wotring study, do not separate the underlying cause of skin eruption as it may be initially difficult to determine. Consequently, the authors of this CLiFF expect some overlap with the CLiFF entitled “Skin Infection.” As it stands, it is not clear whether spaceflight associated skin rashes are secondary to the dysregulation of crewmembers’ immune system, inadequate hygiene, or both (Crucian et al., 2016; Braun et al., 2019). Studies have demonstrated that epidermal thinning results from spaceflight (Dunn et al., 2018; Barratt et al., 2019). Further, exposure to microgravity leads to skin irritation due to vasodilation in 3D in vitro settings (Choi et al., 2021). These changes may explain the higher frequency of dermatitis than expected in a highly screened, healthy, spaceflight population.

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

Spaceflight: The incidence rate was derived two LSAH data gathering events (Walton, 2010; Saile et. al, 2017). Unfortunately, the authors of this CLiFF did not have direct access to the data from those LSAH events. Consequently, information was taken detailing these events from the previous IMM CLiFF entitled "Skin Rash.” Per report, skin infections, petechiae, hyperemia (allergic reaction), dry skin and herpes zoster were not included in incident counts for this condition. The Walton LSAH pull identified 94 cases and the Saile LSAH pull identified 26 cases. The previous CLiFF noted that the initial Walton pull did include some skin infections which presented initially as skin rashes, but these “were counted as two separate events if there were 24 hours or more between rashes in the same crew member.” At the time of this CLIFF completion, a repeat LSAH data gathering event was not possible and missions past 2017 are not represented. Antonsen et al. (2017) was rated less highly than the data in the previous IMM CLiFF as the data in Table 1 could not be adequately reconciled with this specific condition’s definition. For example, Table 1 described 10 cases of rash along with 10 incidents skin irritation. However, two of these cases were EVA related and thus were more applicable to ICL 46 “EVA Related Suit Contact Injury.” The 94 cases described in Table 2 were concordant with the Walton LSAH pull. Of note, it was observed that in the Antonsen et al. paper Table 1 was mislabeled as 'ISS through Exp 40' when it should read ' ISS expeditions 9 and 14 through 40'. In Crucian et al. (2016), electronic medical records were examined from 46 long-duration ISS crew members, representing 20.57 total flight years. Skin rashes were the most reported event (1.12/flight year, 23 events). Although the authors recognized that there may have been seem overlap between skin categories depending on clinical symptoms, they made attempts to separate skin infections from other skin eruptions. Ultimately, this data was downrated given that that the IMM CLiFF encompassed more missions. In Braun et al. (2019), preflight and postflight questionnaires were given to 8 nonatopic astronauts that asked about their terrestrial skin care habits and skin conditions, on-orbit skin care routine and whether any special observations regarding the skin were made during flight. Recorded symptoms included peeling, rash, dryness, reddening, itchiness, bruising, skin sensitivity, bumps, acne and slow healing of contusions and lacerations. This study seemed to correlate that skin symptoms were related to spaceflight hygiene. Data from this study could not be used to calculate an incidence rate but did provide an attempt at a mechanistic explanation of the increased rate of skin eruptions during spaceflight.

ANALOG LITERATURE

In Knapik et al. (2019), medical events were reviewed during the physically demanding Special Forces Assessment and Selection (SFAS) courses between 2015 and 2017. There was a total of 800 soldiers and 708 medical encounters during this 20-day course that was held 12 times. The prevalence of soldiers with one or more injuries was 38.4% (307/800). There were 14 events of “contact dermatitis” which equated to 10.5% of total injuries and illnesses. Of note, skin abrasions, impetigo and blisters were categorized separately. Another study (Tansey et al., 1979) analyzed medical reports from 885 Fleet ballistic missile submarine patrols from 1963-1973 and compared them to illness rates found in crewmembers on surface-level vessels. Within this timespan there was one reported event of “subacute eczema” in a total of 7,650,000 man-days. Of note, other skin conditions were characterized separately as well including “dermatophytosis,” “erysipelas,” “skin infection (unspecified),” and “impetigo.” The authors do comment that they believed the reporting of medical conditions on submarines was artificially low secondary to the lack of medical personnel and fear of retribution. In Thomas et al. (2003), a retrospective analysis was conducted of the medical records between January 1, 1997, and September 30, 2000, of 1389 officers and 11,952 enlisted crew members. This accounted for a total of 215,086 and 1,955,521 person-days at

sea, respectively. The subjects in this study were a highly screened, healthy population and the study was conducted to develop epidemiological data to determine risk in space medicine. “Skin and Subcutaneous Tissue Disorders” had a reported 18 officer events for 3.1/100 person-years and 436 enlisted men events for 8.1/100 person-years. Unfortunately, there were no further details regarding how many of these events could be attributed to non-infectious skin rashes.

TERRESTRIAL LITERATURE

The incidence of occupational skin disease reported to United Kingdom’s The Health and Occupation Reporting (THOR) network between 2002-2005 was analyzed in Turner et al. (2007). In this study, contact dermatitis was reported as either “allergic”, “irritant” or “mixed or unspecified.” Dermatologists reported an incidence rate of contact dermatitis of 68.0 per million (95% CI: 59.8-76.2) and occupational physicians reported a rate of 259.7 per million (95% CI 200.8-318.6). Overall incidence for occupational skin disease was 91.3 per million (95% CI: 81.8-101.1) and 316.6 per million (95% CI: 251.8-381.3) by dermatologists and occupational physicians, respectively. A systematic review of the research from North America and Western Europe between 1996 and 2007 (Thyssen et al., 2007) found that the medial prevalence of a contact allergy to at least one allergen was 21.2% and the weighted average prevalence was 19.5% across all age ranges. In Dietz et al. (2021), incidence rates of occupational contact dermatitis in Denmark were determined between 2007 and 2018. The overall incidence rate was found to be 9.8 per 10,000 workers per year (n= 16,484). Of these events, 71.6% were diagnosed with irritant contact dermatitis and 28.4% were diagnosed with allergic contact dermatitis.

OVERALL INCIDENCE SUMMARY

INCIDENCE

Mean: 2.635 events/person-years; SD: 0.2427

INCIDENCE SUMMARY

The posterior distribution for the incidence rate given the spaceflight data (120 events over 45.49 person-years) under an uninformative prior is Gamma (shape=117.875, rate=44.734) with mean 2.635 and SD 0.2427. Spaceflight data: 120 events over 45.49 person-years. IR 2.638 (95%CI: 2.197, 3.143) IMED shows 120 cases (94 from earlier LSAH pull and 26 new cases. Antonsen shows 96 in Table 2 (as expected matches first pull) and 20 other cases in Table 1. Given the discrepancy, the IMED counts were used as they encompassed more missions.

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
2.63502

SD
0.242702

Gamma
(Shape): 117.875
(Rate): 44.734

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Walton, 2010	Spaceflight	4
Saile et al., 2017	Spaceflight	4
Antonsen et al., 2017	Spaceflight	2
Crucian et al., 2016	Spaceflight	3
Braun et al., 2019	Spaceflight	1
Knapik et al., 2019	Analog	2
Tansey et al., 1979	Analog	2
Thomas et al., 2003	Analog	1
Turner et al., 2007	Terrestrial	2
Thyssent et al., 2007	Terrestrial	1
Dietz et al., 2021	Terrestrial	2

Spaceflight incidence data was rated the highest as there was an appropriate sample size that occurred in space. Analog and terrestrial studies did not accurately reflect the highly screened crewmembers or the spaceflight environmental conditions. Further, there was concern that analog and terrestrial studies would exert an overwhelming influence on the final incidence distribution given their large number of poorly representative subjects.

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

This CLiFF condition is event-based and consequently there are no known preventative measures. However, there is serious interest in the documentation and analysis of healing of skin pathologies during spaceflight. At L-10 days, the crew and flight surgeon undergo training on the use of the 35mm still and digital cameras so that they can document any minor/major infections /allergies /hypersensitivities /injuries inflight. This training is conducted as part of the Medical Operations Preflight Briefing.

BEST CASE SCENARIO DEFINITION

Mild to moderate and uncomplicated skin rash that responds to topical treatment.

WORSE CASE SCENARIO DEFINITION

Moderate to severe skin rash, covering an extensive area and that requires more than 5-7 days of topical treatment, requires a course of oral or IV medications, or is refractory to treatment.

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

None

BEST CASE/WORST CASE PROBABILITY COMMENTS

Generally, it is accepted that if allergic contact dermatitis or atopic dermatitis involves an extensive area of skin (greater than 20 percent) or is in a sensitive area not resolving with topical treatment, systemic steroid therapy may be required (Fonacier et al., 2019; Menga et al., 2017). The authors of this CLiFF effort to not have access to the original LSAH data, but per the prior IMM CLiFF: “Based on Real World System data set, there were 26 events and 3 of them were worst case. Since we now have worst case scenarios, which did not have before, we can use the empirical data so the worst-case scenario would be 11.54% (3/26). Thus the best case scenarios would be 88.46% (23/26) (Saile L., 2017).” Although prospective studies are rare, estimates from systematic reviews cite that 10% of adult patients experiencing a form of dermatitis are prescribed systemic steroids (Menga et al., 2017; Drucker et al., 2018). In a Dutch population-based cross-sectional study, Zhang et al. (2019) found that of physician-diagnosed atopic dermatitis, the “severe” category represented 16.9% of the population.

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

Citation	Source	LOC Value
Saile et al., 2017	Spaceflight	3
Menga et al., 2017	Terrestrial	2
Druker et al., 2018	Terrestrial	2
Zhang et al., 2018	Terrestrial	1

Since the worst-case has occurred in spaceflight, spaceflight data was ranked more highly than the single low-powered terrestrial study. The spaceflight data was in good concordance with systematic reviews, however it is unclear how they arrived these estimates.

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: 2.635; SD: 0.2427	89 - 89	100	0.87	6.51076	24	336	0	0	0	0	0
Treated Worst Case (TWC)		11 - 11	100	0.94	27.6641	120	2016	0	0	1	0	0
Untreated Best Case (UTBC)	N/A	N/A	N/A	0.87	6.51076	24	336	0	0	0	0	0
Untreated Worst Case (UTWC)	N/A	N/A	N/A	0.94	30.0292	120	2016	27.6641	0	10	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

The best-case scenario refers to a minor skin eruption that is either self-resolving or responds to creams or ointments. The worst-case is a skin eruption that either has a prolonged course, is in a sensitive area (i.e., periorbital or genital regions) or covers significant surface area. Relevant pathologies include contact dermatitis or atopic dermatitis. Skin eruptions secondary to infections or allergic reactions (urticaria) or covered in separate CLiFFs. This CLiFF does not include life-threatening skin disease pathologies Steven-Johnson syndrome or Toxic epidermal necrolysis as these are typically secondary to drug reactions or infections. The RTDC surrogate for this condition is hospitalization.

TREATED BEST CASE (TBC) SCENARIO COMMENTS

Treatment in the best-case scenario can range from the application of an over-the-counter moisturizer, applying emollient creams or to even using low-potency topical corticosteroids. In the mildest cases, a one-time application may be enough to resolve the issue, and most review articles recommend one-time dosing (Chan et al., 2021). There is a lack of systematic studies to delineate the optimal duration in the best-case as most regimens recommend continuing moisturizing agents on a as-needed basis, and promptly discontinued when lesions resolve (Eichenfield et al., 2015). In Hon et al. (2009), emollients were prescribed to adolescents with atopic eczema or dermatitis for a period of two weeks. Low potency topical corticosteroids can be prescribed for one or two weeks at a time (Chan et al., 2021; Stacey et al., 2021). RTDC and LOCL are not expected for this scenario.

TREATED WORST CASE SCENARIO (TWC) COMMENTS

By definition, the lower bound for duration is set at five days for the worst-case scenario. Medium-potency steroids (groups III, IV and V) are recommended for the treatment of severe dermatitis events. At most, these topical steroids should only be used for 12 weeks (Stacey et al. 2021; Drake et al., 1996). Oral corticosteroids and other biological agents are also indicated treatments in this worst-case scenario but prescribed in durations shorter than 12 weeks secondary to undesirable side-effects (Brar, 2021; Chan et al., 2021, Drucker et al., 2018). Although there was literature available regarding the incidence of contact dermatitis during hospital admission (from medical supplies, cleansers, and adhesives), there was a paucity of data available regarding the percentage of cases that needed inpatient or advanced medical care. In Storan et al. (2013), patients seen by a dermatology inpatient service at a single academic tertiary center between 2000 to 2010 were reviewed. During that time frame, 301 patients were admitted with atopic dermatitis, and 150 patients were admitted contact dermatitis. Unfortunately, it is not known how this translates into a rate of hospitalization as the number of skin rashes in the general, non-hospitalized was undetermined. However, the surrogate for RTDC is a non-zero value. Consequently, subject matter expertise opinion assigned a value of “1%” for RTDC for this condition to reflect that this would be an extremely unlikely event. LOCL is not expected for this condition.

UNTREATED BEST CASE (UTBC) SCENARIO COMMENTS

There was a lack of systematic studies available to determine duration for the untreated best case. The untreated best case would be expected to last no less than the treated best case. RTDC and LOCL are not expected for this condition.

UNTREATED WORST CASE (UTWC) SCENARIO COMMENTS

There was a lack of systematic studies available to determine duration for the untreated worst case. The untreated worst case would be expected to last no less than the treated worst case and accordingly the same range for duration used. Since Storan et al. did demonstrate that non-infectious skin rashes are hospitalized (n=451 over 10 years), RTDC was set at zero to 10% by subject matter expert consensus; it was expected that the upper-bound would be greater than the treated worst-case condition, but still relatively low. LOCL is not expected for this condition.

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

Citation	Source	LOC Value
Chan et al., 2021	Terrestrial	2
Eichenfield et al., 2015	Terrestrial	
Hon et al., 2009	Terrestrial	
Stacey et al., 2021	Terrestrial	
Brar, 2021	Terrestrial	

Citation	Source	LOC Value
Drucker et al., 2018	Terrestrial	

Duration ranges were taken from several systematic reviews and low-powered and moderately applicable prospective trials.

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Storan et al., 2013	Terrestrial	1

This study was a single institution's inpatient experience; it was limited that it was not a epidemiological study and a rate of hospitalization could not be calculated.

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
N/A	N/A	4

Based on the definitions, loss of crew life is not expected for any of the scenarios associated with this CLiFF.

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

Capabilities and Resourcing Scope

Overview

This condition covers undifferentiated rashes encountered in spaceflight. While spaceflight associated rashes have not been formally classified it is thought that they result from a combination of dry skin, irritant exposure, fungal exposure, mild allergies, and/or poor focal hygiene.

CNES: None

Diagnostic Scope and Resourcing

For both the best and worst case definitions the CRT WG SME consensus was to rely on history and physical for diagnosing the rash.

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): 0.87 hours for history and physical
CP1 WC (Treated or Untreated): 0.94 hour for history and physical of a more extensive skin rash

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

Treatment for the best case includes topical steroids and moisturizing cream. treatment for the worst case adds the capabilities for oral steroids and oral antihistamines.

No additional ground support communications needs are expected for the best case, for the worst case the ability to send images to the ground for specialist consultation is expected. No real time audio or video is necessary.

REFERENCES
Barratt, M.R., Baker, E.S., Pool S.L., Principles of Clinical Medicine for Space Flight, Second Edition. Springer, 2019.

IMM CLIFF RECONCILATION COMMENTS

The predecessor to this CLiFF was entitled “Skin Rash.” In this effort, the modifier “spaceflight associated” was added to the title. The authors of

this CLiFF were not present when it was decided to add this modifier, but after discussing such with several members of the original CliFF definition team, this modifier was added to emphasize that skin rashes are more common (likely to have a higher incidence) in spaceflight. This modifier was not intended to restrict the definition of the best- and worst-case scenarios. For this effort, incidence data was updated with the help of a biostatistician. Durations and RTDC were revised using data from more recent studies.

LIMITATIONS SUMMARY

• There may be some overlap between spaceflight-associated skin rashes and other CLiFF conditions relating to skin eruptions or infections. • Under-reporting for this condition could have occurred during past space missions due to subtle rashes that were not of clinical consequence. This may result in underestimation of the incidence. • The authors did not have access to the original LSAH data and thus there was a dependence on already published sources. • After extensive literature searches performed by the editors for this condition, no studies were found that informed hospitalization rates, likely a result of this condition's mostly benign consequences. • The authors to this CLiFF did not have access to the original LSAH data and thus there was an implied dependence on already published sources. • Given a paucity of data, subject matter expertise was used to assign values for worst case RTDC probabilities.

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)												
Treated Worst Case (TWC)		664										
Untreated Worst Case (UTWC)		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)							34	211	245	3763	0.0651076	6.51076
Untreated Best Case (UTBC)							34	211	245	3763	0.0651076	6.51076
Treated Worst Case (TWC)	132						34	211	1041	3763	0.276641	27.6641
Untreated Worst Case (UTWC)	132						34	211	1130	3763	0.300292	30.0292

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)		664										
	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)	132						34	211	1041	3763	0.276641	27.6641

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