Clinical Finding Form (CliFF)

Branch	Baseline

ICL53_Fracture - Distal Leg

Fracture - Distal leg encompasses any traumatic fracture of the patella, tibia, or fibula. However, fracture - ankle is a separate condition for consideration in future iterations of IMPACT. It is somewhat unclear where a distal leg fracture stops and an ankle fractures starts based on their definitions. For the purposes of this CLiFF the mesh term "ankle" was excluded in literature searches.

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

There have been no published accounts of a distal leg fracture (or any fracture) in spaceflight.

ANALOG LITERATURE

Military analog population data focuses primarily on stress fractures. Stress fractures are not included in this Cliff.

TERRESTRIAL LITERATURE

Wennergren et al, 2018 completed a 5 year retrospective review of tibial fracture incidence in Sweden in patients age 16-101 (stratified ages less than 50 and 50 years and older). The overall incidence of tibial fracture in this population was 51.7/100,000 py, with an incidence of 24.12/100,000 person-years in patients age 16-49. The most common cause of fractures was falls, followed by traffic accidents. Beerekamp et al, 2017 conducted a similar retrospective review of lower leg fractures in the Netherlands in a 9 year study inclusive of 12% of the emergency department patients in the country. The overall incidence in this study was 44.8/100,000 person years.

OVERALL INCIDENCE SUMMARY

INCIDENCE

Surface-Ops EVA: mean 3.183E-7 SD 2.758E-9.

INCIDENCE SUMMARY

This cliff pertains only to traumatic fractures of the distal leg. The incidence of traumatic fractures outside of surface EVA was assumed to approach 0. Thus, the incidence only applies to Surface-ops EVA exposure. It is an incidence proportion, utilizing terrestrial traumatic distal leg fracture data (Beerekamp et al, 2017; Wennergren et al, 2018). This incidence proportion distribution is a Beta(shape1=13319.4, shape2=41845411064) with mean 3.183E-7 and SD 2.758E-9. This is the result of Bayesian analysis generating the posterior of the incidence rate for a meta-analysis of 2 terrestrial references (Beerekamp et al, 2017; Wennergren et al, 2018) (12271 events over 26686430py and 1371 events over 2650000py) and then utilizing the posterior samples to generate a posterior distribution for the probability of observing at least one fracture over a 6-hour EVA. Beerekamp et al, 2017 included information on distal leg fractures, whereas Wennergren included data specific to tibial fractures. Beerekamp et al, 2017 was not age adjusted because, although the female rates increase with age, the male rates decrease with age. If you assume the population is half male and half female, the rates become consistent across the age spans. Given this, the data were not sex or age-adjusted from Beerekamp et al, 2017. Wennergren et al did not provide demographics to allow for sex or age-adjustment. These two data sources were entered into a Bayesian model to get a posterior distribution for the incidence rate. That incidence rate was used to calculate the probability of experiencing at least 1 fracture event over an EVA (assumed to be 6 hours).

TABLE 1. INCIDENCE MODEL

Incidence Details

Incidence Type
EVA
Segment
EVA Surface
Env. Exposure
NA

Sex
Any
Crowns
Any
Contacts
Any

Pregnancy
Any

Incidence Distribution

Occurrence Dist
Binomial
Incidence Dist.
Beta
Mean
3.183E-07
SD
2.758E-09

Beta
(Alpha): 13319.4
(Beta): 4.18454E+10

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Wennergren et al, 2018	Terrestrial	3
Stattin et al, 2018	Terrestrial	0
Beerekamp et al, 2017	Terrestrial	3
Larsen et al, 2016	Terrestrial	1

Wennergren et al, 2018 (Swedish) and Beerekamp et al, 2017 (Dutch) provide retrospective analysis over 5 and 9 years, respectively, of skeletally mature patients of ages 16 years and older. They use national databases to determine the incidence of tibial (Wennergren et al) and lower leg (Beerekamp et al) fractures. Stattin et al, 2018 provides a hazard ratio comparison of all fracture types, including lower leg fractures, in cross-country skiing athletes compared to controls. This data is not well suited for incidence for this CLiFF. Larsen et al, 2016 provides the incidence of all patellar fractures in Denmark from 2005-2014. Patellar fractures are uncommon, thus this article is less applicable to the astronaut corps.

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

Pre-flight requirements include training on exercise devices to prepare for in-flight use. In-flight, on the International Space Station (and previously on Mir), crewmembers are required to exercise for 2.5 hours per day (1 hour of aerobic conditioning and 1.5 hours or resistive exercise) (NASA, MedB 5.2).

BEST CASE SCENARIO DEFINITION

A closed, non-comminuted, non-segmented, non-displaced, or minimally displaced fracture resulting in no neurovascular compromise to the affected limb.

WORSE CASE SCENARIO DEFINITION

A fracture that is: open, comminuted, segmented, moderatlely to severely displaced, intra-articular, or results in neurovascular compromise to the affected limb, likely requiring surgical intervention.

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

Fracture - Knee Fracture - Tibial Shaft Fracture - Proximal Fibular Fracture - Pilon

BEST CASE/WORST CASE PROBABILITY COMMENTS

The definition of this condition is inclusive of multiple traumatic fractures of the lower leg. The best- and worst-case probabilities vary significantly depending on the type of fracture involved. Best-case/worst case scenario probabilities are as follows based on literature from some of the fracture types included in the condition: Tibial Fracture: BC 57.8%, WC 42.20% (Wennergren et al, 2018), Composite "Lower Leg Fracture:" BC 49.5%, WC 50.5% (Beerekamp et al, 2017), Patellar Fracture: BC 23.6%, WC 76.4% (Larsen et al, 2016). For the purposes of this Cliff the "Lower Leg Fracture" best-case (49.5%) and worst-case (50.5%) probabilities will be used since it most closely meets the broad definition of the Cliff, but individual values are included here should they be needed for future efforts.

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

Citation	Source	LOC Value
Wennergren et al, 2018	Terrestrial	3
Stattin et al, 2018	Terrestrial	2
Beerekamp et al, 2017	Terrestrial	3
Larsen et al, 2016	Terrestrial	2

The applicability of these papers to the astronaut corps varies. Wennergren et al and Beerekamp et al included patients from 16 years of age and older. Stattin et al looked at cross-country skiers vs. non-cross country skiers to compare rates of injuries. Larsen et al focuses specifically on patellar fractures. Notably, all of the studies were outside the United States (Swedish, Danish, and Dutch). Regardless, the values for best- and worst-case probability in these studies appear to be valid and coincide with the worst-case scenario definition for this condition based on complications such as open fractures, or need for surgery.

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)	Surface-Ops EVA: mean 3.183E-7 SD 2.758E-9.	49.5 - 49.5	100	1.22	6.93596	168	1680	0	0	1.1	0	0
Treated Worst Case (TWC)		50.5 - 50.5	100	2.07	28.1557	1008	12600	7.0954	0	100	0	4.9
Untreated Best Case (UTBC)	N/A	N/A	N/A	1.22	33.5769	1123	12600	0.58464	0	1.1	0	0
Untreated Worst Case (UTWC)	N/A	N/A	N/A	2.07	46.532	1123	17250	20.5687	0	100	28	50

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 RTDC surrogate was "hospitalization," but the need for surgery was also considered an RTDC surrogate for RTDC probabilities. The definition for this condition encompasses any traumatic fracture involving the distal leg . This broad definition made the literature search for duration, RTDC, and LOCL complicated given that different fracture types and locations have very different prognoses. Thus, data was found for individual fracture types and each scenario was analyzed on an individual level to arrive at the most appropriate values. See specific scenarios below for an explanation of how duration, RTDC, and LOCL were derived.

TREATED BEST CASE (TBC) SCENARIO COMMENTS

The definition of this condition inherently includes multiple fracture types in the distal leg. Thus, durations of treatment for distal leg fractures, tibial plateau and tibial shaft fractures, patellar fractures, and proximal fibular shaft fractures were obtained. The minimum value for duration of healing (168 hours for proximal fibular shaft fracture) and maximum value for duration of healing (1680 hours for patellar fracture) were used for the duration range (Boden et al, 1999; Melvin and Mehta, 2011). RTDC probabilities for tibial plateau fracture (0%) (Porter and Fenton, 2011), patellar fracture (0-1.1%) (Gwinner et al, 2016), and proximal fibular shaft fracture (0%) (Pallin, 2018) were obtained. The range (0-1.1%) was accordingly assigned for RTDC since it is dependent on the type of fracture. No evidence of mortality secondary to a best-case distal leg fracture could be found from tibial plateau fracture (Porter, 2011), patellar fracture (Gwinner et al, 2016), tibial shaft fracture (Schmidt et al, 2003), or proximal fibular fracture (Pallin, 2018). Thus, LOCL probability was assigned as 0%.

TREATED WORST CASE SCENARIO (TWC) COMMENTS

The definition of this condition inherently includes multiple fracture types in the distal leg. Reviewed studies indicate a healing time of 6-8 weeks with surgical intervention for worst-case lower extremity distal leg fractures. The minimum duration was assigned 1,008 hours (6 weeks). This is based on surgical intervention for worst-case tibial plateau fractures (Thomas et al, 2009) and Patellar Fractures (Melvin and Mehta, 2011). The maximum duration, 12600 hours (75 weeks), was re-used from the untreated best-case scenario. Since surgical intervention will be unavailable inflight, it was felt that this was a better approximation for healing time than data based on surgical intervention of these fractures. The RTDC surrogate of need for surgery was used to inform the RTDC probability. RTDC probabilities were obtained from the literature for tibial plateau fracture (100-100%) (Porter and Fenton, 2011), Patellar Fracture (100-100%) (Melvin and Mehta, 2011), Tibial Shaft Fracture (Schmidt et al, 2003) (100-100%) and Proximal Fibular Shaft Fracture (0-87.5%) (Boden et al, 1999). The full range 0-100% was used for RTDC probability. LOCL probability estimates were found in the literature for tibial plateau fracture (0-4.9%) (Elsoe and Larsen, 2020), patellar fracture (0-1.3%) (Larsen and Elsoe, 2018), tibial shaft fractures (0-3%) (Tampe et al, 2018), and proximal fibular fractures (0%) (Pallin, 2018). Accordingly, the LOCL probability range was set at 0-4.9%.

UNTREATED BEST CASE (UTBC) SCENARIO COMMENTS

Due to the paucity of data available regarding untreated distal leg fractures, treated (casting) tibial shaft fracture data were used to estimate the UTBC scenario duration. The minimum duration was assigned 1123 hours (6.7 weeks) and the maximum was assigned 12,600 hours (75 weeks) based on Schmidt et al, 2003. The RTDC probability for this condition is based on need for surgical intervention. By definition, best-case fractures are not anticipated to require surgical intervention. The RTDC probability from the TBC scenario was repeated for this scenario (0-1.1%). No data could be located for RTDC probabilities of traumatic tibial fractures. The full range 0-100% was assigned for RTDC. No data were available to inform the LOCL probability. The LOCL probability was assigned 0% based on SME opinion.

UNTREATED WORST CASE (UTWC) SCENARIO COMMENTS

The duration for the UTBC was repeated for the minimum duration for this scenario. The maximum duration was informed by Pritchett, 1997. It is a small study of 18 patients with too many comorbidities to safely undergo surgery for widely displaced patellar fractures. A third of the patient's died, but of the 12 living patients at 2 years of follow-up 9 reported good outcomes, although all patients had extensor lag of more than twenty degrees. Due to a paucity of data the 2-year follow-up period from this study was used as the upper limit for the duration for this scenario. No data was found informing RTDC for this scenario, thus the RTDC from the TWC scenario was repeated (0-100%). The paucity of data for untreated fractures is most apparent in relation to LOCL probability. The range of 28-50 was taken from the Fracture – Femur cliff data (LOCL of traumatic, displaced intracapsular femur fractures in a non-operative elderly comorbid population - Gregory et al, 2010). SME opinion is that the likelihood of LOCL from a distal leg fracture would not exceed that of a femur fracture.

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

Citation	Source	LOC Value
Thomas et al, 2009	Terrestrial	2
Melvin and Mehta, 2011	Terrestrial	
Schmidt et al, 2003	Terrestrial	
Pallin, 2018	Terrestrial	
Rome et al, 2005	Terrestrial	
Allen et al, 2004	Terrestrial	
Slatyer, 1995	Terrestrial	
Swenson et al, 1997	Terrestrial	
Uvaraj et al, 2007	Terrestrial	
Boden et al, 1999	Terrestrial	
Pritchett, 1997	Terrestrial	

This condition covers multiple different traumatic fracture types in the tibia, fibula, and patella. This is a challenge for duration because the treatment course varies widely between fracture types. The durations listed in Table 4 are the minimum and maximum duration times found in the literature search based on different fracture types when literature was available (tibial shaft fracture, tibial plateau fracture, patellar fracture, proximal fibular fracture). Thus, the durations values have wide distributions. This is a limitation due to the multiple fracture types being combined in this condition.

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Porter and Fenton, 2011	Terrestrial	2
Gwinner et al, 2016	Terrestrial	
Schmidt et al, 2003	Terrestrial	
Pallin, 2018	Terrestrial	
Melvin and Mehta, 2011	Terrestrial	
Boden et al, 1999	Terrestrial	
Uvaraj et al, 2007	Terrestrial	

This condition covers multiple different traumatic fracture types in the tibia, fibula, and patella. This is a challenge for RTDC because the severity/consequence of the fractures varies significantly depending on the location and type of fracture. Therefore, the RTDC probabilities have a wide spread for this condition. Having a lower bound of 0% for some of these scenarios may underestimate the true RTDC probability because it was assigned based on less consequential fracture types/locations.

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Porter and Fenton, 2011	Terrestrial	N/A
Gwinner et al, 2016	Terrestrial	
Schmidt et al, 2003	Terrestrial	
Pallin, 2018	Terrestrial	
Elsoe and Larsen, 2020	Terrestrial	
Larsen and Elsoe, 2018	Terrestrial	
Tampe et al, 2018	Terrestrial	

Citation	Source	LOC Value
Gregory et al, 2010	Terrestrial	

This condition covers multiple different traumatic fracture types in the tibia, fibula, and patella. This is a challenge for LOCL because risk of loss of crew life varies depending on the type and location of the fracture. There is also a paucity of data for untreated fractures.

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

Capabilities and Resourcing Scope
Overview
Distal leg fracture refers to a fracture of the tibia and/or fibula, with the best-case scenario representing uncomplicated fractures and the worst-case scenario representing complicated fractures. Any fracture, if left untreated, could result in further complications such as malunion, loss-of function, and/or chronic pain. A worst-case scenario fracture, left untreated, could result in additional significant complications such as neurovascular compromise.
CNES: Fracture knee (tibial), tibial shaft fracture, proximal fibular fracture, pilon fracture
Diagnostic Scope and Resourcing:
In the best-case scenario, diagnosis is based on history, physical examination (musculoskeletal and neurologic), and imaging. Plain film (X-Ray), CT, and MRI will be unavailable inflight. Musculoskeletal ultrasound was included in the CRT as it may serve as a useful adjunct in diagnosis for some cases, but it was not considered a necessary capability to diagnose distal leg fracture.
In the worst-case scenario, diagnosis is based on history, physical examination (musculoskeletal, neurologic, and vital signs), and imaging. In some cases, musculoskeletal ultrasound may be contraindicated due to risk of contamination of an open fracture, or further displacement of the fracture(s). The utility of musculoskeletal ultrasound would be determined on a case-by-case basis. It was included as a non-necessary capability. This diagnostic framework is consistent with the terrestrial workup for distal leg fracture with the exception of the inability to perform plain film X-Ray (and if warranted CT or MRI), and thereby using Musculoskeletal Ultrasound as a possible surrogate.
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 Clinical Phase 1 duration:
Best Case CP1: 1.22 hours
Worst Case CP1: 2.07 hours
This CRT includes a scope of practice code of 5 (which correlates to an “Experienced procedure trained generalist attending (ED attending)” and was included for musculoskeletal ultrasound and interpretation.
Treatment Scope and Resourcing:
Most best-case distal leg fractures in terrestrial populations resolve with an initial period of splinting, followed by 4-6 weeks of casting. Splinting was considered a necessity, whereas casting was included as a capability but not considered a necessity in this CRT. Although 3D printing offers potential for splinting of musculoskeletal injuries, it remains a largely experimental process and it is not within the scope of this CRT. Depending on the fracture location, non-weightbearing status may be used terrestrially. If the fracture were to occur in microgravity phases of flight, non-weightbearing status is already achieved. Should the fracture occur during surface operations, it was assumed that partial gravity combined with improvised mobility assistance utilizing materials available during surface operations would sufficiently provide non-weightbearing status (i.e. crutches were not included in this CRT). Physical therapy is recommended post-immobilization. Exercise modification is also recommended, but not built into the CRT as this does not represent a clinical resource. Pain is variable depending on the patient. Acetaminophen and NSAIDs were included in the best-case treatment scenario (acetaminophen given a higher primacy due to evidence that NSAIDs may interfere with bone healing).
Terrestrially, all worst-case fractures warrant surgical intervention. Thus, a worst-case distal leg fracture in-flight would present a significant treatment challenge. These fractures would warrant an attempted reduction to achieve more physiologic alignment. Note that nerve blocks for fracture reduction are not included in the scope for IMPACT 1.0 but could be considered in the future. Open fractures inflight would be treated with copious irrigation, wound closure, prophylactic antibiotics and splinting with possible casting after wound healing. Again, both splinting and casting were included as capabilities, but only splinting was considered a necessary capability in this CRT. Both plaster and fiberglass (and their associated means of removal) were included for trade-space analysis. Pain from a worst-case fracture may require narcotic analgesia. Physical therapy would be advised until the end of the mission.
Communications and Support Needs:
While real-time video and audio loop communications are desired for diagnosis and treatment, they were not considered a necessity, particularly in the best-case scenario. For the WC, consultation with ground specialists to facilitate treatment and healing was considered necessary given the limited diagnostic and treatment capabilities in-flight.
REFERENCES
1. Boyd AS, Benjamin HJ, Asplund CA. Splints and Casts: Indications and Methods. AFP 2009; 80:491–9.
2. Nanchahal J, British Association of Plastic R and AS. Standards for the management of open fractures of the lower limb. London: Royal Society of Medicine Press Ltd.; 2009.
3. Clinical Practice Guidel : Distal tibia and-or fibula physeal fractures - Outpatient clinics. Retrieved 1 February 2021 from https://www.rch.org.au/clinicalguide/guideline_index/fractures/ankle_outpatients/

IMM CLIFF RECONCILATION COMMENTS

Fracture – Distal Leg is a new condition, not previously accounted for in the IMM. The closest condition in IMM was “Lower Extremity Stress Fracture.” Because of this, the incidence, duration, and outcomes (RTDC, LOCL), and task impairment are appropriately unique in this CLiFF as compared to the IMM “Lower Extremity Stress Fracture” CLiFF.

LIMITATIONS SUMMARY

This condition covers multiple different traumatic fracture types in the tibia, fibula, and patella. This is a challenge for incidence, duration, RTDC, and LOCL as these numbers vary by fracture type, which can have a protracted treatment course. The durations listed in Table 4 are the minimum and maximum duration times found in the literature search based on different fracture types when literature was available (tibial shaft fracture, tibial plateau fracture, patellar fracture, proximal fibular fracture). Thus, the durations values have wide distributions. Overall the confidence in the duration, RTDC, and LOCL is decreased by combining so many fracture types into one condition.

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)							145					
Untreated Best Case (UTBC)		664		89			145					
Treated Worst Case (TWC)		664					145					
Untreated Worst Case (UTWC)	223	664		89			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						34	211	522	3763	0.138719	13.8719
Untreated Best Case (UTBC)	132	564	414	22	196	34	34	211	2505	3763	0.665692	66.5692
Treated Worst Case (TWC)	132		414	22	196	34	34	211	1852	3763	0.492161	49.2161
Untreated Worst Case (UTWC)	132	564	414	22	196	34	34	211	2728	3763	0.724953	72.4953

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)							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)									0	3763	0	0
Untreated Best Case (UTBC)				22					22	3763	0.0058464	0.58464
Treated Worst Case (TWC)				22			34	211	267	3763	0.070954	7.0954
Untreated Worst Case (UTWC)	132			22	196	34	34	211	774	3763	0.205687	20.5687

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