Clinical Finding Form (CliFF)

Branch Baseline

ICL9_Arthritis, Acute

In adults, arthritis is the most common cause of disability and is among the leading conditions causing work limitations. The estimated number of adults with physician diagnosed arthritis is anticipated to reach 25% of the adult population by 2040 (Watkins-Castillo, 2021). Osteoarthritis (OA), also known as degenerative joint disease, is the most common type of arthritis. It causes progressive damage to the cartilage and other joint tissues, and frequently affects the hand, knees, and hips. Gout is a painful, recurrent form of inflammatory arthritis, caused by deposition of uric acid crystal in joints (Watkins-Castillo, 2021). Symptoms typically consist of intense episodes of painful swelling in single joints, most often in the feet and especially in the big toe. There have been no reported cases of osteoarthritis flares or crystalline arthropathies in spaceflight. Historically, it has been thought that microgravity provides offloading that should decrease the incidence of osteoarthritis in spaceflight, but there is anecdotal evidence of cartilage damage caused by spaceflight. This is a new area of active research. The effect of spaceflight on the incidence of arthritis in-flight is currently unknown.

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

Historically, there are no published cases of either osteoarthritis flares or crystalline arthropathies occurring in spaceflight. It should be noted that OA flares may be less common overall in spaceflight due to microgravity and partial gravity offloading of the cartilage interface of the joint.

ANALOG LITERATURE

Cameron et al, 2011 provides analog incidence values for osteoarthritis among US Military members. It is a retrospective analysis over 10 year period (1999-2008) querying records from the DMSS (Defense Medical Surveillance System) across all branches of the US military. It reports a total of 108,266 incident cases over 13,768,885 person-years. Overall and stratified rates unadjusted and adjusted rates (by sex and age) are provided. Note this is based only on physician-diagnosed cases on OA in the military and thus could be an underestimate of the true incidence. This is based only on physician-diagnosed cases of OA in the military and thus could be an underestimate of the true incidence. Notably, the prevalence of osteoarthritis in the military is higher than that of the general population (26% higher prevalence in age ranges 20-24) and 200% higher in ages 40 years and older), likely as a result of the occupational demands of the military.

TERRESTRIAL LITERATURE

Osteoarthritis: Because osteoarthritis prevalence increases with age, most articles have a population of participants that is older than the astronaut corps. There are few articles that inform the incidence of Osteoarthritis and Crystalline arthropathies. Of the literature identified by the search, two terrestrial papers provided incidence for Osteoarthritis (Parry et al and Skou et al). Parry et al, 2018 provides an incidence value for acute flare-ups of knee osteoarthritis in 67 participants of a diary study (mean age 62, 55% Female, mean BMI 24.6). The average age is higher than the astronaut corps. Skou et al, 2020 provides a cross-sectional analysis of 193 patients with pre-existing knee osteoarthritis and 59 patients with pre-existing hip osteoarthritis who completed an educational and physical therapist-supervised exercise treatment program across 400 primary care facilities in Denmark. Participants performed a 30-second chair-stand test (the number of chair stands that a patient can complete in a 30 second period). The outcome measure was an increase in at least 2 points (self-reported) on a 0-10 pain scale after the chair test. 1 in 3 patients with knee OA, and 1 in 5 patients with hip OA, experienced an increase in at least 2 points with this chair test provocation. Notably, the average age of participants was above the astronaut corps (65.4y for knee OA, 66.8y for hip OA) as was the average BMI (29.1 for hip OA and 27.2 for knee OA). Cisternas et al, 2016 provides a retrospective analysis of the prevalence of osteoarthritis in US adults using data from the MEPS-HC (Medical Expenditure Panel Survey Household Component, Annual National Survey) (respondent-reported medical conditions). It includes adults 18 years and older, n = 31,228-34,920 annual responses. The study matched survey responses to a "probable Dx of OA" based on ICD9-CM Codes 715 (Osteoarthrosis and allied disorders),716 (other and unspecified arthropathies), 719 (Effusion/swelling of joint, unspecified). Sensitivity/specificity for OA using these codes was 62.9% and 93.5%. Based on this, they report a prevalence of 30.8 million adults with osteoarthritis (13.4% of the US population). Crystalline Arthropathies: Savolainen et al, 2003 is a Finnish study that provides incidence of crystalline arthropathies based on data collected in the year 2000. This is the only study identified that provides incidence for crystalline arthropathies. The incidence rate is reported as (overall) 18.7 cases per 100,000 person years, with a male incidence of 24.5/100,000 person years and a female incidence of 13.6/100,000 person years. Notably, the average age of diagnosis was 65yo, which is higher than the astronaut corps. Smith et al 2014, and Chen-Xu et al, 2019 provide prevalence values for gout. Prevalence data is not as useful incidence data for this effort. Smith et al, 2014 provides a global prevalence of gout of

0.076% (year 2010) from a systematic review. Chen-Xu et al, 2019 provide US prevalence of gout, stratified by age based on NHANES survey responses from 2015-2016. The average age of participants was 47.9yo and the overall prevalence was 3.9%, but when stratified by ages more applicable to the astronaut corps, the prevalence's are 0.7% for ages 20-39, and 3.4% for ages 24-59. Gout is more prevalent in developed nations, which explains the large discrepancy in the overall prevalence's presented by Smith et al vs. Chen-Xu et al.

OVERALL INCIDENCE SUMMARY

INCIDENCE

mean: 0.02295
SD: 1.136E-4

INCIDENCE SUMMARY

Terrestrial/analog data was used to inform the incidence for this condition, for crewmembers with no prior history of arthritis. The definition includes both Crystalline Arthropathy and Osteoarthritis, so the incidence for both was considered. Savolainen et al, 2003 provided data for the Crystalline Arthropathy distribution. Cameron et al, 2011 (a military analog) provided data for the Osteoarthritis distribution. The incidence is based on the contribution of both as a sum. For those with no prior history of arthritis: Gamma(shape=40814, rate=1778686) with mean: 0.02295 and SD: 1.136E-4.

TABLE 1. INCIDENCE MODEL

Incidence Details

Incidence Type
General

Segment
All

Env. Exposure
NA

Sex
Any

Crowns
Any

Contacts
Any

Pregnancy
Any

Incidence Distribution

Occurrence Dist
Poisson

Incidence Dist.
Gamma

Mean
0.0229462

SD
0.000113581

Gamma
(Shape): 40814
(Rate): 1.77869E+06

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Parry et al, 2018	Terrestrial	2
Skou et al, 2020	Terrestrial	1
Cameron et al., 2011.	Analog	3
Cisternas et al, 2016.	Terrestrial	1

Citation	Source	LOC Value
Savolainen et al, 2003.	Terrestrial	2
Smith et al, 2014.	Terrestrial	0
Chen-Xu, 2019.	Terrestrial	1

Osteoarthritis (OA): Parry et al, Skou et al, and Cameron et al, provide incidence data for osteoarthritis. Parry et al, 2018 provides an incidence value for acute flare-ups of knee osteoarthritis in 67 participants of a diary study (mean age 62, 55% Female, mean BMI 24.6). The average age is higher than the astronaut corps. Skou et al, 2020 provides a cross-sectional analysis of 193 patients with pre-existing knee osteoarthritis and 59 patients with pre-existing hip osteoarthritis who completed an educational and physical therapist-supervised exercise treatment program across 400 primary care facilities in Denmark. Participants performed a 30-second chair-stand test (the number of chair stands that a patient can complete in a 30 second period). The outcome measure was an increase in at least 2 points (self-reported) on a 0-10 pain scale after the chair test. 1 in 3 patients with knee OA, and 1 in 5 patients with hip OA, experienced an increase in at least 2 points with this chair test provocation. Notably, the average age of participants was above the astronaut corps (65.4y for knee OA, 66.8y for hip OA) as was the average BMI (29.1 for hip OA and 27.2 for knee OA). Cameron et al, 2011 provides analog incidence values for osteoarthritis among US Military members. It is a retrospective analysis over 10 year period (1999-2008) querying records from the DMSS (Defense Medical Surveillance System) across all branches of the US military. It reports a total of 108,266 incident cases over 13,768,885 person-years. Overall and stratified rates unadjusted and adjusted rates (by sex and age) are provided. Note this is based only on physician-diagnosed cases of OA in the military and thus could be an underestimate of the true incidence. Notably, the prevalence of osteoarthritis in the military is higher than that of the general population (26% higher prevalence in age ranges 20-24) and 200% higher in ages 40 years and older), likely as a result of the occupational demands of the military. Cisternas et al, 2016 provides a retrospective analysis of the prevalence of osteoarthritis in US adults using data from the MEPS-HC (Medical Expenditure Panel Survey Household Component, Annual National Survey) (respondent-reported medical conditions). It includes adults 18 years and older, n = 31,228-34,920 annual responses. The study matched survey responses to a "probable Dx of OA" based on ICD9-CM Codes 715 (Osteoarthrosis and allied disorders),716 (other and unspecified arthropathies), 719 (Effusion/swelling of joint, unspecified). Sensitivity/specificity for OA using these codes was 62.9% and 93.5%. Based on this, they report a prevalence of 30.8 million adults with osteoarthritis (13.4% of the US population). While osteoarthritis flares have traditionally been thought to be less common in spaceflight, there is some emerging research into cartilage damage induced by spaceflight. It is unclear at this time what effect spaceflight has on the incidence of osteoarthritis. Crystalline Arthropathies: Savolainen et al, 2003 is a Finnish study that provides incidence of crystalline arthropathies based on data collected in the year 2000. This is the only study found that provides incidence for crystalline arthropathies. The incidence rate is reported as (overall) 18.7 cases per 100,000 person years, with a male incidence of 24.5/100,000 person years and a female incidence of 13.6/100,000 person years. Notably, the average age of diagnosis was 65yo, which is higher than our astronaut corps. Smith et al 2014, and Chen-Xu et al, 2019 provide prevalence values for gout. Prevalence data is not as useful incidence data for this effort. Smith et al, 2014 provides a global prevalence of gout of 0.076% (year 2010) from a systematic review. Chen-Xu et al, 2019 provide US prevalence of gout, stratified by age based on NHANES survey responses from 2015-2016. The average age of participants was 47.9yo and the overall prevalence was 3.9%, but when stratified by ages more applicable to the astronaut corps, the prevalence's are 0.7% for ages 20-39, and 3.4% for ages 24-59.

CREWMEMBER SELECTION/PREVENTION

DISQUALIFYING CONDITIONS

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

PREFLIGHT PREVENTATIVE MEASURES

There are no specific preventive requirements for crewmembers for this condition.

BEST CASE SCENARIO DEFINITION

Acute osteoarthritis flare or crystalline arthropathy with mild to moderate symptoms that responds to treatment. (Note rheumatologic arthropathies are not covered in this condition).

WORSE CASE SCENARIO DEFINITION

Acute osteoarthritis flare or crystalline arthropathy with severe symptoms requiring more than one course of treatment. (Note rheumatologic arthropathies are not covered in this condition).

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

Osteoarthritis, acute Arthropathy, acute - crystalline

BEST CASE/WORST CASE PROBABILITY COMMENTS

The best-case, worst-case definition for this condition stipulates that the worst-case represents severe pain due to osteoarthritis or crystalline arthropathy which requires more than one course of treatment (i.e. the osteoarthritis or crystalline arthropathy is refractory to initial treatment). Fargetti et al, 2012 report that 1% of cases of Gout in the USA are refractory to treatment. Sicras-Mainar et al, 2021 provides a retrospective study in the Spanish National Health System (Spain) in which they determined the proportion of patients age 18yo or greater with chronic moderate to severe OA who were refractory to NSAIDs and Opioids was 10.7%. This is a population with chronic pain due to osteoarthritis, which differs from the astronaut population, but this value is likely an underestimate of those refractory to treatment with just NSAIDs. Due to the paucity of data aligning with the best-case/worst-case scenario definitions, these articles are felt to be as close of an estimation of the best-case/worst-case probabilities as can be obtained at this time. The values provided for gout and osteoarthritis were combined (with appropriate weighting to account for Osteoarthritis being more common than Gout) to arrive at a worst-case scenario probability of 9.7%.

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

Citation	Source	LOC Value
Fargetti et al, 2012.	Terrestrial	3
Sicras-Mainar et al, 2021	Terrestrial	3

The best-case, worst-case definition for this condition stipulates that the worst-case requires more than one course of treatment (i.e. the osteoarthritis or crystalline arthropathy is refractory to initial treatment). Fargetti et al, 2012 report that 1% of cases of Gout in the USA are refractory to treatment. Sicras-Mainar et al 2021 provides a retrospective study in the Spanish National Health System (Spain) in which they determined the proportion of patients age 18yo or greater with chronic moderate to severe OA who were refractory to NSAIDs and Opioids was 10.7%. This is a population with chronic pain due to osteoarthritis, which differs from the astronaut population, but this value is likely an underestimate of those refractory to treatment with just NSAIDs.

TABLE 4. CLIFF TREATMENT & OUTCOME TABLE BY CLINICAL PHASE

Case Scenario	Composite Incidence	Condition Probability %	CP1: Diagnosis		CP2: Treatment			CP3: Condition End State				
			TI%	Duration	TI%	Duration		TI%	RTDC		LOCL	
			Preset	Preset	Preset	Min	Max	Preset	Min%	Max%	Min%	Max%
Treated Best Case (TBC)	mean: 0.02295 SD: 1.136E-4	90 - 90	100	0.3	0	72	120	0	0	0	0	0
Treated Worst Case (TWC)		10 - 10	100	1.2	12.7292	120	360	0	0	0	0	0
Untreated Best Case (UTBC)	N/A	N/A	N/A	0.3	21.9506	168	336	21.9506	0	0	0	0
Untreated Worst Case (UTWC)	N/A	N/A	N/A	1.2	49.2161	336	1080	49.2161	0	0	0	0

TABLE 4 KEY

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

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

Clinical Phase General Comments:

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

Clinical Phase 1: Initial Assessment and Diagnosis:

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

Clinical Phase 2: Stabilization, Treatment, and Convalescence:

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

Clinical Phase 3: Condition End State:

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

SCENARIO OVERVIEW COMMENTS

RTDC surrogate used was hospitalization. See individual scenario comments below for more details.

TREATED BEST CASE (TBC) SCENARIO COMMENTS

A clinical summary resource from American College of Rheumatology was identified, with Dynamed synthesis of the recommendations, which provided information on duration of treatment (per the methods outlined by this rapid systematic review, Dynamed itself was thus cited as a source for duration). Based on the best-and worst-case definitions of the condition both responding to treatment the Clinical & Science Team made the assumption that RTDC would be 0% for this condition. The editor ran the search for RTDC to substantiate this assumption and the RTDC was 0%. The LOCL searches also yielded a probability of 0%.

TREATED WORST CASE SCENARIO (TWC) COMMENTS

A clinical summary resource from American College of Rheumatology was identified, with Dynamed synthesis of the recommendations, which provided information on duration of treatment (per the methods outlined by this rapid systematic review, Dynamed itself was thus cited as a source for duration). The best-case and worst-case scenarios for this condition are both responsive to treatment. Based on these definitions and the lack of data found in the treated best case scenario, it is fair to assume RTDC remains 0% for the worst case scenario. The LOCL search yielded a probability of 0%.

UNTREATED BEST CASE (UTBC) SCENARIO COMMENTS

Dynamed was used as the primary source for duration of treatment. There is a paucity of data regarding the duration of acute OA flares, so the durations are based primarily on data regarding the duration of gout flares. The minimum duration of the best-case treated and untreated scenarios are similar, because there is evidence that gout flares may be self-limited. Based on the best-and worst-case definitions of the condition both responding to treatment the Clinical & Science Team made the assumption that RTDC would be 0% for this condition. No RTDC searches were run for untreated best-case scenario and the RTDC was assigned a 0% probability based on this assumption. No data was identified regarding LOCL, thus it was assigned a probability of 0%

UNTREATED WORST CASE (UTWC) SCENARIO COMMENTS

Dynamed was used as the primary source for duration of treatment. The best-and worst-case definitions did not perfectly fit the definitions provided within the data found from Dynamed. Thus, a conservative approach was taken and a longer duration of treatment, based on the data, was selected for the untreated worst-case scenario duration. There is a paucity of data regarding the duration of acute OA flares, so the durations are based primarily on data regarding the duration of gout flares. The minimum duration of the best-case treated and untreated scenarios are similar, because there is evidence that gout flares may be self-limited. Based on the best-and worst-case definitions of the condition both responding to treatment the Clinical & Science Team made the assumption that RTDC would be 0% for this condition. No RTDC searches were run for untreated worst-case scenario and the RTDC was assigned a 0% probability based on this assumption. No data was identified regarding LOCL, thus it was assigned a probability of 0%.

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

Citation	Source	LOC Value
DynaMed, Record No. T474276, 2018.	Terrestrial	4
DynaMed, Record No. T913180, 2018.	Terrestrial	

Dynamed articles updated in 2018 were used to inform the duration for this CLiFF ("Gout Management - Treatment of Acute Attack" and "Monoarticular Arthritis - Approach to the Patient"). Dynamed synthesizes multiple references (listed within the Dynamed search). The data from this search is based on terrestrial data, but represents a robust source contributing to duration times.

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
n/a	n/a	2

The best-case and worst-case scenarios for this condition are both responsive to treatment. Based on these definitions, the Clinical & Science Team made the assumption that RTDC would be 0% for this condition. The editor conducted a literature search for RTDC

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
n/a	n/a	3

The literature searches for the various scenarios for LOCL identified no relevant articles, leading to the conclusion that the LOCL probability is 0%. Thus, no citations are available for LOCL.

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

Capabilities and Resourcing Scope

Overview

Worst Case Definition: Acute osteoarthritis flare or crystalline arthropathy with severe symptoms requiring more than one course of treatment. (Note rheumatologic arthropathies are not covered in this condition).
Best Case Definition: Acute osteoarthritis flare or crystalline arthropathy with mild to moderate symptoms that responds to treatment. (Note rheumatologic arthropathies are not covered in this condition).

Essentially this is a crystalline arthropathy that is acute in nature.

The CRT condition focuses primarily on the relief of this discomfort whether that requires moderate pain management, or not and with anti-inflammatory medication.

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, physical examination, and joint fluid collection to differentiate the condition from septic arthritis which would be an emergency.

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): 0.30 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): 1.2 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
3 - Synovial fluid collection and analysis

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

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 diagnostic efforts to rule out septic arthritis. Additionally, preventative measures were not included as they are not typically flown and crew are selected who have no history of crystalline arthropathy, so medications such as allopurinol are unlikely to be needed. Therefore, therapy options were limited.

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 RECONCILATION COMMENTS

The best/worst case definitions have changed from the IMM CLiFF. The IMM CLiFF included rheumatologic arthropathies in the best-case scenario and the worst-case scenario was septic arthritis. Neither rheumatologic nor septic arthropathies are included in this CLiFF, which has prompted changes in the incidence, duration, and RTDC. The LOCL probability remains 0% for all scenarios, as it did in the IMM CLiFF.

LIMITATIONS SUMMARY

CST assumed RTDC = 0% probability, so RTDC searches were not performed (editor did perform RTDC search for TBC scenario). There were no articles identified from the student effort for LOCL (although there were many articles identified during the search and no reason for exclusion was provided. It was assumed that they were not applicable to LOCL).

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)							145					
Treated Worst Case (TWC)							145					
Untreated Worst Case (UTWC)		664					145					
	Affected HSTCs (Continued)								TI Calculation			TI Score
	Hand (Dom)	Hand (Any)	Upper Extremity	Lower Extremity	Ambul & Standing (g)	Translation & Stabilization (microgravity)	Don/Doff Equipment	Pressure Ops	Total Tasks Impaired By Condition	Total Human System Category Tasks Full Mission	TI Decimal	TI %
Treated Best Case (TBC)									0	3763	0	0
Untreated Best Case (UTBC)			414	22			34	211	826	3763	0.219506	21.9506
Treated Worst Case (TWC)	132		414	22			34	211	958	3763	0.254584	25.4584
Untreated Worst Case (UTWC)	132		414	22	196	34	34	211	1852	3763	0.492161	49.2161

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)							145					
Treated Worst Case (TWC)												
Untreated Worst Case (UTWC)		664					145					
	Affected HSTCs (Continued)								TI Calculation			TI Score

	Hand (Dom)	Hand (Any)	Upper Extremity	Lower Extremity	Ambul & Standing (g)	Translation & Stabilization (microgravity)	Don/Doff Equipment	Pressure Ops	Total Tasks Impaired By Condition	Total Human System Category Tasks Full Mission	TI Decimal	TI %
Treated Best Case (TBC)									0	3763	0	0
Untreated Best Case (UTBC)			414	22			34	211	826	3763	0.219506	21.9506
Treated Worst Case (TWC)									0	3763	0	0
Untreated Worst Case (UTWC)	132		414	22	196	34	34	211	1852	3763	0.492161	49.2161

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

No Comments

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