Clinical Finding Form (CliFF)

Branch Baseline

ICL14_Bhp - Anxiety

Anxiety is difficult to define given that the medical reference literature uses varying, inconsistent, and often vague terminology. Generally, it implies apprehension or fear from a potential threat that is typically out of proportion to the situation and hinders the ability to function normally. The DSM-5 groups the following under “Anxiety Disorders”: generalized anxiety disorder, panic disorder, phobias, specific phobia, agoraphobia, social anxiety disorder, separation anxiety disorder (Kogan et al., 2016). However, an astronaut may experience isolated episodes of anxiety without being diagnosed with a psychiatric comorbidity. In Roma et al. (2021), “anxiety” was grouped into “negative valence systems” along with “malaise”, “loss of appetite”, and “irritability” using the National Institute of Mental Health’s (NIMH) Research Domain Criteria (RDoC) framework. This study does examined the interactions between spaceflight medical operations and behavioral health and found that negative valence systems occur frequently (53%) with documented medical conditions. In previous IMM efforts, all behavioral pathologies were grouped into a single CLiFF entitled “Behavioral Emergency CLiFF.” For this iteration, with the expertise from NASA’s Behavioral Health and Performance (BHP) program, certain syndromes that were thought to be most relevant to spaceflight were identified for their own CLiFF conditions. Regrettably, previous LSAH pulls did not attempt to classify behavioral conditions. A repeat LSAH pull is not currently possible. Per the prior effort: “to date, no behavioral emergencies have occurred before, during or after any U.S. space flight." Unfortunately, it is unknown how this statement relates to the incidence of transient episodes of anxiety, as this condition is often not characterized as an emergency. Related conditions covered in other CLiFFs include adjustment disorder, depression, grief-reaction, psychosis secondary to depression and sleep disturbance.

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

In Boyd et al. (2007), a questionnaire was used to calculate a depression score among American astronauts and Russian cosmonauts about the International Space Station (ISS). Participants completed a weekly survey during the 4-7 months that they were in space. Although anxiety was a variable utilized, an incidence value could not be calculated with the data supplied. Kanas et al. (2005), analyzed a questionnaire of American and Russian crewmembers and mission control personnel who were involved in international long-duration missions to the Mir space station and the ISS. The authors concluded that there were demonstrated changes in levels of mood and group climate over time. “Tension-anxiety” scores were significantly elevated for mission control subjects over crewmembers. Kanas et al. (2008) analyzed the content of crewmembers’ communications to elucidate psychological emotional status but made conclusions regarding generalizations and not specific psychiatric disorders. “Tension-anxiety” was a variable in this study however incidence could not be calculated with the data present in the article. Roma et al. (2021) used a systematic review to document behavioral health and performance (BHP)-relevant symptoms for each condition in NASA’s exploration medical conditions list. Negative valence systems were associated with the medical conditions 36% of the time. When a condition required medical treatment, negative valence systems were associated with medical conditions 53% of the time. The authors determined from historical prevalence data over 14 years of ISS operations that there were 481 adverse BHP effects of spaceflight medical treatments per person-year. Although this does not reflect primary or isolated anxiety effects, we can assume that negative valence systems would result in 173.16 events per person-year (= 481 events/person-year * 0.36). This is still likely an over-estimation given that negative valence systems encompass malaise, loss of appetite and irritability in addition to anxiety. This source was down-rated as there was significant overlap with the depression, adjustment disorder, grief-reaction and sleep disturbance CLiFF conditions. In a NASA evidence report for the Human Research Program (Slack et al., 2016) the following is detailed: “Data collected through the LSAH reveals that symptoms of anxiety and depression have occurred during space flight (although there are no reports any diagnoses for either have been give). Over 28.84 person-years of NASA space flight, flight and crew surgeons have documented 24 instances of anxiety related symptoms presented in space flight for an incidence rate of 0.832 cases per person-year (NASA 2007a).” This data was only collected during shuttle flights and the authors of this CLiFF do estimate that this is a severe underestimation of transient episodes of anxiety as most episodes are not likely reported. However, transient episodes of anxiety are not likely reported in analog conditions similarly; consequently, the authors rated this source the highest.

ANALOG LITERATURE

There are several polar studies (Palinkas et al., 1995; Palinkas et al., 2004; Weiss et al., 2000, Steine et al. 2003 and Sandal et al., 2006) that analyzed psychological function in arctic and Antarctic participants, however incidence data could not be calculated from data provided in the publications. Further, anxiety as defined in the best-case scenario was not congruent with the definitions in these studies. Bohnker et al. (1992) conducted a descriptive study of 150 patients on an aircraft carrier over the course of 11 months (July 1990 – May 1991). The ships population was

used as a representative control group. This was not a highly screened population as these were surface-line recruits. There were a total of 2827 people onboard the ship and a total of two diagnoses of “panic disorder” and one diagnosis of “simple phobia.” Campbell et al. (2021) performed a retrospective longitudinal study utilizing the military health system datasets for active United States Army individuals from 2005-2011. Although there were three study groups (Deployed, Combat-Exposed; Deployed, Not-Combat-Exposed; and Not Deployed), only deployed, Not-Combat-Exposed would be relevant to our target population. In this study, there were over 84,850 subjects with 7,220 diagnoses of anxiety disorder over 141,782 person-years resulting in an incidence rate of 5.1/100 person-years (Std error:1.1). This study was downrated as the population involved was not highly screened. In Tansey et al. (1979) medical reports from 1963-1973 of 885 fleet ballistic missile submarine patrols were analyzed and compared to illness rates found in crewmembers on surface-level vessels. Within this timespan there were only 25 reported events of anxiety reaction out of a total of 7,650,000 man-days. This study is severely limited by lack of voluntary reporting and psychiatric definition changes. Moore et al. (2021) retrospectively analyze the Defense Medical Epidemiology Database (DMED) to determine incidence rates of behavioral pathologies military firefighters. “General anxiety disorder” had an incidence rate of 20.45 per 10,000 person-years (n= 144) and “panic disorder” had an incidence rate of 11.6 per 10,000 person-years (n=79). Although this highly-screened population fits well with spaceflight participants, data here likely represent the worst-case scenario as opposed to an anxiety reaction.

TERRESTRIAL LITERATURE

Annual incidence rates of generalized anxiety diagnoses and symptoms in a United Kingdom population using retrospective data from The Health Improvement Network (THIN) database was 23.33/1000 person years at risk (PYAR) for women and 11.65/1000 PYAR for men in 2018 (Slee et al., 2018). Studies found by this CliFF’s authors that were limited to American populations presented results in prevalence data and incidence could not be calculated.

OVERALL INCIDENCE SUMMARY

INCIDENCE

mean 0.8318 and SD 0.1715

INCIDENCE SUMMARY

The Bayesian posterior distribution for the incidence rate given the spaceflight data (24 events over 28.84 person-years) under an uninformative prior is Gamma(shape=23.524, rate=28.281) with mean 0.8318 and SD 0.1715.

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
0.831795

SD
0.171499

Gamma
(Shape): 23.524
(Rate): 28.281

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Boyd et al., 2007	Spaceflight	0
Kanas et al., 2005	Spaceflight	0
Kanas et al., 2008	Spaceflight	0
Roma et al., 2021	Spaceflight	2
Slack et al., 2016	Spaceflight	3
Bohnker et al., 1992	Analog	1
Campbell et al., 2021	Analog	2
Tansey et al., 1979	Analog	1
Moore et al., 2021	Analog	2
Slee et al., 2018	Analog	1

Incidence was difficult to calculate given the varying terminologies used across studies. The best-case scenario likely refers to an anxiety reaction as opposed to a psychological disorder. Except for the Slack et al. evidence report and the Roma et al. study, most incidence data from the sources referred to psychological disorders.

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 exists several preflight behavioral evaluations. A cognitive assessment measuring memory, attention reasoning and spatial processing is performed for every crewmember participating in missions greater than 30 days. A behavior observation of training is also required in two preflight training sessions to provide data about individual behavior and crew interactions. An assessment of crew flight readiness is done during the preflight psychiatric/psychologic status check which occurs at both L-240/180 and L-90/30 days.

BEST CASE SCENARIO DEFINITION

Acute anxiety or mild panic symptoms caused by situational factors (e.g. burnout, work overload, performance pressure, significant events) that alleviates without any impact to the mission or personal life. It may require pharmacological therapy PRN, behavioral health intervention and/or increased behavioral health countermeasures.

WORSE CASE SCENARIO DEFINITION

Anxiety Disorders or severe panic symptoms causing significant distress or decline in areas including but not limited to work performance, sleep and interpersonal dynamics. The condition requires long-term pharmacologic therapy (minimum 6 months), and/or behavioral health intervention.

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

BHP - Panic Symptoms

BEST CASE/WORST CASE PROBABILITY COMMENTS

Per the prior related CliFF, there have been no cases of the worst-case scenario. In Roma et al. (2021), it was estimated that negative valence systems were associated with medical conditions 36% of the time. Consequently, we estimated that there were 173.16 events per-person year of possible negative valance systems from 481 potential impacts per person-year. If the next event was the worst-case scenario, we would expect the percentage of the best-case turning into the worst-case be no more than 0.57% (=1/174 *100).

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

Citation	Source	LOC Value
Roma et al., 2021	Spaceflight	2

Studies were limited given the change in definitions in Diagnostic and Statistical Manual of Mental Disorders (DSM) and the wording of the best- and worst-case scenarios which did not align with current definitions of psychological pathologies. The reported worst-case probability is likely to be an over-estimation, however remains a negligible percentage.

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 0.8318 and SD 0.1715	99.43 - 99.43	100	0.7333	5.60723	1	4379	0	0	0	0	0
Treated Worst Case (TWC)		0.57 - 0.57	100	0.7333	29.1257	4380	11096	5.60723	0	3.64	0	0
Untreated Best Case (UTBC)	N/A	N/A	N/A	0.7333	29.1257	1	4379	9.11507	0	0	0	0
Untreated Worst Case (UTWC)	N/A	N/A	N/A	0.7333	29.1257	4380	11096	29.1257	0	3.64	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

Anxiety is often a person's response to a stress, characterized by apprehension or dread. Stress is generally a response to a perceived threat from an external cause. Stress responses are transient. Anxiety can be both transient and persistent. The best-case scenario is an anxiety reaction, but not necessary a psychological disorder. The worst-case scenario involves persistent symptoms that can take the form of any of the anxiety disorders in the DSM-V (generalized anxiety disorder, panic disorder, phobias, specific phobia, agoraphobia, social anxiety disorder, separation anxiety disorder). The RTDC surrogate for this condition was hospitalization.

TREATED BEST CASE (TBC) SCENARIO COMMENTS

In the treated best case, the anxiety reaction occurs and easily resolves. In the most benign case, it was the gestalt of subject-matter-experts, that subjects would experience unproportionate reactions for at least 1 hour; panic attacks typically peak within 10 minutes (Locke et al., 2015). Symptoms in the best-case scenario are transient, especially with medication or behavioral therapy, and would not be expected to progress to an actual disorder defined by the DSM-5. Consequently, the maximum duration is set just below 6-months. RTDC and LOCL are not expected in the treated best case.

TREATED WORST CASE SCENARIO (TWC) COMMENTS

For duration in the treated worst-case, the lower bound was set by the condition's definition. In a three-year longitudinal study in the Netherlands, a psychiatric cohort among the general adult population (n=6646) was followed (ten Have et al., 2020). Of these subjects, there were 158 participants with first or recurrent anxiety disorder. Those with anxiety disorder had a median episode duration was 7.5 months and mean duration was 15.2 months (11096 hours). People with generalized anxiety disorder (GAD) alone were not found to have an increased risk for hospitalization in a UK-based, 10-year prospective study (IRR = 1.07) (Remes et al., 2019). Only those with GAD and concurrent major depressive disorder were found to be at increased risk for hospital admissions. While there was no data on rate of suicide success, subject-matter consensus was that any suicidal attempt would require hospitalization. A different prospective population study in the Netherlands did demonstrate that anxiety disorder is an independent risk factor for suicidal attempts (odds ratio: 3.64; 95% confidence interval, 1.70- 7.83) (Sareen et al., 2005). Although the authors of this CliFF acknowledge that an odds ratio cannot be directly converted into a probability range, we assumed that the probability of the control group (spaceflight participants without GAD) was 1%, allowing us to estimate that the probability range for RTDC was 0 – 3.64%. LOCL is not expected in the treated worst-case scenario.

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 the best-case scenario.

UNTREATED WORST CASE (UTWC) SCENARIO COMMENTS

There was a lack of systematic studies available to determine duration for the untreated worst-case as current convention is to pursue treatment. The untreated worst-case would be expected to last no less than the treated worst-case and accordingly the same range for duration and RTDC was used. Miloyan et al. (2016) conducted a systematic review and meta-analysis of prospective cohort studies that examined the relationship between anxiety disorders and mortality. The authors determined that there was no evidence of increased mortality risk among anxious individuals relative to the controls. Consequently, LOCL is not expected for this scenario.

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

Citation	Source	LOC Value
Locke et al., 2015	Terrestrial	3
ten Have et al., 2021	Terrestrial	

Duration was largely predetermined by the condition's DSM and scenario definitions. The upper-bound of the worst-case scenario duration was estimated to be the longest time-points in prospective, but low-powered studies.

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Remes et al., 2019	Terrestrial	2
Sareen et al., 2005	Terrestrial	

There were no data available regarding the rate of hospitalization in adjustment disorder. RTDC was estimated from odds ratio of suicide attempts.

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Miloyan et al., 2016	1	1

LOCL was not expected for this condition, and a single systematic review and metanalysis confirmed this assumption.

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

Overview

Worst Case Definition: Anxiety Disorders or severe panic symptoms causing significant distress or decline in areas including but not limited to work performance, sleep and interpersonal dynamics. The condition generally requires long-term pharmacologic therapy (minimum 6 months), and/or behavioral health intervention.

Best Case Definition: Acute anxiety or mild panic symptoms caused by situational factors (e.g. burnout, work overload, performance pressure, significant events) that alleviates without any impact to the mission or personal life. It may require pharmacological therapy PRN, behavioral health intervention and/or increased behavioral health countermeasures.

Diagnostic Scope and Resourcing
In the best-case scenario, diagnosis is based on a focused psychiatric history, psychiatric review of systems, mental status exam and assessment and plan. Additionally, vital signs and a cardiopulmonary exam should be conducted

For behavioral health conditions ground communication and further higher-level psychiatric consultation should occur for diagnostic clarification and to ascertain the necessity of prn psychotropic medication for acute anxiety/panic

In the worst-case scenario, diagnosis is based on a focused psychiatric history, psychiatric review of systems, mental status exam and assessment and plan. Additionally, vital signs and a cardiopulmonary exam should be conducted

For behavioral health conditions ground communication and further higher-level psychiatric consultation should occur for diagnostic clarification and to ascertain the necessity of prn psychotropic medication for acute anxiety/panic and additional long term psychotropic medication management.

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): 0.7333 (44 min).

1. Obtain Vital Signs
2. Take a proper history of the patient and psychiatric ROS
3. Perform a cardiopulmonary exam
4. Perform a mental status exam
5. Interpret the history and MSE
6. Obtain a psychiatry consult
7. Establish ground communication

CP1 WC (Treated or Untreated): 0.7333 (44 min)

1. Obtain Vital Signs
2. Take a proper history of the patient and psychiatric ROS
3. Perform a cardiopulmonary exam
4. Perform a mental status exam
5. Interpret the history and MSE
6. Obtain a psychiatry consult

7. Establish ground communication

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

Treatment Scope and Resourcing

Most best-case terrestrial populations resolve with ongoing brief psychotherapeutic interventions and do not require ongoing medication management; in the acute phase, they may require a prn medication to help ameliorate increased anxious distress/panic. The medium acting benzodiazepine Lorazepam as well as the long acting benzodiazepine Diazepam have been shown to be both safe and effective for the acute treatment of anxious distress/panic.

Cognitive behavioral therapy is an effective psychotherapeutic treatment modality for anxiety and in the BC should be provided on a weekly basis for three months and be continued bi-weekly thereafter for the duration of the mission. Furthermore, considering the austere environment and communication barriers that exist on long duration missions it is recommended that there be on board private psychological conferences for the direct administration of psychotherapeutic treatment.

Additionally, The CES devices can be helpful for symptom reduction, are safe, require a minimal footprint and can be self-administered. However, justification as a primary treatment modality over psychotherapy remains controversial. However, they should be considered as an adjunct treatment modality along with therapy.

Terrestrially, worst case conditions generally do require long term psychotropic medication management and antidepressants (SSRIs) remain the pharmacologic treatment of choice. Escitalopram as the S-enantiomer of Citalopram is effective for the treatment of anxiety and has a favorable half-life and side effect profile. It's enantiomer, Citalopram is a racemic compound and has more adverse effects associated with it such as dose related QTc prolongation and thus is not a suitable choice. Fluoxetine and Sertraline are both effective SSRIs for the treatment of anxiety and have favorable side effect profiles. Benzodiazepines play a secondary role and can be helpful for ameliorating severe anxious distress/panic acutely.

As above in the BC , cognitive behavioral therapy is an effective psychotherapeutic treatment modality for anxiety and in the WC should be provided on a weekly basis for six months and be continued bi-weekly thereafter for the duration of the mission. Furthermore, considering the austere environment and communication barriers that exist on long duration missions it is recommended that there be on board private psychological conferences for the direct administration of psychotherapeutic treatment.

CES devices can be helpful for symptom reduction, are safe, require a minimal footprint and can be self-administered. However, justification as a primary treatment modality over medications and therapy remains controversial. However, they should be considered as an adjunct treatment modality with medications and therapy.

Communications and Support Needs

Adjustment disorders generally are self-limited conditions which often resolve when the stressor is removed. In the BC it is recommended that ground communication and a psychiatric consult be established for diagnostic clarification and psychotherapeutic treatment guidance. Further support would include ongoing onboard private psychological conferences to provide direct psychotherapeutic care for the duration of the mission. Following suit, for WC, ground communication and a psychiatric consult should be established for diagnosis and psychotherapeutic treatment guidance. Further support would include ongoing onboard private psychological conferences to provide direct psychotherapeutic care for the duration of the mission.

REFERENCES

Hales, R., Yudofsky, S., Roberts, L.W. (Eds.). (2014). The American Psychiatric Publishing: Textbook Of Psychiatry, Sixth Edition. American Psychiatric Publishing.

CES Devices:
1. Alpha Stim: www.alphastim.com
2. FisherWallace Device: www.fisherwallace.com

IMM CLIFF RECONCILATION COMMENTS

This condition has no previous predecessor as all psychiatric pathologies were encompassed in the previous CLiFF entitled "Behavioral Emergency." Given the breadth of this topic, the former CLiFF did not adequately represent BHP-Anxiety.

LIMITATIONS SUMMARY

• The authors of this CLiFF did not have access to the original LSAH data and thus there was an implied dependence on already published sources which did not adequately apply to this condition • There is some overlap between this condition and other BHP CLiFF conditions. • Several assumptions needed to be made regarding the untreated cases, RTDC and LOCL given lack of available studies. • Terrestrial sources likely overestimate the incidence, RTDC and LOCL values given the extensive preflight screening that occurs in long-duration spaceflight crewmembers. • There is likely underreporting of this condition in spaceflight due to fears of retribution.

TABLE 8. TASK IMPAIRMENT CALCULATION BASED ON AFFECTED HUMAN SYSTEMS TASK CATEGORIES (HSTC)

Clinical Phase 2: Treatment												
	Affected HSTCs											
	Cognitive - Simple	Cognitive - Complex	Communications	Inter-personal Skills	Vision	Hearing	Cardio-pulmonary	Dentition	GI	GU		
Treated Best Case (TBC)												
Untreated Best Case (UTBC)		664		89								
Treated Worst Case (TWC)		664		89								
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)								211	211	3763	0.0560723	5.60723
Untreated Best Case (UTBC)	132							211	1096	3763	0.291257	29.1257
Treated Worst Case (TWC)	132							211	1096	3763	0.291257	29.1257
Untreated Worst Case (UTWC)	132							211	1096	3763	0.291257	29.1257

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		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)									0	3763	0	0
Untreated Best Case (UTBC)	132							211	343	3763	0.0911507	9.11507
Treated Worst Case (TWC)								211	211	3763	0.0560723	5.60723
Untreated Worst Case (UTWC)	132							211	1096	3763	0.291257	29.1257

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