Clinical Finding Form (CliFF)

Branch Baseline

ICL15_Bhp - Depression

Depressive mood characterized by apathy, low-motivation, irritability, can occur in highly screened spaceflight participants to both planned and unexpected events. If that depressive mood persists for more than two weeks and causes significant distress or impairment in social, occupation or other areas of functioning, major depressive disorder may be diagnosed. NASA distinguishes between a behavioral event and a psychiatric disorder by the following: “a behavioral condition is any decrement in mood, cognition, morale, or interpersonal interaction that adversely affects operational readiness or performance; whereas a psychiatric disorder is one that meets the DSM criteria for diagnosis of a disorder” (Slack et al., 2016). Events that may affect spaceflight participants that lead to this condition may include death of family members or friends, crew friction, frustration with ground team, other medical emergencies, delayed return to earth and other unexpected events. Although there have been no behavioral emergencies or diagnoses of major depressive disorder during spaceflight, there have been reports of depressive mood symptoms (Slack et al., 2016). We expect that depressive symptoms in crewmembers are likely underreported given concern to potentially jeopardize future flight status. 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. Related conditions covered in other CLiFFs include adjustment disorder, anxiety, 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 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 the same 28.84 person-years, four astronauts experienced signs and symptoms of depression during space flight for an incidence rate of 0.139 per person-year (NASA, 2007a).” This data was only collected during shuttle flights and certainly is dated. All shuttle flights were about 2 weeks or less in duration. Thus, the flight duration was not sufficiently long to satisfy the criteria for major depressive disorder. Further, the authors of this CLiFF comment that this is likely an over-estimation because symptoms reported may be transient. However, there may be some under-reporting of depressive symptoms by crewmembers. Because of these limitations, an analog study was rated higher. 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 anxiety, malaise, loss of appetite and irritability in addition to anxiety. This source was downrated after discussion with the authors as there is likely significant overlap with the depression, adjustment disorder, grief-reaction, and sleep disturbance CLiFF conditions. Although there are a multitude of other spaceflight studies analyzing depressive behavioral responses during spaceflight (Boyd et al., 2007, Kanas et al., 2005, Kanas et al., 2008), incidence data were not able to be calculated with the data provided in the publications.

ANALOG LITERATURE

In Palinkas et al. (2004), 220 men and 93 women who spent a full winter at either McMurdo or South Pole Antarctic stations were debriefed by three psychiatrists and one clinical psychologist between 1994 and 1997. All participants, who were either military or civilian personnel were required to undergo medical and psychological evaluations prior to deploying to Antarctica. All subjects remained in Antarctica for approximately 12 months. Evaluation of participants consisted of an interview with a U.S. Navy psychiatrist and clinical psychologist and completion of multiple standardized clinical assessments, including the Minnesota Multiphasic Personality Inventory (MMPI) (33), the 16-Personality Factor Test (16-PF) (34) and the Michigan Alcoholism Screening Test (MAST). Although this was a voluntary study and likely limited by underreporting for fear of employment retribution. Still, this was a highly screened population similar to what we might expect from spaceflight crews. This study presented prevalence data, but incidence data was able to be calculated given the data provided. Diagnoses that would apply to this condition include: major depressive disorder—single episode (n=6), major depressive disorder—recurrent (n=2), dysthymic disorder (n=1) and depressive disorder NOS (n=4). There

were a total of 313 subjects and each subject was in Antarctica for 12 months. 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 83,928 subjects with 8,319 diagnoses of mood disorder over 139,545 person-years resulting in an incidence rate of 6.0/100 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 13 cases of “depression, neurotic” and one case of “maladjustment” out of a total of 7,650,000 man-days. This study is severely limited by lack of voluntary reporting and psychiatric definition changes.

TERRESTRIAL LITERATURE

In Kessler et al. (2003), the prevalence of major depressive disorder (defined by the DSM-4) in the United States age 18 an outer was found to be 16.2%. In an Iranian population-based cohort study, Najafipour et al. (2021) demonstrated an incidence rate (person/1000 person-years) as 3.9 for depression.

OVERALL INCIDENCE SUMMARY

INCIDENCE

mean 0.0415 and SD 0.0116

INCIDENCE SUMMARY

The Bayesian posterior distribution for the incidence rate given the Antarctic Analog data (13 events over 313 person-years) under an uninformative prior is Gamma(shape=12.78, rate=307.65) with mean 0.04154 and SD 0.01162.

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
0.0415407
SD
0.0116201

Gamma
(Shape): 12.78
(Rate): 307.65

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Slack et al., 2016	Spaceflight	2
Roma et al., 2021	Spaceflight	2

Citation	Source	LOC Value
Palinkas et al., 2004	Analog	3
Campbell et al., 2021	Analog	1
Tansey et al., 1979	Analog	1
Kessler et al., 2003	Terrestrial	0
Najafipour et al., 2021	Terrestrial	1

The highest rated evidence came from a study in highly screened individuals living in close proximity for a year in Antarctica.

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

Transient apathy, low-motivation, irritability and/or disturbance of mood that resolves without any impact to the mission or personal life and/or requires as needed behavioral health intervention and increased behavioral health countermeasures.

WORSE CASE SCENARIO DEFINITION

A Depressive Disorder causing significant distress or decline in areas including but not limited to work performance, sleep, and interpersonal dynamics. The condition may also include recurrent suicidal ideation. The Depressive Disorder persists and requires pharmacologic therapy (minimum 6 months) and/or behavioral health intervention; may be treatment resistant; or may result in suicide attempt

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

BHP - Apathy BHP - Low Motivation BHP - Irrritability BHP - Mood Disturbance

BEST CASE/WORST CASE PROBABILITY COMMENTS

The worst case, which is likely a diagnosis of severe major depressive disorder, has not occurred in spaceflight to date. However, in an Antarctic analog population, out of 13 mood disorder events, there were two episodes of recurrent major depressive disorder (Palinkas et al., 2004). Consequently probability was estimated to be 15% (= 2/13).

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

Citation	Source	LOC Value
Palinkas et al., 2004	Analog	3

The worst-case scenario has not occurred in spaceflight, however it has existed in analog populations. The following study, albeit low-powered, used high-screened participants that "wintered-over" in polar conditions.

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 0.0415 and SD 0.0116	85 - 85	100	0.78333	1.18257	1	336	0	0	0	0	0
Treated Worst Case (TWC)		15 - 15	100	0.78333	33.2846	336	17520	0	2.6	11.8	0	4.2
Untreated Best Case (UTBC)	N/A	N/A	N/A	0.78333	2.36513	1	336	2.36513	0	0	0	0
Untreated Worst Case (UTWC)	N/A	N/A	N/A	0.78333	66.5692	336	17520	66.5692	2.6	11.8	0	4.2

TABLE 4 KEY

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

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

Clinical Phase General Comments:

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

Clinical Phase 1: Initial Assessment and Diagnosis:

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

Clinical Phase 2: Stabilization, Treatment, and Convalescence:

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

Clinical Phase 3: Condition End State:

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

SCENARIO OVERVIEW COMMENTS

The best case of scenario likely refers to a transient episode of depressive mood. There is some question whether what is termed “neurasthenia” would fall into this condition, defined as a “negative psychological response to the isolation and rigors of long-duration mission” (Slack et al., 2016 and Kanas et al., 2009). This terminology is considered a psychiatric condition of importance to Russian space psychologists however is not included in the DSM-5. The worst-case scenario refers to a severe case of major depressive disorder requiring extensive pharmacological and behavioral intervention. The RTDC surrogate for this condition is hospitalization.

TREATED BEST CASE (TBC) SCENARIO COMMENTS

Duration for the best-case scenario, a transient depressive mood, was determined to be between one hour and two weeks. The upper bound was estimated as the criteria for major depressive disorder (MDD) by the DSM-5, which would be the worst-case scenario, requires at least two weeks of symptoms, along with other specified criterion (Hasin et al., 2018). RTDC and LOCL is not expected for the treated worst case.

TREATED WORST CASE SCENARIO (TWC) COMMENTS

For duration in the treated worst-case, the lower bound was set by the condition’s definition (6 months). Kessler et al. (2003) found in a face-to-face household survey in 48 contiguous United States that episodes of depression could last as long as 12-months (n-9090). In the Netherlands Mental Health Survey and Incidence Study (n=7076), 20% of those diagnosed with major depression had not recovered at 24 months (Spijker et al., 2002). In a national survey of 36,309 US adults, rate of inpatient hospitalization ranged from 2.60% to 11.8% (Hasin et al., 2018). Even in treated cases, LOCL can still occur. In Simon et al. (1998), treated patients with a known diagnosis of MDD still had a 4.2% mortality rate by suicide.

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 and RTDC for the untreated worst-case. Further, although there were several studies regarding suicide attempts for this scenario, but none that detailed mortality. Accordingly, the values used for the treated worst-case were used in this condition as we would not expect it to be less.

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

Citation	Source	LOC Value
Hasin et al., 2018	Terrestrial	2
Kessler et al., 2003	Terrestrial	
Spijker et al., 2002	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 cross-sectional, high-powered studies.

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Hasin et al., 2018	Terrestrial	2

RTDC was determined by a cross-sectional, high powered, terrestrial study.

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Simon et al., 1998	Terrestrial	1

Although there were several terrestrial studies detailing suicide attempts, mortality secondary to major depressive disorder was limited to a single, high-powered retrospective study. The value from this study is likely an over-estimation as this was not a highly screened population and they did possess multiple comorbidities.

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

Capabilities and Resourcing Scope

Overview

Worst Case Definition: A Depressive Disorder causing significant distress or decline in areas including but not limited to work performance, sleep, and interpersonal dynamics. The condition may also include recurrent suicidal ideation. The Depressive Disorder persists and requires pharmacologic therapy (minimum 6 months) and/or behavioral health intervention; may be treatment resistant; or may result in suicide attempt.
Best Case Definition: Transient apathy, low-motivation, irritability and/or disturbance of mood that resolves without any impact to the mission or personal life and/or requires as needed behavioral health intervention and 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, safety and screening.

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 screening for suicidal ideations. And additionally, to ascertain the necessity/course for 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): 0.78333 (47 min).
1. Obtain Vital Signs
2. Take a proper history of the patient and psychiatric ROS
3. Obtain IV access
4. Labs: TSH/Free T4 (necessity = 0)
5. Perform a cardiopulmonary exam
6. Perform a mental status exam
7. Interpret the history, physical exam and MSE
8. Interpret labs
9. Obtain a psychiatry consult
10. Establish ground communication

CP1 WC (Treated or Untreated): 0.78333 (47 min)
1. Obtain Vital Signs
2. Take a proper history of the patient and psychiatric ROS
3. Obtain IV access
4. Labs: TSH/Free T4 (necessity = 0)
5. Perform a cardiopulmonary exam
6. Perform a mental status exam
7. Interpret the history, physical exam and MSE
8. Interpret labs
9. Obtain a psychiatry consult
10. 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 regular ongoing brief psychotherapeutic interventions and do not require ongoing medication management.
Cognitive behavioral therapy is an effective psychotherapeutic treatment modality for depression 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.

Other measures such as crew rest/day off should be implemented as necessary.

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 depression and have favorable side effect profiles.

Additionally, in the WC scenario concern exists for suicidal ideation and behaviors. Some risk factors include, male sex, previous history of suicide attempts or threats, isolation, a prominent history of feelings of hopelessness or personality disorder (borderline). Because of the austere nature of the spaceflight environment it is important to include a period of 1:1 observation for a minimum period of 24 hours.

As above in the BC , cognitive behavioral therapy is an effective psychotherapeutic treatment modality for depression 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.

Other measures such as crew rest/day off should be implemented as necessary.

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.
Other physical treatment modalities to consider in the WC scenario would me the portable repetitive transcranial magnetic stimulation devices. This treatment has been demonstrated to be safe and potentially beneficial for clinical depression that has not been responsive to pharmacotherapy. rTMS should also be considered as an adjunctive therapeutic modality with medications.

Communications and Support Needs
Depression in the aerospace environment is concerning. In the BC it is recommended that ground communication and a psychiatric consult be established for accurate diagnosis, treatment, and symptom management. Further support would include regular 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 accurate diagnosis, treatment, and ongoing psychotropic medication management. Further support would include regular onboard private psychological conferences to provide direct psychotherapeutic care for the duration of the mission.
Additional support may be utilization of the CES devices and potentially a portable rTMS device.

REFERENCES
Hales, R., Yudofsky, S., Roberts, L.W. (Eds.). (2014). The American Psychiatric Publishing: Textbook Of Psychiatry, Sixth Edition. American Psychiatric Publishing.
Nemeroff, C, Schatzberg, A., Essentials of Clinical Psychopharmacology, Third Edition.

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-Depression

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)				89								
Untreated Best Case (UTBC)				89								
Treated Worst Case (TWC)		664		89			145					
Untreated Worst Case (UTWC)		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)									89	3763	0.0236513	2.36513
Untreated Best Case (UTBC)									89	3763	0.0236513	2.36513
Treated Worst Case (TWC)	132	564	414	22	196	34	34	211	2505	3763	0.665692	66.5692
Untreated Worst Case (UTWC)	132	564	414	22	196	34	34	211	2505	3763	0.665692	66.5692

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)				89								
Treated Worst Case (TWC)												
Untreated Worst Case (UTWC)		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)									0	3763	0	0
Untreated Best Case (UTBC)									89	3763	0.0236513	2.36513
Treated Worst Case (TWC)									0	3763	0	0
Untreated Worst Case (UTWC)	132	564	414	22	196	34	34	211	2505	3763	0.665692	66.5692

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.

REFERENCES

Reference
1. Boyd, Jennifer E., Nick Kanas, Vadim I. Gushin, and Saylor Stephanie. 2007. 'Cultural differences in patterns of mood states on board the International Space Station', Acta Astronautica, 61: 668-71.
2. Campbell, M. S., K. O'Gallagher, D. J. Smolenski, L. Stewart, J. Otto, B. E. Belsher, and D. P. Evatt. 2021. 'Longitudinal Relationship of Combat Exposure With Mental Health Diagnoses in the Military Health System', Mil Med, 186: 160-66.
3. Hasin, Deborah S., Aaron L. Sarvet, Jacquelyn L. Meyers, Tulshi D. Saha, W. June Ruan, Malka Stohl, and Bridget F. Grant. 2018. 'Epidemiology of Adult DSM-5 Major Depressive Disorder and Its Specifiers in the United States', JAMA Psychiatry, 75: 336-46.
4. Kanas, N. A., V. P. Salnitskiy, J. B. Ritsher, V. I. Gushin, D. S. Weiss, S. A. Saylor, O. P. Kozerenko, and C. R. Marmar. 2005. 'Human Interactions in Space: ISS versus Shuttle/M.' in, 56th International Astronautical Congress of the International Astronautical Federation, the International Academy of Astronautics, and the International Institute of Space Law (American Institute of Aeronautics and Astronautics).
5. Kanas, N., G. Sandal, J. E. Boyd, V. I. Gushin, D. Manzey, R. North, G. R. Leon, P. Suedfeld, S. Bishop, E. R. Fiedler, N. Inoue, B. Johannes, D. J. Kealey, N. Kraft, I. Matsuzaki, D. Musson, L. A. Palinkas, V. P. Salnitskiy, W. Sipes, J. Stuster, and J. Wang. 2009. 'Psychology and culture during long-duration space missions', Acta Astronautica, 64: 659-77.
6. Kanas, Nick, and Dietrich Manzey. 2008. 'Space psychology and psychiatry'.
7. Kessler, Ronald C., Patricia Berglund, Olga Demler, Robert Jin, Doreen Koretz, Kathleen R. Merikangas, A. John Rush, Ellen E. Walters, and Philip S. Wang. 2003. 'The Epidemiology of Major Depressive DisorderResults From the National Comorbidity Survey Replication (NCS-R)', JAMA, 289: 3095-105.
8. Najafipour, Hamid, Mohadeseh Shojaei Shahrokhabadi, Ghodsyeh Banivaheb, Abdolreza Sabahi, Mitra Shadkam, and Ali Mirzazadeh. 2021. 'Trends in the prevalence and incidence of anxiety and depressive symptoms in Iran: findings from KERCADRS', Family Medicine and Community Health, 9: e000937.
9. Palinkas, L. A., F. Glogower, M. Dembert, K. Hansen, and R. Smullen. 2004. 'Incidence of psychiatric disorders after extended residence in Antarctica', Int J Circumpolar Health, 63: 157-68.
10. Roma, Peter G., Jason S. Schneiderman, Julia M. Schorn, Sara E. Whiting, Lauren Blackwell Landon, and Thomas J. Williams. 2021. 'Assessment of Spaceflight Medical Conditions' and Treatments' Potential Impacts on Behavioral Health and Performance', Life Sciences in Space Research, 30: 72-81.
11. Simon, G. E., and M. VonKorff. 1998. 'Suicide mortality among patients treated for depression in an insured population', Am J Epidemiol, 147: 155-60.
12. Slack, Kelly J., Thomas J. Williams, Jason S. Schneiderman, Alexandra M. Whitmire, and James J. Picano. 2016. "Evidence Report: Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders." In, edited by Behavioral Health and Performance. Lyndon B. Johnson Space Center, Houston, Texas.
13. Spijker, Jan, Ron De Graaf, Rob V. Bijl, Aartjan T. F. Beekman, Johan Ormel, and Willem A. Nolen. 2002. 'Duration of major depressive episodes in the general population: Results from the Netherlands Mental Health Survey and Incidence Study (NEMESIS)', British Journal of Psychiatry, 181: 208-13.
14. Tansey, W. A., J. M. Wilson, and K. E. Schaefer. 1979. 'Analysis of health data from 10 years of Polaris submarine patrols', Undersea Biomed Res, 6 Suppl: S217-46.

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