

Clinical Finding Form (CLiFF)

Branch

Baseline

ICL17_Bhp - Psychosis Secondary To Depression

Although depression is the most common mental health disease in the United States and Europe, psychosis is an uncommon feature of this disorder, affecting 14-19% of those suffering a major depressive episode (Ohayon, 2002). This condition is generally described as depression with psychotic features or psychotic depression. Psychotic features can include auditory or visual hallucinations, delusions, disorganization, catatonia, aggression, and many more. There is significant overlap in the features of this condition and other behavioral emergencies such as schizophrenia, delusional disorder, and brief psychotic disorder (Parker, 2014). No behavioral emergencies have occurred during spaceflight; however, as spaceflight mission duration increases, the probability of these disorders affecting a member of the crew also increases (Slack, 2009).

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

Psychosis secondary to depression has never been documented in spaceflight; therefore, spaceflight data is not informative to this condition at this time.

ANALOG LITERATURE

Data collected from Polaris submarine patrols between 1963 and 1973 found 58 psychiatric diseases out of a total of 1685 medical events that were treated, for an illness rate of 0.002 for 1963-1967 and 0.038 for 1968-1973. Illness rates are documented as new cases/1000 man-days. 4 behavioral health emergencies occurred during this ten year period, including one unspecific psychosis and three suicide gestures. (Tansey, 1979). According to the Behavioral Health Emergency IMM CLiFF, this study demonstrated rates per person year of 0.00073 and 0.01387 (0.002 and 0.038 *365 / 1000), with an average of the two incidence rates of 0.0073 per person-years. Behavioral emergencies accounted for 6.8% (4/58) of total psychiatric events, or a rate of 0.000503; however this was not specific to psychosis or psychotic depression. Additionally, of the depression cases in this study, only 1/24 (4.5%) was documented as psychotic depression, with the remainder listed as neurotic depression. There were 9 total psychotic events out of 58 total psychiatric syndromes (15.5%). (Tansey, 1979). The limited space, prolonged mission length, and other environmental stressors are similar to spaceflight, and submariners must meet certain medical screening criteria to be in that environment. Additional analog data exists in the military population. Again, according to the Behavioral Health Emergency IMM CLiFF: "Epidemiology of psychiatric illnesses experienced by soldiers in combat was obtained by retrospective review of casualty rosters and electronic medical records. Population consisted of 4122 soldiers, 3797 men and 325 women. Age range 18-52, average 27. There were 308 psychiatric casualties, overall 59.8 per 100 soldier combat-years which represented 23% of all disease and non-battle injury (DNBI). All incidence rates are per 1000 at risk combat-years. There were 8 psychosis events. Overall incidence rate was 1.7. By gender, incidence rate was 0 for females and 1.6 for males per 1000 person-years. Psychosis rates per person year are 0.0017 overall, 0 female, and 0.0016 male. By age, 35 years old and older had the lowest adjusted rate ratio while the 18-23 cohort had the highest;1 and 1.8; 95% Confidence Interval (CI) 1.21-2.69. By gender, adjusted rate ratio for males was higher than females; 1 and 1.9; 95% CI 1.39-2.63. Trends are similar to civilian population trends. (Goodman, 2011)" These rates are expected to significantly overestimate the incidence of psychosis secondary to depression for spaceflight as they include all forms of psychosis and the majority of the cases occurred in a much younger population than astronauts. This is not specific to psychotic depression.

TERRESTRIAL LITERATURE

A large systematic review from 60 years of data in England found the pooled incidence of all psychoses was 31.7 per 100,000 person-years (95%CI: 24.6–40.9). Depressive psychoses (which had limited data) pooled incidence was reported as 5.3/100,000 person-years (95% CI: 3.7-7.6). (Kirkbride, 2012) 18,980 subjects across the populations of 5 European countries were interviewed for another study which provides the prevalence of depression and psychosis with depression. The prevalence of major depressive episode with psychotic features was 0.4% (95%CI: 0.35%-0.54%). 18.5% of patients with major depressive episodes had features of psychosis. (Ohayon, 2002). This data will not be used to support incidence as it is prevalence data. This was included for information only given the limited data available for this condition.

OVERALL INCIDENCE SUMMARY

INCIDENCE

mean 4.779E-5 and SD 4.754E-5

INCIDENCE SUMMARY

The Bayesian posterior distribution for the incidence rate of psychosis secondary to depression given the Polaris submariner analog evidence (1 event over 20,944.56 person-years) under an uninformative prior is Gamma(shape=1.0105, rate=21145.53) with mean 4.779E-5 and SD 4.754E-5. Evidence Analog – Tansey 1979 – Analysis of health data from 10 years of Polaris submarine patrols. 1 reported event of psychotic depression over 7,650,000 man-days (20944.56 person-years – 365.25 days/year). IR: 4.775E-5 (95%CI: 0.2389E-5, 23.55E-5)

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

4.77879E-05

SD

4.75389E-05

Gamma

(Shape): 1.0105

(Rate): 21145.5

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Kirkbride, 2012	Terrestrial	2
Ohayon, 2002	Terrestrial	0
Tansey, 1979	Analog	3
Goodman, 2011	Analog	2

Kirkbride 2012: LOC = 2 (neutral) based on large systematic review over 60 years, however not limited to psychotic depression alone. These data are from an unscreened general population. Ohayon 2002: N/A to the incidence as this is prevalence data. Large study across 5 countries in Europe that specified prevalence of depression with psychotic features, although limited by this being a phone survey that probably missed some real disease. Terrestrial data with very different population. Tansey 1979: LOC = 3 (somewhat confident) based on reasonable analog setting (submarines) over 10 year period. These data focus on behavioral health emergencies in general, but do offer some insight and specific incidences for psychotic depression in a large population, with a single case documented. This is the incidence from which we can glean our best estimate for spaceflight. Goodman 2011: LOC = 2 (neutral) based on large analog population under significant stress and data that breaks out different types of relevant psychoses. Population does not correlate with the astronaut population and the data broadly covers psychosis, not psychotic depression.

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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 preflight preventive measures for psychosis secondary to depression. However, active astronauts undergo preflight psychological screening and are provided psychological support.

BEST CASE SCENARIO DEFINITION

An isolated episode secondary to depression, of thoughts and perceptions that are disturbed and difficulty understanding what is real and what is not, which resolves within the day.

WORSE CASE SCENARIO DEFINITION

Severe psychotic symptomology, secondary to depression, that requires more than one day of pharmacologic therapy and behavioral health intervention. The psychosis may not resolve.

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

None

BEST CASE/WORST CASE PROBABILITY COMMENTS

Best case/worst case percentages are estimated as 0-22%/78-100% based on the probability of functional recovery within six months of a first episode of psychosis secondary to depression. It is assumed that worst case scenario psychosis secondary to depression may require hospitalization due to the severity of symptoms which require intensive treatment and may not resolve. Reference: (Tohen, 2012).

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

Citation	Source	LOC Value
Tohen, 2012	Terrestrial	2

LOC = 2 (neutral) based on difficulty finding relevant literature to support best case and worst case definitions. Large terrestrial general population study.

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)	0.0000438 events/person-yr	22 - 22	100	0.85	31.9559	0	24	9.11507	0	0	0	0
Treated Worst Case (TWC)		78 - 78	100	0.85	96.3061	672	1344	93.2501	0	100	0	0.61
Untreated Best Case (UTBC)	N/A	N/A	N/A	0.85	39.8352	0	24	9.11507	0	0	0	0
Untreated Worst Case (UTWC)	N/A	N/A	N/A	0.85	99.6811	1440	5040	99.3622	100	100	0.61	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

This condition would first require the development of new depression in an astronaut, which has never previously been documented, and then psychosis secondary to that depression. Psychological screening during initial and pre-launch assessments should ideally identify and eliminate any existing depression or psychoses, leaving only novel cases during spaceflight. As discussed above, psychosis is an uncommon feature or complication of depression, and is largely limited to major depressive episodes. With ongoing medical and psychological screening during flight, depression should be identified and managed in the early stages. In the Best Case, the symptoms will resolve within 24 hours regardless of treatment - which could include behavioral health interventions or medications, although 24 hours of medications is not the standard of care for psychosis. In the Worst Case, a crewmember who is treated and has symptoms resolve may be able to continue with the mission. Treated or untreated, an astronaut with ongoing psychotic symptoms will ultimately require RTDC in the form of a psychiatric hospitalization; ECT is also a standard of care treatment for this condition, which is not available in spaceflight. Even with medication and behavioral health intervention terrestrially, patients can suffer from severe depression and psychosis for months to many years. The LOCL is primarily related to suicidal ideation. With ongoing psychiatric contact, behavioral health interventions, close team dynamics (and observation), and limited lethal means on the spacecraft, suicide completion is felt to be a substantially lower risk in spaceflight than terrestrially. However, overdoses of medication, laceration trauma, depressurization of the cabin or EVA suit, and other unique means of suicide and homicide are possible.

TREATED BEST CASE (TBC) SCENARIO COMMENTS

By definition the best case scenario psychotic depression resolves within the day (treated or untreated), hence an LOCL and RTDC of 0 and a max duration of 24 hours.

TREATED WORST CASE SCENARIO (TWC) COMMENTS

By definition, the treated worst case can last from 24 hours to indefinitely based on continued need for assessment and treatment, to include medications, ECT, and hospitalization. The 4-8 weeks included would include reasonable length of treatment to stabilize most cases. LOCL expected to be 0% to 0.61% with LOCL most likely to be due to completed suicide. (Dutta, 2010). RTDC 0-100% depending on whether this condition responds to in-flight treatment or must be returned for treatment and hospitalization.

UNTREATED BEST CASE (UTBC) SCENARIO COMMENTS

By definition the best case scenario psychotic depression resolves within the day (treated or untreated), hence an LOCL and RTDC of 0 and a max duration of 24 hours.

UNTREATED WORST CASE (UTWC) SCENARIO COMMENTS

By definition, the untreated worst case is presumed to last indefinitely. With ongoing psychosis, RTDC will be 100%. LOCL anticipated to be higher in psychotic depression than depression alone, up to 4.2% (Simon, 1998).

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

Citation	Source	LOC Value
Rothschild, 2004	Terrestrial	3

LOC = 4 (confident) for best case scenarios based on case definition for best case scenarios. LOC = 3 (somewhat confident) for worst case scenarios based on terrestrial clinical practice guidelines and trial of antidepressants in psychotic depression (Rothschild, 2004).

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Case definitions	Case definitions	4

LOC = 4 (confident) based on best case and worst case definitions.

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Dutta, 2010	Terrestrial	3
Simon, 1998	Terrestrial	

LOC = 4 (confident) for Best Case based on definition of resolution within 24 hours LOC = 3 (somewhat confident) for Worst Case based on a large terrestrial general population study of suicide risk with first episode of psychosis. (Simon, 1998) includes a large sample of over 60,000 person-years of followup data for patients being treated for depression, and stratifies the risk of death by age groups, including those relevant to the astronaut population. As this study reports on death by suicide for all types of depressions, we expect the incidence of suicide in psychotic depression to be at least as high, and likely higher.

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

Capabilities and Resourcing Scope Overview Worst Case Definition: Severe psychotic symptomology, secondary to depression, that requires more than one day of pharmacologic therapy, use of restraints, and/or behavioral health intervention. The psychosis may not resolve. Best Case Definition: An isolated episode secondary to depression, of thoughts and perceptions that are disturbed and difficulty understanding what is real and what is not, which resolves within the day. 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; IV access should be obtained. Additionally, labs: BMP, UA, TSH/FreeT4 should be collected and interpreted to rule out an underlying medical cause for psychosis. (electrolyte abnormalities, infectious etiology, hypo/hyper thyroidism). 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; IV access should be obtained. Additionally, labs: BMP, UA, TSH/FreeT4 should be collected and interpreted to rule out an underlying medical cause for psychosis. (electrolyte abnormalities, infectious etiology, hypo/hyper thyroidism). 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): 0.85 (51 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. Labs: BMP 6. Labs: UA 7. Perform a cardiopulmonary exam 8. Perform a mental status exam 9. Interpret the history, physical exam and MSE 10. Interpret labs 11. Obtain a psychiatry consult 12. Establish ground communication CP1 WC (Treated or Untreated): 0.85 (51 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. Labs: BMP 6. Labs: UA 7. Perform a cardiopulmonary exam 8. Perform a mental status exam 9. Interpret the history, physical exam and MSE 10. Interpret labs 11. Obtain a psychiatry consult 12. Establish ground communication The highest scope of practice code used in this CRT which includes interpretation of diagnosis, performing diagnostic tests, performing treatment, and assessing fitness for duty would be a five, or a practicing specialist. Treatment Scope and Resourcing Most best-case terrestrial populations can resolve with effective treatment of the underlying depressive disorder and do not necessarily require ongoing treatment with antipsychotic agents. BC treatment often involves titrating the antidepressant medication towards an adequate response with only a brief need for antipsychotic agents. Psychotic symptoms can often be very frightening and cause anxiety and agitation acutely. Benzodiazepines should be utilized for ameliorating anxiety/agitation acutely. Direct observation should be maintained for 24 hours in cases of psychosis secondary to depression while the patient is being medically stabilized. Additional support through regular ongoing psychotherapeutic interventions is necessary. It should be noted that psychosis secondary to depression can be due to unrecognized or inadequately treated depression. Hence the addition of antidepressants to this CRT, as we are dealing with a severe manifestation of MDD with a poorer prognosis; this requires on going medication management with antidepressants. Many studies suggest that psychosis secondary to depression has different in pathogenesis than Depression without psychosis. 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. Terrestrially, worst case conditions generally do require long term psychotropic medication management in the case of persistent psychotic symptoms. WC treatment involves titrating the antidepressant medication toward an adequate response, however, due to persistent psychotic features long term use of antipsychotic agents is often necessary. Psychotic symptoms can often be very frightening and cause anxiety and agitation acutely. This is especially concerning in an isolated and confined environment in space. Benzodiazepines should be utilized for ameliorating anxiety/agitation acutely. In WC scenarios restraints might be necessary for severe agitation and grey tape should be utilized along with other de-escalation strategies to include medications. Direct observation should be maintained for 72 hours in WC case of psychosis secondary to depression while the patient is being medically stabilized. It should be noted that psychosis secondary to depression can be due to unrecognized or inadequately treated depression. Hence the addition of antidepressants to this CRT, as we are dealing with a severe manifestation of MDD with a poorer prognosis; this requires on going medication management with antidepressants. Many studies suggest that psychosis secondary to depression has different in pathogenesis than Depression without psychosis. 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. Communications and Support Needs Psychosis 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, symptoms management and ongoing psychotropic medication management. Additional guidance would likely be needed to support use of restraints and treatment of agitation. 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. Sadock, J, Sadock, V, Synopsis of Psychiatry, Eleventh Edition.

IMM CLIFF RECONCILIATION COMMENTS

There is no IMM Cliff for Psychosis secondary to Depression. There is an IMM Cliff for Depression. There is also an IMM Cliff for Behavioral Emergency. Some data from these CLIFFs are relevant, however both are too broad to apply directly to this condition. Psychosis Secondary to Depression (or Psychotic Depression) is a unique condition. Some references were obtained from these CLIFFs.

LIMITATIONS SUMMARY

Depression Secondary to Psychosis is a unique condition that has not previously been specifically addressed. Terrestrially, this is an uncommon condition, and it's diagnosis is complicated by many other conditions that present with depressive or psychotic features. There is no data on behavioral health emergencies in space in general, including this condition. The terrestrial and analog data are somewhat limited, and likely overestimate the incidence of this condition in spaceflight. The definitions of Best and Worst case further complicate the delineation of this condition, with the Best Case resolving within 24 hours regardless of treatment and the worst case scenario having severe symptoms that may last just over 24 hours or never resolve despite treatment. Therefore, there is limited relevant literature to address these specific case definitions.

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)	223	664		89			145					
Untreated Best Case (UTBC)	223	664	113	89		44	145					
Treated Worst Case (TWC)	223	664	113	89	854	44	145					
Untreated Worst Case (UTWC)	223	664	113	89	854	44	145	5	13	6		
	Affected HSTCs (Continued)								TI Calculation		TI Score	
	Hand (Dom)	Hand (Any)	Upper Extremity	Lower Extremity	Ambul & Standing (g)	Translation & Stabilization (microgravity)	Don/Doff Equipment	Pressure Ops	Total Tasks Impaired By Condition	Total Human System Category Tasks Full Mission	TI Decimal	TI %
Treated Best Case (TBC)	132	564					34	211	2062	3763	0.547967	54.7967
Untreated Best Case (UTBC)	132	564	414	22			34	211	2655	3763	0.705554	70.5554
Treated Worst Case (TWC)	132	564	414	22	196	34	34	211	3739	3763	0.993622	99.3622
Untreated Worst Case (UTWC)	132	564	414	22	196	34	34	211	3763	3763	1	100
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)	223	664	113	89	854	44	145					
Untreated Worst Case (UTWC)	223	664	113	89	854	44	145					
	Affected HSTCs (Continued)								TI Calculation		TI Score	

	Hand (Dom)	Hand (Any)	Upper Extremity	Lower Extremity	Ambul & Standing (g)	Translation & Stabilization (microgravity)	Don/Doff Equipment	Pressure Ops	Total Tasks Impaired By Condition	Total Human System Category Tasks Full Mission	TI Decimal	TI %
Treated Best Case (TBC)	132							211	343	3763	0.0911507	9.11507
Untreated Best Case (UTBC)	132							211	343	3763	0.0911507	9.11507
Treated Worst Case (TWC)	132	564	414	22			34	211	3509	3763	0.932501	93.2501
Untreated Worst Case (UTWC)	132	564	414	22	196	34	34	211	3739	3763	0.993622	99.3622

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 requiring use of the alimentary system, 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 Condition 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

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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
CIFF	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