

Clinical Finding Form (ClIFF)

Branch

Baseline

ICL47_Eye - Retinal Injury

Retinal detachment is a common ophthalmic emergency. Retinal detachment is separation of the neurosensory retina from the underlying retinal pigment epithelium. Retinal detachment occurs when the forces of retinal attachment are overcome and fluid accumulates in the subretinal space. Symptoms of retinal detachment include photopsia (flashes), floaters, visual field defects, and decreased visual acuity. Once the retinal detachment extends beyond the fovea (central macula), permanent visual impairment is almost inevitable (Kang, 2008).

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

A thorough, systematic review of comprehensive databases of medical literature did not reveal any spaceflight data on retinal detachment.

ANALOG LITERATURE

Analog studies were a bit of a stretch and were more situational e.g are there higher rates of retinal detachment when the ambient temperature is higher. Results were controversial and did not clearly relate to spaceflight populations. For this reason no analogue papers were included.

TERRESTRIAL LITERATURE

The preponderance of articles on incidence of retinal detachment citations lead to Mitry 2010 or D'amico 2008. In Mitry2010 they are reporting a mean annual incidence rate for retinal detachment at 10.5 (IQR 8.1-13.2) per 100,000 of population. D'amico2008 reported population-based studies: annual incidence is ~12.6cases per 100,000 persons, or 17.9 per 100,000 if we include retinal detachments after cataract extraction (a common risk factor). D'amico2008 also reported based on longitudinal studies that a new retinal tear or detachment occurs in approx. 1% of patients with lattice retinal degeneration. The worst-case scenario for this condition involves the macula or loss of visual acuity. In this setting, these directs complications specifically from retinal detachment were not found. May2000 reports that nearly 2.5 million new eye injuries occur in the USA each year of which 40k-60k patients are diagnosed with trauma-related blindness. They report 1,400 of every 100,000 USA citizens sustain eye injuries (cumulative lifetime occurrence) with 40% of all cases of monocular blindness caused by trauma. The theme of the papers in these studies has been that TRAUMA IS the most common cause of eye injuries and it is AVOIDABLE with EYE PROTECTION. May2000 published the breakdown of serious eye injuries by use of protective eye gear, reading or sun glasses and no eye protection at all. They found 78% of eye injuries occurred in those not wearing any eye form of eye protection. Only 3% of the eye injuries occurred in people wearing regular glasses and only 2% occurred in those wearing safety glasses. It was unknown if any eye protection was worn in the remaining 17%. They also noted that the home (where there are no compulsory requirements to use eye protection) accounted for the highest proportion of eye injuries (41%) vs industrial premises which came in second at 14%. (where in developed nations requirements and access to safety goggles are compulsory). The condition probabilities in Section 5 below of (0-100%) is broad given the extremes in the literature and the evidence that the vast majority of eye injuries are preventable with the use of appropriate eye protection.

OVERALL INCIDENCE SUMMARY

INCIDENCE

mean 1.26E-4 and SD 8.557E-6

INCIDENCE SUMMARY

The posterior distribution for the incidence rate of phakic non-traumatic RRD given the terrestrial reference data (219 events over 1,737,430 person-years) under an uninformative prior is a Gamma(shape=216.8, rate=1720788) distribution with mean 1.26E-4 and SD 8.557E-6.

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
0.000125989
SD
8.55662E-06
Gamma
(Shape): 216.8
(Rate): 1.72079E+06

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Mitry, D., et al., 2008	Terrestrial	2
D'Amico, 2008	Terrestrial	2
May, et al., 2000	Terrestrial	2
Kazahaya, 1995	Terrestrial	2
Katz, et al., 1993	Terrestrial	2

• These studies had estimates for retinal injuries and detachment that were all in the same ball park. Articles (especially Mitry2010) made efforts to acknowledge the role that patients with repeat history of retinal detachments or who experience retinal detachment after cataract or other ocular procedure can inflate and confound the incidence rates. Multiple estimates for incidence have been offered due to this and efforts were made to exclude those that occurred in significant traumas or after ocular surgery. The ranges offered for incidence remained within the same ranges. • The populations studied are not adequate representations for our astronaut populations and the incidences reported here would likely be much lower in our astronauts given that astronauts are more likely to wear appropriate eye protection for tasks, unlikely to engage in drinking or the use of drugs during a mission or to assault each other as these activities were those with the strongest associations with retinal injuries and detachments.

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

Retinal detachment is a common ophthalmic emergency. Retinal detachment is separation of the neurosensory retina from the underlying retinal pigment epithelium. Retinal detachment occurs when the forces of retinal attachment are overcome and fluid accumulates behind the retina.

BEST CASE SCENARIO DEFINITION

A retinal tear, burn, or detachment without involvement of the macula (central vision and visual acuity are preserved).

WORSE CASE SCENARIO DEFINITION

Worst case scenario is defined as a retinal tear, burn, or detachment with involvement of the macula (central vision and visual acuity may be severely reduced).

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

Eye - Retinal Tear Eye - Retinal Burn Eye - Retinal Detachment

BEST CASE/WORST CASE PROBABILITY COMMENTS

The original CLiFF for IMM has a very different definition for BC/WC because it only included detachment rather than also including retinal tears which do not always lead to detachment. For this condition, retinal breaks need to be considered. "Asymptomatic and symptomatic retinal breaks progressed to rhegmatogenous retinal detachment (RRD) in 0-13.8% and 35-47% of cases, respectively." Therefore, if we assume that asymptomatic tears are unlikely to be noticed on a mission, because they are asymptomatic, we can assume that the worst case will be somewhere between 35 and 47% (i.e. a mean of 41%, thus a BC would be 59% and WC would be 41%). An additional consideration is that of detachments that are "less severe" i.e. do not include the macula which is used terrestrially for triage of surgical urgency. If the macula is involved in the detachment, surgery is urgent while if the macula is not involved, surgery may be delayed for days, but not long. 72.9% of detachment conditions do involve the macula, thus leaving 27.1% that do not involve the macula (or are "best case" detachments). But since surgical intervention is needed in either case because, if left untreated, the majority of both will lead to blindness. However, RTDC events need to be considered as this is the ideal use-case for a return to ground support leading to healthcare that could preserve vision of the crew. Therefore, if we use this data, we would conclude that only 72.9% (macula involved) of the 41% (retinal detachments) or 30% are WC, leaving 70% as BC. It is difficult to determine when during the mission RTDC will be possible to mitigate loss of vision, therefore resulting in and RTDC event that will result in a BC for the condition. Therefore, it was the decision of the team to create a range of BC/WC. The BC range is 59-70% (i.e. 59% is the percentage of detachments from tears and 70% are those events that do not present with macular involvement). This leaves a range of 30-41% for WC.

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

Citation	Source	LOC Value
Mitry, 2010	Terrestrial	3
D'Amico, 2008	Terrestrial	3
May, 2000	Terrestrial	3
Kazahaya, 1995	Terrestrial	3
J. Katz, 1993	Terrestrial	3

• These studies had estimates for retinal injuries and detachment that were all in the same ballpark. Articles (especially Mitry2010) made efforts to acknowledge the role that patients with repeat history of retinal detachments or who experience retinal detachment after cataract or other ocular procedure can inflate and confound the incidence rates. Multiple estimates for incidence have been offered due to this and efforts were made to exclude those that occurred in significant traumas or after ocular surgery. The ranges offered for incidence remained within the same ranges. • The populations studied are not adequate representations for our astronaut populations and the incidences reported here would likely be much lower in our astronauts given that astronauts are more likely to wear appropriate eye protection for tasks, unlikely to engage in drinking or the use of drugs during a mission or to assault each other as these activities were those with the strongest associations with retinal injuries and detachments.

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 1.26E-4 and SD 8.557E-6	59 - 70	100	3.3	15.3069	1	504	0	28	100	0	0
Treated Worst Case (TWC)		30 - 41	100	3.3	30.7999	504	504	0	28	100	0	0
Untreated Best Case (UTBC)	N/A	N/A	N/A	3.3	16.4895	1	504	0	28	100	0	0
Untreated Worst Case (UTWC)	N/A	N/A	N/A	3.3	46.7048	504	504	31.8097	28	100	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

Treatment duration without surgical intervention is assumed to continue until end of mission. All crew that develop this condition can be expected to need to evacuate, since no surgical intervention is currently available. No LOC is expected from this condition.

TREATED BEST CASE (TBC) SCENARIO COMMENTS

TBC Duration: There is no "duration of treatment for retinal detachment" because this involves a surgical procedure. However, the BC definition includes a range of conditions that include the possibility of asymptomatic non progressing tears up through peripheral retinal detachment that requires surgery. This makes duration (and outcome measures) difficult to extrapolate. For this effort the low end of duration is given as the time to diagnose an asymptomatic, non progressive case while the high end is the longest identified time in the literature for spontaneous healing. It is worth noting that clinical recommendations all note that symptomatic tears or detachments should be referred to ophthalmology for repair as soon as possible to prevent progression and further loss of vision. Even asymptomatic tears are recommended to be referred within 5 days. One Caveat is that in small tears, the patient is advised to lay down on the side of the affected eye (opposite the visual defect) to mitigate progression however this relies on gravity to effect fluid shifts, not useful in microgravity. Subsequently the type of surgical procedure is dependent on the size of the detachment. TBD RTDC: If a retinal tear is diagnosed promptly before it progresses to retinal detachment, the prognosis is extremely good with appropriate treatment. Given that some diagnoses in the BC definition may heal spontaneously while others require surgery 100% of the time RTDC in this scenario covers the range of these diagnoses. Retinal tears are typically treated with laser or a freezing procedure (cryotherapy) in an office setting, while retinal detachments often require more invasive procedures. TBC LOCL: The eye is not a life support organ and eye failure or even destruction is not, by itself, associated with mortality. Therefore, no mortality is expected.

TREATED WORST CASE SCENARIO (TWC) COMMENTS

TWC Duration: There is no "duration of treatment for retinal detachment" because this involves a surgical procedure. One Caveat is that in small tears, the patient is advised to lay down on the side of the affected eye (opposite the visual defect) to mitigate progression. This may work in the reduced gravity environment of a celestial body but its effectiveness in microgravity during the transit phases of the mission are unknown since it relies on gravity to effect fluid shifts. The required surgical procedure is dependent on the size of the detachment. TWC RTDC: If a retinal tear is diagnosed promptly before it progresses to retinal detachment, the prognosis is extremely good. Retinal tears are typically treated with laser or a freezing procedure (cryotherapy). Treatment is performed in an office setting and is very effective and quite safe. However, surgery is required in all symptomatic cases and cases involving the macula are likely to all be symptomatic given the sensitivity of this visual area. TWC LOCL: The eye is not a life support organ and eye failure or even destruction is not, by itself, associated with mortality. Therefore, no mortality is expected.

UNTREATED BEST CASE (UTBC) SCENARIO COMMENTS

No articles on this condition reviewed throughout this process have identified a population of patients who would fit our criteria for untreated best case scenarios. For future updates on this condition, consider modifying "retinal breaks" as part of the best case definition and retinal detachments as the worse case definition given that "retinal breaks" can resolve with RTDC while "retinal detachment" would not resolve on its own and ultimately needs a procedure. Additionally, since surgical capabilities for retinal repair are not likely to be included on board, and these are the only demonstrably effective treatments, the untreated and treated outcomes are the same.

UNTREATED WORST CASE (UTWC) SCENARIO COMMENTS

No articles on this condition reviewed throughout this process have identified a population of patients who would fit our criteria for untreated best case scenarios. For future updates on this condition, consider modifying "retinal breaks" as part of the best case definition and retinal detachments as the worse case definition given that "retinal breaks" can resolve with RTDC while "retinal detachment" would not resolve on its own and ultimately needs a procedure. Additionally, since surgical capabilities for retinal repair are not likely to be included on board, and these are the only demonstrably effective treatments, the untreated and treated outcomes are the same.

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

Citation	Source	LOC Value
Akduman, 1998	Terrestrial	

Citation	Source	LOC Value
Akduman, 1998	Terrestrial	2
Ivanisević, 1997	Terrestrial	
Ivanisević, 1997	Terrestrial	
Lira, 2010	Terrestrial	

Duration of treatment/time to maximum progression in 'hours' for the worse case definition of a retinal detachment is difficult to assess since this is treated surgically as soon as possible. The low end time comes from (Akduman1998) which was the time to spontaneous healing for tears in the retina in non macular areas. The high end comes from the need to limit activity until repair. Since this may require limited activity until the end of the mission and macular tears are unlikely to recover without surgery, this is expected to last until the end of the mission. Comprehensive literature searches were run and there is useful data for a duration of untreated retinal tears with the parameters listed. Thus the "permanent" duration is for retinal detachment and after a comprehensive literature search was run, there was no evidence of retinal detachment spontaneously resolving. Conversely, a single study was found discussing the natural history of retinal detachment in an untreated population. The authors write —"this condition is mostly progressive until the whole retina is detached and vision is completely lost. Spontaneous reattachment is very rare."— The study follows 22 patients with Retinal detachment (RD) who refused surgery or were very poor candidates for surgery. Duration with RD was 1-28 years (mean 9.6years) and patients were ages 36-84 (mean 72.9 yo). Permanent loss of vision was found in all cases and maximal visual acuity was no more than hand motion in 9.1%(2/22). One other consideration is that CP2 is the duration of treatment, if these conditions are untreated CP2 should be 0 in all conditions.

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Kazahaya, 1995	Terrestrial	3
Ivanisević, 1997	Terrestrial	
May, 2000	Terrestrial	

(Kazahaya,1995). Overall estimates approximate 28% of symptomatic retinal tears have been documented to lead to clinical retinal detachment. Subsequently (Ivanisević 1997) informs us that 100% of retinal detachments will at some point result in permanent vision loss with the best visual acuity of hand-motion.

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
N/A	N/A	4

"comprehensive literature searches were run and there is no evidence of loss of crew life from a retinal injury with the parameters listed. Therefore with known clinical knowledge, LOCL is not expected."

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

Capabilities and Resourcing Scope Overview Retinal injury bears the risk of permanent loss of vision in both the best and worst case. While it is not life threatening this can be extremely disabling to the crewmember and possibly to the mission. There are effective treatments for retinal injuries but they typically require specialist care. These treatments require invasive procedures and bear the risk of loss of vision. However given that the condition itself, if left untreated has the same risk, and that the procedures involve techniques similar to the training of a generalist physician, such as inserting needles and insufflation, the CRT Working Group determined that including these resources would be prudent. If they are present on board, a specialist on Earth could advise the crew to perform a pneumatic retinopexy. If they are not included there is little change of preventing vision loss. Diagnostic Scope and Resourcing Diagnosis for this condition requires a thorough exam of the exterior, anterior, and posterior of the eye. For this reason a panoptic funduscopy is included. Ultrasound capability was thought of as a "nice to have" and is listed but it is not considered essential for the diagnosis since a funduscopy is more sensitive, and specific. This approach is the same for both best and worst case scenarios. 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): 3.3 hours for an external ocular exam, a fundoscopic exam, a history, and an ultrasound. If ultrasound is not included due to its' lack of necessity the time is expected to be significantly less. Using the standard of "longest reasonable time to complete this task for an experienced clinician adjusted for being in the spaceflight environment." CP1 WC (Treated or Untreated): 3.3 hours for an external ocular exam, a fundoscopic exam, a history, and an ultrasound. If ultrasound is not included due to its' lack of necessity the time is expected to be significantly less. This condition requires a scope of practice 5 commensurate with a skilled, procedure trained, generalist physician such as an emergency medicine doctor or a family medicine doctor. However

the procedure of anterior chamber paracentesis and pneumatic retinopathy are beyond the scope of training for such a physician. It is expected that these would only be performed as a last resort and with guidance from a specialist on the ground. Treatment Scope and Resourcing Treatment for both the best and worst case scenarios is the same. It involves observation and treatment with cycloplegics under guidance from specialists on the ground. If indicated a pneumatic retinopathy could be performed along with an anterior chamber paracentesis to relieve intraocular pressure. ophthalmic steroids are also included as well as a device to monitor intraocular pressure. To prevent infection in the less-than-ideal operating room of the spacecraft ophthalmic antibiotics are also included. Progress would be assessed by repeat visual acuity exams. It should also be noted that pneumatic retinopathy may not work as effectively in microgravity. Normally this procedure is paired with a procedure to repair the retinal break but the equipment needed for this is high mass and high volume. For this reason, only the pneumatic portion was considered "necessary" but the cryopexy unit was included as a "nice to have" with a necessity of zero to enable the simulation to model the availability of treatment even if the definitive and ideal treatment is too mass/volume expensive to be included in the simulation. Communications and Support Needs This condition would require significant near real time ground support in the form of audio and video communication with the ground.

IMM CLIFF RECONCILIATION COMMENTS

The original CLIFF for IMM has a very different definition for BC/WC because it only included detachment rather than also including retinal tears which do not always lead to detachment. For this condition, retinal breaks need to be considered. "Asymptomatic and symptomatic retinal breaks progressed to rhegmatogenous retinal detachment (RRD) in 0-13.8% and 35-47% of cases, respectively." Therefore, if we assume that asymptomatic tears are unlikely to be noticed on a mission, because they are asymptomatic, we can assume that the worst case will be somewhere between 35 and 47% (i.e. a mean of 41%, thus a BC would be 59% and WC would be 41%). An additional consideration is that of detachments that are "less severe" i.e. do not include the macula which is used terrestrially for triage of surgical urgency. If the macula is involved in the detachment, surgery is urgent while if the macula is not involved, surgery may be delayed for days, but not long. 72.9% of detachment conditions do involve the macula, thus leaving 27.1% that do not involve the macula (or are "best case" detachments). But since surgical intervention is needed in either case because, if left untreated, the majority of both will lead to blindness. However, RTDC events need to be considered as this is the ideal use-case for a return to ground support leading to healthcare that could preserve vision of the crew. Therefore, if we use this data, we would conclude that only 72.9% (macula involved) of the 41% (retinal detachments) or 30% are WC, leaving 70% as BC. It is difficult to determine when during the mission RTDC will be possible to mitigate loss of vision, therefore resulting in and RTDC event that will result in a BC for the condition. Therefore, it was the decision of the team to create a range of BC/WC. The BC range is 59-70% (i.e. 59% is the percentage of detachments from tears and 70% are those events that do not present with macular involvement). This leaves a range of 30-41% for WC.

LIMITATIONS SUMMARY

Finding data that exactly matched the CLIFF definition was challenging, especially since there are no reports of RD during spaceflight. Terrestrial idiopathic RD incidence data was used for the composite incidence for this CLIFF. This may be a slight underestimate since it does not specifically include other types of RD nor does it specifically include tears and burns. There is considerable uncertainty in the actual incidence rate during microgravity operations. Astronauts have intensive monitoring of their ocular health during and prior to flight, but the microgravity can cause structural changes in the eye that could lead to an increased incidence during long-duration spaceflight.

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)		664					145					
Untreated Best Case (UTBC)		664		89			145					
Treated Worst Case (TWC)	223	664		89	854		145					
Untreated Worst Case (UTWC)	223	664		89	854		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	1152	3763	0.306139	30.6139
Untreated Best Case (UTBC)	132							211	1241	3763	0.32979	32.979
Treated Worst Case (TWC)	132							211	2318	3763	0.615998	61.5998
Untreated Worst Case (UTWC)	132							211	2318	3763	0.615998	61.5998
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)					854							
	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	T1 Decimal	T1 %
Treated Best Case (TBC)									0	3763	0	0
Untreated Best Case (UTBC)									0	3763	0	0
Treated Worst Case (TWC)									0	3763	0	0
Untreated Worst Case (UTWC)	132							211	1197	3763	0.318097	31.8097

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
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