Clinical Finding Form (CliFF)

Branch	Baseline

ICL60_Glaucoma, Acute Angle-Closure

Angle closure glaucoma results from appositional or synechial narrowing of the anterior chamber angle resulting in limited aqueous outflow (Prum et al., 2016). This in turn, results in increased intraocular pressure elevation and optic nerve injury. Primary angle closure is due to pupillary block. Secondary angle closure is caused by any other disorder. There are several pathologies associated with primary angle closure: primary angle closure suspect (PACS), primary angle closure (PAC), and primary angle closure glaucoma (PACG) (Wright et al., 2016). PACG requires optic neuropathy to be present. When angle closure happens acutely, an ocular emergency occurs as vision loss can develop quickly without treatment. This CLiFF condition only covers acute angle glaucoma. Acute angle glaucoma often has a dramatic presentation with blurring of vision, painful red eye, headache, nausea, and vomiting. Most subjects who experience acute angle glaucoma do seek medical care. Gonioscopy is the gold-standard for diagnosis, however other techniques such as tonometry may be employed (Flores-Sanchez et al., 2019). The mainstay of treatment is rapidly lowering the intraocular pressure, preferably by medicinal therapies initially. However, in resistant cases, a procedural or surgical intervention may be necessary more rapidly. In cases where medical management is effective, laser peripheral iridotomy, argon laser peripheral iridoplasty, or lens extraction may be pursued the next day as an outpatient with ophthalmology.

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

Spaceflight literature were derived from two LSAH data gathering events (Walton, 2010; Saile et. al, 2017) and a NASA white paper (Antonsen et al., 2017). Unfortunately, the authors of this CLiFF did not have direct access to the data from those LSAH events. Consequently, information was taken detailing these events from previous IMM CLiFF entitled " Acute Angle-Closure Glaucoma." The statistician of this CLiFF was also able to contact the authors of Antonsen et al. and verify the data (which was also based on the prior LSAH events). During her analysis it was observed that in the Antonsen et al. paper Table 1 was mislabeled as 'ISS through Exp 40' when it should read ' ISS expeditions 9 and 14 through 40'; this CLIFF corrects for that error. From reviewing these resources, an episode of acute angle glaucoma has not occurred in spaceflight. Consequently, these resources were not used in the incidence calculation. At the time of this CLIFF completion, a repeat LSAH data gathering event was not possible and missions past 2017 are not represented.

ANALOG LITERATURE

In Psolka et al. (2007), a retrospective review was conducted of 107 United States military personnel who were referred to the Walter Reed Army Medical Center ophthalmology service between January 1, 2003 and September 30, 2005 with non-battle pathologies. During this time there were three glaucoma events found in the in the 33 months of this study. The total number of cases in this study may underestimate true incidence as patients were initially evaluated by their “primary service” and not every ocular event likely warranted an ophthalmology referral. Unfortunately, this study could not be used to calculate an incidence rate as there was no information provided regarding whole population (only total number of patients).

TERRESTRIAL LITERATURE

These studies were included because they encompass a global population. Tham et al (2014) and Day et al. (2012) provide prevalence data while Park et al (2019) and Baskaran et al (2015) provide incidence data in Korea and the Chinese population in Southwest Singapore, respectively. Glaucoma can be more prevalent in Asian populations, which is why the global prevalence and European-derived population studies were included as well. Baskaran et al (2015) also includes the prevalence of blindness in patients with primary open-angle glaucoma, which is the definition of the worst case scenario. There are limited studies looking at incidence of primary angle-closure glaucoma.

OVERALL INCIDENCE SUMMARY

INCIDENCE

Males: 3.254E-5 and SD 5.871E-7 Females: 8.249E-5 and SD 9.198E-7

INCIDENCE SUMMARY

Males: The posterior distribution for the incidence rate given the data from the 4 relevant references under an uninformative prior is Gamma(shape=3129.226, rate=96165528) with mean 3.254E-5 and SD 5.871E-7. Females: The posterior distribution for the incidence rate given the data from the 4 relevant references under an uninformative prior is Gamma(shape=8042.958, rate=97502218) with mean 8.249E-5 and SD 9.198E-7.

TABLE 1. INCIDENCE MODEL

Incidence Details

Incidence Type
General

Segment
All

Env. Exposure
NA

Sex
Male

Crowns
Any

Contacts
Any

Pregnancy
Any

Incidence Distribution

Occurrence Dist
Poisson

Incidence Dist.
Gamma

Mean
3.254E-05

SD
5.817E-07

Gamma
(Shape): 3129.23
(Rate): 9.61655E+07

Incidence Details

Incidence Type
General

Segment
All

Env. Exposure
NA

Sex
Female

Crowns
Any

Contacts
Any

Pregnancy
Any

Incidence Distribution

Occurrence Dist
Poisson

Incidence Dist.
Gamma

Mean
8.249E-05
SD
9.198E-07

Gamma
(Shape): 8042.96
(Rate): 9.75022E+07

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Walton, 2010	Spaceflight	0
Saile et al., 2017	Spaceflight	0
Antonsen et al., 2017	Spaceflight	0
Psolka et al., 2007	Analog	0
Ng et al., 2018	Terrestrial	2
Bojic et al., 2004	Terrestrial	2
Chua et al., 2018	Terrestrial	2
Park et al., 2010	Terrestrial	2
Channa et al., 2016	Terrestrial	0
Keenan et al., 2009	Terrestrial	0

Only terrestrial studies were used to determine an incidence rate as there have been no cases of acute glaucoma in spaceflight and analog studies were missing data necessary for this calculation. Unfortunately, terrestrial studies did not accurately represent those in spaceflight as they included elderly subjects and patients with comorbid conditions.

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

Crewmembers undergo several preflight ocular examinations. Firstly, at L-21/18 m an MRI (3T or better using specific ocular imaging protocols) is obtained. Then at L-21/18 m and L-9/6 m an eye exam is conducted which is inclusive of the following testing: refraction (manifest and cycloplegic), visual acuity (distance and near), Amsler grid, threshold visual fields, pupil reflexes, contrast sensitivity, biomicroscopy (slit lamp), extraocular muscle balance, tonometry, optical biometry, retinal photography, dilated fundoscopic examination and optical coherence tomography (high resolution) including spontaneous venous pulsations (SVP) videography. Also, at L-9/6 m, 2-D ultrasound imaging and contact lens or spectacle fitting is performed. Lastly, at L-90/30 d the best corrected visual acuity, color vision, refraction (manifest), biomicroscopy (slit lamp), tonometry, fundus exam (undilated) and OCT (if any baseline scans need to be repeated) tests are performed. Of note, crew-members are trained to conduct vision testing, fundoscopy and 2-D ultrasound so that they can conduct in-flight eye examinations. All astronauts must undergo annual medical examination that includes a medical history review and clinical laboratory testing.

BEST CASE SCENARIO DEFINITION

A mild unilateral angle-closure glaucoma that responds to topical and systemic treatment.

WORSE CASE SCENARIO DEFINITION

Bilateral angle-closure glaucoma with intraocular pressure that does not respond to topical and systemic treatment and poses risk for irreversible blindness.

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

None.

BEST CASE/WORST CASE PROBABILITY COMMENTS

There was no spaceflight data or analog studies available to derive a worst-case probability and consequently, terrestrial studies were used. In Baskaran et al., 2015, 3353 Chinese adults aged 40 years or older underwent a slit-lamp ophthalmic examination, applanation tonometry, measurement of central corneal thickness, gonioscopy and a dilated fundus exam. 49 participants were identified that carried the diagnosis of primary acute glaucoma. Of these, 5 of 49 participants (10.2% [95% CI, 4.4%-21.8%]) were “blind secondary to glaucoma.” Per the discussion, it is assumed this is secondary to bilateral glaucoma. In Hillman, 1979, medical records representing 212 eyes (191 patients) between 1971-1974 in Leeds, England were examined retrospectively. Patients ranged from the fourth to ninth decade and 21 (11.0%) patients in this study had bilateral acute glaucoma. Lastly, in Lowe, 1962, 200 cases of acute angle-closure glaucoma were retrospectively reviewed. These cases had presented to Australian hospitals between 1950-1961 and were identified through the Ophthalmic Research Institute and the Research Project No. 13 of the Royal Victorian Eye and Ear Hospital. There were 23 patients out of 200 that presented with bilateral acute glaucoma (11.5%). This paper did determine that over the course of 20 years (with the majority occurring 5-10 years after the first presentation), 58 patients developed bilateral glaucoma (29%); however, this is likely less applicable to spaceflight timeframes/screening---and was not used in this CLiFF, as opposed to the previous CLiFF effort. The weighted mean for these studies (5*0.102 + 21*0.11 + 23*0.115)/(5 + 21 +23) is 11.2%.

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

Citation	Source	LOC Value
Baskaran et al., 2015	Terrestrial	2
Hillman, 1979	Terrestrial	2
Lowe, 1962	Terrestrial	2

Only terrestrial studies were available to determine a worst-case scenario probability. These studies often represented an older age group with more comorbid conditions than would be expected during spaceflight.

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)	Males: 3.254E-5 and SD 5.871E-7 Females: 8.249E-5 and SD 9.198E-7	88.8 - 88.8	100	2.22	17.8315	0.25	24	0	100	100	0	0
Treated Worst Case (TWC)		11.2 - 11.2	100	2.22	77.9431	24	192	66.8084	100	100	0	0
Untreated Best Case (UTBC)	N/A	N/A	N/A	2.22	61.241	1	336	66.8084	100	100	0	0
Untreated Worst Case (UTWC)	N/A	N/A	N/A	2.22	83.0853	24	336	66.8084	100	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

The best case is an acute angle closure glaucoma that is amenable to medical management to lower intraocular pressure. However, terrestrial guidelines do state that peripheral iridotomy should still be pursued as quickly as possible, even if initial medical management is successful. The worst case involves bilateral acute angle closure glaucoma that cannot be medically managed initially. In this scenario, procedural or surgical management is rapidly necessary. Almost all patients who experience the best- and worst-case scenarios will seek medical care. Terrestrially, emergency medicine and primary care physicians can stabilize the best-case scenario, however these patients would still require an urgent ophthalmology consultation for further treatment. RTDC surrogate for this CLiFF is procedural or surgical intervention, as the resources to implement such are not available in spaceflight.

TREATED BEST CASE (TBC) SCENARIO COMMENTS

Rapid reduction of intraocular pressure is an important step in treating acute angle glaucoma. In the best-case scenario, this is easily accomplished in the acute phase with the use of topical and systemic treatments. In Choong et al., 1999, patients diagnosed with acute angle closure glaucoma at the general infirmary in Leeds between September 1994 to February 1997 underwent a new medical treatment protocol consisting of initially acetazolamide, topical beta blocked and a topical steroid. After 60 minutes, pilocarpine was given and after 90 minutes, if the pressure was not reduced, intravenous glycerol or mannitol was given. All patients achieved adequate intraocular pressure within 1-7 hours (mean 3hr). In Lam et al., 2002, 73 eyes of 64 patients diagnosed with acute primary angle-closure glaucoma received either immediate argon laser peripheral iridoplasty or conventional systemic medical therapy: topical pilocarpine, topical timolol maleate, 200 ml of 20% intravenous mannitol if the intraocular pressure was greater than 60 mmHg, 500 mg of intravenous acetazolamide (followed by 250 mg 4 times daily) and 600 mg of oral potassium twice daily. Of the medication group, some participants had intraocular pressures less than 20 mmHg at 15 minutes after starting the treatment regimen. After 24 hours of medical treatment, the mean of the medical group was less than 20 mmHg, however later data points were not carried out. Once the acute attack has finished (intraocular pressure is normalized), definitive treatment for glaucoma involves preventing further angle closure with a procedure, typically peripheral iridotomy or primary lens extraction (Chan et al., 2019, Wright et al, 2016). Peripheral iridotomy is usually performed as rapidly as corneal transparency allows. In spaceflight, this not an option given lack of available expertise (should be performed by an ophthalmologist) and onboard procedural/surgical capabilities. Studies have shown that peripheral iridotomy should be performed rapidly (within 48 hours) as delaying the procedure is associated with increased morbidity (Lee et al., 2009). Consequently, given the likely progression to vision loss if definitive care is not obtained, RTDC is 100%. LOCL is not expected for any of the ocular pathologies.

TREATED WORST CASE SCENARIO (TWC) COMMENTS

In the treated worst-case scenario, medical treatment with both topical and systemic medication do not alleviate the acute attack. In terrestrial conditions, these patients would undergo an immediate procedure to lower intraocular pressure. In spaceflight, the ability to adequately treat this condition does not exist. Duration for this condition is expected to be no less than the upper bound of the best-case scenario. In Lam et al., 2002, duration of the of an acute angle glaucoma account prior to presentation was noted to range from 2-168 hours. Given that in the same study treatment could last up to an additional 24 hours, total time would be 192 hours prior to iridotomy. Similar to the best-case scenario, RTDC would be 100% and LOCL is not expected for ocular conditions.

UNTREATED BEST CASE (UTBC) SCENARIO COMMENTS

Even in the best case, acute angle glaucoma is considered an ocular crisis and will proceed onto blindness without treatment. There are limited studies available regarding the timeline of the untreated condition. Many guidelines state that without treatment, vision loss and even blindness can occur quickly during the attack, “over hours to days,” but do not get more specific (Prum et al., 2016; Flores-Sánchez et al, 2019). In one case study of acute angle glaucoma, a 73-year-old patient developed monocular blindness 15 days after blepharoplasty (Wride et al., 2004). He developed ocular pain on postoperative day one and was treated for conjunctivitis later in the week. However, by day 15, when the patient presented to the ophthalmologic department, his eye was non-seeing. RTDC is expected to be 100% due to the threat of monocular blindness, however LOCL is not expected.

UNTREATED WORST CASE (UTWC) SCENARIO COMMENTS

In the untreated worst case, recovery is not expected. Duration is expected to be no less than the treated worst-case. RTDC is 100% given the risk of permanent binocular blindness. LOCL is not expected for ocular conditions.

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

Citation	Source	LOC Value
Choong et al., 1999	Terrestrial	2
Lam et al., 2002	Terrestrial	
Prum et al., 2016	Terrestrial	
Flores-Sánchez et al, 2019	Terrestrial	
Wride et al., 2004	Terrestrial	

Available studies to determine durations for treated cases involved retrospective studies and review papers. There was one consensus guidelines available, however it did not provide definitive timelines. Due to the increasingly more rigorous Institutional Review Board guidelines at institutions, literature for untreated best and worst cases were limited and this information was often extrapolated from single, low-powered studies.

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Wright et al, 2016	Terrestrial	1
Chan et al., 2019	Terrestrial	
Lee et al., 2009	Terrestrial	

RTDC for all conditions was determined to be 100% as literature stated that even for the best case scenario, a procedure/intervention other than pure medical management should be completed.

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
N/A	N/A	4

Based on the definitions, loss of crew life is not expected for any of the scenarios associated with this CLiFF.

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

Capabilities and Resourcing Scope Overview The best case of this condition responds to treatment with topical agents. The worst case carries the risk of a refractory condition. With this in mind the CRT Working Group agreed that the risk of blindness from refractory acute angle closure glaucoma warranted the inclusion of anterior chamber paracentesis since in the spaceflight environment the benefits of attempting this procedure even with a non specialist physician may outweigh the risk. It is expected that the decision to perform this procedure would be made in consultation with terrestrial experts. CNES: None Diagnostic Scope and Resourcing Diagnosis for both the best case and the worst case for this condition is based on history, physical exam, anterior segment OCT, and intraocular pressure measurement using a small, hand held device. 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): 2.22 hours for a functional eye exam (APD, EOM, appearance, etc.…), anterior segment OCT, and intraocular pressure measurements. 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): 2.22 hours for a functional eye exam (APD, EOM, appearance, etc.…), anterior segment OCT, and intraocular pressure measurements. The scope of practice for this condition is listed as requiring a specialist for fitness for duty assessments. However, if an anterior chamber paracentesis is warranted, as may occur in the worst case scenario, this procedure should be performed only after discussion with a specialist terrestrially since the risk of a non expert performing it is substantial. Treatment Scope and Resourcing For the best case management includes, 2timolol, apraclonidine, pilocarpine, and acetazolamide since this is the most effective way to gain control of the condition quickly. Visual acuity checks are also included. For the worst case, the additional capability of performing an anterior chamber paracentesis is included since the potential benefit of a non expert performing this procedure likely will outweigh the risk of not treating refractory acute angle closure glaucoma. IT is expected that the decisions and procedure would be performed under the guidance of terrestrial experts. The capability for high dose anxiolysis with oral valium is also added in case such a procedure is necessary. Communications and Support Needs This condition would likely require consultation with terrestrial based experts in both the best and worst case. Audio and visual transmission capability is included as a necessary capability.

IMM CLIFF RECONCILATION COMMENTS

This CLiFF is the successor to the previous IMM CLiFFs entitled "Acute Angle-Closure Glaucoma Cliff." CLiFF condition definitions for the ocular conditions were changed from the previous excluding this condition, which has remained identical. The incidence calculation was updated using more relevant studies. Duration and RTDC values have changed given extensive literature review.

LIMITATIONS SUMMARY

• Literature regarding the untreated worst-case scenario was extremely limited and several parameters are based on subject matter expert opinion. • Terrestrial studies for BC/WC calculations probably overstate WC because these studies are older and better pharmacologic treatments are available now. • Generally, acute angle closure glaucoma is an extremely rare event. We expect this event to be even more unusual for spaceflight crews given their extensive preflight ocular screening. • The incidence of acute angle glaucoma is different for varying ethnicities. The ethnic composite of future spaceflight crews is unknown. • Because of the large sample size, the study used to compute the composite incidence most likely overestimates the confidence we have in the assigned value.

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)					854		145					
Untreated Best Case (UTBC)		664		89	854		145					
Treated Worst Case (TWC)	223	664		89	854		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	1342	3763	0.35663	35.663
Untreated Best Case (UTBC)	132							211	2095	3763	0.556737	55.6737
Treated Worst Case (TWC)	132	564	414	22			34	211	3352	3763	0.890779	89.0779
Untreated Worst Case (UTWC)	132	564	414	22	196	34	34	211	3739	3763	0.993622	99.3622

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)		664		89	854							
Treated Worst Case (TWC)		664		89	854							
Untreated Worst Case (UTWC)		664		89	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	TI Decimal	TI %
Treated Best Case (TBC)									0	3763	0	0
Untreated Best Case (UTBC)	132	564						211	2514	3763	0.668084	66.8084
Treated Worst Case (TWC)	132	564						211	2514	3763	0.668084	66.8084
Untreated Worst Case (UTWC)	132	564						211	2514	3763	0.668084	66.8084

TABLE 8 KEY

Human System Task Category (HSTC) Definitions: Cognitive-Simple: Tasks requiring simple cognitive involvement (low levels of attention, following simple checklists, and not requiring extensive decision making) in conjunction with inputs from other systems. Cognitive-Complex: Tasks requiring complex cognitive involvement (requiring constant attention, frequent interpretation of outside stimuli to inform real-time situations) in conjunction with inputs from other systems. Communication: Tasks requiring primarily communication, via hearing and speaking. Interpersonal Skills: Tasks requiring interpersonal, social interaction between crew including complex technical tasks that require extended crew interaction. Vision: Tasks in which visual information is required. Hearing: Tasks in which primarily auditory information is required, excluding communication, e.g. hearing alarms, medical auscultation, OOHAs. Cardiopulmonary: Tasks requiring greater-than-baseline cardiopulmonary effort, e.g. physically strenuous activities. Dentition: Tasks requiring use of teeth for mastication. GI (Gastrointestinal): Tasks requring use of the alimentary sytem, e.g. solids/liquids consumption and solids excretion. GU (Genitourinary): Tasks requiring use of the male/female genitourinary systems. Hand (Dominant): Tasks performed using primarily the hand, requiring use of the dominant hand (piloting, medical procedures, dental procedures). Hand (Any): Tasks performed using primarily the hand(s), with no preference for dominance, with equivalent bilateral effectiveness. Upper Extremity: Tasks requiring specific use of the upper extremities, excluding hands. Lower Extremity: Tasks requiring specific use of the lower extremities (excluding ambulation and standing in the presence of gravity), e.g. using exercise equipment. Ambulation and Standing (g): Tasks requiring use of both lower extremities to accomplish ambulation or standing in the presence of gravity. Translation and Stabilization (microgravity): Tasks requiring use of either the upper or lower extremities to accomplish translational movement and stabilization (securing oneself to remain stationary) in the setting of microgravity. Don/Doff Equipment: Tasks requiring the donning of personal equipment (including pressure suit, exercise harness, EVA equipment, etc). Pressure Ops: EVA/contingency tasks performed while pressurized in a suit.

Criteria for Assignment of Conditions to HSTCs (any of the following):

1) Is affected crew member physically incapable of performing the human system task category, without impairment, with the condition?
2) Would the treatment (e.g. medications) impair the crewmember's ability to perform the human system task category? (Does not apply to UTx)
3) Does the condition have a high likelihood of causing a significant aeromedical contraindication with an associated human system task category
4) Would performing tasks in an associated task category worsen the condition? (If so, it is affected).
5) Does pain associated with the condition impair any further human system categories?

TASK IMPAIRMENT COMMENTS

CP2: No comment. CP3: No comment.

EVIDENCE COLLECTION PROCESS

Mesh terms that most closely resembled the best-case and worst-case scenarios, and associated Conditions Included but Not Explicitly Stated (CNES), were utilized to build incidence, duration, RTDC, and LOCL searches by best- and worst-case.

Incidence:

Databases searched for spaceflight and analog incidence data included: PubMed, Google Scholar, NASA Technical Reports Server (NTRS) public search, Defense Technical Information Center (DTIC), and Barratt MR, Baker E, Pool SL. Principles of Clinical Medicine for Space Flight. New York, NY: Springer; 2019. 2nd Edition. Databases searched for terrestrial incidence included: DynaMed, PubMed, and Google Scholar.

Duration, RTDC, LOCL:

Databases searched for duration, RTDC, and LOCL included: Dynamed, Cochrane, PubMed, and Google Scholar. Note, that if duration, RTDC, or LOCL data was found in a DynaMed search, the other search engines were not included. Relevant articles were selected and reviewed. If applicable, the article was included in the CLiFF.

LEVEL OF CONFIDENCE (LOC) SCORING

Articles obtained to update the evidence behind this CLiFF were scored by ExMC editors, based on their applicability to the Exploration Spaceflight environment using the following grading scale:

4 – Confident
3 – Somewhat confident
2 – Neutral
1 – Somewhat unconfident
0 – Not confident

The following considerations factor into the grading scale above:

• How closely does the paper describe the medical condition as defined by the IMPACT 1.0 Condiltion List (relevance)?
• How closely does the population included resemble the astronaut population?
• Quality of the paper (number of subjects, methods, etc.)
• How much does the editor trust the source of the evidence?
• How closely does the editor think that the data represents the exploration spaceflight environment?
• Other considerations, at the discretion of the editor, supported in the comments for LOE scoring.

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ACRONYMS

ACRONYM	PHRASE
AAOMS	American Association of Oral and Maxillofacial Surgeons
AMA	American Medical Association
ARCL	All Remaining Conditions List
ARS	Acute Radiation Sickness

BHP	Behavioral Health and Performance
CAC	Coronary Artery Calcium
CHS	Crew Health and Safety
CL	Condition List
CliFF	Clinical Finding Form
CMO	Crew Medical Officer
COMFORT	Clinical Outcome Metrics for Optimization of Robust Training
CP1	Clinical Phase 1
CP2	Clinical Phase 2
CP3	Clinical Phase 3
CRL	Clinical Resource Level
CRT	Capability Resource Table
CST	Clinical Science Team
DCS	Decompression Syndrome
DRM	Design Reference Mission
ED	Emergency Medicine Doctor
EL	Evidence Library
EMCL	Exploration Medical Condition List
EMT	Emergency Medical Technician
EVA	Extravehicular Activity
EXMC	Exploration Medical Capability
HRP	Human Research Program
ICD	International Classification of Disease
ICL 1.0	IMPACT 1.0 Medical Conditions List
ICU	Intensive Care Unit
IMCL	iMED Condition List
iMED	Integrated Medical Evidence Database
IMM	Integrated Medical Model
IMPACT-MD	Impact Medical Database
IP	Incidence Proportion
IR	Incidence Rate
ISS	International Space Station
IV	Intravenous
JSC	Johnson Space Center
LEO	Low-Earth orbit
LEVA	Lunar Extravehicular Activity
LOCL	Loss of Crew Life
LOM	Loss of Mission
LSAH	Lifetime Surveillance of Astronaut Health
LSO	Lunar Surface Operations
MCL	Master Condition List
MEVA	Medical Extravehicular Activity
NASA	National Aeronautics and Space Administration

N/A	Not Applicable
NP	Nurse Practitioner
OBGYN	Obstetrics and Gynecology
OR	Occurrence Rate
PA	Physician Assistant
PDQ	Pain Disability Questionnaire
PFCL	Proposed Future Conditions List
PPE	Personal Protective Equipment
PTRS	Project Technical Requirements Specification
PRL	Pharmaceutical Resource Level
QTL	Quality Time Lost
RCL	Removed Conditions List
REP	Rochester Epidemiology Study
RTDC	Removal to Definitive Care
SANS	Spaceflight-Associated Neuro-ocular Syndrome
SAS	Space Adaptation Syndrome
SEVA	Spaceflight Extravehicular Activity
SME	Subject Matter Expert
SoP	Standard Operating Procedure
SPE	Solar Particle Event
TBD	To Be Determined
TI	Task Impairment