Clinical Finding Form (CliFF)

Branch | **Baseline**

ICL115_Trauma - Severe Head

Traumatic Brain Injury (TBI) occurs as a result of a "violent blow" or jolt to the head (Mayo, 2021). This CLiFF pertains only to severe TBI. Unfortunately, there is no globally accepted definition of severe TBI and multiple classifications systems exist. The classification is complicated by the heterogeneity of presentations with TBI. Classification systems can be based on symptoms, pathoanatomic, etiologic, mechanistic, or prognostic. A post-resuscitative Glasgow Coma Scale (GCS) score of < 9 is often used as one of the criteria for severe TBI. (Hawryluk and Manley, 2015) This CLiFF uses a GCS of < 9. Most severe TBI injuries involve a loss of consciousness and many classification systems also describe a length of loss of consciousness as part of their criteria. Because of the heterogeneity between these classification systems, this was not considered for the definition of this CLiFF. Symptoms of severe TBI may include loss of consciousness, headache, nausea and vomiting, convulsions/seizures, pupillary changes, weakness or numbness, loss or coordination, and/or cerebrospinal fluid leaking from the nose or ears (Mayo, 2021). Note that seizures are a separate CLiFF (ICL 83 - Seizures) and not considered in this CLiFF.

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

Scheuring et al, 2009 was the only source of spaceflight data identified. The study evaluated the incidence musculoskeletal in-flight injuries among astronauts, as well as skin abrasions, contusions, and lacerations in a review spanning Mercury - Expedition 13 of the ISS Program. Unfortunately, head injuries were not categorized by type. Anecdotally, there have been no TBI injuries in spaceflight. Thus, the data on head injuries from this source, if used, would drastically overestimate the incidence of TBI in spaceflight. This source was not used to inform the incidence for this CLiFF.

ANALOG LITERATURE

Levin, 2021 provides unpublished analog incidence compiled from University-National Oceanographic Laboratory System data. It provides an incidence of 96.6/person day. Although the crew characteristics from UNOLS data may be a closer approximation to the astronaut corps (i.e. medical pre-screening), the ocean environment is inherently different from the spaceflight environment. Rough seas present more opportunities for head injuries in general (and possibly TBI). Thus, these data were felt to be an overestimate of the risk in spaceflight and this source did not inform the incidence for this condition.

TERRESTRIAL LITERATURE

The Peterson et al, 2017 provides incidence of TBI based on 2016 and 2017 Healthcare Cost and Utilization Project's (HCUP) National Inpatient Sample sponsored by the Agency for Healthcare Research and Quality. These data allow for restriction by age, and removal of common terrestrial causes of TBI that are not expected in spaceflight (e.g. motor vehicle accident, assault, war), which would over-estimate the incidence of TBI in spaceflight. This source was used to inform the incidence for this condition. Marin et al, 2014 provides incidence of various head injury types between 2006-2010 from data extracted from the Nationwide Emergency Department Sample (NEDS) database. All comer incidence of TBI from this source is 637/100,00 person years. After removing the unspecified head injury, concussion, and cerebral laceration/contusion, the incidence of severe head injury from this study is 79/100,000 person years. An additional source provided an incidence of 285/100,000 person years based on data from the 2017 Global Burden of Disease data (Feigin et al, 2021). However, it did not provide a case definition for severe head injury, and is therefore anticipated to be an overestimate.

OVERALL INCIDENCE SUMMARY

INCIDENCE

Mean: 1.96E-4 SD: 1.037E-6

INCIDENCE SUMMARY

The incidence for this condition is informed from the CDC 2016/2017 report, Traumatic Brain Injury-related Hospitalizations and Deaths by Age Group, Sex, and Mechanism of Injury. Table 1 reports numbers and rates by age group, year, and mechanism of injury. These numbers will be used to estimate an age-adjusted (to flown astronauts) incidence rate from the relevant mechanisms. Crude overall incidence rate (from relative age categories and mechanisms) IR: 5.438E-4 (95%CI: 5.416E-4, 5.46E-4). The incidence of this condition in microgravity was assumed to be 0. Therefore, the incidence should be applied only to surface operations. Similarly, during an EVA, the helmet would protect against head injuries. Currently MEDPRAT does not have the capability to exclude surface EVA time from surface operations, but in the future, this is recommended when the capability exists. The posterior distribution for the age-adjusted (to flown astronauts) incidence rate given the terrestrial evidence, under an uninformative prior, is Gamma(shape=35723.55, rate=182263019) with mean 1.96E-4 and SD 1.037E-6.

TABLE 1. INCIDENCE MODEL

Incidence Details

Incidence Type
UNK

Segment
Surface

Env. Exposure
NA

Sex
Any

Crowns
Any

Contacts
Any

Pregnancy
Any

Incidence Distribution

Occurrence Dist
Poisson

Incidence Dist.
Gamma

Mean
0.000196

SD
1.037E-06

Gamma
(Shape): 35723.6
(Rate): 1.82263E+08

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Feigin et al, 2021	Terrestrial	2
Marin et al, 2014	Terrestrial	2
Peterson et al, 2017	Terrestrial	3
Levin, 2021	Analog	2
Scheuring et al, 2009	Spaceflight	1

Feigin et al, 2021 provides incidence of TBI based on a systematic analysis of the 2017 Global Burden of Disease study. This used data from the US from 1990-2017. The definition for TBI was not clear in this study. Marin et al, 2014 provides incidence of various head injury types between 2006-2010 from data extracted from the Nationwide Emergency Department Sample (NEDS) database. The Peterson et al, 2017 provides incidence of TBI based on 2016 and 2017 Healthcare Cost and Utilization Project's (HCUP) National Inpatient Sample. The data is granular enough to be age restricted an remove common terrestrial sources of TI that would not be expected to occur in spaceflight (e.g. motor vehicle accidents and war). Levin, 2021 provides unpublished analog incidence compiled from University-National Oceanographic Laboratory System. Although this represents ocean vessel crewmembers who received medical pre-screening, and occurs in confined ocean vessels, it is less applicable to exploration missions because of a difference in environment. The UNOLS data is anticipated to overestimate incidence of head injuries, thereby TBI, based on increased risk of head injury during rough sea conditions. Scheuring et al, 2009 evaluated the incidence musculoskeletal in-flight injuries among astronauts from Mercury - Expedition 13 of the ISS Program. Head injuries were not categorized by type limiting the applicability to the category 1 and category

2 scenarios in this CLiFF.

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

Engineering measures are taken to prevent injury to crewmembers, including head injury. Further, on EVA the helmet of the EMU provides protection from head injury.

BEST CASE SCENARIO DEFINITION

This condition does not have a "best-case" and "worst-case" scenario. Rather, it has a "Category 1" scenario encompassing severe non-surgical TBI resulting in diffuse axonal injury (DAI) or persistent vegetative state (PVS) and a "Category 2" scenario encompassing severe surgical TBI, including intracranial bleeding, risk of herniation, and open skull fracture.

Category 1 Scenario Definition: Severe non-surgical TBI (initial GCS < 9) including diffuse axonal injury or other persistent vegetative state

WORSE CASE SCENARIO DEFINITION

This condition does not have a "best-case" and "worst-case" scenario. Rather, it has a "Category 1" scenario encompassing severe non-surgical TBI resulting in diffuse axonal injury (DAI) or persistent vegetative state (PVS) and a "Category 2" scenario encompassing severe surgical TBI, including intracranial bleeding, risk of herniation, and open skull fracture.

Category 2 Scenario Definition: Severe surgical TBI (GCS < 9) including Epidural Hematoma, extensive subdural hematoma, swelling causing risk of imminent herniation, or open skull fracture

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

Traumatic Brain Injury Intracranial Hematoma, Epidural Intracranial Hematoma, Subdural Diffuse Axonal Injury

BEST CASE/WORST CASE PROBABILITY COMMENTS

This condition does not have a "best-case" and "worst-case" scenario. Rather, it has a "Category 1" scenario encompassing severe non-surgical TBI resulting in diffuse axonal injury (DAI) or persistent vegetative state (PVS) and a "Category 2" scenario encompassing severe surgical TBI, including intracranial bleeding, risk of herniation, and open skull fracture. It is feasible that some surgical TBIs may also result in DAI or PVS (i.e. the categories do not have to be mutually exclusive). It was not possible in the literature to separate survival vs. non-surgical TBIs that result in DAI or PVS. However, two sources were found that provide insight into DAI/PVS in severe TBI overall. The StatPearls article titled "Diffuse Axonal Injury" (DAI) provides an incidence of 10% for DAI in TBI patients (Mesfin et al, 2021). A meta-analysis of 21 cohort studies with an outcome of persistent vegetative state, assessed 6 months following severe traumatic brain injury, reports a prevalence of 2.77% (Tang et al, 2017). Therefore, the Category 1 scenario for this condition was assigned a proportion of 2.77-10% and the Category 2 scenario was assigned a proportion of 90-97.23%.

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

Citation	Source	LOC Value
Mesfin et al, 2021	Terrestrial	3
Tang et al, 2017	Terrestrial	3

The StatPearls article titled "Diffuse Axonal Injury" (DAI) provides an incidence of 10% for DAI in TBI patients (Mesfin et al, 2021). A meta-analysis of 21 cohort studies with an outcome of persistent vegetative state, assessed 6 months following severe traumatic brain injury, reports a prevalence of 2.77% (Tang et al, 2017).

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: 1.96E-4 SD: 1.037E-6	2.77 - 10	100	1.82	100	96	70080	100	100	100	25	35
Treated Worst Case (TWC)		90 - 97.23	100	1.82	54.5575	0	2568	9.115	100	100	37	65
Untreated Best Case (UTBC)	N/A	N/A	N/A	1.82	100	0	336	100	100	100	100	100
Untreated Worst Case (UTWC)	N/A	N/A	N/A	1.82	100	0	64.8	100	100	100	100	100

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 ExMC Clinical and Science Team pre-determined that the RTDC probability for both Category 1 and Category 2 of this condition is 100%. Therefore, no literature searches were performed for RTDC. There is a paucity of data regarding untreated TBI with a GCS < 9. Thus, based on treatment measures required to sustain life in the literature, the assumption was made that in both untreated scenarios the LOCL probability is 100%. See specific scenario comments below.

TREATED BEST CASE (TBC) SCENARIO COMMENTS

A retrospective study of 102 Diffuse Axonal injury (DAI) patients, spanning 19 years, at the San Raffaele Scientific Institute in Milan, Italy reports variable lengths of time for return to consciousness. The shortest duration was 4 days and the longest duration was 180 days. (Notably 180 days is when the study period was terminated and 12/102 patients remained comatose at 180 days). The Merck Manual states, regarding patients with Persistent Vegetative State (PVS) that "If the cause was a head injury, recovery is unlikely after 12 months. However, a few people improve over a period of months or years. Rarely, improvement occurs late. After 5 years, about 3% of people recover the ability to communicate and understand, but few can live independently, and none can function normally." The Multi-Society Task Force on Persistent Vegetative State (PVS) (1994) corroborates that after 12 months of unconsciousness it is unlikely that consciousness will be regained, citing 7 of 434 patients (1.6%). However, there are patients that remain alive but never regain consciousness when comatose. Kitzinger and Kitzinger (2018) report a duration of PVS of less than a year to 8 years. This is based on a qualitative narrative interview study with 21 members of 12 families, between 2013-2017, who had a relative in a prolonged disorder of consciousness (coma, vegetative or minimally conscious state) who had died after court-approved withdrawal of artificial hydration and nutrition in the UK. While it is possible that someone in a coma could live longer than 8 years, they reported an average of 4-5years, thus 8 years will be used to approximate the maximum duration. (Kitzinger and Kitzinger, 2018) Therefore, the duration was assigned a range of 96-70,080h (4 days - 8 years). The ExMC Clinical and Science Team pre-determined that the RTDC probability for both Category 1 and Category 2 of this condition is 100%. Therefore, no literature searches for RTDC were performed. Mesfin et al, 2021 estimate that 25% of DAI diagnoses result in death. Thee Multi-Society Task Force on Persistent Vegetative State (PVS) reported a probability of death between 3-6 months of 32-35% (1994). A prospective cohort study of patients with DAI at the Neurosurgical Outpatient Clinic and Trauma at the Central Institute of Hospital da Clinicas da Faculdade de Medicinea da Universidade de Sao Paulo in Sao Paulo, Brazil has similar findings for patients with DAI. 24/78 patients (mean age 32yo) with DAI from July 2013-February 2014 had died by 6 months of follow-up. Inclusion criteria included GCS ≤ 8 at time of admission, age 18-60yo, and a CT/MRI with either normal outcome or signs of DAI. Exclusion criteria: admitted to the hospital more than 6 hours post-trauma, transferred from another hospital with a previous diagnosis of TBI, psychiatric disorders, or other injuries to the head or spinal cord with an AIS ≥ 3. (de Cassia Almeida Vieira et al, 2016) Therefore the LOCL probability for this scenario was assigned a range of 25-35%. Notably, the Ashwal et al, 1994 reports markedly higher mortality rates at longer intervals (82% at 3 years and 95% at 5 years). However, given the DRM of 210 days, the 3-6 month values will be used to approximate LOCL probability. If DRMs of 3 or more years are used in the future, this LOCL probability should be increased accordingly based on the aforementioned data.

TREATED WORST CASE SCENARIO (TWC) COMMENTS

In a retrospective analysis of 121 patients (age 16-24) with epidural hematoma presenting to emergency departments of 14 hospitals in the Queensland Trama Registry (Australia) between 2005-2007, the mean length of hospitalization was 12.9 days (2 SD range: 0-44 days). Skull fracture was also present in 75% of these patients. (Irie et al, 2011) Another study from Queensland, Australia examined outcomes in 117 TBI patients (median age 28, median GCS score 6) who received speech pathology care for dysphagia after their injury. The mean length of hospitalizationwas 39.8 days (2 SD range: 0-106.6). Thus, the duration was assigned a range of 0-107 days for this scenario. The ExMC Clinical and Science Team pre-determined that the RTDC probability for both Category 1 and Category 2 of this condition is 100%. Therefore, no literature searches for RTDC were performed. The minimum probability of LOCL for this scenario is based on a retrospective study of TBI in Latin America. Of 484 patients whom six-month outcomes were available for, 37% died. (Bonow et al, 2017) A retrospective study of 256 patients who underwent surgical intervention for non-penatrating trauma resulting in acute subdural hematoma between March 1998 and March 2008 at Masan Samsung Hospital at Sungkyunkwan Universtiy School of Medicine in Korea reported a mortality rate of 55.4% for patients with a GCS score of 3-8 (Kim, 2009). In a retrospective study of 7,191 patients with head trauma in a Trauma-registry based study at the Los Angeles County and University of Southern California Trauma Center from 1993-2002, Demetriades et al report a mortality rate of 30.5% in patients with a GCS of 4-8 and 65.4% in patients with a GCS of 3 during the study period. Thus, the LOCL probability for this scenario was assigned a range of 37-65.4%.

UNTREATED BEST CASE (UTBC) SCENARIO COMMENTS

There is a paucity of data regarding untreated Diffuse Axonal Injury (DAI) or Persistent Vegetative State (PVS) after head trauma. Therefore, data regarding withdrawal of nutrition and hydration in patients with a coma, PVS, or minimally conscious state was used to inform the duration for the untreated category 1 scenario. The minimum duration was assigned a value of 0 hours because it assumed that many patients with a severe TBI and GCS < 9 would perish rapidly without treatment. Kitzinger and Kitzinger (2018) was used to inform the maximum duration. They performed a qualitative narrative interview study with 21 members of 12 families, between 2013-2017, who had a relative in a prolonged disorder of consciousness (coma, vegetative or minimally conscious state) who had died after court-approved withdrawal of artificial hydration and nutrition in the UK. The article reports that most of these patients died within 9-14 days after removal of their feeding tube and hydration. Therefore, the duration for this scenario was assigned a range of 0-336 hours (0-14 days). The ExMC Clinical and Science Team pre-determined that the RTDC probability for both Category 1 and Category 2 of this condition is 100%. Therefore, no literature searches were performed. Mesfin et al (2021) describes that treatment of DAI focuses on prevention of secondary injuries due to hypotension, hypoxia, cerebral edema, and elevated intracranial pressure. Thus, most patients are maintained under general anesthesia with extensive, and sometimes invasive, monitoring. Similarly, Kitzinger and Kitzinger (2018) discuss patients with PVS being maintained by tube feeding, hydration, suctioning, and extensive care requirements. Thus, the assumption was made that all severe TBI cases resulting in DAI and/or PVS would result in death without treatment. Therefore, the LOCL probability for this scenario was assigned 100%.

UNTREATED WORST CASE (UTWC) SCENARIO COMMENTS

There is a paucity of data regarding untreated severe TBI. Therefore, data regarding delay of transfer in combat patients requiring craniotomy was used to inform this duration. The minimum duration was assigned a value of 0 hours because it assumed that many patients with a severe TBI and GCS < 9 would perish rapidly without treatment. Shackelford et al, 2018 performed a retrospective review, utilizing the Defense Trauma Registry and Joint Trauma System Role 2 Registry, of servicemembers in Iraq or Afghanistan between 2005-2015 who required craniotomy for severe head trauma. They report delays for craniotomy spanning from 0.5 hours - 2.7 days. Notably, this is not true lack of treatment because these patients received intensive care while awaiting craniotomy. Therefore, these durations may be an overestimate. However, given the paucity of data for untreated severe TBI, 2.7 days was assigned as the maximum duration. Thus, the duration was assigned a range of 0-64.8 hours. The ExMC Clinical and Science Team pre-determined that the RTDC probability for both Category 1 and Category 2 of this condition is 100%. Therefore, no literature searches were performed. In a retrospective systematic review from 2000-2003 of 76 patient who required emergent craniotomy for acute traumatic epidural and/or subdural hematoma at the Department of Neurosurgery, University Hospital Bern, in Switzerland, all patients with a GCS < 8 required intubation in the field prior to transfer to the hospital (Taussky et al, 2018). Severe TBI patients with a GCS < 9 require extensive lifesaving measures and ongoing treatment. Thus, the assumption was made that all severe TBI cases as outlined in the Category 2 scenario would result in death without treatment. Therefore, the LOCL probability for this scenario was assigned 100%.

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

Citation	Source	LOC Value
Calvi et al, 2011	Terrestrial	3
Maiese, 2020	Terrestrial	
Kitzinger and Kitzinger, 2018	Terrestrial	
Irie et al, 2011	Terrestrial	
Ward et al, 2007	Terrestrial	
Shackelford et al, 2018	Analog	

The durations for the Category 1 treated scenario are based on literature regarding DAI and PVS. The durations for the Category 2 treated scenario are based on severe TBI literature, with one study being specific to traumatic epidural hematoma (Irie et al, 2011). Data regarding the duration of untreated scenarios are limited. The durations for the untreated Category 1 scenario utilize data regarding withdrawal of life support. For the Category 2 untreated scenario, data regarding delayed transfer of combat patients (Shackelford et al, 2018) was utilized. Notably, this scenario does not reflect true lack of treatment since servicemembers received intensive care while awaiting transport and therefore may be an overestimate of the duration.

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
N/A	N/A	4

The ExMC Clinical and Science Team pre-determined that the RTDC probability for both Category 1 and Category 2 of this condition is 100%. Therefore, no literature searches were performed. This is an assumption that can be made with confidence given that a TBI with a GCS of < 9 would exceed the medical capabilities of the mission.

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Kim, 2009	Terrestrial	
Bonow et al, 2017	Terrestrial	

Citation	Source	LOC Value
de Cassia Almeida Vieira et al, 2016	Terrestrial	3
Mesfin et al, 2021	Terrestrial	
Ashwal et al, 1994	Terrestrial	
Taussky et al, 2008	Terrestrial	
Demetriades et al, 2006	Terrestrial	
Kitzinger and Kitzinger, 2018	Terrestrial	

For treated scenarios the LOCL probabilities are based on literature according to the specified definitions for category 1 and 2 and hold a high level of confidence. There is a paucity of data regarding untreated TBI with a GSC of < 9. Thus, the untreated LOCL probabilities were assumed to be 100% based on known treatment methodologies required to sustain life in the setting of a severe TBI.

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

Capabilities and Resourcing Scope Overview Trauma – Severe Head – This is a broad range of conditions related to traumatic brain injury, skull fractures, and associated complications related to increasing pressure within the cranium (which is a fixed non-expandable space). This condition also includes the convalescent phases of severe head injury which can have significant and long lasting symptoms for weeks to years. CNES: N/A Diagnostics Scope and Resourcing The Best Case and Worst Case definitions are not truly on a spectrum but represent separate but overlapping severe head injury conditions. In the best-case scenario, a severe non-surgical traumatic brain injury (TBI) including diffuse axonal injury and other persistent vegetative state is Diagnosed by history, physical examination, and ultrasound studies. Ultimately these severe coma-like states are Diagnosed by the lack of clinical improvement over many hours. Lab tests do not contribute to the Diagnosis although a sodium level is used to look for complications of treatment. In the worst case scenario, a severe surgical TBI, including hematomas, swelling causing risk of herniation, or open skull fracture, the Diagnosis is made by history, physical examination, and ultrasound studies. Lab tests do not contribute to the Diagnosis although a sodium level is used to look for complications of treatment. 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): 1.82 hours CP1 WC (Treated or Untreated: 1.82 hours This CRT includes a scope of practice code of 5 (which correlates to an “Experienced procedure trained generalist attending” and was included for management decisions, Diagnostics ultrasound, medication management, and fitness for duty. Treatment Scope and Resourcing Terrestrially, these patients are clinically stabilized in an emergency department after rapid evaluation in a CT scanner, airway control with intubation, and typically are admitted to a neurosurgical intensive care unit where they may or may not undergo neurosurgical procedures such as intracranial pressure monitors, drainage or a hematoma, or others. Additional critical care interventions such as central line, invasive arterial blood pressure monitoring, numerous infusions, prolonged paralysis, IV nutrition, and more are also the terrestrial standard of care. Many of these patients are managed for days to months in the intensive care unit before improvement is noted or a poor prognosis can be made. Almost none of the ICU-level standard of care are available in spaceflight nor are the gold standard Diagnostics. Prolonged coma and death are expected outcomes in these cases. Survivors of severe head injuries may have significant residual safety- and mission- threatening issues such as psychosis, agitation, intractable vomiting, cognitive deficits, and others for weeks to months as well.

The capability to perform a burr hole was included in this CRT. Terrestrially this is accompanied by 1 day of prophylactic antibiotics. Given that this CRT also includes open skull fracture, the antibiotics used for other open fracture conditions in the ICL 1.0 were also provided here to cover both burr hole and open skull fracture. Ertapenem and Ceftriaxone are provided for antibiotic prophylaxis for open fractures. Although ertapenem is not traditionally used terrestrially, it was selected due to its broad spectrum, daily dosing, and ability to be dosed IM – decreasing mass/volume requirements associated with IV medications

Communications and Support Needs Communication with ground based support through video would contribute to the initial evaluation and ongoing management of these severe and complicated cases. REFERENCES American College of Surgeons Committee on Trauma. ACS TQIP best practices in the management of traumatic brain injury. January 2015. Pages 1-33. Mesfin FB, Gupta N, Shapshak AH, Taylor RS. Diffuse Axonal Injury. NCBI Bookshelf; StatPearls. Jan 2021. Hawryluk GWJ, Rublano AM, Totten AM, et al. Guidelines for the management of severe traumatic brain injury: 2020 update of the decompressive craniectomy recommendations. Neurosurgery; 87(3):427-434. Tenny S and Thorell W. Intracranial Hemorrhage. NCBI Bookshelf; StatPearls. Jan 2021.

IMM CLIFF RECONCILATION COMMENTS

IMM contains a “Head Injury” CLiFF that is exclusive of traumatic brain injury. This is a new condition exclusive to IMPACT. Therefore, the incidence, durations, and outcomes (RTDC and LOCL) are unique to this condition.

LIMITATIONS SUMMARY

• The Category 1 and Category 2 scenarios for this condition may not be mutually exclusive in clinical practice, but for the purposes of this CLiFF they were treated as mutually exclusive. • Calvi et al, 2011 was used to inform the Category 1 treated duration. The maximum duration of 180 days reflects the end of the study period in this paper. No other data were available to determine the true maximum duration. • The LOCL probability for the treated Category 1 scenario is based on data with a 3-6 month follow-up period. Data from the same reference (Ashwal et al, 1994, 2014) presented much higher mortality rates for 3- and 5-year follow-up (82% and 95%, respectively). Given the DRM of 210 days, the 3-6-month values will be used to approximate LOCL probability. If DRMs of 3 or more years are used in the future, this LOCL probability should be increased accordingly. • The maximum duration for the Untreated Category 2 scenario may be an overestimate. It is based on data regarding delay of transfer out of combat for craniotomy after sustaining a severe TBI. However, this is not true lack of treatment because these patients received intensive care while awaiting craniotomy. • There is a paucity of data regarding untreated severe TBI presenting with a GCS < 9. There is literature available regarding the treatment interventions needed for TBI, however. Based on the treatment modalities mentioned in the literature, the assumption was made that both untreated scenarios would result in LOCL with a 100% probability.

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	113	89	854	44	145	5	13	6		
Untreated Best Case (UTBC)	223	664	113	89	854	44	145	5	13	6		
Treated Worst Case (TWC)	223	664	113	89	854	44	145	5	13	6		
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	414	22	196	34	34	211	3763	3763	1	100
Untreated Best Case (UTBC)	132	564	414	22	196	34	34	211	3763	3763	1	100
Treated Worst Case (TWC)	132	564	414	22	196	34	34	211	3763	3763	1	100
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)	223	664	113	89	854	44	145	5	13	6		
Untreated Best Case (UTBC)	223	664	113	89	854	44	145	5	13	6		
Treated Worst Case (TWC)												
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	414	22	196	34	34	211	3763	3763	1	100
Untreated Best Case (UTBC)	132	564	414	22	196	34	34	211	3763	3763	1	100
Treated Worst Case (TWC)	132							211	343	3763	0.0911507	9.11507
Untreated Worst Case (UTWC)	132	564	414	22	196	34	34	211	3763	3763	1	100

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