Clinical Finding Form (CliFF)

Branch | **Baseline**

ICL114_Trauma - Minor Head

This CLiFF includes concussion, post-concussion syndrome, and non-operative intracranial bleeds resulting in concussive or post-concussive symptoms. Most sources consider a concussion to be a mild, temporary, traumatic brain injury. Concussions are cause by impact with the head or body that causes the brain to move rapidly within the skull (CDC, 2021). Symptoms of concussion vary, but can include headache, nausea, vomiting, fatigue, changes in vision, confusion, amnesia, dizziness, changes in speech and response time, and forgetfulness (Mayo, 2021). Concussive symptoms typically resolve within 3 months. Post-concussive syndrome involves persistent concussive symptoms. (Mayo, 2021)

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 data regarding minor head trauma as defined by this CLiFF are lacking. Scheuring et al, 2009 provides an incidence of head trauma of 34,026 events/100,000 person-years, but this is felt to be a gross overestimation as it includes all head injuries, not exclusively those resulting in the aforementioned. Therefore, it 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 869 events/100,000 person-years. 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. This was not used to inform the incidence for this CLiFF.

TERRESTRIAL LITERATURE

Data on the terrestrial incidence of minor head trauma is reported as 212 events / 100,000 person-years for the 2010 year [Marin, 2014]. These authors conducted a population-based descriptive epidemiological study of TBI visits to EDs in the United States from 2006 through 2010, using the Nationwide Emergency Department Sample (NEDS) database, a nationally representative data source including 25 million to 50 million visits from more than 950 hospitals each year. US Census data was used to determine the number of person years for 2010. Because NEDS database represented a 20% stratified sampling of emergency departments, the authors applied prescribed weighting procedures to account for the unequal sampling probabilities, stratification, and clustering and to produce a national estimate of 212, with a 95% confidence interval of 195-230 events per 100,000 person-years.

OVERALL INCIDENCE SUMMARY

INCIDENCE

Mean: 0.001937
SD: 3.911E-6

INCIDENCE SUMMARY

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 Marin et al, 2014 Research Letter – Trends in Visits for Traumatic Brain Injury to Emergency Departments in the United States was used to inform the incidence for this condition. Using Concussion numbers for 2006 and 2010, we see there were 108,993 and 142,376 events with incidence rates of 174 and 212 kpy, respectively. This implies person-years of 62,639,655 and 67,158,491 respectively. 2006 IR: 1.74E-3 (95%CI: 1.73E-3, 1.75E-3) and 2010: 2.12E-3 (95%CI: 2.109E-3, 2.131E-3).The posterior distribution for the incidence rate given the terrestrial evidence, under an uninformative prior, is Gamma(shape=245292.1, rate=126635068) with mean 0.001937 and SD 3.911E-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
0.001937

SD
3.911E-06

Gamma
(Shape): 245292
(Rate): 1.26635E+08

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

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

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, based on increased risk of head injury during rough sea conditions. Marin et al, 2014 provides incidence of various head injuries (including concussion) between 2006-2010 from data extracted from the Nationwide Emergency Department Sample (NEDS) database. This study included all age groups. Scheuring et al, 2009 evaluated the incidence musculoskeletal in-flight injuries among astronauts from Mercury - Expedition 13 of the ISS Program. Head injuries ("minor trauma" to the head) were not categorized by type limiting the applicability to the best and worst-case 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

Head trauma resulting in a concussion that impacts mission objectives for less than 2 weeks (this includes concussive symptoms caused by non-surgical intracranial bleeds meeting the above criteria).

WORSE CASE SCENARIO DEFINITION

Head trauma resulting in post-concussive syndrome interfering with mission objectives or requiring medications for longer than 2 weeks.

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

Concussion Post-Concussive Syndrome Intracranial Bleed (Non-surgical)

BEST CASE/WORST CASE PROBABILITY COMMENTS

The prevalence of post-concussive syndrome (PCS) in a well-designed prospective trial that observed 90 mild TBI patients compared to non-TBI trauma controls was found to be 5.7% at three month follow up, as diagnosed by Impact Post-Concussion Symptom Inventory (Ponsford et al, 2011). In another prospective study, using the DSM-IV criteria, the rate of PCS was diagnosed in 19 of 161 patients (11.8%) at three-month follow up (Boake et al, 2005). Finally, in a prospective cohort of 107 mild TBI patients, 24 (22%) met criteria for PCS at 3-months as determined by the BIPQ questionnaire (Hou et al, 2012). These studies were pooled to reveal a rate of post-concussive syndrome after mild traumatic brain injury of 13%. It should be noted that the definition of "traumatic brain injury" varies in the literature and between the three aforementioned studies. Ponsford et al, 2011 used the following inclusion criteria: (1) recent (< 24 h) history of trauma or acceleration-deceleration movement applied to the head resulting in loss of consciousness (LOC) < 30 min, post-traumatic amnesia (PTA) < 24 h, and a Glasgow Coma Scale (GCS) score of 13–15 on presentation to the ED; (2) age 18 years or over; and (3) English-speaking. Participants were excluded if they: (1) were intubated or required general anesthesia following injury; (2) had a breath alcohol reading > 0.05 mg/L at the time of recruitment; (3) were under the influence of illicit substances at the time of injury; (4) had focal neurological signs, seizures, and/or intracerebral abnormalities on CT; (5) had a dominant upper limb injury that precluded them from using a computer mouse; (6) were under spinal precautions and not able to sit upright; (7) had a history of previous cognitive impairment, neurological illness, significant alcohol or drug abuse, or other psychiatric impairment currently affecting daily functioning; or (8) were unavailable for follow-up. (Ponsford et al, 2011) Hou et al, 2012 had similar criteria, but notably the allowable time for PTA amnesia differed: A traumatically induced physiological disruption of brain function, as manifested by at least one of the following: (1) any loss of consciousness; (2) any loss of memory for events immediately before or after the accident; (3) any alteration in mental state at the time of the accident (e.g., feeling dazed, disoriented or confused); and (4) lack of focal neurological deficit(s), but where the severity of the injury did not exceed the following: (1) loss of consciousness not more than 15 min; (2) an initial Glasgow Coma Scale (GCS) score of 13-15; and (3) post-traumatic amnesia not more than 60 min. (Hou et al, 2012) Boake et al, 2005 had the most liberal definition of TBI which included any GCS greater than 8. Inclusion criteria included: nonpenetrating TBI; lowest post resuscitation Glasgow Coma Scale (GCS) score >8 ; computed tomography (CT) scan of the brain performed within 24 hours of arrival; and if mild TBI, no surgery under general anesthesia during the admission. (Boake et al, 2005) The rate of PCS in the literature is highly variable, with some studies reporting rates as high as 58% using the Rivermead Post-Concussion Questionnaire (Theadom, 2016), or 64% when using ICD-10 codes (Boake et al, 2005). These studies were excluded however, as there is a very high rate of variability with ICD-10-derived estimates ranging from 6-64% (Polinder, 2018) and several studies suggesting the Rivermead Questionnaire may have very low specificity for concussion related symptoms (Dean, 2012) (Voormolen, 2019).

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

Citation	Source	LOC Value
Ponsford et al, 2011	Terrestrial	2
Hou et al, 2012	Terrestrial	2
Theadom, 2016	Terrestrial	0

Ponsford et al, 2011, Boake et al, 2005, and Hou et al, 2012 were all ranked as 2. These studies were well designed but are all in small terrestrial populations, and have an earliest follow-up assessment at 3 months (rather than 2 weeks as defined in this CLiFF) which may underestimate the worst-case scenario probability at 2 weeks. Theadom, 2016 utilized the Rivermead Post-Concussion Questionnaire, which was shown in other studies to have a high rate of false-positives for post concussion syndrome (45% of a healthy cohort) (Voormolen, 2019) and poor specificity to symptoms from head trauma (Dean, 2012).

TABLE 4. CLIFF TREATMENT & OUTCOME TABLE BY CLINICAL PHASE

Case Scenario	Composite Incidence	Condition Probability %	CP1: Diagnosis		CP2: Treatment			CP3: Condition End State				
			TI%	Duration	TI%	Duration		TI%	RTDC		LOCL	
			Preset	Preset	Preset	Min	Max	Preset	Min%	Max%	Min%	Max%
Treated Best Case (TBC)	Mean: 0.001937 SD: 3.911E-6	87 - 87	100	0.783	32.979	24	168	0	7.4	10.3	0	0.6
Treated Worst Case (TWC)		13 - 13	100	0.783	55.6737	336	744	0	10.3	17.8	0	0.6
Untreated Best Case (UTBC)	N/A	N/A	N/A	0.783	41.9081	24	336	0	7.4	10.3	0	0.6
Untreated Worst Case (UTWC)	N/A	N/A	N/A	0.783	64.6027	336	8760	0	10.3	17.8	0	0.6

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 RTDC surrogate for this condition is hospitalization. The literature doesn't elucidate a difference in need for hospitalization based on prior treatment vs. no prior treatment. Thus, the RTDC probabilities for the treated and untreated best-case scenarios are the same. Likewise, the RTDC probabilities for the treated and untreated worst-case scenarios are the same. The LOCL probability is the same for all scenarios because neither treatment, nor development of post-concussive syndrome (the worst-case scenario), are expected to affect the probability of LOCL for this condition. See detailed comments for each scenario below.

TREATED BEST CASE (TBC) SCENARIO COMMENTS

Minor head trauma with medical evaluation typically resolves in 7 days based on a retrospective study of NCAA collegiate football players (McCrea et al, 2003) but symptoms can resolve as quickly as 24 hours (McCrea et al, 2003). Therefore, the duration for this scenario was assigned 24-336 hours (1-7 days). RTDC (surrogate measure of hospitalization) is required in a minority of cases. Babcock et al, 2013 report that 7.4% of mild traumatic brain injury cases (as defined by the following inclusion criteria: Blow to the head or acceleration/deceleration movement of the head resulting in 1 or more of the following: LOC < 30 min, amnesia < 24 hour or any alteration in mental state, and GSC of 13 or more 30 minutes or more after injury) required hospitalization. Notably, this study was exclusive to children and adolescents, which limits it's generalizability to the astronaut corps. Rhame et al, 2021 reported a hospitalization rate of 10.3% for mild TBI patients in a retrospective chart review from Jan 2016-Dec 2017 for patients admitted through the University of Cincinnati Emergency Department under their mild TBI observation protocol. Inclusion criteria included: mild TBI with GCS of 14 or 15 within 24 hours of injury. Non-surgical intracranial bleeds were included unless they met exclusion criteria. Exclusion criteria were: requirement for neurosurgery, focal neurologic deficits, coagulopathy, admission required for other injuries, abnormal vital signs, other active comorbid conditions, and non-impact seizures. (Rhame et al, 2021) Thus, the RTDC range was assigned 7.4-10.3% for this scenario. Mortality following minor head trauma is very rare. In a retrospective study of 2484 patients with mild head injury presenting to an Emergency Department in Madrid, Spain between December 1991 and April 1993, there was an overall mortality rate of 0.6% (15 deaths). Inclusion criteria included: age > 15 years, GCS of 13-15, experienced a blow to the head independently of whether there were or were not signs of brain dysfunction, such as a transient loss of consciousness (LOC), posttraumatic amnesia (PTA) or associated injuries. Patients were excluded if they had isolated facial trauma, those deteriorating to a GCS of less than 13 within 4h of injury and those showing a lucid interval who were referred from local hospitals after they developed neurological deterioration. (Gomez et al, 1996). Therefore, the LOCL probability was assigned 0-0.6%. Note, this is the same as the probability for all other scenarios in this CLiFF neither treatment, nor development of post-concussive syndrome are expected to affect the probability of LOCL for this condition.

TREATED WORST CASE SCENARIO (TWC) COMMENTS

Persistent symptoms after minor head trauma are defined as starting at 14-days duration, and measurable deficits in cognition and memory usually resolve by one month (Barbosa et al, 2012). Thus the duration was assigned 336-744 hours (14-31 days). Rhame et al, 2021 reported a hospitalization rate of 10.3% for mild TBI patients in a retrospective chart review from Jan 2016-Dec 2017 for patients admitted through the University of Cincinnati Emergency Department under their mild TBI observation protocol. Inclusion criteria included: mild TBI with GCS of 14 or 15 within 24 hours of injury. Non-surgical intracranial bleeds were included unless they met exclusion criteria. Exclusion criteria were: requirement for neurosurgery, focal neurologic deficits, coagulopathy, admission required for other injuries, abnormal vital signs, other active comorbid conditions, and non-impact seizures. (Rhame et al, 2021) Babcock et al, 2013 report that 17.8% of mild traumatic brain injury cases (as defined by the following inclusion criteria: Blow to the head or acceleration/deceleration movement of the head resulting in 1 or more of the following: LOC < 30 min, amnesia < 24 hour or any alteration in mental state, and GSC of 13 or more 30 minutes or more after injury) that went on to develop post-concussive syndrome required hospitalization in a retrospective review. Notably, this study was exclusive to children and adolescents, which limits it's generalizability to the astronaut corps. Thus the RTDC probability for this scenario was assigned 10.3-17.8%. Mortality following minor head trauma is very rare. In a retrospective study of 2484 patients with mild head injury presenting to an Emergency Department in Madrid, Spain between December 1991 and April 1993, there was an overall mortality rate of 0.6% (15 deaths). Inclusion criteria included: age > 15 years, GCS of 13-15, experienced a blow to the head independently of whether there were or were not signs of brain dysfunction, such as a transient loss of consciousness (LOC), posttraumatic amnesia (PTA) or associated injuries. Patients were excluded if they had isolated facial trauma, those deteriorating to a GCS of less than 13 within 4h of injury and those showing a lucid interval who were referred from local hospitals after they developed neurological deterioration. (Gomez et al, 1996). Therefore, the LOCL probability was assigned 0-0.6%. Note, this is the same as the probability for all other scenarios in this CLiFF neither treatment, nor development of post-concussive syndrome are expected to affect the probability of LOCL for this condition.

UNTREATED BEST CASE (UTBC) SCENARIO COMMENTS

Minor head trauma symptoms can resolve as quickly as 24 hours (McCrea et al, 2003) or last longer than 14 days (McCrory et al, 2017). The Consensus Statement on Concussion in Sport (5th International Conference in Berlin) reports that the expected timeframe for "normal clinical recovery" in an adult is 10-14 days and anything longer than this is considered, "Persistent symptoms" which require a referral. Duration greater than 14 days meets criteria for the worst-case condition, and therefore is not discussed here. Therefore, the duration for this scenario was assigned 24-336 hours (1-14 days). RTDC and LOCL were assumed to be the same in this scenario as in the best-case treated scenario. (The effect of treatment is reflected, rather, in the task impairment). Thus what follows is identical to the best-case treated scenario. RTDC (surrogate measure of hospitalization) is required in a minority of cases. Babcock et al, 2013 report that 7.4% of mild traumatic brain injury cases (as defined by the following inclusion criteria: Blow to the head or acceleration/deceleration movement of the head resulting in 1 or more of the following: LOC < 30 min, amnesia < 24 hour or any alteration in mental state, and GSC of 13 or more 30 minutes or more after injury) required hospitalization. Notably, this study was exclusive to children and adolescents, which limits it's generalizability to the astronaut corps. Rhame et al, 2021 reported a hospitalization rate of 10.3% for mild TBI patients in a retrospective chart review from Jan 2016-Dec 2017 for patients admitted through the University of Cincinnati Emergency Department under their mild TBI observation protocol. Inclusion criteria included: mild TBI with GCS of 14 or 15 within 24 hours of injury. Non-surgical intracranial bleeds were included unless they met exclusion criteria. Exclusion criteria were: requirement for neurosurgery, focal neurologic deficits, coagulopathy, admission required for other injuries, abnormal vital signs, other active comorbid conditions, and non-impact seizures. (Rhame et al, 2021) Thus, the RTDC range was assigned 7.4-10.3% for this scenario. Mortality following minor head trauma is very rare. In a retrospective study of 2484 patients with mild head injury presenting to an Emergency Department in Madrid, Spain between December 1991 and April 1993, there was an overall mortality rate of 0.6% (15 deaths). Inclusion criteria included: age > 15 years, GCS of 13-15, experienced a blow to the head independently of whether there were or were not signs of brain dysfunction, such as a transient loss of consciousness (LOC), posttraumatic amnesia (PTA) or associated injuries. Patients were excluded if they had isolated facial trauma, those deteriorating to a GCS of less than 13 within 4h of injury and those showing a lucid interval who were referred from local hospitals after they developed neurological deterioration. (Gomez et al, 1996). Therefore, the LOCL probability was assigned 0-0.6%. Note, this is the same as the probability for all other scenarios in this CLiFF neither treatment, nor development of post-concussive syndrome are expected to affect the probability of LOCL for this condition.

UNTREATED WORST CASE (UTWC) SCENARIO COMMENTS

8Persistent symptoms after minor head trauma are defined as starting at 14-days duration. Although measurable deficits in cognition and memory usually resolve by one month, they can last longer, with most patients exhibiting clinical recovering within 3-12 months (Barbosa et al, 2012). It is assumed that without treatment, the clinical recovery would take longer. Thus the duration was assigned 336-8750 hours (14-365 days) for this scenario. The literature doesn't elucidate a difference in need for hospitalization based on prior treatment vs. no prior treatment. Thus, the RTDC for this scenario will be approximated using the same RTDC as the treated worst-case scenario. Rhame et al, 2021 reported a hospitalization rate of 10.3% for mild TBI patients in a retrospective chart review from Jan 2016-Dec 2017 for patients admitted through the University of Cincinnati Emergency Department under their mild TBI observation protocol. Inclusion criteria included: mild TBI with GCS of 14 or 15 within 24 hours of injury. Non-surgical intracranial bleeds were included unless they met exclusion criteria. Exclusion criteria were: requirement for neurosurgery, focal neurologic deficits, coagulopathy, admission required for other injuries, abnormal vital signs, other active comorbid conditions, and non-impact seizures. (Rhame et al, 2021) Babcock et al, 2013 report that 17.8% of mild traumatic brain injury cases (as defined by the following inclusion criteria: Blow to the head or acceleration/deceleration movement of the head resulting in 1 or more of the following: LOC < 30 min, amnesia < 24 hour or any alteration in mental state, and GSC of 13 or more 30 minutes or more after injury) that went on to develop post-concussive syndrome required hospitalization in a retrospective review. Notably, this study was exclusive to children and adolescents, which limits it's generalizability to the astronaut corps. Thus the RTDC probability for this scenario was assigned 10.3-17.8%. Mortality following minor head trauma is very rare. In a retrospective study of 2484 patients with mild head injury presenting to an Emergency Department in Madrid, Spain between December 1991 and April 1993, there was an overall mortality rate of 0.6% (15 deaths). Inclusion criteria included: age > 15 years, GCS of 13-15, experienced a blow to the head independently of whether there were or were not signs of brain dysfunction, such as a transient loss of consciousness (LOC), posttraumatic amnesia (PTA) or associated injuries. Patients were excluded if they had isolated facial trauma, those deteriorating to a GCS of less than 13 within 4h of injury and those showing a lucid interval who were referred from local hospitals after they developed neurological deterioration. (Gomez et al, 1996). Therefore, the LOCL probability was assigned 0-0.6%. Note, this is the same as the probability for all other scenarios in this CLiFF neither treatment, nor development of post-concussive syndrome are expected to affect the probability of LOCL for this condition.

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

Citation	Source	LOC Value
McCrea et al, 2003	Terrestrial	3
McCrory et al, 2017	Terrestrial	
Barbosa et al, 2012	Terrestrial	

Terrestrial data regarding concussions in collegiate athletes (McCrea et al, 2003) and an international consensus statemetn on concussions in sports (McCrory et al, 2017) were used to inform the best-case scenario durations. These sources provided a range for the duration of concussive symptoms. The lower end of the range was assigned to the best-case treated scenario and the best-case untreated scenario duration was extended to include the upper end of the range cited in this literature. Barbosa et al, 2012, a practice management guideline for mild traumatic brain injuries developed from a review of 112 articles spanning 1998-2011, was used to inform the duration of the worst-case scenarios. Again, a range was presented and the lower end of the range was assigned to the treated worst-case scenario and the untreated worst-case scenario was extended based on these data.

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Rhame et al, 2021	Terrestrial	2
Babcock et al, 2013	Terrestrial	

Two studies informed the RTDC probabilities for this condition. The literature doesn't elucidate a difference in need for hospitalization based on prior treatment vs. no prior treatment. Thus, the RTDC probabilities for the best-case treated and untreated scenarios are the same and the worst-case treated and untreated scenarios are the same. Rhame et al, 2021 reported a hospitalization rate of 10.3% for mild TBI patients in a retrospective chart review from Jan 2016-Dec 2017 for patients admitted through the University of Cincinnati Emergency Department under their mild TBI observation protocol. Inclusion criteria included: mild TBI with GCS of 14 or 15 within 24 hours of injury. Non-surgical intracranial bleeds were included unless they met exclusion criteria. Exclusion criteria were: requirement for neurosurgery, focal neurologic deficits, coagulopathy, admission required for other injuries, abnormal vital signs, other active comorbid conditions, and non-impact seizures. (Rhame et al, 2021) This case definition is consistent with the best-case scenario definition of this CLiFF. Babcock et al, 2013 was a prospective cohort study involving patients with TBI who participated in a TBI registry funded by the National institues of Health. The cohort was recruited at pediatric and adult Emergency Departements of the University of Rochester Medical Center from January 7, 2003 - September 6, 2004. However, the data presented only pertain to children and adolescents, minimizing the generalizability of this study to the astronaut corps. This study stratified hospitalizations according to our best and worst-case scenarios, reporting a different proportion of hospitalizations for mild traumatic TBI vs. post-concussive syndrome. Mild traumatic brain injury cases were defined by the following inclusion criteria: Blow to the head or acceleration/deceleration movement of the head resulting in 1 or more of the following: LOC < 30 min, amnesia < 24 hour or any alteration in mental state, and GSC of 13 or more 30 minutes or more after injury. Notably, studies that present information based on patients presenting to the emergency department may be skewed towards more severe manifestations of minor head trauma (vs. those who present as outpatients or don't present at all).

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Gomez et al, 1996	Terrestrial	2

Data regarding mortality secondary to minor head trauma were lacking. One retrospective study of 2484 patients with mild head injury presenting to an Emergency Department in Madrid, Spain between December 1991 and April 1993, was found to inform the LOCL probability. Inclusion criteria included: age > 15 years, GCS of 13-15, experienced a blow to the head independently of whether there were or were not signs of brain dysfunction, such as a transient loss of consciousness (LOC), posttraumatic amnesia (PTA) or associated injuries. Patients were excluded if they had isolated facial trauma, those deteriorating to a GCS of less than 13 within 4h of injury and those showing a lucid interval who were referred from local hospitals after they developed neurological deterioration. (Gomez et al, 1996). This provided the maximum probability for all scenarios because neither treatment, nor development of post-concussive syndrome are expected to affect the probability of LOCL for this condition. Notably, studies that present information based on patients presenting to the emergency department may be skewed towards more severe manifestations of minor head trauma (vs. those who present as outpatients or don't present at all), so this estimate would be the maximum probability of LOCL. The generalizability of this study in Spain may be somewhat limited.

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

Overview
Minor head trauma under this definition refers to an injury severe enough to cause a concussion without risk of permanent anatomical injury. The BC is a short duration concussion less than 2 weeks while the worst case lasts longer. Deficits in this case largely cognitive, irritability, and mental endurance and are expected to improve with time. There are no specific disease modifying treatments for concussions or treatments that will shorten duration but symptom control can help limit task impairments.

CNES: None

Diagnostic Scope and Resourcing
In both the best-case and worst-case scenario, diagnostics would include a history, primary assessment, and physical exam inclusive of vital signs, and a thorough neurological exam

Clinical Phase 1 Duration and Rationale
This version of IMPACT presumes physician level knowledge, skill, and ability will be present on the mission. The CRT working group SME consensus duration is as follows:

CP1 BC (Treated or Untreated): 0.783 hours for history, physical exam, and a thorough
neurological exam
CP1 WC (Treated or Untreated): 0.783 hours. The initial evaluation is the same for BC and
WC since the difference in definitions is the duration.

The highest scope of practice required for performance of a full neurological exam and interpretation of the physical exam which was rated a 4. Intern level training is also necessary for management decisions and determining fitness for duty.

Treatment Scope and Resourcing
Treatment is symptom focused since no disease or duration modifying treatments exist at present that are supported by robust clinical evidence. Symptomatic care includes antiemetics, NSAIDs, medications to facilitate sleep, and ant vertiginous medications.

Communications and Support Needs
While a best-case scenario will require ground communication with video and audio to facilitate the recovery phase by assisting with schedule planning, neurological reassessments, and fitness for duty assessment.

IMM CLIFF RECONCILATION COMMENTS

IMM had a condition called, “Head Injury.” Head injury was defined in this CLiFF as, “An injury that is clinically evident on physical examination and is recognized by the presence of ecchymoses, lacerations, deformities, or cerebrospinal fluid leakage. The CLiFF specifically states that traumatic brain injury is a separate entity and defines TBI as, “An injury to the brain itself and is not always clinically evident; if unrecognized, it may result in an adverse outcome.” This CLiFF is unique from the prior IMM CLiFF as it includes concussion, post-concussive syndrome, and non-operative intracranial bleeding, all of which are outside the scope of the definition of “head injury” used in the prior CLiFF. Therefore, this CLiFF has unique incidence, RTDC, LOCL, and TI values as compared to the IMM CLiFF.

LIMITATIONS SUMMARY

• There are few data in the literature regarding non-operative intracranial bleed as it is described in the best-case scenario. Thus, the data informing this CLiFF focus primarily on mild TBI (some of which includes intracranial bleed) and concussion for the best-case scenario. The worst-case scenario is informed by literature regarding post-concussive syndrome. • The best-case treated and untreated RTDC probabilities are the same, as are the worst-case treated and untreated RTDC probabilities due to a lack of data representing the need for hospitalization after head injury dependent on initial treatment vs. lack of treatment. • Babcock et al, 2013 informed the worst-case scenario RTDC probabilities. This is a pediatric study, limiting its generalizability to the astronaut corps. • The LOCL probabilities for all scenarios are the same based on the assumption that the worst-case scenario (post-concussive syndrome) does not increase risk of mortality and the assumption that lack of treatment does not increase mortality (rather, lack of treatment extends the duration, which is reflected by increased durations for the untreated scenarios). • Gomez et al, 1996 informed all LOCL probabilities. This study was conducted in Spain, which may limit its generalizability to the astronaut corps.

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		89			145					
Untreated Best Case (UTBC)	223	664	113	89			145					
Treated Worst Case (TWC)		664		89	854		145					
Untreated Worst Case (UTWC)	223	664	113	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	1241	3763	0.32979	32.979
Untreated Best Case (UTBC)	132							211	1577	3763	0.419081	41.9081
Treated Worst Case (TWC)	132							211	2095	3763	0.556737	55.6737
Untreated Worst Case (UTWC)	132							211	2431	3763	0.646027	64.6027

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)												
	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)									0	3763	0	0
Treated Worst Case (TWC)									0	3763	0	0
Untreated Worst Case (UTWC)									0	3763	0	0

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