Clinical Finding Form (CliFF)

Branch	Baseline

ICL56_Fracture - Wrist

The wrist is an anatomic linkage bridging the hand to the forearm. The hand relative to the forearm can flex, extend, pronate, supinate, and deviate radially and ulnarly. Malfunction of the wrist occurs when the structural alignment of the bones has changed, i.e. distal radius malunion and acute fracture of carpal bones (Steinberg, 2002). For the purposes of this CLiFF, a “Wrist Fracture” includes a fracture of the distal radius or ulna, or fracture of any of the carpal bones (scaphoid, lunate, triquetrum, trapezoid, trapezium, capitate, hamate, and pisiform). Distal radius fractures are the most common type of wrist fracture, and one of the most common fractures in adults (Baawa-Ameyaw et al, 2020). The most injured carpal bone is the scaphoid where 70% of carpal fractures occur (Steinberg, 2002). Potential mechanisms of injury for wrist fracture in space include impact to structure from an outstretched hand during intra-vehicular translation, hyperflexion or a direct blow to the wrist such as while stowing equipment, or excessive forces exerted such as doing a repair during an EVA (Scheuring, 2009). Acute fractures results in pain, tenderness, swelling and potential deformity. Crewmembers may be faced with substantial morbidity if fracture healing is delayed or results in clinically significant deformity. Worst-case fractures pose additional risks of complex regional pain syndrome, infection, and neurovascular compromise. All best-case fractures are terrestrially recommended to be treated with splinting, followed by casting. All worst-case fractures terrestrially are treated with surgical intervention. Spaceflight-induced bone atrophy is due to the mechanical unloading of the skeletal system and is targeted to specific regions of the skeleton. These site-specific losses occur at normally weight-bearing skeletal areas (on Earth) suggesting that the regions that experience the larger deficits in mechanical loading undergo the greater adaptation. In low Earth orbit operations, the degree of BMD loss in the wrist has not been substantial. Radiation increases bone resorption and outside low earth orbit; BMD may be greater. In microgravity demineralization may be potentiated by the poor absorption of vitamin D. A deficiency in vitamin D could lead to malabsorption of calcium in the intestine and poor re-absorption by the proximal tubules of the kidney. The failure to conserve calcium because of vitamin D deficiency will limit the availability of calcium to support the anabolic effects of exercise and physical activity on bone and muscles. It is noted that the hands and wrists are the primary means of ambulation on orbit. The possible effect of mineralization or de-mineralization of wrist bones is not known (Sibonga, 2008).

INCIDENCE DATA INCLUDED IN THE MODEL

The model imports the following incidence information from the MEDPRAT Evidence Library Database: incidence data category, space adaption status, EVA status, incidence data type, incidence and occurrence distribution data and incidence data characteristics. Data category defines the type of data available for incidence calculations (i.e. raw data vs. adjusted data). Space adaptation identifies medical events that where onset occurs in the first 5-7 days of flight and does not reoccur. EVA-related incidence values identify medical events that occur only during an EVA. Incidence values types vary by data category and define the number of medical events per person-year (rates) or medical events per person at-risk (proportion) for each medical condition. Incidence values can be modified by crew characteristics such as gender sex and certain crew medical history characteristics. Modifying characteristics are noted below and incidence values are listed individually for each characteristic. Distributions are assigned to medical events incidence values and occurrences in the model. For each crewmember in a given trial, the incidence and number of occurrences of each medical condition are randomly selected from these probability distributions. Detailed descriptions of the distributions are included in the MEDPRAT Technical Description Document.

INCIDENCE DATA

SPACEFLIGHT LITERATURE

There have been no reported wrist fractures during spaceflight. Lewandowski et al (2008) used predictive modeling to derive a probability of wrist fracture sustained from a fall during an EVA on a Mars mission to be: Male: 0.0128; Female: 0.0240. Nelson et al. (2009) published findings from the Bone Fracture Risk Model (used in IMM) to estimate the probability of wrist fracture on missions to the moon of 14 days or less to be < 1%, short-duration Mars missions (344d) to be 1-2.5%, and long-duration Mars Missions (918d) to be < 1.5%.

ANALOG LITERATURE

A retrospective 8-year study (1998-2006) by Wolf et al (2009) found an incidence of 1.21 scaphoid fractures/1000 person-years among active duty military members. Nice and Hilton (1990) report a combined incidence of carpal fractures onboard 20 US naval ships of 4.08/1000 person-years.

TERRESTRIAL LITERATURE

Terrestrial data was found from studies which utilized national databases to collect incidence data. Karl et al (2009) performed a retrospective study of all upper extremity fractures, but provided incidence data for distal radius/ulnar fractures of 16.2/100,000 person-years, scaphoid fractures of 1.09/100,000 person-years, and all other carpal fractures of 2.38/100,000 person-years. Duckworth et al (2012) reported an incidence limited to scaphoid fractures of 29/100,000 person-years from a 1-year prospective study of adults 13yo and older presenting to the Edinburgh Orthopaedic Trauma Unit, Royal Infirmary of Edinburgh, Edinburgh, United Kingdom.

OVERALL INCIDENCE SUMMARY

INCIDENCE

Males: mean: 0.0052, SD: 0.0052 Females: mean:0.004, SD: 0.004

INCIDENCE SUMMARY

NASA's bone fracture risk model (BFxRM) was chosen to be best for predicting wrist bone fracture risk (incidence). The incidence is being linked to surface operations during EVA for Lunar missions (the risk of wrist fracture in microgravity is assumed to be 0). ExMC is in pursuit of updated predictions from the modeling team but in the meantime, a Beta distribution is being used to approximate the prediction distribution cited in Lewendowski et al 2008, " Forecasting proximal femur and wrist fracture caused by a fall to the side during space exploration missions to the Moon and Mars." The means and variance of those probability predictions are specified in Table 2 of the manuscript. A Beta distribution will be used to approximate the simulated distributions until new predictions can be incorporated. For males on the lunar surface, the distribution is Beta(shape1=0.00207, shape2=1.615), mean: 0.00128, SD: 0.0221. For females on the lunar surface, the distribution is Beta(shape1=0.2128, shape2=25.39), mean:0.00831, SD: 0.0176

TABLE 1. INCIDENCE MODEL

Incidence Details

Incidence Type
EVA

Segment
EVA Surface

Env. Exposure
NA

Sex
Male

Crowns
Any

Contacts
Any

Pregnancy
Any

Incidence Distribution

Occurrence Dist
Binomial

Incidence Dist.
Beta

Mean
0.0052

SD
0.0052

Beta
(Alpha): 0.00207
(Beta): 1.615

Incidence Details

Incidence Type
EVA

Segment
EVA Surface

Env. Exposure
NA

Sex
Female

Crowns
Any

Contacts
Any

Pregnancy
Any

Incidence Distribution

Occurrence Dist

Binomial

Incidence Dist.

Beta

Mean

0.004

SD

0.004

Beta

(Alpha): 0.2128

(Beta): 25.39

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Duckworth et al, 2012.	Terrestrial	0
Karl et al, 2009.	Terrestrial	2
Wolf et al, 2009.	Analog	0
Nice et al, 1990.	Analog	1
Lewandowski et al, 2008.	Spaceflight	3
Nelson et al, 2009.	Spaceflight	3

Duckworth et al, 2012 presents terrestrial scaphoid fractures. Wolf et al, 2009 presents scaphoid fractures, but in military personnel. While scaphoid fractures are the most common carpal bone fracture, they are less common than distal radius fractures (the most common type of wrist fracture). Using scaphoid fractures alone as an estimate for incidence would not provide an accurate picture of wrist fractures (inclusive of distal radius/ulna and carpal bones). Nice et al, 1990 presents incidence data for carpal fractures (expanding upon lone scaphoid fractures) in Naval submarines. However, again this disregards the most common wrist fracture, the distal radius. While military analogs can be well matched to the astronaut population in age and elite health status, fractures in military members are suspected to be less representative of fractures seen in spaceflight (particularly those sustained in combat). Of the two military analog papers (Wolf et al, 2009 and Nice et al 1990), Nice et al is likely more representative given the isolated, confined environment of a submarine. Of the terrestrial and analog data sources, the most inclusive of all types of wrist fracture is Karl et al, 2009. It provides incidence for distal radius/ulnar fractures, scaphoid fractures, and "other carpal bones." Despite this, terrestrial data (whether analog or not) is suspected to over-estimate risk of in-flight fracture due to 1G on earth as compared to microgravity inflight, vs. 1/6G Lunar and 1/3G Martian surfaces. Lewandowski et al, 2008 and Nelson et al, 2009 are papers presenting NASA's Bone Fracture Risk Model (BFxRM) designed for use with IMM to predict fracture probability in different spaceflight environments. The Lewandowski et al 2008 paper specifically presents wrist fracture probabilities for Martian and Lunar surfaces for the astronaut population, thus information presented in this paper is used for incidence for Wrist Fracture as it is the most representative provided in the data set.

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

All crewmembers undergo DXA scanning pre- and post-flight. Pre-flight at L-21/18 month; and L-180/30 day (As close to launch as possible). Post-flight at R+5/30, then as clinically indicated to assess BMD recovery.

BEST CASE SCENARIO DEFINITION

A closed, non-comminuted, non-segmented, non-displaced, or minimally displaced fracture resulting in no neurovascular compromise to the affected limb.

WORSE CASE SCENARIO DEFINITION

A fracture that is: open, comminuted, segmented, moderately to severely displaced, intra-articular, or results in neurovascular compromise to the affected limb, likely requiring surgical intervention.

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

Fracture of the carpal bones, distal radius, distal ulna.

BEST CASE/WORST CASE PROBABILITY COMMENTS

The WC probability was assigned 16-39% based on a relative weighting of distal radius fractures (which account for approx. 20 of all fracture types) and scaphoid fractures (which account for approx. 1.8% of all fracture types). The 54% WC probability seen during the UK COVID lockdown quoted in Baawa-Ameyaw et al, 2020 was not considered in this calculation as it was felt to be an outlier. Therefore 11-36% was weighted for distal radius fractures and 68.9% was weighted for scaphoid fractures

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

Citation	Source	LOC Value
Duckworth et al, 2012.	Terrestrial	2
Baawa-Ameyaw et al, 2020.	Terrestrial	3
Earnshaw et al, 2002.	Terrestrial	3
Lindau et al, 1999.	Terrestrial	2
DeWeber, 2022	Terrestrial	N/A
Meena et al, 2014	Terrestrial	N/A

Duckworth et al, 2012 gave a WC probability of 68.9% for scaphoid fractures. Baawa-Ameyaw et al, 2020 looked at distal radius fractures that met radiographic criteria for surgery in patients in the UK during the first COVID-19 lockdown (during which time the UK made the decision not to operate on any distal radius fractures). Unfortunately, no follow-up data was available for patients who ultimately required surgery after the lockdown (i.e. failed non-surgical treatment). The article presented a 54% WC probability during the first lockdown, but also contrasted this incidence with a WC probability of 36% pre-COVID. (Both values were used in this average). Earnshaw et al, 2002 is a historic reference from Queen's Medical Center in the UK that IMM used. At 5 weeks post- distal radius fracture there was a WC probability of 25%. Lindau et al 1999 is another historic article from the IMM effort, looking at a series of 341 athletes from Sweden) that presented a WC probability of 11% for distal radius fractures.

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: mean: 0.0052, SD: 0.0052 Females: mean:0.004, SD: 0.004	61 - 84	100	1.23	5.46107	672	1512	0	3	6.7	0	0
Treated Worst Case (TWC)		16 - 39	100	2.52	19.2931	2160	8760	10.0186	100	100	0	0
Untreated Best Case (UTBC)	N/A	N/A	N/A	1.23	35.3973	672	1512	10.0186	3	6.7	0	0
Untreated Worst Case (UTWC)	N/A	N/A	N/A	2.52	50.1063	2160	8760	27.7172	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 RTDC surrogate used for the CLiFF was open reduction and internal fixation (ORIF) or permanent disability. This data collection effort for this CliFF was unable to identify data for untreated scenarios (see details below).

TREATED BEST CASE (TBC) SCENARIO COMMENTS

Duration and RTDC for the treated, best-case scenario, were based on distal radius and scaphoid fractures only and did not include the other bones of the wrist. The duration articles (Beleckas and Calfee 2017), (Winston and Welland 2017), are specific to athlete populations. The RTDC surrogate chosen was open reduction and internal fixation (ORIF) or permanent disability. All fracture types in the BC definition (closed, non- or minimally-displaced, non-comminuted, non-segmented) are recommended to be managed non-surgically. Among those managed non-surgically, the complication considered that could lead to permanent disability was complex regional pain syndrome (CRPS). Roh et al (2014) provided incidence data on Complex Regional Pain Syndrome based on a study including 498 patients (roughly evenly split between M/F) ages 56.9 +/- 18.7 presenting to a tertiary care center (Gil Medical Center, Gachon University School of Medicine, Incheon, Korea) with distal radius fractures. Non-comminuted distal radius fractures had an incidence of CPRS of 17/286, (whereas comminuted distal radius fractures, more in line with WC scenario, had incidence of CPRS of 25/191). Extra-articular distal radius fractures had an incidence of CPRS of 16/238 (intra-articular 26/239). Aro and Koivunen (1991) examined long-term functional outcomes of patients with varying degrees of radial shortening following distal radius fractures. 47 patients age 54 +/- 18 with no radiographic deformity were included in the study. 2/47 patients had "unsatisfactory" long-term outcomes. Dias and Kantharuban (2017) described complication rates in scaphoid fractures, citing incidence of CRPS at 3% with non-operative management. LOCL was deemed 0% probability, which is appropriate for a BC wrist fracture (Duckworth et al, 2012), (Karl et al, 2009).

TREATED WORST CASE SCENARIO (TWC) COMMENTS

The same search was used for treated best case and treated worst case duration in Dynamed (Distal Radius and Scaphoid Fractures). RTDC for treated worst case searches was limited to Distal Radius and Scaphoid Fractures and the RTDC surrogate chosen was “ORIF / Permanent disability incidence.” This disregards the possibility of Compartment Syndrome as an RTDC surrogate. However, all worst-case wrist fractures should receive surgical intervention based on clinical practice guidelines (Lichtman et al, 2010) so RTDC was assigned a 100% probability (which would not have changed if compartment syndrome was included). The LOCL probability search was limited to distal radius and scaphoid fractures. LOCL probability was determined to be 0% (Duckworth et al, 2012) (Karl et al, 2015). However, this does not include the complication of compartment syndrome, which may present a probability of death > 0%. Thus, LOCL may underestimate the true probability of LOCL in the model.

UNTREATED BEST CASE (UTBC) SCENARIO COMMENTS

The literature search was unable to identify any duration or RTDC probability data for untreated wrist fractures. Thus, the duration and RTDC probability for untreated is using treated best-case data, i.e. the duration and RTDC for treated and untreated BC scenario will be identical. This is a limitation of the data. The duration (Beleckas and Calfee, 2017), (Winston and Weiland 2017) and RTDC probability (Roh et al, 2014), (Aro and Koivunen, 1991), (Dias and Kantharuban, 2017) are based on distal radius and scaphoid fractures. It was assumed that the LOCL probability would remain 0% for the BC untreated scenario based on data from the BC treated scenario (Duckworth et al, 2012), (Karl et al, 2009).

UNTREATED WORST CASE (UTWC) SCENARIO COMMENTS

The literature search was unable to identify any duration, RTDC probability, or LOCL probability data for untreated worst-case wrist fractures. The duration for untreated WC is using treated WC data, i.e. the duration probability for treated and untreated WC scenario will be identical (MacDermid et al, 2001). This is a limitation of the data. One additional source was found comparing radiographic outcomes of delayed vs. immediate surgical intervention of distal radius fractures (Lee at al, 2020). Lee et al presented a small cohort study of distal radius fractures with 25 cases (delayed surgery, average 24.8 days post-fracture) and 50 controls (immediate surgery average 5.6 days post-fracture). Subjects spanned ages 18-87. Notably, open fractures and concomitant fractures of carpal bones were excluded. The authors found no significant difference in radiographic outcomes of healing with delayed vs. immediate surgery. However, they did note that delayed surgery, based on operative notes review, “revealed that an extended surgical approach and invasive dissection techniques were utilized more frequently in the delayed group.” This study was felt to support a WC untreated duration that is equivalent to the WC treated duration. This assumes the ability to RTDC for definitive surgical care within an average of 24.8 days post-fracture and is limited to a closed, distal radius fracture. The lack of available data for untreated worst-case is a limitation of this CliFF. The assumption was made that, given the RTDC probability for the treated WC is 100% (i.e. for all fracture types under the WC definition, the recommended treatment is surgery), the RTDC for the untreated WC scenario would also have to be 100% (Lichtman et al, 2010). The LOCL probability from the worst-case treated scenario was used for the worst-case untreated scenario since no additional data was available (Duckworth et al, 2012), (Karl et al, 2015). Whereas this is likely an appropriate assumption to make for LOCL probability for the BC scenario, there is a higher risk of underestimating LOCL probability for the WC untreated scenario, particularly in reference to infection from untreated open fracture and compartment syndrome (neither infection or compartment syndrome were considered specifically in searches for LOCL, which is a limitation of the data supporting this CLiFF). Thus, worst-case untreated LOCL probability is suspected to be an underestimate, a limitation of this CLiFF.

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

Citation	Source	LOC Value
Beleckas et al, 2017	Terrestrial	3
Winston et al, 2017	Terrestrial	
MacDermid et al, 2001	Terrestrial	
Lee et al, 2020	Terrestrial	

Unique data for untreated scenarios was unable to be obtained, so treated and untreated durations are identical. Becleckas et al, 2017 is a review article for distal radius fractures in athletes age 18-60. Winston et al, 2017 is a review of scaphoid fractures in athletes. Macdermid et al 2001 is a prospective study of distal radius fractures in adults. Lee et al, 2020 is a small cohort study of delayed surgical intervention (24.8 days post-fracture) vs. immediate surgery (5.6 days post-fracture) for distal radius fracture. Notably, it excludes open or concomitant carpal bone fractures, but was used to help inform worst-case, untreated duration.

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Roh et al, 2014	Terrestrial	3
Aro and Koivunen, 1991	Terrestrial	
Dias and Kantharuban, 2017	Terrestrial	
Lichtman et al, 2010	Terrestrial	

Unique data for untreated scenarios was unable to be obtained, so treated and untreated RTDCs are identical. The RTDC surrogate is open reduction and internal fixation (ORIF) or permanent disability. All fracture types in the BC definition are recommended to be managed non-surgically. Among those managed non-surgically, the complication that could lead to permanent disability that was considered was complex regional pain syndrome (CRPS) - which represents a small percentage for RTDC (3-6.7%) in best case scenarios. All fracture types in the WC definition are recommended to be managed surgically, thus RTDC for WC scenarios is 100%.

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Duckworth et al, 2012.	Terrestrial	1
Karl et al, 2009.	Terrestrial	

Unique data for untreated scenarios was unable to be obtained, so treated and untreated LOCLs are identical. Loss of Crew Life secondary to a wrist fracture was considered to have a 0% probability based on the literature. This is likely an underestimate for untreated scenarios, particularly the worst-case untreated scenario.

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

Overview Wrist fracture refers to a fracture of the carpal bones (and/or the distal radius/ulna), with the best-case scenario representing uncomplicated fractures and the worst-case scenario representing complicated fractures. Any fracture, if left untreated, could result in further complications such as malunion, loss-of function, and/or chronic pain. A worst-case scenario, left untreated, could result in additional significant complications such as neurovascular compromise. CNES: Fracture of the carpal bones, distal radius, distal ulna Diagnostic Scope and Resourcing: In the best-case scenario, diagnosis is based on history, physical examination (musculoskeletal and neurologic), and imaging. Plain film (X-Ray), CT, and MRI will be unavailable inflight. Musculoskeletal ultrasound was included in the CRT as it may serve as a useful adjunct in diagnosis for some cases, but it was not considered a necessary capability to diagnose wrist fracture. In the worst-case scenario, diagnosis is based on history, physical examination (musculoskeletal, neurologic, and vital signs), and imaging. In some cases, musculoskeletal ultrasound may be contraindicated due to risk of contamination of an open fracture, or further displacement of the fracture(s). The utility of musculoskeletal ultrasound would be determined on a case-by-case basis. It was included as a non-necessary capability. This diagnostic framework is consistent with the terrestrial workup for wrist fracture with the exception of the inability to perform plain film X-Ray (and if warranted CT or MRI), and thereby using Musculoskeletal Ultrasound as a possible surrogate. 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 Clinical Phase 1 duration: Best Case CP1: 1.23 hours Worst Case CP1: 2.52 hours Treatment Scope and Resourcing: Most best-case wrist fractures in terrestrial populations resolve without reduction, with an initial period of splinting, followed by 4-6 weeks of casting. Splinting was considered a necessity, whereas casting was included as a capability but not considered a necessity in this CRT. Physical therapy is recommended post-immobilization. Pain is variable depending on the patient. NSAIDs and Acetaminophen were included in the best-case treatment scenario. Terrestrially, all worst-case fractures warrant surgical intervention. Thus, a worst-case wrist fracture in-flight would present a significant treatment challenge. These fractures would warrant an attempted reduction to achieve more physiologic alignment. Open fractures inflight would be treated with copious irrigation, wound closure, prophylactic antibiotics and splinting with possible casting after wound healing. Again, both splinting and casting were included as capabilities, but only splinting was considered a necessary capability in this CRT. Both plaster and fiberglass (and their associated means of removal) are included for trade-space analysis. Pain from a worst-case fracture may require narcotic analgesia. Physical therapy would be advised until the end of the mission. Exercise modification is also recommended, but not built into the CRT as this does not represent a clinical resource. 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: While real-time video and audio loop communications are desired for diagnosis and treatment, they were not considered a necessity, particularly in the best-case scenario. For the WC, consultation with ground specialists to facilitate treatment and healing was considered necessary given the limited diagnostic and treatment capabilities in-flight. References 1. American Academy of Orthopedic Surgeons. Management of Distal Radius Fractures: Evidence-Based Clinical Practice Guideline. 2020. Retrieved from https://www.aaos.org/globalassets/quality-and-practice-resources/distal-radius/drfcpg.pdf 2. Daniels JM, Zook EG, Lynch JM. Hand and Wrist Injuries: Part II. Emergent Evaluation. AFP 2004; 69:1949–56. 3. Phillips TG, Reibach A, Slomiany WP. Diagnosis and Management of Scaphoid Fractures. AFP 2004; 70:879–84. 4. Open-fractures_ADULT.pdf. Retrieved 23 January 2021 from http://www.med.umich.edu/asp/pdf/adult_guidelines/Open-fractures_ADULT.pdf

IMM CLIFF RECONCILATION COMMENTS

It was a challenge for the IMM to find untreated BC/WC data and thus used durations that were similar between best and worst case scenarios in the IMM (i.e. the duration of treated best case was similar to untreated best case, and the duration of the treated worst case was similar to the untreated worst case). This same assumption is being made in this CLiFF. The paucity of data for untreated scenarios remains a limitation in this effort. The durations for this effort are considerably longer for the worst-case scenarios (12-52 weeks vs. 6-12 weeks) based on the updated evidence review. The RTDC probabilities are similar between IMM and IMPACT. Both IMM and IMPACT assume a 0% probability of LOCL for any scenario, although as stated previously this is likely an underestimate for the worst-case, untreated scenario which may have a greater than 0% of LOCL in the event of untreated open fracture or fracture resulting in untreated compression syndrome.

LIMITATIONS SUMMARY

• Analog articles examining wrist fracture in the context of fragility fractures/osteopenia/osteoporosis were disregarded by the student effort at not applicable. However, fractures that occur in spaceflight would be most similar to these types of fractures terrestrially. This is a limitation of the search. • Searches for incidence did not consistently use the same mesh words. For instance, distal radius fractures were included for terrestrial incidence data, but not for spaceflight or analog incidence searches. It is appropriate to include distal radius/ulna fractures in the searches, but they should be included for all searches, not just some to make it uniform. Of note, distal radius fractures are incredibly common, terrestrially. This could be artificially inflating the terrestrial incidence value. Students documented concerns about inconsistency in the terrestrial data studies. Scaphoid fracture was used as a surrogate in many cases (which is the most common carpal bone fracture, but not as common as distal radius fracture). • Duration, RTDC, and LOCL were based on distal radius and scaphoid fractures only and did not include the other bones of the wrist. • The RTDC surrogate chosen was “ORIF / Permanent disability incidence.” This does disregard the possibility of Compartment Syndrome as an RTDC surrogate. • The literature search was unable to identify any duration, RTDC of LOCL data for untreated wrist fractures. Thus, the duration and RTDC for untreated scenarios is using treated data, i.e. the duration and RTDC %, and LOCL % for treated and untreated scenarios will be identical. This is a limitation of the data. The paucity of data for untreated scenarios remains a limitation in this effort. • LOCL probability was determined to be 0% for both best and worst-case scenarios (Duckworth et al, 2012) (Karl et al, 2015). However, in the worst-case scenario this does not include the complication of compartment syndrome, which may present a probability of death > 0%. It seems intuitive that the risk of death from an untreated WC fracture - comminuted, open - that isn’t treated could be > 0% (infection, sepsis, compartment syndrome). There was no data available for the untreated scenario, so treated was used (0%). Thus, LOCL may underestimate the true probability of LOCL in the model, especially in the WC, untreated scenario.

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)												
Untreated Best Case (UTBC)		664		89			145					
Treated Worst Case (TWC)		664										
Untreated Worst Case (UTWC)	223	664		89			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					34	34	211	411	3763	0.109221	10.9221
Untreated Best Case (UTBC)	132	564	414			34	34	211	2287	3763	0.60776	60.776
Treated Worst Case (TWC)	132					34	34	211	1075	3763	0.285676	28.5676
Untreated Worst Case (UTWC)	132	564	414	22	196	34	34	211	2728	3763	0.724953	72.4953

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)	132						34	211	377	3763	0.100186	10.0186
Treated Worst Case (TWC)	132						34	211	377	3763	0.100186	10.0186
Untreated Worst Case (UTWC)	132		414	22	196	34	34	211	1043	3763	0.277172	27.7172

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: In the worst-case treated scenario, pain medications assumed to impair complex cognitive tasks. In all untreated scenarios, pain from the wrist fracture was assumed to prevent the use of the hands. CP3: No comments.

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