Clinical Finding Form (CliFF)

Branch | **Baseline**

ICL71_Nephrolithiasis

Kidney stones form as a result of physicochemical or genetic derangements leading to super saturation of the urine with stone-forming salts or, less commonly, from recurrent urinary tract infection with unease-producing bacteria. Stasis in the upper urinary tract due to local anatomic anomalies may also promote or enhance stone formation in susceptible individuals. Spaceflight is associated with biochemical alterations that promote kidney stone formation. Microgravity associated bone demineralization has been shown to result in hypercalciuria, and hypocitraturia, and reductions in urinary pH. Citrate, an inhibitor of stone formation, was shown to be reduced particularly in early spaceflight. Dietary intake known to be protective of stone formation was also found to be reduced including protein, potassium phosphorus and magnesium. (Whitson, 1997); (Whitson, 1993). Hypercalciuria is a characteristic of the skeletal adaptation to space, and contributes to the increased super saturation of urine such as with calcium phosphate or calcium oxalate. However, whether a renal stone forms in supersaturated urine depends upon other risk factors. The presence of these aggregates in the renal collection or excretion system can potentially result in renal colic, hematuria, infection, and can obstruct urine flow to cause hydronephrosis (Sibonga, 2008). Factors contributing to dehydration on orbit include dehydration associated with space motion sickness in the first few days of flight, and decreased urine output due to lower oral fluid intake associated with depressed appetite, increased workload and exercise (Jones, 2008). There has been one reported episode of an inflight renal stone occurrence in a cosmonaut during a long duration mission. This episode was associated with severe pain and significantly impacted mission operations. Symptoms subsided, the stone apparently passed spontaneously over a period of days, and the mission was completed. (Barratt, 2019). There are no instances of symptomatic kidney stone formation during spaceflight among U.S. astronauts. There have been 7 cases within 12 months of landing postflight. NASA's Glenn Research Center (GRC) prepared a Bayesian Analysis for the IMM to provide an estimate of the incidence of kidney stones among astronauts inflight (Gilkey, 2012). Future work may include updating the estimate of incidence of symptomatic inflight kidney stones based on the inclusion of more recent data and the use of inflight renal stone modeling currently under development at GRC which accounts for the biochemical alterations and environmental factors of spaceflight. Additional future work may include accounting for future medical technologies that allow for the noninvasive treatment of kidney stones inflight on the outcomes of these events.

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 are no instances of symptomatic kidney stone formation during spaceflight in U.S. astronauts. There is an anecdotal report of a Russian cosmonaut who passed a kidney stone inflight. Leedey cited in (Sibonga, 2008).

ANALOG LITERATURE

Articles discussed physiology or treatment of renal stones in space analogs but did not refer to incidence. Articles discussing nephrolithiasis were generally dated before 1990.

TERRESTRIAL LITERATURE

NASA's Glenn Research Center prepared a Bayesian Analysis for the incidence of kidney stones (Gilkey, 2012). When looking at the astronaut population data for the medical events investigated, the population and the occurrences are very low. Due to this low occurrence, Bayesian methods are deemed necessary in order to better predict probability estimates for incidence rates of these medical events. The Bayesian process allows researchers to make inferences to determine the probability that a hypothesis is true, conditional on all available evidence. An estimate of the probability of an astronaut developing a renal stone during or after space flight was estimated using data from LSAH (Wear, 2007) and the Center for Disease Control (CDC) (Litwin, 2004). Information from these sources was combined using a Bayesian update approach to estimate the average rate of stone formation. By making the average rate assumption, a Poisson probability distribution was assumed to govern the probability of stone formation. This model uses only data pertaining to stone occurrence, not data related to blood or urine chemistry. To begin to estimate the probability of renal stone formation in the astronaut corps, control populations and the general U.S. population, there is an assumption that the rates of renal stone incidences is constant over the period of interest. This in turn leads to the assumption of the probability of occurrence following a Poisson distribution. These assumptions are likely erroneous in the larger sense, based on LSAH temporal distribution of stone formation provided to the GRC-IMM team. However, it is believed that the assumption is currently the "best approximation" based on non-attributable data from short duration mission (less than 20 days) participants. Only one data point is available on the occurrence associated with long duration missions (~180 days) at this time. From the CDC as of 2004 (Litwin, 2004), the incidence of renal stones per 1000 persons per year varied; for males, the range was one to three incidents while the female range was 0.6 to 1 incidents per 1000 persons per year. For this analysis gender differences were not considered, and the average incidence rate of renal stones was 0.0018. An EF of 2.236 was found by taking the square root of the ratio 3 to 0.6 (Gilkey, 2012). The LSAH maintains an astronaut control population database, primarily made up of JSC personnel. This data was of interest, as renal stone incidence is geographically dependent, due to factors including dietary habits, lifestyle, and so on. The JSC astronaut analog population was used to capture these discrepancies due to geography. The incidence rate of renal stones for this ground-based comparison population from Pietrzyk et al. (Pietrzyk, 2007) Out of 927 participants there were 74 occurrences of renal stones over 17740.8 person-years yielding an incidence rate of 0.0042 events per person-year. Primarily occurring post-flight of short duration missions, there have been a number of renal stone incidences in the astronaut population. Out of 332 astronauts there were 14 occurrences over 5434.5 person-years yielding an incidence rate of 0.0026 events per person year. (Pietrzyk, 2007) Two things should be noted on this data. The first is that this counts all occurrences, including repeat occurrences (two known). Second, ~40 percent of the occurrences occur within 30 months of return, and the remainder occurred after 66 months post return. This may negate the assumption of an average rate for the entire period of interest. The total number of person years reported includes the time frame for both inflight and post-flight data. To improve the estimate of the rate of occurrence in the astronaut corps and provide a first-order approximation suitable for use in the GRC-IMM modeling effort, the following approach was taken using the numerical Bayesian update code WinBUGS. One Bayesian update was performed such that no gender distinction was made. The data from the CDC (Litwin, 2004) was used to form an informed lognormal conjugate prior for the incidence rate of renal stones among the general U.S. population. This prior was used to update LSAH astronaut control population in Step 1 of Bayesian implementation, yielding a posterior for the updated incidence rate of renal stones. In Step 2, the posterior of Step 1 was used as the prior and updated LSAH pre-flight/in-flight astronaut data in WinBUGS. The result is the estimation for the incidence rate of renal stone formation among astronauts during an exploration mission. This process returned an estimate of the rate of renal stone formation in the astronaut core (most representative of post-flight) with respect to the general population and the LSAH control population. This rate can be used as the input rate to a Poisson distribution probability model to estimate the probability of a renal stone occurrence. The mean incidence rate of renal stone formation among astronauts was 0.00396 events per person-year. Standard deviation is 0.00046 (Gilkey, 2012). This model should be considered very limited in that it assumes an average occurrence rate of renal stones, irrespective of the stone type or environmental conditions. Additionally, the inclusion of repeated occurrences could influence the predicted rate of occurrence as it is know that the occurrence of one stone increases the likelihood of subsequent stones. Use should be treated with understanding of these limitations. However, it is likely a reasonable representation of the rate of stone formation given the occurrence data available and given the assumptions made during construction of the estimate. More accurate estimates can be made with further analysis of the periods of renal stone occurrence in post-flight sufferers and the urinary/serum chemistry values that pertain to stone formation. The current model data will serve as the baseline for future estimates that utilize such biochemical stone forming/inhibiting parameters.

OVERALL INCIDENCE SUMMARY

INCIDENCE

mean 0.00396 and SD 0.00046

INCIDENCE SUMMARY

Using a GRC Bayesian analysis of terrestrial data and LSAH astronaut and ground control data, the resulting distribution for the incidence rate is lognormal(mean=0.00396, variance=2.116E-7) which has mean 0.00396 and SD 0.00046. Evidence: GRC Bayesian analysis that combined terrestrial data with LSAH ground controls, and astronaut data. From the CDC (Litwin 2004) estimates of the generate population were 1-3 per 1,000 person-years in males and 0.6 to 1 per 1,000 person-years in females. For LSAH ground controls, out of 927 participants, there were 74 events over 17740.8 person-years. IR: 4.171E-3 (95%CI: 3.299E-3, 5.207E-3). For 332 included astronauts, there were 14 events over 5434.5 person-years. IR: 2.576E-3 (95%CI: 1.466E-3, 4.22E-3). Resulting distribution for the incidence rate is lognormal(mean=0.00396, variance=2.116E-7) which has mean 0.00396 and SD 0.00046.

TABLE 1. INCIDENCE MODEL

Incidence Details

Incidence Type
General

Segment
All

Env. Exposure
NA

Sex
Any

Crowns
Any

Contacts
Any

Pregnancy
Any

Incidence Distribution

Occurrence Dist
Poisson

Incidence Dist.
Log-Normal

Mean
0.00396
SD
0.00046

Log-Normal
(Mean): 0.00396
(SD): 0.00046

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Gilkey, et al. 2012	Terrestrial	3

NASA's Glenn Research Center prepared a Bayesian Analysis for the incidence of kidney stones (Gilkey, 2012). LOC = 3 (somewhat confident).

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

There are no specific preflight preventive measures for astronauts with no history of kidney stones. However, preflight surveillance ultrasound is performed on all mission-assigned astronauts to detect any preflight kidney stones.

BEST CASE SCENARIO DEFINITION

A renal stone that responds to conservative treatment (e.g. analgesics and hydration).

WORSE CASE SCENARIO DEFINITION

A renal stone that does not respond to conservative treatment (e.g. requires lithotripsy or surgical treatment).

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

None

BEST CASE/WORST CASE PROBABILITY COMMENTS

Best case/worst case percentage = 74%/26% based on terrestrial study indicating that 26% of kidney stone cases required surgical treatment (Burgher, 2004).

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

Citation	Source	LOC Value
Burgher, et al. 2004	Terrestrial study	3

26% of kidney stone cases required surgical treatment.

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 0.00396 and SD 0.00046	74 - 74	100	1.848	15.3069	197	293	0	0	0	0	0
Treated Worst Case (TWC)		26 - 26	100	1.848	15.3069	936	960	0	100	100	0	0
Untreated Best Case (UTBC)	N/A	N/A	N/A	1.848	63.3138	197	293	26.7606	0	0	0	0
Untreated Worst Case (UTWC)	N/A	N/A	N/A	1.848	63.3138	936	960	26.7606	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 management of kidney stones in spaceflight is currently limited to analgesics, hydration, and tamsulosin. This treatment is adequate for best case scenario kidney stones. Worst case scenario kidney stones would require lithotripsy or surgical treatment. Neither of these treatments are available in spaceflight. RTDC surrogates apply to the worst case scenarios in which these required treatments are not available.

TREATED BEST CASE (TBC) SCENARIO COMMENTS

The treated best case scenario results in temporary task impairment with 0% probability of RTDC and 0% probability of LOCL.

TREATED WORST CASE SCENARIO (TWC) COMMENTS

The treated worst case scenario results in temporary task impairment with 100% probability of RTDC and 0% probability of LOCL. CP3 task impairment of 0% should be reconsidered since the management of kidney stones in spaceflight is currently limited to analgesics, hydration, and tamsulosin. Studies examining death in cases of kidney stones report that death is due to complications of obstructing stones. The stone itself is not fatal but hydronephrosis leading to renal failure or infection that eventually causes sepsis can lead to death. Since hydronephrosis leading to renal failure and death would require bilateral kidney involvement which is very unlikely and since sepsis is a separate condition, LOCL is 0% for this condition (Nephrolithiasis).

UNTREATED BEST CASE (UTBC) SCENARIO COMMENTS

The untreated best case scenario results in permanent task impairment (duration of mission) with 0% probability of RTDC and 0% probability of LOCL.

UNTREATED WORST CASE (UTWC) SCENARIO COMMENTS

Untreated worst case scenario results in permanent task impairment (duration of mission) with 100% probability of RTDC and 0% probability of LOCL. Studies examining death in cases of kidney stones report that death is due to complications of obstructing stones. The stone itself is not fatal but hydronephrosis leading to renal failure or infection that eventually causes sepsis can lead to death. Since hydronephrosis leading to renal failure and death would require bilateral kidney involvement which is very unlikely and since sepsis is a separate condition, LOCL is 0% for this condition (Nephrolithiasis).

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

Citation	Source	LOC Value
Miller, 2019	Terrestrial study	3

Represents the time to stone passage. Since the best case represents stones that are likely to pass on their own, the average duration of stone passage should be between 8.2 days (197 hours) and 12.2 days (293 hours). For stones > 4mm, the average duration of stone passage is 39 days (936 hours), Almost all stones that will spontaneously pass do so in 40 days (960 hours) or less. LOC = 3 (somewhat confident) based on a terrestrial general population study.

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
N/A	N/A	4

Best case scenario RTDC = 0% (based on best case definition). Best case scenario is defined as a renal stone that responds to conservative treatment (e.g. analgesics and hydration). Therefore, based on the best case scenario definition, best case scenarios (stones not requiring intervention) should not result in hospitalization or mortality (RTDC or LOCL). Worst case scenario RTDC = 100% based on the need for lithotripsy or surgical treatment which is not expected to be available on spaceflight missions. LOC = 4 (confident).

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
N/A	N/A	4

LOCL is not expected for best case or worst case scenarios. Best case scenario is defined as a renal stone that responds to conservative treatment (e.g. analgesics and hydration). Therefore, based on the best case scenario definition, best case scenarios (stones not requiring intervention) should not result in hospitalization or mortality (RTDC or LOCL). Studies examining death in cases of kidney stones report that death is due to complications of obstructing stones. The stone itself is not fatal but hydronephrosis leading to renal failure or infection that eventually causes sepsis can lead to death. Since hydronephrosis leading to death would require bilateral kidney involvement which is very unlikely and since sepsis is a separate condition, LOCL is 0% for this condition (Nephrolithiasis). LOC = 4 (confident).

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

ICL #71, Nephrolithiasis

Capabilities and Resourcing Scope

Overview

When renal colic begins, the first priority is to rule out conditions other acute abdominal processes, however, concerning symptoms for nephrolithiasis include intermittent abdominal and flank pain, nausea, vomiting, malaise, and potentially fevers and chills (when a kidney stone leads to concomitant infection). Complete urinary obstruction leading to anuria and hydronephrosis can further increase the risk of infection and cause irreversible loss of kidney function. Utilizing urinary studies and imaging can help reveal what type of stone as there are multiple types (Calcium oxalate, calcium phosphate, cystine, struvite, or uric acid).

CNES: None

Diagnostic Scope and Resourcing

The medical history should review any personal or family history of kidney stones, diet, current medications, and any conditions associated with an increased risk of kidney stones. Workup begins with urinalysis and renal ultrasound. Non-contrast CT, plain radiography with urography, straining the urine for stone analysis, and urine culture will not be possible in spaceflight. While a urinalysis and creatine in a basic metabolic panel are reasonable first laboratory examinations, a complete blood count with differential, liver function panel, lipase, and urine pregnancy test should also be evaluated as part of the differential diagnosis. Labs like uric acid, parathyroid hormone, ionized calcium, urine microscopy for crystals, or testing for cystinuria are unlikely currently during spaceflight. In addition to the renal ultrasound, abdominal and pelvic ultrasounds can also be completed to evaluate for other intra-abdominal pathologies in the differential diagnosis. Per the definitions, BC and WC diagnostic work up will be the same.

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): 1.848
CP1 WC (Treated or Untreated): 1.848

The highest scope of practice required for diagnosis includes the interpretation of the ultrasounds which is SOP 5 (attending).

Treatment Scope and Resourcing
Irrespective, of stone type, conservative management terrestrially includes pain control (NSAIDs first line), and medical expulsive therapy with an alpha blocker. Tamsulosin is likely to be present in the formulary, however, doxazosin will not be available. In addition to mild pain medications like NSAIDs and Tylenol, oral narcotics may be needed acutely. Oral hydration and PO or IM antiemetics are also needed in the best-case scenario.

In the worst-case scenario, the renal stone is not responding to conservative treatment and is severe enough to require lithotripsy or surgical treatment. IV hydration and IV antiemetics are added to the treatment scope. Further, ultrasound-guided percutaneous nephrolithotomy may be considered to help drain urine from the obstructed kidney and a sedation protocol utilizing narcotics, midazolam, or ketamine can be used if needed. Functional ultrasound is a hopeful future capability, however, not currently scoped for this condition.

Lifestyle modifications such as increased fluid intake, thiazide diuretics, allopurinol, or citrates can be prescribed for recurrent calcium stones. If pyelonephritis occurs, this diagnosis is a separate condition covered by its own CLiFF. While continued recurrences refractor to lifestyle modification is beyond the scope of this condition, thiazide diuretics, allopurinol, and citrate supplementation can help in preventing calcium stones.

Communications and Support Needs

While a best-case scenario may only require ground communication for confirmation of diagnosis and management, ground support with video or pictures will be necessary for the worst case scenario to help guide management and guide RTDC decisions as the diagnosis warrants surgical management.

REFERENCES

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IMM CLIFF RECONCILATION COMMENTS

The IMM CliFF Nephrolithiasis was used as the basis for this CliFF (ICL71 - Nephrolithiasis). The incidence values from the IMM CliFF are used for the ICL71 CliFF. The main difference between the CliFFs is the updated best case/worst case percentages from 36%-85%/15%-64% to 74%/26% based on the (Burgher, 2004) study. This change decreases the uncertainty of the best case/worst case percentages. Future work may include updating the incidence estimates for inflight symptomatic kidney stones with more recent terrestrial general population and astronaut data, and attempting to incorporate spaceflight environmental and physiological factors.

LIMITATIONS SUMMARY

There are no instances of symptomatic kidney stone formation during spaceflight among U.S. astronauts. Therefore, terrestrial general population studies and astronaut terrestrial data are used for incidence and outcomes. It is unknown to what extent spaceflight environmental and physiological factors may increase the likelihood of the development of symptomatic kidney stones inflight. There is limited information regarding untreated kidney stones. Treatment options being investigated include moving an obstructing stone or shattering it with ultrasound. This CLiFF does not consider these as therapeutic options at this time and are not considered in the calculations. If such treatment becomes available on-board the space vehicle, this calculation will need to be reconsidered.

TABLE 8. TASK IMPAIRMENT CALCULATION BASED ON AFFECTED HUMAN SYSTEMS TASK CATEGORIES (HSTC)

Clinical Phase 2: Treatment												
	Affected HSTCs											
	Cognitive - Simple	Cognitive - Complex	Communications	Inter-personal Skills	Vision	Hearing	Cardio-pulmonary	Dentition	GI	GU		
Treated Best Case (TBC)		664					145					
Untreated Best Case (UTBC)	223	664	113	89	854	44	145		13	6		
Treated Worst Case (TWC)		664					145					
Untreated Worst Case (UTWC)	223	664	113	89	854	44	145		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							211	1152	3763	0.306139	30.6139
Untreated Best Case (UTBC)	132	564	414	22	196	34	34	211	3758	3763	0.998671	99.8671
Treated Worst Case (TWC)	132							211	1152	3763	0.306139	30.6139
Untreated Worst Case (UTWC)	132	564	414	22	196	34	34	211	3758	3763	0.998671	99.8671

Clinical Phase 3: Condition End State												
	Affected HSTCs											
	Cognitive - Simple	Cognitive - Complex	Communications	Inter-personal Skills	Vision	Hearing	Cardio-pulmonary	Dentition	GI	GU		
Treated Best Case (TBC)												
Untreated Best Case (UTBC)		664										
Treated Worst Case (TWC)												
Untreated Worst Case (UTWC)		664										
	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							211	1007	3763	0.267606	26.7606
Treated Worst Case (TWC)									0	3763	0	0
Untreated Worst Case (UTWC)	132							211	1007	3763	0.267606	26.7606

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.

REFERENCES

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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