Clinical Finding Form (CliFF)

Branch	Baseline

ICL58_Gastritis/Reflux/Esophagitis

Gastritis is a broad term that typically refers to inflammation of the esophagus, stomach, or duodenum (Azer et al. 2021; Kashiwagi 2005). Symptoms of gastritis in mild cases often include epigastric burning, abdominal discomfort, nausea, postprandial fullness, and progress to abdominal or chest pain and hematemesis in severe cases. Importantly, this CLiFF condition does not cover gastroenteritis, sepsis or shock which are covered in other CLiFF conditions. Also, this CLiFF only pertains to acute gastritis with neutrophil predominance as the likelihood of a crew member experiencing chronic gastritis (as can be seen in Crohn's disease, Barrett's esophagus, esophageal malignancy, chronic delayed gastric emptying/manometry disorders, functional dyspepsia or improper NSAID use) is minimal given the pre-mission medical screening (Michael et al. 2019). Given the breadth of medical complaints this condition encompasses, key-word lists were formed to differentiate between resources for the best and worst cases. Best Case Keywords: acute gastritis, gastroesophageal reflux disease (GERD), acute esophagitis, indigestion, dyspepsia, heartburn, esophageal disease, epigastralgia, digestive-system disorders (excluding gastroenteritis), gastrointestinal diseases (excluding gastroenteritis) Worst Case Keywords: peptic ulcer disease, gastric ulcer, duodenal ulcer, acute nonvariceal upper-gastrointestinal bleeding, helicobacter pylori and any keyword included above with a more prolonged course than a single incident.

INCIDENCE DATA INCLUDED IN THE MODEL

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

INCIDENCE DATA

SPACEFLIGHT LITERATURE

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

ANALOG LITERATURE

Analog studies involved all branches of the military and included larger sample sizes than than the spaceflight literature. However Thomas et al., 2003 analyzed medical events involving United States Navy officers on 240 submarine patrols between 1997 and 2000 for the purpose of creating an analog population for future spaceflight missions. Although medical events that pertatined to this CLIFF definition were categorized broadly as 'digestive system disorders', 'gastroenteritis' was a seperate condition. In Storms et al. (2016), dyspeptic and peptic ulcer events were recorded in a retrospective review of active duty Air Force airmen. Incidence data from this study were gathered from only flyer events, although non-flyer event data was available. This popultation included members of the aircrew who likely had comorbid conditions, and was not as highly screened as the population in Thomas et al. One of the largest analog populations came from a retrospective review of active members of the Army, Navy, Air Force, Marine Corps and Coast Guard between January 1, 2005 and December 31, 2014 (Daniele et al, 2015). Although subjects in this study certaintly were not as highly screened as spaceflight participants, medical conditions were categorized in a manner similar to the definitions in this CLiFF. The remainder of the analog studies (Lindren et al., 2012; Belmont et al., 2010; Lyons et al., 1990; Tansey et al., 1979) were limited in how they defined their incidence data, applicability of population and sample size.

TERRESTRIAL LITERATURE

Terrestrial literature (Eusebi et al., 2018; Ford et al., 2015) were large meta-analyses pertaining to the conditions 'dyspepsia' and 'GERD.' These studies presented data as prevelance rather than incidence rates. North American populations were not highly screened and represented the general public with a high liklihood of comorbid conditions. Populations in these studies were also skewed towards the elderly (albeit included subjects older than 15 years of age).

OVERALL INCIDENCE SUMMARY

INCIDENCE

mean: 0.034 SD: 0.00734

INCIDENCE SUMMARY

Using a Bayesian meta-analysis to combine top-rated data sources, mean: 0.034 SD: 0.00734 which is approximated by a Gamma(shape=21.45, rate=631.08) The graph below shows the distribution. I changed the line types via ratings, more dash less rated. I annotated with the reference for the 4 1s and 2s

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.
Gamma

Mean
0.0339894

SD
0.00733887

Gamma
(Shape): 21.45
(Rate): 631.08

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Antonsen et al., 2017	Spaceflight	3
Thomas et al., 2003	Analog	3
Walton, 2010	Spaceflight	2
Saile et al., 2017	Spaceflight	2
Storms et al., 2016	Analog	2
Daniele et al., 2015	Analog	2
Lindgren et al., 2012	Analog	1
Belmont et al., 2010	Analog	1
Lyons et al., 1990	Analog	1
Tansey et al., 1979	Analog	1

Citation	Source	LOC Value
Eusebi et al., 2018	Terrestrial	1
Ford et al., 2015	Terrestrial	1

Although the Antonsen, Walton and Saile resources are derived directly from spaceflight data, confidence in these resources is diminished given that reports did not always accurately represent the best- and worst-case conditions and were subject to interpretation by the data-gatherer. Further, upon direct discussion with those who had participated in prior missions, astronauts did not always report real-time symptoms in apprehension of disqualification from tasks or future missions. However, the statistician for this CLIFF was able to talk to the authors of the Antonsen paper and verify how incidence data was derived, increasing the confidence rating of this source; this was unavailable for the other spaceflight resources. Studies that had highly screened populations that were designed for the purpose of creating a spaceflight analog, had comparable confidence rankings. Lastly, the terrestrial data had lower levels of confidence despite their large sample populations; data in these studies often included populations with comorbid conditions and age-ranges that were not consistent with spaceflight groups.

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 that will be on missions greater than 30 days do undergo H. Pylori Testing at L-21/18 AME L-9/6 m (if needed). Crew members initially undergo serological screening for H. Pylori antibodies, and if negative, no further testing is required. If positive, they subsequently undergo a non-invasive breath test. If this is positive, they undergo an accepted current treatment regimen and are re-tested after 4 weeks. (Of note, serologic evaluation to determine H. pylori infection is no longer considered clinically useful by the American College of Gastroenterology and the American Gastroenterology Association)

BEST CASE SCENARIO DEFINITION

Mild indigestion, most likely due to gastro-esophageal reflux (GERD), esophagitis, or gastritis, that resolves with minimal or no treatment.

WORSE CASE SCENARIO DEFINITION

Moderate or severe indigestion, including duodenal and/or gastric ulceration, either requiring prolonged treatment, or leading to complications such as gastrointestinal bleeding.

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

GI - Indigestion, GERD, GI Ulcer - Duodenal, GI Ulcer - Gastric, GI bleed (upper)

BEST CASE/WORST CASE PROBABILITY COMMENTS

There have been no worst-case events recorded in spaceflight and as such data were limited to analog and terrestrial studies. The most specific data came from Storms et al. (2016) in which a weighted average of Air Force pilots and crewman who experienced severe 'peptic ulcer events' was calcuated to be 0.6% over the course of 13 years (74100 person-years). This is in good concordance with terrestrial data which estimates worst case probability to be betweeen 0.1 to 6.0% (Lanast et al., 2007; Garrow et al.,2010)

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

Citation	Source	LOC Value
Storms et al., 2016	Analog	2
Hayashi et al., 2003	Analog	0
Lyons et al., 1990	Analog	0
Lanas et al., 2017	Terrestrial	0
Garrow et al., 2010	Terrestrial	0

More confidence was held in analog studies (Storms et al., 2016; Hayashi et al., 2003) as terrestrial populations (Lanas et al., 2017; Garrow et al., 2010) often had comorbid conditions and age ranges not applicable to spaceflight despite their large sample sizes and appropriate handling of data, Although the Hayashi et al., 2003 study did use an apporopriate analog occupation (pilots), it too was eventually excluded from the final worst case probability as subjects were only of Japanese race and were subjected to different diets and H. pylori rates than expected NASA crewmembers.

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: 0.034 SD: 0.00734	99 - 99	100	0.47	0	0	24	0	0	0	0	0
Treated Worst Case (TWC)		1 - 1	100	1.72	15.4797	336	1344	0	0.1	1	0.00021	0.021
Untreated Best Case (UTBC)	N/A	N/A	N/A	0.47	2.97635	0	24	0	0	0	0	0
Untreated Worst Case (UTWC)	N/A	N/A	N/A	1.72	31.3972	672	2016	29.47	0.08	1	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 hospitalization or unresolving upper gastrointestinal bleeding.

TREATED BEST CASE (TBC) SCENARIO COMMENTS

Determining the duration of the treated best case (TBC) scenario is difficult as this definition is an episode of indigestion that resolves with minimal or no treatment. Most literature pertaining to duration of gastritis results from studies of functional dyspepsia, gastroesophageal reflux disease or peptic ulcer disease. These pathologies contrast to the single episode of gastritis described in the TBC which may result from stress, changes in diet or sleep, the microgravity environment or even acute viral illness. The previous IMM CLIFF used a duration of zero to 24 hours of duration based on subject matter expert consensus. The treated best case is unlikely to be handled with therapeutics that modify the gastric pH but rather those that solely alleviate symptoms (Savarino et al., 2017). Several studies have demonstrated that a single episode of untreated indigestion can vary from 0 to 3.75 hours however they often can reoccur over the course of 24 hours (Batista et al. 2019; Pehlivanov et al. 2001; Portale et al. 2007). Treated events can be expected to have shorter symptomatic periods, but there are no studies actually demonstrating such. Consequently, a duration of zero to 24 hours was assumed for the TBC (and also the UTBC described in the subsequent section). By definition, events that would lead to RTDC and LOCL are not expected for this condition.

TREATED WORST CASE SCENARIO (TWC) COMMENTS

In the treated worst case (TWC) condition, mucosal defects are expected in the gastric or duodenal walls. Definitive testing to differentiate between the causes of severe gastritis, whether it be Helicobacter pylori (H. pylori) or peptic ulcer induced, is unlikely in space given limited resources and training. Active treatment, usually with at least a proton pump inhibitor (PPI) is recommended between six to eight weeks, albeit there are studies that have demonstrated efficacy in two weeks (Lau et al. 2011; Sigterman et al. 2013). Accordingly, duration of CP2 for this condition was chosen to range from two to eight weeks. Of note, other therapies such as antibiotics and histamine 2 receptor antagonists (H2RAs) may have other ranges of treatment, but they are recommended within the duration of this timeline. The RTDC surrogate for this condition was hospitalization or unresolving upper-gastrointestinal bleeding. Terrestrial consensus guidelines recommend that all acute upper-gastrointestinal bleeding (both non-variceal, which pertains to this condition and variceal, which is excluded from this condition) be at least evaluated in an emergency department; most will require hospitalization (Laine et al. 2012). However, this worst case condition is highly unlikely as 'gastrointestinal ulcer with complication' possesses a pooled incidence rate estimated at 1.0 per 1,000 person-years (Hernández-Díaz et al. 2002; Klein et al. 2015). The mortality rate of this condition is even lower, estimated to be at 2.1% of admitted patients with this pathology (Tielleman et al. 2015).

UNTREATED BEST CASE (UTBC) SCENARIO COMMENTS

Similar to the rationale used in TBC, the untreated best case (UTBC) is still a self-limited illness. Again, most literature pertaining to duration of gastritis results from studies of functional dyspepsia, gastroesophageal reflux disease or peptic ulcer disease. Since treatment of the best case is focused solely on symptomatic control as opposed to modifying the pathogenesis or physiology of the condition, it can follow that the duration for the untreated condition would be similar to its treated counterpart. Likewise, the RTDC and LOCL parameters are unchanged from the TBC.

UNTREATED WORST CASE (UTWC) SCENARIO COMMENTS

Applicable studies for the untreated worst case (UTWC) were limited to those published before the year 2000 as the current standard of care is to initiate pharmaceuticals at the time of diagnosis. The shortest duration, four weeks, was taken from a study during which the placebo (control) group experienced 36% healing of their duodenal ulcers (Lam et al. 1997). Although it is likely that those experiencing the UTWC could have shorter durations, studies discerning such were unavailable. Further, it is expected that the untreated worst case would have a longer CP2 duration than the TWC. The same study demonstrated that without intervention over 64 percent of these ulcers would be healed and the patients would be asymptomatic by 12 weeks. Other studies seemed to support this timeline but only followed patients to six and eight week timpoints (Scheurer et al. 1977; Massarrat et al. 1981; Darle et al. 1984). Of note, one study reported that patients with endoscopy-confirmed duodenal ulcers still had significant disease after two years (Kaneko et al. 1989). However, limitations of this study include the inability to differentiate between disease reoccurrence or clinically-significant pathology as patient symptomology was unknown. Still, the same study was useful in determining RTDC as it reported that out of its 456 male office workers over the age of 40 with confirmed gastric or duodenal ulcerations, only four had a complicated course involving gastrointestinal bleeding requiring escalation of care. Similarly, a Finnish study reported that between 2006-2008 there was an incidence rate of 37 per 100,000 persons hospitalized for severe complications and only 44.4% of this population had been treated with either a PPI or H2-receptor antagonist, prostaglandins, or antibiotics for H.pylori the year prior (Malmi et al. 2014). Since data indicated that the maximum TWC RTDC was approximately 1.0% and it would be expected that the maximum UTWC RTDC (calculated to be 0.08% by the above studies) would be equivalent or greater, the UTWC RTDC was raised to 1%. Given the definition, LOCL is not expected for this condition as sepsis and shock are covered in other CLiFFs.

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

Citation	Source	LOC Value
Portale 2007	Terrestrial	2
Batista 2019	Terrestrial	
Pehlivanov 2001	Terrestrial	
Weberg 1989	Terrestrial	
Sigterman 2013	Terrestrial	
Lau 2011	Terrestrial	
Scheurer 1977	Terrestrial	
Massarrat 1981	Terrestrial	
Darle 1984	Terrestrial	
Kaneko 1989	Terrestrial	

The best available studies to determine durations for treated and untreated best cases were based on ex-vivo experiments with low sample sizes. Meta-analysis data were available for the TWC. Due to the increasingly more rigourous Institutional Review Board guidelines of American institutions, literature for the UTWC are dated and largely limited to European countries.

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Klein 2015	Terrestrial	2
Hernández-Díaz 2002	Terrestrial	
Kaneko 1989	Terrestrial	
Malmi 2014	Terrestrial	

RTDC percentages for the TBC and UTBC are expected to be zero given the conditions' definitions; as such articles were not reviewed for these conditions. In the TWC, RTDC was determined from a dated systematic review and updated narrative review. For the UTWC, data was extropoliated from studies with low sample sizes in European countries.

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Tielleman 2015	Terrestrial	2

Based on the definitions, loss of crew life is not expected for any of the conditions. However, to validate the assumption that mortality was neglible a literature search was still conducted and this narrative review does indeed provide a negligiable mortality for United States hospitalized patients.

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

Overview: Gastritis refers to mucosal inflammation secondary to gastric injury.(Azer et al. 2021) There are numerous pathophysiologies associated with this condition including anatomic abnormalities, delayed gastric emptying, increased acid production, NSAID use, inappropriate diet, infection, inflammatory disease and iatrogenic injuries.(Kashiwagi 2005; Lanas et al. 2017) Differentiating between the causes of gastritis is unlikely during a space-flight mission given limited resources and training. This CRT will pertain to acute gastritis with neutrophil predominance; the likelihood of a crew member experiencing chronic gastritis, as can be seen in Crohn’s disease, is minimal given the pre-mission medical screening. Terrestrial consensus guidelines advocate for outpatient management in the Best Case (BC) scenario.(Kahrilas et al. 2008) Most terrestrial populations experiencing the BC often do not seek physician or provider advice. Consequently, in this CRT, scope of practice is defined at the first-responder level. The Worst Case (WC) scenario does require the ability to interpret lab work and imaging along with prescribing adequate therapeutics. As such, the scope of practice in this CRT for the WC is at the Intern/PA/NP level. Of note, the WC scenario can include gastrointestinal bleeding and RTDC is persistent gastrointestinal bleeding. However, this CRT does not include conditions requiring large resuscitative efforts such as hypovolemic shock, bowel or stomach perforation, peritonitis and sepsis as in concordance with our task-impairment (TI) consensus (worst case, untreated TI% 29.5). CNES: GI - Indigestion, GERD, GI Ulcer - Duodenal, GI Ulcer - Gastric, GI bleed (upper) Diagnostic Scope and Resourcing: In the BC condition, diagnostics are based on clinical symptoms and physical exam. For the WC scenario, in terrestrial conditions, a simple differential should be explored including an upright chest-x-ray for possible pneumonia or visceral perforation and an electrocardiogram and troponin for acute cardiac syndrome. In this CRT, given the significance of missing an acute cardiac syndrome event, resources for an EKG and a troponin were allocated. The severity of disease can be assessed by bloodwork for anemia and electrolyte derangements in addition to a stool hemoccult for upper-gastrointestinal bleeds. However, a stool guaiac test is not absolutely essential to treat this condition. To avoid not being able to treat gastritis if a stool hemoccult was not available, for this iteration the necessity of this capability was placed as ‘0’. Definitive testing that would occur in terrestrial care such as endoscopy, gastric mucosal biopsy, histology, urea breath testing, stool antigen testing, immunologic testing, double contrast barium swallows, esophageal manometry and ambulatory esophageal pH monitoring (Azer et al. 2021; Kashiwagi 2005) are not likely to occur on the proposed missions given the increased medical specialization needed and the current limits on allocated area. 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: 0.47 hours This is the time estimated to remove the crew member from duties, perform hand hygiene and conduct a simple physical exam. Worst Case CP1: 1.72 hours This is the time estimated to remove the crew member from duties, perform hand hygiene, conduct a systems-based physical exam, obtain bloodwork, and perform and interpret ultrasound imaging. Treatment Scope and Resourcing: Most cases of mild gastritis in terrestrial populations resolve without any treatment.(Savarino et al. 2017) However, should mild symptoms persist, a bland and scheduled diet and sleep modifications can be pursued prior to initiating pharmacological treatment. When medications are required for mild GERD, Histamine 2 receptor antagonists (H2RAs) are preferred over proton pump inhibitors (PPIs). Further symptomatic relief can be addressed with as-needed antiacids or aluminum sucrose sulfate. In the WC, PPIs are found to be more effective than H2RAs.(Lanas et al. 2017; Young et al. 2020) The terrestrial standard of care is to not treat for Helicobacter pylori (H. pylori) unless definitive diagnosis is made.(Meltzer et al. 2015). Given the high unlikelihood of an H. pylori infection, it was the consensus of the CRT team that resources should not be allocated for this specific condition. Communications and Support Needs: Realtime medical direction from ground control is only likely to be necessary in the worst-case scenario as there is little-to-no risk in foregoing treatment in the best-case scenario. References Azer, S. A., and H. Akhondi. 2021. 'Gastritis.' in, StatPearls (Treasure Island (FL)). Kahrilas, Peter J., Nicholas J. Shaheen, and Michael F. Vaezi. 2008. 'American Gastroenterological Association Medical Position Statement on the Management of Gastroesophageal Reflux Disease', Gastroenterology, 135: 1383-91.e5. Kashiwagi, H. 2005. 'Ulcers and gastritis', Endoscopy, 37: 110-5. Lanas, A., and F. K. L. Chan. 2017. 'Peptic ulcer disease', Lancet, 390: 613-24. Meltzer, Andrew C., Lauren E. L. Winter, Paige Kulie, Cameron Benedict, Kelvin Lim, Otabek Ishmukhamedov, and Melissa L. McCarthy. 2015. 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IMM CLIFF RECONCILATION COMMENTS

This CLiFF is the successor to the previous IMM CLiFF entitled "Indigestion." There is some concern that the person-years for the LSAH data gathering (Walton M 2010; Saile L. 2017) was calculated incorrectly. Further a previous NASA internal whitepaper (Antonsen et al. 2017) had a table mislabeled as ‘ISS through Exp 40’ when in actuality, the data included in the table was for only expeditions nine, and 14 through 40. Thus, the spaceflight incidence in this CLiFF does differ from what was reported previously. Lastly, it was recognized by the contributors to this CLiFF that reported illnesses in spaceflight were subjected to interpretation by both the medical operations and the data-gatherers from the LSAH reports. Therefore, analog literature was given more influence in this CliFF’s composite incidence compared to its precursor

LIMITATIONS SUMMARY

• ‘Gastritis’ is a broad term not consistently used in medical practice and can be taken to describe a variety of conditions. Therefore, it was difficult to find terrestrial evidence that encompassed all the possible nuances of “gastritis.” • Although H. pylori resources were not included for this condition’s CRT; however, studies used in this CLIFF to determine certain parameters may have incorporated this condition. It is not believed that this significantly impacts the veracity of the parameters although H. pylori in the worst case scenario is still a possibility. • Under-reporting for this condition could have been significant during past space missions and may result in underestimation of the incidence. There is the possibility that sufficient medication to treat gastroenteritis will not be carried on board if the condition incidence used is too low. • The statistical methods being used strongly weight the mean incidence towards studies with large sample sizes. Since spaceflight datasets, by their very nature, have small sample sizes, they may have a negligible influence on the calculation of mean incidence when included with larger sample size terrestrial studies.

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)	0	0	0	0	0	0	0	0	0	0		
Untreated Best Case (UTBC)	0	0	0	0	0	0	0	0	13	0		
Treated Worst Case (TWC)	0	664	0	0	0	0	145	0	13	0		
Untreated Worst Case (UTWC)	0	664	0	89	0	0	145	0	13	0		
	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	0	0	0	0	0	0	0	0	3763	0	0
Untreated Best Case (UTBC)	0	0	0	0	0	0	0	211	224	3763	0.059527	5.9527
Treated Worst Case (TWC)	132	0	0	0	0	0	0	211	1165	3763	0.309593	30.9593
Untreated Worst Case (UTWC)	132	0	0	0	0	0	0	211	1254	3763	0.333245	33.3245

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)	0	0	0	0	0	0	0	0	0	0		
Untreated Best Case (UTBC)	0	0	0	0	0	0	0	0	0	0		
Treated Worst Case (TWC)	0	0	0	0	0	0	0	0	0	0		
Untreated Worst Case (UTWC)	0	664	0	89	0	0	0	0	13	0		
	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	0	0	0	0	0	0	0	0	3763	0	0
Untreated Best Case (UTBC)	0	0	0	0	0	0	0	0	0	3763	0	0
Treated Worst Case (TWC)	0	0	0	0	0	0	0	0	0	3763	0	0
Untreated Worst Case (UTWC)	132	0	0	0	0	0	0	211	1109	3763	0.294712	29.4712

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

The TI process endeavored to use the middle ground of the condition definitions for its process. Consequently, the definition for the worst case scenario (which covers multiple different medical conditions), was duodenal and/or gastric ulcer. CP2: In the treated worst-case scenario, complex cognition was considered impaired as a conservative measure since the clinical course can vary. In the untreated best-case scenario, EVA was aeromedically contraindicated due to lack of symptom control. CP3: The worst-case scenario includes multiple different medical conditions, that could have different outcomes (e.g. ulceration could get worse, GI bleed without treatment would likely result in death, whereas untreated indigestion would likely cause less impairment). In light of this, in the untreated worst-case scenario, CP3 was kept largely the same as CP2 (i.e. assuming no improvement, but not worsening). The exception is that the cardiopulmonary system was not considered to be impaired in CP3 due to chronic compensation.

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