Diarrhea Cliff

Branch Baseline

Diarrhea is defined as three or more loose or watery stools per day (Farthing, 2008) or a definite decrease in consistency and increase in frequency based upon an individual baseline. (Wanke, 2008)

Diarrhea results mainly from excess fecal water, which in our population, can have infectious, drug-induced (i.e. antibiotics), or food-related causes. Four mechanisms that induce diarrhea are increased osmotic load, increased secretion, inflamation, and decreased absorption time. Complications include dehydration and electrolyte loss.

In industrialized countries, the incidence is lower and generally stable. In most cases, acute diarrhea is a self-limiting illness that resolves with or without symptomatic treatment in a few days. (Carre, 2001)

Due to the effects of microgravity in space, there are unique challenges regarding the clinical evaluation of hydration status and the response to perenteral fluid admninistration. (Marshburn, 2008) In the US space program several events of diarrhea due to multiple causes have been reported in space flight. (Walton, 2010)

Incidence Data Included in the Model

The model imports the following incidence information from the IMM database: incidence data category, space adaption status, incidence data, 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. fixed data). Space adaptation identifies medical events that onset occurs in the first 5 days of flight and does not reoccur. Incidence values vary by data category and define the number of medical events per person-year or medical events per person-at-risk for each medical condition. Incidence values can be modified by crew characteristics such as gender. 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 crew member 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 IMM Technical Description Document.

Incidence	
Data Category:	In-flight
Space Adaptation:	No
Incidence Type:	Rate

Distribution Data	
Incidence:	Gamma
Occurrence:	Poisson

Data Characteristics	
Events:	40
Person Years:	45.49
Space Flight Incidence Rate (Events / Person Years):	40 / 45.49 = 0.87931413497472

Incidence Comments

In the US space program 33 events of diarrhea have been reported in space flight. (Walton, 2010)

Of 31 cases, 14 had unknown duration, 7 lasted less than 24 hours, 9 lasted 24 hours, 2 lasted 48 hours, and 1 lasted 120 hours (5 days). One crew member reported several events. All other events occurred to different crew members. (Walton, 2010)

The incidence data was updated to integrate the Real World System observed events including the person at risk from our validation data set. There was 3 ISS and 4 STS events added. Plus 18.17 persons years added. This data set included the remaining Shuttle missions and ISS Expedition 31/32 through Expedition 39/40 (Saile, 2017).

Updated the Person-Years based on the revised real world system integrated incidence data. The integrated person years changed from 18.17 to 18.13 so the conditions person years changed from 45.53 to 45.49 (Saile L., 2017)

Information Regarding Prevention

Selection criteria

Disqualifying conditions in the abdomen/digestive system include: Chronic diseases or disorders of the alimentary tract that interfere with performance of duties, chronic gastritis or chronic abdominal pain, ulcerative colitis, Crohn's disease, chronic diarrhea, regardless of cause, irritable bowel syndrome. In infectious diseases: Acute or chronic infectious diseases, until appropriately treated, that might compromise mission operations, performance of duties, or crew health or safety; the presence of pathological intestinal bacteria or parasites proven by laboratory stool testing. In the general category: Any medical condition that, in the judgment of the MSMB, may compromise mission operations, performance of duties, or crew health or safety. (International Space Station Program, 2009)

Incidence Level of Evidence (LOE)

The IMM level of evidence appropriate assessment of the quality of the IMM input data. Since IMM incorporates input data from a wide variety of sources including astronaut population, terrestrial or analog populations, and external models, an innovative approach to assess the quality of input data was required. Information obtained from the astronaut population and/or space flight is the more relevant so it is assigned the highest level of evidence and less relevant data sources are assigned a lower level of evidence.

Citation	LOE Value	LOE Category
Walton, 2010	1	Incidence
Saile L., 2017	1	Incidence

Alternative Incidence Data

Analog Populations

An analysis of 10 years of data collected on US Navy Polaris submarine patrols over the ten year period 1963-1973 reported a total of 1685 medical events treated. Illness rates are indicated as new/cases/1000 man-days. There were a total of 229 gastrointestinal diseases during the 1963-73 period with an illness rate of 0.05 and 0.03; for the 1963-67 and 1968-73 periods respectively. There were a total of 13 events of enteritis (diarrhea); causing 13 sick days, range 1 to 4 days, during the 1963-1973 period. (Tansey, 1979)

Incidence rate 0.03 per 1000 man-days (0.03*365 = 10.95/ 1000) equals 0.01095 person-years for the period 1963-1967 and 0.05 per 1000 man-days (0.05 *365 / 1000 person years) equals 0.01825 person-years for the period 1968-1973. The average of these two incidence rates is 0.0146 per person-years. Enteritis (13/229) accounted for 5.68% of total gastrointestinal events, or a rate of 0.00082928. Six EVACs occurred but there is no information by condition.

Thomas reported on health of US Navy submarine crews during periods of isolation. There were 3 events of non-infective gastroenteritis among officers and 27 among enlisted men, ICD9 code 558. The incidence rate for non-infective gastroenteritis was 0.5 for officers and enlisted crew, per 100 person years. Effect of illness was minimal 0.75 (officers) to 1 day (enlisted men). Digestive diagnoses were the second most common cause of limited or no duty. Only 4.2% of officers and 7% of enlisted men had greater than 2 days illnesses. Thomas concluded that officers are most analogous to current astronauts. Majority of medical events reported were minor, non-life-threatening, with little or no impact on unit mission. (Thomas, 2003) The incidence rate per person-years is 0.005 (0.5/100). Diarrhea may have been reported with ICD9 code 780-799, signs, symptoms and ill defined conditions, but we cannot segregate the diarrhea data, ICD9 code 787.91, from this group.

Among military personnel in operations Iraqi Freedom and Enduring Freedom less than half sought care for their diarrhea symptoms. (Brown, 2009)

A repeated cross-sectional survey using a convenience sample of US military personnel deployed to Iraq, Afghanistan, and surrounding areas collected from surveillance sites at Incirlik Air Base, Turkey, or Camp Arifjan, Kuwait, where US military personnel were transiting during redeployment, or at Camp As Sayliyah, Qatar, at a rest and recuperation program. Overall, 26% of respondents reported at least 1 episode of diarrhea during their deployment. The mean duration of illness reported was 2.7 days. Overall incidence of self-reported diarrhea from April 2006 to March 2007 was 12.1 episodes; 95% confidence interval (CI) 11.4, 12.7, per 100 person-months. Hospitalization rates were 0; 4.0; and 2.0% in Afghanistan, Iraq and Kuwait respectively. (Riddle, 2008) Mean hospitalizations is 2% similar to civilian United States population. Per person years, incidence rate is 1.452 (12.1 /100 * 12) and the 95% CI 1.368-1.524 (11.4 and 12.7 / 100 * 12).

Non-Analog Populations

To assess trends in the burden of acute diarrheal illness, the Foodborne Diseases Active Surveillance Network (FoodNet) conducted a population-based telephone survey during 1998-1999, using a random-digit-dialing, single-stage Genesys-ID sampling method. During the 12-month study period, 12,755 persons were interviewed; after the exclusion of persons with chronic diarrheal illnesses, 12,075 persons were included in the analysis; 6% (n=645) reported having experienced an acute diarrheal illness at some point during the 4 weeks preceding the interview (annualized rate, 0.72 episodes per person-year). Rates of diarrheal illness were highest among children aged less than 5 years and were lowest in persons aged 65 years or older, 1.1 and 0.32 episodes per person-year respectively. Twenty-one percent of persons with acute diarrheal illness sought medical care as a result of their illness. By age, cohorts of interest 25-44 and 45-64, self reported annualized rates were 1.7 and 1.2 respectively for acute diarrhea episodes (prevalence) and 0.99 and 0.56 for acute diarrheal illness.

Nine percent of persons with a diarrheal illness who visited a health care provider and 2% of all persons with a diarrheal illness were hospitalized for at least 1 night. The median duration of hospitalization was 3 nights (25% and 75% quartiles, 2 and 10 nights, respectively; range, 1–20 nights). Confidence intervals or standard deviations were not published. (Imhoff, 2004)

Treatment and Outcomes

Based on the best evidence available best and worst case percentage ranges are assigned. The medical condition is divided into three clinical phases in all three clinical phases a functional impairment is assigned. The clinical phase I and II's functional impairments remain for the duration for that respective clinical phase. The function impairment in clinical phase III represents final impairment for this medical condition and remains for the rest of the mission. Other mission end states include evacuation and loss of crew life.

The IMM checks medical resource availability once the number of medical events and scenarios has been established. If there is not sufficient essential resources called out in the CliFF, then the medical condition will go down an untreated best or worst case scenario pathway.

The table below summarizes the treated and untreated best and worst case scenarios.

	Clinical Phase I Diagnosis & Initial Treatment[1]		**Clinical Phase II On-going Treatment / Convalescence[2]**		**Clinical Phase III Recovered / Mission End State[3]**		
	FI* (%)	**Duration (hrs)**	**FI* (%)**	**Duration (hrs) (Min - ML - Max)**	**FI* (%)**	**EVAC** (%)**	**LOCL** (%)**
ISS-based Treatment (best case scenario %: 97.56 - 100)	100	0.25	0 - 9	0 - 12 - 24	0	0	0
ISS-based Treatment (worst case scenario %: 0 - 2.44)	100	0.5	1 - 20	24 - 72 - 120	0 - 9	0 - 1	0
Untreated Best Case	0	0	1 - 20	0 - 12 - 24	0 - 9	0	0
Untreated Worst Case	0	0	12 - 38	24 - 72 - 120	1 - 38	0 - 100	0

[1]Clinical Phase I: Clinical phase I covers only the initial assessment of the affected crew member to define his or her medical condition, and completion of appropriate initial treatment to stabilize the crew member. While the affected crew member is being assessed, he or she is not able to perform any assigned tasks, thus Functional Impairment during this phase is considered 100%. In the untreated case, there is no diagnosis performed or treatment given, therefore Functional Impairment and Duration will always be "not applicable".

[2]Clinical Phase II: On-going Treatment and Convalescence- During clinical phase II, the affected crew member is receiving any appropriate follow-on treatment for his or her medical condition to allow the crew member to recover as much as he or she is able to recover in the ISS environment. Clinical phase II also encompasses relapses or reoccurrences of the same original medical condition in clinical phase I necessitating additional treatment or recovery time due to unsuccessful primary treatment response. The duration in Clinical Phase II is expressed in minimum, most likely (ML) and maximum hours. This was updated for future capabilities in IMM but is currently not being used by the model.

[3]Clinical Phase III: Recovered/Mission End State- Clinical phase III is reached once the affected crew member has recovered from the medical condition as much as he or she is able to recover in the ISS environment. This may or may not be recovery from the given medical condition to the full extent possible. If this "recovered" state results in an evacuation or loss of the crew member, this will be noted in the mission end state results.

*Functional Impairment (FI) is a measure of the affected crew member's health and performance ability.

**Two mission end state results are addressed in the CliFF: 1) Evacuation (EVAC) - crew and patient are evacuated from the spacecraft due to the medical condition, and 2) Loss of crew (LOCL) - death of affected crew member due to medical condition. EVAC is considered as an end state result if any of the following criteria are met: 1) potential LOCL, 2) potential significant permanent impairment, or 3) potential intractable pain. Probability distributions are assigned for each range of values within the Table of Treatments and Outcomes.

Refer to the Integrated Medical Model Technical Document for more information on how risk is reported by the IMM, Crew Health Index (CHI) and Quality Adjusted Mission Time calculations.

Definition and Probability of Best and Worst Case Scenario: (includes definitions of best and worst case scenarios and identifies the probability of those scenarios.)

Scenario Comments

Best case scenario is defined as mild diarrhea that resolves spontaneously, or with one dose of medication.

Worst case scenario is defined as copious, severe and prolonged diarrhea that may lead to dehydration and electrolyte imbalance, and requires treatment with intravenous fluids.

Infectious diarrhea and dehydration causing hypovolemic shock are addressed in the Gastroenteritis and the Hypovolemic Shock CliFFs respectively.

The **percentages of how often best versus worst case scenario occur b**ased on the Real World Systems data there were no worst cases so to integrate this data into the BC/WC percentage the algorithm developed with the original data set was used for all the medical events in both data sets. Therefore, if the next case is a worst case we would 1/41 or 2% of cases as worst cases. If the next case is best case, we would have 41/41 or 100%. Thus the percentage for Worst case is 0-2% (Saile L., 2017)

Best Case Comments

Diarrhea's functional impairments (FI) calculation follows the IMM mild non-space adaptation template. Colonic & Rectal Disorders ratings are based on Table 6-5, p-114. (American Medical Association, 2008)

By definition in Clinical Phase I, FI is 100%. Duration of physical exam as described in ISS checklist for the best case scenario is estimated as 15 minutes. During Clinical Phase II, FI is estimated to be 0 to 9%. Duration is estimated from 0 to 24 hours, In Clinical Phase III, full recovery is expected and FI is 0%. By definition EVAC and LOCL are not expected for the best case scenario.

Worst Case Comments

Diarrhea's functional impairments (FI) calculation follows the IMM mild non-space adaptation template. Colonic & Rectal Disorders ratings are based on Table 6-5, p-114. (American Medical Association, 2008)

By definition in Clinical Phase I, FI is 100%. Duration of physical exam and IV procedure, as described in ISS Medical Checklist, is estimated as 30 minutes. During Clinical Phase II, FI is estimated to be 1 to 20%. Duration is estimated as 24 to 120 hours (1-5 days), based on in-flight data. (Walton, 2010) In Clinical Phase III, full recovery may or may not occur and FI is estimated to be 0-9%. Abdominal pain with bloody diarrhea requiring hospitalization has occurred in the astronaut corps on the ground. Class IIC, manageable with HMS but may necessitate emergent evacuation if condition does not improve or worsens. (Johnston, 2008) To allow for uncertainty EVAC is estimated at 0-1%. By definition, LOCL is not expected for this condition.

Untreated Best Case Comments

Diarrhea's functional impairments (FI) calculation follows the IMM mild non-space adaptation template. Colonic & Rectal Disorders ratings are based on Table 6-5, p-114. (American Medical Association, 2008)

During Clinical Phase II, FI is estimated to be 1 to 20%. Duration is 0 to 24 hours, similar to the treated best case scenario. In Clinical Phase III, recovery may or may not occur without treatment. FI is estimated to be 0-9%. By definition, EVAC and LOCL are not expected for this condition.

Untreated Worst Case Comments

Diarrhea's functional impairments (FI) calculation follows the IMM mild non-space adaptation template. Colonic & Rectal Disorders ratings are based on Table 6-5, p-114. (American Medical Association, 2008)

During Clinical Phase II, FI is estimated to be 12 to 38%. Duration is estimated as 24-120 hours (1-5 days), similar to the treated worst case scenario. In Clinical Phase III, recovery is unlikely and FI is estimated to be 1-38%. Dehydration without available treatment may require EVAC. To allow for uncertainty EVAC is estimated at 0-100%. LOCL is not expected for this scenario.

Treatment and Options Level of Evidence (LOE)

The IMM level of evidence appropriate assessment of the quality of the IMM input data. Since IMM incorporates input data from a wide variety of sources including astronaut population, terrestrial or analog populations, and external models, an innovative approach to assess the quality of input data was required. Information obtained from the astronaut population and/or space flight is the more relevant so it is assigned the highest level of evidence and less relevant data sources are assigned a lower level of evidence.

Citation	LOE Value	LOE Category
American Medical Association, 2008	3	FI
Johnston, 2008	2	EVAC
Saile L., 2017	1	BCWC

The Resource Table (RT)

Resource	Units Required Best Case	Units Required Worst Case	Units Available At Start Of Mission	Consumable	Essential	Rationale
Blood Pressure Cuff (regular, large)	0	1	2	No	Yes	Measure blood pressure
Blood Pressure Monitor	0	1	1	No	Yes	Monitor blood pressure
BZK wipes	0	1	60	Yes	No	Cleanse skin.
Gauze pads (4x4)	0	2	50	Yes	No	To absorb blood or fluids from skin
Imodium (loperamide HCL) 2 mg tablet	1	16	40	Yes	Yes	Anti-diarrhea
IV administration set	0	1	3	Yes	Yes	IV Fluids infusion
IV Cap	0	1	5	Yes	No	To attach IV fluids to Y-type catheter
IV Catheter (18G, 20G, or 22G)	0	1	14	Yes	Yes	IV fluid administration
IV Fluid 1L (1000mL)	0	2	5	Yes	Yes	To replenish fluids
IV Fluid Air Filter	0	1	3	Yes	No	To filter air from IV line
IV pressure infuser	0	1	1	No	No	IV Fluids infusion
Medical tape	0	0.03	5	Yes	No	Single-coated tape pressure adhesive tape
Nitrile gloves (large, medium, and small) (pair)	0	1	30	Yes	No	Personal Protective equipment
Sharps container	0	1	40	No	No	To dispose of medical waste such as used medical needles, scalpels, IV catheters, razors, vials
Thermometer	1	1	1	No	No	To measure temperature
Tourniquet	0	1	1	No	No	To stop blood flow and engorge vein, this facilitates IV insertion

Resource Comments

The table was revised on 8/16/11. We added water as a resource and rationales. Oral electrolyte solution, normally used before landing, is available for use at the discretion of the Flight Surgeon on console.

The ISS Medical Checklist includes Diarrhea as a medical condition. All resources included in the resource table are available on board (Mission Operations Directorate (MOD), 2011).

Dehydration causing hypovolemic shock is addressed in the Hypovolemic Shock CliFF. Infectious diarrhea is addressed in the Gastroenteritis CliFF.

Comparison of ISS Med Checklist procedures versus clinical guidelines

Practice guidelines for acute diarrhea recommend to assess hydration, document duration, fever and cramping, rehydration volume and other symptomatic treatment. Fecal analysis if severe, bloody or persistent diarrhea. (Farthing, 2008) ISS Medical Checklist treatment is similar to terrestrial clinical guidelines with the exception of fecal analysis is not available on board.

Required Resources Level of Evidence (LOE)

The IMM level of evidence appropriate assessment of the quality of the IMM input data. Since IMM incorporates input data from a wide variety of sources including astronaut population, terrestrial or analog populations, and external models, an innovative approach to assess the quality of input data was required. Information obtained from the astronaut population and/or space flight is the more relevant so it is assigned the highest level of evidence and less relevant data sources are assigned a lower level of evidence.

Citation	LOE Value	LOE Category
NASA Mission Operations Directorate (MOD), 2011	2	Resources

Level Of Evidence

Input Data	LOE Average
Incidence	1
Functional Impairment	3
Best Case / Worst Case	1
EVAC / LOCL	2
Resources	2
QUALITY OF EVIDENCE	**1.8**

Description	Range
Excellent	1-2
Good	2.1-3
Fair	3.1-4
Poor	4.1-5

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