Urinary Tract Infection Cliff

Branch Baseline

Urinary tract infection (UTI) can include infections of the upper and lower urinary tract. In adults from the ages of 20-50 they are 50 fold more common in women. Risk factors for females include a history of recurrent UTIs and for males a history of recurrent prostate disease. Symptoms include dysurea, urinary frequency, urgency, occasionally incontinence. It may also accompanied by cloudy and foul-smelling urine, pain in the lower abdomen or flank, and fever. Urine reagent dipstick urinalysis will confirm positive for leukocyte esterase, nitrates, and sometimes hemoglobin. Complications include pylonephritis. Treatment consists of oral hydration, antibiotics and symtomatic relief. UTIs have been reported in the US space program. (Jones, 2008)

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

Male Data Characteristics	
Events:	5
Person Years:	37.31
Space Flight Incidence Rate (Events / Person Years):	5 / 37.31 = 0.13401232913428

Female Data Characteristics	
Events:	7
Person Years:	8.18
Space Flight Incidence Rate (Events / Person Years):	7 / 8.18 = 0.855745721271394

Incidence Comments

The source of model incidence data is a compliation of available in flight medical events (Walton, 2010). The combined incidence for both femail and male is 9 total cases during 27.36 person-years of space flight, which equals 0.33.

Integrated the real world system incidence data. Added 1 ISS and 1 STS event to the female incidence. Added 1 STS event to the male incidence. Added 4.47 to the persons years in the female incidence for a total of 8.18 and 13.7 person years to the male incidence for total of 37.38 person years (Saile, 2017).

Updated the Person-Years based on the revised real world system integrated incidence data. The integrated person years changed from 3.61 to 3.60 so the conditions person years changed from 37.35 to 37.31 (Saile L., 2017).

Information Regarding Prevention

Information regarding Prevention

Disqualifying events in the genitourinary category include disease, injury, or other disorders of the kidneys or GU tract that could require emergency medical treatment or interfere with successful mission completion; history of prostatitis or evidence of prostatic hypertrophy or other significant prostatic diseases interfering with micturition and potentially requiring emergency medical treatment; and any disabling disorders of the reproductive system or associated anatomical structures that could potentially require emergency medical care (International Space Station Program Medical Standards for ISS Crewmembers Working Group, 2009).

Vehicle requirement(s): Conditions affecting urinary health are pre-launch, launch, and entry suit, (Jones, 2008).

Other: Mission schedules, inadequate fluid intake, and redistribution of body fluids may affect urinary output. Some medications used for motion sickness may cause urinary retention or have anticholinergic side effects (Jones, 2008). The ISS Medical Checklist side effects includes urinary retention for Atropine, Vicodin and Metaxalone (Skelaxin) (International Space Station Program Medical Standards for ISS Crewmembers Working Group, 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

Incidence data not included in the model

The model pulls the incidence information from the IMM database ... the information shown below does not go into the model.

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

Distribution Data	
Incidence:	Gamma
Occurrence:	Poisson

Data Characteristics	
Events:	9
Person Years:	27.36
Space Flight Incidence Rate (Events / Person Years):	9 / 27.36 = 0.328947368421053

Incidence Comments

Overall incidence 9 events/27.36 person-years for inflight events is calculated based on two separate rates: male 4 events/23.65 years, and female 5/3.71 years.

(Walton, 2010)

Alternative Incidence Data

There is no national surveillance system describing prevalence and incidence across all urologic diseases (Litwin MS, 2007). Various governmental and non-governmental agencies in the United States maintain data sets that can provide useful health statistics. In the NIH's Urologic Diseases of America is noted that the prevalence rates in the Veterans Administration (VA) data are much lower than those in National Health National Health and Nutrition Examination Survey (NHANES) because the VA identifies only UTIs for which patients sought medical attention in one year, whereas NHANES relies on self-reported UTI over a lifetime, i.e. prevalence (Griebling, 2007). Also, VA offers the most recent results.

The total frequency of UTI diagnosis for outpatient care is 2,334 for male and 5,552 for female. While the inpatient hospital stays by adults with urinary tract infection listed as primary diagnosis, stratified by gender and age were: 35-44 age cohort, count 17,009, rate 75, 95% CI (71–79%); 45-54 age cohort, count 16,633, rate 89, 95% CI (85–93); 55-64 age cohort, count 18,375, rate 150, 95% CI (144–157) for females. Rate per 100,000 based on 2000 population estimates from Current Population Survey (CPS) (Griebling, 2007).

35-44 age cohort, count 8,764, rate 40, 95% CI (38–42%); 45-54 age cohort, count 11,165, rate 63, 95% CI (59-66); 55-64 age cohort, count 13,360, rate 120, 95% CI (113–126) for males. Rate per 100,000 based on 2000 population estimates from Current Population Survey (CPS), (Griebling, 2007).

The hospitalization rates for UTI, listed as primary diagnosis, based in 2000 population estimates were for females 35-44 0.00075, 45-54 0.00089; and 55-64 0.0015. For males 0.0004; 0.00063, and 0.0012 respectively. These rates amount to less than 1% of the total number of UTI cases, so we are estimating the risk of evacuation to be 0 to 1%

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 %: 84.62 - 92.31)	100	0.33	0 - 9	72 - 120 - 168	0	0	0
ISS-based Treatment (worst case scenario %: 7.69 - 15.38)	100	0.33	1 - 19	240 - 288 - 336	0 - 9	0 - 1	0
Untreated Best Case	0	0	1 - 19	72 - 120 - 168	0 - 9	0	0
Untreated Worst Case	0	0	11 - 29	240 - 288 - 336	1 - 29	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

The **best case scenario** is Urinary Tract Infection (UTI) with mild symptoms and responds to first line antibiotics.

The **worst case scenario** is UTI with moderate to severe symptoms, requiring second line antibiotics.

Percentages of how often best versus worst case scenarios occur: based on Real World System data set, there were 3 events and 1of them were worst case. Since we now have worst case scenarios, which did not have before, we can use the empirical data so the worst case scenario would be 33.33% (1/3). Thus the best case scenarios would be 66.67% (2/3) (Saile L., 2017).

Best Case Comments

During **Clinical Phase I,** Functional Impairment (FI) is 100%. Following ISS procedures for diagnosis is 20 minutes. FIs are derived from Table 7-4, Bladder Disease, page 139 of the Guides to the Evaluation for Permanent Impairment (American Medical Association, 2008). For detailed description of grading refer to the CliFF Appendix. During **Clinical Phase II,** FI is estimated to be 0 to 9%. BC duration of symptoms is expected for 3-7 days depending on response to treatment. (International Space Station Integrated Medical Group, 2006). Updated clinical guidelines recommend 3 days treatment for women and 7 days for men. (Orenstein, 2009), (ECRI Institute, 2009). In this scenario, UTI will resolve in **Clinical Phase III** and FI is 0%. EVAC or LOCL has never occurred in flight. It is not estimated to occur in the best case scenario. (Inflight Compilation Lockdown, 2008).

Worst Case Comments

During **Clinical Phase I,** FI and duration are similar to the best case scenario. FIs are derived from Table 7-4, Bladder Disease, page 139 of the Guides to the Evaluation for Permanent Impairment (American Medical Association, 2008). For detailed description of grading refer to the CliFF Appendix. During **Clinical Phase II,** FI is estimated to be 1 to 19%. Duration is estimated to be 10 to 14 days. (Orenstein, 2009) In the worst case scenario, UTI may partially resolve in **Clinical Phase III** and FI is 0 to 9%. Based on terrestrial data (Griebling, 2007) (Griebling, 2007). EVAC is estimated from 0 to 1% of UTIs requiring hospital admission for the worst case scenario. LOCL is unlikely to occur.

Untreated Best Case Comments

FIs are derived from Table 7-4, Bladder Disease, page 139 of the Guides to the Evaluation for Permanent Impairment (American Medical Association, 2008). For detailed description of grading refer to the CliFF Appendix. During **Clinical Phase II,** FI is estimated to be 1 to 19%. Duration may be from 14 to 20 days. (Orenstein & Wong, 2009). In the best case scenario, UTI may resolve without treatment in **Clinical Phase III** and there is 0 to 9% FI. EVAC and LOCL are not likely to occur.

Untreated Worst Case Comments

FIs are derived from Table 7-4, Bladder Disease, page 139 of the Guides to the Evaluation for Permanent Impairment (American Medical Association, 2008). For detailed description of grading refer to the CliFF Appendix.

During **Clinical Phase II,** FI is estimated to be 11 to 29%. The duration is estimated to be 10 to 14 days (Orenstein & Wong, 2009). By definition there is no treatment available in this scenario. During **Clinical Phase III** UTI will not resolve without treatment and FI is estimated in 1 to 29%. Risk of worsening infection exists and EVAC is estimated in 0 to 100 % to account for uncertainty. LOCL is not likely to occur

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
Griebling, 2007	4	EVAC
Saile L., 2017	1	BCWC

Additional Comments

We searched PubMed using the terms: Urinary Tract Infection (UTI), UTI Complicated, UTI uncomplicated, UTI female, and UTI male.

The Resource Table (RT)

Resource	Units Required Best Case	Units Required Worst Case	Units Available At Start Of Mission	Consumable	Essential	Rationale
Bactrim DS (Sulfamethoxazole/Trimethoprim) 800 mg/160 mg tablet	14	0	40	Yes	Yes	Antibiotic, first line
Cotton swabs	1	1	6	Yes	No	To collect urine sample
Levaquin (levofloxacin) 500mg	0	7	50	Yes	Yes	Antibiotic, third line
Motrin (Ibuprofen) 400mg	0	9	400	Yes	Yes	Pain relief
Nitrile gloves (large, medium, and small) (pair)	1	1	30	Yes	No	Personal Protective equipment for CMO
Thermometer	1	1	1	No	No	To measure temperature
Urine chemstrips	2	2	10	Yes	Yes	Urine test for ph, leukocytes, protein, glucose, ketones, blood, and nitrites
Urine Color Chart	1	1	1	No	No	To interpret chemstrips.

Resource Comments

Updated clinical guidelines recommend 3 days treatment for women and 7 days for men, (Orenstein, 2009), (ECRI Institute, 2009)while ISS recommended treatment is 7 days. Resources reviewed and updated based on new ISS Medical Kit (Mission Operations Directorate (MOD), 2011).

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	4
Resources	2
QUALITY OF EVIDENCE	**2.2**

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

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