Respiratory Infection Cliff

Branch Baseline

Respiratory tract infections in this Clinical Finding Form include the common cold, bronchitis and pneumonia.

Upper respiratory tract infection (URI) represents the most common acute illness evaluated in the outpatient setting. The common cold is typically a mild, self-limited, catarrhal syndrome of the nasopharynx. URIs involve direct invasion of the mucosal lining the upper airway. Person-to-person spread of viruses accounts for most URIs. (Meneghetti, 2011)

Bronchitis is characterized by inflammation of the bronchial tubes or bronchi, the air passages that extend from the trachea into the small airways and alveoli. Acute bronchitis is manifested by cough and, occasionally, sputum production that lasts for no more than 3 weeks. (Fayyaz, 2011)

Pneumonia can be defined as inflammation of the lung parenchyma, characterized by consolidation of the affected segment and a filling of the alveolar air spaces with exudates, inflammatory cells, and fibrin. Infection by bacteria or viruses are the most common cause. (Kamangar, 2011)

Respiratory infections have been reported in space in spite of efforts to mitigate this risk with a 7 day pre-launch quarantine. The diagnosis can be challenging since similar symptoms have been attributed to a cephalad fluid shift and the dry spacecraft cabin atmosphere. Establishing the diagnosis of pneumonia posses another unique challenge due to reliance on stethoscope auscultation possibly by a non-physician CMO in a noisy cabin environment. Susceptability to infection is increased due to an impaired immune response seen in astronauts during space missions. (Marshburn, 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

Data Characteristics	
Events:	35
Person Years:	45.49
Space Flight Incidence Rate (Events / Person Years):	35 / 45.49 = 0.76939986810288

Incidence Comments

There have been 33 events of respiratory irritation/respiratory infection that have been reported in space flight. (In-flight Compilation Lockdown revised, 2010)

All events have been mild and uncomplicated. There were 2 respiratory irritation events of environmental etiology, i.e. fiberglass and dry gases; 15 cough events and 16 "respiratory infections", including 7 “head colds.” Of note, pharyngitis and sinus infections are not included in this incidence rate. (Walton, 2010)

Added 2 events and 18.17 person years based on the real world systems incidence information (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 nose, sinuses, mouth, and throat category include: Deformities, injuries, or destructive diseases of the mouth, nose, throat, pharynx, or larynx that interfere with breathing, speech, mastication, and/or the swallowing of ordinary food, unless surgically corrected with normal function restored. In the lungs and chest wall category: any condition of the lungs, pleura, mediastinum or chest wall that could interfere with performance of duties; pulmonary tuberculosis; history of untreated spontaneous pneumothorax or pneumomediastinum; chronic obstructive pulmonary disease, e.g. chronic bronchitis or emphysema, with evidence of pulmonary dysfunction of significant severity so as to cause functional impairment or increased risk for pulmonary barotrauma; current asthma of any degree; bronchiectasis; pulmonary blebs, bullae or cysts; abscess of the lung; chronic or acute mycotic or protozoal infection of the lung, history of pulmonary embolus; history of pleural effusion of unknown etiology; active hemoptysis. In general: any medical condition that, in the judgment of the MSMB, may compromise mission operations, performance of duties, or crew health or safety. In the infectious diseases category: acute or chronic infectious diseases, until appropriately treated that might compromise mission operations, performance of duties, or crew health or safety. (International Space Station Program, 2009)

Other

Pre-flight quarantine program was established to limit viral or bacterial infections to crew members; however, breaches are possible. Pulmonary problems unique to space flight include exposure to exotic atmospheric and environmental contaminants which may cause irritation of the upper airways or disruption of pulmonary capillary and alveolar integrity. Pulmonary infections do not seem to occur at a higher rate in space flight than on Earth. (Marshburn, 2008)

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 185 respiratory diseases during the 1963-73 period with an illness rate of 0.07 and 0.03; for the 1963-67 and 1968-73 periods respectively. There were a total of 80 pneumonia events; causing 386 sick days, mean duration 4.8 days; 43 upper respiratory infection events (URI), with 87 sick days; mean duration 2.02 days; 36 acute bronchitis events, with 107 sick days; mean duration of 3 days; all during the 1963-1973 period. (Tansey, 1979)

Incidence rates for the period 1963-1967 and 1968-1973 were 0.02555 (0.07 *365 / 1000) and 0.01095 (0.03 *365 / 1000) person years. The average of these two incidence rates is 0.01825 per person-years. Respiratory infections (159/185) accounted for 86% of the respiratory disease events, or a rate of 0.015695 person-years. URI include ear nose and throat (ENT). Pneumonia and bronchitis accounted for 63% (116/185) of respiratory events. Incidence rate for respiratory infections, excluding ENT is 0.0114975 person-years. Seven EVACs occurred but there is no information by condition.

Thomas reported on health of US Navy submarine crews during periods of isolation. There were 55 events of upper respiratory infections among officers and 502 among enlisted men. The incidence rate for respiratory infection was 9.5 for officers and 9.6 for enlisted crew, per 100 person years. Effect of illness was minimal 0.75 (officers) to 1 day (enlisted men). Digestive illness was 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 space program participants. 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 0.093 (9.3/100) and includes ICD9 codes 460-519. We cannot segregate the pneumonia/bronchitis data.

Nice reported on the nature of medical communications and Medevacs among Navy personnel. A total of 752 medical communications and 743 Medevacs were documented. Respiratory conditions are not included with a percentage in the list of Medevacs. There was a significant higher probability of a Medevac following a communication if the diagnosis was related to injury, digestive system or mental problems. (Nice, 1987)

A study was conducted to analyzed incidence and risk factors for acute respiratory illness (ARI) using self-report data from two sources collected from troops deployed to Iraq, Afghanistan and the surrounding region during 2005-2006. Overall, 39.5% reported having at least one ARI. Of these, 18.5% sought medical care and 33.8% reported having decreased job performance. Of those reporting respiratory infections, 33.8% (n = 377) reported the respiratory illness decreased job performance. Fourteen percent (n = 155) of those with self-reported respiratory infections were confined to quarters (given bed rest) or put on light duty (restricted work) and 1.2% (n = 13) reported requiring hospitalization due to the respiratory infection. The rate of self-reported ARI was 15 episodes per 100 person-months among those taking the voluntary survey, (95% CI 14.3–15.6), and 24.7 episodes per 100 person-months among those taking the clinic health questionnaire, (95% CI 23.2–26.5). Negative binomial regression analysis found female sex, Navy branch of service and lack of flush toilets to be independently associated with increased rates of ARI. Deployment to Operation Iraqi Freedom, increasing age and higher rank were also positively associated with ARI risk. This rate is considerably higher compared to an expected acute respiratory illness rate of circa10% for those seeking medical attention among a military population in garrison (at home base) for a similar time period in the United States. Those with severe infections may have been medically evacuated from theater and would not be available to participate in our study. Duration of illness was 4 to 7 days. (Soltis, 2009) The estimated annual rates are 1.8 (15 * 12 / 100) for the survey to 2.97 (24.7 * 12 / 100) for the clinical questionnaire., 95% CIs are 1.71-1.87 (14.3 & 15.6 * 12 / 100) and 2.78-3.18 (23.2 & 26.5 * 12 / 100) respectively. A study was conducted to identify trends of selected disease and non-battle injuries (NBI) incidence among US military personnel deployed in ongoing military operations in Southwest Asia and the Middle East. Participants completed an anonymous questionnaire concerning diarrhea, acute respiratory illness (ARI), and NBIs. ARI for operations Iraqi Freedom and Enduring Freedom have been reported in 69% of deployed personnel, with 17% of them seeking medical care. Overall ARI incidence among troops deployed to the region between April 2006 and March 2007 was estimated at 7.1 cases, 95% Confidence Interval (CI) 6.4, 7.8 per 100 person-months. ARI rates remained relatively unchanged across time. Gender, rank, military component and unit type, and deployment history were not found to be associated with differential ARI rates. (Riddle, 2008) The incidence rate for acute respiratory infections is 0.852 (7.1* 12 / 100), CI 0.768 - 0.936 (6.4 & 7.8 * 12 / 100).

Non-Analog Populations

Incidence of URIs for the United States population is challenging to estimate because most cases are untreated and are not reported. URIs are the most common infectious illness in the general population. URIs are the leading reasons for people missing work or school, and they represent the leading acute diagnosis in the office setting. The incidence of the common cold varies by age. Adolescents and adults have approximately 2-4 colds a year. (Meneghetti, 2011)

Acute lower respiratory tract infections cause more disease and death than any other infection. More than 3 million cases occur annually in the United States. Pneumonia is more prevalent during the winter months and in colder climates. (Kamangar, 2011)

Bronchitis is one of the top conditions for which patients seek medical care. In one study, acute bronchitis affected 44 of 1000 adults annually, and 82% of episodes occurred in fall or winter. Although found in all age groups, acute bronchitis is most frequently diagnosed in children younger than 5 years. By gender bronchitis affects males more than females. (Fayyaz, 2011)

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 %: 97.22 - 100)	100	0.25	0 - 9	96 - 132 - 168	0	0	0
ISS-based Treatment (worst case scenario %: 0 - 2.78)	100	0.25	2 - 23	168 - 204 - 240	0 - 10	0 - 1	0
Untreated Best Case	0	0	2 - 23	96 - 132 - 168	0 - 10	0	0
Untreated Worst Case	0	0	11 - 40	168 - 204 - 240	2 - 40	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 defined as a respiratory irritation or infection, common cold or mild bronchitis, that resolves spontaneously.

The worst case scenario is defined as a respiratory infection, bronchiolitis or pneumonia, that requires treatment.

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 13/425 or 3% of cases as worst cases. If the next case is best case, we would have 12/425 or 3%. Thus the percentage for best case is 97% (Saile L., 2017)

The previous BC and WC scenario percentages also were determined using space flight data and were the same with the RWS data integration. (Walton, 2010) We assume all cases have been best cases. If the next case is a worst case (1/34) 3% would be worst cases. If the next case is a best case 0% would be worst cases. Our estimate for worst case scenario is 0 to 3 %. Thus, the best case scenario is 97-100%

Septic Shock is addressed in the Sepsis Clinical Finding Form.

Best Case Comments

Respiratory Infection's functional impairments (FI) calculation follows the IMM mild non-space adaptation template. Pulmonary dysfunction ratings are based on Table 5-4, p.88 (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 to be 15 minutes. During Clinical Phase II, FI is estimated at 0 to 9%. Duration is estimated to be from 96 to 168 hours (4-7 days). (Meneghetti, 2011) In Clinical Phase III, by definition, full recovery is expected. FI is 0%; EVAC and LOCL are not expected for the best case scenario.

Worst Case Comments

Respiratory Infection's functional impairments (FI) calculation follows the IMM mild non-space adaptation template. Pulmonary dysfunction ratings are based on Table 5-4, p.88 (American Medical Association, 2008).

By definition in Clinical Phase I, FI is 100%. Duration of physical exam as described in ISS checklist is estimated to be 15 minutes. During Clinical Phase II, FI is estimated at 2 to 23%. Duration is estimated to be from 168 to 240 hours (7-10 days) based on terrestrial and analog data. (Cunha, 2011) (Soltis, 2009) and duration of antibiotic treatment. In Clinical Phase III, full recovery may or may not occur and FI is estimated at 0-10%. Based on analog data (Soltis, 2009) EVAC is estimated at 0-1% for severe cases requiring hospital admission on the ground. LOCL is not expected for this condition.

Untreated Best Case Comments

Respiratory Infection's functional impairments (FI) calculation follows the IMM mild non-space adaptation template. Pulmonary dysfunction ratings are based on Table 5-4, p.88 (American Medical Association, 2008).

During Clinical Phase II, FI is estimated to be 2 to 23%. Duration is 96 to 168 hours (4-7 days), similar to the treated best case scenario. In Clinical Phase III, by definition, full recovery is expected and FI is 0%. EVAC and LOCL are not expected for the best case scenario.

Untreated Worst Case Comments

Respiratory Infection's functional impairments (FI) calculation follows the IMM mild non-space adaptation template. Pulmonary dysfunction ratings are based on Table 5-4, p.88 (American Medical Association, 2008).

During Clinical Phase II, FI is estimated to be 11 to 42%. Duration is estimated to be 168 to 240 hours (7-10 days), similar to the treated worst case scenario. In Clinical Phase III, recovery is unlikely without treatment. FI is estimated at 2-40%. EVACs and hospitalization have occurred in analog populations. (Soltis, 2009); (Belmont, 2010) To allow for uncertainty EVAC is estimated at 0-100% for the untreated worst case. 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
Soltis, 2009	2	EVAC
Belmont, Jr., 2010	2	EVAC
Walton, 2010	1	BCWC
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
Benzonatate (Tessalon Perles) 100mg	10	20	30	Yes	Yes	To suppress cough
Blood Oximeter	1	1	1	No	Yes	Monitors the oxygen saturation of a patient's blood
Dextromethorphan (Robitussin) 15mg capsule	10	20	20	Yes	Yes	Cough expectorant
Stethoscope	1	1	2	No	Yes	To listen to lung sounds
Thermometer	1	1	1	No	No	To measure oral temperature
Zithromax (Azithromycin) 250 mg	0	6	18	Yes	Yes	Treatment of infection

Resource Comments

The table was revised on 8/22/2011. We added Azithromycin.

The ISS medical checklist includes cough assessment and treatment. Bronchitis and pneumonia are not addressed in the checklist. Resources for these two conditions are based on terrestrial guidelines.

All resources included in the resource table are available on board (MOD, 2011).

Septic Shock is addressed in the Sepsis Clinical Finding Form.

Comparison of ISS Med Checklist procedures versus clinical guidelines

ISS medical checklist the recommended treatment for cough is similar to terrestrial guidelines. (Irwin, 2006)

Bronchitis and pneumonia are not addressed in the ISS checklist. Supportive treatment for bronchitis, is similar to the treatment for cough. (Braman, 2006) Pneumonia treatment is based on terrestrial guidelines. (Mandell, 2007)

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
Braman, 2006	3	Resources
Mandell, 2007	3	Resources

Level Of Evidence

Input Data	LOE Average
Incidence	1
Functional Impairment	3
Best Case / Worst Case	1
EVAC / LOCL	2
Resources	2.66666666666667
QUALITY OF EVIDENCE	**1.93333333333333**

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

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