Insomnia (space adaptation) Cliff

Branch Baseline

Insomnia is a sleep disorder resulting in as a lack of adequate restful sleep. It is usually characterized by complaints of difficulty sleeping, and or difficulty falling and staying asleep.

Early insomnia, space adaptation syndrome, due is usually attributed to the first 3-5 days of a space mission during adaptation to microgravity, very short and multiple light-dark cycles per work day, abnormally long work periods, variations in sleep-wake schedules, shift work, temperature, humidity and noise.

Prevention includes sleep-shifting pre-flight, private sleep quarters, noise-reducing ear plugs, window covers and blindfolds. Treatment includes short acting hypnotics. (Putcha, 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:	Yes
Incidence Type:	Proportion

Distribution Data	
Incidence:	Beta
Occurrence:	Bernoulli

Data Characteristics	
Occurrence Hour Range:	24 to 120
Peak Occurrence Hours:	24
Events:	381
Persons At Risk:	807
Space Flight Incidence Rate (Events / Persons at Risk):	381 / 807 = 0.472118959107807

Incidence Comments

Source of incidence data is a compliation of available in flight medical events (Walton, 2010). Incidence just for STS 0.194 to 0.500 events/person reported for shuttle missions.

Integrated real world system incidence data (Saile, 2017).

Updated the Persons at Risk based on the revised real world system integrated incidence data. The integrated RWS persons at risk from 144 to 143 so the conditions integrated iMED value went from 808 to 807. (Saile L., 2017)

Information Regarding Prevention

Preventive treatment(s): Non-pharmacological means include time-shifting during pre-flight, quarantine and use of noise reducing personal devices (ear plugs, etc) as a sleep aid.

Vehicle requirement(s): Sleep stations are provided on ISS for privacy and comfort, window covers are placed to allow for a dark environment, noise limits are more stringent for rest periods.

Contingency measure(s): An earth sleep baseline may be obtained for each individual astronaut. An individual confidence level is developed for each individual astronaut for sleep-related fatigue. These clinical ranges require regular re-evaluation and update. (NASA, 2007)

Other: Insomia may be a side effect of some of the medications in the ISS medical kits. The ISS Medical Checklist (International Space Station Integrated Medical Group, 2006) lists insomnia as a possible side effect for the following: Amiodarone, Celecoxib, Ciprofloxacine, Doxycycline, Metoprolol, Ofloxacin, Risperidone, Venlafaxine, and also some of the Russian only medications which are not listed here.

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

Ohayon determined that 19% of the population has complaints about insomnia and provides data stratified by age and type of complaint. Sample size was 25579 in 7 European countries. The 35-44 years old prevalence was 29.5%, 45-54 years old prevalence was 34.4% and 54-65 years old prevalence was 42%. Symptoms included were difficulty initiating sleep, difficulty maintaining sleep, early morning awakening, and non-restorative sleep. Symptoms have to be present at least 3 nights during a week. Primary insomnia, i.e. not related to other disorders was 3.9 % of 13,295 female and 2% of 12,284 male, with a 95% confidence interval, while total insomnia diagnoses were 8.6% for female and 4.6% for male. (Ohayon, 2009)

The Sleep in America Poll, conducted by the National Sleep Foundation, revealed that almost 50 percent of people surveyed had complaints of frequent insomnia, but only 6 percent were formally diagnosed. Moreover, approximately, 30 to 35 percent of respondents complained of nightly insomnia. This translates to 0.30-0.35 prevalence rate. (Buscemi, 2005)

NIH used the same definition criteria, and differentiated between chronic, i.e. over 30 days, and acute insomnia. (National Institutes of Health State of the Science, 2005)

The incidence rate of insomnia is noted to be higher in spaceflight than terrestrially. This is most likely due the spaceflight environment and its effect on human function and performance. Putcha and Marshburn both note factors affecting sleep are microgravity, ultra short light-dark cycles, abnormally long working period, deviations in sleep-wake schedule duration, shift work, and noise. (Putcha, 2008) Use of sleep medications in flight has increased from reported 15% in 1990 to 45% in 2008. (Slack, 2009)

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 %: 95.81 - 96.07)	100	0.5	0 - 5	0 - 36 - 72	0	0	0
ISS-based Treatment (worst case scenario %: 3.93 - 4.19)	100	0.5	1 - 10	72 - 96 - 120	0	0	0
Untreated Best Case	0	0	1 - 10	0 - 36 - 72	0	0	0
Untreated Worst Case	0	0	6 - 30	72 - 96 - 120	0	0	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 definition: Insomnia occurring within the first 5 days of spaceflight that is mild and is effectively treated with appropriate crew scheduling/sleep-shifting and the available hypnotic medications. All the insomnia cases of space adaptation reported to date appear to be consistent with this best case scenario definition. (Walton, 2010)

Worst case scenario: Insomnia space adaptation occurs with the first 5 days of spaceflight that is severe or refractory to treatment. There were no findings of severe or intractable space adaptation insomnia cases reported during space flight. (Walton, 2010)

Best Case/Worst Case Percentagess: Based on the Real World System's data set there were 82 events and of those events 15 were classified as worst case. Therefore, 81.71% of space adaptation insomnia cases will be best case and 18.29% will be worst case (Saile L., 2017).

Best Case Comments

During **Clinical Phase I**, Functional impairment (FI) is by definition 100% is derived from Table 13-6, page 329 of the "AMA Guides to the Evaluation of Permanent Impairment" (American Medical Association, 2008). Refer to Appendix A for description of grading. FI is estimated in 0 to 5%. Mild cases of insomnia should effectively respond to treatment within 72 hours, the **Clinical Phase II** or treatment phase will most-likely be less than 72 hours in duration**. Clinical Phase III**: FI is 0%. There should be no residual impairment for effectively treated mild cases of insomnia. Based on in-flight data there is no risk of EVAC or LOCL (Walton, 2010).

Worst Case Comments

The diagnosis and initial treatment of **Clinical Phase I** is similar to the "best case scenario". Functional impairment is derived from Table 13-6, page 329 of the "AMA Guides to the Evaluation of Permanent Impairment" (American Medical Association, 2008). Refer to Appendix A for description of grading**. Clinical phase II** or the ongoing treatment would presumably last longer and result in higher functional impairment, of 1 to10%. These cases of insomnia may require 72 hours to 120 hours to resolve. ISS Medical Checklist advises the crew to contact the surgeon if sleeping medications are required for more than 3 nights in a row. During **clinical phase III** insomnia resolves and FI is 0%. There is no risk of EVAC or LOCL (Walton, 2010).

Untreated Best Case Comments

Functional impairment is derived from Table 13-6, page 329 of the "AMA Guides to the Evaluation of Permanent Impairment" (American Medical Association, 2008). **Clinical phase II** functional impairment is estimated in 1 to10%. Untreated space adaptation insomnia may persist for up to 3 days. During **clinical phase III** insomnia resolves and impairment is 0%. There is no significant risk of EVAC or LOCL (Walton, 2010).

Untreated Worst Case Comments

Untreated worst case is severe untreated insomnia that may persist from 3 to 5 days. Functional impairment is derived from Table 13-6, page 329 of the "AMA Guides to the Evaluation of Permanent Impairment" (American Medical Association, 2008). Refer to Appendix A for description of grading. For **Clinical Phase II** FI is estimated in 6 to 30%. During **clinical phase III** untreated severe insomnia is expected to resolve and FI will return to 0%. There is no significant risk of EVAC or LOCL.

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
Walton, 2010	1	EVAC
Saile L., 2017	1	BCWC

Additional Comments

Pubmed search with keywords: insomnia and incidence, insomnia and epidemiology, insomnia and statistics yielded large amount of results. Articles were reviewed and incidence data were not found. Lack of incidence data on insomnia has also been reported by NIH (National Institutes of Health State of the Science, 2005) and Buscemi (Buscemi, 2005). We selected articles that included prevalence data.

The Resource Table (RT)

Resource	Units Required Best Case	Units Required Worst Case	Units Available At Start Of Mission	Consumable	Essential	Rationale
Zolpidem (Ambien) 5mg tablet	1	2	200	Yes	Yes	Sleep aid

Resource Comments

Both Ambien and Sonata are required recources for the treatment of insomnia. Crew members may choose either, based on personal preference and ground testing of these medications (MOD, 2011). In addition, preliminary validation of resource utilization incidates underforecasting of Sonata use by IMM.

Required Resources Level of Evidence (LOE)

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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	1
Resources	2
QUALITY OF EVIDENCE	**1.6**

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

Reference List

Reference
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