Sleep Disorder Cliff

Branch Baseline

Sleep disorder occurs following the first 5 days of space flight and is not related to space adaptation. Sleep disorders are not uncommon after space adaptation is completed. A combination of sleep shifts, workload and crew motivation have been attributed to causes of chronic sleep debt. (Marshburn, 2008) These may be treated with non-benzodiazipine hypnotics and melatonin. (Slack, 2009) Regular daily exercise is known to significantly contribute to good sleep hygiene. (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:	233
Person Years:	45.49
Space Flight Incidence Rate (Events / Person Years):	233 / 45.49 = 5.12200483622774

Incidence Comments

Source of incidence data is a compliation of the available in flight medical events (Walton, 2010).

Added 100 new medical events and 18.17 person years based on the real world system's incidence data (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)

Duplicate was found in the ISS Real World System events, thus 1 ISS event was removed.

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) for sleep aid.

Vehicle requirement(s): Sleep stations are provided on Station 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: Insomnia 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

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. Factors affecting sleep are microgravity, ultra short light-dark cycles, abnormally long working period, deviations in sleep-wake schedule duration, shift work, and noise. (Marshburn, 2008)

Use of sleep medications in flight has increased from reported 15% in 1990 to 45% in 2008 (Slack, 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. (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)

Ohayon determined that 19% of the population have complaints about insomnia and provides data stratified by age and type of complain. Sample size was 25579 in 7 European countries. 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 and Reynolds, III 952-60)

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 %: 98.72 - 99.15)	100	0.5	0 - 5	24 - 48 - 72	0	0	0
ISS-based Treatment (worst case scenario %: 0.85 - 1.28)	100	0.5	1 - 10	72 - 96 - 120	0 - 5	0	0
Untreated Best Case	0	0	1 - 10	24 - 48 - 72	0 - 5	0	0
Untreated Worst Case	0	0	6 - 30	72 - 96 - 120	1 - 30	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: Sleep disorders include insomnia that is not related to space adaptation and occurs after flight day 5. It can alsoinclude sleep shifting and sleep prophylaxis for Extravehicular Activities (EVAs). It is mild in nature. It can be effectively treated with appropriate crew scheduling/sleep-shifting and the available hypnotic medications. All inflight cases of sleep disorders appeared to meet these criteria.

Worst case scenario definition: As in the best case scenario, the criteria for sleep disorders apply. A small percentage of these cases in spaceflight might be severe or refractory to treatment.

Best Case/Worst Case Percentages: There were 98 events in the Real World System data. In this data set there were 2 WC so empirical data is being used to determine BC/WC percentages. Therefore, it is calcuated that 98% (96/98) of cases of sleep disorders will be best case and 2% (2/98) of cases of sleep disorders will be worst case (Saile L., 2017)

From CHS corrections of translation of incidence and best/worst case numbers, the total number of events were 233, of which 231 were best case. (There was 1 worst case event in ISS and 1 worst case event in STS). Using empirical data, as above, the best case is calculated as 99% (231/233) and the worst case as 1% (2/233).

Best Case Comments

ISS-based Treatment (best case scenario): During Clinical Phase I the duration is estimated to 30 mintures., Functional impairment (FI) is by definition 100% . FI is derived from from Table 13-6, Sleep and Arousal Disorders p 329, of the “AMA Guides to the Evaluation of Permanent Impairment”. During Clinical Phase II treatment will most-likely at least 24 hours but less than 72 hours in duration and 0 to 5% functional impairment. In Clinical Phase III there should be no residual impairment for effectively treated mild cases of insomnia. Based in our in-flight data there is no risk of EVAC or LOCL.

Worst Case Comments

ISS-based Treatment (worst case scenario): The diagnosis and initial treatment, Clinical phase I would be similar to the “best case scenario”, the ongoing treatment. In Clinical phase II would presumably last longer and result in higher functional impairment, of 1 to10%. FI is derived from from Table 13-6, Sleep and Arousal Disorders p 329, of the “AMA Guides to the Evaluation of Permanent Impairment” (American Medical Association, 2008). These cases of insomnia may require 72 to 120 hours to resolve. ISS Medical Checklist (International Space Station Integrated Medical Group, 2006) advises the crew to contact the surgeon if sleeping medications are required for more than 3 nights in a row. During clinical phase III, residual impairment of 0 to 5% occurs due to ineffective treatment or the ongoing use of sleeping medications. There is no risk of EVAC or LOCL (In-flight Compilation Lockdown revised, 2010).

Untreated Best Case Comments

Untreated best case: 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 at 1 to10%. Untreated best case late insomnia may will last at least 24 hours and may persist to 72 hours. During clinical phase III insomnia may not resolve with residual impairment of 0-5%. There is no significant risk of EVAC or LOCL.

Untreated Worst Case Comments

Untreated worst case: In Clinical Phase II the duration may last from 72 housrs to 120 hours and the functional impairment is assigned from 6 to 30% resulting from the potential to reduced alertness. This range is derived from Table 13-6, page 329 of the “AMA Guides to the Evaluation of Permanent Impairment” (American Medical Association, 2008). During clinical phase III untreated severe insomnia may persist so FI is estimated frrom 1 to 30% range. 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
Lopez, 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. We did not find incidence data during the articles review. 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 including 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 available resources for the treatment of insomnia on ISS. The crew may choose either based on personal preference and ground testing of these medications (MOD, 2011). Some of the preliminary validation of resources utlization indicates under-forecasting of Sonata use by IMM.

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	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

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