Headache (space adaptation) Cliff

Branch Baseline

Headaches that occur in the first 3-5 days in flight are usually attributed to space adaptation. The mechanism of these headaches is thought to be due to the cephalad fluid shifts that occur shortly after orbital insertion in microgravity. These headaches are considered self-limited and usually resolve within 72 hours along with other symptoms attributed to space adaptation. Oral analgesics are often recommended and seem to be helpful. Other endogenous or exogenous causes should always be considered whenever headaches occur during a mission. (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:	Yes
Incidence Type:	Proportion

Distribution Data	
Incidence:	Beta
Occurrence:	Bernoulli

Data Characteristics	
Occurrence Hour Range:	24 to 240
Peak Occurrence Hours:	24
Events:	281
Persons At Risk:	807
Space Flight Incidence Rate (Events / Persons at Risk):	281 / 807 = 0.34820322180917

Incidence Comments

Headache (Space Adaptation) includes headaches that began during Days 1 to 5 and for which no other attribution, such as CO or CO2 exposure, caffeine withdrawal, toxic exposure or DCS, had been determined. When a crew member took an analgesic and the reason indicated was headache, we counted that as a headache event. Source of incidence data is a compliation of available in flight medical events (Walton, 2010).

Integrated the 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

Disqualifying events in the neurological area include: Any post-traumatic syndrome manifested by changes in personality, deterioration of higher intellectual functions, anxiety, headaches, or disturbances of equilibrium; vascular, migrainous or cluster headache of sufficient severity or frequency to interfere with normal function or that might pose a risk to the mission. Frequent or severe headaches due to other causes also are disqualifying.

General disqualifying conditions: In general, any medical condition that, in the judgment of the Multilateral Space Medicine Board, may compromise mission operations or crew safety, or require urgent medical treatment while a resident on the ISS (International Space Station Program, 2009).

Other: Headache is listed as a side-effect of the following medications in the ISS medical checklist (International Space Station Integrated Medical Group, 2006): Adenosine, Ambien (Zolpidem), Bactrin (Sulfamethoxazole/trimethoprim), Benadryl (Dyphenhidramine), Ceftriaxone (Rocephin), Celebrex, Cimetidine (Tagamet), Decadron (Dexamethasone), Deltasone (Prednisone), Dexedrin (Dextroanphetamine), Diflucan (Fluconazole), Effexor (Venlafaxine), Entex PSE (Pseudoephedrine/Guaifenesin), Flagyl (Metronidazole), Flumazenil (Romazicon), Haldol (Haloperidol), Isoptin (Verapamil), Metaxalone (Skelaxin), Nitroglycerin, Norethindrone/Ethinyl Estradiol, Omeprazole (Prilosec), Ondansetron (Zofran), Oseltamivir (Tamiflu), Pseudoephedrine (Sudafed), Risperdal (Risperidone), Sertraline (Zoloft), Sonata (Zaleplon), and Valacyclovir (Valtrex).

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

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 %: 94.33 - 94.68)	100	0.25	0 - 10	1 - 4.5 - 8	0	0	0
ISS-based Treatment (worst case scenario %: 5.32 - 5.67)	100	0.25 - 1	3 - 18	1 - 60.5 - 120	0	0	0
Untreated Best Case	0	0	3 - 18	1 - 4.5 - 8	0	0	0
Untreated Worst Case	0	0	11 - 32	1 - 60.5 - 120	0	0 - 1.5	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 having an uncomplicated course of space adaptation syndrome-related headache, which resolves spontaneously or with minor symptomatic treatment.

The **worst case scenario** is defined as a severe space adaptation related headache poorly responsive to available treatment.

Percentages of how often best versus worst case scenarios occur Based on the Real World System data set there were 48 events and of those events 1 was the worst case. Since there is a worst case the percentage can be calculated from the empirical data. The worst case is 2.08% (1/48), while the best case is 97.92% (47/48) (Saile L., 2017).

Best Case Comments

Best case scenario: includes description of the medical conditions under the best case scenario. Along with explanation of how 1] the FI in all 3 Clinical Phases was derived 2] the duration in Clinical Phases I & II, and 3] the mission end-states and their percentages.

Headache is not included as a condition in the American Medical Association guides to the Evaluation of Permanent Impairment. The calculation of functional impairments (FI) follows the IMM standard template for space adaptation conditions; we combined two tables: Migraine and Complex Regional Pain Syndrome (Upper Extremity). Migraine ratings are based on Table 13-18, p.342 (American Medical Association, 2008). The ratings for Whole Person Impairment are in the same table. Complex Regional Pain Syndrome (CRPS-UE) gradings are based on Table 15-16, p. 454 (American Medical Association, 2008). The CRPS is converted to Whole person impairment based on table 15-1, page 385 (American Medical Association, 2008). Combined FI ratings are calculated using the Combined Values Chart as indicated in Appendix A, pp 604-606 (American Medical Association, 2008).

For **Clinical Phase I,** by definition FI is 100% and duration is estimated in 15 minutes to evaluate headache as described in the ISS medical checklist. During **Clinical Phase II,** FI is estimated in 0 to 10%, and duration is estimated in 1 to 8 hours considering it may take up to 2 doses for relief of headache as indicated in the ISS medical checklist.

During **Clinical Phase III,** headache (space adaptation) is expected to resolve and FI is 0%. Based in space flight data (In-flight Compilation Lockdown revised, 2010) EVAC and LOCL are not expected.

Worst Case Comments

The worst case scenario includes description of the medical conditions under the best case scenario and how the percentage was derived. Along with explanation of how 1] the FI in all 3 Clinical Phases was derived 2] the duration in Clinical Phases I & II, and 3] the mission end states and their percentages.

Headache is not included as a condition in the American Medical Association guides to the Evaluation of Permanent Impairment. The calculation of functional impairments (FI) follows the IMM standard template for space adaptation conditions; we combined two tables: Migraine and Complex Regional Pain Syndrome (Upper Extremity). Migraine ratings are based on Table 13-18, p.342 (American Medical Association, 2008). The ratings for Whole Person Impairment are in the same table. Complex Regional Pain Syndrome (CRPS-UE) gradings are based on Table 15-16, p. 454 (American Medical Association, 2008). The CRPS is converted to Whole person impairment based on table 15-1, page 385 (American Medical Association, 2008). Combined FI ratings are calculated using the Combined Values Chart as indicated in Appendix A, pp 604-606 (American Medical Association, 2008). For **Clinical Phase I,** by definition FI is 100%. Duration is estimated in 15 to 60 minutes to evaluate headache as described in the ISS medical checklist, which requires PMC and assessing VS for severe headaches. During **Clinical Phase II,** FI is estimated in 3 to 18%, and duration is estimated in 1 to 120 hours based on IMM assumptions that space adaptation syndrome occurs in days 1 to 5. During **Clinical Phase III,** headache (space adaptation) is expected to resolve and FI is 0%. Based in space flight data EVAC and LOCL are not expected (In-flight Compilation Lockdown revised, 2010).

Untreated Best Case Comments

Untreated Best Case scenario includes explanation of how 1] the FI in Clinical Phases 2 & 3 was derived, 2] the duration in Clinical Phase II and 3] the mission end states and their percentages. Duration is the same as for treated best case scenario.

Headache is not included as a condition in the American Medical Association guides to the Evaluation of Permanent Impairment. The calculation of functional impairments (FI) follows the IMM standard template for space adaptation conditions; we combined two tables: Migraine and Complex Regional Pain Syndrome (Upper Extremity). Migraine ratings are based on Table 13-18, p.342 (American Medical Association, 2008). The ratings for Whole Person Impairment are in the same table. Complex Regional Pain Syndrome (CRPS-UE) gradings are based on Table 15-16, p. 454 (American Medical Association, 2008). The CRPS is converted to Whole person impairment based on table 15-1, page 385 (American Medical Association, 2008). Combined FI ratings are calculated using the Combined Values Chart as indicated in Appendix A, pp 604-606 (American Medical Association, 2008).

During **Clinical Phase II,** FI is estimated in 3 to 18%, and duration is estimated in 1 to 8 hours similar to treated best case. During **Clinical Phase III,** headache (space adaptation) is expected to resolve and FI is 0%. Based in space flight data EVAC and LOCL are not expected.

Untreated Worst Case Comments

Untreated Worst case scenario includes explanation of how 1] the FI in Clinical Phases 2 & 3 was derived, 2] the duration in Clinical Phase II and 3] the mission end states and their percentages. Duration is the same as for treated worst case scenario.

Headache is not included as a condition in the American Medical Association guides to the Evaluation of Permanent Impairment. The calculation of functional impairments (FI) follows the IMM standard template for space adaptation conditions; we combined two tables: Migraine and Complex Regional Pain Syndrome (Upper Extremity). Migraine ratings are based on Table 13-18, p.342 (American Medical Association, 2008). The ratings for Whole Person Impairment are in the same table. Complex Regional Pain Syndrome (CRPS-UE) gradings are based on Table 15-16, p. 454 (American Medical Association, 2008). The CRPS is converted to Whole person impairment based on table 15-1, page 385 (American Medical Association, 2008). Combined FI ratings are calculated using the Combined Values Chart as indicated in Appendix A, pp 604-606 (American Medical Association, 2008).

During **Clinical Phase II,** FI is estimated in 11 to 32%, and duration is estimated in 1 to 120 hours, similar to treated worst case. During **Clinical Phase III,** headache (space adaptation) is expected to resolve and FI is 0%. Based on in-flight data, no EVAC has occurred for headache. In order to keep uncertainty and allow for the risk of headache being a symptom of a more serious neurological disorder, we are estimating 0 to 1.5% risk of EVAC, based on Ang's study that 1.5 (18/1276) of patients presenting to the ED with headache were admitted for a potentially serious condition, e.g. intracranial hemorrhage, stroke, TIA, and meningitis (Ang, 2009). Based in space flight data LOCL is not expected.

Of note, the International Headache Society describes migraine without aura lasting 4 to 72 hours, untreated or unsuccessfully treated. (Headache Classification Subcommittee of the International Headache Society, 2010)

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
American Medical Association, 2008	3	FI
American Medical Association, 2008	3	FI
Lopez, 2010	1	EVAC
Saile L., 2017	1	BCWC

Additional Comments

We searched PubMed using the key terms headache and space medicine, headache and astronauts, headache and microgravity, headache and hospitalization. Then we refined our search by relevance and date of publication.

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	Measure blood pressure
Motrin (Ibuprofen) 400mg	1	12	400	Yes	Yes	Pain relief
Thermometer	0	1	1	No	No	To measure temperature

Resource Comments

The ISS checklist recommends that if headache is particularly severe, or does not respond to any of the medications in Table 1, contact ground and schedule a PMC (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	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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