

Headache (Late) Cliff

Branch Baseline

Terrestrially tension headaches are the most frequent cause of headaches in general and the high workload of crewmembers during a mission makes tension headache a likely diagnosis for in-flight headaches after the first 5 days on orbit. (Marshburn, 2008) There have been several headache events in this category reported on orbit. Most have resolved within a couple hours, and were readily treatable with available medication. (Walton, 2010)

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:	73
Person Years:	45.49
Space Flight Incidence Rate (Events / Person Years):	$73 / 45.49 = 1.60474829632886$

Incidence Comments

Headache (Late) includes headaches that began after Day 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 compilation of available in flight medical events (Walton, 2010)

In STS There were 39 events for male and 5 for female crew members (Walton, 2010) in 23.65 and 3.71 person-years respectively (1.64 and 1.34 incidence), 1:0.81 ratio; which is different from terrestrial incidence 1:3 (Lyngberg, 2005)

Added 25 total medical events and 18.17 person years based on the real world system 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)

Decreased ISS from 17 to 16 events to account for the duplicate events in the ISS Real World System events.

Information Regarding Prevention

Selection criteria

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**)

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	2	Incidence
Saile L., 2017	1	Incidence

Alternative Incidence Data

Analog populations

Vein's study surveyed 17 ESA astronauts to assess clinical characteristics of headache. The sample size is small, but it classified the types of space headache by intensity making it the best available source. Majority of astronauts reported having disabling headaches while in space but not on earth. Age range was 28-58 years. There was no difference in occurrence of headache between short and long duration missions. The 12 astronauts with headaches (71%) reported a total of 21 events, nine during launch, nine during stay at the space station, one during EVA and one during landing. One severe event was reported during launch and none later. Mean headache duration was 98 minutes for stay at the space station. (Vein, 2009)

Russian MIR astronauts have reported headaches caused by environmental contamination and associated with fatigue. No primary headache was reported. {Gontcharov, 2005 2720 /id

Non Analog population

A longitudinal study of the incidence and risk factors for primary headache disorders was conducted in Denmark to assess the incidence of migraine and tension-type headache in a general population, during the period 1989–2001. Of 740 persons aged 25–64 years examined in 1989, 673 were eligible in 2001 and 549 (81.6%) participated. The overall incidence of frequent tension-type headache was 14.2 per 1,000 person-years (male: female ratio, 1:3). In total, there were 53 incident cases of tension-type headache among 337 subjects at risk. Both rates decreased with age. Annual incidence rates were calculated from cumulative incidence rates. To minimize diagnostic impurity, subjects with migraine in 1989 were excluded from the group at risk of tension-type headache. Incidence rates per person year and 95% confidence intervals (CI) by age were: 35-44 cohort 0.0128, 95% CI (0.0064 to 0.0197); 45-54 cohort 0.0135, 95% CI (0.0069 to 0.0205); 55-64 cohort 0.0035, 95% CI (0.0004 to 0.0125). (Lyngberg, 2005)

A study to determine clinical characteristics and outcomes of primary headaches in Denmark, reported that attack duration for episodic tension headache in 2001 was 30 minutes to 4 hours for 25.7%; 4 hours to 1 day for 53.3%; 1 to 3 days for 16.2 % and, more than 3 days for 4.8%. By intensity 25.9% of headaches were mild, 72.2% moderate and 1.9% severe. (Ashina, 2010)

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 %: 98.65 - 100)	100	0.25	0 - 10	1.5 - 12.75 - 24	0	0	0
ISS-based Treatment (worst case scenario %: 0 - 1.35)	100	0.25	3 - 18	1.5 - 36.75 - 72	0 - 10	0	0
Untreated Best Case	N/A	N/A	3 - 18	1.5 - 12.75 - 24	0 - 10	0	0
Untreated Worst Case	N/A	N/A	11 - 32	1.5 - 36.75 - 72	3 - 32	0	0

¹Clinical 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".

²Clinical 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.

³Clinical 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 a tension type headache, which resolves spontaneously or with minor symptomatic treatment. Late headache includes headaches occurring on or after the 6th flight day.

The **worst case scenario** is defined as a moderate or severe headache poorly responsive to available treatment.

Percentages of how often best versus worst case scenarios occur The previous percentages used were determined using Vein's and Ashina's studies. (Vein, 2009) (Ashina, 2010) Vein's study surveyed 17 astronauts; 71% of them reported headache. They had not suffered from headache on earth. The sample size is small, but it classified the types of space headache by intensity making it the best available source for space flight. No severe headaches were reported during stay at the space station. (Vein, 2009) Ashina provided clinical characteristics of episodic tension type headaches among 106 subjects terrestrially of which 1.9% reported severe headache. (Ashina, 2010)

Based 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 1/75 or 1% of cases as worst cases. If the next case is best case, we would have 75/75 or 100%. Thus the percentage for worst case is 0-1% (Saile L., 2017)

Best Case Comments

Headache is not included as a condition in the American Medical Association guides to the Evaluation of Medical Impairment. The calculation of functional impairments (FI) follows the IMM standard template for mild non-space adaptation conditions; we combined two tables: Migraine and Complex Regional Pain Syndrome - Upper Extremity (CRPS-UE). 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) ratings 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). Final FI ratings are calculated using the Combined Values Chart as indicated in Appendix A, pp 604-606 (American Medical Association, 2008). For further information refer to the ClIFF Appendix.

For **Clinical Phase I**, by definition FI is 100%. Duration is estimated in 15 minutes to evaluate headache as described in the ISS medical checklist for sick call. (Mission Operations Directorate (MOD), 2011) During **Clinical Phase II**, FI is estimated at 0 to 10%, and duration is estimated at 1.5 to 24 hours based on Vein's and Ashina's studies. (Vein, 2009); (Ashina, 2010)

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

Worst Case Comments

Headache is not included as a condition in the American Medical Association guides to the Evaluation of Medical Impairment. The calculation of functional impairments (FI) follows the IMM standard template for mild non-space adaptation conditions; we combined two tables: Migraine and Complex Regional Pain Syndrome - Upper Extremity (CRPS-UE). 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) ratings 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). Final FI ratings are calculated using the Combined Values Chart as indicated in Appendix A, pp 604-606 (American Medical Association, 2008). For further information refer to the ClIFF Appendix.

For **Clinical Phase I**, by definition FI is 100%. Duration is estimated in 15 minutes similar to the best case scenario. During **Clinical Phase II**, FI is estimated in 3 to 18%. Duration is estimated in 1.5 to 72 hours since it is poorly responsive to available treatment. During **Clinical Phase III**, headache (late) may or may not to resolve and FI is estimated at 0-10%. Based in space flight data, EVAC and LOCL are not expected. (Walton, 2010)(In-flight Compilation Lockdown revised, 2010)

Untreated Best Case Comments

Headache is not included as a condition in the American Medical Association guides to the Evaluation of Medical Impairment. The calculation of functional impairments (FI) follows the IMM standard template for mild non-space adaptation conditions; we combined two tables: Migraine and Complex Regional Pain Syndrome - Upper Extremity (CRPS-UE). 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) ratings 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). Final FI ratings are calculated using the Combined Values Chart as indicated in Appendix A, pp 604-606 (American Medical Association, 2008). For further information refer to the ClIFF Appendix.

During **Clinical Phase II**, FI is estimated in 3 to 18%, and duration is estimated in 1.5 to 24 hours, similar to treated best case. During **Clinical Phase III**, headache (late) may or may not to resolve and FI is estimated at 0-10%. Based in space flight data EVAC and LOCL are not expected.

Untreated Worst Case Comments

Headache is not included as a condition in the American Medical Association guides to the Evaluation of Medical Impairment. The calculation of functional impairments (FI) follows the IMM standard template for mild non-space adaptation conditions; we combined two tables: Migraine and Complex Regional Pain Syndrome - Upper Extremity (CRPS-UE). 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) ratings 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). Final FI ratings are calculated using the Combined Values Chart as indicated in Appendix A, pp 604-606 (American Medical Association, 2008). For further information refer to the ClIFF Appendix.

During **Clinical Phase II**, FI is estimated in 11 to 32%. Duration is estimated in 1.5 to 24 hours, similar to treated worst case. During **Clinical Phase III**, headache (late) may or may not to resolve without treatment and FI is estimated at 3-32%. Based on in-flight data, no EVAC or LOCL is expected.

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
Walton, 2010	1	EVAC
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
Blood Oximeter	0	1	1	No	Yes	To measure crew oxygen levels.
Blood Pressure Cuff (regular, large)	0	1	2	No	Yes	Measure blood pressure
Blood Pressure Monitor	0	1	1	No	Yes	Measure blood pressure
BZK wipes	0	1	60	Yes	No	To clean thermometer prior to stowage
Motrin (Ibuprofen) 400mg	0	15	400	Yes	Yes	Second line pain relief should first fail.
Thermometer	0	1	1	No	No	To measure temperature
Toradol (Ketorolac) 30mg/mL, 2mL single dose vial	0	4	3	Yes	Yes	For pain relief
Tylenol (Acetaminophen) 325 mg	2	6	150	Yes	Yes	Pain relief

Resource Comments

Headache is not included in the ISS Medical Checklist (2011) (Mission Operations Directorate (MOD), 2011). Simple analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) are recommended for the treatment of episodic tension type headache (TTH) in Europe (Bendtsen, 2010) while American clinical guidelines recommend the same treatment and aspirin. (Beithon, 2011) The resources included in the table are available on board.

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
Bendtsen, 2010	3	Resources
Beithon, 2011	3	Resources

Level Of Evidence

Input Data	LOE Average	Description	Range
Incidence	1.5	Excellent	1-2
Functional Impairment	3	Good	2.1-3
Best Case / Worst Case	1	Fair	3.1-4
EVAC / LOCL	1	Poor	4.1-5
Resources	3		
QUALITY OF EVIDENCE	1.9		

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