Headache (CO_2 induced) Cliff

Branch Baseline

A carbon dioxide induced headache results from the build up of ambient carbon dioxide. Several cases have been reported in the US space program. Ambient carbon dioxide levels above 2% are known to cause headaches and lethargy. The nominal levels recorded on US spacecraft have been 0.26%. It is thought that pockets of small poorly ventilated volumes in modules may be responsible. Headaches could also be a sign that at carbon dixoide scrubber system has failed. Symptoms typically resolve rapidly and spontaneously with improvement of intramodular airflow. Analgesics are available to be used as needed. (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:	69
Person Years:	45.49
Space Flight Incidence Rate (Events / Person Years):	69 / 45.49 = 1.51681688283139

Incidence Comments

CO_2 is a natural metabolic byproduct, exhaled at a rate of about 200 mL of CO2 per minute at rest and up to 4.0 L/min at maximal exercise (Williams, 2009). If not removed from the atmosphere of a closed environment, CO2 can accumulate quickly from respiratory sources alone. Other sources of CO2 include combustion, decay of organic matter, and fire suppression systems.

The effects of ambient carbon dioxide and exposure limits have been well studied on Earth. However, informal crew reports on the International Space Station have suggested that astronauts are developing CO2-related symptoms such as headache and lethargy at lower than expected CO2 levels and that symptoms tend to resolve when CO2 level is decreased. These anecdotes and several studies, reviewed by Law et al (Law, Watkins, & Alexander, 2010)and Cronyn et al (Cronyn, Watkins, & Alexander, 2011) support an association between elevated ppCO2 and CO2-related symptoms. While causality remains to be proven, it is speculated that headaches reported by crewmembers that improve when environmental CO_2 levels are lowered were caused by the elevated levels of CO_2 (Law et al., 2010);(James, 2007).

The incidence was derived from the compliation of inflight medical events (Walton, 2010).

Added 49 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)

Information Regarding Prevention

Vehicle requirement(s) CO_2 removal systems are used to scrub the spacecraft or space-station atmosphere, as part of the air revitalization system.

Contingency measure(s): If the CO_2 levels rise above the pre-determined Spacecraft Maximum Allowable Concentrations (SMAC levels) due to failure of the nominal air revitalization system or due to a larger number of crewmembers onboard (for example due to visiting vehicles or vehicle contingencies), additional capability to scrub CO_2 out of the cabin atmosphere is utilized. (James, 2008) (Bacal, Beck, & Barratt, 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

Incidence data not included in the model

The model pulls the incidence information from the IMM database ... the information shown below does not go into the model.

Incidence	
Data Category:	Fixed
Space Adaptation:	No
Incidence Type:	Rate

Distribution Data	
Incidence:	Fixed
Occurrence:	Poisson

Data Characteristics	
Fixed Rate:	0.0082

Incidence Comments

The National Poison Data System (NPDS) (Bronstein et al., 2009) is a national database which automatically uploads data from 61 US poison centers. NPDS reported 8.2 exposures per thousand population for 2008, thus the incidence rate is 0.0082. From ths study 427 cases of carbon dioxide poisoning were recorded out of a total of 34,237 cases of fumes/gases/vapors poisoning (0.01); 379 were unintentional (0.89). Outcomes were: 57 none (0.13), 67 minor (0.16), 22 moderate (0.05), 1 major (0.002) and 0 deaths for 2008. 80 cases were treated in a healthcare facility (0.19)

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 %: 95.71 - 97.14)	100	0.25	0 - 10	1 - 4.5 - 8	0	0	0
ISS-based Treatment (worst case scenario %: 2.86 - 4.29)	100	0.25 - 0.5	3 - 18	1 - 4.5 - 8	0 - 10	0 - 1	0
Untreated Best Case	0	0	3 - 18	1 - 4.5 - 8	0 - 10	0	0
Untreated Worst Case	0	0	11 - 32	1 - 4.5 - 8	3 - 32	0 - 19	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 CO_2-induced headache, which resolves spontaneously or with minor symptomatic treatment, and involves minimal functional impairment

The **worst case scenario** is defined as a moderate CO_2-induced headache which involves a moderate level of functional impairment. Because CO2 headaches are promptly treated in-flight, the severity of the headache is not expected to be severe.

Percentages of how often best versus worst case scenarios occur were determined using the Real World System data set. There wer 49 events and of those events 2 were worst case. Thus the percentage of worst case scenario is 4.08% (2/49) and best case scenario is 95.92% (47/49) (Saile L., 2017)

Best Case Comments

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 mild non-space adaptation conditions; we combined two tables: Migraine and Complex Regional Pain Syndrome (Upper Extremity). Migraine Whole Person Impairment ratings are based on Table 13-18, p.342 (American Medical Association, 2008). Complex Regional Pain Syndrome (CRPS-UE) gradings for upper extremity impairment are based on Table 15-16, p. 454 (American Medical Association, 2008). The CRPS is converted from localized 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). See the CliFF Appendix for detailed description of grading.

For **Clinical Phase I,** by definition FI is 100% and duration is estimated as 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 as 1 to 8 hours considering it may take up to 2 doses for relief of headache as indicated in the ISS medical checklist or resolve spontaneously (Headache Classification Subcommittee of the International Headache Society, 2010).

During **Clinical Phase III,** headache (CO_2 induced) is expected to resolve and FI is 0%. Based on space flight data (Walton, 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 mild non-space adaptation conditions; we combined two tables: Migraine and Complex Regional Pain Syndrome (Upper Extremity). Migraine Whole Person Impairment ratings are based on Table 13-18, p.342 (American Medical Association, 2008). Complex Regional Pain Syndrome (CRPS-UE) gradings for upper extremity impairment are based on Table 15-16, p. 454 (American Medical Association, 2008). The CRPS is converted from localized 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). See the CliFF Appendix for detailed description of grading.

For **Clinical Phase I,** by definition FI is 100% and duration is estimated as 15-30 minutes to evaluate headache as described in the ISS medical checklist and perform atmospheric CO_2 evaluation. During **Clinical Phase II,** FI is estimated as 3 to 18%, and duration is estimated as 1 to 8 hours considering it may take up to 2 doses for relief of headache as indicated in the ISS medical checklist (Headache Classification Subcommittee of the International Headache Society, 2010)or for the headache to resolve spontaneously with a change on the environmental parameters (lowering of the ambient CO2).

During **Clinical Phase III,** headache (CO_2 induced) is expected to resolve or improve and FI is expected to be 0 to 10%. Based in space flight data (Walton, 2010) EVAC and LOCL have never occurred and are unlikely. To maintain uncertainty we are estimating 0 to 1% risk of evacuation based on terrestrial data (Bronstein, 2009)

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 (Include references for duration and FI. 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 mild non-space adaptation conditions; we combined two tables: Migraine and Complex Regional Pain Syndrome (Upper Extremity). Migraine Whole Person Impairment ratings are based on Table 13-18, p.342 (American Medical Association, 2008). Complex Regional Pain Syndrome (CRPS-UE) gradings for upper extremity impairment are based on Table 15-16, p. 454 (American Medical Association, 2008). The CRPS is converted from localized 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). See the CliFF Appendix for detailed description of grading.

During **Clinical Phase II,** FI is estimated as 3 to 18%, and duration is estimated as 1 to 8 hours, similar to the treated best case scenario. During **Clinical Phase III,** headache (CO_2 induced) is expected to resolve or improve and FI is expected to be 0 to 10%. Based on space flight data (Walton, 2010) 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 (Include references for duration and FI. 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 mild non-space adaptation conditions; we combined two tables: Migraine and Complex Regional Pain Syndrome (Upper Extremity). Migraine Whole Person Impairment ratings are based on Table 13-18, p.342 (American Medical Association, 2008). Complex Regional Pain Syndrome (CRPS-UE) gradings for upper extremity impairment are based on Table 15-16, p. 454 (American Medical Association, 2008). The CRPS is converted from localized 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). See the CliFF Appendix for detailed description of grading.

During **Clinical Phase II,** FI is estimated as 11 to 32%, and duration is estimated as 1 to 8 hours similar to the treated worst case scenario.

During **Clinical Phase III,** headache (CO_2 induced) is expected to either improve or remain the same with FI ranging from 3 to 32%. Based on space flight data (Walton, 2010) EVAC and LOCL have not occurred and are not expected. To maintain uncertainty we are estimating 0 to 19 % risk of evacuation (Bronstein, 2009).

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
Bronstein, 2009	4	EVAC
Saile L., 2017	1	BCWC

Additional Comments

A PubMed search was conducted using the key terms, poisoning and carbon dioxide, then refined our search for relevance and date.

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
Thermometer	0	1	1	No	No	Measure pemperature
Tylenol (Acetaminophen) 325 mg	0	4	150	Yes	Yes	Pain relief

Resource Comments

The ISS checklist includes the following warning for Headache:

If more than one crewmember develops a headache at the same time or if headaches develop in a certain region of the ISS, it is vital that that the atmosphere be sampled with the Compound Specific Analyzer for Combustion Products (CSA-CP) and the portable Carbon Dioxide Monitor (CDM). Headaches occurring at night in a sleep station or other more enclosed area are possibly due to local CO2. Ventilation should be increased to this area if possible (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	4
Resources	2
QUALITY OF EVIDENCE	**2.2**

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

Reference List

Reference
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