

Altitude Sickness Cliff

Branch Baseline

Hypoxia is a state of oxygen deficiency sufficient to cause impairment of function. A cabin leak may result in reduced cabin pressure resulting in hypobaric hypoxia. An environmental control mishap in which cabin pressure is maintained but oxygen level is inadequately sustained may cause normobaric hypoxia. Once hypoxia has been recognized, resolving the oxygen deficiency is the indicated treatment. In space travel, hypoxia can also occur with inadequate gas mixing and uneven cabin ventilation. Either the rapid or gradual onset of hypoxia can be dangerous. An acute hypoxic exposure is an operational emergency. Immediate corrective action or escape is required. (Bacal, 2008)

Altitude sickness represents a spectrum of pathologic states initiated by an exaggerated vascular response to hypoxia. Syndromes include acute mountain sickness (AMS), high altitude cerebral edema (HACE), high altitude pulmonary edema (HAPE), and high altitude retinal hemorrhage. The potential for AMS in space operations exists during staged decompression prior to EVA or following inadvertent pressure reduction due to partial loss of spacecraft atmosphere. (Clark, 2008)

An AMS worksheet has been developed for space flight, which is a modification of the Lake Louise AMS self-report questionnaire and clinical functional assessment. Fatigue and headache are common during space flight, with or without hypoxia. Changes in these symptoms are not necessarily diagnostic, but providing a numerical score may be useful to monitor treatment and resolution. (Clark, 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:	Model
Space Adaptation:	No
Incidence Type:	Rate

Distribution Data

Incidence:	Lognormal
Occurrence:	Poisson

Data Characteristics

Mean:	5.43E-05
Standard Deviation:	6.32E-05

Incidence Comments

Altitude sickness has not occurred among US astronauts in flight. (Walton, 2010) Lacking in-flight data IMM requested a risk trade study. The likelihood is based on the probability of loss of function of the oxygen generation systems on ISS. It does not reflect the rate of change of ppO₂ levels or the probability of various ppO₂ levels. The version 1.2 interim 10A PRA model was run for a 6 month mission time to extract the event probabilities from the model end states. The results of this analysis include probability of occurrence over a 6 month period and the same probabilities expressed as failure rates, in number of failures per hour. (Haines, 2008) The incidence rate and standard deviation were calculated from the PRA analysis results by the IMM biostatistician: 5.43 X 10⁻⁵ events per year and 6.32 X 10⁻⁵ SD respectively. (Minard, 2011)

Information Regarding Prevention

Selection criteria

Disqualifying conditions in general, are any medical condition that, in the judgment of the MSMB, may compromise mission operations, performance of duties, or crew health or safety. Crew members must meet medically specific standards for periodic altitude chamber exposures to 10,000 meters. Appearance of subjective symptoms, such as pain, nausea, dizziness, dyspnea, weakness, visual darkening, itching, bends, or other subjective feelings of discomfort; or certain specific cardiovascular symptoms may require the individual to undergo further training to accomplish the altitude chamber training objectives. They are not in themselves disqualifying for ISS crewmember duties, unless they are determined to be due to a pathological condition after subsequent medical testing. (International Space Station Program, 2009)

Vehicle requirements

Oxygen supply.

Contingency measures

Immediate treatment for altitude hypoxia is with oxygen, preferably with the Quick-Don Mask which delivers 100% oxygen. Periodic crew training in an altitude chamber and drills on orbit allow crewmembers to recognize their own hypoxia symptoms. In the case of a loss of cabin pressure, mitigating factors for the prevention of Altitude Sickness (altitude hypoxia) on orbit for ISS are: Immediate use of Quick-Don Mask and connect to ship's oxygen supply, or Walk Around Bottle (100% oxygen). Isolate crewmembers from the module that is losing pressure if possible, by sealing off module and translating to another module or to the Soyuz. Flight rules require EVAC of the International Space Station if the oxygen level drops to greater than or equal to 10,000 feet cabin altitude for longer than 24 hours. (Bacal, 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
Haines, 2008	2	Incidence

Alternative Incidence Data

Each year, the US Antarctic Program rapidly transports scientists and support personnel from sea level (SL) to the South Pole (SP), 2835 m (9301 feet) providing a unique natural laboratory to quantify the incidence of acute mountain sickness (AMS). The incidence of AMS at SP tended to be higher than previously reports in other geographic locations at similar altitudes. (Anderson, 2011)

Acute mountain sickness (AMS) is a syndrome typically arising in the first 1–2 days at a higher altitude and is characterized by the presence of a headache along with sleep disturbance, gastrointestinal symptoms, fatigue, and dizziness or lightheadedness. High altitude cerebral edema (HACE) is a syndrome often diagnosed in the presence of acute mountain sickness when mental status changes or ataxia emerge. High altitude pulmonary edema (HAPE), usually occurs after 2–4 days at altitude and may present rapidly in individuals with no signs of AMS. Each of these syndromes presents a health risk to polar workers and may significantly impair judgment or disrupt work productivity. The case definition for AMS utilized the standard Lake Louise Symptom Scoring System (LLSS) which requires the presence of a headache and an overall symptom score of 3 or greater. (Anderson, 2011)

This group was 70% male with a mean age of 36.8 +/-10.6 years. Shortness of breath with activity was the most commonly reported symptom (87%), followed by sleeping difficulty (74%), headache (66%), fatigue (65%), dizziness/lightheadedness (46%) and general functional limitation (41%). Overall symptoms peaked on Day 2 (LLSS = 2.5 +/- 2.1). Using strict Lake Louise Criteria, 52% of subjects satisfied acute mountain sickness criteria at some point during their visit to altitude. On Day 1, 24% met acute mountain sickness criteria, and 33% met criteria on Day 2, with steadily decreasing values from 15 to 4% on Days 3 to 7. During the 2006 season, 2.8% (7 of 246) workers were evacuated from the South Pole for symptoms consistent with HAPE. (Anderson, 2011)

A survey was conducted to estimate the incidence of high altitude illness among 3628 unacclimatized persons who had no previous high altitude experience and who traveled to Tibet by air to an altitude of 3600 m (11811 feet.) These subjects were asked to answer questions in a written questionnaire about symptoms associated with high altitude illnesses that occurred within 2 weeks of their first arrival, their severity, and possible contributing factors. Physical examination and appropriate laboratory tests were also performed for hospitalized subjects. They found that 2063 respondents had mild acute mountain sickness with an incidence of 57.2%, and 249 (12.07%) of them were hospitalized for treatment. The incidence of high altitude pulmonary edema was 1.9%, while no case of high altitude cerebral edema was found. Additionally, there was no report of death. Psychological stresses and excessive physical exertions possibly contributed to the onset of HAPE. Acute mountain sickness is common among unacclimatized persons after their acute ascent to Tibet. The incidence of HAPE and HACE, however, is very low among them. (Ren, 2010)

HAPE/HACE

The incidence of HAPE is not known. Epidemiology applies numerous different diagnostic criteria and HAPE severity varies across population, thus numerator and denominators have been estimates. The incidence of HAPE is estimated to be one order of magnitude less than that of acute mountain sickness. Hall reported, based on different studies, HAPE ranging from 0.01% at 2,500m (8202 feet), 1.9 at 3600m (11,811 feet) and 2.5 to 5% at 4,300m (14,107 feet). Data above 4,500m (14,764 feet) is less reliable and generally related to mortality (Hall, 2011). The largest study today (Ren, 2010) reported HAPE at 1.9%, while a study with 262 subjects found 15% had chest rales or interstitial edema on radiograph after ascent (Cremona, 2002).

Incidence of HACE ranges from 0.01% at 2000m (6561.7 feet), 1.2% in the Indian armed forces at altitudes of 5,500m (18044.6 feet) to 1.8% in trekkers at 4,300 meters (14107.6 feet). (Roach, 2002)

The **mortality** rate for combined HACE/HAPE is 0.12% (Windsor, 2009) at extreme altitude and 0.022% at 6194m (20321.5 feet) in Alaska (McIntosh, 2008) . In a number of cases, HAPE and HACE coexist. Up to 20% of those who present with HAPE also demonstrate signs of HACE, while up to 50% of those who died from HAPE also had evidence of HACE on autopsy. (Windsor, 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 %: 97 - 100)	100	0.5	3 - 46	24 - 36 - 48	0	0	0
ISS-based Treatment (worst case scenario %: 0 - 3)	100	0.5 - 1	21 - 70	48 - 60 - 72	0 - 70	100	0 - 100
Untreated Best Case	0	0	21 - 70	24 - 36 - 48	0 - 46	0 - 100	0
Untreated Worst Case	0	0	48 - 100	48 - 60 - 72	48 - 100	100	100

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

Acute mountain sickness (AMS) is a syndrome typically arising in the first 1–2 days at an elevated altitude. It is diagnosed by the presence of a headache along with sleep disturbance, gastrointestinal symptoms, fatigue, and dizziness or lightheadedness. High altitude cerebral edema, is a syndrome often diagnosed in the presence of acute mountain sickness when mental status changes or ataxia emerge. High altitude pulmonary edema, usually occurs after 2–4 days at altitude and may present rapidly in individuals with no signs of AMS. (Anderson, 2011)

The **best case scenario** is defined as a mild case of altitude sickness, which resolves with oxygen use and acetazolamide (Diamox), or return to standard environmental conditions.

The **worst case scenario** is defined as moderate to severe altitude sickness, which may lead to high altitude pulmonary edema (HAPE) and high-altitude cerebral edema (HACE) which are life-threatening if untreated.

The **percentage of how often best versus worst case scenario occur** was estimated considering the incidence of HAPE and HACE in terrestrial studies. A group of military recruits ascending by plane to Tibet, 3600m (11,811 feet) reported 1.9% HAPE incidence and no cases of HACE (Ren, 2010) In Antarctica (SP, 2835 m (9301 feet), the incidence of HAPE has been reported at 2.84% (7/246) and no cases of HACE. (Anderson, 2011). The incidence of HACE is lower and it ranges from 0.01% in the western United States to 1.8% in Mount Everest. (Roach, 2002) To allow for uncertainty our worst case scenario is estimated at 0-3%, thus our best case percentage is 97-100%.

Best Case Comments

Altitude Sickness is a multi-system medical condition and it 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 severe conditions. It requires combining two tables. Pulmonary Dysfunction ratings are based on Table 5-4, p.88 (American Medical Association, 2008) and Consciousness and Awareness ratings are based on Table 13-4, p. 327 (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). Refer to the ClIFF Appendix for further information.

By definition during **Clinical Phase I**, FI is 100% and duration is estimated to be 30 minutes for health exam as called out in the ISS medical checklist. During **Clinical Phase II**, Functional Impairment is estimated to be 3-46%. Duration is estimated to be 24 to 48 hours based on the Antarctic analog. (Anderson, 2011) During **Clinical Phase III**, FI is 0%. By definition complete recovery is expected with no EVAC or LOCL.

Worst Case Comments

Altitude Sickness is a multi-system medical condition and it 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 severe conditions. It requires combining two tables. Pulmonary Dysfunction ratings are based on Table 5-4, p.88 (American Medical Association, 2008) and Consciousness and Awareness ratings are based on Table 13-4, p. 327 (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). Refer to the ClIFF Appendix for further information.

By definition during **Clinical Phase I**, FI is 100% and duration is estimated to be 30 to 60 minutes. Including physical exam, respiratory support and starting intravenous fluids. During **Clinical Phase II**, Functional Impairment is estimated at 21-70%. Estimated duration in the Antarctic was up to 7 days. IMM estimated duration at 48-72 hours, 2 to 3 days, based on time when symptoms peak (Anderson, 2011 4111 /id } and time to EVAC. During **Clinical Phase III**, recovery may or may not occur; FI is estimated at 0-70%. Hospitalization has occurred at a rate of 12% in the military (Ren, 2010) and EVAC has occurred among Antarctic workers at a rate of 2.8% (Anderson, 2011). Mortality rates have been estimated to be 0.0012 for HACE and HAPE (Windsor, 2009). To allow for uncertainty EVAC and LOCL are estimated to be 100%.

Untreated Best Case Comments

Altitude Sickness is a multi-system medical condition and it 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 severe conditions. It requires combining two tables. Pulmonary Dysfunction ratings are based on Table 5-4, p.88 (American Medical Association, 2008) and Consciousness and Awareness ratings are based on Table 13-4, p. 327 (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). Refer to the ClIFF Appendix for further information.

During **Clinical Phase II**, Functional Impairment is estimated to be 21-70%. Duration is estimated to be 24-48 hours, similar to the treated best case scenario. During **Clinical Phase III**, FI is 0-46%. Without treatment available, EVAC is estimated at 0-100%. LOCL is estimated at 0%.

Untreated Worst Case Comments

Altitude Sickness is a multi-system medical condition and it 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 severe conditions. It requires combining two tables. Pulmonary Dysfunction ratings are based on Table 5-4, p.88 (American Medical Association, 2008) and Consciousness and Awareness ratings are based on Table 13-4, p. 327 (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). Refer to the ClifF Appendix for further information.

During **Clinical Phase II**, Functional Impairment is estimated to be 48-100%. Duration is estimated at 48 to 72 hours, similar to the treated worst case scenario. During **Clinical Phase III**, FI remains 48 to 100%. EVAC and LOCL are expected at 100% without available treatment.

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
Ren, 2010	4	BCWC
Anderson, 2011	2	BCWC
Roach, 2002	4	BCWC
American Medical Association, 2008	3	FI
American Medical Association, 2008	3	FI
American Medical Association, 2008	3	FI
Windsor, 2009	4	EVAC

Additional Comments

On October 5, 1993, U.S. Astronaut Dr. Henry died of High Altitude Pulmonary Edema (HAPE) on Mount Everest, after reaching an altitude of 21,000 feet, (Carr, 1993), (National Aeronautics and Space Administration (NASA), 2007).

The Resource Table (RT)

Resource	Units Required Best Case	Units Required Worst Case	Units Available At Start Of Mission	Consumable	Essential	Rationale
Ambu bag and mask	0	1	1	No	Yes	Hand-held device used to provide positive pressure ventilation to a patient who is not breathing or is breathing inadequately
Blood Oximeter	1	1	1	No	Yes	Monitors the oxygen saturation of a patient's blood
Blood Pressure Cuff (regular, large)	1	1	2	No	Yes	Measure blood pressure
Blood Pressure Monitor	1	1	1	No	Yes	Measure blood pressure
BZK wipes	0	1	60	Yes	No	Cleanse skin.
CMRS	0	1	1	No	No	Restrain crew member to ensure safety
Dexamethasone (Decadron) 10mg injectable	0	2	20	Yes	Yes	Administered for the anti-inflammatory effect
Diamox (Acetazolamide) 250 mg tablets	6	0	100	Yes	Yes	Administered for the effects of symptoms of altitude sickness.
ECG Monitor (Device, USB Charge Cable, Lead Set Cable, Cue Card)	0	1	1	No	Yes	Measure and monitor ECG
Endotracheal Stylet	0	1	1	No	Yes	To provide ventilation
Endotracheal Tube 7.0/8.0	0	1	4	Yes	Yes	Establish and maintain patent airway and ventilation
EtCO2 Monitor with EMMA adapter	0	1	1	No	Yes	Measure end tidal CO2
IV administration set	0	1	3	Yes	Yes	IV Fluids infusion
IV Cap	0	1	5	Yes	No	To maintain IV when not in use
IV Catheter (18G, 20G, or 22G)	0	1	14	Yes	Yes	IV fluid administration
IV Fluid 1L (1000mL)	0	2	5	Yes	Yes	To replenish fluids
IV Fluid Air Filter	0	1	3	Yes	No	To filter air from IV set
IV pressure infuser	0	1	1	No	No	IV Fluids infusion
Ketamine 50 mg/mL, 10 mL multi dose vial	0	0.3	6	Yes	Yes	For sedation in case of intubation/ventilation.
King Supraglottic Airway (SGA) Tube (size 3/size 4)	0	1	2	Yes	Yes	Establish and maintain patent airway and ventilation
Laryngoscope (blade)	0	1	1	No	Yes	For intubation
Laryngoscope handle	0	1	1	No	Yes	For intubation
Medical tape	0	0.03	5	Yes	No	Single-coated tapepressure adhesive tape

Resource	Units Required Best Case	Units Required Worst Case	Units Available At Start Of Mission	Consumable	Essential	Rationale
Nasal Airway (6mm, 7mm)	0	1	2	No	Yes	Airway management
Needle (23G)	0	7	20	Yes	Yes	For medication administration.
Oral Airway	0	1	2	No	Yes	Airway management
Pack of 12 ECG electrodes	0	1	5	Yes	Yes	Measure and monitor ECG
PEEP Valve	0	1	1	No	Yes	provide positive pressure ventilation
Phenergan (Promethazine tablet) 25 mg	6	0	100	Yes	Yes	For N/V.
SGA Cue Card	0	1	1	No	Yes	Guidance for use of supraglottic airway
Sharps container	0	1	40	No	No	For needle and syringe disposal
Stethoscope	1	1	2	No	Yes	To auscultate lungs, heart, and blood flow in arteries and veins
Suction Cartridge	0	1	1	No	Yes	Provide suction
Suction device	0	1	1	No	Yes	To aspirate secretions or vomit
Suction device collection bag	0	1	2	Yes	No	To collect fluids suctioned from mouth/airway
Suction device syringe	0	1	1	No	Yes	To remove fluids, secretions, vomit from mouth
Suction tip - mouth (curette)	0	1	1	No	Yes	Used for suction by inserting into the end of a suction tube
Suction Tubing - Endotracheal Tube	0	1	1	Yes	Yes	Provide suctioning of airway
Surgical Lubricant	0	1	6	Yes	No	Provide lubrication during the ILMA insertion.
Syringe (35cc)	0	1	1	Yes	Yes	Inflation of SGA tube
Syringe (3cc)	0	8	20	Yes	Yes	For medication administration and flushing the IV catheter as appropriate.
T-adapter	0	1	1	No	Yes	Ventilation tubing setup
Tourniquet	0	1	1	No	No	To stop blood flow and engorge vein, facilitating IV insertion
Tylenol (Acetaminophen) 325 mg	18	0	150	Yes	Yes	For headache
Valium (Diazepam) 5 mg/mL, 2 mL syringe	0	1	2	Yes	Yes	for sedation with intubation
Variable Oxygen System	1	1	1	No	Yes	To provide ventilation
VOS Intubated Patient Hardware (Ventilator/Respirator)	0	1	1	No	Yes	Mechanical ventilation

Resource Comments

The table was revised on December 15, 2011. IV set, Oxygen tubing, ET tube, ET connector, 3 cc syringe, BP cuff. Added IV set, Oxygen tubing, ET tube, ET connector, 3 cc syringe, BP cuff, and BP-ECG were added.

ISS medical checklist include procedures for altitude illness (AMS) (Mission Operations Directorate (MOD), 2011). HAPE and HACE are not addressed. Resources for worst case scenario have been added based on Wilderness Clinical Guidelines (Luks, 2010).

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
Luks, 2010	3	Resources

Level Of Evidence

Input Data	LOE Average	Description	Range
Incidence	2	Excellent	1-2
Functional Impairment	3	Good	2.1-3
Best Case / Worst Case	3.33333333333333	Fair	3.1-4
EVAC / LOCL	4	Poor	4.1-5
Resources	2.5		
QUALITY OF EVIDENCE	2.96666666666667		

Reference List

Reference

- American Medical Association. Guides to the Evaluation of Permanent Impairment. 6th ed. Chicago: American Medical Association Press; 2008.
- American Medical Association. Pulmonary System. In: Rondinelli R, editor. Guides to the Evaluation of Permanent Impairment. 6th ed. Chicago: American Medical Association Press; 2008. p. 77-99.
- American Medical Association. Central and Peripheral Nervous System. Guides to the Evaluation of Permanent Impairment. 6th ed. Chicago: American Medical Association Press; 2008. p. 321-45.
- Anderson PJ, Miller AD, O'Malley KA, Ceridon ML, Beck KC, Wood CM, et al. Incidence and Symptoms of High Altitude Illness in South Pole Workers: Antarctic Study of Altitude Physiology (ASAP). Clin Med Insights Circ Respir Pulm Med 2011;5:27-35.
- Bacal K, Beck G, Barratt MR. Hypoxia, Hypercarbia, and Atmospheric Control. In: Barratt M, Pool S, editors. Principles of Clinical Medicine for Space Flight. New York: Springer; 2008. p. 445-73.
- Carr J. Former Astronaut Karl Henize Dies on Mt. Everest Expedition. Johnson News . 10-8-1993. Houston, TX, NASA. 12-19-2011.
- Clark J. Decompression Related Disorders Pressurization Systems, Barotrauma, and Altitude Sickness. In: Barratt M, Pool S, editors. Principles of Clinical Medicine for Space Flight. New York: Springer; 2008. p. 247-71.
- Cremona G, Asnaghi R, Baderna P, Brunetto A, Brutsaert T, Cavallaro C, et al. Pulmonary extravascular fluid accumulation in recreational climbers: a prospective study. Lancet 2002 Jan 26;359(9303):303-9.
- Haines R. Probabilistic Risk Assessment (PRA) Risk Trade Study - Altitude Sickness. PROGRAM INTEGRATION AND CONTROL CONTRACT NNJ04AA01C. Houston, TX: ARES Corporation; 2008 Apr 28. Report No.: ISS-PRA-08-04.
- Hall DP, Duncan K, Baillie JK. High altitude pulmonary oedema. J R Army Med Corps 2011 Mar;157(1):68-72.
- International Space Station Program. Medical Standards for ISS Crewmembers - MED Vol A. 3.2 ed. NASA; 2011.
- Luks AM, McIntosh SE, Grissom CK, Auerbach PS, Rodway GW, Schoene RB, et al. Wilderness Medical Society consensus guidelines for the prevention and treatment of acute altitude illness. Wilderness Environ Med 2010 Jun;21(2):146-55.
- McIntosh SE, Campbell AD, Dow J, Grissom CK. Mountaineering fatalities on Denali. High Alt Med Biol 2008;9(1):89-95.
- Minard C. Altitude Sickness, Incidence Rate & Standard Deviation. Lopez V, editor. 12-15-2011.
- NASA Mission Operations Directorate (MOD). International Space Station Integrated Medical Group Medical Checklist. Mission Operations Directorate (MOD), Systems Operations Data File (SODF) . 6-24-2011. Houston, TX, National Aeronautics and Space Administration (NASA).
- National Aeronautics and Space Administration (NASA). Karl G. Henize, Biographical Data. National Aeronautics and Space Administration (NASA) Johnson Space Center . 2007. Houston, TX. 12-19-2011.
- Ren Y, Fu Z, Shen W, Jiang P, He Y, Peng S, et al. Incidence of high altitude illnesses among unacclimatized persons who acutely ascended to Tibet. High Alt Med Biol 2010;11(1):39-42.
- Roach R, Stepanek J, Hackett P. Acute Mountain Sickness and High-Altitude Cerebral Edema. In: Pandolf KB, Burr RE, editors. Medical Aspects of Harsh Environments. Washington, DC: Office of The Surgeon General Department of the Army, United States of America, Borden Institute; 2002. p. 760-88.
- Walton M, Kerstman E, IMM. In-flight Compilation v20100414_Incidence_calculation. 2010.
- Windsor JS, Firth PG, Grocott MP, Rodway GW, Montgomery HE. Mountain mortality: a review of deaths that occur during recreational activities in the mountains. Postgrad Med J 2009 Jun;85(1004):316-21.