Altitude Sickness CLIFF Peer Review

1. *Strength of evidence presented in CLIFF in modeling the characteristics and mission impact of this medical condition within the spaceflight environment?*

   Score: 3

   Grading Scale:

   4 - Confident

   3 - Somewhat confident

   2 – Neutral

   1 – Somewhat unconfident

   0 – Not confident

2. How confident are you that these data accurately represent the spaceflight environment?	*Tables 1, 2* *Composite Incidence and Level of Confidence*	*Table 3, 4 BC/WC* *Loss of Crew and probability*	*Table 4 - Clinical Phase 1, 2 durations* *Table 5 – CP 2 Loss of Crew*	*Table 4 – RTDC %* *Table 6 – RTDC Loss of Crew*	*Table 4 – Loss of Crew Life %* *Table 7 – Loss of Crew Life, Loss of Crew*	*Table 8 – TI*
Score	*4*	*2*	*3*	*3*	*2*	*3*

Comments and limitations:

1. **General comments.** This CLiFF characterizes altitude sickness during spaceflight which occurs when there is hypoxia to the extent that it causes impairment of normal function. This could occur because of low ambient pressures without a compensating increase in oxygen concentration, a cabin or EVA suit leak, poor cabin ventilation with local areas of low oxygen concentration, or a failure of the ECLSS system which causes improper gas mixing. There may be various pathologic states resulting from hypoxia including acute mountain sickness (AMS), high altitude cerebral edema (HACE), high altitude pulmonary edema (HAPE), and high altitude retinal hemorrhage. The greatest risk occurs when there is a planned decompression of the entire vehicle or a smaller space, such as an airlock, in preparation for an EVA. EVA crewmembers are at risk of altitude sickness if there is a suit leak large enough to exceed the capacity of the EMU tanks to compensate and the crewmember is not able to return promptly to the airlock. The best case is high altitude headache or acute mountain sickness (AMS), which resolves spontaneously or with oxygen use, acetazolamide (Diamox), or descent (to a normal pressure or oxygen level). The worst case is high altitude pulmonary edema (HAPE) or high-altitude cerebral edema (HACE).

2. **Incidence.** There have been no cases of altitude sickness reported during manned spaceflight except for catastrophic accidents (i.e., Challenger and Columbia). The analog and terrestrial data is inadequate to replicate the environment and scenarios associated with a loss of cabin or EMU pressure. The incidence calculation is confined to EVA crewmembers because it is assumed that if there is a loss of cabin pressure sufficient to cause hypoxia in a habitat or spacecraft, the condition is probably not survivable. Therefore, the incidence is calculated on a per-EVA basis for each crewmember who participates. The probability of loss of suit pressure then becomes an engineering assessment, and the EMU SPLAT suit leak analysis and PRA estimate were utilized. The probability of a suit leak is estimated at approximately 0.0001 per EVA. Since there are no uncertainty estimates included, the incidence proportion is fixed rather than a probability distribution. This resulted in the incidence of altitude sickness per individual spacewalk. The best case/worst case probabilities of 97.8/2.2% were derived from a terrestrial study that showed the number of hikers experiencing AMS who had severe symptoms that correspond to the WC definition. CP2 duration, return to definitive care (RTDC) and loss of crew life probabilities are supported by terrestrial evidence. All RTDC and loss of crew life probabilities are 0 except for the UTWC which could have an elevated risk of loss of crew life. It is assumed that "treated" is equivalent to reversing the hypoxia that caused AMS by returned to a pressurized airlock. The meaning of "untreated" becomes confusing since it implies that a return to normal pressures could not be accomplished. For the untreated worst case, the assumption is that the affected crewmember returned to the airlock but required a higher level of care because of complications such as HAPE or HACE. The composite probability density curve that was derived appears to be a reasonable representation of the data presented. The incidence is fixed; thus, there is no associated standard deviation.

3. **Clinical phase data**. I am in agreement with the clinical phase 1 durations entered in this CLIFF. This data was compiled by a team of expert clinicians, and I was involved in the discussions leading to the calculation of the clinical phase durations. The phase 2 duration was modified during the course of the review, and I am in agreement with the changes made.

4. **Task impairment**. The analysis was performed and reviewed by a separate team of expert clinicians. I am aware of the methods that were used but did not directly participate in the discussions.

5. **Dependence on mission phase or duration of mission**. This medical condition is mission phase dependent. It is postulated to occur only during the pressure changes associated with EVA. The risk is considered to be zero during periods when the cabin pressure remains constant; i.e., depressurization is not occurring.

6. **Limitations**

- The EMU SPLAT suit leak analysis and PRA estimate were utilized. The probability of a suit leak is estimated at approximately 0.0001 per EVA. Since there are no uncertainty estimates included, the incidence proportion is fixed rather than a probability distribution.
- The meaning of "untreated" becomes confusing since it implies that a return to normal pressures could not be accomplished. For the untreated worst case, the assumption is that the affected crewmember returned to the airlock but required a higher level of care because of complications such as HAPE or HACE.
- The "untreated" best case is ambiguous because the treatment is return to the airlock. If that doesn't happen, the crewmember can't survive.

- The condition dictates that the crew will need to return to a habitable volume and survive a return journey. As such, a catastrophic leak occurring in a lunar habitat, lunar lander, orbiting station, or Orion that leads to LOCL is not considered. Only events that result in hypoxia during EVA with “treatment” being a return to the airlock are considered. There may be circumstances in which emergency evacuation is survivable, but these are felt to be highly unlikely.
- Events such as a loss of pressure on Gateway that will lead to LOCL are ignored because the medical kit will not be sufficient to resolve these issues. Therefore, a major limitation of this analysis is that moderate leaks that lead to modified missions could not be quantified and are ultimately not considered.
- The ability to repressurize a crew member in the setting of a leak is paramount to management. Mission phase will heavily impact this capability; however, the details of mission stages or duration are yet to be determined
- Moderate leaks that lead to modified missions could not be quantified and are ultimately not considered because these contingencies cannot be accurately calculated.

Reviewed by:

David C. Hilmers