

Spaceflight Associated Headache 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 LOC and probability	Table 4 - Clinical Phase 1, 2 durations Table 5 – CP 2 LOC	Table 4 – RTDC % Table 6 – RTDC LOC	Table 4 – Loss of crew life % Table 7 – Loss of crew life LOC	Table 8 – TI
Score	3	3	3	4	4	3

Comments and limitations:

1. General comments. Headaches are a common complaint in astronauts during spaceflight just as they are on earth. During the first 5 days after insertion into orbit, many headaches are a result of increased intracranial pressure from microgravity-associated fluid shifts. Once a new equilibrium has been established, it is felt that most headaches are tension-type although cephalad fluid shift may still play some role. Previously, space motion sickness syndrome was inclusive of this condition, but it is now recognized as a separate disorder. There has been acknowledgment that space adaptation headaches often do not occur concomitantly with motion sickness. It is possible that headaches may occur during the first 5 days of space travel that are associated with stress, lack of sleep, or environmental conditions within the cabin but are not secondary to fluid shifts. These would be considered SAS-related headaches and thus might be mis-classified. It is likely that astronauts also may under-report SAS-related headaches as many are mild and resolve quickly. Other conditions that are related but not covered in this CLIFF include: headache, headache-CO2 and altitude sickness which are the subjects of their own CLIFFs. The best case is considered to be an uncomplicated course of space adaptation syndrome-related headache, which resolves spontaneously or with minor symptomatic treatment. The worst case is a severe space adaptation related headache poorly responsive to available treatment.

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2. Incidence. Since this condition only occurs during spaceflight, LSAH data represents the best source to inform the incidence calculation. It is felt that analog studies, such as head-down tilt investigations, are not an exact duplication of the spaceflight environment and not as valuable as LSAH data. Unfortunately, there have been no new LSAH drops since the corresponding IMM CLIFF was developed, and the same information is being used. There have been 281 events reported over a total of 807 person-missions. Person-missions is being used for SAS-related conditions because each crewmember goes through this period once during each mission, no matter what the flight duration might be. This was an enhancement over the IMM CLIFF in which person-years was used. The best case/worst case probabilities were calculated using data from the previous IMM effort in which 48 events were analyzed and of those events, one was the worst case, yielding a best case/worst case probability of 98%/2%. The clinical phase durations, RTDC and Loss of crew life probabilities are supported by spaceflight as well as terrestrial evidence, and I am in agreement with their calculation. RTDC and Loss of crew life were considered to be zero for all scenarios given that there has never been a loss of life or evacuation because of this condition during manned US space missions. The probability density curve that was derived appears to be a reasonable representation of the data presented.

3. Clinical phase data. I am in agreement with the clinical phase 1 duration 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 duration. CP2 was supported by terrestrial evidence.

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. By definition, this medical condition only occurs during the first five days of spaceflight.

6. Limitations

- It is likely that astronauts may under-report SAS-related headaches as many are mild and resolve quickly. This could cause an under-estimation of the true incidence.
- The authors of this CLIFF did not have access to the original LSAH data, and thus there was an implied dependence on already published sources.
- There is some overlap between this condition and other CLIFF conditions such as headache, headache-CO₂, altitude sickness.
- It is possible that headaches may occur during the first 5 days of space travel that are associated with stress, lack of sleep, or environmental conditions within the cabin but are not secondary to fluid shifts. These would be considered SAS-related headaches and thus might be mis-classified.
- Several assumptions needed to be made regarding duration and the untreated cases given lack of available studies.

Reviewed by:

David C. Hilmers