Space Adaptation Space Motion 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: 4

   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	*4*	*3*	*4*	*3*	*4*	*3*

Comments and limitations:

1. **General comments.** Space Motion Sickness (SMS) is a condition unique to spaceflight that occurs in a large percentage of astronauts during the first five days after transition from gravity to microgravity. The symptoms are varied but often result in general malaise, nausea, gastrointestinal discomfort, and fatigue. Crewmembers who experience this condition try to limit their movements, their oral intake, and often feel the desire to sleep. There are several hypotheses about the pathophysiology of this phenomenon including cephalad fluid shifts and neuroanatomical sensory conflicts. SMS is considered to be one component of Space Adaptation Syndrome. This disorder is usually self-limited and resolves on its own although the use of drugs such as promethazine have proven helpful in alleviating symptoms. This CLiFF condition only includes SMS which occurs during the transition from gravity to microgravity. Entry Motion Sickness (EMS) or Earth-readaptation syndrome is a similar condition that results from transitioning from microgravity to gravity and is covered in a different CLiFF. Based on this reviewer's experience in spaceflights, the condition has probably been unreported in the past. Some crewmembers minimized the symptoms out of concern over future crew assignments. Very mild symptoms may have also gone unreported. The best case is considered to be space motion sickness that result in mild to moderate symptoms (e.g. loss of appetite, malaise, stomach awareness, 2 or fewer episodes of emesis, resolves within 72 hours, causes no or minimal performance decrement) while the worst case is SMS with severe and

persistent symptoms (e.g. need to keep head from moving, greater than 2 episodes of emesis, significant performance decrement, persists for greater than 72 hours)..

2. **Incidence.** Since SMS only occurs during the transition between a gravity environment and microgravity, only spaceflight data can be used for the incidence calculation. Individuals who are resistant to motion sickness, air sickness, or sea sickness on earth may be quite susceptible to SMS. There is quite a bit of data from prior missions that has been compiled. However, there has not been a new LSAH data drop since 2017, so there is little new information to update this CLiFF from the IMM version. There have been 419 events over 588 person-missions after careful review of crew reports. The IMM CLiFF was improved by using person-missions rather than person-years to reflect the fact that on past missions each crewmember was subject to this condition once during the mission. This may need to be refined during future missions where there are gravity well operations. The incidence should be considered a floor as some crewmembers may have minimized or denied their symptoms over fear of not being considered for future crew assignment.

The best case/worst case probabilities are somewhat problematic as definitions of mild, moderate and severe cases differed between various sources. The most recent data available was used to make this calculation. The clinical phase durations, RTDC and Loss of crew life probabilities are supported by data from spaceflight reports, and I am in agreement with their calculation. Both RTDC and Loss of crew life probabilities were considered to be zero given prior spaceflight experience. 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**. This medical condition only occurs during the transition from a gravity environment and microgravity.

6. **Limitations**

- The incidence should be considered a floor as some crewmembers may have minimized or denied their symptoms over fear of not being considered for future crew assignment. This was probably more of an issue during the Shuttle era when spaceflight lasted 2 weeks or less than it is during long-duration flights.
- The authors did not have access to the original LSAH data and thus there was an implied dependence on already published sources. In the prior IMM CLiFF, the Walton LSAH pull was not used, and the authors of this CLiFF were unable to reconcile their calculations.
- There may be some overlap between this condition and other CLiFF conditions, such as space adaptation headache.
- Several assumptions needed to be made regarding duration and the untreated cases given lack of available studies.

Reviewed by:

David C. Hilmers