Gravity Well Orthostatic Intolerance 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: 2

   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	*2*	*1*	*2*	*3*	*3*	*3*

Comments and limitations:

1. **General comments.** This CLiFF characterizes entry orthostatic intolerance in a "gravity well" defined as the return to a partial gravitational field after having spent time in microgravity. This could include landing on the lunar or the Martian surface after orbiting or directly approaching these bodies. Orthostatic intolerance describes the collection of physiologic changes such as tachycardia, dizziness, tunnel vision, nausea, and even syncope that occur when central perfusion is not maintained upon reacclimating to a positive gravitational field from a microgravity environment. Based on prior low earth orbit missions with a terrestrial return, it is usually a self-limited condition, milder in severity for shorter missions, that responds well to rest, restriction of provocative movements, and rehydration. This description, however, is derived from the experience with return to 1 g conditions, primarily with shuttle flights. None of the 12 Apollo astronauts experienced such symptoms upon entering the 1/6 g environment on the lunar surface while nearly two-thirds of astronauts returning to earth experienced some type of orthostatic intolerance. Based on these differences, the strength of the gravitational field appears to have an important influence on the incidence. The best case is considered to be mild gravity well orthostatic intolerance that spontaneously resolves. The worst case is gravity well orthostatic intolerance that requires IV fluids

or results in a syncopal episode. Since the gravity transition will be from microgravity to 1/6 g or 3/8 g instead of 1 g, the editor anticipates that all orthostatic intolerance events will be best case scenarios.

2. **Incidence.** The incidence of gravity well orthostatic intolerance (specifically defined as readaptation occurring on return to a partial gravitational field from microgravity) has been estimated based on the Apollo moon landings. There is no other analog that can be used to compute incidence. There were 0 documented events of orthostatic intolerance among the 12 astronauts who have walked on the moon compared to nearly two-thirds of astronauts returning to earth who experienced some type of orthostatic intolerance. It is unknown what the effect of the 3/8 g Martian gravitational field will be on the incidence of orthostatic intolerance. The editor states that all episodes of this condition will be mild; thus, the best-case probability is 100%. As a result, all worst-case data is listed as zero. The clinical phase durations are based on astronaut re-entry data that have shown a resolution of orthostatic intolerance by 3 days after landing. RTDC and Loss of crew life probabilities are estimated to be zero which is a reasonable assumption. 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 is dependent on mission phase as it only occurs when there is re-entry from microgravity to a partial gravity field such as landing on the lunar or Martian surface.

6. **Limitations**

- There is very limited data to support this CLiFF. Only 12 astronauts have experienced a microgravity to lunar gravity transition and none of them reported orthostatic intolerance.
- There are known reports of gender differences in terrestrial re-entry orthostatic intolerance. However, the only available data to support this CLiFF comes from the 12 males who landed on the lunar surface.
- There may have been under-reporting of symptoms related to orthostatic intolerance among the Apollo astronauts. In addition, the Apollo astronauts who walked on the moon did not undergo orthostatic testing after landing.
- There is no data to support the incidence of orthostatic intolerance upon entering the Martian 3/8 gravitational field. It is possible that the incidence will be somewhere between the Apollo moon landing experience and that of shuttle astronauts.
- At some future point, it would be advisable to calculate separate incidences for Martian and lunar landings, given the difference in gravitational fields.
- The assumption that there will be no worst case is questionable. However, it is not currently known whether there will be any critical piloting tasks needed to safely land a spacecraft on the lunar or Martian surfaces. While there were no reported problems with orthostatic intolerance during Apollo missions, the data set is small and future critical tasks will be dependent on spacecraft design.
- As a result of the current BC/WC probabilities, all entries for worst case are zero.

- The incidence calculates the probability of having orthostatic intolerance for each crewmember onboard. However, the consequences of these disturbances depend on the individual crew responsibilities. For example, there would be more potential mission impact if the pilot or commander of the landing vehicle became incapacitated than if a crewmember without mission-critical responsibilities became ill.

Reviewed by:

David C. Hilmers