BHP Sleep Disturbance 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	*3*	*3*	*2*	*4*	*3*	*3*

Comments and limitations:

1. **General comments.** This CLiFF characterizes sleep disturbances that affect the quantity or quality of sleep after the initial adaptation to spaceflight. There is a separate CLiFF, ICL 95 Space Adaptation Insomnia, that examines sleep disturbances during the first 5 days after launch. Sleep disturbance is a very common condition among astronauts, contributing factors include noisy environments, shift work, workload and crew motivation resulting in chronic sleep debt. Sleep disturbances may affect crew performance and hinder the accomplishment of mission objectives. The best case is considered to be transient, mild to moderately disturbed sleep (after day 5 of space flight) caused by but not limited to: environmental factors, sleep shifting, poor sleep hygiene and/or exhaustion, that is effectively treated with appropriate crew scheduling/sleep- shifting, sleep aids or behavioral health interventions. The worst case is a Sleep-Wake Disorder (after day 5 of spaceflight) such as Insomnia Disorder or Circadian Rhythm Sleep-Wake Disorders that are severe or refractory to treatment with appropriate crew scheduling/sleep-shifting, sleep aids and behavioral health interventions. Sleep disturbance can lead to or be the result of conditions covered in other behavioral CLiFFs including relational problems, anxiety, depression, grief-reaction, psychosis secondary to depression and adjustment disorder. These conditions may, and often do, coexist.

2. **Incidence.** There is fairly robust data describing sleep disturbances during spaceflight. Data from the last LSAH data drop and additional cases reported through the real world system's incidence data base were used to calculate the composite incidence. The calculated incidence is high, but even so, this may be an underestimate because of mild sleep disturbances that may go unreported. The best case/worst case probabilities were calculated from the same data set as above. The total number of sleep disturbance events were 233, of which 231 met the best case definition. The best case probability is therefore calculated as 99% (231/233) and the worst case as 1% (2/233). The clinical phase durations were based on spaceflight studies showing the range of time that sleep disturbances last with the use of treatment. There is a paucity of data to support the estimation of clinical phase times for the untreated cases. The return to definitive care RTDC and Loss of crew life probabilities were considered to be zero based on the available data and subject matter expert opinion. The probability density curve that was derived appears to be a reasonable representation of the data present

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**. The incidence of this medical condition may vary over the course of the mission. The "3rd quarter effect" is the observation that psychological problems peak during the 3rd quarter of the mission and then decrease as the mission nears completion.

6. **Limitations**

- The incidence of this medical condition may vary over the course of the mission. The "3rd quarter effect" is the observation that relationship problems peak during the 3rd quarter of the mission and then decrease as the mission nears completion.
- There is some overlap between this condition and other BHP CLiFF conditions, including anxiety, depression, grief-reaction, psychosis secondary to depression and relational problems. These conditions may, and often do, coexist and sleep disturbances may be the result or may be the cause of other BHP conditions.
- The TBC and UTBC CP2 durations are identical as are TWC and UTWC durations. This seems to indicate that treatment does not matter. However, the definitions of worst case (and sometimes best case) indicate that therapy is required. Since there is no data to support a different estimation of these times, the durations were left as suggested by the editor with the limitation as noted herein.
- There is a lack of clear delineation between the best- and worst-case scenarios
- Many spaceflight studies did not differentiate between insomnia caused by space adaptation and inherent microgravity effects
- Several assumptions needed to be made regarding the untreated cases given lack of available studies.
- 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.
- The calculated incidence may be an underestimate because of mild sleep disturbances that may go unreported.

Reviewed by:

David C. Hilmers