

BHP Anxiety 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	3	2	3	2	3

Comments and limitations:

1. General comments. This CLIFF characterizes anxiety that may arise during spaceflight. Anxiety is generally understood to mean apprehension or fear from a potential threat or unexpected event that is out of proportion to the harm that the event poses. It can encompass a wide range of anxiety disorders that are defined by DSM-5 and thus the term “anxiety” can be used in a variety of contexts, making data integration difficult. LSAH data releases do not classify behavioral conditions up until now and therefore spaceflight data is of limited value. There are probably many short-lived episodes of anxiety that are part of the normal reaction to stressful events. These probably go unreported and thus lead to an underestimation of the true incidence of anxiety. This is a new CLIFF that is a refinement of the IMM CLIFF that dealt with behavioral emergencies as a single entity and that was not categorized by behavioral pathology. Studies of analog environments have shown a “third quarter phenomenon” in which psychologic issues may peak in the 3rd quarter of a mission and generally improve in the 4th. The best case is considered to be acute anxiety or mild panic symptoms caused by situational factors (e.g. burnout, work overload, performance pressure, significant events) that alleviate without any impact to the mission or personal life. It may require pharmacological therapy PRN, behavioral health intervention and/or increased behavioral health

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countermeasures. The worst case are anxiety disorders or severe panic symptoms causing significant distress or decline in areas including but not limited to work performance, sleep and interpersonal dynamics. The condition requires long-term pharmacologic therapy (minimum 6 months), and/or behavioral health intervention. Related conditions covered in other CLIFFs include adjustment disorder, relationship problems, depression, grief-reaction, psychosis secondary to depression and sleep disturbance. These conditions may, and often do, coexist.

2. Incidence. The incidence calculation is based on a report to the Human Research Program in 2016 that examined LSAH data for cases of anxiety during spaceflight. There were 24 documented cases of anxiety-related symptoms in the 28.84 person years studied. This data is limited to space shuttle flights only and therefore does not include extended duration missions. Incidence is difficult to calculate given the lack of a uniform definition of anxiety. The authors noted that this incidence rate is probably an underestimate since many cases of transient anxiety are probably not reported. The best case/worst case probabilities were derived from a study which examined the number of medical problems occurring during spaceflight that had been associated with negative “valence” (feelings or reactions). This occurred 36% of the time out of a total of 481 events yielding 174 events with negative valence. Since there have been no documented cases of anxiety that have met the worst-case criteria, the worst case probability is estimated to be less than 1%. A 99%/1% split for BC/WC was assigned. The clinical phase durations were based on clinical studies showing the range of therapy needed based on the definitions used in the CLIFF. The data is weak to support the estimation of clinical phase times. Since there is little to no data for untreated cases, the UTBC was assigned the same CP2 durations as the TBC, and a similar assignment was made for the UTWC and the TWC. The maximum duration of the worst case in terrestrial studies was 3 years, so this was used for CP2 maximum durations for TWC and UTWC. The best case return to definitive care (RTDC) and loss of crew life probabilities were considered to be zero based on terrestrial studies. The worst case probabilities for RTDC have a maximum value of 3.64% which is based on hospitalization rates, considered to be a surrogate for RTDC. Loss of crew life was considered to be zero for all cases of anxiety. 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.

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- There is a paucity of published spaceflight data relating specifically to anxiety as defined by this CLIFF due to the lack of classification of behavioral problems by DSM diagnostic category.
- Analog and terrestrial data have limitations when applied to the spaceflight environment.
- There is some overlap between this condition and other BHP CLIFF conditions, including adjustment disorder, depression, grief-reaction, psychosis secondary to depression and sleep disturbance. These conditions may, and often do, coexist.
- Several assumptions needed to be made regarding the untreated RTDC and LOCL values given lack of available studies.
- 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.
- 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 which did not adequately apply to this condition.
- The incidence data is limited to space shuttle flights only and therefore does not include extended duration missions.
- Terrestrial sources likely overestimate the incidence, RTDC and Loss of crew life values given the extensive preflight screening that occurs in long-duration spaceflight crewmembers.
- There is likely underreporting of this condition in spaceflight due to mild cases that are felt to be a normal reaction and due to fears of retribution in more severe cases of anxiety.

Reviewed by:

David C. Hilmers