

BHP Depression Disorder 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	2	3	2	3	3

Comments and limitations:

1. **General comments.** This CLIFF characterizes depression that may arise during spaceflight. Depression can develop even in well-screened individuals such as astronauts and can result in apathy, lack of motivation, irritability, sleep disturbance and a variety of other physical and emotional manifestations. By definition, if this mood lasts for more than two weeks and causes significant impairment in activities and interactions with other crewmembers, it may be diagnosed as major depressive disorder. NASA distinguishes between a behavioral event and a psychiatric disorder by the following: “a behavioral condition is any decrement in mood, cognition, morale, or interpersonal interaction that adversely affects operational readiness or performance; whereas a psychiatric disorder is one that meets the DSM criteria for diagnosis of a disorder.” There have been no documented reports of a behavioral emergency resulting from depressive mood or major depression during previous missions. The best analysis of depressive symptoms was limited to shuttle flights, all of which were about 2 weeks or less in duration. Thus, the flight duration was not sufficiently long to satisfy the criteria for major depressive disorder. 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

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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 transient apathy, low-motivation, irritability and/or disturbance of mood that resolves without any impact to the mission or personal life and/or requires as needed behavioral health intervention and increased behavioral health countermeasures. The worst case is a Depressive Disorder causing significant distress or decline in areas including but not limited to work performance, sleep, and interpersonal dynamics. The condition may also include recurrent suicidal ideation. The Depressive Disorder persists and requires pharmacologic therapy (minimum 6 months) and/or behavioral health intervention; may be treatment resistant; or may result in a suicide attempt. Related conditions covered in other CLIFFs include adjustment disorder, anxiety, grief-reaction, psychosis secondary to depression, personal relationship problems and sleep disturbance. These conditions may, and often do, coexist.

2. Incidence. There is a lack of robust data describing depression during spaceflight. The best analysis of depressive symptoms was limited to shuttle flights, almost all of which were about 2 weeks or less in duration. Thus, the flight duration was not sufficiently long to satisfy the criteria for major depressive disorder. The incidence calculation was based on a study of 313 individuals who spent a winter in Antarctica. They were debriefed by qualified psychiatrists and a psychologist and had undergone psychologic evaluation prior to starting their deployment. Thirteen events were described as meeting the definition of depression. While Antarctica is not a perfect analog for spaceflight, this study specifically categorized depressive disorders, and the demographics of the cohort studied are similar to those of astronauts. The best case/worst case probabilities were derived from the same Antarctica study. Out of 13 recorded events, 2 of them represented recurrent major depressive disorder which meets the worst case definition. Consequently, the BC/WC probabilities were calculated to be 85%/15%. The clinical phase durations were based on clinical studies showing the range of therapy needed based on the definitions used in the CLIFF. 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 range of 2.6% to 11.8%, which are based on hospitalization rates, considered to be a surrogate for RTDC. The worst case Loss of crew life was as high as 4.2% based on the increased risk of suicide in individuals with major depressive disorder. 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 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, such as depression, peak during the 3rd quarter of the mission and then decrease as the mission nears completion.

6. Limitations

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- The incidence of depression 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 a paucity of published data relating specifically to spaceflight-related depression as defined by this CLIFF due to the lack of classification of behavioral problems by DSM diagnostic category.
- There is some overlap between this condition and other BHP CLIFF conditions, including anxiety, adjustment disorder, 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 Loss of crew life values given lack of available studies.
- Terrestrial sources likely overestimate the incidence, RTDC and Loss of crew life values given the extensive pre-flight screening of long-duration spaceflight crewmembers.
- 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
- There is likely under-reporting of this condition in spaceflight due to fears of retribution or unwillingness to disclose emotional issues.

Reviewed by:

David C. Hilmers