BHP Psychosis Secondary to Depression 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*	*2*	*3*	*2*	*3*	*3*

Comments and limitations:

1. **General comments.** This CLiFF characterizes psychosis that is secondary to 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. Rarely (in about 15% of depressed individuals), psychosis may occur. Psychotic features may include auditory or visual hallucinations, delusions, disorganization, catatonia, and aggressive behavior. There have been no documented reports during previous missions of a behavioral emergency resulting from psychosis of any type, including from depressive mood or major depression. This is a new CLiFF that is a refinement of the IMM CLiFF that dealt with behavioral emergencies as a single entity and that CLiFF 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 an isolated episode secondary to depression, of thoughts and perceptions that are disturbed and difficulty understanding what is real and what is not, which resolves within the day. The worst case is severe psychotic symptomology, secondary to depression, that requires more than one day of pharmacologic therapy and behavioral health intervention. The

psychosis may not resolve. Related conditions covered in other CLiFFs include adjustment disorder, anxiety, grief-reaction, depression without psychosis, personal relationship problems and sleep disturbance. These conditions may, and often do, coexist.

2. **Incidence.** There are no reports of psychosis arising from depression during spaceflight. The best available analog to spaceflight that reported incidents of psychotic depression was a Polaris submariner study done in the 1960's and 1970's. This population has some similarities to astronauts. Submariners are screened prior to entry at the Naval Submarine School to assess their ability to adjust to both the school and subsequent submarine service. The close quarters, underwater environment, and long patrols are also similar to exploration space missions. The paper reported one case of psychotic depression over the course of nearly 21,000 person years, so the incidence in a screened population is very low, as expected. The best case/worst case probabilities are difficult to ascertain given that the best case is defined as lasting 24 hours or less which is felt to be unlikely. The BC/WC probability split was based on a terrestrial study that estimated that the chance of functional recovery within six months of the first episode of depression-triggered psychosis was 0 to 22%. This leaves a WC probability of 78-100%. The best case clinical phase durations were based on the BC definition (lasting 24 hours or less). The worst case CP2 times were based on the shortest time generally needed to stabilize a case and the length of the DRM (210 days). The best case RTDC and Loss of crew life probabilities were considered to be zero based on terrestrial studies. The treated worst case probabilities for return to definitive care (RTDC) have a range of 0-100%, showing the uncertainty in the efficacy of treatment. On the other hand, untreated worst case RTDC probabilities were considered to be 100%. 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 TWC and UTWC CP2 durations are identical. This seems to imply that treatment does not matter. However, the definitions of worst 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**

- The incidence of depression leading to psychosis 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.

BHP Psychosis Secondary to Depression CLIFF Peer Review

- There is a paucity of published data relating specifically to spaceflight-related psychosis secondary to 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, major 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.
- The TBC and UTBC CP2 durations are identical as are TWC and UTWC durations. This seems to imply that treatment does not matter. However, the definitions of worst 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 no data on behavioral health emergencies in space in general, including this condition. The terrestrial and analog data are somewhat limited, and likely overestimate the incidence of this condition in spaceflight because of intense screening of astronauts.
- The definitions of Best and Worst case further complicate the delineation of this condition, with the Best Case resolving within 24 hours regardless of treatment and the worst case scenario having severe symptoms that may last just over 24 hours or never resolve despite treatment. Therefore, there is limited relevant literature to address these specific case definitions.

Reviewed by:

David C. Hilmers