

Seizures 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	3	3	3

Comments and limitations:

1. General comments. This CLIFF characterizes seizures that might occur during spaceflight. There are a number of different types of seizures of varying etiologies and severity, but they stem from pathologic electrical signals in the brain that cause undesired physical effects. Astronauts are screened for seizures and presumably no astronaut would have a history of a seizure disorder (epilepsy). The major concern is for an unprovoked seizure that arises *de novo* during the mission and is the subject of this CLIFF. Secondary causes might include an infection or traumatic brain injury, but these are the subject of separate CLIFFs (individual infections and mild-moderate and severe head trauma). There have been no recorded cases of seizures during spaceflight. The best case for this CLIFF is a single seizure that resolves spontaneously or responds to drug therapy and does not recur. The worst case is defined as status epilepticus (a seizure lasting longer than 5 minutes, or with two or more discrete seizures between which there is incomplete recovery of consciousness).

2. Incidence. As there are no reports of seizures during spaceflight, a predictive model for astronauts developed at the Glenn Research Center was used to estimate the composite incidence.

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This model used data from LSAH (terrestrial astronaut data as well as spaceflight) and a large terrestrial study. Information from these sources was combined using a Bayesian update approach to estimate the average rate of first unprovoked seizures, using age-appropriate data. From the output of this model an incidence calculation was made. The best case/worst case percentage is based on a terrestrial study indicating that the incidence status epilepticus in patients with epilepsy is about 1-5%. This should be a reasonable estimate for worst case, leaving a BC/WC probability split of 95-99%/1-5%. The clinical phase durations, RTDC, and Loss of crew life probabilities are supported by terrestrial evidence and the case definitions, and I am in agreement with their calculation. Both TWC and UTWC RTDC probabilities were considered to be 100% based on the high morbidity/mortality associated with status epilepticus. The TBC and UTBC RTDC and Loss of crew life are all estimated to be zero based on the best case definition. There could be some slight overlap with the respiratory failure CLIFF since some deaths from status epilepticus are caused by airway compromise. 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 not dependent on mission phase. However, once an astronaut experiences a seizure, the likelihood of having a subsequent seizure increases significantly.

6. Limitations

- There are no instances of seizures during spaceflight among U.S. astronauts. Therefore, terrestrial general population studies and astronaut terrestrial data were modelled and used for incidence and outcomes.
- Since the model used looked at spaceflights through 2012 and no reports of seizures have occurred since then, the model is probably an overestimation of the true spaceflight incidence. The effect size is probably small, however.
- This medical condition is not dependent on mission phase. However, once an astronaut experiences a seizure, the likelihood of having a subsequent seizure increases significantly.
- There could be some slight overlap with the respiratory failure CLIFF since some deaths from status epilepticus are caused by airway compromise. Also, there could be overlap with CLIFFs that deal with secondary causes of seizures (infections and head trauma, for example).

Reviewed by:

David C. Hilmers