

Gastroenteritis 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	4	4	3	3	3

Comments and limitations:

1. General comments. Gastroenteritis is a non-specific term for various pathologic states of the gastrointestinal tract. The CLIFF researchers focused on the symptom of diarrhea. Gastroenteritis is often accompanied by symptoms of nausea, vomiting, anorexia, abdominal pain/cramping, bloating, and bowel gas. Viruses, bacteria, toxins, and parasites are the most common causes of gastroenteritis in the terrestrial setting. However, the threat of many of these infections is likely low in the spaceflight environment where there is good hygiene and access to clean food and water. Workup of gastroenteritis in spaceflight will be limited as infectious testing will likely not be available. In addition, if there is a significant radiation exposure, the lower gastrointestinal tract would likely be one of the first organ systems affected. Another potential case that hasn't been considered is the possibility of antibiotic-associated colitis, usually from *C. difficile*. There will be some antibiotic use during missions and there is a possibility that the antibiotics could affect the gut microbiome with resulting *C. diff* overgrowth and diarrhea/colitis. *C. difficile* is very contagious and could easily be spread. The crew probably won't have the diagnostic tools to recognize it and effectively treat it. *C. difficile* is often recurrent and can rarely lead to complications such as toxic megacolon. Including this pathogen could change our worst-case definition to include recurrent *C.*

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difficile infection and its complications. If we need to request oral vancomycin or fidaxomicin to treat this condition, we will need to flag this for the pharmacists.

2. Incidence. The incidence data uses spaceflight data that is fairly robust dating from the space shuttle and station eras. There is probably significant under-reporting of diarrhea as it is often self-limited, and the crew most likely has self-medicated in the past without reporting the condition to the ground. This could potentially impact the calculation of the amount of anti-diarrheal medication that needs to be carried on board. The best case/worst case probabilities, clinical phase durations, RTDC and Loss of crew life probabilities are supported by terrestrial evidence. 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 durations 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 durations.

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 should not be dependent on mission phase.

6. Limitations

- Under-reporting for this condition could have been significant during past space missions and may result in underestimation of the incidence. There is the possibility that sufficient medication to treat gastroenteritis will not be carried on board if the condition incidence used is too low.
- The condition did not consider *C. difficile* infection. If this condition occurs on board, it could present a significant health hazard for the crew if not recognized. If not covered within this CLIFF, it is recommended that it be considered as a separate condition.
- Radiation colitis could occur if the crew encounters a significant radiation event. This is not considered in this CLIFF.
- The worst case scenarios used data from resource-poor countries. This probably leads to a highly conservative estimate of worst case probabilities given the higher level of hygiene in the spaceflight environment.
- Infectious diarrhea can be very contagious and also recurrent. Once an episode occurs, the incidence of further cases will likely increase significantly.

Reviewed by:

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