

Urinary Tract Infection 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	2	3	3	3

Comments and limitations:

1. General comments. The subject of this CLIFF is urinary tract infections (UTI). UTI's can originate from the lower urinary tract (cystitis) or the upper tract (pyelonephritis). The microgravity environment predisposes astronauts to UTI's by promoting the formation of urinary tract calculi and relative dehydration through fluid shifts and decreased oral intake. Females are at increased risk from an anatomical standpoint and have a higher incidence of UTI's. There are well-documented cases of UTI's during spaceflight. The best case for this CLIFF is defined as a UTI that is responsive to oral antibiotics while the worst case is a UTI or pyelonephritis requiring IV antibiotics.

2. Incidence. UTI's in space are well-documented, and the diagnosis is usually fairly straightforward. Because of the unique space environment and the relative good health of astronauts, terrestrial studies were not considered and spaceflight data was used alone in the composite incidence decision. Since there is a higher incidence in females, two distributions were created, differentiated by gender. The best case/worst case probability was based on a prospective terrestrial study showing that of 147 UTIs diagnosed, 138 were cystitis and 5 were pyelonephritis (a proportion of 3.6%) at initial diagnosis. Other studies showed that pyelonephritis constitutes 1-5%

Urinary Tract Infection CLIFF Peer Review

of all UTIs. At the lower end, a meta-analysis revealed that 2 out of 582 UTI's progressed to pyelonephritis yielding a WC percentage of 0.34%. Taking into account these terrestrial studies and the increased risk of UTI's during spaceflight, the worst case probability of 1% was derived. The clinical phase durations, RTDC and LOCL probabilities are supported by terrestrial evidence, and I am in agreement with their calculation. A limitation was the lack of untreated worst-case data. The RTDC probability was based on studies looking at rates of hospitalization. Using this criterion may overestimate the actual need to RTDC as adequate treatment (IV antibiotics) will be available onboard. The LOCL number is also problematic in that many severe cases can lead to sepsis, which is a separate condition. 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.

6. Limitations

- There was a paucity of untreated worst-case data to inform the WC probabilities.
- The RTDC probability was based on studies looking at rates of hospitalization. Using this criterion may overestimate the actual need to RTDC as adequate treatment (IV antibiotics) will be available onboard.
- The LOCL probability is problematic in that many severe cases can lead to sepsis, which is a separate condition.

Reviewed by:

David C. Hilmer