

## Upper Respiratory 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<br>Composite Incidence and Level of Confidence | Table 3, 4<br>BC/WC<br>Loss of Crew and probability | Table 4 -<br>Clinical Phase 1, 2 durations<br><br>Table 5 – CP 2 Loss of Crew | Table 4 – RTDC %<br><br>Table 6 – RTDC Loss of Crew | Table 4 – Loss of Crew Life %<br><br>Table 7 – Loss of Crew Life, Loss of Crew | Table 8 – TI |
| Score                                                                                      | 3                                                          | 3                                                   | 2                                                                             | 2                                                   | 3                                                                              | 3            |

Note: Tab 9B still contains old information and needs to be updated. Tab 3E shows updated mean incidence, but this has not been transferred to tab 9B. The minimum and maximum % for LOCL should have a number instead of “N/A.” All empty data positions should be completed.

Comments and limitations:

**1. General comments.** Upper respiratory infection (URI), as defined in this CLIFF, includes the common cold, sinusitis, and rhinitis. By far the most common pathogens are viral, but bacterial infections also occur with some frequency. Upper respiratory tract infection (URI) represents the most common acute illness evaluated in the outpatient setting. Person-to-person spread of viruses accounts for most URIs. Respiratory infections have been reported in space in spite of efforts to mitigate this risk with a pre-launch quarantine. The diagnosis can be challenging since similar symptoms have been attributed to a cephalad fluid shift and the dry spacecraft cabin atmosphere. While the risk of infection is reduced because of pre-launch quarantine and the filtered atmosphere in the crew cabin, susceptibility to infection is increased due to an impaired immune response during

## Upper Respiratory Tract Infection CLIFF Peer Review

space missions. Data to inform this CLIFF comes from direct crew reporting and from analysis of medication usage for upper respiratory tract infections by the crew.

**2. Incidence.** Crew reporting of URI showed approximately 1 infection per person year (Crucian) which was consistent with analogue data showing a nearly equivalent rate. However, it was felt that there is significant under-reporting of URI's as it is often self-limited, and astronauts most likely self-medicate without reporting the condition to the ground. In this case evidence as to actual usage of medication to treat URI's is available in the paper by Wotring that shows an incidence more than 4 times the reported rate. Actual usage probably represents the best evidence for the presence of a URI. The reported and usage data were combined statistically to derive the mean incidence and probability distribution curve. The resulting incidence of approximately 2 cases per person-year and the probability distribution curve appear to be a reasonable representation of the data presented.

The CP 2 times are difficult to determine, partially because of the paucity of data on worst case results. However, the times as defined are difficult to understand. The maximum duration of the treated best case is longer than the treated worst case, which should not be the case. The same is true for treated worst case vs untreated worst case. Also, the probabilities of RTDC are higher for the treated worst case than for the untreated worst case which also should not be. The best case/worst case clinical probabilities are supported by terrestrial evidence.

**3. Clinical phase data.** I am in agreement with the clinical phase durations entered in this CLIFF except as noted in paragraph 2 for clinical phase 2. Clinical phase 1 duration 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 upper respiratory infections will not be carried on board if the condition incidence used is too low.
- Since URI's are very contagious, once an episode occurs, the incidence of further cases through droplet spread will likely increase significantly.
- The untreated worst case data is extremely sparse. This is most likely because treatment is generally readily available and untreated disease is usually self-limited.
- Many of the terrestrial and analogue papers were unhelpful as the populations studied were significantly different than astronauts.

Reviewed by:

David C. Hilmers