

Lower 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 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	3	3	3	2	3

Comments and limitations:

Note: The CLIFF data was not completely compiled at the time of this review.

1. **General comments.** Lower respiratory tract infections are defined as any infections in the lungs, airway, or pleura below the level of the larynx. There are a number of potential pathogens, but most commonly the infectious etiologies are viral and bacterial, with fungal and parasitic infections less likely. A lower respiratory tract infection can affect the airways, such as with tracheitis or bronchitis, the bronchioles or alveoli in the lungs (pneumonia), or the pleura (pleuritis or empyema). For purposes of this CLIFF the best case scenario was defined as an influenza-like illness or viral bronchitis that resolves with symptomatic treatment. The worst case scenario is a bacterial superinfection after a viral illness, bacterial bronchitis or bacterial pneumonia that requires treatment with antibiotics but does not result in ARDS or respiratory failure. Since astronauts are quarantined prior to flight, are in excellent general health, and are living in a sanitary environment in the spacecraft, it would be expected that this would be a very uncommon occurrence. It is also unlikely that astronauts will under-report this condition because of its potential seriousness.

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2. Incidence. These infections have been very rarely reported in space. Data from spaceflights on the ISS show only one case of what was diagnosed as “bronchitis”. Since the spaceflight data is so sparse and “bronchitis” can be an imprecise diagnosis, it was not felt that this data could be highly informative. The best epidemiologic data comes from papers by Broulette and MacFarlane. The Broulette paper looked at the incidence of community acquired pneumonia in a general population. “Community acquired pneumonia” would comprise the majority of the infections that are included in the case definition but is not all-encompassing. The MacFarlane paper, on the other hand, studied community acquired lower respiratory infections as a whole and has a higher incidence rate. The two papers were considered equally informative. There is one analogue paper that was also used that reports a significantly higher rate of infections than the other two papers. The sample size of the Broulette study is massive and completely overwhelms the influence of the other two study when combined, as the statistical methods being used strongly weight the mean incidence towards studies with large sample sizes. The probability distribution curve also shows an extremely narrow distribution with a tight variance centered near the incidence reported. This most likely overstates the precision of the data considered as there are significant difference in the reported incidences in the individual papers as well as differences with which the conditions studied correspond to the definition used in the CLIFF. I feel that lower respiratory tract infections are very unlikely to occur in space, so there is no basic disagreement with the mean incidence that was calculated. The best case/worst case probabilities, clinical phase durations, RTDC and Loss of crew life probabilities are supported by terrestrial evidence.

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. However, it should be noted that if someone develops pneumonia or other lower respiratory tract infection once, his/her risk of re-infection increases, and the subsequent incidence rate will increase.

6. Limitations

- Spaceflight incidence data are based on only a few cases and the diagnostic criteria may not be reliable. Thus, the spaceflight data was not deemed to be highly informative.
- The Broulette study contained an extremely large number of subjects. The statistical methods being used strongly weight the mean incidence towards studies with large sample sizes. Thus, the mean incidence rate calculated was very close to that quoted in the Broulette paper.
- The overall confidence that we have in the mean incidence value is probably overstated because of the large sample size of the Broulette paper.
- Collecting appropriate data for the untreated scenarios was very difficult since few, if any, studies address not providing treatment for medical conditions.
- Obtaining accurate data for CP2 durations was difficult.
- Once an episode occurs, the incidence of further cases will likely increase significantly.

Reviewed by:

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David C. Hilmers