Space Adaptation Nasal Congestion 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: 2

   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*	*2*	*2*	*3*	*3*	*3*

Comments and limitations:

1. **General comments.** This CLiFF addresses nasal congestion that occurs as a result of the hydrostatic fluid shifts that occur within the first five days after orbital insertion. The feeling of fullness in the face, sinuses, and nasal cavities is experienced by nearly all crewmembers, to some extent. In most cases it resolves spontaneously as a new fluid equilibrium is reached within a few hours or days. Although this condition can be uncomfortable, it usually has little mission impact and little associated morbidity. Since the condition is so common and is expected as a physiologic phenomenon after reaching orbit, many cases probably go unreported. This condition needs to be distinguished from ICL 82 "Respiratory Tract Infection – Upper" which may be also associated with nasal congestion but is usually associated with a viral infection rather than with fluid shifts. ICL 82 deals with URI's that occur anytime during the mission, not just during the first five days. It is possible that some URI's may be erroneously categorized as SAS-related if they occur during the first five days of flight. The best case is considered to be nasal congestion that resolves spontaneously while the worst case is nasal congestion requiring treatment.

2. **Incidence.** Four papers describing the incidence of "nasal stuffiness" or "rhinitis" during different eras of manned spaceflight were used to determine the composite incidence. The data represents occurrences, so it is unclear whether multiple episodes were attributed to the same crewmember. It was difficult to parse from this data how many cases of nasal congestion occurred as a result of fluid shifts and how many occurred after the first five mission days. Thus, the incidence may be overestimated. However, since crewmembers are aware of the cause of the nasal congestion and the impact is relatively minor, many cases may go unreported. This would result in an off-setting underestimation of the incidence. The best case/worst case probabilities used data from a pharmacologic study in which 55% of crewmembers on ISS missions who reported symptoms of nasal congestion used medication to treat the condition. This data was used to inform the worst case scenario. It should be noted that this data was collected throughout the flight, not only during the first five days. In my experience, this is likely to be an overestimation of the number of astronauts who use medications to treat SAS-related congestion. Thus, the worst case probability may be overestimated. The clinical phase durations are based on terrestrial studies as there is no corroborating spaceflight data, Both RTDC and Loss of crew life probabilities were considered to be zero given the medical condition definition. 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 dependent on mission phase as it only occurs during the first five mission days.

6. **Limitations**

- It was difficult to parse from the papers used for the incidence calculation how many cases of nasal congestion occurred as a result of fluid shifts after insertion into orbit and how many occurred after the first five mission days. The preponderance of the incidence data does not stratify onset of symptoms to these first 5 days. Thus, the incidence may be overestimated.
- Since crewmembers are aware of the cause of SAS-related nasal congestion, and the impact is relatively minor, many cases may go unreported. This would result in an off-setting underestimation of the incidence.
- The best case/worst case probability used data collected on medication usage for nasal congestion throughout entire ISS missions. Therefore, the amount of medication used to treat SAS-related nasal congestion (worst case scenario) during the first five mission days may not be accurate. In my experience as a crewmember, a worst case of 55% is likely to be an overestimation of the number of astronauts who use medications to treat SAS-related congestion. It is likely that the worst case probability is lower than that stated.
- Data comes from a handful of observational studies of actual symptoms and pharmacologic use in spaceflight. The definitions of nasal congestion are subjective and medicine usage by astronauts, a key stratification in this condition, is widely driven by preference for symptomatic relief, rather than any firm criteria. As suggested in the pre-

flight mitigation activities [i.e. clean air filters], some symptoms may not be purely related to cephalad fluid shifts, but to air quality as well. One key limitation is that by definition, space adaptation conditions only occur in the first 5 days after orbital insertion.

- This condition needs to be distinguished from ICL 82 "Respiratory Tract Infection – Upper" which may be also associated with nasal congestion but is usually associated with a viral infection rather than with fluid shifts. ICL 82 deals with URI's that occur anytime during the mission, not just during the first five days. It is possible that some URI's may be erroneously categorized as SAS-related nasal congestion if they occur during the first five days of flight.

Reviewed by:

David C. Hilmers