

Epistaxis 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	3	2	2	3	3

Comments and limitations:

1. **General comments.** Epistaxis, or nosebleed, is a common event that most often does not require medical treatment. Only 6% of people who experience an epistaxis event will ever seek medical attention. There have been 14 recorded events during spaceflight. This condition has been divided into space adaptation-related epistaxis which occurs within the first 5 days of achieving orbit, and cases of epistaxis that occur beyond the first five days on orbit. This somewhat arbitrary distinction was chosen as it is thought that one of the major contributors to epistaxis, cephalad fluid shift with consequent increased intravascular pressures, leads to an increased risk of epistaxis. It should be noted that this cephalad shift equilibrates but a component of it remains after five days. Other conditions that can contribute to epistaxis such as low humidity, circulating debris, and trauma, continue to exist after the space adaptation period is over. This CLIFF considered the post-space adaptation syndrome case. The best-case scenario was epistaxis that resolves with little or no treatment while the worst case was a bleed requiring nasal packing and/or surgery.

2. **Incidence.** The composite incidence was calculated using only spaceflight data as there are no good terrestrial analogs to the spaceflight environment. Of the 14 spaceflight recorded events 6 of

them were recorded during the first five days (space adaptation-related), 2 of them after 5 days, and the remaining 6 were not time-stamped. The biostatistician proportionately assigned the indeterminate 6 cases according to the relative ratios of the other 8 cases. This is a possible source of error but is an appropriate assumption. There is probably significant under-reporting of epistaxis as it is often self-limited and mild, and the crew most likely has self-treated in the past without reporting the condition to the ground. The best case/worst case probabilities are supported by terrestrial evidence. Literature regarding the untreated worst-case scenario was extremely limited and several parameters are based on subject matter expert opinion. Due to the increasingly rigorous Institutional Review Board guidelines of American institutions, literature for untreated best and worst cases were limited to extrapolation from dated case studies. RTDC percentages for the TBC and UTBC were assigned to be zero given the conditions' definitions and no articles were reviewed for these conditions. In the TWC, RTDC was determined from retrospective reviews. The UTWC RTDC used the same studies as the TWC along with subject matter expert consensus given the lack of available literature detailing this scenario. The probability density curve that was derived appears to be a reasonable representation of the data presented. The variance is fairly broad, reflecting the uncertainty in the mean incidence.

3. Clinical phase data. I am in agreement with the clinical phase 1 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. Clinical phase 2 duration assignment required a number of assumptions, given the paucity of data about untreated cases. However, the final estimations appear to be appropriate.

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 and a separate CLIFF has been assigned to epistaxis during the first five days of spaceflight. After five days of flight, the condition is considered to have a constant incidence through the rest of the mission except for possible gravity well-related changes.

6. Limitations

- Assignment of 6 inflight events of epistaxis whose mission time was indeterminate was based on the proportion of known events occurring after 5 days. While a logical assumption to make, there is the possibility of significant assignment error.
- The separation of 'day 5' for space adaption epistaxis versus the condition characterized in this CLIFF is largely based on anecdotal experience.
- The exact start dates of several inflight occurrences of epistaxis are unknown.
- Literature regarding the untreated worst-case scenario was extremely limited and several parameters are based from subject matter expert opinion.
- Due to the increasingly more rigorous Institutional Review Board guidelines of American institutions, literature for untreated best and worst cases were limited to extrapolation from dated case studies.
- Under-reporting for this condition could have been significant during past space missions and may result in underestimation of the incidence.

Reviewed by:

David C. Hilmers