Abnormal Uterine Bleeding 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*	*1*	*1*	*2*	*3*

Overview:

Comments and limitations:

1. **General comments.** Abnormal uterine bleeding is a very common condition in women, estimated to affect 5-25% of menstruating females. For this CLIFF it is defined to be irregular bleeding between menses, menses > 8 days in length, or heavy menses (requiring tampon/pad changes < Q2H, or passing clots larger than the size of a quarter). Spaceflight evidence is limited because of probable under-reporting, privacy issues, and lack of pharmacologic usage data. The worst-case scenarios are delineated by the need for mechanical or surgical intervention. Surgical modalities are assumed to not exist on board and mechanical interventions such as tamponade with a Foley catheter are temporizing measures at best. Terrestrial data varies widely because of differences in definitions and in study populations. Therefore, a number of parameters were derived from a combination of terrestrial data and subject matter expertise. Fortunately, the editor has published previously on this condition and is very familiar with the extant literature.

2. **Incidence.** The only non-survey terrestrial paper available was used to determine composite incidence. The resulting value most likely is conservative given that there is a range of hormonal and non-hormonal preventive treatments available to female astronauts that may not be options in the

general population. This may be somewhat offset by possible under-reporting of the condition to the ground by female astronauts. The study that was used has a very large sample size; therefore, the small variance most likely overestimates the confidence that we have in the composite incidence. The best case/worst case probabilities were based on a range of probabilities cited in terrestrial studies. A best guess estimate was made between the extremes of probabilities reported. It was particularly difficult to calculate clinical phase durations, return to definitive care (RTDC) and loss of crew life probabilities because of the wide range of variables involved, and the uncertainty in the efficacy of onboard measures to stop a hemorrhage. The probability density curve that was derived appears to be a reasonable representation of the data presented; however, it most likely overestimates the overall confidence we have in the composite incidence.

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 1 durations. As stated above, clinical phase 2 durations are based on assumptions documented in the CLIFF and on subject matter expertise.

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**

- There has been no formal tracking of AUB in spaceflight and little published details are available about known events.
- Female astronauts have a wide range of interventions available to prevent AUB that may not be options to many women who were subjects of terrestrial studies. This may skew the terrestrial data that was used when applied to the female astronaut population.
- Terrestrial literature on AUB does not specifically analyze outcomes by non-hormonal, cyclical hormonal, continuous hormonal, or type of contraception.
- Under-reporting for this condition may be significant given privacy issues.
- Inability to predict the efficacy of on-board methods of control, such as mechanical tamponade, could have a profound effect on the CP2 duration, RTDC and LOCL probabilities.
- The RTDC and LOCL calculations are based on a 210 day lunar mission where RTDC is possible within 14 days. These will probably need to be modified if a Martian mission is baselined.

Reviewed by:

David C. Hilmers