Vaginal Yeast Infections 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*	*2*	*3*	*3*	*3*	*3*

Comments and limitations:

1. **General comments.** Vulvovaginal candidiasis is the subject of this CLIFF and is defined as a yeast infection of the vulva and/or vagina. It is mainly caused by Candida albicans although other candida species may be involved. It is characterized by pruritis, discomfort/pain, abnormal vaginal discharge, dysuria, and/or dyspareunia. It is quite common and up to 75% of women will have at least one episode during their lifetimes. Severe cases are more common in immunocompromised patients but can also occur as a consequence of systemic antibiotic therapy. The best case in this CLIFF is defined as: uncomplicated vulvovaginal candidiasis, with mild to moderate, sporadic, or infrequent vulvar irritation, including itching and discomfort of the vulvar skin and vaginal epithelium, vaginal discharge, and/or discomfort with voiding which responds to all azole treatment regimens including single-dose oral, and intra-vaginal therapy. The worst case is a complicated, severe, or recurrent vulvovaginal candidiasis requiring extended oral treatment. It is expected that very mild cases might go unreported or unnoticed during spaceflight. Since the immune system may be compromised during long-term spaceflight, female astronauts may be more disposed to candidal infections as the mission progresses.

2. **Incidence.** Two terrestrial studies that investigated the incidence of vulvovaginal candidiasis were combined to calculate the composite incidence. These studies had similar incidence rates. Because mild cases may go unnoticed or unreported, it is possible that this number represents an underestimate. The best case/worst case probability used CDC estimates of complicated cases and a terrestrial study that examined the recurrence rate. The value obtained of 10% worst case probability is a reasonable estimate using these two sources. The clinical phase durations are supported by terrestrial evidence, and I am in agreement with their calculation. Both RTDC and LOCL probabilities were considered to be zero given the medical condition definition. The probability density curve for the composite incidence 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 duration 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 might have a higher incidence as the mission progresses. This is based on research that shows that immune dysregulation increases with the length of the spaceflight.

6. **Limitations**

- Under-reporting for this condition may occur because of very mild disease that could go unnoticed. This may result in underestimation of the incidence.
- There was a paucity of data regarding the incidence of this condition in spaceflight. This limitation is overcome by robust terrestrial studies.
- The best case to worst case probability is limited by the broad worst case definition which includes both severe infections and recurrent infections.
- Untreated worst-case duration is nearly impossible to calculate because this is a scenario where treatment would always be given.

Reviewed by:

David C. Hilmers