Appendicitis 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*	*3*	*2*	*2*	*3*

Comments and limitations:

1. **General comments.** This CliFF characterizes acute appendicitis which is inflammation or infection of the appendix. Usually this occurs with a small appendicolith or other obstruction causing blockage of the lumen of the appendix. While the diagnosis is often clinical, based on typical signs and symptoms, ultrasound (which will be carried onboard) can be of limited use in confirming the diagnosis in the hands of a trained operator. Antibiotics have increasingly been used to treat non-complicated appendicitis and will probably be the mainstay of therapy if a case were to occur during a mission. It is unlikely appendectomy will be an option during exploration missions. There have been no reported cases of appendicitis during spaceflight. The best case is considered to be an uncomplicated case of appendicitis which responds to conservative medical treatment (antibiotics and symptomatic treatment). The worst case is appendicitis resulting in a perforation or intra-abdominal infection.

2. **Incidence.** There have been no confirmed inflight reports of acute appendicitis. A model that was used to estimate the incidence of appendicitis was developed by Gilkey, et al. The model incorporates astronaut terrestrial data as well as the spaceflight experience to generate a risk of appendicitis. Because there has not been a case of appendicitis in space, the study used a Bayesian analysis to calculate the risk of appendicitis occurring by combining baseline incidence data in analogous populations and the two cases in astronauts who had appendicitis on earth. Since then, no cases of appendicitis have occurred in spaceflight, so the incidence may be lower than estimated in this paper. The best case/worst case probabilities used data from two terrestrial studies that showed that 22.5% to 37.4% of patients with appendicitis who were initially treated with antibiotics failed therapy and required surgery. The clinical phase durations, Removal to Definitive Care (RTDC) and *Loss of Crew Life* probabilities are supported by terrestrial evidence and the case definitions, and I am in agreement with their calculation. The best case *Loss of Crew Life* was estimated as 0% by condition definition, and the worst case RTDC was set at 100% based on the case 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 not dependent on mission phase as appendicitis may occur during any time during the mission.

6. **Limitations**

- There are no instances of appendicitis during spaceflight among U.S. astronauts. Therefore, terrestrial general population studies and astronaut terrestrial data were modelled and used for incidence and outcomes.
- It is unknown to what extent spaceflight environmental and physiological factors increase the likelihood of the development of appendicitis during spaceflight.
- The diagnosis of appendicitis may be difficult to make during spaceflight due to the lack of imaging. It may be confused with other causes of acute abdominal pain such as ovarian torsion, ectopic pregnancy, biliary colic, cholecystitis or cholangitis, etc.
- There is a paucity of data to inform the *Loss of Crew Life* and RTDC probabilities for the untreated cases.
- There have been no new cases of appendicitis that have occurred in spaceflight since the Gilkey paper was published, so the incidence may be lower than estimated in this paper.

Reviewed by:

David C. Hilmers