

Diverticulitis 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	3	3	3

Comments and limitations:

1. General comments. This CLIFF characterizes acute diverticulitis that could occur during spaceflight. Diverticulitis results from inflammation in an outpouching of the organs of the digestive tract called diverticula. This can lead to a localized infection or to more serious complications such as abscess, perforation, fistula or obstruction. Most commonly, diverticulitis occurs in the colon but can occur in other parts of the digestive tract. Symptoms include pain, nausea/vomiting, fever, anorexia, and constipation or diarrhea. CT scan is the preferred diagnostic modality. Since CT most likely will not be available in space, the diagnosis will need to be made clinically although ultrasound could provide some insight. Surgery is required in about 12-30% of patients admitted with diverticulitis who fail conservative therapy with intravenous fluids and antibiotics. Risk factors for diverticulitis include smoking, obesity, sedentary lifestyle, and low dietary fiber intake, the prevalence of which would tend to be lower in the astronaut population. There are no case reports of diverticulitis during crewed spaceflight. The best case is considered to be an uncomplicated case of diverticulitis that is self-limited or that responds to oral or IV antibiotics. The worst case is a complicated case of diverticulitis (i.e., abscess, perforation, fistula, obstruction), requiring IV antibiotics and/or percutaneous or surgical intervention.

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2. Incidence. Since there are no spaceflight reports of diverticulitis, the incidence calculation was based on data from a large terrestrial epidemiological project in Olmsted County, Minnesota from 2000-2007. The data was stratified by age, and the age group best characterizing flown astronauts was used. As there is also a slight difference in incidence between males and females, two separate distributions were made based on gender. There is no indication that the incidence of diverticulitis in astronauts would be different for them in space than on earth. However, astronauts probably have fewer risk factors for the development of diverticulitis than the general population that was studied, and it is expected that the incidence is overestimated. In addition, diverticulitis often recurs in individuals who have had a previous episode, and these cases would be reported in the incidence data. Since astronauts are well-screened, they would be much less likely to have a recurrent case. Since the incidence was based on a large epidemiologic study, the variance is small which may underestimate the uncertainty in the incidence calculation. The best case/worst case probabilities were derived from terrestrial studies showing that 12-30% of patients presenting with diverticulitis required surgery. Thus, a range of BC 70-88% and WC 12-30% was chosen to define the BC/WC split. Of note, the WC definition also includes the need for IV antibiotics, so the BC/WC split could be a slight underestimation since the studies only looked at the need for surgery. The clinical phase durations, RTDC and Loss of crew life probabilities are supported by terrestrial evidence, and I am in agreement with their calculation. The surrogate for RTDC is the need for hospitalization. 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; however, once an astronaut has a case of diverticulitis, the probability of a recurrent case increases significantly.

6. Limitations

- Risk factors for diverticulitis include smoking, obesity, sedentary lifestyle, and low dietary fiber intake, the prevalence of which would tend to be lower in the astronaut population. This could lead to an overestimation of the incidence in astronauts vis a vis the general population.
- Since the incidence was based on a large epidemiologic study, the variance is small which may underestimate the uncertainty in the incidence calculation.
- The WC definition includes the need for IV antibiotics, so the BC/WC split could be a slight underestimation since the studies utilized in the calculation only looked at the need for surgery. However, it is expected that most cases requiring surgery will also require IV antibiotics.
- This medical condition is not dependent on mission phase; however, once an astronaut has a case of diverticulitis, the probability of a recurrent case increases significantly.
- The study used to calculate incidence included recurrent cases of diverticulitis. It is assumed that once an astronaut had a case of diverticulitis, they would either have definitive care via

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surgery or be disqualified from spaceflight. This may lead to overestimation of the incidence of diverticulitis in the astronaut population.

- For the untreated best-case scenario, all studies used except Bolkentstein et al, 2018 are based on initially hospitalized patients and may therefore not reflect the true duration, RTDC, or Loss of crew life for acute uncomplicated diverticulitis since they do not include data from patients treated as outpatients.
- There is a paucity of data regarding untreated worst-case diverticulitis. The untreated worst-case scenario duration is based on diverticular disease with an associated abscess treated with antibiotics only. The RTDC is based on the proportion of complicated diverticulitis patients who required surgery in the listed studies. The Loss of crew life is based on a study of patients presenting with perforation requiring emergent surgery (delayed/advanced presentation) and the upper limit of 100% was conservatively assigned since data does not exist to inform this value.

Reviewed by:

David C. Hilmers