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*	*3*	*3*	*3*	*3*

Comments and limitations:

1. **General comments.** This CliFF characterizes tendinopathy, tendinitis, tenosynovotis, and bursitis of the lower extremity. Although overuse injury is specified in the definition as a separate condition, it is the cause of many of the cases described in this CLiFF and is not categorized separately. Symptoms of tendinopathy and bursitis include pain, swelling, and reduced function. Treatment may include rest, activity modification, physical therapy, medications, injections, and surgery. There are no documented episodes of tendinopathy or bursitis in spaceflight. Therefore, terrestrial studies are used to estimate the incidence and outcomes of this condition in spaceflight. Since many cases included in this CLiFF are of minor consequence, they may go unreported, whether in space or on earth. The best case is considered to be tendinopathy/enthesopathy, bursitis, or overuse injury which can be managed symptomatically (e.g. rest, non-opioid analgesics, physical therapy) and does not impact mission objectives. The worst case is a a tendinopathy/enthesopathy, bursitis, or overuse injury which requires treatment (e.g. corticosteroid injection, dry needling, physical therapy, nitroglycerin patches), or impacts mission objectives. Elective surgery may be necessary post-mission in the worst case.

2. **Incidence.** There are no documented episodes of these conditions during spaceflight; therefore, terrestrial studies were used to estimate the incidence and outcomes. Although military populations are usually younger and more active than astronauts during spaceflight, the best data to describe the subject of this CLiFF came from a Naval Special Forces study. This research studied the incidence of these conditions in Special Forces operators, categorized by their location in the upper or lower extremities (the former of which is the subject of a related CLiFF, ICL 108). No other paper could be found that met the medical condition as closely or specified their anatomic location as closely as this one. Given that this study took place in unit gravity, utilizing its data may result in an overestimation of the incidence and impact of this condition since the microgravity environment of spaceflight typically results in decreased forces on joints, muscles, and tendons of the lower extremities. However, exercise countermeasures during the microgravity phase of spaceflight missions and terrestrial EVAs under partial G conditions could contribute to the development of these conditions. The best case/worst case probabilities are based on the percentage of patellar tendinopathy and Achilles tendinopathy cases (30-38%) that are unable to participate in sports or eventually require surgery. The clinical phase durations, RTDC and LOCL probabilities 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 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, the incidence may be increased during periods of heavy activity and partial gravity.

6. **Limitations**

- Under-reporting for this condition could have occurred during past space missions due to subtle overuse injuries that were not of clinical consequence. This may result in underestimation of the incidence.
- No spaceflight data are available for this medical condition.
- The population studied to calculate incidence was Special Forces operators. They are more likely to be younger and more active than astronauts during spaceflight.
- The group studied may result in an overestimation of the incidence and impact of this condition since the microgravity environment of spaceflight typically results in decreased forces on joints, muscles, and tendons of the lower extremities. Since we don't have access to incidence data about the joint site and condition distribution, we assumed independence in the probabilities of MSK conditions occurring, i.e. where the injury occurs is independent of which type of injury. This is a noted limitation of this incidence approach for both the upper and lower extremity CliFFs.
- The incidence and outcomes for overuse injuries was not included because relevant incidence data was not available for overuse. However, many of the other conditions described in this CLiFF result from overuse injuries.

Reviewed by:

David C. Hilmers