

Acute Arthritis 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	3	3

Note: The CRT documentation (CP1 durations in Table 4 and CAPABILITY RESOURCE TABLE (CRT) OVERVIEW row 114) are unavailable until June 15th. I have left them highlighted yellow in this CLIFF as a placeholder for when the information is available.

Comments and limitations:

1. General comments. In adults, arthritis is the most common cause of disability and is among the leading conditions causing work limitations. Although arthritis prevalence is higher in those over 65 years, nearly two-thirds of the adults reporting doctor diagnosed arthritis are younger than 65 years. This CLIFF does not cover inflammatory arthritides such as rheumatoid arthritis nor does it include septic arthritis, but does include osteoarthritis and crystalline arthropathies. Osteoarthritis, also known as degenerative joint disease, is the most common type of arthritis. It causes progressive damage to the cartilage and other joint tissues, and frequently affects the hand, knees, and hips. Gout is a painful, episodic and recurrent form of crystalline arthritis, caused by deposition of crystal

in joints and elsewhere. Symptoms typically consist of intense episodes of painful swelling in single joints, most often in the feet and especially in the great toe.

There have been no reported cases of osteoarthritis flares or crystalline arthropathies in spaceflight. However, since many of the astronauts are in the 5th or 6th decade of life, it is likely that a significant number will have arthritis to some degree. It might be intuitive that the off-loading of joints in microgravity leads to a decreased incidence of osteoarthritis. However, data from terrestrial hind-limb unloading (HLU) animal experiments and human bed-rest studies demonstrate that reduced mechanical forces associated with joint unloading and immobilization can lead to proteoglycan loss in articular cartilage. Joint trauma and unloading studies support the notion that a normal range of mechanical forces are critical for maintaining healthy joints. Thus, microgravity may actually lead to a progression of arthritic changes. Radiation may further degrade articular cartilage once astronauts leave the protective environment of low earth orbit. In summary, it is unclear whether exploration missions will lead to an increase or decrease in the incidence of acute arthritis.

2. Incidence. A suggestion was made that the composite incidence be divided into two separate distributions, one for astronauts with a diagnosis of arthritis and another for those without. I did not feel that this was justified for the following reasons. First, a large segment of the population will have some evidence of arthritis in at least one joint, upon close examination, by the time they reach the age of most astronauts. Many astronauts who have done EVA training will develop arthritis in the glenohumeral joints. Also, the definition of when degenerative changes become “arthritis” is not clear cut. Do we only define “arthritis” if it is severe? It is easier to distinguish if there is a history of gouty arthritis or not with some precision, but osteoarthritis is much less clear. The Parry paper that was going to be used to inform the distribution of astronauts with a known diagnosis of arthritis only had 67 subjects with an average age of 62 and was a diary study of knee osteoarthritis. Most patients with significant knee osteoarthritis have daily pain. It was unclear in this paper that an acute flare occurred whenever the diary said that there was pain. The incidence that the paper indicated was 200 times higher than the non-arthritic mean. Given that the paper includes few subjects, who were older, and who were self-reporting, there was a low level of confidence in this paper. Therefore, putting all astronauts without distinction into the same distribution was preferred. The fact that there has never been a reported case of acute arthritis in spaceflight adds weight to using the lower mean incidence rate. The best case/worst case probabilities and clinical phase durations are supported by terrestrial evidence. The CST assumed that return to definitive care (RTDC) had a zero probability, so no searches were made. Loss of crew life was also assumed to be zero for all cases, which appears to be a reasonable assumption. The probability density curve that was derived appears to be a reasonable representation of the data presented. It should be noted that because of the large number of subjects in the Cameron study, the computed variance in the distribution is small and represents an overconfidence in the precision of the incidence.

3. Clinical phase data. I am in agreement with the clinical phase durations 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 durations.

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

- Because of the large number of subjects in the Cameron study, the computed variance in the distribution is small and represents an overconfidence in the precision of the incidence.
- CST assumed RTDC = 0% probability, so RTDC searches were not performed (editor did run RTDC search for TBC scenario).
- There were no articles identified from the student effort for loss of crew life.

Reviewed by:

David C. Hilmer