

Pregnancy 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: 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	1	3	3	3	2	3

Comments and limitations:

1. General comments. This CLIFF characterizes the medical condition of pregnancy during spaceflight. There is currently little research that has examined the effects of microgravity and the spaceflight environment on either the mother or fetus. However, it is estimated from terrestrial data that about 98-99% of pregnancies are intrauterine while 1-2% are ectopic. Thus, the most likely outcome of a pregnancy would be the need to return to definitive care which would carry a significant mission impact. This CLIFF is part of a pair of pregnancy-related CLIFFs, the other one being ICL 76, Risk of Pregnancy which calculated the risk of becoming pregnant. This CLIFF examines the medical complications and mission impact if a pregnancy were to occur, and builds on the data collected in ICL 76 on the expected rate of intercourse. The assumption is made that only first trimester pregnancies are considered. It is assumed that the pregnancy will be discovered and RTDC will be completed prior to the pregnancy extending to the second trimester. This assumption is not valid for Mars missions. The best case is a first trimester intrauterine pregnancy inclusive of uncomplicated early pregnancy loss not requiring surgical management. The worst case is defined as ectopic pregnancy OR complicated early pregnancy loss requiring surgical management.

Pregnancy CLIFF Peer Review

2. Incidence. There have been no reports of a pregnancy during manned missions. In addition, there is not data that shows the type or utilization rates of various forms of contraceptives by female astronauts. The best analog study available investigated pregnancy rates in deployed female military officers. This data was adjusted for the proportion of pre-menopausal astronauts flown in ICL 76, Risk of Pregnancy. It can only be applied in the model when there are mixed crews (neither all male nor all female). There are a number of uncertainties including whether the rate of pregnancy complications (miscarriage, ectopic, etc) would be similar in space as it is on earth. What the utilization and effectiveness of contraception or emergency contraceptives are or will be among female astronauts are unknown. The recent discovery of venous thromboembolism (VTE) during an ISS mission may change the hormonal contraceptive practices among females on future missions as these types of pharmaceuticals can increase the risk of VTE. The best case/worst case probabilities were based on rates of ectopic vs intrauterine pregnancies in a terrestrial study. This investigation showed a 98% intrauterine pregnancy rate and a 2% ectopic rate which was chosen as the BC/WC probability split. It is unknown how well this corresponds to the female astronaut population based on the differences in environment and the possible increased risk of ectopic pregnancy in microgravity. 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 maximum CP2 time is 13 weeks (end of the first trimester) for each case. RTDC times are all considered to be 100% because of the unknown risks of spaceflight on the mother and fetus and the need to return for definitive care. Loss of crew life probabilities are based on the failure rates of methotrexate for pregnancy termination in the TWC. The Loss of crew life for the UTWC is higher than the TWC and was estimated by subject matter expertise. 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, but intercourse might be expected to be more likely later in a mission and also during periods of less intense mission activities. It also might be expected that once a couple has decided to engage in intercourse, the frequency of this activity might increase from baseline and thus raise the risk of pregnancy. This CLIFF assumes that RTDC would be performed prior to the end of the first trimester. This assumption is not valid for Mars missions.

6. Limitations

- The assumption is made that only first trimester pregnancies are considered. It is assumed that the pregnancy will be discovered and RTDC will be completed prior to the pregnancy extending to the second trimester. This assumption is not valid for Mars missions.
- Although the deployed female military officer population is probably the best analog available, there are still major differences in the privacy and time available for intimate relations during military deployments and during spaceflight in a small vehicle or habitat.

Pregnancy CLIFF Peer Review

- The rate of contraceptive use or type among female astronauts is not tracked nor is the compliance rate.
- Since the use of chemical abortion to terminate pregnancy is a personal choice and individual crewmembers may decide not to use it, its utilization and impact on the mission is difficult to predict.
- It is unknown how the space environment affects the rate of miscarriage or ectopic pregnancy.
- The recent discovery of venous thromboembolism (VTE) during an ISS mission may change the hormonal contraceptive practices among females on future missions as these types of pharmaceuticals can increase the risk of VTE. Increased risk of VTE may impact the rate of miscarriage.
- This medical condition is not dependent on mission phase, but intercourse might be expected to be more likely later in a mission and also during periods of less intense mission activities. It also might be expected that once a couple has decided to engage in intercourse, the frequency of this activity might increase from baseline and thus raise the risk of pregnancy. Increased frequency of intercourse may cause depletion of the supply of emergency contraception.
- There are difficulties combining multiple pathologic outcomes such as miscarriage and ectopic pregnancy into one definition despite their differences
- The calculation of Loss of crew life is extremely limited given we do not even have terrestrial data on mortality rates for ectopic pregnancy during modern times when surgical interventions are widely available and utilized.
- it is unknown if risks inherent to the space environment may increase the risk of ectopic pregnancy or complicated early pregnancy loss or interfere with medical treatment leading to the need for surgical management.

Reviewed by:

David C. Hilmers