

Risk for 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	2	3	3	3	3

Comments and limitations:

1. General comments. This CLIFF characterizes the risk 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. Thus, the most likely outcome of a pregnancy would be the need to return to definitive care which, of course, carries a significant mission impact. This CLIFF is part of a pair of pregnancy-related CLIFFs, the second one being ICL 123, Pregnancy. This CLIFF actually calculates the expected incidence of intercourse and its accompanying risk for pregnancy when performed with or without emergency contraception. The intent of this CLIFF is to allow resourcing of interventions such as emergency contraception to prevent pregnancy from occurring and to inform ICL 123, Pregnancy. The best case is vaginal intercourse involving a male and pre-menopausal female crewmember in which emergency contraception is used to prevent pregnancy. It is also considered a BC scenario if a crewmember involved is using a long-acting reversible contraceptive (LARC) or undergone procedure for permanent sterility. The worst case is defined as vaginal intercourse involving a male and pre-menopausal female crewmember who is not using a long-acting reversible contraceptive (LARC) or has not undergone a procedure for permanent sterility AND emergency contraception was either not used or was not successful.

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2. Incidence. There is no spaceflight data available that defines the incidence of intercourse during manned missions. In addition, there is no data that shows the type or utilization rates of various forms of contraceptives by female astronauts. The best analog that is available is deployed female military officers. The pregnancy rate among this cohort was adjusted for age, fecundity, and the estimated rate at which intercourse leads to pregnancy. From this data, the estimated incidence of intercourse that would be needed to cause the observed pregnancy rate was calculated. There are a number of uncertainties in this method including whether the rate of pregnancy from a single act of intercourse would be similar in space as it is on earth. What the utilization rate and type of contraception is or will be among female astronauts are also 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 data from a study investigating the risk of failure of emergency contraception (EC), calculated to be about 2%. This was adjusted for the possibility that female crewmembers may choose not to use EC or the supply of EC may be depleted. A best case/worst case split of 90%/10% was chosen based on the rate of failure of EC and expert opinion. The clinical phase durations, RTDC and Loss of crew life probabilities are supported by terrestrial evidence, and I am in agreement with their calculation. Loss of crew life probabilities are assumed to be zero. 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. More frequent intercourse could deplete the supply of EC.

6. Limitations

- 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.
- The rate of contraceptive use or type among female astronauts is not tracked nor is the compliance rates. However, the studies that were used to calculate intercourse investigated pregnancy rates in women who would have had the same access to contraceptives as female astronauts, so contraceptive use patterns should not have a significant effect on the incidence calculations.
- One of the factors that was adjusted to derive a rate of intercourse was fecundity. Historic percentages of female astronauts who were pre-menopausal and post-menopausal were used. It is unknown what this will be in the future.

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- Since the use of emergency contraception is a personal choice and individual crewmembers may decide not to use it, its utilization is difficult to predict.
- It is unknown how the space environment affects the rate of pregnancy from a single act of intercourse.
- 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.
- 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. More frequent intercourse could deplete the supply of EC.
- The best case and worst case definitions do not consider the use of non-long acting contraceptives such as barrier contraception, pills, patch, ring. However, the use of one of these methods in addition to EC would presumably lower the risk of pregnancy vis a vis not using any form of contraception.
- We do not know whether crews will be mix-gendered, what their sexual orientation may be, what the crew dynamic would be, what their fertility status is, or what their ages are. Age is an important factor that affects fertility as well as pregnancy risks, however.
- The data is adjusted for the proportion of pre-menopausal vs. post-menopausal astronauts who have flown historically. Not all pre-menopausal women are fertile, and thus the CLIFF incidence is not calculated to adjust perfectly to age-matched fertility outcomes.

Reviewed by:

David C. Hilmers