

Menstrual Cycle Control in Female Astronauts and the Associated Risk of Venous Thromboembolism

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Background:

Venous thromboembolism (VTE) is a common and serious condition in which a blood clot develops within the venous circulation. The Centers for Disease Control and Prevention quotes an incidence of approximately 1-2 per 1000 people in the USA yearly. Risk factors are numerous and can be divided into acquired (e.g. age, trauma, surgery, medical conditions, medication), inherited (e.g. antithrombin deficiency, protein S deficiency) and mixed (e.g. hyperhomocysteinemia).

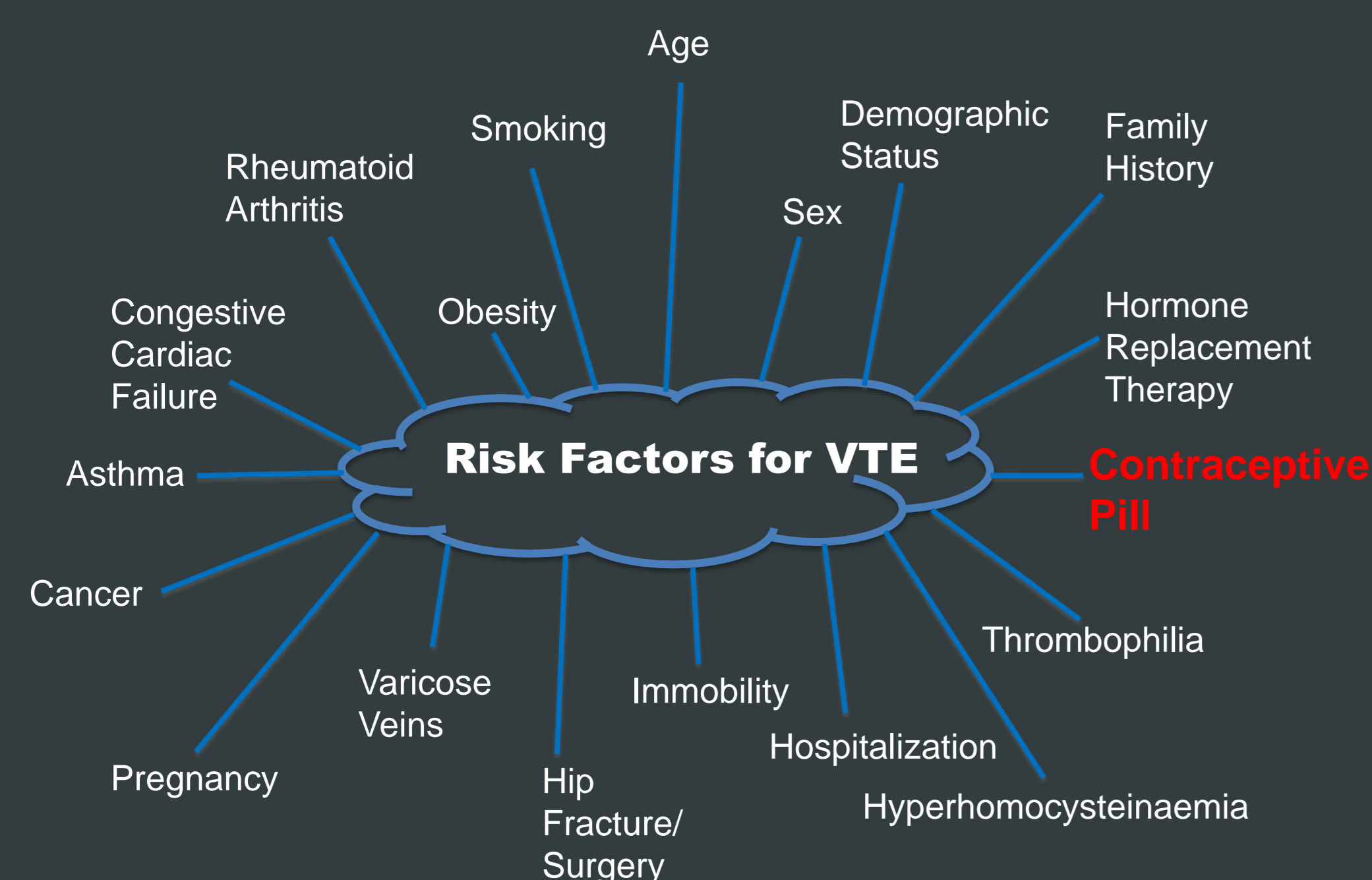
Use of estrogen-containing medications is a known risk factor for VTE. There have been no documented case reports of VTE in female astronauts during spaceflight in the published literature. The oral contraceptive pill (OCP) is the most commonly reported method of menstrual cycle suppression, but OCP usage doubles the risk of VTE. Current VTE risk prediction models do not include the spaceflight environment or the physiological changes associated with it.

Objectives:

Identify and estimate the specific risk of VTE for female astronauts as a result of taking hormonal contraception for menstrual cycle control.

Hypothesis:

We predict spaceflight does not increase the risk of VTE compared to the terrestrial population because of the excellent health of the crewmembers, which in turn, reduces their risk from all the other known risk factors.



Method:

A systematic review of the literature was conducted to identify and quantify the terrestrial risk factors for VTE. Studies involving analogue populations, e.g. military personnel, were also reviewed due to similarities in usage of the OCP for menstrual suppression. The Lifetime Surveillance of Astronaut Health (LSAH) department at NASA provided data on each terrestrial risk factor before and after a spaceflight mission per female astronaut. This permitted an estimate of the change in each risk predictor in relation to spaceflight to be calculated.

Results:

The most commonly identifiable terrestrial risks for VTE are not applicable to the female astronaut population. This is likely due to selection processes as well as training practices astronauts need to maintain.

Potential risks relevant to female astronauts include:

- Hormonal contraception – OCP usage increases the VTE risk to 9-10 per 10,000 per year compared to 4-5 per 10,000 per year when not using hormonal contraception
- Multiple long distance flights during training – When flights are ≥ 4 hours, risk of VTE is 21.5 per 100,000 flights, however, concurrent OCP use increases this risk to 55.3 per 100,000 flights. Any two hour increase in air travel duration increases the VTE risk by 26%.
- Immobility during Soyuz training – physical inactivity for >41 hours per week increases the risk of pulmonary embolism by 2.34 (95% CI 1.3 – 4.2)
- Minor injuries as a result of pre-flight or in-flight activities – a minor injury in the past prior three months leads to an adjusted odd ratio of 3.5 for developing a VTE (95% CI 2.8 – 4.3)
- Hematological factors – anaemia (microcytic and macrocytic), thrombocytosis, hyperhomocysteinemia and nutrient deficiencies all increase the risk of VTE.

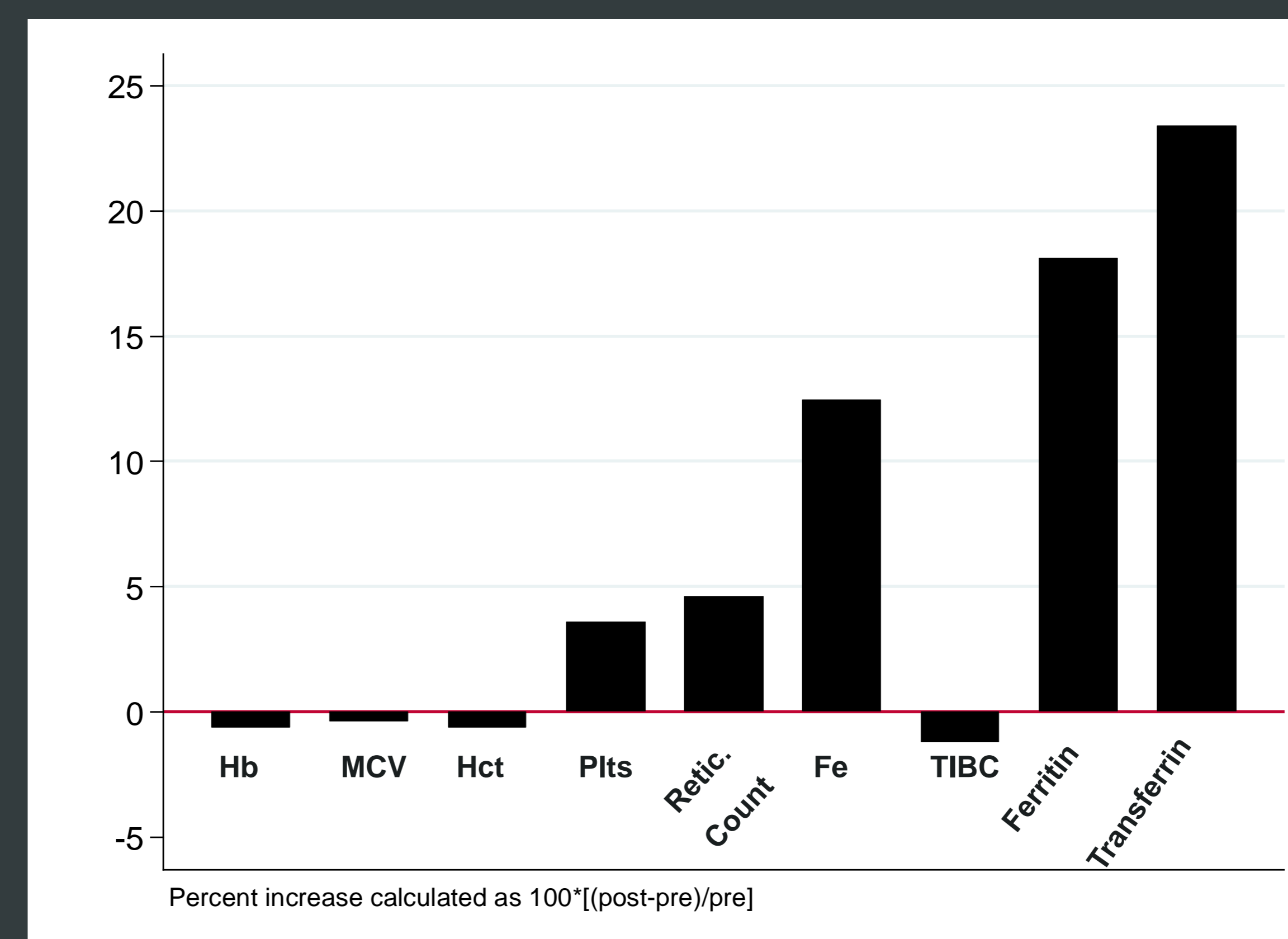
The majority of female astronauts on long duration missions chose to use the oral contraceptive pill pre-flight and in-flight.

Results:

This pilot analysis used grouped data from 27 female crewmembers who used oral contraceptives on either long or short duration missions. Values are presented as means. Hematological factors for which LSAH data was requested included:

- Hemoglobin (Hb) – With an Hb <1st centile, the odds ratio of VTE risk is 3.4. This was **not** the case for our female astronaut population. Hematinics also did not reflect nutrient deficiencies amongst our astronaut population.
- A Mean Corpuscular Volume (MCV) <1st centile or >99th centile has an adjusted odds ratio of VTE risk of 1.95 and 2.65 respectively. This was **not** depicted in our data set.
- Hematocrit (Hct) – a 5% rise in Hct increases the risk of VTE by 1.25. The Hct did **not** rise in our astronaut population after spaceflight.
- Increased reticulocyte counts indicate new red blood cell formation and potential increase in blood viscosity and thus risk of VTE. This rose but only by **4.6%**. High platelet counts indicate a hypercoagulable blood status and therefore an increased risk of VTE. The overall rise was **3.6%**.

The Percent Increase of Known VTE Risk Factors after Short or Long Duration Spaceflight in Female Astronauts Taking the Oral Contraceptive Pill



Conclusions

This study is still in progress and data is awaited on muscle injury rates in-flight as well as homocysteine levels in relation to spaceflight. Estimations are yet to be made on immobility times during specific training activities. Additional statistical analyses and comparisons of short vs. long-duration mission data are planned.

With the data that are available, we conclude the risk for VTE in female astronauts is not higher than the general population also using hormonal contraception. The crewmembers are a fit and healthy group of individuals. Astronaut selection processes are likely to “select-out” the most common terrestrial risk factors for VTE. There are, however, training activities which could increase periodic risk of VTE amongst the female astronauts. Care should be taken during these times.

References

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Disclosure Statement

The authors are employed by their respective associated institutions. We will not be discussing off-label use or investigational use in this presentation.