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3 **COVID-19 vaccine related menstrual irregularities: A cause of vaccine**
4 **hesitation?**

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11 To,

12 The Editor-in-Chief

13 Vaccination against Coronavirus Disease of 2019 (Covid-19) has shown remarkable
14 progress in controlling the ongoing pandemic. Currently, over nine billion doses of
15 Covid-19 vaccines have been administered worldwide(1), and although this widespread
16 vaccination has shown great progress in managing the pandemic, multiple side effects
17 have been noted. Most of these side effects are mild such as pain at injection site, fever,
18 rash, etc., but some are serious and long-lasting like myocarditis and other
19 cardiovascular complications.

20 Recently, there have been reports of several women experiencing menstrual
21 irregularities after being administered Covid-19 vaccines, and that has created hesitation
22 amongst women to get their shot.(2) Table 1. summarizes the number of menstrual
23 disturbances recorded by Medicines and Healthcare products Regulatory Agency
24 (MHRA) Yellow Card Scheme until 22nd December 2021.

25 While several factors have been implicated to be the cause of these irregularities, a
26 definitive reason still remains to be established. A recent meta-analysis by Sharifian-
27 Dorche M et al. has shown that Covid-19 vaccines induce thrombocytopenia.(3) This
28 can result in the loss of endometrial haemostasis, and consequently, vaccinated women

29 might experience increased blood loss/heavy menstrual bleeding (HMB). Moreover,
30 since body's immune system is activated by Covid-19 vaccines(4), immune cells lining
31 the uterus can contribute to early shedding of uterine wall, and that may manifest as
32 intermenstrual bleeding (IMB) or postmenopausal bleeding (PMB). Women who have
33 recovered from Covid-19 infection continue to suffer from menstrual irregularities for
34 prolonged times. Therefore, the possibility of Long Covid Syndrome causing these
35 menstrual disturbances cannot be disregarded.(5) Additionally, the prevailing gender
36 bias in pre-and post-covid literature has led to under-reporting of events related to
37 female reproductive health, further limiting our understanding of this subject.

38 In conclusion, to minimize vaccine hesitation among women, it is imperative that a
39 better understanding of these side effects should be sought. Further research should be
40 encouraged to investigate vaccines' short- and long-term effects on reproductive health.
41 Questions regarding menstrual cycle should be included in clinical trials for Covid-19
42 vaccines, and women should be encouraged to report any unusual post-vaccination
43 changes in menstrual cycles to their doctors. Moreover, strict pharmacovigilance should
44 be practiced to monitor people with pre-existing coagulopathies, and those on certain
45 medications in order to limit the possibility of life-threatening conditions such as
46 cerebral venous sinus thrombosis (CVST) after taking the Covid-19 vaccines. Lastly, to
47 remove any mistrust, clinicians should inform women about all the risks and benefits of
48 vaccination so they can make the right choice to protect themselves, and their families.

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51 publication elsewhere, and no parts of this manuscript have been presented in a meeting
52 orally, or by a poster, anywhere to date.

53 **Conflict of interest:** None to declare.

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88 **Table: Summary of menstrual irregularities in women living in UK by MHRA(6–**
 89 **8)**

Adverse Events	Number of Adverse Events Reported (<i>n</i>)**		
	Pfizer-BioNTech	Moderna	AstraZeneca
Menstruation with Decreased Bleeding	6359	776	4363
Menstruation with Increased Bleeding	6383	933	5363
Intermenstrual Bleeding	1142	186	694
Postmenopausal Bleeding	101	13	302
Other Menstrual Disorders	8533	1182	5468

90 **~51.1 million doses of Covid-19 vaccines have been administered to women in the
 91 UK until 22nd December, 2021

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