


# Association between COVID-19 vaccination and menstruation: a state of the science review

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## ABSTRACT

**Introduction** Menstrual health is a key patient-reported outcome beyond its importance as a general indicator of health and fertility. However, menstrual function was not measured in the clinical trials of COVID-19 vaccines. The purpose of this review was to synthesise the existing literature on the relationship between COVID-19 vaccination and menstrual health outcomes.

**Methods** A PubMed search to 31 October 2023 identified a total of 53 publications: 11 prospective cohort studies, 11 retrospective cohort studies or registry-based cohort studies, and 31 cross-sectional or retrospective case-control studies.

**Results** Identified studies were generally at moderate-to-high risk of bias due to retrospective design, interviewer bias, and failure to include a non-vaccinated control group. Nonetheless, the bulk of the literature demonstrates that COVID-19 vaccine is associated with temporary changes in menstrual characteristics (cycle length and flow) and menstrual pain. Follicular phase (at the time of vaccination) is associated with greater increases in cycle length. Evidence suggests temporary post-vaccine menstrual changes in adolescents, abnormal vaginal bleeding in postmenopausal individuals, and a potential protective effect of using hormonal contraception.

**Conclusions** In this review we found evidence supporting an association between the COVID-19 vaccine and menstrual health outcomes. Given the importance of menstrual function to overall health, we recommend that all future vaccine trials include menstruation as a study outcome. Future vaccine studies should include rigorous assessment of the menstrual cycle as an outcome variable to limit sources of bias, identify biological mechanisms, and elucidate the impact of stress.

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Menstrual health data were not collected as part of the clinical trials for the COVID-19 vaccines, and anecdotal reports of menstrual cycle changes after vaccination encouraged independent research to evaluate these outcomes. Individual research studies have evaluated this question, but data have not been summarized in a comprehensive review.

## WHAT THIS STUDY ADDS

⇒ We found that most published studies reflected a moderate or high risk of bias due to methodological issues. However, the existing data suggest temporary changes in menstrual cycle length, flow and menstrual pain following COVID-19 vaccination.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE, OR POLICY

⇒ This review suggests the importance of measuring and monitoring the menstrual cycle as a key outcome in future vaccine clinical trials and may also be used to counsel individuals about potential menstrual changes following COVID-19 vaccination.

## INTRODUCTION

Half the population will experience menstruation at some point in their lives. Among individuals with a uterus, menstruation occurs for approximately 5–7 days each month for 40 years. Menstrual health, whether characterised in terms of cycle length, days of flow, volume/intensity of flow, regularity or associated symptoms, is a key patient-reported outcome beyond its importance as a general indicator of

health and fertility. Menstrual health outcomes are not routinely included in clinical trials and have not been a consideration for vaccine trials.<sup>1–4</sup> Numerous reports of menstrual disturbances following COVID-19 vaccination, the complete absence of evidence, and the lack of attention to this sex-specific issue contributes to vaccine hesitancy, causes public mistrust, and directly impacts preventable morbidity and mortality (see online supplemental file 1).<sup>5–10</sup> The purpose of this review was to summarise the existing evidence on the relationship between COVID-19 vaccination and menstrual health.

## Methods

To identify potentially relevant publications, we used the following search terms in PubMed to identify articles published on or before 31 October 2023: ‘COVID-19’, ‘vaccination’, ‘vaccine’, ‘menstruation’, ‘menses’ and ‘menstrual changes’. After excluding case series or case reports and publications based solely on postmenopausal individuals, we identified a total of 53 publications: 11 prospective cohort studies, 11 retrospective cohort studies or registry-based cohort studies, and 31 cross-sectional or retrospective case–control studies. These papers were then rated by the co-authors and a research staff member for risk of bias using the ROBINS-E tool, which provides a structured method for evaluating risk of bias in non-randomised epidemiological studies.<sup>11</sup> Authors of any of the included papers were not involved in the risk assessment of these papers. In the results, we have highlighted key studies while summarising the evidence. Additionally, we provide study details for the identified prospective and retrospective cohort studies or registry-based cohort studies in [tables 1 and 2](#), respectively. Study details for cross-sectional studies or retrospective case–control studies are presented in online supplemental file 2.

## RESULTS

### Cycle length

Cycle length is a distinct measurement defined as the time period from the first day of the last menstrual period until the day before the next menses starts. The bulk of research on COVID-19 vaccination and menstrual health has been focused on cycle length as it is a well-defined and, often, routinely tracked outcome. Formal passive reporting systems and public reports described *both* longer and shorter cycle lengths in the cycle during which COVID-19 vaccination occurs.<sup>12,13</sup> The first prospective study to identify an association between COVID-19 vaccination and temporary alterations to menstrual cycle length was a retrospective cohort study of prospectively tracked menstrual cycles in approximately 4000 US-based individuals.<sup>14</sup> The study utilised de-identified period tracking data from the Food and Drug Administration (FDA)-cleared menstrual tracking application Natural Cycles to

compare cycle length differences between vaccinated and unvaccinated individuals. The population analysed had to be not recently pregnant, naturally cycling (no use of hormones) and demonstrate normal menstrual cycle length pre-vaccination. As compared with the unvaccinated control group, vaccinated individuals experienced a slightly longer cycle of less than 1 day after vaccination. A subsequent study broadening the population to include individuals outside the United States confirmed the findings with data from nearly 20000 individuals and additionally found that for most individuals the increase in cycle length resolved in the cycle following vaccination.<sup>15</sup>

Although the average cycle length change observed in these population analyses was small, there were individuals in both the vaccinated and unvaccinated groups who experienced a greater magnitude of change. Of the total, 1342 participants experienced a change in cycle length of eight or more days, comprising 6.2% of vaccinated individuals and 5.0% of unvaccinated individuals. Individuals who were younger and who had a longer cycle length before vaccination were more likely to experience the increase. This study also found no difference in the type of COVID vaccine (eg, mRNA, attenuated virus, etc.) and no change in menstrual cycle length (eg, days of bleeding).

With regard to menstrual cycle phase at the time of vaccination, one retrospective cohort study of individuals using a menstrual tracking application demonstrated that individuals who received vaccine in the follicular phase were more likely to experience a cycle length disturbance than those who received vaccine in the luteal phase.<sup>16</sup> This study was not designed to determine causation as it did not include a control group or use a validated ovulation date.

Much less is known about the extent to which adolescent girls experience menstrual cycle changes following COVID-19 vaccination – likely given the greater difficulties in studying this vulnerable population. One study included 39 adolescent girls (aged 12–16 years) and assessed menstrual regularity following vaccination. Although this study did not include a control group, the data showed that eight girls (of the 23 with pre-vaccine regular cycles) reported some kind of menstrual irregularity 3 months post-vaccination.<sup>17</sup> A separate study in Norway asked mothers of both vaccinated and unvaccinated adolescent girls to retrospectively report any menstrual cycle disturbances in their daughters.<sup>18</sup> The data showed mothers reported more menstrual disturbances (shorter and longer cycles, increased pain, and increased heavy bleeding) in the girls who had been vaccinated compared with those who were not, although the authors mentioned that menstrual disturbances were common in both groups.

The published literature has continued to demonstrate that COVID-19 vaccination is associated with a slightly longer average cycle length among reproductive-aged individuals who prior to vaccination

**Table 1** Prospective cohort studies of premenopausal individuals

First author (reference)	Publication year	Study design	Location	Sample size	Age of participants	Study period	Vaccine types	Outcome(s)	Control variables	Main results	Overall risk of bias rating
Alvergne <sup>19</sup>	2022	Two cohorts: retrospective+prospective	UK	Prospective: 79 Retrospective: 1273	≥18 years	Retrospective: 7/2021–10/2021 Prospective: not provided	Pfizer, Moderna, AstraZeneca, Janssen	Timing and flow of menses	None	<ul style="list-style-type: none"> <li>▲ Post-vaccine menses: 2.3 days late on average (prospective cohort)</li> <li>▲ No meaningful change in flow</li> <li>▲ No association by brand - those on progesterogen-only contraception: more likely to report heavy flow</li> </ul>	High
Boucharid <sup>18</sup>	2022	Prospective cohort	North America	76	18–42 years	Not provided	Pfizer or Moderna mRNA vaccines	Prospectively collected daily diary data on: cycle length, days of flow, volume, luteal phase length, signs of ovulation. Secondary outcomes: perceived menstrual changes attributed to vaccination	None (time-invariant variables controlled as part of pre-post design)	75 women provided 588 cycles for analysis (227 pre-vaccine cycles, 145 vaccine cycles, 216 post-vaccine cycles), 22% perceived changes in their menstrual cycle post-vaccination but there were no significant differences in menstrual cycle length or days of flow comparing pre-vaccine, vaccine and post-vaccine cycles	Moderate
Chiang <sup>20</sup>	2023	Prospective cohort study	Taiwan	20	≥20 years	Not provided	Moderna, Pfizer, AstraZeneca	Cycle length, bleed length	None (pre-post design)	Bleed length: 6.08 (pre) vs 6.45 (first dose) vs 6.00 days (second dose). Cycle length: 29.42 (pre) vs 30.84 (first dose) vs 30.30 days (second dose)	High
Duijster <sup>29</sup>	2023	Prospective cohort event monitoring study+spontaneous reports	The Netherlands	13 567	16–55 years	1/2/2021–29/3/2022	AstraZeneca, Janssen, Moderna or Pfizer vaccine	Amenorrhoea/oligomenorrhoea, dysmenorrhoea, heavy menstrual bleeding, intermenstrual bleeding, irregular bleeding, reduced blood loss, and withdrawal blood loss abnormal	Age	Increased odds of any menstrual abnormality for Janssen (OR 1.83; 95% CI 1.33 to 2.49), Moderna (OR 2.44; 95% CI 1.86 to 3.20) and Pfizer (OR 3.04; 95% CI 2.36 to 3.93) vs AstraZeneca. Most menstrual abnormalities (63.8%, n=352) occurred after second dose of vaccination vs first dose (36.2%). Overall, median time to resolution of abnormalities was 7 days (IQR 4–14 days)	Moderate
Edelman <sup>15</sup>	2022	Prospective cohort study	Global	19 622	18–45 years	10/2020–11/2021	Pfizer, Moderna, AstraZeneca, Janssen	Cycle length, menses length	Age, BMI, education, parity, relationship status, global region	Adjusted difference (β) in change in cycle length between vaccinated and unvaccinated: first dose: 0.71 (95% CI 0.47 to 0.96); second dose: 0.56 (95% CI 0.28 to 0.84). After second dose: –0.11 (95% CI –0.33 to 0.10). Adjusted difference in change in menses length for vaccinated vs unvaccinated: first dose: 0.07 (95% CI 0.00 to 0.13); second dose: 0.13 (95% CI 0.06 to 0.20)	Low

Continued

Table 1 Continued

First author (reference)	Publication year	Study design	Location	Sample size	Age of participants	Study period	Vaccine types	Outcome(s)	Control variables	Main results	Overall risk of bias rating
Edelman <sup>14</sup>	2022	Prospective cohort study	US	3959	18–45 years	10/2020–9/2021	Pfizer, Moderna, Janssen	Cycle length, menses length	Age, race/ethnicity, BMI, parity, relationship status, education	Cycle length: first dose: $\beta=0.64$ (0.27 to 1.01); second dose: $\beta=0.79$ (0.40 to 1.18); Days of flow: first dose: $\beta=0.08$ (–0.04 to 0.19); second dose: $\beta=0.08$ (–0.04 to 0.20)	Low
Gibson <sup>16</sup>	2022	Prospective cohort study	US	9652	$\geq 18$ years	11/2019–11/2022	Moderna, Pfizer, Janssen	Cycle length	Age, BMI, seasonality	All vaccinations: first dose of mRNA vaccine (0.50 days, 95% CI 0.22 to 0.78); second dose of mRNA vaccine (0.39 days, 95% CI 0.11 to 0.67); Janssen vaccine: 1.26 days longer (95% CI 0.45 to 2.07) than pre-vaccination cycles. Follicular phase vaccination: first dose of mRNA vaccine (0.97 days, 95% CI 0.53 to 1.42); second dose of mRNA vaccine (1.43 days, 95% CI 1.06 to 1.80); Janssen dose (2.27 days, 95% CI 1.04 to 3.50)	Low
Mohr-Sasson <sup>17</sup>	2023	Prospective cohort	Israel	35	12–16 years	6/2021–7/2021	Pfizer	Change in: cycle regularity, cycle length, cycle intensity, AMH during 3-month period	Age, BMI, side effects	31.8% of regularly menstruating girls had irregular periods after vaccination; 50% of pre-menarcheal girls reported menarche on 3-month follow-up; AMH levels not appreciably different pre- and post-vaccination	High
Rogers <sup>23</sup>	2022	Prospective cohort	UK	11 475	18–59 years	2/2021–10/2021	AstraZeneca, Pfizer, Spikevax	Cycle changes	None	Reported HR for first dose of AstraZeneca (reference) with second dose of AstraZeneca, first dose of Pfizer, and second dose of Pfizer. All null	Moderate
Wang <sup>21</sup>	2022	Prospective cohort study	US and Canada	3858	21–56 years (all premenopausal)	4/2020–11/2021	mRNA and adenovirus-vector	Cycle length	Sociodemographic and behavioural factors: spandemic stressors	Vaccination was associated with longer cycles after vaccination (0–6 months: OR 1.67 (95% CI 1.05 to 2.64); 7–9 months: OR 1.43 (95% CI 0.96 to 2.14); >9 months: OR 1.41 (95% CI 0.91 to 2.18)) and among those whose cycles were short, long or irregular before vaccination (OR 2.82 (95% CI 1.51 to 5.27); OR 1.10 (95% CI 0.68 to 1.77) for those with normal length, regular cycles before vaccination). mRNA and adenovirus-vectored vaccines were both associated with this change	Low

Continued

Table 1 Continued		Overall risk of bias rating									
First author (reference)	Publication year	Study design	Location	Sample size	Age of participants	Study period	Vaccine types	Outcome(s)	Control variables	Main results	
Wesselink <sup>22</sup>	2023	Prospective cohort study	US and Canada	1137	21–45 years	6/2021–8/2022	Moderna, Pfizer, Janssen	Cycle regularity, cycle length, bleed length, heaviness of bleed and menstrual pain	Sociodemographic, lifestyle, medical and reproductive factors	Participants had 1.1-day longer cycles after the first dose of vaccine (95% CI 0.4 to 1.9) and 1.3-day longer cycles after the second dose (95% CI 0.2 to 2.5). Associations were attenuated at the second cycle post-vaccination. There was little association with cycle regularity, days of flow, menstrual volume or pain	Low

AMH, anti-Müllerian hormone; BMI, body mass index; CI, confidence interval; HR, hazard ratio; IQR, interquartile range; mRNA, messenger RNA; OR, odds ratio; UK, United Kingdom; US, United States;  $\beta$ , mean difference.

had regular cycles.<sup>16 19–22</sup> We now know the COVID-19 vaccine is associated with changes in cycle length, at least in adult populations, and although a small change in menstrual cycle length may not be meaningful to healthcare professionals and researchers as it does not signify the need for a clinical workup or intervention, the significance of this body of research is that unanticipated, even small disturbances for a key patient outcome like menstrual health can trigger an exponential rise in concerns, as has been the case with the COVID-19 vaccine.

#### Cycle irregularity/missed periods/intermenstrual bleeding

Studies investigating altered menstrual patterns (ie, missed periods, intermenstrual bleeding and cycle irregularity) remain sparse. These outcomes, specifically missed periods and cycle irregularity, overlap somewhat with one another and with cycle length outcomes and may be viewed and defined differently by patients and the scientific community. Intermenstrual bleeding is more straightforward to define, any bleeding that occurs outside of menses, but the data have not been available prospectively or have been inconsistently tracked by patients. Just three prospective cohort studies in the United States and the UK have reported on pre- and post-vaccination menstrual cycle characteristics; all concluded that COVID-19 vaccination was not associated with a change in menstrual regularity.<sup>21–23</sup> Additionally, one Swedish national register-based cohort study found that COVID-19 vaccinations were not associated with incident menstrual cycle irregularity that was “at least of sufficient concern to warrant seeking medical care” among premenopausal women.<sup>24</sup>

The evidence is less clear regarding any impact of COVID-19 vaccination on other bleeding disorders. Evidence from any longitudinal studies is absent. We found seven cross-sectional surveys of individuals reporting missed periods and intermenstrual bleeding after receiving COVID-19 vaccination (especially in subsequent and booster doses compared with the first dose).<sup>25–31</sup> However, none of the studies was able to ascertain the extent to which these findings were attributable to a natural menstrual variation, selection bias, or causally affected by the vaccines given the cross-sectional study design.

At the present time, the current evidence is insufficient to determine if COVID-19 vaccination is associated with cycle irregularity or other altered menstrual patterns.

#### Flow effects/bleeding intensity, quantity and duration

Menstrual flow is truly a patient-oriented outcome where the patient determines what is heavy or light; thus any reported change from an individual’s baseline is the outcome of interest.<sup>32</sup> Reported menstrual flow effects around COVID-19 vaccination have been mainly retrospectively collected but duration of menses

**Table 2** Retrospective cohort studies or registry-based cohort studies of premenopausal individuals

First author (reference)	Publication year	Study design	Location of study	Sample size	Age of participants	Study period	Vaccine types	Outcome(s)	Control variables	Main results	Overall risk of bias rating
Alahmadi <sup>41</sup>	2022	Retrospective cohort study	Saudi Arabia	673	18–45 years	1/2021–11/2022	Moderna, AstraZeneca, Pfizer-BioTech	Menstrual length, days of flow, volume, pain regarding pre- and post-COVID-19 vaccination	None (pre-post comparison)	Changes in menstruation after both vaccine doses were observed for 47%; 23% more pain after first dose and 21% after second dose. Moderna vaccine was associated with greatest changes (65.4%), AstraZeneca was associated with fewest changes (44.9%). Duration of changes in cycles after vaccination (one dose or both) was <1 month for 42% and ≥3 months for 27.1%. Vaccination was associated with minor and transient increase in menstrual pain	High
Barabás <sup>51</sup>	2022	Retrospective cohort study	Hungary	1563	18–65 years	Recruited: 9/2021–12/2021 Data collected: 2019–2022	Pfizer, Moderna, AstraZeneca, Sputnik, Janssen, Sinopharm	Cycle length, menses length, cycle regularity	None	40.4% reported menstrual changes; 29.9% shorter cycles; 22.2% longer cycles; 13.9% missed period; 7.8% prolonged bleeding; 12.2% irregular bleeding; 4.3% heavier bleeding; 2.8% strong menstrual cramps; 2.0% period reappearance	High
Biggaard Jensen <sup>49</sup>	2023	Registry-based cohort study	Denmark	13648	18–65 years	2021–12/2021	Pfizer-BioNTech, Moderna, other or mixed	Longer menstrual cycle, shorter menstrual cycle, heavier menstrual bleeding, lighter menstrual bleeding, more regular menstrual cycle, more irregular menstrual cycle, menstrual cycle, menstrual absence, prolonged bleeding, shortened bleeding, menstrual pain, intermenstrual bleeding, 2-monthly menstrual bleedings, duration of any menstrual changes	Vaccine symptoms, prior COVID-19 infection, concerned about vaccine, stress, age, smoking, health, use of hormonal contraception; alcohol use, physical activity, weight, pre-vaccination menstrual regularity, vaccine type	30% women reported any menstrual change (95% CI 29.31 to 30.86). Less than 10% of women reported either longer or shorter cycles, heavier or lighter bleeding, more regular or irregular cycles, or other menstrual changes	High

Continued



Table 2 Continued

First author (reference)	Publication year	Study design	Location of study	Sample size	Age of participants	Study period	Vaccine types	Outcome(s)	Control variables	Main results	Overall risk of bias rating
Caspersen <sup>18</sup>	2023	Population-based cohort study	Norway	7565	12–15 years	8/2021–10/2021	Cominaty vaccine	Mother's report of daughter's periods before vs after vaccination: (1) heavier bleeding than usual, (2) prolonged menses, (3) shorter interval between menses than usual, (4) longer interval between menses than usual, (5) spotting between menses and (6) greater menstrual pain	None (self-matched case series study)	RR for heavier bleeding 1.60 (95% CI 1.43 to 1.80); RR for prolonged bleeding 1.39 (95% CI 1.22 to 1.59); RR for shorter interval 1.19 (95% CI 1.07 to 1.32); RR for longer interval 1.15 (95% CI 1.05 to 1.27); RR for spot bleeding 1.06 (95% CI 0.92 to 1.23); RR for stronger period pain 1.14 (95% CI 1.04 to 1.26); RR for period pains without bleeding 1.00 (95% CI 0.90 to 1.11); RR for other pelvic symptoms 0.97 (95% CI 0.76 to 1.25)	High
Darney <sup>33</sup>	2023	Retrospective cohort study	Five global regions	9555	18–44 years	10/2020–5/2022	Pfizer, Moderna, AstraZeneca, Janssen, Covishield and Sputnik, Covaxin, Sinopharm and Sinovac	Mean number of heavy bleeding days and changes in bleeding quantity at three time points (first dose, second dose and post-exposure menses)	Age, race, ethnicity, parity, BMI, education, relationship status, region.	About 66% reported no change in heavy bleeding days, regardless of vaccination status. Little difference in heavy bleeding days by vaccination status. A larger proportion of vaccinated individuals experienced increases in total bleeding quantity (34.5% unvaccinated, 38.4% vaccinated; $\beta$ =4.0%, 99.2% CI 0.7 to 7.2)	Low
Dellino <sup>60</sup>	2022	Retrospective cohort study	Italy	100	18–45 years	4/2021–4/2022	Pfizer, Moderna, AstraZeneca	Late period, abnormal uterine bleeding	None	23% had menstrual delay, 77% had AUB	High
Hallberg <sup>61</sup>	2022	Registry-based cohort study	Sweden	1.6 million	15–49 years	12/2020–1/2022	Pfizer, Moderna, AstraZeneca	CD-10 codes: N91 (absent, scanty, rare menstruation), N92 (excessive, frequent, irregular menstruation), N93 (other abnormal uterine/vaginal bleeding)	None	Standardised incidence ratios (comparing with unvaccinated patients in 2019): N91: 0.93 (0.86 to 1.00); N92: 1.04 (1.01 to 1.07); N93: 1.23 (1.17 to 1.28)	High
Hasdemir <sup>62</sup>	2023	Retrospective cohort study	Turkey	258	"Reproductive-aged women"	Not provided	CoronaVac, Pfizer	"Menstrual dysregulation"	None	Prevalence of new-onset menstrual dysregulation following vaccination was 20.6% and it differed compared with baseline. Menstrual pattern returned to normal in 59.6% of vaccinated women	High

Continued

Table 2 Continued

First author (reference)	Publication year	Study design	Location of study	Sample size	Age of participants	Study period	Vaccine types	Outcome(s)	Control variables	Main results	Overall risk of bias rating
Ljung <sup>24</sup>	2023	Registry-based cohort study	Sweden	2 946 448	12–74 years	12/2020–2/2022	BNT162b2, mRNA-1273, ChAdOx1 nCoV-19, AZD1222	Healthcare contact (admission to hospital or visit) for menstrual disturbance or bleeding before or after menopause (ICD-10 codes N91, N92, N93, N95)	Age, country of birth, employed in healthcare, marital status, education, health-seeking behaviours, comorbidity, and treatments	Postmenopausal: highest risks observed after third dose, in 1–7-day risk window (HR 1.28, 95% CI 1.01 to 1.62) and 8–90-day risk window (HR 1.25, 95% CI 1.04 to 1.50). There was a 23–33% increased risk after 8–90 days with BNT162b2 and mRNA-1273 after the third dose, but association with ChAdOx1 nCoV-19 was unclear. Premenopausal: no association with menstrual disturbances or bleeding	Moderate
Trogstad <sup>63</sup>	2023	Retrospective cohort study (Norwegian Young Adult Cohort)	Norway	39 772	18–30 years	5/2021–10/2021	Data from National Immunisation Registry (SYSVAK), Pfizer, Moderna, AstraZeneca (through 3/2021 only)	Menstrual disturbances (heavier bleeding than usual, prolonged bleeding, shorter interval between menstruations, longer interval between menstruations, spot bleedings, stronger pain during menstruation, period pain without bleeding) before and after the first and second dose of COVID-19 vaccine.	Self-controlled case series design	In the first cycle after vaccination: increased occurrence of unusually heavy and prolonged bleeding, spot bleeding, interval changes, and increased pain during periods vs last cycle prior to vaccination. The association was strongest for heavy menstrual bleeding increasing from 8% before vaccination to 14–15% after vaccination, corresponding to RR of 1.90 (95% CI 1.69 to 2.13 after first vaccine dose; RR 1.84, 95% CI 1.66 to 2.03 after second dose). The association between vaccination and menstrual disturbances did not differ by vaccine brand, use of hormones, or history of gynaecological conditions	Moderate

Continued



Table 2 Continued

First author (reference)	Publication year	Study design	Location of study	Sample size	Age of participants	Study period	Vaccine types	Outcome(s)	Control variables	Main results	Overall risk of bias rating
Wong <sup>48</sup>	2022	Retrospective cohort study (vaccine surveillance)	US	62 679	≥18 years	12/2020–1/2022	Pfizer, Moderna, Janssen	Menstrual irregularities or vaginal bleeding	None	63 815 respondents reported on menstrual irregularities or vaginal bleeding, which included 62 679 female respondents (1.0% of 5 975 363 female respondents aged ≥18 years). Common themes identified included timing of menstruation (70 981 (83.6% responses) and severity of menstrual symptoms (56 890 (67.0% responses). Other themes included menopausal bleeding (3439 (4.0% responses) and resumption of menses (2378 (2.8% responses)	Moderate

AUB, abnormal uterine bleeding; CI, confidence interval; HR, hazard ratio; ICD-10, International Classification of Diseases, 10th Revision; OR, odds ratio; RR, relative risk; US, United States;  $\beta$ , mean difference.

or number of bleeding days have been more available prospectively as they are tracked routinely by individuals and are a main data point captured by menstrual tracking applications.

A large-scale investigation of 9555 menstruating individuals (7401 vaccinated and 2154 unvaccinated) who tracked menstrual cycles using an app found no differences in number of heavy bleeding days, although vaccinated individuals did report greater total bleeding quantity in the cycle when the vaccine was received.<sup>33</sup> Other studies have found no significant changes in self-reported menstrual flow in a large prospective and retrospective sample of women<sup>19</sup> and no differences in relative risk of reporting “heavier” or “lighter” periods in those vaccinated compared with those who were not.<sup>34</sup> Similar self-report studies have found no differences in menstrual flow following vaccination.<sup>35</sup> However, contradictory findings have also been published suggesting there are changes to menstrual flow following vaccination, with many participants reporting “heavier” menstrual flow.<sup>12 36 37</sup> These findings also have support from research demonstrating changes to menstrual flow following vaccination,<sup>31 38</sup> although there have also been a mix of reported changes including “heavier” and “lighter” flow.<sup>39</sup> Despite these mixed findings, the UK Medicines and Healthcare products Regulatory Agency (MHRA) determined that “heavy flow” be included as a potential vaccine side effect, given the strength of the evidence supporting this outcome, and Pfizer and Moderna product information has now added this as a possible side effect.<sup>40</sup>

### Menstrual pain and endometriosis

Menstrual pain is a self-reported outcome measure, defined as pain and discomfort in and around the pelvic region that begins with the onset of menstruation. Data on menstrual pain and COVID-19 vaccination are limited, although existing studies do suggest increased menstrual pain after COVID-19 vaccination, affecting around 20–40% of menstruating people after vaccination; estimated prevalence was similar after both the first and second vaccination dose.<sup>28 41–43</sup> Heterogeneity by type of vaccination in relation to post-vaccination menstrual pain experience remains inconclusive.<sup>39 41</sup> However, a longitudinal study that included pre-pandemic and pre-vaccination follow-up data did not observe that menstrual cycle pain complaints varied appreciably according to vaccination status.<sup>22</sup> Importantly, post-vaccination change in menstrual pain could also be attributed to background variability in menstrual pain driven by, for example, between-cycle fluctuations, age-related menstrual changes or pandemic-related stress.<sup>44</sup> Unlike menstrual length and regularity, menstrual pain and other menstruation-related symptoms can be perceived differently when reported in real time versus recalled and influenced by the format of questions, increasing the risk of misclassification or recall bias.

One of the most common medical conditions associated with menstrual pain is endometriosis. Endometriosis is a disease where the lining of the uterus (the endometrium) grows outside of the uterus. Endometriosis is associated with other painful conditions including dyspareunia, dysuria and dyschezia, and can be a source of chronic pelvic pain. It is associated with inflammatory processes, and thus, individuals with endometriosis may be particularly susceptible to effects from the COVID-19 vaccine. Emerging research suggests that people with endometriosis immunised with SARS-CoV-2 mRNA vaccines perceived worsening menstrual cycle abnormalities – namely fatigue, pain and regularity disorders – compared with those without a history of endometriosis.<sup>43 45</sup> Among people with endometriosis, those taking hormonal treatment reported less change in menstrual-associated symptoms,<sup>43</sup> suggesting a possible protective or stabilising effect of oestrogen or progesterone. Notably, in these studies, endometriosis was confirmed by either transvaginal sonography or by hospital record, so it is not clear if participants received surgical confirmation of endometriosis at any point, which is the gold standard for diagnosis.

#### Postmenopausal individuals

The diagnosis of menopause is quite clear, diagnosed 12 months after an individual's last period. Although one small study of 64 postmenopausal Lebanese women found no evidence of vaginal bleeding following receipt of the COVID-19 vaccine,<sup>46</sup> many larger studies examining population data have found evidence of a slightly increased risk of bleeding in postmenopausal women. In an examination of clinical records of 485 644 postmenopausal women, there was a small but statistically significant increase in the likelihood of receiving an abnormal bleeding diagnostic code in the 16 weeks following COVID-19 vaccination.<sup>47</sup> However, the authors note that this temporary increase was so small that it translated to fewer than 1 in 1000 women experiencing this change. Another study of over 1.5 million Swedish postmenopausal women also reported a small but significantly increased risk of bleeding, particularly after receiving a third dose of the vaccine.<sup>24</sup> An evaluation of reports of COVID-19 vaccine side effects to “v-safe” – an independent and voluntary vaccine monitoring system for individuals in the United States – found that approximately 4% of the 84 943 responses of menstrual disturbances reported postmenopausal bleeding.<sup>48</sup> Additionally, a supplementary analysis of 14 577 Danish self-reported postmenopausal women showed 2% (n=347) reported some “menstrual changes” following vaccination.<sup>49</sup> Postmenopausal women, by definition, are not menstruating, although the authors did not clarify the specific “menstrual” changes reported by postmenopausal women. Taken together, it does appear that many postmenopausal individuals experienced some abnormal

vaginal bleeding following COVID-19 vaccination and this information is critically important information for this population to know when considering the potential side effects of the COVID-19 vaccination.

#### Hormonal contraception users

Hormonal contraception encompasses a wide range of methods, method delivery systems and dosing, and can contain only progestogen or oestrogen combined with a progestogen. The few studies that have specifically evaluated the impact of hormonal contraception on menstrual cycle changes following COVID-19 vaccination have suggested that hormonal use has a protective effect against changes to the menstrual cycle but not all studies are able to differentiate between different methods.

One large study including prospective and retrospectively collected self-report data found a delay in the menstrual period following vaccination of 0.37 days, which was a smaller delay than in those not using hormonal contraception. There were no significant changes to menstrual flow following vaccination in those using hormonal contraception generally; although when type of hormone was analysed separately, those using progesterone-only hormones reported heavier flow following vaccination.<sup>19</sup> A separate study also reported heavier menstrual flow post-vaccine among those using hormonal contraception, although type of hormonal contraceptive was not analysed separately. Those using hormonal treatments also reported more breakthrough bleeding.<sup>12</sup> However, one additional study reported *fewer* menstrual cycle changes and less bleeding changes following each of the first and second dose vaccinations in those using hormonal contraceptives compared with those who were not.<sup>43</sup>

#### Stress

The term “stress” is a broad and wide-ranging term that encompasses a number of areas related to psychological distress, worry or concern.<sup>50</sup> Many different measures can reflect different aspects of stress including depression, anxiety, perceived stress and COVID-19 pandemic-related stress. There have been mixed results with regard to the impact of psychological stress on menstrual disturbances following receipt of the COVID-19 vaccine. Wang and colleagues reported that adult vaccinated women had a higher risk of increased cycle length compared with unvaccinated women, and this finding persisted after accounting for pandemic-related stress, which was assessed as depression, anxiety, posttraumatic stress, perceived stress and worry about COVID-19.<sup>21</sup> Similarly, another study found no relationship between perceived stress and vaccination status or menstrual cycle characteristics.<sup>22</sup> However, another study found that changes in menstrual cycle characteristics were correlated with symptoms of depression, suggesting that the menstrual

cycle effects of the vaccine may be related to changes in mood.<sup>51</sup> However, these inconsistent findings may result from different assessments of stress and how those measures related to changes in the menstrual cycle.

#### Long/short pre-vaccination cycles

Almost all of the research published to date is focused on individuals with regular pre-vaccination menstrual cycles.<sup>32</sup> The restriction of analyses to this ‘normal’ cycle population was by design, otherwise it would have been impossible to determine if an actual signal existed due to the vaccine. Individuals with baseline irregular cycles did report menstrual disturbances through official passive reporting systems (Vaccine Adverse Event Reporting System, VAERS) and social media-based surveys. However, due to the inherent increased variability with irregular cycles, it will be a challenge to determine what changes are due to the vaccine.

### AREAS OF FUTURE RESEARCH

#### Optimisation of study design and risk of bias

Cross-sectional and retrospective case–control studies, which select participants after both vaccination and menstrual changes have already occurred, are more prone to selection bias than prospective studies because selection is more likely to be dependent on both exposure and outcome. Another common concern about many studies is that participants were asked to report data on changes in menstruation in relation to vaccination, or participants were asked to provide data on vaccination and menstrual changes on the same questionnaire, both of which are likely to increase potential for spurious positive associations. The studies at lowest risk of bias are those that: (1) did not select participants in a way that depended on outcome status, (2) collected data prospectively in time (ie, vaccination data were collected before data on the occurrence of menstrual changes), (3) included a comparison group of non-vaccinated participants and (4) followed participants for at least two menstrual cycles to assess the extent to which menstrual changes persisted over time. Ideally, a study would use vaccine data on brand, dose and dates from a population vaccine registry (gold standard), but only a small subset of studies had access to vaccination records. Nevertheless, studies that collected data proximal in time to the occurrence of vaccination are likely to have reasonably valid exposure classification. Prospective cohort studies in which participants were asked to report any changes in menstruation attributed to vaccination should still be considered at relatively higher risk of bias. Overall, based on these criteria, there is a moderate-to-high risk of bias in the vast majority of published studies on this topic.

#### Biological mechanisms

While we still do not know the mechanism for vaccine-induced menstrual changes, in retrospect it is not

surprising that temporary changes to the menstrual cycle could occur with vaccination. Prior evidence exists demonstrating that the reproductive and immune systems ‘cross-talk’, and a large body of literature has demonstrated the role of oestrogen receptors and their impact on immune function,<sup>52–53</sup> although the extent to which the reverse is true (ie, influence of immune responses on oestrogen) is not well documented. The menstrual cycle is orchestrated through the hypothalamic–pituitary–ovarian (HPO) axis with a series of well-timed hormonal events.<sup>54</sup> The follicular phase of the menstrual cycle or the first half of the menstrual cycle prior to ovulation is the portion of the cycle that is the most variable in its duration while the luteal phase is a consistent duration (typically 14 days).<sup>55</sup> It is quite plausible that both stress and inflammation would impact the balance of ovarian hormones that determine menstrual cyclicality.<sup>56</sup> Future research exploring these potential mechanisms is warranted.

### DISCUSSION

This review has summarised the existing literature on the relationship between COVID-19 vaccination and menstrual cycle changes. Overall, data from published studies indicate small transient changes in menstrual cycle length (ie, longer cycle length) following vaccination. Additionally, there is some evidence that other menstrual characteristics such as menstrual pain, menstrual flow and intermenstrual bleeding also occur following vaccination. Less is known about how these effects impact unique populations, including postmenopausal individuals and adolescents, although the limited data available suggest that breakthrough bleeding or menstrual cycle changes, respectively, may occur. Data from several studies suggest estrogen-containing hormonal contraception may protect against changes, which may be due to combined hormonal contraception’s inherent, dominant effect on the endometrium or perhaps a unique oestrogen-inflammatory interaction. Additionally, preliminary evidence exists suggesting that menstrual cycle phase at the time of vaccination impacts the degree of menstrual changes, although much more research is needed in this area. The role of stress and long/short pre-vaccination cycles is much less clear due to the very limited data available.

Despite the range of studies included in this review, outcome measures varied from study to study, likely reflecting the lack of established measures for assessing menstrual characteristics or use of whatever data were available in attempts to try to answer the question. Although efforts have been made to provide guidelines for menstrual cycle outcome measures,<sup>57</sup> this remains a significant gap in menstrual-related research. Additionally, lack of standardised measures creates further obstacles for future clinical trials to evaluate and assess the impact of interventions on the menstrual cycle. The menstrual cycle is a significant indicator of women’s health outside of fertility and pregnancy, and the lack



**Box 1 Additional educational resources (Source)**

Sharp GC, Fraser A, Sawyer G, *et al.* The COVID-19 pandemic and the menstrual cycle: research gaps and opportunities. *Int J Epidemiol.* 2022 Jun 13;51(3):691-700. doi: 10.1093/ije/dyab239  
 NIH COVID-19 website. <https://covid19.nih.gov/news-and-stories/covid-19-vaccines-and-menstrual-cycle>.  
 COVID-19 vaccination and menstruation. <https://www.science.org/doi/10.1126/science.ade1051>

of attention to this critical health indicator suggests much work is still needed to address women's health disparities (Box 1).

We now have a solid evidence base from data over the past 3 years demonstrating the impact of the COVID-19 vaccine on the menstrual cycle. However, it should be noted that the majority of these papers are published in obstetrics/gynaecology or low-impact health journals. The lack of publication of vaccine/menstrual cycle papers in general medical journals suggests that much of academic medicine does not see this information as important for public health. Unfortunately, many providers and members of the public may not learn about these results because of decreased visibility or availability of the published articles. General medical journals may want to reconsider publication priorities in light of the impact of women's health outcomes on public health; given the paucity of evidence in the field, even a small or negative finding is important for both patients and providers. Going forward, we encourage the measurement and monitoring of menstrual health as a key outcome in future clinical trials.

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**REFERENCES**

- Polack FP, Thomas SJ, Kitchin N, *et al.* Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020;383:2603-15.
- Oliver SE. The Advisory Committee on Immunization Practices' interim recommendation for use of Moderna COVID-19 vaccine — United States. *MMWR Morb Mortal Wkly Rep*; 2020. Available: <https://www.cdc.gov/mmwr/volumes/69/wr/mm695152e1.htm>
- Sadoff J, Gray G, Vandebosch A, *et al.* Safety and efficacy of single-dose Ad26.Cov2.S vaccine against COVID-19. *N Engl J Med* 2021;384:2187-201.
- Baden LR, El Sahly HM, Essink B, *et al.* Efficacy and safety of the mRNA-1273 SARS-Cov-2 vaccine. *N Engl J Med* 2021;384:403-16.
- Male V. Menstruation and COVID-19 vaccination. *BMJ* 2022;o142.
- COVID-19 vaccination and menstrual cycle changes: a United Kingdom (UK) retrospective case-control study | medRxiv. 2022. Available: <https://www.medrxiv.org/content/10.1101/2021.11.23.21266709v3>
- Townsel C, Moniz MH, Wagner AL, *et al.* COVID-19 vaccine hesitancy among reproductive-aged female tier 1A healthcare workers in a United States medical center. *J Perinatol* 2021;41:2549-51.
- Characterizing menstrual bleeding changes occurring after SARS-Cov-2 vaccination | medRxiv. 2021 Available: <https://www.medrxiv.org/content/10.1101/2021.10.11.21264863v1>
- Stoeklé HC, Sekkate S, Angellier E, *et al.* Refusal of anti-coronavirus disease 2019 vaccination in cancer patients: is there a difference between the sexes? *Eur J Cancer* 2021;155:54-5.
- Simms KT, Hanley SJB, Smith MA, *et al.* Impact of HPV vaccine hesitancy on cervical cancer in Japan: a modelling study. *Lancet Public Health* 2020;5:e223-34.
- Higgins JPT, Morgan RL, Rooney AA, *et al.* A tool to assess risk of bias in non-randomized follow-up studies of exposure effects (ROBINS-E). *Environ Int* 2024;186:108602.
- Lee KMN, Junkins EJ, Luo C, *et al.* Investigating trends in those who experience menstrual bleeding changes after SARS-Cov-2 vaccination. *Sci Adv* 2022;8:eabm7201.
- Zhang B, Yu X, Liu J, *et al.* COVID-19 vaccine and menstrual conditions in female: data analysis of the Vaccine Adverse Event Reporting System (VAERS). *BMC Womens Health* 2022;22:403.
- Edelman A, Boniface ER, Benhar E, *et al.* Association between menstrual cycle length and coronavirus disease 2019 (COVID-19) vaccination: a U.S. cohort. *Obstet Gynecol* 2022;139:481-9.
- Edelman A, Boniface ER, Male V, *et al.* Association between menstrual cycle length and COVID-19 vaccination: global,

- retrospective cohort study of prospectively collected data. *BMJ Med* 2022;1:1. Available: <https://bmjmedicine.bmj.com/content/1/1/e000297>
- 16 Gibson EA, Li H, Fruh V, *et al.* Covid-19 vaccination and menstrual cycle length in the Apple Women's Health Study. *NPJ Digit Med* 2022;5:165.
  - 17 Mohr-Sasson A, Haas J, Sivan M, *et al.* The effects of COVID-19 mRNA vaccine on adolescence gynecological well-being. *Arch Gynecol Obstet* 2023;307:1625–31.
  - 18 Caspersen IH, Juvet LK, Feiring B, *et al.* Menstrual disturbances in 12- to 15-year-old girls after one dose of COVID-19 Comirnaty vaccine: population-based cohort study in Norway. *Vaccine* 2023;41:614–20.
  - 19 Alvergne A, Woon EV, Male V. Effect of COVID-19 vaccination on the timing and flow of menstrual periods in two cohorts. *Front Reprod Health* 2022;4:952976.
  - 20 Chiang MR, Shih LC, Lu CC, *et al.* The COVID-19 vaccine did not affect the basal immune response and menstruation in female athletes. *Physiol Rep* 2023;11:e15556.
  - 21 Wang S, Mortazavi J, Hart JE, *et al.* A prospective study of the association between SARS-Cov-2 infection and COVID-19 vaccination with changes in usual menstrual cycle characteristics. *Am J Obstet Gynecol* 2022;227:739.
  - 22 Wesselink AK, Lovett SM, Weinberg J, *et al.* COVID-19 vaccination and menstrual cycle characteristics: a prospective cohort study. *Vaccine* 2023;41:4327–34.
  - 23 Rogers A, Rooke E, Morant S, *et al.* Adverse events and overall health and well-being after COVID-19 vaccination: interim results from the Vac4Covid cohort safety study. *BMJ Open* 2022;12:e060583.
  - 24 Ljung R, Xu Y, Sundström A, *et al.* Association between SARS-Cov-2 vaccination and healthcare contacts for menstrual disturbance and bleeding in women before and after menopause: nationwide, register based cohort study. *BMJ* 2023;381:e074778.
  - 25 Namiki T, Komine-Aizawa S, Takada K, *et al.* The association of three doses of the BNT162b2 mRNA vaccine with abnormal bleeding and an irregular menstrual cycle among premenopausal females: a single institute observation study. *J Obstet Gynaecol Res* 2022;48:2903–10.
  - 26 Rodríguez Quejada L, Toro Wills MF, Martínez-Ávila MC, *et al.* Menstrual cycle disturbances after COVID-19 vaccination. *Womens Health (Lond)* 2022;18.
  - 27 Muhaidat N, Alshrouf MA, Azzam MI, *et al.* Menstrual symptoms after COVID-19 vaccine: a cross-sectional investigation in the MENA region. *Int J Womens Health* 2022;14:395–404.
  - 28 Farland IV, Khan SM, Shilen A, *et al.* COVID-19 vaccination and changes in the menstrual cycle among vaccinated persons. *Fertil Steril* 2023;119:392–400.
  - 29 Al-Furaydi A, Alrobaish SA, Al-Sowayan N. The COVID-19 vaccines and Menstrual disorders. *Eur Rev Med Pharmacol Sci* 2023;27:1185–91.
  - 30 Taşkaldıran I, Vuraloğlu E, Bozkuş Y, *et al.* Menstrual changes after COVID-19 infection and COVID-19 vaccination. *Int J Clin Pract* 2022;2022:3199758.
  - 31 M M Al-Mehaisen L, A Mahfouz I, Khamaiseh K, *et al.* Short term effect of corona virus diseases vaccine on the menstrual cycles. *Int J Womens Health* 2022;14:1385–94.
  - 32 Munro MG, Critchley HOD, Fraser IS, *et al.* FIGO Menstrual Disorders Committee. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. *Int J Gynaecol Obstet* 2018;143:393–408.
  - 33 Darney BG, Boniface ER, Van Lamsweerde A, *et al.* Impact of coronavirus disease 2019 (COVID-19) vaccination on menstrual bleeding quantity: an observational cohort study. *BJOG* 2023;130:803–12.
  - 34 Alvergne A, Kountourides G, Argentieri MA, *et al.* A retrospective case-control study on menstrual cycle changes following COVID-19 vaccination and disease. *iScience* 2023;26:106401.
  - 35 Saleh Alzahrani H, Ali Algashami S, Abdulaziz Alharkan A, *et al.* The effect of COVID-19 vaccination on the menstrual cycle in female in Riyadh, Saudi Arabia. *Saudi Pharm J* 2023;31:746–51.
  - 36 Qashqari FSI, Dahlawi M, Assagaf HM, *et al.* Effect of the COVID-19 vaccine on the menstrual cycle among females in Saudi Arabia. *Ethiop J Health Sci* 2022;32:1083–92.
  - 37 Sualeh M, Uddin MR, Junaid N, *et al.* Impact of COVID-19 vaccination on menstrual cycle: a cross-sectional study from Karachi, Pakistan. *Cureus* 2022;14:e28630.
  - 38 Matar SG, Nourelden AZ, Assar A, *et al.* Effect of COVID-19 vaccine on menstrual experience among females in six Arab countries: a cross sectional study. *Influenza Other Respir Viruses* 2023;17:e13088.
  - 39 Qazi TB, Dkhar SA, Quansar R, *et al.* Impact of COVID-19 vaccination on menstrual cycle in women of reproductive age. *Int J Gynaecol Obstet* 2023;162:1086–90.
  - 40 GOV.UK. Coronavirus vaccine - summary of Yellow Card reporting. 2024. Available: <https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting>
  - 41 Alahmadi AM, Aljohani AH, Fadhoun RA, *et al.* The effect of the COVID-19 vaccine on the menstrual cycle among reproductive-aged females in Saudi Arabia. *Cureus* 2022;14:e32473.
  - 42 Baena-García L, Aparicio VA, Molina-López A, *et al.* Premenstrual and menstrual changes reported after COVID-19 vaccination: the EVA project. *Womens Health (Lond)* 2022;18.
  - 43 Martínez-Zamora MÁ, Feixas G, Gracia M, *et al.* Evaluation of menstrual symptoms after coronavirus disease 2019 vaccination in women with endometriosis. *Womens Health (Lond)* 2023;19.
  - 44 Sharp GC, Fraser A, Sawyer G, *et al.* The COVID-19 pandemic and the menstrual cycle: research gaps and opportunities. *Int J Epidemiol* 2022;51:691–700.
  - 45 Gilan A, Laster-Haim S, Rottenstreich A, *et al.* The effect of SARS-Cov-2 BNT162b2 vaccine on the symptoms of women with endometriosis. *Arch Gynecol Obstet* 2023;307:121–7.
  - 46 Farah S, Hijazi M, Aoun E, *et al.* Effect of COVID-19 vaccinations on menstrual cycle and postmenopausal bleeding among health care workers: a cross-sectional study. *Int J Gynaecol Obstet* 2023;162:532–40.
  - 47 Suh-Burgmann EJ, Tierney C, Hung YY, *et al.* Association between vaccination against COVID-19 and postmenopausal bleeding. *Am J Obstet Gynecol* 2022;227:907–8.
  - 48 Wong KK, Heilig CM, Hause A, *et al.* Menstrual irregularities and vaginal bleeding after COVID-19 vaccination reported to v-safe active surveillance, USA in December, 2020–January, 2022: an observational cohort study. *Lancet Digit Health* 2022;4:e667–75.
  - 49 Bisgaard Jensen C, Bech BH, Hansen SN, *et al.* Prevalence of and risk factors for self-reported menstrual changes following

- COVID-19 vaccination: a Danish cohort study. *Hum Reprod* 2023;38:1825–34.
- 50 Stress. n.d. Available: <https://www.who.int/news-room/questions-and-answers/item/stress>
- 51 Barabás K, Makkai B, Farkas N, *et al.* 2022 Influence of COVID-19 pandemic and vaccination on the menstrual cycle: a retrospective study in Hungary. *Front Endocrinol (Lausanne)* 13:974788.
- 52 Kovats S. Estrogen receptors regulate innate immune cells and signaling pathways. *Cell Immunol* 2015;294:63–9.
- 53 Straub RH. The complex role of estrogens in inflammation. *Endocr Rev* 2007;28:521–74.
- 54 Valsamakis G, Chrousos G, Mastorakos G. Stress, female reproduction and pregnancy. *Psychoneuroendocrinology* 2019;100:48–57.
- 55 Reed BG, Carr BR. The normal menstrual cycle and the control of ovulation. In: Feingold KR, Anawalt B, Blackman MR, eds. *Endotext*. South Dartmouth, MA: MDText.com, Inc., 2000.
- 56 Rahimi Mansour F, Keyvanfar A, Najafiarab H, *et al.* Menstrual disturbances following COVID-19 vaccination: a probable puzzle about the role of endocrine and immune pathways. *J Reprod Immunol* 2023;158:103952.
- 57 Schmalenberger KM, Tauseef HA, Barone JC, *et al.* How to study the menstrual cycle: practical tools and recommendations. *Psychoneuroendocrinology* 2021;123.
- 58 Bouchard TP, Schneider M, Schmidt M, *et al.* Menstrual cycle parameters are not significantly different after COVID-19 vaccination. *J Womens Health (Larchmt)* 2022;31:1097–102.
- 59 Duijster JW, Schoep ME, Nieboer TE, *et al.* Menstrual abnormalities after COVID-19 vaccination in the Netherlands: a description of spontaneous and longitudinal patient-reported data. *Br J Clin Pharmacol* 2023;89:3126–38.
- 60 Dellino M, Lamanna B, Vinciguerra M, *et al.* SARS-Cov-2 vaccines and adverse effects in gynecology and obstetrics: the first Italian retrospective study. *Int J Environ Res Public Health* 2022;19:13167.
- 61 Hallberg E, Sundström A, Larsson M, *et al.* Association between menstrual cycle length and coronavirus disease 2019 (COVID-19) vaccination: a U.S. cohort. *Obstet Gynecol* 2022;139:940–1.
- 62 Hasdemir PS, Senol Akar S, Goker A, *et al.* The effect of COVID-19 vaccinations on menstrual cycle and serum anti-Mullerian hormone levels in reproductive age women. *Hum Fertil* 2023;26:153–61.
- 63 Trogstad L, Laake I, Robertson AH, *et al.* Heavy bleeding and other menstrual disturbances in young women after COVID-19 vaccination. *Vaccine* 2023;41:5271–82.



### Supplement 1: Relevant historical perspective on COVID-19 vaccine and menstrual disturbances

In the Spring of 2021, shortly after the introduction of the novel COVID-19 vaccine, public reports of menstrual cycle disturbances began appearing both through formalized passive surveillance systems (e.g., US Centers for Disease Control Vaccine Adverse Event Reporting System; VAERS) and via social media (e.g., Twitter; now X). Individuals reported a range of potential vaccine-related menstrual cycle changes including but not limited to shorter and longer cycles, heavier, lighter or no flow during menses, more or fewer days of menses, and intermenstrual bleeding. These reported menstrual cycle disturbances also raised concerns regarding future fertility given menstrual health is a general indicator of health and fertility. A 2021 Kaiser family foundation poll reported that two-thirds of parents were concerned that COVID-19 vaccines will impact their child's future fertility. Women in the US make approximately 80% of health care decisions for their families and thus play a key role in household vaccination decisions, thereby highlighting the need to better understand any links between menstrual health and vaccines.

This universal knowledge deficit, the extent to which vaccines influence menstrual health, limited the ability to counsel menstruating individuals and their families about what to expect with vaccination at a critical time in the COVID-19 pandemic when infection rates were high, pandemic 'panic' was rampant, health care capacity was overtaxed, and there was growing mistrust of the medical system. It also drew attention to long-standing sex-specific research inequities especially around menstrual health, as well as the adverse patient experiences within the healthcare system when reporting concerns around menstrual health. The National Institutes of Health responded with a rapid-response funding opportunity in order to support further research (NOSI NOT-HD-21-035 COVID-19 Vaccination and Menstruation). The grant funding had strict inclusion criteria (reproductive-age, naturally cycling US-based individuals) as its purpose was to identify a causal relationship among healthy menstruating

individuals not using exogenous hormones. Here, we take the opportunity to report on both the latest research supported by this NIH funding as well as additional research from the scientific community that helps create a foundation of understanding of the effects of vaccination on menstrual health.

Supplement Table 1. Cross-sectional studies or retrospective case-control studies of pre-menopausal individuals

First Author (Reference #)	Publication Year	Study Design	Location of Study	Sample Size	Age of Participants	Study Period	Vaccine Types	Outcome(s)	Control Variables	Main Results	Overall Risk of Bias Rating
Abdollahi (1)	2022	Cross-sectional study	Iran	427	No age exclusions; mean age=29 years	6/2021-8/2021	Sinopharm, AstraZeneca, SputnikV, Covaxin	Menstrual disturbances, metrorrhagia, hirsutism	None	Menstrual disturbances: AstraZeneca 10.7%; SputnikV 5%, Covaxin 17.6%, Sinopharm 8%; Metrorrhagia: AstraZeneca 6.3%, SputnikV 2.5%, Covaxin 11.8%; Sinopharm 3.5% Hirsutism: AstraZeneca 3.6%, SputnikV 1.3%, Covaxin 2.9%, Sinopharm 0.5%	High
Aldali (2)	2022	Cross-sectional study	Riyadh, Saudi Arabia	604	16-17 years	12/2021-2/2022	Pfizer, Moderna	"Menstrual disorder"	None	Adolescents who took the first dose and had chronic disease had 2.4 times higher odds of having menstrual disorder than non-chronic disease patients.	High
Al-Furaydi (3)	2023	Cross-sectional study	Saudi Arabia	216	18-45 years	2/2022-3/2022	Pfizer, Moderna, AstraZeneca	Self-report of 8 possible menstrual changes: longer interval between menstruations, missed period, shorter interval between menstruations, more heavy bleeding than usual, less bleeding than usual, stronger pain during menstruation, less pain during menstruation, short menstruation Also asked if the changes persisted for 1, 2, or 3+ cycles	None	65% of participants reported at least one menstrual change Most common changes were longer intervals between menstruations (44%) and stronger pain during menstruation (33%).	High
Al-Mehaisen (4)	2022	Cross-sectional study	Global	1,506	≥18 years	5/2021-6/2021	Pfizer, Sinopharm, AstraZeneca, USSR	Changes in the menstrual cycle regularity, duration, volume (flow), new-onset dysmenorrhea, intermenstrual bleeding (IMB), or postcoital bleeding (PCB) in first period since receiving the vaccine.	None (pre-post comparison)	No effect estimates provided. 76% reported no changes in cycle duration and 60% reported no changes in days of flow. There were no new episodes of dysmenorrhea post vaccination. "The association between the date of the last vaccine dose with menstrual timing, duration, flow, and dysmenorrhea after vaccine and period timing and period volume was found to be statistically significant." There was no association of vaccine type with menstrual complaints, with exception of AstraZeneca being associated with dysmenorrhea.	High
Alvergne (5)	2023	Retrospective case-control study	UK	12,579	18-45 years	3/2021-6/2021	AstraZeneca and Pfizer	Perceived vaccine side effects on menses; FIGO classification system for AUB parameters: frequency, regularity, duration, volume, and inter-menstrual bleeding; cycle length; skipped menstrual periods; regularity; days of flow; intensity of flow; inter-menstrual bleeding.	Menstrual characteristics before pandemic, age, BMI, hormonal contraceptive use, reproductive disease	82% did not experience menstrual changes or "abnormal" cycle parameters (as defined by FIGO) after vaccination.	High
Amer (6)	2022	cross-sectional study	Saudi Arabia, Syria, Egypt, Libya, Sudan	1,254	15-50 years	5/2021-	Pfizer, Astrazeneca, Senopharm	Self-reported menstrual changes (amount, duration, symptoms)	None	38.4% reported menstrual changes, 27.8% reported amenorrhea 55.1% of menstrual changes were still present >9 months later	High
Baena-García (7)	2022	cross-sectional study	Spain	14,153	18-55 years	6/2021-9/2021	Pfizer-BioNTech, Moderna	Perceived changes in the amount and duration of menstrual	None	11,017 (78%) reported experiencing menstrual cycle changes after vaccination. The most common menstrual changes were more	High

							Oxford/AstraZeneca, and Johnson & Johnson/Janssen	bleeding, presence of clots, cycle length, and premenstrual symptoms after vaccine administration compared to the six previous menstruations (13 questions)		menstrual bleeding (43%), more menstrual pain (41%), delayed menstruation (38%), fewer days of menstrual bleeding (34.5%), and shorter cycle length (32%).	
Dabbousi (8)	2022	cross-sectional study	Lebanon	505	≥18 years	9/2021-10/2021	Pfizer, Astrazeneca, Sputnik, Sinopharm, Moderna	Heavy bleeding, light bleeding, pain, duration, regularity	None (pre-post comparison)	Heavy bleeding: 39.4% pre, 33.3% post Light bleeding: 26.7% pre, 33.5% post Pain: 75.4% pre, 75.2% post Duration: 7.9% pre, 9.9% post Irregular cycles: 12.5% pre, 20.4% post	High
Farland (9)	2023	cross-sectional study	US	545	18-45 years	5/2021-12/2021	Moderna, Pfizer, Janssen	Changes in menses since vaccination, when changes occurred (by dose), and when they resolved: missed periods, infrequent menstruation (>35 days), irregular menstruation, abnormal bleeding or spotting between the menstrual periods, abnormally light bleeding, abnormally heavy or prolonged bleeding, increased menstrual pain.	None	About 25% of vaccinated reported a change in their cycle after vaccination; most reported changes after their 2nd dose (56%) as compared with 1st (18%) and 3rd (14%) doses. Most common changes: irregular menses (43%), increased pain (30%), and abnormally heavy or prolonged bleeding (31%). Participants with a history of SARS-CoV-2 infection were less likely to report menstrual changes after vaccination vs. those without such history (OR=0.58; 95% CI: 0.32-1.04).	High
Filfilan (10)	2023	Cross-sectional study	Northern Africa, Middle East, Asia, Eastern Europe, Australia	2,381	15-49	1/2022-6/2022	Pfizer, Moderna, Astrazeneca, Janssen	Changes in cycle length, days of menstrual flow, dysmenorrhea, flow intensity, and intermenstrual bleeding	None	Changes in menstrual cycles were found for all types of vaccines. In 36% of vaccinated (2 doses), cycles became irregular, and in 29% of vaccinated (2 doses), cycles became prolonged (>35 days). Abnormalities were also experienced in the quantity of menstrual flow, with heavy flow reported in 31% of vaccinated. Severe dysmenorrhea was also a common post-vaccine menstrual change reported in 47% of vaccinated.	High
Gilan (11)	2023	Cross-sectional study	Israel	174	18-45 years	7/2021-11/2021	Pfizer-Blotech	Changes in amount or length of bleeding, intermenstrual bleeding and worsening in dysmenorrhea	BMI, age, background disease, hormonal treatment and parity.	Endometriosis patients were more likely to experience changes in bleeding patterns following vaccination (endometriosis: 39.5%, controls: 31.0%) and worsening in endometriosis symptoms with a 4.3-fold worsening in dysmenorrhea [95% CI 1.9-9.9]	High
Hariton (12)	2023	Cross-sectional study	US	5,314	18-55 years	3/3/2022-7/4/2022	Three exposure groups: not infected & not vaccinated (control), vaccinated but not infected, and infected but not vaccinated. Vaccine types: Pfizer, Moderna, Janssen	Users "Glow" app with a minimum of 6 months of continuous logging of menstrual cycles before and after April 2021. Primary outcome: changes in average cycle length and difference in cycle length in the 6 months before vs. each month after each event. Restricted to participants with cycles of 21-40 days.	Age, race, trying to conceive status, or symptoms associated with each event (results not shown)	No differences in average cycle length in the 6 months preceding or 6 months after vaccination. Participants with SARS-CoV-2 infection were more likely to report a longer first cycle after infection (0.35 days; 95% CI -0.15 to 0.56) than those without infection or vaccination, but difference was not clinically meaningful, and no difference observed in the month of infection or 2-6 months after infection.	Low

Kajiwara (13)	2023	cross-sectional study	Japan	55	18–22 years	10/2021-3/2022	Moderna, Pfizer	Regularity of menstruation; length of menstrual cycle; and day one date of menstruation around vaccination	None	Difference between predicted and actual menstrual cycle length was $1.9 \pm 3.0$ , $1.6 \pm 2.8$ , and $2.5 \pm 3.8$ days before vaccination and after 1st and 2nd dose of vaccine, respectively. In participants who received vaccinations twice within single menstrual cycle, this difference was $1.3 \pm 3.5$ and $3.9 \pm 3.3$ days before and after vaccination, respectively. Menstrual cycle length was slightly longer after 2nd dose.	Moderate
Khan (14)	2023	Cross-sectional study	Saudi Arabia	383	18-55 years	6/25/22-8/11/22	AstraZeneca, Pfizer, Moderna	Menstrual regularity, intermenstrual bleeding, menstrual flow, and menstrual pain	Age, PCOS, contraceptive use, identified vaccine skeptics	Reports of menstrual irregularity increased from 30% pre-vaccine to 70% post-vaccine, intermenstrual bleeding from 40% pre-vaccine to 60% post-vaccine, and extreme menstrual pain from 39% pre-vaccine to 61% post-vaccine. Women with PCOS reported greater menstrual pain post-vaccine. Vaccine skepticism was associated with greater reported menstrual changes post-vaccine.	High
Kumar (15)	2023	Cross-sectional study	India	5709	18-45 years	Not provided	COVISHIELD, COVAXIN	Frequent cycles, prolonged cycles, inter-menstrual bleeding, excessive bleeding, scanty bleeding, amenorrhea, cycle length, cycle regularity	None	333 (6%) reported post-vaccination menstrual disturbances, with 33% having frequent cycles, 64% prolonged cycles, and 4% inter-menstrual bleeding. 301 (5%) noticed changes in the amount of bleeding, with 50% excessive, 49% scanty, and 1% amenorrhea followed by heavy bleeding. Irregularities of menstrual cycle and length were higher in the COVAXIN group (7%) vs. COVISHIELD (5%) group.	High
Laganà (16)	2022	Cross-sectional study	Italy	164	mean age: $35.8 \pm 7.2$ years	9/10/2021-10/10/2021	AstraZeneca, Pfizer, Moderna, Janssen	frequency, length, and quantity of the menstrual cycle after vaccine administration	None	About 50-60% of participants who received the first dose of the COVID-19 vaccine reported menstrual cycle irregularities, regardless of the type of administered vaccine. Occurrence of menstrual irregularities seems to be slightly higher (60-70%) after the second dose. Menstrual irregularities after both 1st and 2nd doses resolved in ~50% of cases within two months.	High
Lee (17)	2022	Cross-sectional study	Not reported	39,129	18-45 years (pre-menopausal) 55-80 years (post-menopausal)	4/2021 - 6/2021	Pfizer, Moderna, AstraZeneca, Janssen, NovaVax, Other	Heavier menstrual flow Breakthrough bleeding	Age, race/ethnicity, postvaccine adverse effects of fever or fatigue, reproductive conditions, contraceptive hormone use, history of bleeding in pregnancy, history of postpartum hemorrhage	42% with regular menstrual cycles bled more heavily than usual, while 44% reported no change after being vaccinated. Among respondents who typically do not menstruate, 71% on long-acting reversible contraceptives, 39% of people on gender-affirming hormones, and 66% of postmenopausal participants reported breakthrough bleeding.	High
Lessans (18)	2023	Cross-sectional study	Israel	219	18-50 years	7/2021-10/2021	Pfizer, Moderna	Primary: irregular bleeding following vaccination. Secondary: presence of any menstrual change, including irregular bleeding, mood changes, or dysmenorrhea following the vaccine.	None (self-matched study)	Overall, 23.3% (n=51) experienced irregular bleeding and 40% (n = 83) reported any menstrual change after vaccination. Parity and presence of medical comorbidities were higher among patients who experienced irregular bleeding.	High

Marcelino (19)	2023	Cross-sectional study	Brazil	1012	20-39 years	12/31/21-2/8/22	Not reported.	Menstrual changes, menstrual cyclicity, days of menstrual flow, bleeding quantity	Age, ethnicity, cohabitation status, education, family income, contraception method, BMI, number of pregnancies, deliveries, and abortions, COVID infection	29.9% of women reported menstrual changes after vaccination. 9.4% reported irregular cycles, 19.2% reported changes to menstrual flow, and 18.8% reported changes to bleeding quantity. Contraceptive use was associated with fewer menstrual changes.	High
Martínez-Zamora (20)	2023	Cross-sectional study	Spain	848	>18 years (pre-menopausal)	9/2021-3/2022	Moderna, Pfizer-BioNTech	Worsened or new menstrual-associated symptoms in the first and second menstrual cycle after completed COVID-19 vaccination.	Age, hormonal treatment, smoking, parity	Similar % in both endometriosis and non-endometriosis groups reported menstrual changes the first (52.6% vs. 48.8%, respectively) and second cycle after vaccination (29.0% vs. 28.1%, respectively). Bleeding frequency/regularity disorders were found to be more frequent in the non-endometriosis group in the first cycle after vaccination.	High
Matar (21)	2023	Cross-sectional study	North Africa, Middle East	4,942	≥18 years	11/2021-12/2021	AstraZeneca, Janssen, Pfizer, Sinopharm, Sputnik	Heaviness of flow, cycle length, pelvic pain, days of bleeding	None	Heavy periods: 24.6% vs. 22.0% Cycle length >36 days: 1.6% in both groups; Pelvic pain: 83.8% vs. 81.6% Period-related pelvic pain in past three months: 85.3% vs. 81.6%	Moderate
Mínguez-Esteban (22)	2022	Cross-sectional study	Spain	746	18-45 years	2/2022-6/2022	Pfizer, Moderna	Menstrual pain intensity, menstrual bleeding, menstrual cycle duration	None	Sixty-five percent perceived changes in their menstrual cycle after vaccination, irrespective of type of vaccine or number of doses. An increase—rather than a reduction—in duration, bleeding, and pain during their menstrual cycles was reported after vaccination. The percentage that reported alterations after their last dose remained strongly constant across time, ranging from 64 to 65%.	High
Muhaidat (23)	2022	Cross-sectional study	MENA region	2,269	> menarche	7/2021-8/2021	Pfizer, Sinopharm, AstraZeneca	irregular menstruation, cramps, increased period frequency, menorrhagia, increased duration of menses, skipped periods, intermenstrual bleeding	None	35.3% of participants reported menstrual abnormalities pre-vaccination; 66.8% reported menstrual abnormalities after vaccination	High
Namiki (24)	2022	Cross-sectional study	Japan	309	≥18 years (premenopausal)	12/27/2021-3/5/2022	Pfizer, Moderna	Abnormal bleeding and menstrual irregularity.	None	The prevalence of abnormal bleeding was 0.6%, 1.0%, and 3.0% for the first, second, and third doses, respectively. Irregular menses were more common than abnormal bleeding: 1.9%, 4.9%, and 6.6% for the first, second, and third doses, respectively. COVID vaccination was not markedly associated with abnormal bleeding or irregular menstrual cycles.	High
Qazi (25)	2023	Cross-sectional study	India	300	15-49 years	11/20/2021-11/27/2021	Covaxin, Covishield	Cycle regularity, cycle length, heaviness of bleed, and menstrual pain	None	After vaccination, 10% experienced change in menstrual regularity (20% had a prolonged cycle, 30% had a missed cycle, 50% had delayed cycle) and 11% experienced change in cycle duration (55% had decreased duration, and 27% had increased duration). 33% reported cramps along with pain after vaccination. Duration of pain increased in 6% after vaccination. 25% reported change in menstrual flow after vaccination: increased flow (16%), decreased flow (59%).	High



Qashqari (26)	2022	Cross-sectional study	Saudi Arabia	2338	≥12 years (premenopausal)	8/2021-2/2022	Pfizer, AstraZeneca, and Moderna	Changes in heaviness of flow, cycle length, menstrual cramps.	None	>50% had not noticed any menstrual abnormalities after COVID vaccination. After receiving the first dose, small percentages reported that their next period was heavier than usual (14.5%), later than usual (27.7%), and cramps were worse than usual (26.5%). After receiving a second dose, small percentages reported that their period was heavier than usual (17.1%), later than usual (24.7%), and cramps were worse than usual (26.8%).	High
Rodríguez Quejada (27)	2022	Cross-sectional study	Online survey, 89% lived in South America	184	18-40 years	7/2021-9/2021	Pfizer, SinoVac, Janssen, Moderna, AstraZeneca, Other	Cycle regularity, menses length, bleed volume	None	- 51% regular, 43% irregular, 6% amenorrhea after vaccination - 65% normal duration of menses, 26% long menses, 9% amenorrhea/absent - 42% heavy bleeds, 21% light bleeds, 7% absent	High
Saleh Alzahrani (28)	2023	Cross-sectional study	Saudi Arabia	1066	12-50 years	12/2021-6/2022	Pfizer, AstraZeneca, and Moderna	Abnormal menstruation before vs. after COVID-19 vaccines, defined as shorter or longer cycle length, cycle irregularity, fewer or more days of flow, lighter or heavier intensity of flow, amenorrhea.	Occupation, gynecological conditions	Neither type of vaccine nor number of vaccine doses was associated with menstrual abnormality after vaccination.	High
Sarfraz (29)	2022	Cross-sectional study	Global	510	Not provided	6/2021-7/2021	Details not provided	Changes in cycle length	None	OR for change in cycle length of vaccinated vs. unvaccinated=3.17 (95% CI: 0.47, 21.43); only 3% of cohort unvaccinated	High
Sualeh (30)	2022	Cross-sectional study	Pakistan	384	≥18 years	11/2021-2/2022	Details not provided	Variations in flow, intensity, duration, or regularity of menses	None	After taking the COVID-19 vaccine, 33 participants (21.4%) reported a decrease in their menstrual cycle length. The menstrual flow of 40 participants (15.1%) became heavier.	High
Taşkaldıran (31)	2022	Cross-sectional study	Turkey	542	18-50 years	5/31/2022-7/31/2022	Pfizer, Sinovac, Other	Cycle shortened, cycle delayed, period shorter, period longer, bleeding lighter, bleeding heavier, intermenstrual bleeding	None	Shorter cycle=3.7%, delayed cycle=5.7%, intermenstrual bleeding=2.4%, heavier bleeding=3.7%, lighter bleeding=2.6%, shorter period=2.4%, longer period=2.9%	High

Abbreviations: AUB = abnormal uterine bleeding,  $\beta$  = mean difference, CI = confidence interval, OR = odds ratio, RR = relative risk, UK = United Kingdom, US = United States.

1. Abdollahi A, Naseh I, Kalroozi F, Kazemi-Galougahi MH, Nezamzadeh M, Sabeti Billandi S, et al. Comparison of Side Effects of COVID-19 Vaccines: Sinopharm, AstraZeneca, Sputnik V, and Covaxin in Women in Terms of Menstruation Disturbances, Hirsutism, and Metrorrhagia: A Descriptive-Analytical Cross-Sectional Study. *Int J Fertil Steril*. 2022 Aug 21;16(3):237–43.
2. Aldali JA, Alotaibi FT, Alasiri GA, Almesned RA, Alromih AM, Almohandes AM, et al. Evaluate the side effect associated with COVID-19 vaccine on adolescents in Riyadh, Saudi Arabia: A cross-section study. *Saudi Med J*. 2022 Nov;43(11):1248–53.
3. Al-Furaydi A, Alrobaish SA, Al-Sowayan N. The COVID-19 vaccines and menstrual disorders. *Eur Rev Med Pharmacol Sci*. 2023 Feb;27(3):1185–91.
4. M M Al-Mehaisen L, A Mahfouz I, Khamaiseh K, N Al-Beitawe S, Al-Kuran OAH. Short Term Effect of Corona Virus Diseases Vaccine on the Menstrual Cycles. *Int J Womens Health*. 2022;14:1385–94.
5. Alvergne A, Kountourides G, Argenti MA, Agyen L, Rogers N, Knight D, et al. A retrospective case-control study on menstrual cycle changes following COVID-19 vaccination and disease. *iScience*. 2023 Apr 21;26(4):106401.
6. Amer AA, Amer SA, Alrufaidi KM, Abd-Elatif EE, Alafandi BZ, Yousif DA, et al. Menstrual changes after COVID-19 vaccination and/or SARS-CoV-2 infection and their demographic, mood, and lifestyle determinants in Arab women of childbearing age, 2021. *Front Reprod Health*. 2022;4:927211.
7. Baena-García L, Aparicio VA, Molina-López A, Aranda P, Cámara-Roca L, Ocón-Hernández O. Premenstrual and menstrual changes reported after COVID-19 vaccination: The EVA project. *Womens Health (Lond)*. 2022;18:17455057221112237.
8. Dabbousi AA, El Masri J, El Ayoubi LM, Ismail O, Zreika B, Salameh P. Menstrual abnormalities post-COVID vaccination: a cross-sectional study on adult Lebanese women. *Ir J Med Sci*. 2023 Jun;192(3):1163–70.
9. Farland LV, Khan SM, Shilen A, Heslin KM, Ishimwe P, Allen AM, et al. COVID-19 vaccination and changes in the menstrual cycle among vaccinated persons. *Fertil Steril*. 2022 Dec 17;S0015-0282(22)02110-0.

10. Filfilan NN, Bukhari S, Rizwan M, Bukhari NM, Aref NK, Arain FR, et al. Effects of Different Types of COVID-19 Vaccines on Menstrual Cycles of Females of Reproductive Age Group (15-49): A Multinational Cross-Sectional Study. *Cureus*. 2023 May;15(5):e39640.
11. Gilan A, Laster-Haim S, Rottenstreich A, Porat S, Lessans N, Saar TD, et al. The effect of SARS-CoV-2 BNT162b2 vaccine on the symptoms of women with endometriosis. *Arch Gynecol Obstet*. 2023 Jan;307(1):121–7.
12. Hariton E, Morris JR, Ho K, Chen C, Cui E, Cedars MI. THE EFFECT OF THE COVID-19 VACCINE AND COVID-19 INFECTION ON MENSTRUAL CYCLE LENGTH: AN ANALYSIS OF 12 MONTHS OF CONTINUOUS MENSTRUAL CYCLE DATA FROM 5,314 PARTICIPANTS. *Fertility and Sterility [Internet]*. 2023 May 23 [cited 2023 May 30];0(0). Available from: [https://www.fertstert.org/article/S0015-0282\(23\)00535-6/fulltext?dgcid=raven\\_jbs\\_aip\\_email](https://www.fertstert.org/article/S0015-0282(23)00535-6/fulltext?dgcid=raven_jbs_aip_email)
13. Kajiwara S, Akiyama N, Baba H, Ohta M. Association between COVID-19 vaccines and the menstrual cycle in young Japanese women. *J Infect Chemother*. 2023 May;29(5):513–8.
14. Khan GA, Althubaiti A, Alsharif A, Alsayed Z, Jifree H. Dysmenorrhea, intermenstrual bleeding, menstrual flow volume changes, and irregularities following COVID-19 vaccination and the association with vaccine skepticism: A retrospective observational study. *Womens Health (Lond)*. 2023;19:17455057231210094.
15. Kumar N, Gangane N, Mohapatra I, Rukadikar C, Sharmila V, Pushpalatha K, et al. Effect of COVID-19 Vaccination on Menstrual Cycle Patterns of Reproductive-Age Women: A Multi-centric Observational Study. *Curr Drug Res Rev*. 2023 Jun 8;
16. Laganà AS, Veronesi G, Ghezzi F, Ferrario MM, Cromi A, Bizzarri M, et al. Evaluation of menstrual irregularities after COVID-19 vaccination: Results of the MECOVAC survey. *Open Med (Wars)*. 2022 Mar 9;17(1):475–84.
17. Lee KMN, Junkins EJ, Luo C, Fatima UA, Cox ML, Clancy KBH. Investigating trends in those who experience menstrual bleeding changes after SARS-CoV-2 vaccination. *Science Advances*. 2022 Jul 15;8(28):eabm7201.
18. Lessans N, Rottenstreich A, Stern S, Gilan A, Saar TD, Porat S, et al. The effect of BNT162b2 SARS-CoV-2 mRNA vaccine on menstrual cycle symptoms in healthy women. *International Journal of Gynecology & Obstetrics*. 2023;160(1):313–8.
19. Marcelino AC, Fim AB, da Cunha Pereira P, Monteiro I, Darney BG, Bahamondes L. Association between COVID-19 and vaccination on menstrual cycle. *Int J Gynaecol Obstet*. 2024 Feb;164(2):571–7.
20. Martínez-Zamora MÁ, Feixas G, Gracia M, Rius M, Quintas L, de Guirior C, et al. Evaluation of menstrual symptoms after Coronavirus disease 2019 vaccination in women with endometriosis. *Womens Health (Lond)*. 2023;19:17455057231176751.
21. Matar SG, Noureldin AZ, Assar A, Bahbah EI, Alfryjat AM, Hasabo EA, et al. Effect of COVID-19 vaccine on menstrual experience among females in six Arab countries: A cross sectional study. *Influenza Other Respir Viruses*. 2023 Jan;17(1):e13088.
22. Mínguez-Esteban I, García-Ginés P, Romero-Morales C, Abuíñ-Porras V, Navia JA, Alonso-Pérez JL, et al. Association between RNAm-Based COVID-19 Vaccines and Permanency of Menstrual Cycle Alterations in Spanish Women: A Cross-Sectional Study. *Biology (Basel)*. 2022 Oct 27;11(11):1579.
23. Muhaidat N, Alshrouf MA, Azzam MI, Karam AM, Al-Nazer M, Al-Ani A. Menstrual Symptoms After COVID-19 Vaccine: A Cross-Sectional Investigation in the MENA Region. *IJWH*. 2022 Mar;Volume 14:395–404.
24. Namiki T, Komine-Aizawa S, Takada K, Takano C, Trinh QD, Hayakawa S. The association of three doses of the BNT162b2 mRNA vaccine with abnormal bleeding and an irregular menstrual cycle among premenopausal females: A single institute observation study. *J Obstet Gynaecol Res*. 2022 Nov;48(11):2903–10.
25. Qazi TB, Dkhar SA, Quansar R, Khan SMS. Impact of COVID-19 vaccination on menstrual cycle in women of reproductive age. *Int J Gynaecol Obstet*. 2023 Sep;162(3):1086–90.
26. Qashqari FSI, Dahlawi M, Assaggaf HM, Alsafi R, Gari A, Abudawood A, et al. Effect of the COVID-19 Vaccine on the Menstrual Cycle among Females in Saudi Arabia. *Ethiop J Health Sci*. 2022 Nov;32(6):1083–92.
27. Rodríguez Quejada L, Toro Wills MF, Martínez-Ávila MC, Patiño-Aldana AF. Menstrual cycle disturbances after COVID-19 vaccination. *Womens Health (Lond)*. 2022 Jul 7;18:17455057221109375.
28. Saleh Alzahrani H, Ali Algashami S, Abdulaziz Alharkan A, Sultan Alotaibi N, Waseem Algahs N. The effect of COVID-19 vaccination on the menstrual cycle in female in Riyadh, Saudi Arabia. *Saudi Pharm J*. 2023 May;31(5):746–51.
29. Sarfraz A, Sarfraz Z, Sarfraz M, Nadeem Z, Felix M, Cherrez-Ojeda I. Menstrual irregularities following COVID-19 vaccination: A global cross-sectional survey. *Ann Med Surg (Lond)*. 2022 Sep;81:104220.
30. Sualeh M, Uddin MR, Junaid N, Khan M, Pario A, Ain Q. Impact of COVID-19 Vaccination on Menstrual Cycle: A Cross-Sectional Study From Karachi, Pakistan. *Cureus*. 2022 Aug;14(8):e28630.
31. Taşkaldıran I, Vuraloğlu E, Bozkuş Y, Turhan İyidir Ö, Nar A, Başçıl Tütüncü N. Menstrual Changes after COVID-19 Infection and COVID-19 Vaccination. *Int J Clin Pract*. 2022;2022:3199758.