**Effect of COVID-19 vaccination on menstrual periods: a retrospective cohort study**

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**Abstract (249 words)**

Objective. Clinicians and regulators are receiving reports of changes to menstrual periods following COVID-19 vaccination. However, it is unclear if the two are biologically linked. If they are, people using hormonal contraception are predicted to be less likely to report a change and spontaneously cycling people vaccinated prior to ovulation more likely. The objective was to test these hypotheses.

Design. Retrospective cohort study.

Setting. UK.

Population. 1273 people who had received at least one dose of a COVID-19 vaccination, have periods or withdrawal bleeds and keep a record of the dates of these.

Methods. Participants reported whether they use any hormonal contraception and, for each dose of the vaccine, on which day of their menstrual cycle they were vaccinated and details of how the timing and flow of their next period compared to their normal experience.

Main outcome measures. Association between 1. the use of hormonal contraception and reported changes to timing or flow of the next menstrual period, and 2. the timing of vaccination within the menstrual cycle and reported changes to timing or flow of the next menstrual period.

Results. The data from this cohort did not support the pre-specified hypotheses that people using hormonal contraception would be less likely to report a change, or that spontaneously cycling people vaccinated prior to ovulation would be more likely to report a change.

Conclusions. This study did not detect strong signals supporting the idea that COVID-19 vaccination is linked to menstrual changes in most people.

Funding. No specific funding.

Keywords. COVID-19, vaccine, menstruation, periods, contraception.

**Tweetable abstract (109 characters)**

This retrospective cohort study found no strong signals to suggest COVID-19 vaccination affects menstruation.

**Introduction**

Changes to periods and unexpected vaginal bleeding are not currently listed as common side effects of COVID-19 vaccination, but primary care practitioners and those working in reproductive health are increasingly being approached by people who have experienced these events following vaccination. In the UK, the MHRA’s surveillance scheme, Yellow Card, had received 39,026 reports of these events by 7 December 2021 [1]. It is important to note that most people who report such a change following vaccination find that their period returns to normal the following cycle [2] and that there is no evidence that COVID-19 vaccination adversely affects female fertility [3-8]. Nonetheless, people are concerned by these reports. Investigating the potential link between COVID-19 vaccination and menstrual changes is important for maintaining public trust in the vaccination programme and, if a link is found, to allow people to plan for potential changes to their cycles [9].

We currently know very little about how vaccination may affect the menstrual cycle, but there is some evidence that HPV vaccination may be associated with heavier or irregular periods [10]. There is also evidence that viral infection, including with SARS-CoV2 itself, can alter the menstrual cycle [11,12]. Taken together, this may suggest that immune stimulation can affect the menstrual cycle. Biologically plausible mechanisms by which this could occur include effects mediated by immunological influences on the hormones driving the menstrual cycle [13] or by immune cells in the lining of the uterus, which are involved in the cyclical build-up and breakdown of this tissue [14].

The purpose of this study was to assess the association between receipt of a COVID-19 vaccine and changes to the timing and flow of the next menstrual period, in a retrospectively recruited cohort of 1273 people. The data from this cohort allows us to test pre-specified hypotheses about how COVID-19 vaccination and menstrual changes may be biologically connected.

**Methods**

*Population*

2241 people who were over 18, had received at least one dose of a COVID-19 vaccination, have periods or withdrawal bleeds and who have a record of the dates of these, and the date or dates on which they received the vaccine were recruited by advertising on social media and in newsletters with a largely female readership in the UK. Participants used a web-based form, which was open between 27 July and 17 October 2021, to anonymously report their age, length of their normal menstrual cycle, whether they use any hormonal contraception, whether they are breastfeeding, whether they have ever been diagnosed with a menstrual or gynaecological condition and, for each dose of the vaccine, which brand they received, on which day of their cycle they were vaccinated and details of how the timing and flow of their next period compared to what they normally experience.

The analysis plan was pre-specified and registered before the data was examined. <https://osf.io/pa3nd>

The following responses were removed from the data set: 0. Responses made in preview mode (survey tests for ethical approval; n = 7). 1. Responses in which the normal cycle length was not given (n = 33). 2. Responses where the normal cycle length was given as less than or equal to 19 days; the majority of these responses were in the range of 3-7 days, suggesting that respondents may have given the length of their menses, rather than their menstrual cycle (n = 646). 3. Responses where the normal cycle length was given as more than or equal to 40 days (n = 25). 4. Responses where the normal cycle length was given by a range, where the range was >3 days (n = 36). 5. Responses where there was a text indication that cycle length was unpredictable or irregular (n = 38). 6. Responses in which the day of the cycle that the vaccine was given was not specified (n = 140). 7. Respondents who did not have a period after the vaccine, but were able to specify the reason for this (eg. became pregnant in the same cycle that they were vaccinated, opted to skip a withdrawal bleed if taking a contraceptive pill; n = 28). 8. Respondents who indicated that they did not receive the vaccine (n = 2). 9. Respondents who noted that they had made an error, and would resubmit a fresh version (n = 1). 10. Respondents who noted that they do not normally have periods or withdrawal bleeds, not already removed from the dataset (n = 9).

After data cleaning, 1273 records remained, of which 813 had data for both the first and second dose of the vaccine. The majority of these responses (n = 1121, 88%) were confirmed as coming from IP addresses in the UK. Details of the respondents are given in Table 1.

*Statistical analysis*

Where participants gave a range for their normal cycle length, the median cycle length was used for analysis. For examination of the effect of the day of the cycle on which the vaccine was given, the day of ovulation was estimated by cycle length – 14, based on the observation that the luteal phase of the menstrual cycle is normally constant at around 14 days [15]. The day on which the vaccine was given, relative to the predicted day of ovulation, was therefore calculated by cycle day of vaccination – (cycle length – 14).

Independence between ten pairs of variables was determined using Chi squared tests.

1. Brand of vaccination and timing of next period; 2. Brand of vaccination and flow of next period. For tests 1 and 2, respondents who had either received Janssen or did not specify the brand of vaccine received (n = 13) were excluded from the analysis.

3. Use of hormonal contraception and timing of next period; 4. Use of hormonal contraception and flow of next period. For tests 3 and 4, respondents who did not clearly specify the form of contraception they use (n = 15) were excluded from the analysis.

5. Timing of vaccination and timing of next period; 6. Timing of vaccination and flow of next period. For tests 5 and 6, only those who were not on hormonal contraception were included (n = 1117). Menstrual cycle days on which fewer than 5 respondents had been vaccinated were excluded (n = 16 respondents vaccinated more than 17 days before the predicted day of ovulation), as were days on which the respondent was already overdue for their period (n = 70), since these respondents would, by definition, report that their period was later than usual.

7. Timing of period following dose 1 and Timing of period following dose 2; 8. Flow of period following dose 1 and flow of period following dose 2.

9. Pre-existing diagnosis of menstrual or gynaecological conditions and timing of the period following vaccination; 10. Pre-existing diagnosis of menstrual or gynaecological conditions and flow of the period following vaccination.

For tests 1-6, 9 and 10, data from both first and second doses were included. For tests 7 and 8, records in which only first dose data was available (n = 460) were excluded.

A total of 10 Chi squared tests were carried out. The Holm-Bonferroni sequential correction was used to correct for multiple hypothesis testing. Tests in which the adjusted p value (p’) is less than or equal to 0.05 are indicated and categories in which the standardised residual is greater than the critical value for residuals (1.96) are indicated by \*. These categories have more responses in them than would be expected if the variables under investigation were independent.

Statistical analysis was performed with Prism version 9.0.0.

*Patient and public involvement*

This study was carried out as a result of a number of unsolicited messages from members of the public, who felt that they had experienced a change to their periods following COVID-19 vaccination, and thought that more research should be done into this. Tests 9 and 10 were added as exploratory analyses following a series of webinars on COVID-19 vaccination and reproductive health issues, because the potential for people with pre-existing gynaecological diagnoses to experience worse menstrual effects emerged as a common concern in the audience questions.

**Results**

*Association between brand of vaccination and changes in timing and flow of next period*

Menstrual changes have been reported to the Yellow Card surveillance scheme after receiving all brands of vaccines [1], suggesting that no particular brand or strategy (mRNA vs adenovirus-vectored) is clearly associated with menstrual changes. In line with these reports, in this dataset there was no association between brand of vaccine received and self-reported change to timing or flow of the next period (Figure S1a,b).

*Association between hormonal contraception and changes in timing and flow of next period*

If there is a link between COVID-19 vaccination and changes to periods, and it is mediated by changes to sex hormones as has been suggested [13], then people in whom exogenous sex hormones are supplied by hormonal contraception are expected to be less likely to experience a menstrual change following vaccination.

There was no association between hormonal contraception and timing of the next period (Figure 1a) but, contrary to the pre-specified hypothesis, people on hormonal contraception were more likely to report that the flow of the period following vaccination was different from usual (Figure 1b).

*Association between timing of vaccination and changes in timing and flow of next period*

The most commonly-reported menstrual change following vaccination is a delay to the next period [1]. Vaccination produces an inflammatory response and inflammation is associated with follicular dynamics during the menstrual cycle [16,17]. Further, the length of the luteal phase is considered to be relatively stable, with variation in cycle length arising from variation in the follicular phase [15]. Therefore, vaccination in the follicular phase could delay or prevent ovulation lengthening the cycle. In this case, later than usual periods would be predicted to be associated primarily with vaccination in the follicular phase.

There was a significant association between timing of vaccination within the menstrual cycle and the timing of the next period (Figure 2a). Examination of the standardised residuals revealed that this association was due to respondents vaccinated the day that their period was due, or the day before their period was due, who were more likely to report that their next period was late. This is perhaps unsurprising, since the timing of vaccination meant that these people were already moving towards having a later than usual period: there was no association to support the pre-specified hypothesis. There was no association between timing of vaccination and flow of the next period (Figure 2b).

*Association between menstrual changes following dose 1 and dose 2*

For both timing (Figure S2a) and flow (Figure S2b), there was a strong association between the reports for dose 1 and dose 2, with people most likely to report the same experience following dose 2 as they had following dose 1.

*Association between pre-existing gynaecological conditions and changes in timing and flow of the period following vaccination*

One concern commonly expressed by people with pre-existing gynaecological or menstrual conditions is that, since they already experience heavy of otherwise difficult periods, any menstrual changes following COVID-19 vaccination might be more pronounced for them. This concern is a major contributor to vaccine hesitancy in this group.

To address this concern, an exploratory analysis was added to determine how having a pre-existing diagnosis of a menstrual or other gynaecological condition might affect the timing or flow of the period following vaccination. There was no association between having had a diagnosis of any gynaecological or menstrual condition and the reported flow of the period following vaccination (Figure 3b). However, there was a significant association between the timing of the period following vaccination and having a pre-existing diagnosis (Figure 3a) with those with a diagnosis of endometriosis more likely to report an earlier than usual period, and those with a diagnosis of polycystic ovaries more likely to report a later than usual period.

**Discussion**

*Main findings*

Among 1273 people recruited retrospectively who kept a record of their periods and the date of their COVID-19 vaccination, people using hormonal contraception were more likely to report a change to the flow of the period immediately following COVID-19 vaccination. An association was detected between having a dose of COVID-19 vaccine in the last two days of the menstrual cycle and the subsequent period being later than usual, although this is likely to be accounted for by the period or withdrawal bleed in these cases already being late at the time of vaccination.

These findings did not support the pre-specified hypotheses.

In an exploratory analysis, participants who had a pre-existing diagnosis of endometriosis were more likely to report an earlier than usual period immediately post-vaccination, and those with a diagnosis of polycystic ovaries were more likely to report a later than usual period.

*Strengths and limitations*

The major strength of this study is the collection of detailed data about use of hormonal contraception and the timing of vaccination within the menstrual cycle. This allows us to examine the possibility that there is a biological link between COVID-19 vaccination and menstrual changes, by testing pre-specified hypotheses. The hypotheses to be tested and data analysis plan were registered in advance of data analysis, increasing the robustness of the findings.

The major limitation of the study is that, because the participants were recruited retrospectively, the data is likely to be enriched for those who noticed a change, who might be more motivated to participate in the study. Therefore, this data cannot be used to determine the frequency with which people experience menstrual changes following COVID-19 vaccination. Approaches in which participants are recruited prospectively or using menstrual cycle data collected for other reasons, for example, datasets from menstrual cycle tracking apps with linked data about dates of vaccination, are better equipped to answer these questions. Approaches using menstrual cycle tracking apps are likely to be particularly powerful because the large number of cycles logged and the granularity of the data powers the studies to detect small and rare changes to post-vaccination menstrual cycles. Further, where the app uses additional data (for example, basal body temperature, results of LH tests) to determine the day of ovulation, the date of vaccination relative to ovulation can be determined with greater accuracy than the crude estimate used here.

It is also important to note that the majority of the participants in this study were from the UK, so these findings may not be applicable to other countries. In particular, this dataset cannot tell us about any potential associations between menstrual changes and vaccines that are not approved for use in the UK, such as Sinovac, Sinopharm or Sputnik V. In the UK, the recommended interdose interval is at least 8 weeks, whereas most other countries use a 3- or 4-week interval [18]. This could also mean that different effects may be seen in countries vaccinating with these schedules, even when they are using the same vaccines.

*Interpretation*

This study was designed to test the idea that there is a biological link between COVID vaccination and changes to menstrual periods or withdrawal bleeds. If any such link was mediated by sex hormones, people on hormonal contraception would be less likely to report a change to their bleeds than those spontaneously cycling but, unexpectedly, people using hormonal contraception were in fact more likely to report a change to the flow of the period immediately following COVID-19 vaccination. This is in line with the results of a large survey of menstrual experiences following COVID vaccination, which also found that people using hormonal contraception were significantly more likely to report a change in flow than people who were spontaneously cycling [19]. These findings do not support the idea that any change to vaginal bleeding following COVID-19 vaccination is mediated by changes to hormones. However, many people use hormonal contraception at least partially to make their bleeds lighter and more regular [20,21], so people on hormonal contraception may therefore have found any change that they did experience more noticeable.

Similarly, this study did not find evidence to support the idea that later than expected periods were associated with vaccination in the follicular phase of the menstrual cycle, as would be expected if these effects were mediated by delayed ovulation or anovulation.

The reported timing and flow of the period following first vaccination dose was strongly predictive of the report following second vaccination dose. This could be consistent with interindividual factors affecting the nature of the menstrual response to vaccination, but there are other potential explanations for this observation. In this UK-based cohort, vaccine doses would have been given at around 8 weeks apart [18], meaning that any change, whether vaccine-related or otherwise, that affected the post-dose 1 period could potentially still be in effect for the post-dose 2 period.

Respondents who had a diagnosis of a menstrual or gynaecological condition were not more likely to report a change in flow than those who did not have such a diagnosis, and those with a diagnosis of heavy or abnormal menstrual bleeding or uterine fibroids were not more likely to report a change in timing. However, there was an increase in the frequency of people with endometriosis who reported an earlier than usual period, and in the frequency of those with polycystic ovaries who reported a later than usual period. This could suggest that people who are already vulnerable to experiencing menstrual changes might be more likely to experience some changes following vaccination and it will be important to follow this up to determine whether this is a genuine phenomenon. In the interim, these findings should not be used to counsel people who have these diagnoses against vaccination. Indeed, it is important for those who are particularly concerned about changes to their menstrual cycles to be reminded that COVID infection itself may cause this [11,12].

**Conclusions**

This retrospective cohort study of 1273 participants did not detect strong signals to support the idea that COVID-19 vaccination is linked to menstrual changes in most people. However, there was a weaker signal to suggest that people who are already vulnerable to menstrual disruptions may be more likely to experience these shortly after vaccination. Larger, prospectively recruited studies are required to more firmly confirm or refute any link. In the interim, these findings should not be used to counsel people who have these diagnoses against vaccination.

**Data availability**

Cleaned, fully anonymised data, together with our analysis files, are available from the Open Science Framework at <https://osf.io/6jf4u/>

**Preprint**

The data presented in this manuscript have been submitted to MedRXiv as a preprint. This version of the manuscript differs from the preprint in that it has been rewritten to conform to BJOG style requirements.

<https://www.medrxiv.org/content/10.1101/2021.11.15.21266317v1.full.pdf>

**Details of ethical approval**

This retrospective cohort study was approved by the Research Governance and Integrity Team at Imperial College London, study number 21IC6988.

**Funding**

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**Disclosure of interests**

None to declare.

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| Demographic characteristics |  |
| Age in years (Median, IQR) | 33 (29 – 39) |
| Cycle length in days (Median, IQR) | 28 (27 – 30) |
| *Hormonal contraception* |  |
| No hormonal contraception | 1117 (87.6%) |
| Combined pill | 53 (4.2%) |
| Progesterone only pill | 17 (1.3%) |
| Contraceptive implant | 2 (0.2%) |
| Contraceptive injection | 2 (0.2) |
| Contraceptive patch | 3 (0.2%) |
| Intrauterine system | 47 (3.7%) |
| Vaginal ring | 2 (0.2%) |
| Other | 10 (0.8%) |
| Not specified | 5 (0.4%) |
| *Menstrual and gynaecological diagnosis* | |
| Abnormal menstrual bleeding | 22 (1.7%) |
| Heavy menstrual bleeding | 150 (11.8%) |
| Endometriosis | 60 (4.7%) |
| Polycystic ovaries | 87 (6.8%) |
| Uterine fibroids | 21 (2.4%) |
| *Breastfeeding* |  |
| No | 1179 (92.5%) |
| Yes | 89 (7.1%) |
| Not specified | 5 (0.4%) |
| *Previous pregnancies* |  |
| 0 | 572 (45%) |
| 1 | 219 (17.2%) |
| 2 | 220 (17.3) |
| 3 or more | 252 (19.8) |
| Not specified | 10 (0.8%) |
| *Vaccine* |  |
| AstraZeneca | 346 (27.1%) |
| Janssen | 8 (0.6%) |
| Moderna | 136 (10.7%) |
| Pfizer | 778 (61%) |
| Not specified | 5 (0.4%) |

**Table 1.** Participant characteristics

**Figure legends**

**Figure 1.** A. The proportional area charts depict the proportion of respondents who reported a change to the timing of the period following vaccination broken down by whether the respondent was spontaneously cycling or taking hormonal contraception. B. The proportional area charts depict the proportion of respondents who reported a change to the flow of the period following vaccination broken down by whether the respondent was spontaneously cycling or taking hormonal contraception.

**Figure 2.** A. The proportional area charts depict the proportion of respondents who reported a change to the timing of the period following vaccination, broken down by the day in the cycle on which they received the vaccine. The predicted day of ovulation is defined as “0” with days before ovulation indicated by negative values, and days after ovulation indicated by positive values. B. The proportional area charts depict the proportion of respondents who reported a change to the flow of the period following vaccination, broken down by the day in the cycle on which they received the vaccine.

**Figure 3.** A. The proportional area charts depict the proportion of respondents who reported a change to the timing of the period following vaccination, broken down by whether the respondent reported having a pre-existing diagnosis of any menstrual or gynaecological condition. B. The proportional area charts depict the proportion of respondents who reported a change to the flow of the period following vaccination, broken down by whether the respondent reported having a pre-existing diagnosis of any menstrual or gynaecological condition.