FRONT MATTER

Title: Characterizing menstrual bleeding changes occurring after SARS-CoV-2 vaccination

Short title: Menstrual bleeding after SARS-CoV-2 vaccination

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Abstract

Many people began sharing that they experienced unexpected menstrual bleeding after SARS-CoV-2 inoculation. This emerging phenomenon was undeniable yet understudied. We investigated menstrual bleeding patterns among currently and formerly menstruating people, with a research design based off our expectations that these bleeding changes related to changes in clotting or inflammation, affecting normal menstrual repair. In this sample, 42% of people with regular menstrual cycles bled more heavily than usual, while 44% reported no change, after being vaccinated. Among people who typically do not menstruate, 71% of people on long-acting reversible contraceptives, 39% of people on gender-affirming hormones, and 66% of post-menopausal people reported breakthrough bleeding. We found increased/breakthrough bleeding was significantly associated with age, other vaccine side effects (fever, fatigue), history of pregnancy or birth, and ethnicity. Changes to menstrual bleeding are not uncommon nor dangerous, yet attention to these experiences is necessary to build trust in medicine.

Teaser

Increased bleeding can occur post SARS-CoV-2 vaccines; this study characterizes patterns to enable future hypothesis testing.

MAIN TEXT

Introduction

Menstruating and formerly menstruating people began sharing that they experienced unexpected bleeding after being administered a SARS-CoV-2 vaccine in early 2021. Vaccine trial protocols do not typically monitor for major adverse events for more than seven days, and additional follow up communications do not inquire about menstrual cycles or bleeding. Therefore, manufacturers had no way of addressing the extent to which this observation was a coincidence or a potential side effect of the vaccines. In mainstream media coverage, medical doctors and public health experts hastened to say that there was "no biological mechanism" or "no data" to support a relationship between vaccine administration and menstrual changes. In other cases experts declared that these changes were more likely a result of "stress"(*1–4*).

Unfortunately, dismissal by medical experts fueled greater concerns, as both vaccine hesitant and anti-vaccine individuals and organizations began to conflate the possibility of short-term menstrual changes with long-term harms to fertility. Pundits, politicians, religious leaders, and wellness influencers worked the oft-used framing of protecting women to advise against the vaccine (*5–9*). As the SARS-CoV-2 vaccine became available to adolescents, calls to understand the menstrual changes associated with the vaccine increased as parents felt they were weighing their child's pubertal development and future fertility against their risk of getting COVID-19(*10, 11*).

There are in fact multiple plausible biological mechanisms to explain a relationship between an acute immune challenge like a vaccine (*12*), its corresponding and well-known systemic effects on hemostasis and inflammation (*13*), and menstrual repair mechanisms of the uterus (*14–17*), The uterine reproductive system is flexible and adaptable in the face of stressors, in order to weather short-term challenges in a way that leaves long-term fertility intact (*18, 19*). We know that running a marathon may influence hormone concentrations in the short term while not rendering that person infertile (*20*); that short-term calorie restriction that results in a loss of menstrual cycling can be overcome by resuming normal feeding (*21*); that inflammation influences ovarian hormones (*22–24*); and that psychosocial stressors can correspond to cycle irregularity and yet resilience can buffer one from these harms (*25–27*). Less severe, short-term stressors can and do influence menstrual cycling and menstruation, and this has been established over forty years of cycle research (*19, 20, 28–30*); However this work has also established that while sustained early stressors can influence adult hormone concentrations, short-term stressors resolve and do not produce long-term effects (*31*); This is quite different from the sustained immune assault of COVID-19 itself: studies and anecdotal reports are already demonstrating that menstrual function may be disrupted long-term, particularly in those with long COVID (*32*).

Vaccines function by mobilizing the immune system to protect from disease if exposure occurs. This immune activation is important, although it may also produce a cascade of other localized (e.g., soreness at injection site) or systemic (e.g., fatigue, fever) inflammatory responses. Studies that assess the direct effect of vaccination on the menstrual cycle are few and far between. A study from 1913 identified that the typhoid vaccine was associated with menstrual irregularities, which included missed, late, and early menstruation, discomfort, and heavy bleeding in more than half of their female sample (*33*). Hepatitis B studies have also indicated that menstruation could be altered (*34*), and a HPV post-market safety study found that over a quarter of participants reported menstrual irregularity (*35*). The speed and coverage of the current COVID-19 pandemic vaccination campaign may have inadvertently highlighted a previously under-recognized side effect of especially immunogenic vaccines administered in adulthood, which is that systemic inflammatory responses may in some individuals invoke downstream responses in target organs such as the uterus.

The question of whether and when the particular acute immune challenge of the current SARS-CoV-2 vaccines affects menstrual cycling or menstruation is an emerging one with limitations on study design. Given the vaccines' overall established safety generally (*36–38*), and in relation to fertility and pregnancy (*39–43*), and the multiple waves of viral spread and variant emergence the world has endured with this deadly pandemic, a prospective design with a control group of unvaccinated individuals was unethical. Early on in anecdotal reports of menstrual cycle experiences, it was unclear the nature and breadth of the cycle changes: among those experiencing side effects were people experiencing earlier, later, heavier, lighter periods? Were other menstrual cycle phenomena also altered, like midcycle and premenstrual experiences? Were formerly menstruating people (e.g., those on menstrual suppression therapies or postmenopausal people) affected?

For this reason, we established an emergent, exploratory, mixed methods survey instrument intended to capture a wide range of responses from current and formerly menstruating adults. Given the multiple possible mechanisms at play, it was unclear the extent to which preexisting reproductive, immune, or hemostatic conditions, hormonal treatments, or menopausal status might play a role in an individual's post-vaccine experience. What's more, the bulk of mainstream reporting on this issue focused on the lived experiences of cisgender women who were currently menstruating, despite the fact that anecdotal reports of breakthrough bleeding by trans, non-binary, and/or postmenopausal people abounded (*3*, *44*). The feelings of frustration and mistrust were palpable, and thus another goal of this instrument was to demonstrate listening and attention.

Here we share results from our first round of analyses of this instrument (N=39,129), as well as the ways that this early exploration has made it possible to establish the parameters of the phenomenon of post-vaccine menstrual change. We focus specifically on data related to menstrual bleeding (in people who menstruate regularly) or breakthrough bleeding (in people who do not currently menstruate) from the first three months of data collection in order to provide a timely description of trends to clinicians and the public alike. Specifically, we sought to answer the following research questions:

- What is the range of menstrual bleeding changes reported by regularly menstruating respondents after being administered the SARS-CoV-2 vaccine?
- To what extent are non-menstruating respondents reporting breakthrough bleeding after being administered the SARS-CoV-2 vaccine?
- Are there trends among those with a changed bleeding pattern to help determine proximate mechanisms acting on the uterus?

Answers derived from this sample can help shape the narrative around the nature of short-term menstrual changes, help clinicians working with vaccine hesitant patients understand differences between fecundity and fertility, and develop the necessary, on-the-ground data on this new phenomenon to design future prospective, mechanistic studies on the relationship between vaccine immune responses and menstrual repair. Projects that take the time to establish trends and listen to respondents are important first steps to understanding details of emerging health concerns and how they affect people in the absence of other types of evidence such as structured, hypothesis-driven methodologies (*45*).

Results

Demographics and summary statistics

After data cleaning and aggregation of the first three months of data collection (Fig. 1), participants in our sample (N=39,129) were between 18 to 80 years old (median=33 years; M_{age}=34.22 years, SD=9.18). All participants were fully vaccinated (at least fourteen days after all

required doses) and had not contracted COVID-19 (diagnosed or suspected). This sample was 35,572 (90.9%) woman-only identifying and 3,557 (9.1%) gender diverse; 32,983 (84.3%) white-only identifying and 6,146 (15.7%) racially diverse; and 31,134 (79.6%) non-Hispanic or Latinx and 7,995 (20.4%) Hispanic, Latinx, or other (summary demographics in Table 1; detailed demographics in Table S1).

Respondents in this sample were vaccinated with Pfizer (N=21,620), Moderna, (N=13,001), AstraZeneca (N=751), Johnson & Johnson (N=3,469), Novavax (N=61), or other (N=204) vaccines, with 23 not reporting vaccine type. Self-report of localized vaccine side effects (soreness at injection site) after the first dose and second dose were 87.6% and 77.4%, respectively, across all vaccine types. Systemic vaccine side effects (headache, nausea, fever, and/or fatigue) were experienced by 54.3% and 74.6% of participants after the first and second dose, respectively. Of those that reported systemic vaccine side effects, 40.6% experienced systemic effects after both doses.

Vaccine symptoms, period changes (flow and length), period symptoms, and timing of period symptoms reported by study respondents are presented by age categories (Table 2, detailed reporting by vaccine type in Table S2). The Johnson & Johnson vaccine, being the only single dose vaccine at the time of survey, was excluded from later analyses.

Summary statistics of menstrual changes and breakthrough bleeding occurrences

We examined menstrual experiences overall and by conservatively defined subgroups, based upon self-reported typical pre-vaccine menstrual cycle status. We identified two major groups – those who regularly menstruate, and those who do not currently menstruate but have in the past. The subgroups of regularly menstruating people are 1) premenopausal people (ages 18-45) with spontaneous menstrual cycles and 2) premenopausal people (ages 18-45) with hormonally contracepting cycles who still bleed regularly. The subgroups of non-menstruating people are 1) premenopausal people (ages 18-45) on hormonal treatments that suppress menstruation (e.g., hormonal contraceptives, long-acting reversible contraception (LARC), testosterone), and 2) postmenopausal people (ages 55-80, no period for at least 12 months). Our analyses seeking to characterize the range of typical experiences focus on regularly cycling respondents without diagnosed reproductive conditions. We include respondents with reproductive conditions in our additional analyses of trends of which groups appear to be more at risk for changed bleeding patterns. Our analyses of breakthrough bleeding include people with and without diagnosed reproductive conditions after initial inspection did not reveal those groups to be significantly different. See Fig. 1 and Methods for data cleaning details and detailed subgroup descriptions; subgroup demographics are in Table S3.

We first report descriptive statistics, including the proportions of our sample who experienced changes in bleeding heaviness and duration (for people who regularly menstruate) or breakthrough bleeding (for those who typically do not menstruate), overall and by subgroups. We then analyzed associations between menstrual changes and age, race, and ethnicity, vaccine type (restricted to the most common 2-dose vaccines, Pfizer and Moderna), vaccine symptoms, typical period experience, reproductive history, and diagnosed reproductive conditions focusing on the same sub-groups. As these sample sizes were large, we used alpha threshold $p<.001$ when testing for associations within subgroups greater than 800, which meant respondents on gender-affirming treatments and postmenopausal respondents we used the typical alpha threshold $p<.05$.

Reported menstrual changes in regularly menstruating people

The menstrual changes in the full group of pre-menopausal regularly menstruating people (N=21,380) included period flow change and period length change. The highest proportion of respondents reported noticing changes to their reported period symptoms 14 or more days after receiving their vaccines (Dose 1: 29.94%; Dose 2: 26.85%).

Due to the proportion of people experiencing heavy flow after at least one of the vaccines, we grouped regularly cycling individuals with any heavier flow into one condition ("heavier"; N=7,429 of 17,642; 42.11%), people who experienced no change in flow after either dose into the second condition ("no change"; N=7,684; 43.56%), and the remainder of people who experienced a combination of lighter and no change after their doses into a smaller third condition ("not heavier", N=2,529; 14.34%). In total, 727 were missing dose 1 period flow information and 3,031 were missing dose 2 period flow information (Table S5). We similarly grouped people reporting any longer bleeding into one condition ("longer"; N=5,9780 of 17,366; 34.42%), people who experienced no change in period length after either dose into a second group ("no change", N=8,914; 51.33%), and the remainder of people who experienced a combination of shorter and no change to period length across doses into a smaller group ("not longer", N=2,474; 14.25%). Period length information was missing for 776 people following dose 1 and 3,342 people following dose 2. If information was missing at either dose, we treated it as pairwise missingness, so the respective menstrual change variable was missing. Thus, period flow change is described as heavier, no change, or not heavier and period length change is described as longer, no change, or not longer. Since lighter flow or shorter duration bleeding is meaningful but less common in this sample, we include this condition in our analyses but focus mainly on factors associated with heavier bleeding as compared to no change in bleeding.

Among spontaneously cycling premenopausal people with regular menstrual cycles and no diagnosed reproductive conditions, 45.81% (4,388 of 9,579) of people experienced no change in their bleeding heaviness and 40.83% (3,911) experienced heavier bleeding after vaccination (Fig. 2). Nearly a third of this subgroup also experienced a longer duration of menstrual bleeding Premenopausal people using hormonal contraceptives who report regular menstrual cycles and no diagnosed reproductive conditions reported similar trends, 42.8% (1,384 of 3,237) of people experienced no change in their bleeding heaviness and 41.2% (1,334) experienced heavier bleeding after vaccination. More than a third of this subgroup reported a longer duration of menstrual bleeding (Table S4). Differences between the regularly menstruating groups in post-vaccine menstrual flow and duration were statistically significant, with hormonally contracepting people being less likely to experience no change in flow ($\chi^2(2, N=12{,}816)=17.338$, $p=0.0002$) and more likely to experience a longer menstrual duration ($\chi^2(2, N=12{,}608)=49.689$, $p=1.62\text{E-}11$).

When comparing spontaneously cycling and hormonally contracepting regularly menstruating respondents, we found differences between these groups in past pregnancy, parity, usual period flow, usual period length, race, ethnicity, and age ($N_{sp}=11{,}700$ and $N_{hc}=3{,}855$; Table S6). Vaccine type and local/systemic symptoms did not differ between subgroups.

Non-menstruating respondents and breakthrough bleeding

The majority of non-menstruating pre-menopausal people using LARC experienced breakthrough bleeding, 70.49% overall (1,089 out of 1,545). Fewer people on gender-affirming hormones experienced breakthrough bleeding, 38.52% (104 out of 270). Among post-menopausal people who were not on any hormonal treatments, breakthrough bleeding was reported by 65.97% of respondents (157 out of 238).

Associations with trends in flow change and breakthrough bleeding in this sample

For the regularly cycling subgroups, we tested for associations between relevant demographic factors, vaccine type, reported systemic side effects, typical menstrual experiences, reproductive history, and diagnosed reproductive conditions with flow change; in the non-menstruating subgroups we examined whether these factors were associated with the occurrence of breakthrough bleeding. We discuss each of these factors in the next sections. Full results are reported in Tables 3-5.

Age, gender, race, and ethnicity

We tested for significant differences between age and change to one's period flow after vaccination within the regularly cycling subgroups. Age was significantly different only in the spontaneously cycling subgroup ($F_{(2, 9,576)}$=34.1, p=1.70E-15). Those who reported heavier flow change were older (M=32.9 years) than those with no change (M=31.7; p=8.18E-15) or not heavier change (M=31.7; p=8.06E-08).

No significant associations were found in either of the regularly cycling subgroups when we tested for any association between racial group and changes to period flow after vaccination. When we examined for an association with ethnicity, we found a significant relationship in the spontaneously cycling subgroup (χ^2(2, N=9579)=34.81, p=2.75E-08). Heavier flow was experienced by 43.7% of people of Hispanic/Latinx or other ethnicity compared to 40.0% by people who are Non-Hispanic/Latinx (OR=1.16, 95%CI[1.05, 1.28]). The Cramér's V effect size was small for this relationship (φc=0.060).

We examined for significant differences between age and presence of breakthrough bleeding post-vaccination within the non-menstruating subgroups. Age was significantly different only in the post-menopause subgroup (t(147.99) = -2.255, p=0.026), where post-menopausal people who experienced breakthrough bleeding were slightly younger (M=59.8 years) than those who did not (M=61.4 years).

There was not a significant relationship found with race in the non-menstruating groups (those on LARC and those receiving gender-affirming hormonal treatments). We could not run a test of whether breakthrough bleeding was associated with race in the post-menopausal subgroup because of the small number of non-white identifying individuals. Ethnicity was associated with breakthrough bleeding in post-menopausal people (χ^2(1, N=238)=4.1338, p=0.042), and heavier flow was reported by 76.92% of people of Hispanic/Latinx or other ethnicity compared to 61.85% of Non-Hispanic/Latinx ethnicity in this sample (OR=2.05, 95%CI [1.03, 4.26]). Non-Hispanic individuals were less likely to report breakthrough bleeding than Hispanic or other ethnicity individuals (φc=0.142).

Vaccine type

There was no difference in post-vaccination menstrual flow or rate of occurrence of breakthrough bleeding between Pfizer or Moderna in any of the subgroups, and sample sizes for the other vaccine types were too small for analysis in this sample. Results for regularly cycling subgroups are reported in Table 4 and for non-menstruating subgroups are reported in Tables 5 and 6.

Systemic side effects

We examined whether fatigue and/or fever, as notable systemic vaccine side effects, were associated with change in bleeding. Fever and post-vaccine menstrual flow change were associated in spontaneous regularly cycling respondents (χ^2(2, N=9,579)=40.11, p=1.95E-09), with heavier flow more likely to be reported by people who had fever than people who did not report fever (43.2% vs 39.1%; OR=1.18, 95%CI [1.09, 1.28]). Fatigue was also significantly associated with post-vaccine menstrual flow change in spontaneous regularly cycling respondents (χ^2(2, N=9579)=44.51, p=2.16E-10), and heavier flow was experienced by 42.03% of spontaneously cycling respondents who had fatigue compared to 35.25% of those who did not have fatigue (OR=1.33, 95%CI [1.19, 1.49]). We found no significant associations with systemic side effects and breakthrough bleeding.

Typical menstrual experiences

We tested for associations between a respondent's usual menstrual blood flow and whether they experienced a change to that flow after the vaccine in regularly cycling subgroups.

There was a significant relationship with typical menstrual blood flow and change to menstrual blood flow in the regularly cycling groups (spontaneously cycling: $\chi^2(4, N=9{,}537)=61.07$, $p=1.73E-12$; hormonally contracepting: $\chi^2(4, N=3{,}222)=19.56$, $p=0.0006$). People who report typically having a heavy flow were less likely to experience an even heavier flow following the vaccine (spontaneously cycling: OR=0.82, 95%CI [0.73, 0.92]; hormonal contraception: OR=0.92, 95%CI[0.69, 1.22]), though the effect size was small (spontaneously cycling: φc=0.057; hormonally contracepting: φc=0.055). There was also a significant relationship between a respondent's usual menses length and whether they experienced a change to length of menses after the vaccine in spontaneous regularly cycling respondents, ($\chi^2(6, N=9{,}395)=66.66$, $p=1.98E-12$; small effect estimate, φc=0.0596; see Table S8).

Reproductive history

Four study variables were considered regarding reproductive history: past pregnancy, vaginal bleeding during pregnancy, parity, and post-partum hemorrhage. We compared all four variables in the regularly cycling subgroups and compared pregnancy and parity in the non-menstruating subgroups when there were an adequate number of responses (>20) per cell (Tables 3-5). In both the spontaneously cycling and hormonally contracepting cycle subgroups, respondents who have been pregnant reported heavier flow post-vaccine more often than people who have not (spontaneously cycling: 46.7% versus 37.5%, OR=1. 46, 95%CI [1.35, 1.60]; hormonally contracepting: 47.3% versus 39.2%, OR=1.39, 95%CI [1.18, 1.64]). In the spontaneously cycling subgroup, respondents who have given birth reported heavier flow more often than people who have not $\chi^2(2, N=9{,}579)=50.20$, $p=1.26E-11$ (46.2% versus 38.2%) (OR=1.37, 95%CI [1.25, 1.50]).

In the LARC subgroup, respondents who have been pregnant were more likely (79.6% versus 67.42%) to report breakthrough bleeding ($\chi^2(1, N=1{,}544)=20.06$, $p=7.50E-06$; OR=1.88, 95%CI [1.42, 2.52]). The effect size in this group was small (φc=0.1156). Respondents in the LARC subgroup who have given birth were also more likely to report heavier flow (78.5% versus 68.4%; $\chi^2(1, N=1{,}545)=11.73$, $p=0.0006$; OR=1.68, 95%CI [1.25, 2.29]). The effect size was small (φc=0.0889). We did not have enough responses in the gender-affirming subgroup to run this comparison. Prior pregnancy and parity were not significantly associated with breakthrough bleeding in post-menopause individuals.

Neither vaginal bleeding during pregnancy nor post-partum hemorrhage was associated with post-vaccine flow change in regularly cycling subgroups. This was true despite having a large number of respondents reporting these experiences (824 reporting vaginal bleeding during pregnancy and 306 individuals reporting post-partum hemorrhage).

Because age, pregnancy, and parity were all associated with a heavier flow in our sample, and these variables have a tendency to be associated with each other, we tested for average age differences in those with past pregnancy/no pregnancy and parous/not parous. Respondents with a history of pregnancy or who were parous were significantly older (pregnancy: $t_{(10{,}738)}=-77.73$, $p<2.2E^{-16}$; parity: $t_{(9{,}440)}=-80.678$, $p < 2.2E^{-16}$). People who had been pregnant were older ($M_{age}=37.47$) than people with no history of pregnancy ($M_{age}=29.08$), and parous respondents were also older ($M_{age}=38.13$) than non-parous ($M_{age=}29.54$). Finally, we looked only at respondents with no history of pregnancy and tested for age differences to try to separate the effect of age and reproductive history. We found those who reported a heavier flow post-vaccine were more likely to be older ($F(2, 6{,}093)=9.091$, $p=0.0001$). Again, the heavier condition was older ($M_{age}=29.60$) than those who reported no change to their flow ($M_{age}=28.82$; $t(4{,}724.8)=4.217$, $p=2.038e-05$).

Reproductive conditions

We then made comparisons for those diagnosed with a specific reproductive condition against the appropriate (i.e., spontaneously cycling or hormonally contracepting) larger sample without any diagnosed conditions (Table 6). In spontaneously cycling subgroups, a higher proportion of respondents with endometriosis (52.4%), menorrhagia (44.6%), and/or fibroids (46.3%) reported experiencing a heavier menstrual flow post-vaccine than the non-diagnosed respondents (40.8%). In the hormonally contracepting subgroup, a higher proportion of respondents with fibroids (56.4%) reported experiencing a heavier menstrual flow post-vaccine than the non-diagnosed respondents (41.2%).

Discussion

We present initial summary statistics and descriptive analyses of changes to menstrual bleeding in a large and diverse sample of currently and formerly menstruating adults after SARS-CoV-2 vaccination. This is the very first characterization of the full range of post-vaccine menstrual experiences for a gender-diverse sample of pre- and post-menopausal people with and without diagnosed reproductive conditions. We cannot estimate prevalence or incidence based on our methodological approach of this emergent phenomenon. However, our results highlight that these changes affect a large number of people and some of the trends we observe support hypothesis development for additional prospective study in hemostatic and inflammatory changes to the endometrium after an acute immune response (Fig. 4).

In this first analysis, we focus on the heavier bleeding of currently menstruating and breakthrough bleeding of formerly menstruating people, which we define as an increased bleeding phenotype. The increased bleeding phenotype appeared to be the most common post-vaccination change within our sample. Initial forays into our qualitative data suggest a widely variable experience of the increased bleeding phenotype, confounding a straightforward case definition. At this time, we suggest that rather than a threshold quantity to define the increased bleeding phenotype, vaccinated people and providers instead consider menstrual changes in the context of what is typical for the vaccinated person. For instance, many hormonal treatments reduce or suppress menses, and therefore a change in bleeding among individuals prescribed these treatments can look substantially different than bleeding changes for spontaneously cycling people.

Increased bleeding is often distressing, and it can (and often should) lead providers towards diagnostic procedures to assess its origins (*46–48*). This is especially true when it comes to breakthrough bleeding among formerly menstruating people, for whom this symptom can be an early sign of cancer. When possible bleeding-related side effects to a treatment are not shared with the clinical or patient population, it may lead to unnecessary, painful, and expensive diagnostic procedures. In a related example, several studies have now shown that epidurals likely increase the risk of increased bleeding among regularly cycling and/or postmenopausal people (*49, 50*). In one recent study, 17% of postmenopausal respondents reported breakthrough bleeding after injection, and 7% from a control group. Of the thirty one respondents who reported this bleeding to their physician, thirteen had endometrial biopsies collected, and two had transvaginal ultrasounds. While all results were benign, endometrial biopsies are known to be intensely painful and invasive procedures (*51, 52*). Though these data have been reported in the literature for at least a decade, no patient-facing information about epidurals that we could find makes note of the risk of unexpected bleeding, which means potentially unnecessary, expensive, painful diagnostic procedures may continue today.

Unexpected bleeding has other major and even life-threatening consequences. Trans men, trans masculine people, and masculine of center genderqueer people, many of whom suppress periods with a combination of LARC and masculinizing therapies, may find themselves suddenly navigating public bathrooms or workplaces while menstruating. Therefore, this unexpected

bleeding runs the risk of psychological distress for those who experience gender dysphoria with menstruation, and physical harm for people for whom managing menstruation in public is dangerous (*53*, *54*).

In addition to our finding of a significant proportion of respondents experiencing some form of increased bleeding, we noticed some trends in who was more likely to have this phenotype. Among premenopausal respondents, those who were older and/or Hispanic (using U.S. census demographic approaches) were more likely to report heavier bleeding post-vaccine. Prior pregnancy and prior birth also were associated with a greater risk of heavier bleeding. Finally, premenopausal, spontaneously cycling respondents who were diagnosed with endometriosis, menorrhagia, and/or fibroids were more likely to report experiencing heavier bleeding post-vaccine compared to those without any diagnosed reproductive condition. We also find that many respondents who had post-vaccine changes did not have them until fourteen days or longer post-inoculation, which extends beyond the typical seven days of adverse symptom reporting in vaccine trials.

The responsiveness of menstrual cycles and bleeding patterns to external stressors is well known (*55*). Responsiveness to external stressors is one reason menstrual cycles are often thought of as reflecting overall health status, or a so-called "vital sign" in clinical practice (*56–58*). Thus, many people are attuned to menstrual cycles and take note of changes as potentially indicating other underlying health concerns. For many people, menstruation matters for reasons beyond current conceptive intentions: menstruation relates to their experiences of gender and gender dysphoria, to their intuitive connections to bodily processes, and to their fears and embarrassments surrounding menstrual stigma (*53*, *59*, *60*). Therefore, unexpected and unplanned menstrual changes can cause concern, distress, or other negative responses, in addition to discomfort and physical pain.

Despite this, menstruation is seldom considered a variable during vaccine trials aside from determining last menstrual period as part of established protections against volunteers being or getting pregnant. The vast majority of research that has been conducted regarding reproductive and menstrual function centers around whether or not live and attenuated vaccines are safe to give someone who is pregnant (*61–64*), or if it affects fertility (*65*, *66*). The research that has been conducted on menstrual cycles specifically is often not able to establish a causal link, as the data is obtained through retrospective surveys or data mining (*67*, *68*) and randomized controlled trials often do not allow a mechanism for reporting these changes (*44*). Data mining and signal detection in VAERS has resulted in the identification of several possible effects on menstruation that suggest further research is needed (*67*, *68*); however, queries about changes in menstruation are still not a standard part of vaccine trials despite recent calls for more study (*69*).

Menstruation is an inflammatory and hemorrhagic event that must be resolved quickly to restore uterine function and prevent infection and continued hemorrhage (*14*, *70*). Disruption of the normal coagulation pathway of the endometrium may delay the repair mechanisms that allow menses to end quickly. A few of our findings suggest that vaccination is less likely to be affecting periods via ovarian hormone pathways, and more likely along these inflammatory pathways. We found very little difference between respondents with spontaneous and hormonally contracepting cycles in the rate of post-vaccine heavy menstrual flow. We also found a significant proportion of formerly menstruating people, including post-menopausal participants with presumably dormant ovaries, experienced breakthrough bleeding. Further, the greater presence of this increased bleeding phenotype among regularly cycling premenopausal respondents who were older and/or parous points to ways in which mature and established menstrual repair mechanisms may create a vulnerability to this short-term phenomenon. In addition, the greater proportion of people with endometriosis, menorrhagia, and/or fibroids points to a vulnerability among those with hyperproliferative and/or vascular/hemostatic conditions. Respondents with polycystic ovary

syndrome, which often causes amenorrhea and therefore infrequent menstrual repair, were not more likely to experience increased bleeding after vaccination.

Data used in these analyses are unable to represent population prevalence of post-vaccine menstrual changes. They may be biased towards those who noted some change in their own menstrual or bleeding experiences, particularly if that change was uncomfortable, painful, frightening, or concerning. That said, a significant portion of the respondents who took part reported no menstrual change. Evidence suggests that people with other types of negative experiences are less, not more likely to participate in surveys where they suspect they will be expected to recount such material (*71*, *72*). A large number of qualitative responses alluded to the fact that people who are interested in science or cared about the research participated despite not having adverse menstrual experiences post-vaccine. Further, the rate of localized and systemic side effects reported in this sample were similar to that reported in vaccine trials (*36*–*38*). suggesting this sample is not grossly unrepresentative of the wider population. Awareness of selection bias is important to contextualize survey findings. That said, the sample size for this survey is large enough to suggest that the observed trends are real and are affecting a large number of vaccinated people.

An additional limitation of these analyses is due to the fact that our sample has a very high percentage of people who identify as white and as not Hispanic/Latinx. There are several potential causes for this, including that this data may reflect early trends in vaccination (*73*), it may be related to internet access (though the survey was tested for smartphone functionality), it may be related to participant trust in academic research, and/or it may be a function of how information about the survey was disseminated across social media and traditional media platforms. Social media allows for dissemination, but it also often creates insular communities due to differences in user demographics (*74*). Whatever the cause, we note the under-representation of Black, Indigenous, Latinx, and other respondents of color as a limitation in this research that seeks to understand menstrual experiences after vaccination. One of the ways we have sought to correct this underrepresentation is through the creation of a Spanish language version of the survey, which is still in its initial recruitment phase.

Comparisons between people on hormonal contraception and people with spontaneous cycles should be interpreted with caution, as the decision to use hormonal contraception is not independent of other health and life circumstances. This is especially true in people who have diagnosed reproductive conditions, which are often managed with hormonal contraceptives. Thus, differences between these groups may also reflect underlying differences in severity of the conditions or effectiveness of treatment approaches for managing symptoms. Future hypothesis development should focus on the ways in which these changes to menstrual bleeding may be acting via hemostatic, inflammatory, and/or immune pathways related to menstrual repair mechanisms of the uterus. Furthermore, there remains incredible potential for applying knowledge gained in understanding the mechanisms underlying the increased menstrual bleeding after vaccines that we describe to treating symptoms of reproductive conditions which have been vastly understudied.

Gaps in knowledge, such as better understanding the ways menstrual cycles respond to acute and chronic immune and inflammatory stressors, can also be understood as a form of ignorance which is produced and reproduced based upon structural, cultural, and political decisions (*75*). The data presented and discussed here highlights how anthropological mixed-methods research approaches that engage in attentive listening rather than strictly *pro forma* hypothesis-driven research is necessary to attend to gaps in knowledge during emerging phenomena. Taking the time to listen and notice allows us to observe things that may not fit into our established narratives and to take responsibility for our role in knowledge dissemination as scientists (*76*, *77*). Furthermore, examination of the narratives and stories that we use to understand the world around us can illuminate the ways scientific narratives can shape and

reproduce inequitable power structures of the world. Research which notices and attends to the experiences of people is a necessary first step to restore trust and create transparency in science.

We have documented a phenotype of increased menstrual bleeding across a diverse set of currently and formerly menstruating people as a post-vaccine response. In doing so, we help provide evidence and context for clinicians regarding the validity of these experiences and we note future avenues of inquiry for researchers. Recognizing and attending to this emerging phenomenon of bleeding changes can help bolster trust between people who menstruate and medical providers, which is an area that has a long history of medical misogyny and gaslighting (*78–81*). Current and historic focus on fertility and reproduction in research and clinical trials is insufficient for addressing the changes in bleeding patterns that cause concern in many people. We urge other researchers and funding bodies to increase investment in understanding queer, trans, and nonbinary menstrual experiences, because there is a dearth of existing literature to understand the biosocial context of menstrual bleeding in these groups. Furthermore, we note that postmenopausal bleeding is still massively understudied. Mixed-methods and community based participatory research to address questions that matter to those historically excluded from reproductive and menstruation science is needed in order to provide adequate and culturally and physically relevant care to these populations.

Materials and Methods

Recruitment

This research was designated as exempt by the University of Illinois Institutional Review Board and Washington University in St. Louis Institutional Review Board. Data were collected and managed using REDCap hosted at the University of Illinois at Urbana-Champaign (*82*, *83*). REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies. The survey launched on April 7, 2021, and data collection is closing on October 7, 2021 after 6 months of data collection. Results presented here are from data downloaded on June 29, 2021 (approximately 12 weeks of data collection). The survey was initially announced on Twitter (*84*, *85*), but quickly propagated through multiple social media platforms. Media coverage (TV news, public radio, online journalism, print journalism, science blogs, etc.) of the study included links to the survey and provided additional wide-spread participant recruitment. Additionally, many participants learned of the survey after performing an online search to investigate their own menstrual experiences and finding social media and/or news coverage of this project. Thus, the data collected by this survey represents extensive snowball sampling via many channels.

Sample

At the time of downloading, 92,529 participants had completed the informed consent and submitted the survey. This included only unique email IDs with duplicate emails being sorted by timestamp and the more recent timestamp responses retained (N=205). There were 5 individuals removed for inappropriate and/or hostile responses. Ages greater than 99 (N=26) were manually re-coded by the first two number entered (e.g., 323 was coded as 32) or by calculating the age from the birth year entered (e.g., 1990 was coded as 31). Then, we removed participants under age 18 (N=12). Responses missing more than 90% of survey items were removed (N=11,999). From the remaining responses (N=80,513), we retained only those that reported having not been diagnosed with COVID-19 (N=65,241; removing N=4,494 with diagnosed COVID-19; 5,761 with suspected but undiagnosed COVID-19; 4,870 who were unsure about prior COVID-19, and 103 reporting “other”). There were 42,097 who had received two vaccine doses, 19,161 who had not received a second dose, and 3,983 who did not respond. Two-dose vaccinated individuals were restricted to those who submitted the survey at least 14 days after their second vaccination date (N=35,660). Individuals reporting only one dose (N=23,144) were restricted to Johnson &

Johnson vaccine and 14 days after first dose vaccination date (N=3,469). In total, we removed those that were not at least 14 days after full vaccination (N=26,112), i.e., two weeks after second dose for two-dose vaccines or two weeks after vaccination for single-dose vaccines. The final sample was 39,129 participants for general sample descriptive statistics. The vaccines received by participants were as follows: 751 received AstraZeneca, 3,469 Johnson & Johnson, 13,001 Moderna, 61 Novavax, 21,620 Pfizer, 204 other (which includes those who received different types across dose 1 and 2), and 23 missing.

We focused on the 35,660 individuals who received a two-dose COVID-19 vaccination for statistical analyses of menstrual changes and vaccine experiences. Of these respondents, the menstrual cycles were self-described as regular (N=27,143), irregular (N=4,358), or absent (N=4,136), with 23 individuals not responding to this item and thus excluded from analyses beyond sample description. Analyses focus on narrowly defined subsamples with additional restrictions to reduce the confounding influence of variables that likely influence menstrual cycles or differences between people in menstrual experiences. We specifically focus on the following main groups: premenopausal people with spontaneous regularly occurring menstrual cycles (age 18-45, predictable menstrual cycles, no diagnosed reproductive conditions, and not taking exogenous hormones), regularly cycling people on hormonal contraception (age 18-45, predictable menstrual cycles, no diagnosed reproductive conditions), non-menstruating pre-menopausal people (age 18-45, separated into people using long-acting reversible contraceptives (LARC) and people using gender-affirming hormones), pre-menopausal people with reproductive conditions (age 18-45, self-reported diagnoses, separated in to spontaneous regularly menstruating people, regularly menstruating people using hormonal contraception, and non-menstruating people on LARC or gender-affirming hormones), post-menopausal people (with and without diagnosed reproductive conditions, and not on any hormonal treatments). Note that the pre-menopausal sample was restricted to age below 45 and post-menopausal sample was restricted above age 55, due to the variability expected throughout perimenopause. People who reported having irregular menstrual cycles, selected perimenopause, or were coded based on text as perimenopausal or an uncertain menopause stage are not included in these analyses. Additional detail for groups can be found in the supplemental information.

Unlike regularly menstruating people where usual period flow and length are expected to differ between those with and without diagnosed reproductive conditions, the presence of hormonal treatments and/or reproductive dormancy reduces the potential for major differences within our non-menstruating groups based on diagnosed reproductive conditions. In LARC subgroups, those non-diagnosed (N=943) did not differ from those diagnosed (N=602) with reproductive conditions on prevalence of breakthrough bleeding, timing of period symptoms at dose 1 [or 2], vaccine type, experience of side effects at dose 1 [or 2], fever, fatigue, past pregnancy, parity, race, ethnicity, or age. In gender-affirming subgroups, those undiagnosed (N=183) did not differ from those diagnosed (N=87) on any of the study variables compared (breakthrough bleeding, vaccine type, fever, fatigue, race, ethnicity, and age). We did not run tests for association with timing of symptoms, any side effects at dose 1 [or 2], or reproductive history, because there were too few respondents in each cell. Finally, in post-menopause subgroups, those undiagnosed (N=117) and diagnosed (N=121) with reproductive conditions did not differ on any study variables compared (breakthrough bleeding, vaccine type, fever, fatigue, past pregnancy, parity, race, ethnicity, and age). Thus, we combined people diagnosed with reproductive condition with those who are not diagnosed with reproductive conditions within the three non-menstruating subgroups (LARC, gender-affirming care, post-menopausal).

Data Analytic Strategy

We started with descriptive statistics of the full sample of 39,129 fully vaccinated individuals grouped into age categories. The descriptive report of the full sample omits all the

second dose variables for the single-dose Johnson & Johnson vaccine. As these effects we observed were an emerging phenomenon we focus primarily on descriptive statistics and trends.

In each subgroup we focused on menstrual changes following vaccination. In regularly cycling subgroups, changes to menstrual flow and menstrual length were investigated. These were defined as 'heavier', 'not heavier', or 'no change'. In non-menstruating subgroups, breakthrough bleeding was investigated. We describe the approximate frequency of breakthrough bleeding as 'after both', 'only dose 2', 'only dose 1', or 'none'. We examined for differences based on whether respondents reported any breakthrough (see measures in online Supplemental for more details).

Chi-square test of independence were used in two ways—to examine whether a study variable was associated with bleeding outcomes and to determine whether there was an association between study variables and the subgroup defined as spontaneous versus hormonally contracepting or without versus with diagnosed reproductive conditions. Study variables were not compared either within or across subgroups when the sample sizes per cell were less than 20. For regularly cycling subgroups, we omitted respondents with missing data and respondents who selected 'other' usual menstrual flow or length, most of whom gave detailed unique descriptions via text entry. Association with vaccine type was restricted to Pfizer and Moderna due to a largely US based sample and, therefore, large sample numbers for these vaccines for the early April – early July time period.

We investigated other factors likely to be associated with reported bleeding experiences by analyzing each subgroup. We calculated the proportions within each independent variable that were associated with each bleeding outcome (flow change or breakthrough depending on the subsample). Chi-square tests of independence were run within each sample subgroup to test for significant associations between bleeding condition and study variables. Pairwise missingness was used to handle missing data. All study variables were nominal, except age. When the contingency table was 2x2, Yate's continuity correction was applied. Alongside the chi-square tests for associations with bleeding outcomes, we calculated Cramér's V (φ_c) to estimate effect sizes. For comparisons of 2x2 or 2x3 contingency tables, the effect size estimates are considered small when φ_c is 0.10 to 0.30 and medium when 0.30 to 0.50. For 3x3 contingency tables, the estimates are small at 0.07 to 0.20 and medium at 0.20 to 0.35.(*86*) We calculated 95% confidence intervals for effect sizes. Age differences were tested using Welch's two sample t-test for unequal variances when comparing two conditions or one-way ANOVA when comparisons were between three conditions.

In our large samples (N > 870) at a significance threshold of $p<.001$ we had 90% power to detect a small-medium (*86*) effect size of 0.178, and for smaller samples we used the standard $p<.05$ which means we have 28% power to detect a similar effect. As a result of large sample sizes in select subgroups, we did expect to find significant associations that related to small differences in proportions. In most subgroups, we had the power to detect an effect of 7% proportion differences with 90% power at $p<.001$, minimum sample size per proportion was 993, and 3% proportion differences required a minimum of 4,724 individuals per proportion. To detect a 7% proportion difference, we required 993 individuals per sample proportion. With similar proportion differences at 90% power with alpha threshold at $p<.05$, we required samples of 499 for 7% differences and 2,374 for 3% differences. Therefore, the smallest subgroups where $p<.05$ was the alpha threshold, namely people using gender-affirming hormones and post-menopause people, we had 90% power to detect 25% proportion differences and less than 20% power to detect 7% proportion differences. As the main goal of this paper was to describe the experiences of a wide range of people, we acknowledged the limitation of these significance tests and focus on effect estimates and the odds ratio for significant associations. Following the results of the chi-square tests, the comparative odds of bleeding conditions, namely heavier flow change and breakthrough bleeding, were calculated for significant associations using odds ratio.

All analyses were run in R Studio (*87*). `DescTools` was used for chi-square test power analysis (*88*), `rcompanion` for Cramer's *V* (*89*), `questionr` for odds ratio (*90*), and `ggplot2` for figures (*91*). Supplemental materials and survey instrument are available: https://osf.io/6rvxk/?view_only=f91f1247658f49e3bbf59b2f6cfd3898 .

References

1. A. Cuda, Is there a link between COVID vaccine and "funky" menstrual periods? Experts say it's too soon to know. *Connecticut Post* (2021), (available at https://www.ctpost.com/news/coronavirus/article/Is-there-a-link-between-COVID-vaccine-and-16112418.php).

2. S. Lilly, Can COVID-19 vaccine impact your menstrual cycle? Doctors address side-effects concerns. *WTVR* (2021), (available at https://www.wtvr.com/news/coronavirus/covid-vaccine-menstrual-cycle-impacts).

3. N. Stock, Some people are reporting abnormal periods after a COVID-19 vaccine. U. of I. professor is looking for answers. *chicagotribune.com* (2021), (available at https://www.chicagotribune.com/coronavirus/vaccine/ct-vaccine-side-effects-period-menstruation-20210420-i4fy7a7tnnbchi654z3o64a7my-story.html).

4. A. Villarreal, 'No data' linking Covid vaccines to menstrual changes, US experts say. *The Guardian* (2021), (available at https://www.theguardian.com/world/2021/apr/23/covid-vaccines-periods-menstruation-changes-data-experts).

5. A. North, Why false claims about Covid-19 vaccines and infertility are so powerful. *Vox* (2021), (available at https://www.vox.com/22639366/covid-19-vaccine-fertility-pregnancy-myths).

6. S. Stecklow, A. Macaskill, SPECIAL REPORT The ex-Pfizer scientist who became an anti-vax hero. *Reuters* (2021), (available at https://www.reuters.com/business/healthcare-pharmaceuticals/special-report-ex-pfizer-scientist-who-became-an-anti-vax-hero-2021-03-18/).

7. G. Brumfiel, The Life Cycle Of A COVID-19 Vaccine Lie. *npr* (2021), (available at https://www.npr.org/sections/health-shots/2021/07/20/1016912079/the-life-cycle-of-a-covid-19-vaccine-lie).

8. H. Dreyfus, Why Some Orthodox Jewish Women Won't Get Vaccinated. *The New York Times* (2021), (available at https://www.nytimes.com/2021/06/11/nyregion/orthodox-jewish-vaccinations.html).

9. K. Ronayne, M. R. Blood, Gov. Newsom calls GOP rivals 'anti-vax,' but are they? *AP* (2021), (available at https://apnews.com/article/business-health-coronavirus-pandemic-b6049fa972077f6baa2d0c9d3278debd).

10. J. Gerson, Why this mom got the COVID-19 shot but hesitates for her daughter. *Modern Healthcare* (2021), (available at https://www.modernhealthcare.com/safety-quality/why-this-mom-got-covid-19-shot-hesitates-her-daughter).

11. J. Grose, They're Not Anti-Vaccine, but These Parents Are Hesitant About the Covid Shot. *The New York Times* (2021), (available at https://www.nytimes.com/2021/05/12/parenting/vaccine-children.html).

12. K. R. Talaat, N. A. Halsey, A. B. Cox, C. L. Coles, A. P. Durbin, A. Ramakrishnan, J. H. Bream, Rapid changes in serum cytokines and chemokines in response to inactivated influenza vaccination. *Influenza Other Respi Viruses*. **12**, 202–210 (2018).

13. G. Grignani, A. Maiolo, Cytokines and hemostasis. *Haematologica*. **85**, 967–972 (2000).

14. H. O. Critchley, R. W. Kelly, D. T. Baird, R. M. Brenner, Regulation of human endometrial function: mechanisms relevant to uterine bleeding. *Reprod Biol Endocrinol*. **4**, S5 (2006).

15. J. Evans, L. A. Salamonsen, Inflammation, leukocytes and menstruation. *Rev Endocr Metab Disord*. **13**, 277–288 (2012).

16. M. Berbic, I. S. Fraser, Immunology of Normal and Abnormal Menstruation. *Womens Health (Lond Engl)*. **9**, 387–395 (2013).

17. A. Azlan, L. A. Salamonsen, J. Hutchison, J. Evans, Endometrial inflammasome activation accompanies menstruation and may have implications for systemic inflammatory events of the menstrual cycle. *Human Reproduction*. **35**, 1363–1376 (2020).

18. K. B. H. Clancy, P. T. Ellison, G. Jasienska, R. G. Bribiescas, Endometrial thickness is not independent of luteal phase day in a rural Polish population. *Anthropol Sci*. **117**, 157–163 (2009).

19. P. T. Ellison, C. Panter-Brick, S. F. Lipson, M. T. O'Rourke, The ecological context of human ovarian function. *Human Reproduction*. **8**, 2248–2258 (1993).

20. J. C. Prior, B. H. Yuen, P. Clement, L. Bowie, J. Thomas, Reversible luteal phase changes and infertility associated with marathon training. *The Lancet*. **320**, 269–270 (1982).

21. R. J. Mallinson, N. I. Williams, M. P. Olmsted, J. L. Scheid, E. S. Riddle, M. J. De Souza, A case report of recovery of menstrual function following a nutritional intervention in two exercising women with amenorrhea of varying duration. *J Int Soc Sports Nutr*. **10**, 34 (2013).

22. K. B. H. Clancy, A. R. Baerwald, R. A. Pierson, *American Journal of Physical Anthropology*, in press, doi:10.1002/ajpa.22976.

23. K. B. H. Clancy, L. D. Klein, A. Ziomkiewicz, I. Nenko, G. Jasienska, R. G. Bribiescas, Relationships between biomarkers of inflammation, ovarian steroids, and age a menarche in a rural Polish sample. *Am J Hum Biol*. **25**, 389–398 (2013).

24. H. Shattuck-Heidorn, M. W. Reiches, A. M. Prentice, S. E. Moore, P. T. Ellison, Energetics and the immune system: Trade-offs associated with non-acute levels of CRP in adolescent Gambian girls. *Evol Med Public Health*. **2017**, 27–38 (2017).

25. J. E. Allsworth, S. Zierler, N. Krieger, B. L. Harlow, Ovarian Function in Late Reproductive Years in Relation to Lifetime Experiences of Abuse. *Epidemiology*. **12**, 676–681 (2001).

26. J. E. Allsworth, J. Clarke, J. F. Peipert, M. R. Hebert, A. Cooper, L. A. Boardman, The Influence of Stress on the Menstrual Cycle among Newly Incarcerated Women. *Women's Health Issues*. **17**, 202–209 (2007).

27. S. Palm-Fischbacher, U. Elhert, Dispositional resilience as a moderator of the relationship between chronic stress and irregular menstrual cycle. *Journal of Psychosomatic Obstetrics & Gynecology* (2014), doi:10.3109/0167482X.2014.912209.

28. J. C. Prior, M. Naess, A. Langhammer, S. Forsmo, Ovulation Prevalence in Women with Spontaneous Normal-Length Menstrual Cycles – A Population-Based Cohort from HUNT3, Norway. *PLoS ONE*. **10**, e0134473 (2015).

29. M. J. de Souza, J. Van Heest, L. M. Demers, B. L. Lasley, Luteal Phase Deficiency in Recreational Runners: Evidence for a Hypometabolic State. *The Journal of Clinical Endocrinology & Metabolism*. **88**, 337–346 (2003).

30. V. J. Vitzthum, H. Spielvogel, Epidemiological transitions, reproductive health, and the Flexible Response Model. *Economics & Human Biology*. **1**, 223–242 (2003).

31. P. T. Ellison, in *On fertile ground* (Harvard University Press, Cambridge, MA, 2001).

32. M. Cohut, How does long COVID affect periods? (2021), (available at https://www.medicalnewstoday.com/articles/long-covid-and-periods-the-unspoken-impact-on-female-well-being).

33. A. R. Lamb, EXPERIENCES WITH PROPHYLACTIC TYPHOID VACCINATION: ITS EFFECT ON MENSTRUATION. *Arch Intern Med (Chic)*. **XII**, 565 (1913).

34. T. Shingu, T. UCHIDA, M. NISHI, K. HAYASHIDA, S. KASHIWAGI, J. HAYASHI, M. KAJI, Menstrual Abnormalities after Hepatitis B Vaccine. *The Kurume Medical Journal*. **29**, 123–125 (1982).

35. S. Suzuki, A. Hosono, No association between HPV vaccine and reported post-vaccination symptoms in Japanese young women: Results of the Nagoya study. *Papillomavirus Research*. **5**, 96–103 (2018).

36. F. P. Polack, S. J. Thomas, N. Kitchin, J. Absalon, A. Gurtman, S. Lockhart, J. L. Perez, G. Pérez Marc, E. D. Moreira, C. Zerbini, R. Bailey, K. A. Swanson, S. Roychoudhury, K. Koury, P. Li, W. V. Kalina, D. Cooper, R. W. Frenck, L. L. Hammitt, Ö. Türeci, H. Nell, A. Schaefer, S. Ünal, D. B. Tresnan, S. Mather, P. R. Dormitzer, U. Şahin, K. U. Jansen, W. C. Gruber, Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *N Engl J Med*. **383**, 2603–2615 (2020).

37. L. R. Baden, H. M. El Sahly, B. Essink, K. Kotloff, S. Frey, R. Novak, D. Diemert, S. A. Spector, N. Rouphael, C. B. Creech, J. McGettigan, S. Khetan, N. Segall, J. Solis, A. Brosz, C. Fierro, H. Schwartz, K. Neuzil, L. Corey, P. Gilbert, H. Janes, D. Follmann, M. Marovich, J. Mascola, L. Polakowski, J. Ledgerwood, B. S. Graham, H. Bennett, R. Pajon, C. Knightly, B. Leav, W. Deng, H. Zhou, S. Han, M. Ivarsson, J. Miller, T. Zaks, Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *N Engl J Med*. **384**, 403–416 (2021).

38. L. Chu, R. McPhee, W. Huang, H. Bennett, R. Pajon, B. Nestorova, B. Leav, A preliminary report of a randomized controlled phase 2 trial of the safety and immunogenicity of mRNA-1273 SARS-CoV-2 vaccine. *Vaccine*. **39**, 2791–2799 (2021).

39. E. O. Kharbanda, J. Haapala, M. DeSilva, G. Vazquez-Benitez, K. K. Vesco, A. L. Naleway, H. S. Lipkind, Spontaneous Abortion Following COVID-19 Vaccination During Pregnancy. *JAMA* (2021), doi:10.1001/jama.2021.15494.

40. R. S. Morris, SARS-CoV-2 spike protein seropositivity from vaccination or infection does not cause sterility. *F&S Reports*, S2666334121000684 (2021).

41. R. Orvieto, M. Noach-Hirsh, A. Segev-Zahav, J. Haas, R. Nahum, A. Aizer, Does mRNA SARS-CoV-2 vaccine influence patients' performance during IVF-ET cycle? *Reprod Biol Endocrinol*. **19**, 69 (2021).

42. T. T. Shimabukuro, S. Y. Kim, T. R. Myers, P. L. Moro, T. Oduyebo, L. Panagiotakopoulos, P. L. Marquez, C. K. Olson, R. Liu, K. T. Chang, S. R. Ellington, V. K. Burkel, A. N. Smoots, C. J. Green, C. Licata, B. C. Zhang, M. Alimchandani, A. Mba-Jonas, S. W. Martin, J. M. Gee, D. M. Meaney-Delman, Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons. *N Engl J Med*. **384**, 2273–2282 (2021).

43. L. H. Zauche, B. Wallace, A. N. Smoots, C. K. Olson, T. Oduyebo, S. Y. Kim, E. E. Petersen, J. Ju, J. Beauregard, A. J. Wilcox, C. E. Rose, D. M. Meaney-Delman, S. R. Ellington, Receipt of mRNA Covid-19 Vaccines and Risk of Spontaneous Abortion. *N Engl J Med*, NEJMc2113891 (2021).

44. archaeologistswerebaffled, A COVID and Periods Masterpost. *An Archeology of My Desk* (2021), (available at https://archaeologistswerebaffled.tumblr.com/post/664334182030458880/a-covid-and-periods-masterpost).

45. C. Panter-Brick, A. Fuentes, in *Health, Risk, and Adversity*, C. Panter-Brick, A. Fuentes, Eds. (Berghahn Books, NED-New edition, 1., 2009; http://www.jstor.org.proxy2.library.illinois.edu/stable/j.ctt9qdbxg.7), pp. 1–10.

46. G. Robertson, Screening for endometrial cancer. *Medical Journal of Australia*. **178**, 657–659 (2003).

47. M. A. Clarke, B. J. Long, A. Del Mar Morillo, M. Arbyn, J. N. Bakkum-Gamez, N. Wentzensen, Association of Endometrial Cancer Risk With Postmenopausal Bleeding in Women: A Systematic Review and Meta-analysis. *JAMA Internal Medicine*. **178**, 1210–1222 (2018).

48. N. Wouk, M. Helton, Abnormal Uterine Bleeding in Premenopausal Women. **99**, 10 (2019).

49. O. Y. Çok, H. E. Eker, T. Çok, Ş. Akin, A. Ariboğan, G. Arslan, Abnormal Uterine Bleeding: Is It an Under-Reported Side Effect after Epidural Steroid Injection for the Management of Low Back Pain? *Pain Med*. **12**, 986–986 (2011).

50. E. Suh-Burgmann, Y.-Y. Hung, J. Mura, *American Journal of Obstetrics and Gynecology*, in press, doi:10.1016/j.ajog.2013.06.045.

51. H. Cengiz, H. Dağdeviren, C. Kaya, A. Yeşil, S. S. Çaypınar, Comparing the efficacy of intrauterine lidocaine and paracervical block in decreasing the pain associated with endometrial biopsy: a randomised trial. *Arch Gynecol Obstet*. **289**, 609–614 (2014).

52. C. M. Leclair, J. K. Zia, C. M. Doom, T. K. Morgan, A. B. Edelman, Pain Experienced Using Two Different Methods of Endometrial Biopsy: A Randomized Controlled Trial. *Obstetrics & Gynecology*. **117**, 636–641 (2011).

53. A. J. Lowik, "Just because I don't bleed, doesn't mean I don't go through it": Expanding knowledge on trans and non-binary menstruators. *International Journal of Transgender Health*. **22**, 113–125 (2021).

54. J. C. Chrisler, J. A. Gorman, J. Manion, M. Murgo, A. Barney, A. Adams-Clark, J. R. Newton, M. McGrath, Queer periods: attitudes toward and experiences with menstruation in the masculine of centre and transgender community. *Culture, Health & Sexuality*. **18**, 1238–1250 (2016).

55. M. P. Rogers-LaVanne, K. B. H. Clancy, in *The Routledge Handbook of Anthropology and Reproduction*, S. Han, C. Tomori, Eds. (Routledge, NY, ed. 1st, 2021).

56. American Academy of Pediatrics, Committee on Adolescence, American College of Obstetricians and Gynecologists, Committee on Adolescent Health Care, Menstruation in Girls and Adolescents: Using the Menstrual Cycle as a Vital Sign. *Pediatrics*. **118**, 2245–2250 (2006).

57. Menstrual Cycles as a Fifth Vital Sign. *https://www.nichd.nih.gov/*, (available at https://www.nichd.nih.gov/about/org/od/directors_corner/menstrual-cycles).

58. K. Li, I. Urteaga, C. H. Wiggins, A. Druet, A. Shea, V. J. Vitzthum, N. Elhadad, Characterizing physiological and symptomatic variation in menstrual cycles using self-tracked mobile-health data. *npj Digit. Med.* **3**, 79 (2020).

59. N. I. Mondragon, M. B. Txertudi, Understanding menstruation: Influence of gender and ideological factors. A study of young people's social representations. *Feminism & Psychology*. **29**, 357–373 (2019).

60. B. Fahs, There will be blood: Women's positive and negative experiences with menstruation. *Women's Reproductive Health*. **7**, 1–16 (2020).

61. M. Arora, R. Lakshmi, Maternal vaccines-safety in pregnancy. *Best Pract Res Clin Obstet Gynaecol*, S1521-6934(21)00017–1 (2021).

62. P. Bozzo, A. Narducci, A. Einarson, Vaccination during pregnancy. *Can Fam Physician*. **57**, 555–557 (2011).

63. P. Cohen, S. J. Scadron, The effects of active immunization of the mother upon the offspring. *Journal of Pediatrics*. **29**, 609–619 (1946).

64. F. M. Munoz, J. A. Englund, Vaccines in Pregnancy. *Infectious Disease Clinics of North America*. **15**, 253–271 (2001).

65. O. R. Orta, E. E. Hatch, A. K. Regan, R. Perkins, A. K. Wesselink, S. K. Willis, E. M. Mikkelsen, K. J. Rothman, L. A. Wise, A prospective study of influenza vaccination and time to pregnancy. *Vaccine*. **38**, 4246–4251 (2020).

66. N. B. Schmuhl, K. E. Mooney, X. Zhang, L. G. Cooney, J. H. Conway, N. K. LoConte, No association between HPV vaccination and infertility in U.S. females 18–33 years old. *Vaccine*. **38**, 4038–4043 (2020).

67. D. Little, Quadrivalent Human Papillomavirus Vaccine and the Young Ovary: Review of Safety Research Following Two Case Series of Premature Ovarian Insufficiency. *Journal of Immunology and Infectious Diseases* (2017), doi:10.15744/2394-6512.4.101.

68. L. Gong, H. Ji, X. Tang, L. Pan, X. Chen, Y. Jia, Human papillomavirus vaccine-associated premature ovarian insufficiency and related adverse events: data mining of Vaccine Adverse Event Reporting System. *Sci Rep*. **10**, 10762 (2020).

69. V. Male, Menstrual changes after covid-19 vaccination. *BMJ*, n2211 (2021).

70. M. K. Spooner, Y. Y. Lenis, R. Watson, D. Jaimes, A. L. Patterson, The role of stem cells in uterine involution. *Reproduction*. **161**, R61–R77 (2021).

71. N. N.Rosenthal, J. J. Freyd, Sexual Violence on Campus: No Evidence that Studies Are Biased Due to Self-Selection. *Dignity: A Journal of Analysis of Exploitation and Violence*. **3** (2018), doi:10.23860/dignity.2018.03.01.07.

72. L. M. Greco, E. H. O'Boyle, S. L. Walter, Absence of malice: A meta-analysis of nonresponse bias in counterproductive work behavior research. *Journal of Applied Psychology*. **100 (1)**, 75–97 (2015).

73. A. Kolbe, "Disparities in COVID-19 Vaccination Rates across Racial and Ethnic Minority Groups in the United States" (Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services, Washington, D.C., 2021), pp. 1522–1527.

74. B. Auxier, M. Anderson, Social Media Use in 2021. *Pew Research Center: Internet, Science & Tech* (2021), (available at https://www.pewresearch.org/internet/2021/04/07/social-media-use-in-2021/).

75. *Agnotology: The Making and Unmaking of Ignorance* (Stanford University Press, Stanford, 2008; http://www.sup.org/books/title/?id=11232).

76. A. L. Tsing, in *The Mushroom at the End of the World: On the Possibility of Life in Capitalist Ruins* (Princeton University Press, 2015; https://doi.org/10.2307/j.ctvc77bcc.6.), pp. 17–25.

77. A. Shotwell, in *Against Purity: Living Ethically in Compromised Times* (2021; http://www.jstor.org/stable/10.5749/j.ctt1hch845.6), p. 33.

78. J. C. A. Shaw, The Medicalization of Birth and Midwifery as Resistance. *Health Care for Women International*. **34**, 522–536 (2013).

79. S. Verbiest, C. K. Malin, M. Drummonds, M. Kotelchuck, Catalyzing a Reproductive Health and Social Justice Movement. *Matern Child Health*, 741–749 (2016).

80. S. Vedam, K. Stoll, D. N. McRae, M. Korchinski, R. Velasquez, J. Wang, S. Patridge, L. McRae, R. E. Martin, G. Jolicoeur, CCinBC Steering Committee, Patient-led decision making: Measuring autonomy and respect in Canadian maternity care. *Patient Education and Counseling*. **102**, 586–594 (2019).

81. P. M. Niles, K. Stoll, J. J. Wang, S. Black, S. Vedam, "I fought my entire way": Experiences of declining maternity care services in British Columbia. *PLOS ONE* (2021), doi:https://doi.org/10.1371/journal.pone.0252645.

82. P. A. Harris, R. Taylor, R. Thielke, J. Payne, N. Gonzalez, J. G. Conde, Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of Biomedical Informatics*. **42**, 377–381 (2009).

83. P. A. Harris, R. Taylor, B. L. Minor, V. Elliott, M. Fernandez, L. O'Neal, L. McLeod, G. Delacqua, F. Delacqua, J. Kirby, S. N. Duda, The REDCap consortium: Building an international community of software platform partners. *Journal of Biomedical Informatics*. **95**, 103208 (2019).

84. Dr. Kate Clancy 🏳️‍🌈, Our survey was approved and made it through production! VACCINATED MENSTRUATORS ASSEMBLE: https://is.gd/pd_vax (This is a project to explore whether the covid vaxes affect the periods - if you have menstruated before and got the vax, take 15 min to tell us your experiences!). *@KateClancy* (2021), (available at https://twitter.com/KateClancy/status/1379847815636135941).

85. Dr. Katie Lee, PhD, Have you gotten the vaccine for COVID-19? Do you now/have you ever menstruated? Our research team wants to know about your menstrual experiences after vaccination! Link to informed consent and survey here: https://is.gd/pd_vax. *@ResourcefulSqrl* (2021), (available at https://twitter.com/ResourcefulSqrl/status/1379855580484014083).

86. J. Cohen, *Statistical Power Analysis for the Behavioral Sciences* (Routledge, NY, ed. 2nd, 1988).

87. R Core Team, "R: A language and environment for statistical computing" (manual, Vienna, Austria, 2019), (available at https://www.R-project.org/).

88. A. et mult. al. Signorell, "DescTools: Tools for descriptive statistics" (manual, 2021), (available at https://cran.r-project.org/package=DescTools).

89. S. Mangiafico, "rcompanion: Functions to support extension education program evaluation" (manual, 2021), (available at https://CRAN.R-project.org/package=rcompanion).

90. J. Barnier, F. Briatte, J. Larmarange, "questionr: Functions to make surveys processing easier" (manual, 2020), (available at https://CRAN.R-project.org/package=questionr).

91. H. Wickham, *Ggplot2: elegant graphics for data analysis* (Springer-Verlag New York, 2016; https://ggplot2.tidyverse.org).

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Figures and Tables

Fig. 1. Flowchart of data cleaning and aggregation. Note that totals in the yellow boxes do not add up to the numbers in the grey boxes due to uncertain menopause stage (n=1,522), currently or recently lactating (n=2,498), having had a hysterectomy (n=43), discrepant responses (e.g., self-reported period details did not align with self-reported menstrual group), and the divisions made to the samples. Further details can be found in Supplemental Materials.

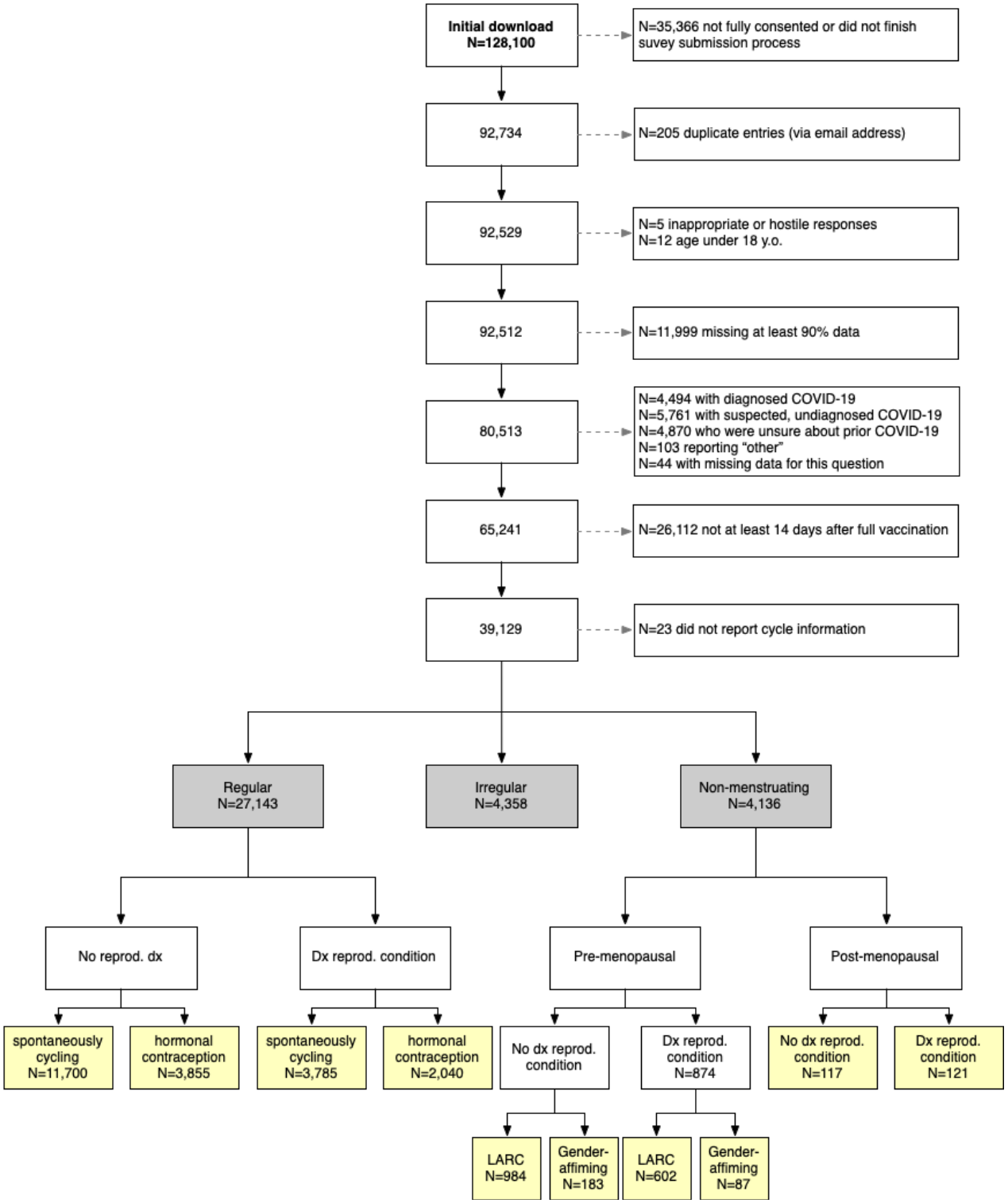

Fig. 2. Menstrual flow changes in regularly cycling individuals. Displayed on the x-axis are the percentage of individuals reporting each flow change condition (y-axis). In the left column are the hormonally contracepting subgroups (HC) and in the right, the spontaneous cycling subgroups (Sp). Only the specific diagnoses with large sample sizes are shown.

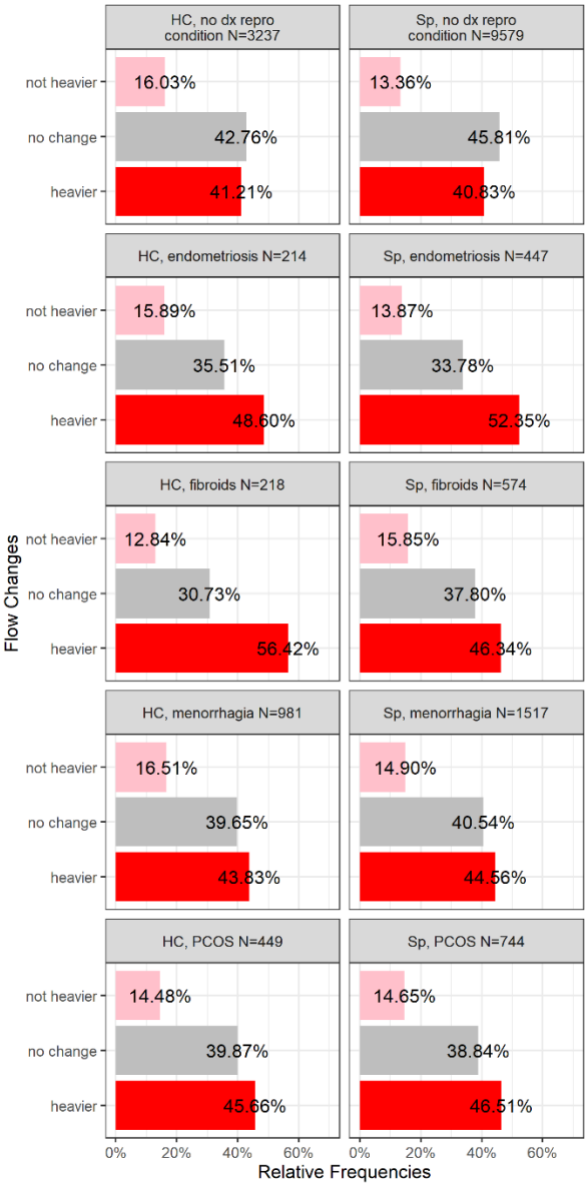

Fig. 3. Breakthrough bleeding in non-menstruating individuals. Displayed on the x-axis are the percentage of individuals reporting breakthrough bleeding (y-axis) after both doses, only following dose 2, only following dose 1, or no breakthrough bleeding during vaccination time.

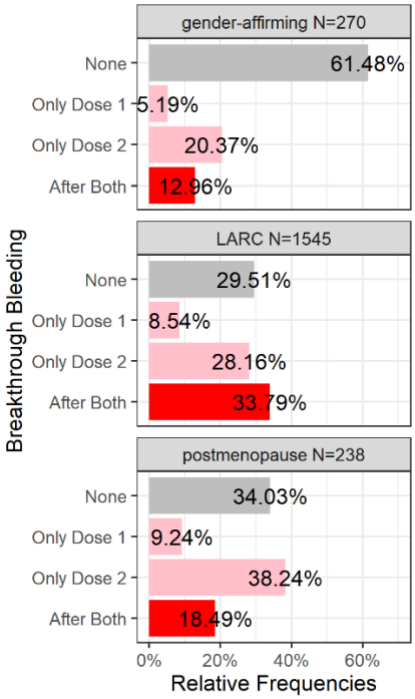

Fig 4. Summary of key results

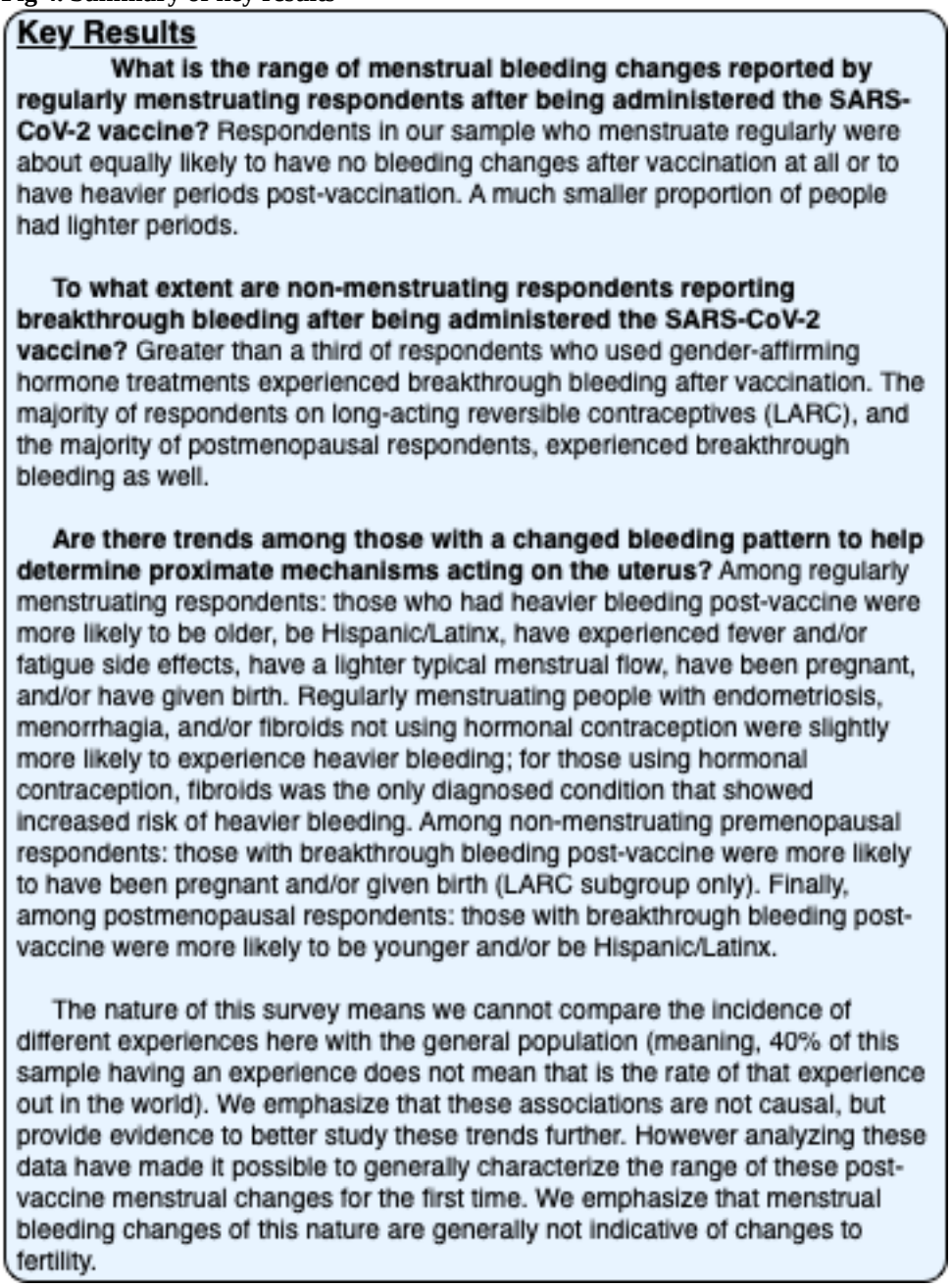

Table 1. Sample summary information. Demographics and sample background in life stages corresponding to later sample subgroups (pre-menopausal 18-45, menopause transition or perimenopause 46-54, post-menopause 55+).

	Total (N=39,129)		18-24 (N=6,332)		25-34 (N=14,797)		35-45 (N=13,096)		46-54 (N=4,304)		55+ (N=600)	
Age	34.22 (9.18)		21.69 (1.85)		29.63 (2.84)		39.43 (3.10)		49.10 (2.38)		59.34 (4.94)	
Vaccine*												
Pfizer	21,620	55.3%	3,646	57.6%	8,246	55.7%	7,135	54.5%	2,287	53.1%	306	51.0%
Moderna	13,001	33.2%	1,916	30.3%	4,898	33.1%	4,521	34.5%	1,448	33.6%	218	36.3%
Johnson& Johnson	3,469	8.9%	634	10.0%	1,260	8.5%	1,126	8.6%	406	9.4%	43	7.2%
Other	1,016	2.6%	133	2.1%	388	2.6%	304	2.3%	159	3.7%	32	5.3%
Gender												
Identifies woman-only	35,572	90.9%	4,535	71.6%	13,449	90.9%	12,751	97.4%	4,245	98.6%	592	98.7%
Gender diverse	3,557	9.1%	1,797	28.4%	1,348	9.1%	345	2.6%	59	1.4%	<10	-
Race												
Identifies white-only	32,983	84.3%	4,978	78.6%	12,336	83.4%	11,393	87.0%	3,743	87.0%	533	88.8%
Racially diverse	6,146	15.7%	1,354	21.4%	2,461	16.6%	1,703	13.0%	561	13.0%	67	11.2%
Ethnicity												
Non-Hispanic/Latinx	31,134	79.6%	4,896	77.3%	11,791	79.7%	10,597	80.9%	3,409	79.2%	441	73.5%
Hispanic/Latinx or other	7,995	20.4%	1,436	22.7%	3,006	20.3%	2,499	19.1%	895	20.8%	159	26.5%
IUDs												
hormonal	3,746	9.6%	547	8.6%	1,744	11.8%	1,158	8.8%	280	6.5%	17	2.8%
copper/non-hormonal	1,532	3.9%	156	2.5%	722	4.9%	537	4.1%	112	2.6%	<10	-
Hormonal Treatments												
Hormonal Contraceptive	7,438	19.0%	1,980	31.3%	3,588	24.2%	1,583	12.1%	277	6.4%	10	1.7%
Other Hormonal Treatments	2,980	7.6%	377	6.0%	867	5.9%	1,082	8.3%	518	12.0%	136	22.7%
Cycle Regularity												
Regular	28,811	73.6%	4,418	69.8%	11,513	77.8%	11,167	85.3%	2,662	61.8%	51	8.5%
Irregular	4,768	12.2%	1,206	19.0%	1,903	12.9%	989	7.6%	632	14.7%	38	6.3%
Non-menstruating	4,525	11.6%	707	11.2%	1,377	9.3%	931	7.1%	1,003	23.3%	507	84.5%
Usual Period Flow†												
light	6,030	15.4%	870	13.7%	2,561	17.3%	1,938	14.8%	632	14.7%	-	-
moderate	22,230	56.8%	3,738	59.0%	8,672	58.6%	7,689	58.7%	2,050	47.6%	-	-
heavy	6,880	17.6%	1,092	17.2%	2,336	15.8%	2,615	20.0%	803	18.7%	-	-
non-menstrual	3,727	9.5%	579	9.1%	1,138	7.7%	795	6.1%	778	18.1%	-	-
other	235	0.6%	51	0.8%	83	0.6%	56	0.4%	33	0.8%	-	-
Usual Period Length‡												
1-3 days	4,804	12.3%	562	8.9%	1,936	13.1%	1,725	13.2%	562	13.1%	-	-
3-5 days	17,454	44.6%	2,736	43.2%	6,864	46.4%	6,144	46.9%	1,648	38.3%	-	-
5-7 days	11,482	29.3%	2,094	33.1%	4,288	29.0%	3,926	30.0%	1,123	26.1%	-	-
7+ days	1,491	3.8%	315	5.0%	512	3.5%	471	3.6%	183	4.3%	-	-
non-menstrual	3,730	9.5%	589	9.3%	1,142	7.7%	787	6.0%	768	17.8%	-	-
other	127	0.3%	31	0.5%	42	0.3%	29	0.2%	15	0.3%	-	-
Medical history												
Past pregnancy	16,859	43.1%	167	2.6%	3,980	26.9%	8,841	67.5%	3,403	79.1%	468	78.0%
Parity	14,579	37.3%	66	1.0%	3,049	20.6%	7,939	60.6%	3,099	72.0%	426	71.0%
Reproductive conditions												
Menorrhagia or heavy bleeding	6,864	17.5%	876	13.8%	2,123	14.3%	2,529	19.3%	1,119	26.0%	217	36.2%
Endometriosis	1,735	4.4%	142	2.2%	536	3.6%	749	5.7%	266	6.2%	42	7.0%
PCOS	3,238	8.3%	391	6.2%	1,325	9.0%	1,194	9.1%	293	6.8%	35	5.8%
Fibroids	2,449	6.3%	6,300	99.5%	14,458	97.7%	11,945	91.2%	3,530	82.0%	447	74.5%
Adenomyosis	277	0.7%	11	0.2%	57	0.4%	136	1.0%	64	1.5%	<10	-
other	2,612	6.7%	351	5.5%	956	6.5%	963	7.4%	292	6.8%	50	8.3%

Note: <10 was used for any cells with fewer than 10 individuals.

* = 23 missing two-dose vaccine type. † = 27 missing usual flow report. ‡ = 41 missing usual length report. Usual period flow/length was blank for 55 and up ages because some selected options other than non-menstrual to describe what was true of them when they menstruated.

Ages are binned based on approximate life stages and the later subgroup analysis.

Other vaccines includes Novavax, AstraZeneca, and self-reported other. These percentages do not add up to 100% because while all responded appropriately to whether they had two doses, some did not report the vaccine-type.

Table 2. Self-reported side effects. Vaccine side effects and menstrual changes reported after each vaccine dose in age groups corresponding to life stage and sample subgroups.

	Full sample		18-24		25-34		35-45		46-54		55+	
Dose 1	N=39,129		N=6,332		N=14,797		N=13,096		N=4,304		N=600	
Vaccine side effectss												
any side effects	34,397	87.9%	5,548	87.6%	13,253	89.6%	11,498	87.8%	3,613	83.9%	485	80.8%
arm-soreness	34,291	87.6%	5,636	89.0%	13,354	90.2%	11,333	86.5%	3,517	81.7%	451	75.2%
fatigue	18,468	47.2%	3,172	50.1%	7,152	48.3%	6,085	46.5%	1,813	42.1%	246	41.0%
headache	10,745	27.5%	1,980	31.3%	4,177	28.2%	3,443	26.3%	1,021	23.7%	124	20.7%
fever	4,211	10.8%	839	13.3%	1,755	11.9%	1,230	9.4%	339	7.9%	48	8.0%
nausea	3,557	9.1%	759	12.0%	1,410	9.5%	1,071	8.2%	282	6.6%	35	5.8%
other	3,828	9.8%	402	6.3%	1,270	8.6%	1,517	11.6%	550	12.8%	89	14.8%
Period changes & symptoms												
*Period flow**												
lighter	3,103	7.9%	470	7.4%	1,233	8.3%	1,112	8.5%	284	6.6%	-	-
no change	18,667	47.7%	2,842	44.9%	7,382	49.9%	6,968	53.2%	1,451	33.7%	-	-
heavier	6,087	15.6%	782	12.3%	2,173	14.7%	2,459	18.8%	662	15.4%	-	-
*Period length**						0.0%		0.0%		0.0%		
shorter	2,998	7.7%	406	6.4%	1,141	7.7%	1,169	8.9%	279	6.5%	-	-
no change	19,630	50.2%	3,045	48.1%	7,759	52.4%	7,292	55.7%	1,512	35.1%	-	-
longer	5,166	13.2%	638	10.1%	1,866	12.6%	2,048	15.6%	602	14.0%	-	-
Symptoms						0.0%		0.0%		0.0%		
had a period	29,867	76.3%	4,729	74.7%	11,483	77.6%	10,688	81.6%	2,823	65.6%	144	24.0%
spotting	10,109	25.8%	1,733	27.4%	4,018	27.2%	3,289	25.1%	957	22.2%	112	18.7%
other menstrual bleeding	4,476	11.4%	661	10.4%	1,636	11.1%	1,561	11.9%	551	12.8%	67	11.2%
no period symptoms	5,086	13.0%	908	14.3%	1,827	12.3%	1,269	9.7%	806	18.7%	276	46.0%
Dose 2	N=35,660		N=5,698		N=13,537		N=11,970		N=3,898		N=557	
Vaccine side effects												
any side effects	32,775	91.9%	5,223	91.7%	12,535	92.6%	11,024	92.1%	3,526	90.5%	467	83.8%
arm-soreness	30,298	85.0%	4,962	87.1%	11,660	86.1%	10,134	84.7%	3,135	80.4%	407	73.1%
fatigue	27,149	76.1%	4,331	76.0%	10,551	77.9%	9,123	76.2%	2,802	71.9%	342	61.4%
headache	19,413	54.4%	3,349	58.8%	7,716	57.0%	6,248	52.2%	1,866	47.9%	234	42.0%
fever	13,818	38.7%	2,342	41.1%	5,608	41.4%	4,377	36.6%	1,354	34.7%	137	24.6%
nausea	8,793	24.7%	1,708	30.0%	3,545	26.2%	2,665	22.3%	784	20.1%	91	16.3%
other	8,367	23.5%	840	14.7%	3,063	22.6%	3,251	27.2%	1,084	27.8%	129	23.2%
Period changes & symptoms												
*Period flow**												
lighter	3,167	8.9%	494	8.7%	1,283	9.5%	1,120	9.4%	263	6.7%	-	-
no change	10,811	30.3%	1,696	29.8%	4,475	33.1%	3,905	32.6%	723	18.5%	-	-
heavier	8,454	23.7%	1,110	19.5%	2,954	21.8%	3,449	28.8%	922	23.7%	-	-
*Period length**												
shorter	2,862	8.0%	387	6.8%	1,127	8.3%	1,099	9.2%	242	6.2%	-	-
no change	12,459	34.9%	1,969	34.6%	5,072	37.5%	4,588	38.3%	816	20.9%	-	-
longer	6,743	18.9%	903	15.8%	2,407	17.8%	2,625	21.9%	792	20.3%	-	-
Symptoms												
had a period	25,335	71.0%	4,022	70.6%	9,654	71.3%	8,905	74.4%	2,585	66.3%	169	30.3%
spotting	9,824	27.5%	1,639	28.8%	3,893	28.8%	3,161	26.4%	968	24.8%	163	29.3%
other menstrual bleeding	5,269	14.8%	750	13.2%	1,862	13.8%	1,837	15.3%	721	18.5%	99	17.8%
no period symptoms	4,326	12.1%	789	13.8%	1,699	12.6%	1,238	10.3%	470	12.1%	130	23.3%

Note: * = non-menstruating individuals were not asked these items.
Dose 1 and dose 2 sample sizes differ because the Johnson&Johnson vaccine does not have a second dose, so participants do not report on any dose 2 survey items.
Dose 1 and 2 period flow were used to calculate flow changes in regularly menstruating age groups. Period symptoms (had a period, spotting, and other menstrual bleeding) were used to calculate whether breakthrough occurred in non-menstruating age groups.

939 **Table 3.** Menstrual and medical history variables related to changes in flow across regularly cycling subgroups.

	No dx reproductive conditions *Flow change conditions*				**Dx reproductive conditions** *Flow change conditions*				Chi-square results			Effect size	
Spontaneously menstruating	Heavier	Not heavier	No change	*N*	Heavier	Not heavier	No change	*N*	*df*	χ^2	*p*	φ_c	φc 95% CI
Usual period flow													
heavy	36.8%	19.0%	44.2%	1,556	43.5%	15.5%	41.0%	1,190					
light	46.0%	10.1%	43.9%	938	47.9%	10.7%	41.4%	215	4	61.07	**1.73e^{-12}**	0.057	[0.044, 0.074]
moderate	41.1%	12.6%	46.3%	7,043	47.4%	14.1%	38.5%	1,674	4	6.78	.1479	0.033	[0.019, 0.063]
Vaccine type													
Pfizer	39.6%	13.4%	47.0%	5,814	45.4%	14.1%	40.5%	1,810	2	7.77	.0206	0.029	[0.011, 0.050]
Moderna	42.5%	13.0%	44.5%	3,499	47.0%	14.0%	39.0%	1,175	2	0.82	.6626	0.017	[0.006, 0.056]
Vaccine symptoms													
fever	43.2%	14.7%	42.1%	4,051	48.4%	12.9%	38.7%	1,350	2	40.11	**1.95e^{-09}**	0.065	[0.047, 0.086]
no fever	39.1%	12.4%	48.5%	5,528	44.1%	15.5%	40.4%	1,751	2	7.26	.0265	0.048	[0.019, 0.084]
fatigue	42.0%	13.8%	44.2%	7,877	47.1%	14.5%	38.4%	2,651	2	44.51	**2.16e^{-10}**	0.068	[0.050, 0.089]
no fatigue	35.3%	11.6%	53.1%	1,702	39.3%	13.8%	46.9%	450	2	12.08	.0024	0.062	[0.032,0.101]
Medical history													
parous	46.2%	11.6%	42.2%	2,896	47.0%	14.5%	38.5%	1,274	2	50.20	**1.26e^{-11}**	0.072	[0.051, 0.093]
not parous	38.5%	14.1%	47.4%	6,683	45.2%	14.3%	40.5%	1,827	2	1.23	.5412	0.02	[0.006, 0.059]
PPH	46.4%	11.8%	41.8%	306	45.8%	16.4%	37.8%	177	2	0.03	.9838	0.003	[0.005, 0.054]
no PPH	46.1%	11.6%	42.3%	2,582	47.2%	14.1%	38.7%	1,094	2	0.66	.7183	0.023	[0.006, 0.091]
pregnant	46.7%	11.9%	41.4%	3,478	47.7%	14.6%	37.7%	1,561	2	78.94	**<2.2e^{-16}**	0.091	[0.070, 0.111]
not pregnant	37.5%	14.2%	48.3%	6,096	44.2%	14.2%	41.6%	1,540	2	5.07	.0794	0.04	[0.014, 0.076]
vaginal bleeding during pregnancy	46.6%	12.3%	41.1%	824	45.0%	14.9%	40.1%	531	2	0.23	.8937	0.008	[0.004, 0.048]
no vaginal bleeding during pregnancy	46.8%	11.6%	41.6%	2,634	48.8%	14.5%	36.7%	1,020	2	2.20	.3333	0.038	[0.010, 0.094]
Race													
White-only identifying	40.8%	12.9%	46.3%	7,981	45.3%	14.3%	40.4%	2,576	2	12.56	.0019	0.036	[0.016, 0.058]
Racially diverse	40.9%	15.9%	43.2%	1,598	48.9%	14.9%	36.2%	525	2	3.26	.1960	0.032	[0.010, 0.071]
Ethnicity													
Non-Hispanic/ Latinx	40.0%	12.7%	47.3%	7,483	45.5%	14.1%	40.4%	2,454	2	34.82	**2.75e^{-8}**	0.06	[0.042, 0.081]
Hispanic/Latinx or other	43.6%	15.9%	40.5%	2,096	47.6%	15.3%	37.1%	647	2	2.33	.3124	0.027	[0.007, 0.069]
N	3911	1280	4388		1425	446	1230						
Menstruating on HC	Heavier	Not heavier	No change	*N*	Heavier	Not heavier	No change	*N*	*df*	χ^2	*p*	φ_c	φc 95% CI
Usual period flow													
heavy	39.4%	16.0%	44.6%	231	44.3%	16.9%	38.8%	343					
light	45.3%	12.6%	42.1%	1,075	47.3%	13.9%	38.8%	474	4	19.56	**.0006**	0.055	[0.037, 0.083]
moderate	39.1%	18.0%	42.9%	1,916	42.3%	17.8%	39.9%	901	4	4.69	.3203	0.037	[0.021, 0.078]
Vaccine type													
Pfizer	40.5%	16.7%	42.8%	1,917	43.0%	16.4%	40.6%	1,029	2	2.10	.3496	0.026	[0.007, 0.064]
Moderna	42.5%	15.0%	42.5%	1,251	45.8%	16.8%	37.4%	668	2	1.83	.4007	0.033	[0.009, 0.088]
Vaccine symptoms													
fever	44.1%	16.4%	39.5%	1,362	46.8%	17.8%	35.4%	765	2	10.85	.0044	0.058	[0.031, 0.094]
no fever	39.1%	15.8%	45.1%	1,875	41.8%	15.4%	42.8%	960	2	9.76	.0076	0.075	[0.030, 0.128]
fatigue	42.6%	15.6%	41.8%	2,722	45.8%	16.6%	37.6%	1,486	2	13.32	.0013	0.064	[0.032, 0.099]
no fatigue	34.0%	18.4%	47.6%	515	33.0%	15.5%	51.5%	239	2	17.70	**.0001**	0.101	[0.056, 0.150]
Medical history													
parous	46.2%	15.9%	37.9%	649	49.4%	15.7%	34.9%	421	2	9.43	.0089	0.054	[0.022, 0.091]
not parous	39.9%	16.1%	44.0%	2,588	42.3%	16.7%	41.0%	1,304	2	6.92	.0315	0.063	[0.025, 0.111]
PPH	42.8%	15.9%	41.3%	63	38.5%	20.5%	41.0%	39	2	0.36	.8335	0.024	[0.010, 0.113]
no PPH	46.5%	15.9%	37.6%	585	50.4%	15.3%	34.3%	379	2	2.09	.3521	0.071	[0.016, 0.180]
pregnancy	47.2%	15.7%	37.1%	817	50.5%	15.8%	33.7%	505	2	17.96	**.0001**	0.075	[0.042, 0.109]
no pregnancy	39.2%	16.1%	44.7%	2,417	41.4%	16.7%	41.9%	1,219	2	13.13	.0014	0.087	[0.048, 0.138]
VB in pregnancy	45.4%	16.1%	38.5%	218	48.3%	17.6%	34.1%	176	2	0.44	.8037	0.023	[0.008, 0.107]
no VB in pregnancy	48.0%	15.5%	36.5%	598	51.7%	14.9%	33.4%	329	2	0.81	.6673	0.040	[0.013, 0.142]
Race													
White-only identifying	40.7%	15.6%	43.7%	2,787	42.9%	16.3%	40.8%	1,462	2	7.12	.0285	0.047	[0.019, 0.084]
Racially diverse	44.4%	18.5%	37.1%	450	50.2%	17.1%	32.7%	263	2	6.45	.0398	0.061	[0.022, 0.110]
Ethnicity													
Non-Hispanic/ Latinx	40.5%	15.3%	44.2%	2,658	43.6%	15.9%	40.5%	1,443	2	13.48	.0012	0.065	[0.034, 0.101]
Hispanic/Latinx or other	44.4%	19.3%	36.3%	579	45.7%	19.5%	34.8%	282	2	4.08	.1302	0.049	[0.015, 0.100]
N	1,334	519	1,384		759	284	682						

940 Note: These proportions are calculated without inclusion of missing or omitted categories in the total sample size in
941 each flow change condition displayed at the bottom (displayed percentages should equal 100%). Independent
942 variables are displayed in the rows, and the dependent variable is displayed in the columns. The column N reported is
943 the total N per level of the independent variable used in analysis. The chi-square results refer to the left hand-side (no
944 diagnosed condition) on top then directly below the same comparison in the diagnosed conditions subgroups
945 (shaded).
946 HC is hormonal contraception, PPH is post-partum hemorrhage, VB is vaginal bleeding
947

Table 4. Breakthrough bleeding in premenopausal people. Vaccine and medical history related to breakthrough bleeding across pre-menopause non-menstruating subgroups.

	LARC *Breakthrough bleeding*			**Gender-Affirming** *Breakthrough bleeding*			Chi-square results			Effect size	
	Yes	No	*N*	Yes	No	*N*	*df*	χ^2	*p*	φ_c	φc 95% CI
Vaccine type											
Pfizer	70.1%	29.9%	938	39.3%	60.7%	178	1	0.02	.899	0.004	[0.001, 0.063]
Moderna	70.6%	29.4%	568	37.8%	62.2%	90	1	0.01	.910	0.015	[0.002, 0.137]
Vaccine symptoms											
fever	72.9%	27.1%	657	43.1%	56.9%	109	1	3.02	.082	0.046	[0.004, 0.100]
no fever	68.7%	31.3%	888	35.4%	64.6%	161	1	1.32	.250	0.078	[0.004, 0.194]
fatigue	70.3%	29.7%	1,308	-	-	-	1	0.05	.823	0.008	[0.001, 0.059]
no fatigue	71.3%	28.7%	237	-	-	-					
Medical history											
parous	78.5%	21.5%	316	-	-	-	1	11.73	**.0006**	0.089	[0.036, 0.132]
not parous	68.4%	31.6%	1,229	-	-	-					
pregnant	79.6%	20.4%	387	-	-	-	1	20.06	**$7.5e^{-06}$**	0.116	[0.069, 0.163]
not pregnant	67.4%	32.6%	1,157	-	-	-					
Race											
White-only identifying	69.9%	30.1%	1,350	36.0%	64.0%	225	1	1.83	.176	0.037	[0.002, 0.082]
Racially diverse	74.9%	25.1%	195	51.1%	48.9%	45	1	3.01	.083	0.116	[0.009, 0.242]
Ethnicity											
Non-Hispanic/Latinx	69.4%	30.6%	1,297	36.4%	63.6%	220	1	4.33	.037	0.055	[0.008, 0.103]
Hispanic/Latinx or other	76.2%	23.8%	248	48.0%	52.0%	50	1	1.86	.172	0.093	[0.007, 0.220]
N	1,089	456		104	166						

Note: Associations with breakthrough bleeding were investigated on the binary outcome. The *N* at the bottom of the table corresponds to total individuals in each breakthrough condition. The *N* within the column corresponds to the number of individuals in each level of the independent variables that were included in the chi-square tests of independence. Alpha thresholds for LARC were $p<.001$ and for gender-affirming were $p<.05$.

Table 5. Breakthrough bleeding in post-menopausal people. Vaccine and medical history related to breakthrough bleeding across post-menopause subgroup.

	Post-menopause *Breakthrough bleeding*			Chi-square results			Effect size	
	Yes	No	*N*	*df*	χ^2	*p*	φ_c	φc 95% CI
Vaccine type								
Pfizer	66.1%	33.9%	124					
Moderna	60.4%	39.6%	96	1	0.54	.464	0.059	[0.004, 0.198]
Vaccine symptoms								
fever	67.7%	32.3%	62					
no fever	65.3%	34.7%	176	1	0.04	.851	0.022	[0.002, 0.147]
fatigue	67.1%	32.9%	164					
no fatigue	63.5%	36.5%	74	1	0.15	.698	0.035	[0.002, 0.168]
Medical history								
parous	64.9%	35.1%	168					
not parous	68.6%	31.4%	70	1	0.16	.691	0.035	[0.003, 0.160]
pregnant	64.7%	35.3%	187					
not pregnant	70.6%	29.4%	51	1	0.38	.536	0.051	[0.004, 0.174]
Race								
White-only identifying	-	-	-					
Racially diverse	-	-	-					
Ethnicity								
Non-Hispanic/ Latinx	61.8%	38.2%	173					
Hispanic/Latinx or other	76.9%	23.1%	65	1	4.13	**.042**	0.142	[0.021, 0.268]
N	157	81						

Note: Associations with breakthrough bleeding were investigated on the binary outcome. Alpha thresholds for post-menopause were $p<.05$.

Table 6. Associations with diagnosed reproductive conditions. Comparisons between pre-menopausal regular-cycling reproductive condition diagnoses and comparison non-diagnosed subgroup.

		Flow change conditions			Chi-square results				Effect sizes	
	Total N	Heavier	Not heavier	No change	*df*	*N*	χ^2	*p*	Odds Ratio	Odds Ratio 95%CI
Spontaneous	11,700	40.8%	13.4%	45.8%						
Endometriosis	536	52.3%	13.9%	33.8%	2	10,026	27.439	**1.1e^{-06}**	1.59	[1.31, 1.96]
PCOS	908	46.5%	14.7%	38.8%	2	10,323	13.637	.0011	1.26	[1.08, 1.47]
Menorrhagia	1,866	44.6%	14.9%	40.5%	2	11,096	14.749	**.0006**	1.16	[1.04, 1.30]
Fibroids	708	46.3%	15.9%	37.8%	2	10,153	14.137	**.0009**	1.25	[1.05, 1.49]
Hormonally contracepting	3,855	41.2%	16.0%	42.8%						
Endometriosis	251	48.6%	15.9%	35.5%	2	3,451	5.1195	.0773	1.35	[1.01, 1.80]
PCOS	533	45.6%	14.5%	39.9%	2	3,686	3.2462	.1973	1.20	[0.98, 1.47]
Menorrhagia	1,150	43.8%	16.5%	39.7%	2	4,218	3.0687	.2156	1.11	[0.96, 1.29]
Fibroids	262	56.4%	12.9%	30.7%	2	3,455	19.547	**5.7e^{-05}**	1.85	[1.39, 2.46]

Note. The reproductive conditions are compared to the first listing (spontaneous or hormonally contracepting). Diagnoses were not mutually exclusive, so some individuals might be represented in the endometriosis as well as the fibroids group, for example, or have other listed diagnoses with too few respondents to make comparisons. The Odds Ratio is calculated for risk of heavier bleeding in the diagnosed group.