

# COVID-19 and Gynecologic Health

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# Gynecologic Health in the Pandemic

Menstruation

Fertility

Health Inequity

Miscarriage

Sexual health

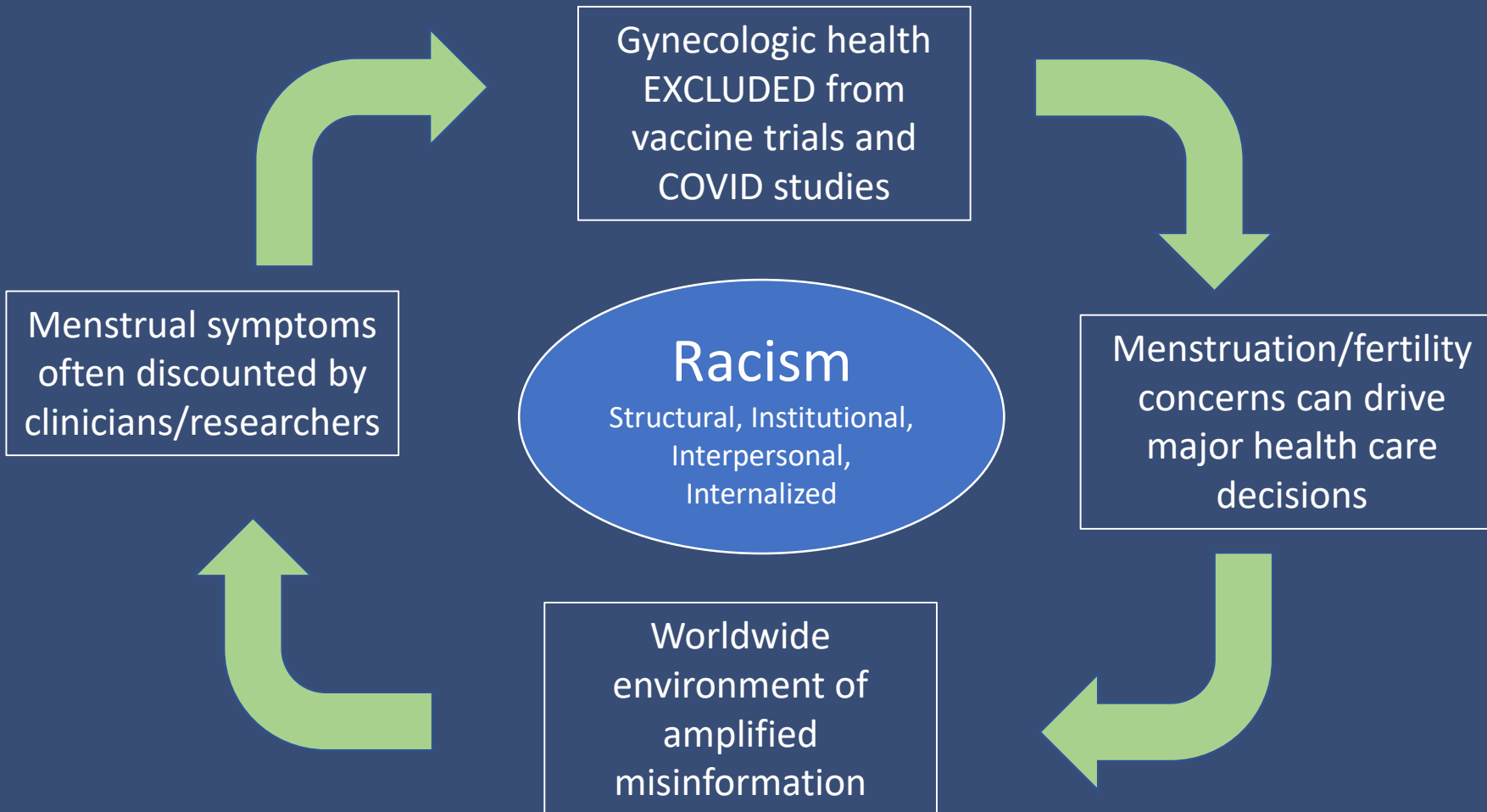
Urinary Symptoms

And many more.....

COVID-19 Infection

COVID-19 Vaccine

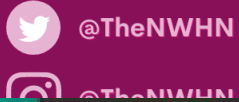
# Gynecologic Health in the Pandemic



SINCE YOU ASKED

## Can the COVID-19 vaccine effect your period?

PSST! THE ANSWER IS: WE'RE NOT SURE YET



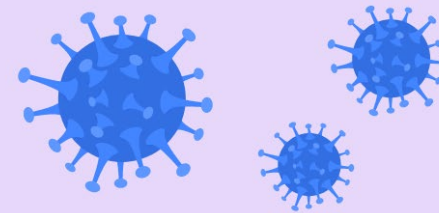
Thousands report  
after COVID-19 va

**FACT:** Being near someone who's received a COVID-19 vaccine can't affect your menstrual cycle.



[cdc.gov/coronavirus](https://cdc.gov/coronavirus)

## Does the COVID-19 vaccine cause infertility?



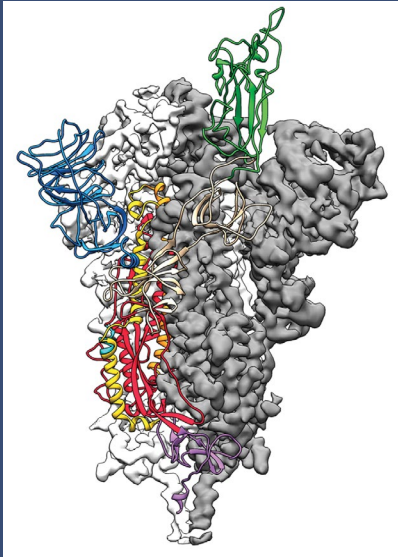
No. There is no evidence that the COVID-19 vaccine (or any vaccine) causes infertility.



## pandemic has affected periods

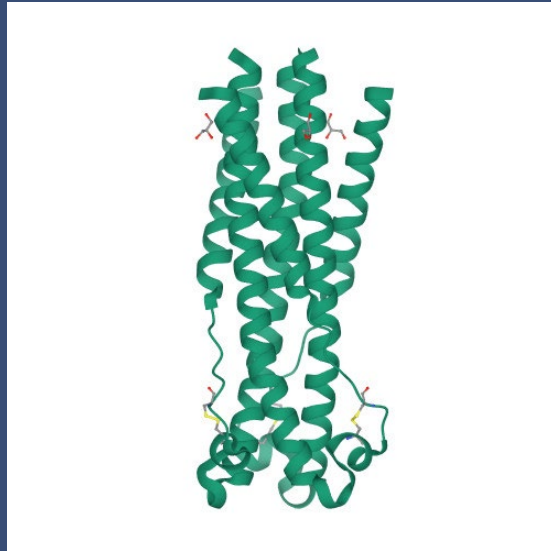
ccines and pandemic stress have all been linked to distributions to on cycles.

# Vaccines and Female Infertility



## Spike Protein

SARS-CoV-2 mRNA vaccines  
create antibodies to Spike



## Syncytin-1

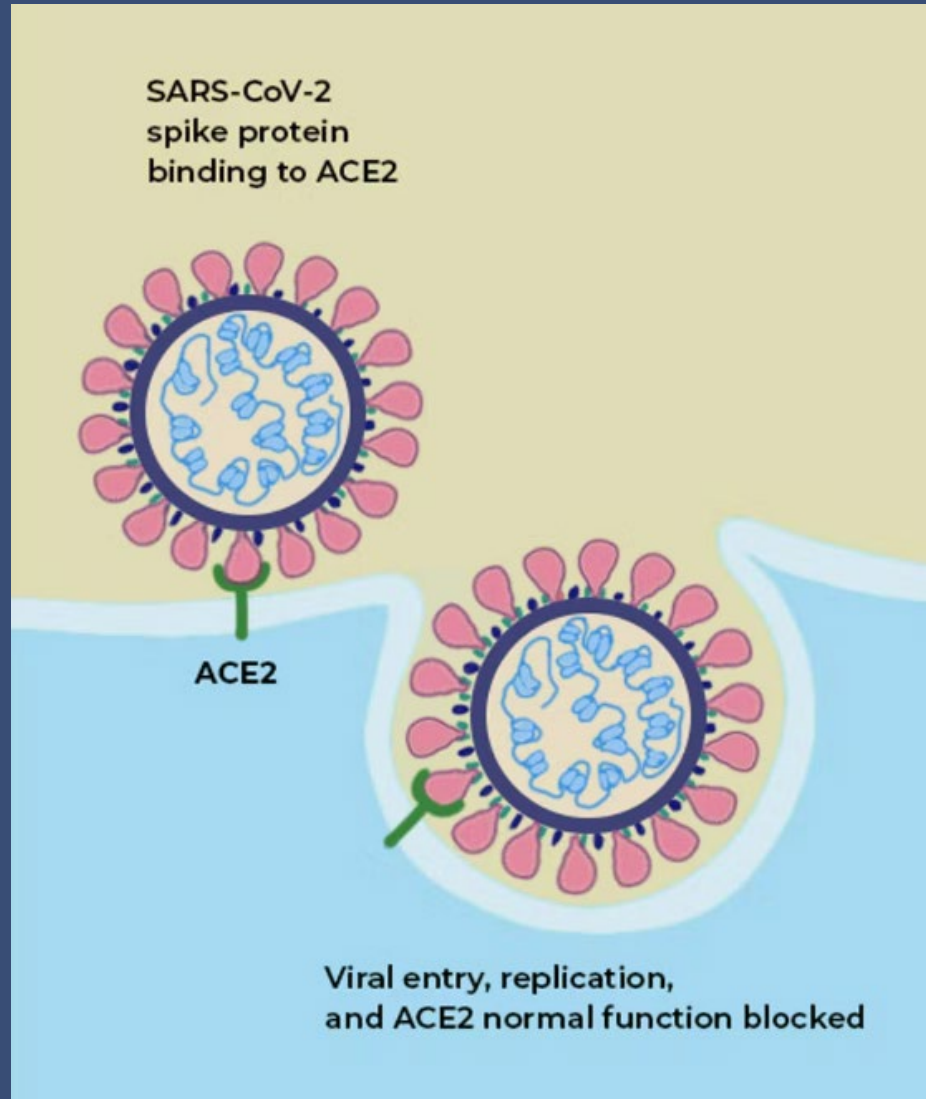
Placenta protein involved  
in pregnancy growth

SARS-CoV-2 Vaccines do not  
contain mRNA for Syncytin-1

Antibodies against Spike do  
not impact Syncytin-1

**Vaccines do not cause female  
infertility**

# SARS-CoV-2 in the Reproductive Tract



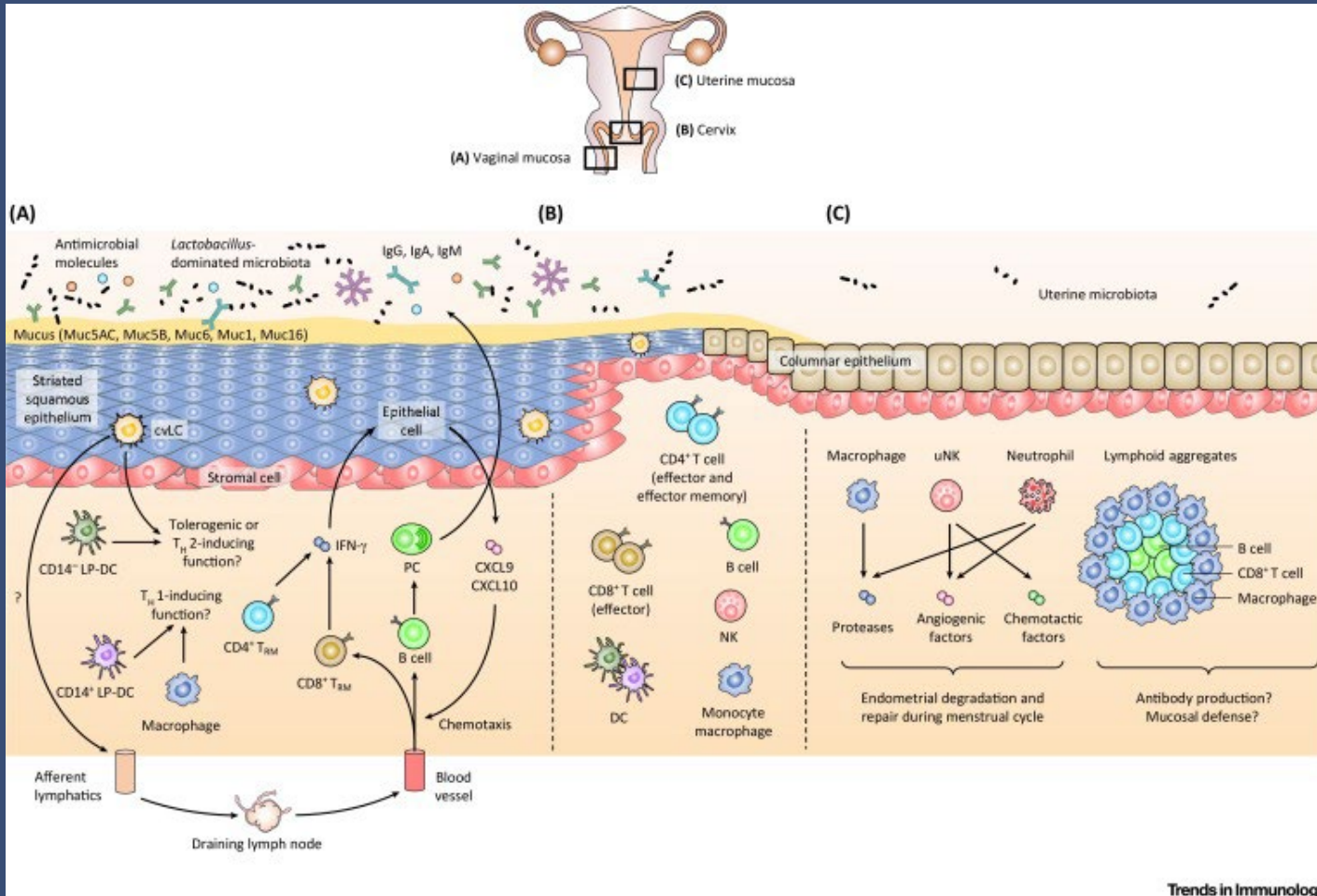
*Very low* gene expression of SARS-CoV-2 receptors ACE-2 and proteases (TMPRSS2) in uterus, ovary, fallopian tubes

**No SARS-CoV-2 found in endocervical or vaginal swabs or endometrial biopsies**

Goad, et al, PLOS One, Dec 2020  
Herarejos-Castillo, et al, Fertility and Sterility, Aug 2020  
Soilen et al, Rev Chilena Infectol, Oct 2021  
Takmaz et al, PLOS, Sept 2021  
Miguel-Gomez, AJOG, March 2022



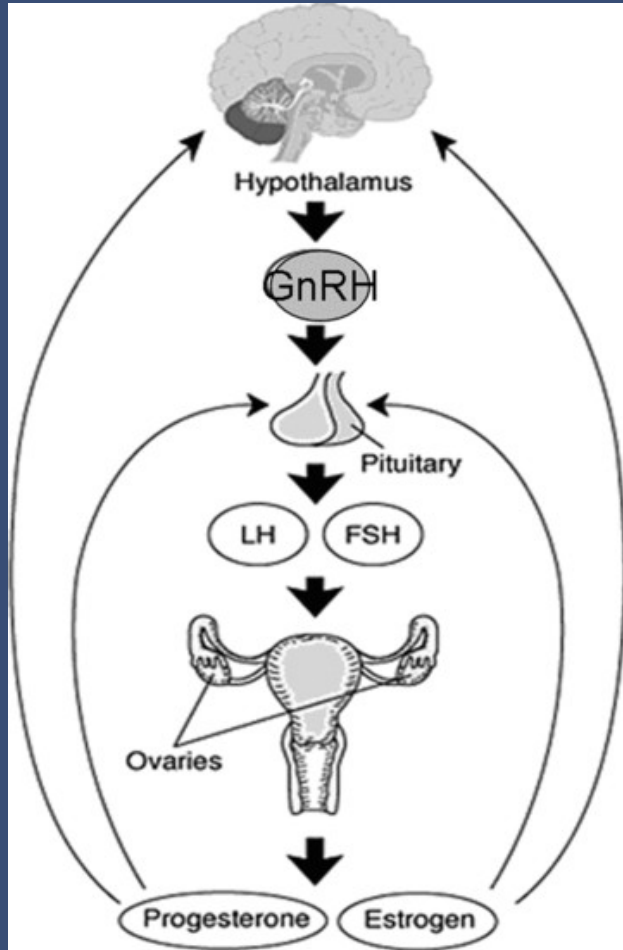
# Immune Activity in Reproductive Tract



Vagina, Cervix, Uterus  
have immune activity

Endometrium produces  
prostaglandins and cytokines  
(eg IL-1, IL-6, TNFα)

# Regular Timed Menstruation



Hypothalamic-Pituitary-Ovarian (HPO) messaging supports regular timed monthly menses but.....

30% of females will have some type of abnormal uterine bleeding by age 50



# What can cause changes to the menstrual cycle?

Weight change

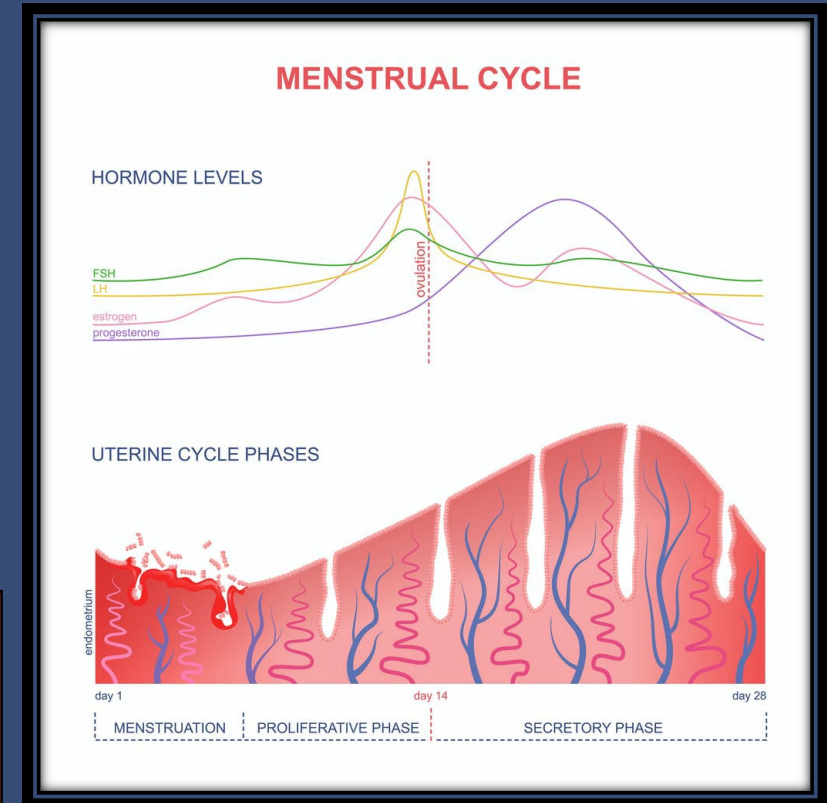
Exercise

Sleep

Depression/Anxiety

Acute and Chronic illness

**Any stress** can increase cortisol and disrupt GnRH secretion



# Menstrual Changes during Pandemic



Several studies with online surveys report increase in menstrual changes during pandemic

## Limitations

Cross-sectional (one point in time)

Bias in who answers surveys

Majority are white

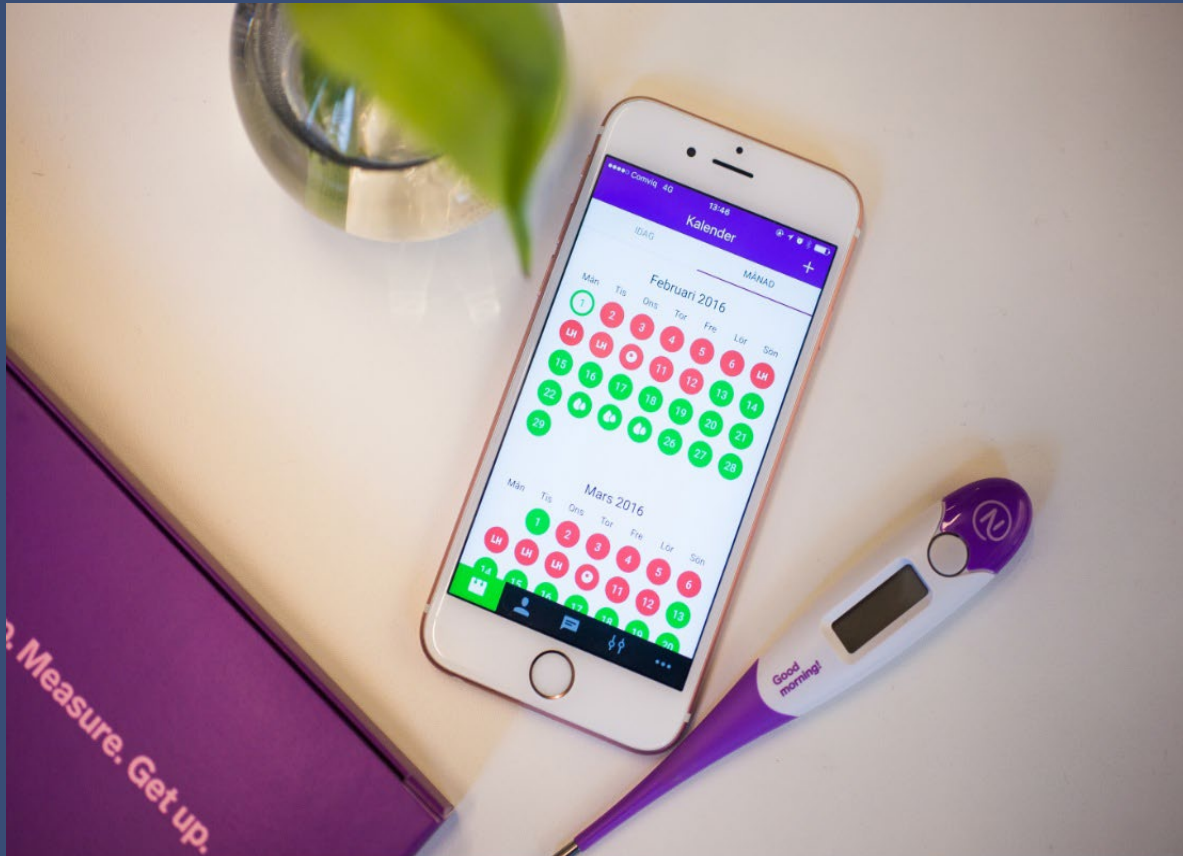
Demir, et al, Triangle of COVID, anxiety, menstrual cycle, Jo of Ob and Gyn, 2021

Phelan et al, Impact of COVID-19 Pandemic on Women's Reproductive Health, Front Endocrin, March 2021

Preethi et al, Pandemic induced stress and obesity leading to abnormal uterine bleeding, Health Science Reports, Feb 2022

Images from United Nations Population Fund

# Menstrual Changes during Pandemic



- 18,000 menstrual app users
- Mean age 33 years, 80%  $\geq$  college
- 29% Great Britain, 23% USA
- 2019 PRE-pandemic vs March-Sept 2020

# Menstrual Changes during Pandemic

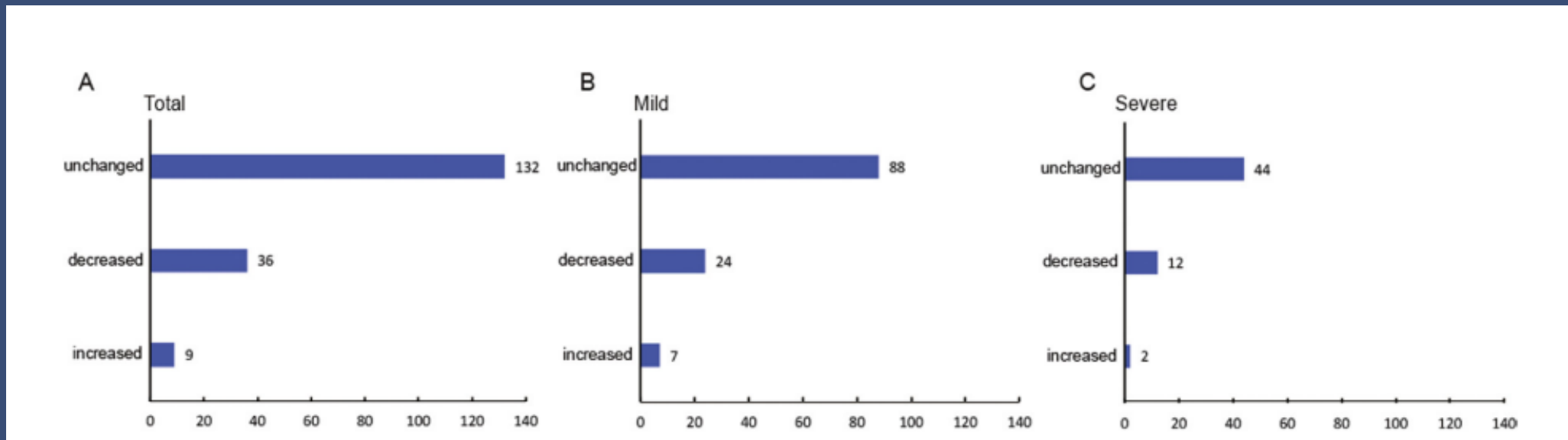
	Pre-COVID:	During COVID:
	Mar-Sep 2019	Mar-Sep 2020
	(n = 108,021 cycles)	(n = 106,405 cycles)
	Mean (95%CI)	Mean (95%CI)
Cycle length	29.40 (29.34–29.46)	29.16 (29.10–29.22)
Menstrual duration	4.21 (4.19–4.23)	4.32 (4.30–4.34)

- No clinically significant differences in menstruation during pandemic
- High pandemic stress not associated with abnormal cycle
- Fewer anovulatory cycles DURING pandemic

# Menses and COVID-19 Infection

# Menses Volume change with COVID-19

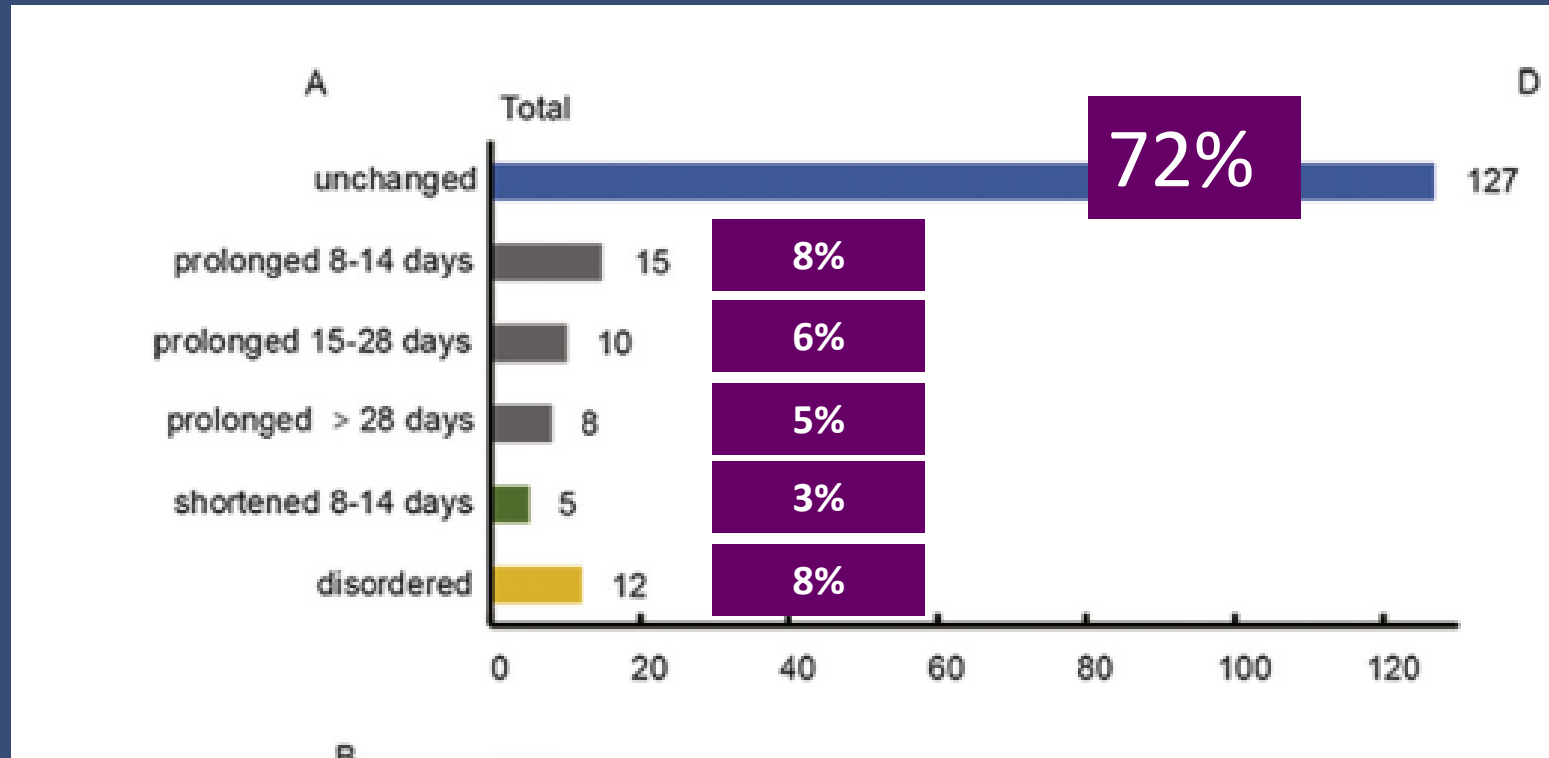
- N=177, hospitalized in China with COVID
- 75% unchanged, 20% decreased, 5% increased
- No difference by disease severity





# Cycle length change after COVID-19

- 28% with menstrual cycle changes
- 99% returned to normal within 2 months
- More cycle changes than controls without COVID



# Menstrual Changes *after* COVID

- N=158 in Indonesia, hospitalized with COVID
- Menses before infection by reported history and 3 months after

Menstrual parameter	Before COVID-19 Infection (n = 158)	After COVID-19 Infection (n = 158)	p value
Mean cycle length (n [%]) <ul style="list-style-type: none"><li>• &lt; 24 days</li><li>• 24–32 days</li><li>• &gt; 32 days</li></ul>	17 (10.8%) 125 (79.1%) 16 (10.1%)	24 (15.2%) 103 (75.1%) 31 (19.6%)	0.001*
Menstrual irregularity (n [%])	28 (17.7%)	56 (35.4%)	< 0.001*
Heavy menstrual bleeding (n [%])	43 (27.2%)	53 (33.5%)	0.041*

Persistent abnormalities in cycle length 3 months after COVID

Worse mental health associated with menstrual changes

# Menstrual Changes *after* COVID

- N=127 in Arizona (CoVHORT study)
- 16% reported change in menses after COVID (cycle length, duration, flow)
- More COVID symptoms=more likely to have abnormal menses

Characteristics	COVID-19 positive participants	
	SARS-CoV-2-positive participants who reported a change in their menstrual cycle after infection <sup>a,b</sup> (n = 20; 15.7%)	SARS-CoV-2-positive participants who did not report a change in their menstrual cycle after infection <sup>a,c</sup> (n = 107; 84.3%)
Increase in premenstrual syndrome symptoms (ie, greater than usual mood swings, feelings of anxiety or depression, tiredness, trouble sleeping, bloating or stomach pain, breast tenderness, changes in appetite or sex drive)	9 (45.0)	—
Most common COVID-19 symptoms, n (%)		
Fatigue	15 (79.0)	29 (27.1)
Headache	11 (57.9)	21 (19.6)
Body aches and pains	10 (52.6)	17 (15.9)
Shortness of breath	10 (52.6)	17 (15.9)

# Menses and COVID-19 Infection

There may be transient changes to menses but..

Data is very limited: More research needed!

Small sample sizes

Often hospitalized patients

Short-term or no follow-up

Recall bias vs. Prospective follow-up

# Menstrual Changes *after* Vaccination

- Survey studies have reported changes in cycle length, duration, volume
- July 15, 2022: Online survey of 39, 129 vaccinated people, 18-80 years

**56% : Change in menstrual flow**  
**42%: Heavier bleeding**  
**No difference by use of hormonal contraception**

**High rates of breakthrough bleeding in people who do not menstruate**  
**Gender-affirming hormones (39%), LARC (71%), postmenopausal (66%)**

**LIMITATIONS:** Sample of app users,  
84% white, no pre-vaccine data,  
no comparison group of unvaccinated

# Menstrual Changes *after* Vaccination

- 3,959 people with menstrual cycles tracked on app “Natural Cycles”
- Age 18-45 years, US residents, vaccinated *vs* unvaccinated
- Prospectively collected data, 3 months prior vs 3 months after vaccine

		Cycle Length		Menses Length	
	n	Change in Length (d)	Adjusted Difference in Change vs Unvaccinated Individuals (d)*	Change in Length (d)	Adjusted Difference in Change vs Unvaccinated Individuals (d)*
1st dose					
Unvaccinated	1,556	0.07 (−0.22 to 0.35)	—	−0.09 (−0.18 to 0.00)	—
Vaccinated	2,403	0.71 (0.47–0.94)	0.64 (0.27–1.01)	−0.01 (−0.09 to 0.06)	0.08 (−0.04 to 0.19)
2nd dose					
Unvaccinated	1,556	0.12 (−0.15 to 0.39)	—	−0.09 (−0.18 to −0.01)	—
Vaccinated	1,919	0.91 (0.63–1.19)	0.79 (0.40–1.18)	−0.01 (−0.09 to 0.07)	0.08 (−0.04 to 0.20)

Data are mean (98.75% CI) unless otherwise specified.  
 \* Differences are from mixed-effects models with random intercepts and random slopes at the individual level, an interaction between vaccination status and prevaccination–postvaccination timing, and adjusted for age, race, body mass index, educational attainment, parity, and relationship status.

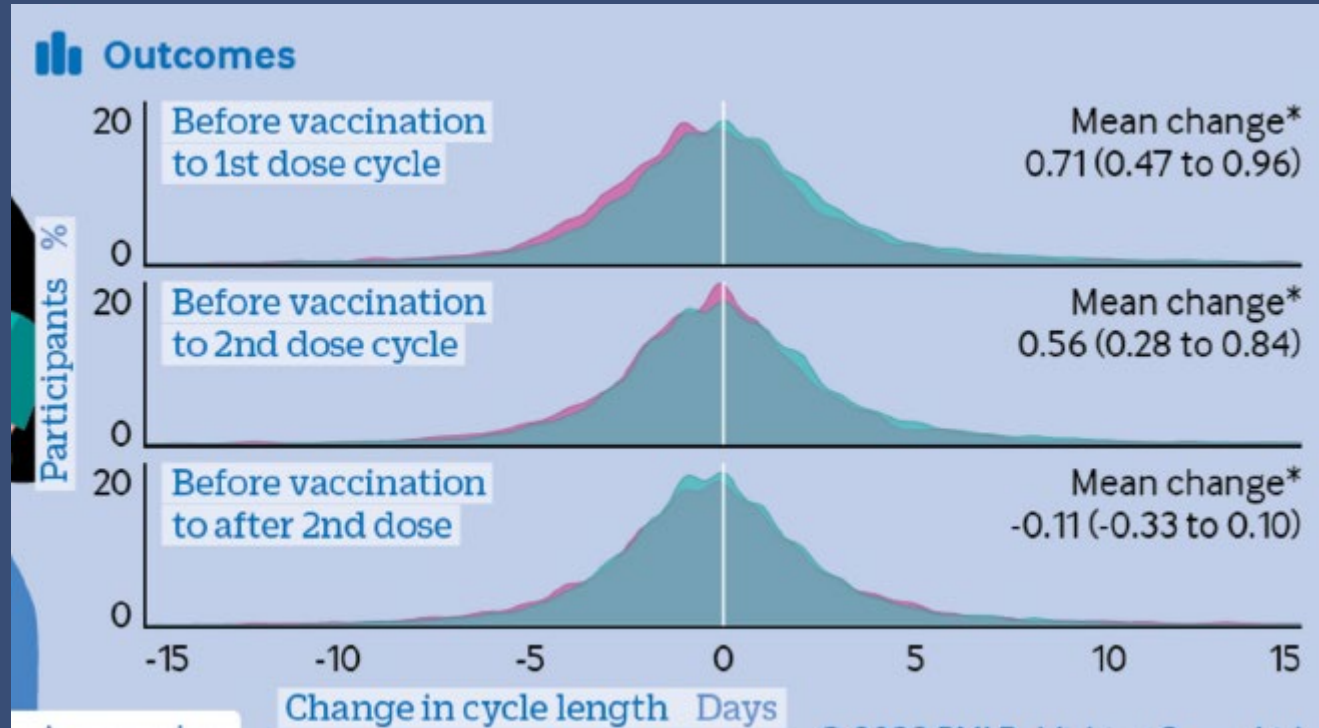
<1 day difference in cycle length between vaccinated and unvaccinated

If both doses within one menstrual cycle, cycle 2.32 days longer



# Menstrual Changes *after* Vaccination

- 19,622 people with menstrual cycles tracked on app “Natural Cycles”
- Age 18-45 years, **global** population (Europe/Canada/US)
- Vaccinated *vs* unvaccinated (all vaccines)
- Prospectively collected data, 3 months prior vs 3 months after vaccine



<1 day difference in cycle length  
between vaccinated and  
unvaccinated

If both doses within one  
menstrual cycle,  
3.91 (CI 2.5-5.3) days longer

# Menstrual Changes *after* Vaccination

Small, temporary changes in cycle length of <1 day  
No change in menstruation duration

Limitations of these studies:

Sample is app users

Missing demographic data

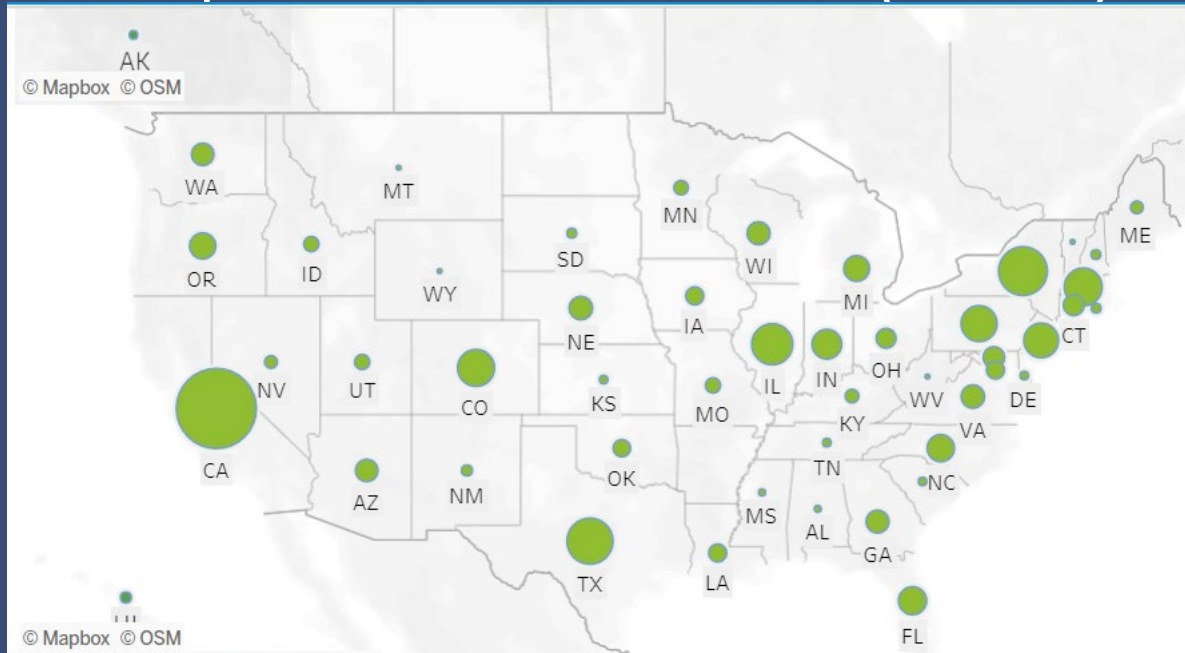
Restricted to normal cycles pre-COVID

# COVID-19 and Early Pregnancy

Multiple studies have found ***no increased risk of miscarriage with COVID-19 infection***

## PRIORITY Study

Prospective nationwide cohort (N=1330)

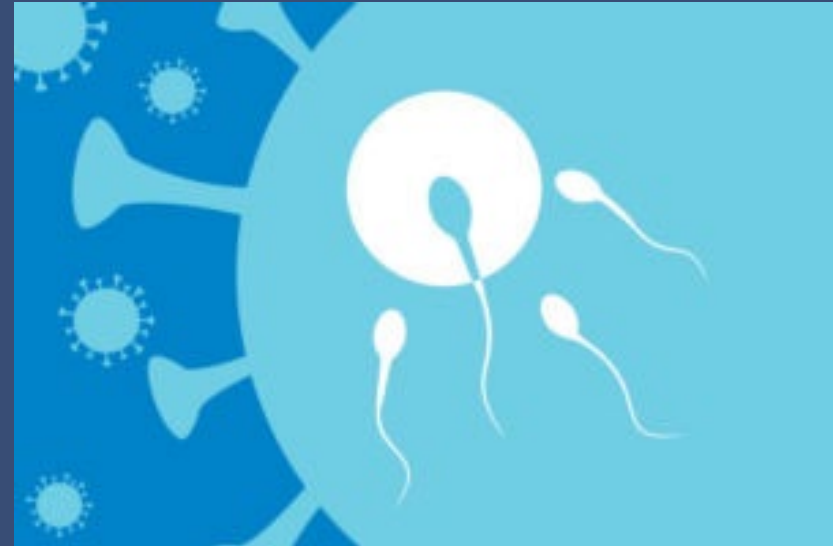


- 139 enrolled <14 weeks gestation
  - 6% loss <20 weeks in *both* COVID+ (n=94) and COVID- (n=15)
- Upper CI for loss 13.4% vs 10% in clinically recognized pregnancies

# COVID-19 and Female Fertility

Most studies show...

- No change in AMH, FSH, Estradiol with infection
- No impact on ability to get pregnant without assistance
- No impact on IVF outcomes



# COVID-19 and Gynecology

	Vaccine	COVID-19 Infection
<b>Menstruation</b>	Small, transient change in cycle length	Possible changes, more data needed
<b>Female fertility</b>	No impact	No impact
<b>Miscarriage</b>	No impact	No impact

# RECOVER and Gynecologic Health

**RECOVER participants answer questions about...**

*menstruation, sexual function, menopause, urinary symptoms, fertility*

## **Strengths of RECOVER**

*Large sample (10,000 females), Diverse US population, Longitudinal follow-up*



**RECOVER**

Researching COVID to Enhance Recovery