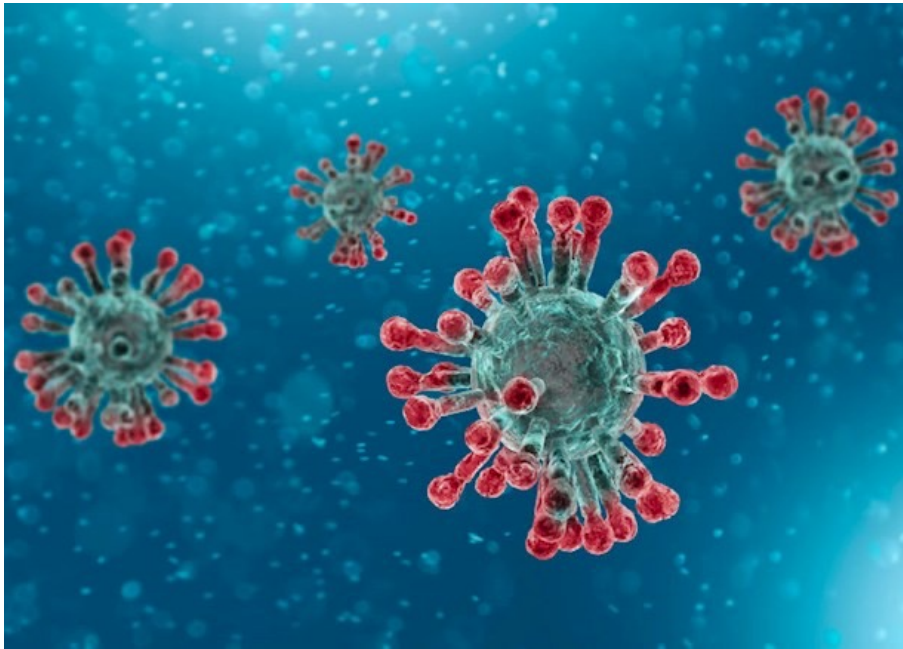


# COVID-19 Vaccines in Pregnancy and Lactation



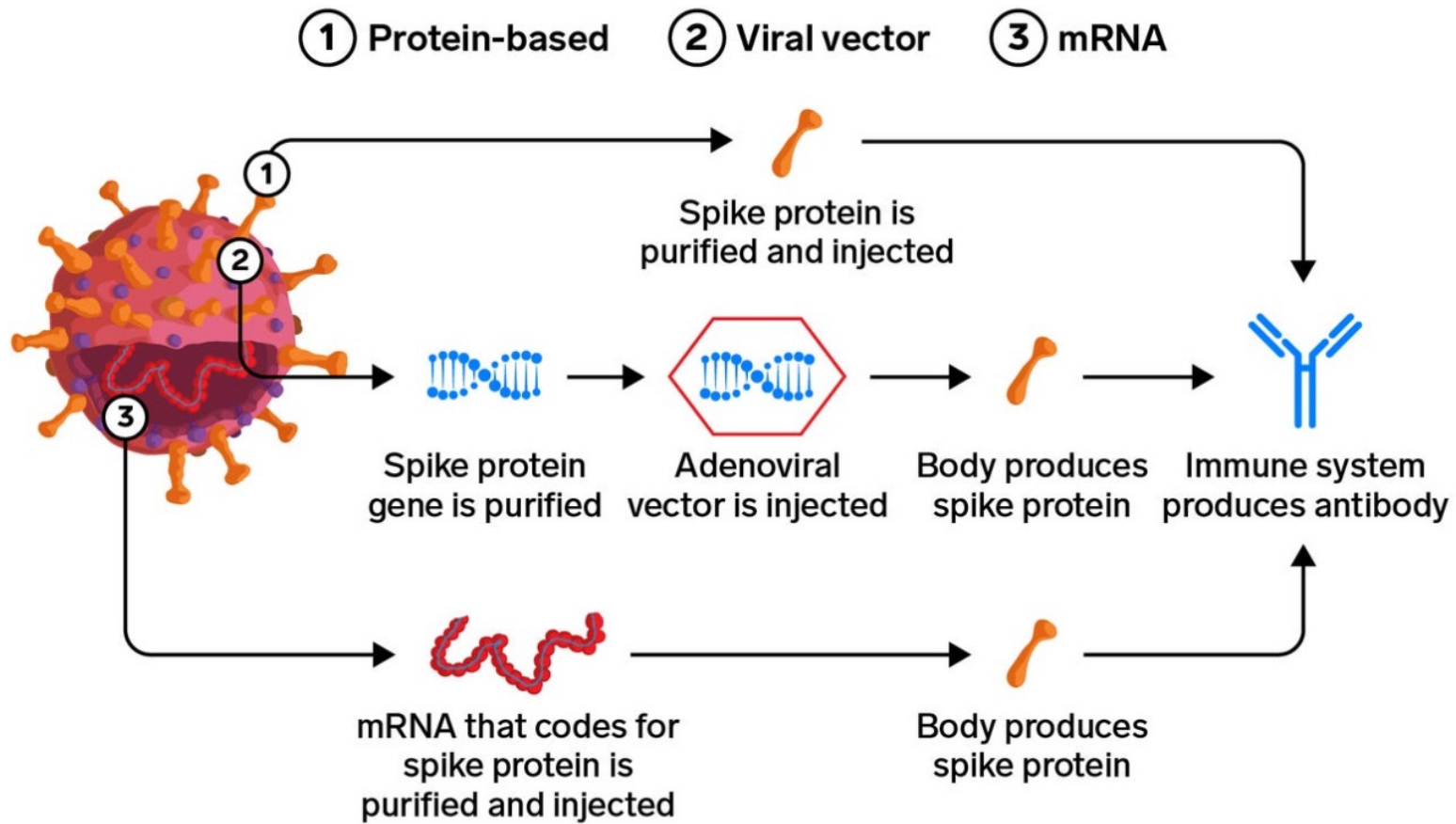
Stephanie L. Gaw, MD, PhD  
Assistant Professor  
Maternal Fetal Medicine  
UC San Francisco

*May 13, 2021*

**I have no disclosures.**



# Three types of coronavirus vaccines in development



Source: National Institutes of Health presentation at Senate hearing on September 9, 2020

INSIDER

# How some of the different Covid-19 vaccines compare



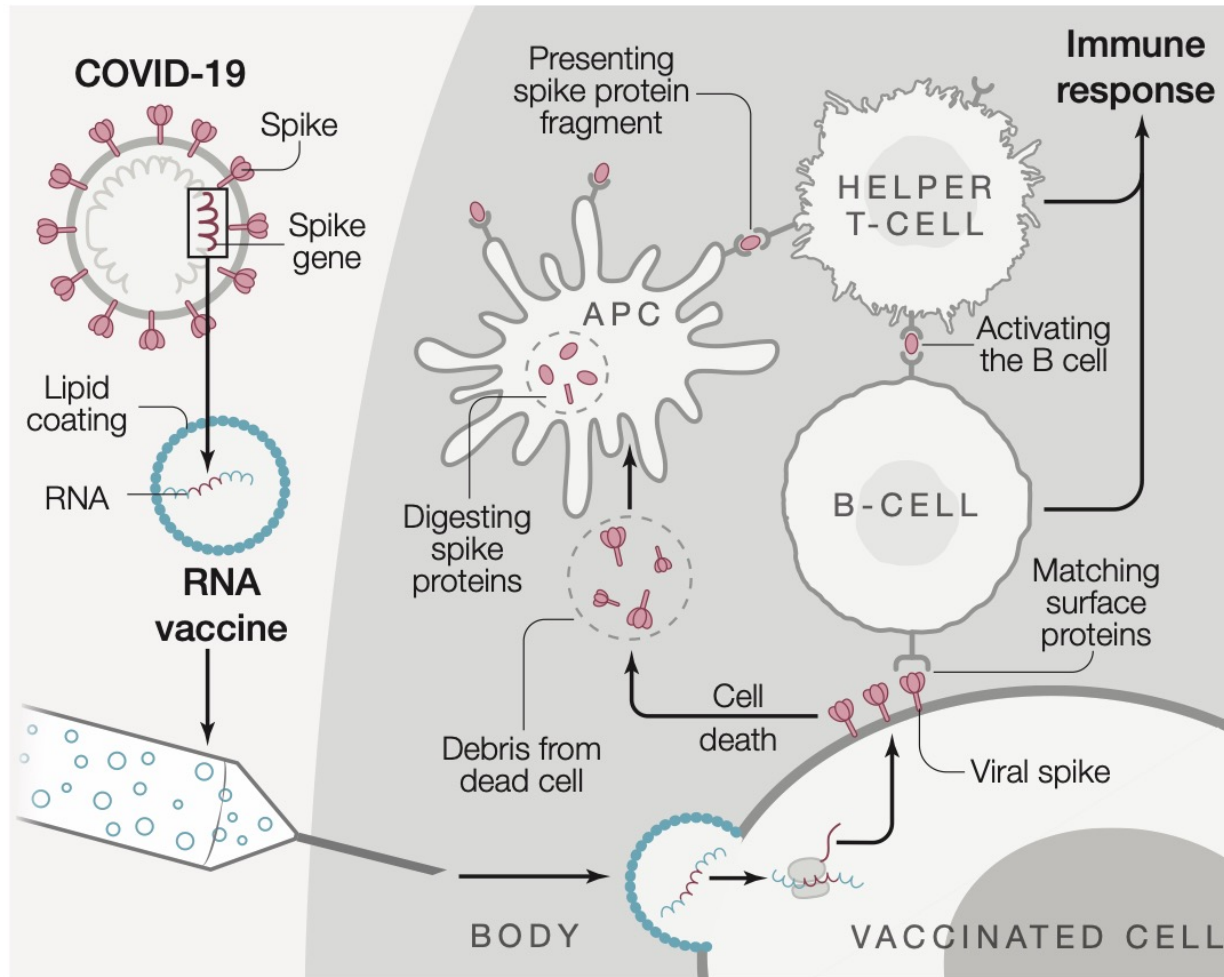
Dec 2020 →

Feb 2021 →

Technology / company	Suitable for people with weak immune systems	Number of doses	Storage	Other vaccines using this technology
<b>RNA</b> Pfizer-BioNTech Moderna	✓		<b>Pfizer-BioNTech:</b> -70C and 2-8C for up to 5 days  <b>Moderna:</b> -20C for 6 months and 2-8C for 30 days	No other licensed vaccines
<b>Viral vector</b> Oxford-AstraZeneca CanSino Biologics Gamaleya Research Institute Johnson & Johnson	✓ (Depending on viral vector used)	 to 	 2-8C	Ebola
<b>'Whole' virus</b> Sinovac (inactivated) Bharat Biotech (inactivated) Sinopharm (inactivated) Medicago Inc. (virus-like particle)	✓		 2-8C	Whooping cough (inactivated) Rabies (inactivated) Hepatitis A (inactivated) HPV/cervical cancer (virus-like particle)
<b>Protein subunit</b> Novavax Chinese Academy of Sciences	✓		 2-8C	Hepatitis B

As of 6 January 2021. Source: Company data/Gavi

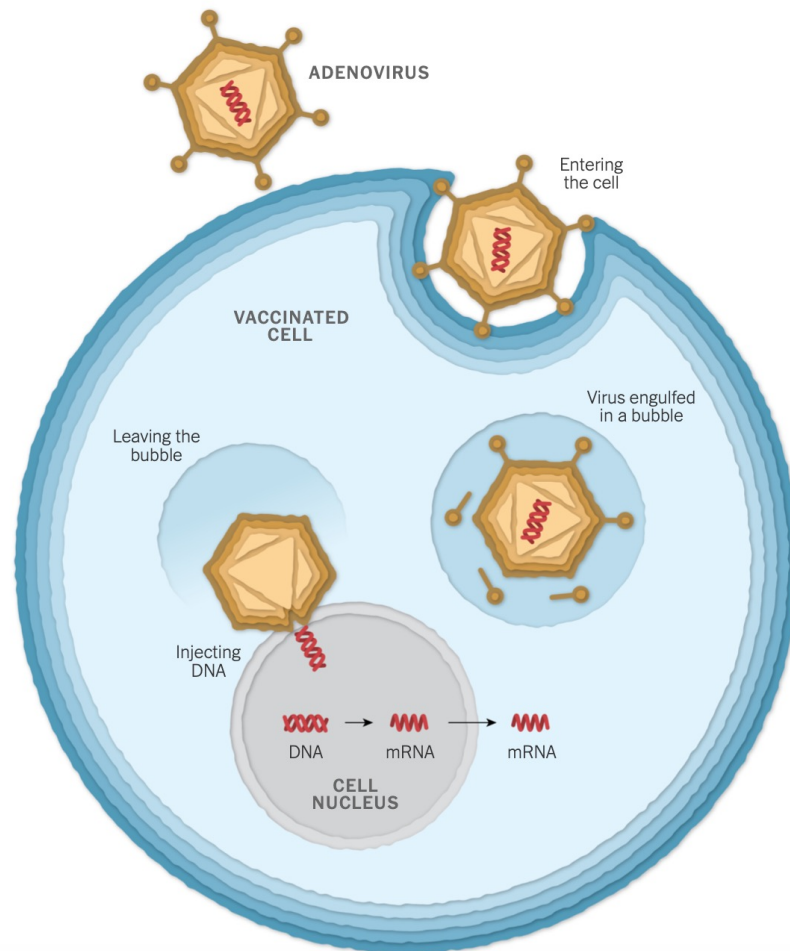
# How mRNA vaccines work



No live virus  
=  
No risk of  
infection

From Topol, Cell 2021

# How adenovirus-DNA vaccines work



No replicating  
virus  
=  
No risk of  
infection

From NY Times

## Coronavirus vaccines weren't tested on pregnant women — here's why that's a problem

"Pregnant immune systems are a little different ... we don't have any direct data on whether it's safe," one doc said

By **NICOLE KARLIS** DECEMBER 9, 2020 11:29PM (UTC)



Ultrasound pregnancy examination of a young woman in a Medical Clinic during COVID-19 outbreak (Getty Images)



# Why are pregnant and lactating people excluded from vaccine and therapeutics trials?

- To protect them
- Pregnant individuals wouldn't want to take the risk
- Increases cost and complexity of trials
  - Pregnancy follow-up
  - Neonatal follow-up
- Administrative and regulatory disincentives
  - “Protection of women and children”
  - “Inclusion of vulnerable populations”

**But, this approach is actually harmful ...**

# Why pregnant and lactating people should be included unless exclusion is justified:

- Pregnancy is a risk factor for severe disease and complications
  - H1N1, SARS-CoV-2
- Many at-risk are pregnant or lactating
  - Health care workers
  - Medical comorbidities
- Pregnant and lactating mothers are forced to make a decision ***without data***
  - Data collected outside of a clinical trial is sub-optimal
  - Not controlled
  - Often rely on registries-> introduces bias

**Protect pregnant people *through* research, not *from* research.**

## ***Pregnant Women Get Conflicting Advice on Covid-19 Vaccines***

The W.H.O. and the C.D.C. provide differing views, and experts partly blame a lack of data because expectant mothers have been excluded from clinical trials.



A pregnant woman being vaccinated in Tel Aviv. The C.D.C. and the W.H.O. differ in their guidance for expectant mothers. Jack Guez/Agence France-Presse — Getty Images



By Apoorva Mandavilli and Roni Caryn Rabin

Published Jan. 28, 2021 Updated Feb. 2, 2021

# Guidance from Regulatory, Public Health and Professional Societies

	Pregnancy	Lactation
Not eligible	First Round: UK, WHO	First Round: UK, WHO
Should not be routinely given	UK, WHO → Revised to “consider in high-risk situations”	
Do not deny access	FDA	FDA
Should be <b>offered</b>	ACOG, SMFM	UK, WHO, ABM, ACOG
<b>Recommended</b>	CDC (April 2021)	CDC, SMFM

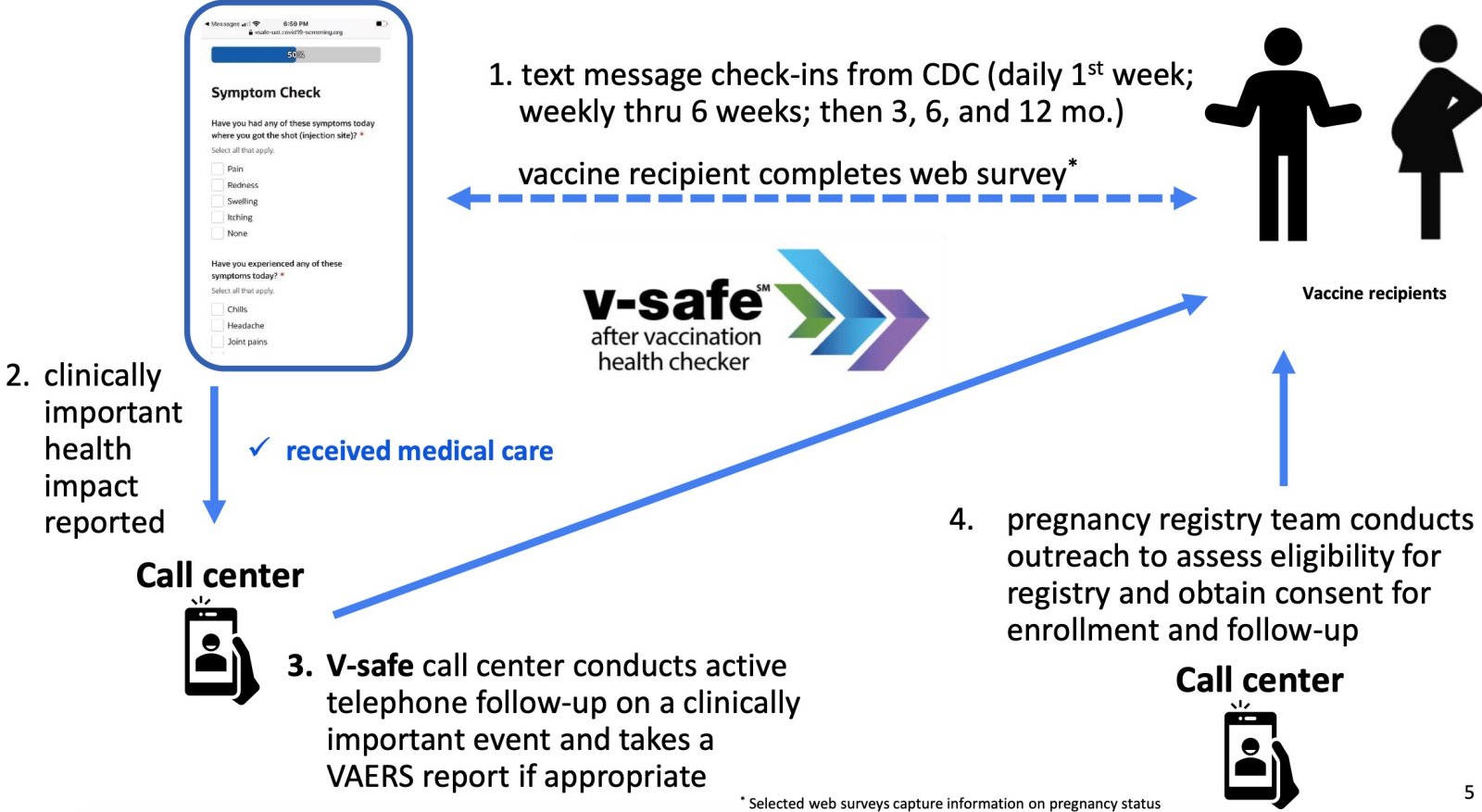
# Unknowns regarding COVID vaccines in pregnancy and lactation

- **Efficacy- Do they work?**
  - Are immune responses similar to non-pregnant?
  - Does duration of immunity change with pregnancy?
  - Should dosing amount/schedule change?
- **Safety- Are they safe for mom and baby?**
  - Immediate side effects of vaccine in pregnancy?
  - Does vaccine cross the placenta, or into breastmilk?
  - Does the vaccine cause placental/fetal inflammatory response?
  - Adverse pregnancy outcomes? Miscarriage, stillbirth, birth defects, complications?
- **Benefits to fetus/infant**
  - Passive immunity to baby in utero or breastmilk?
  - Optimal timing of vaccination in pregnancy?

# Early data



# CDC V-SAFE Registry



ORIGINAL ARTICLE

# Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons

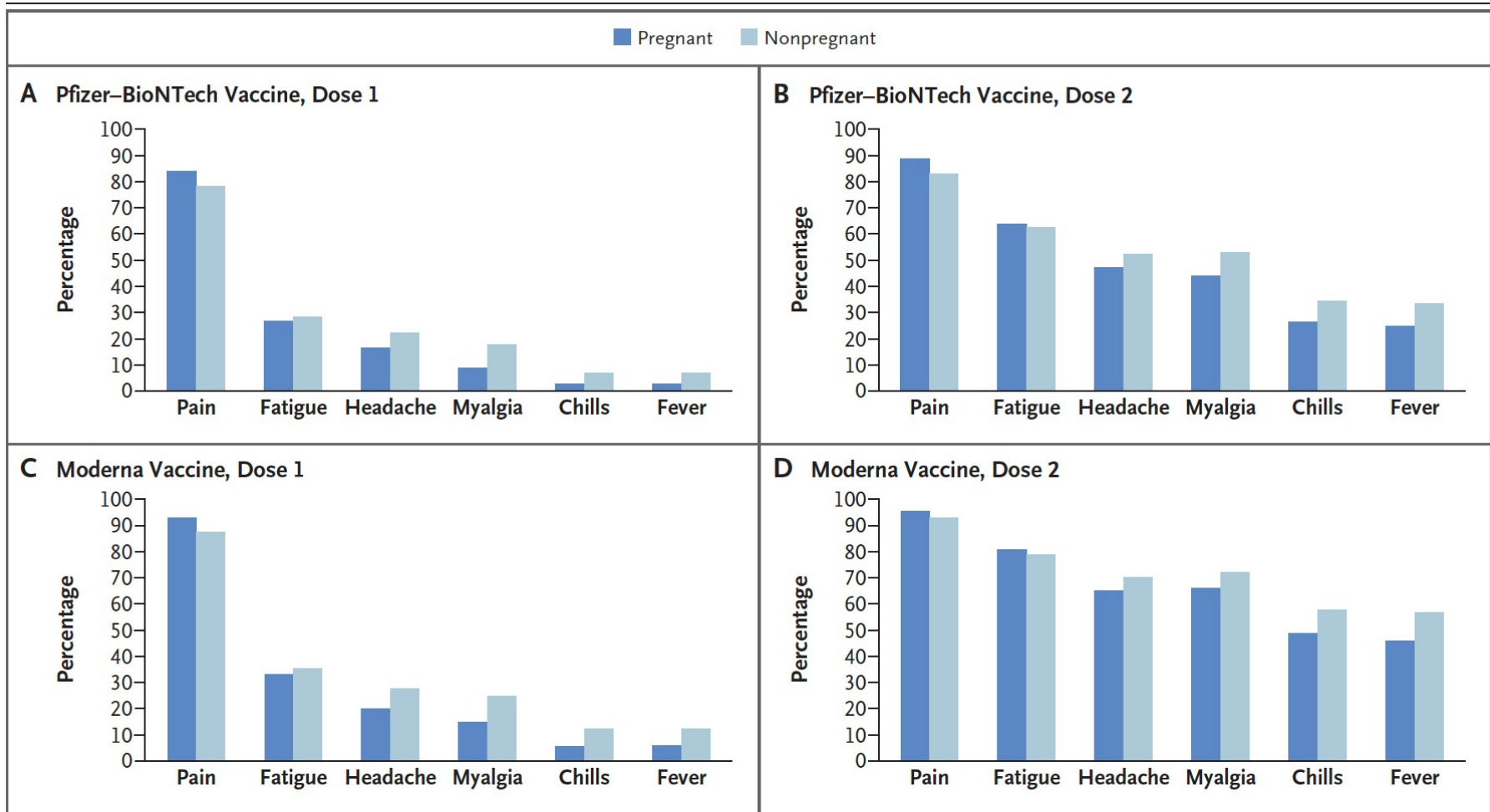
Tom T. Shimabukuro, M.D., Shin Y. Kim, M.P.H., Tanya R. Myers, Ph.D.,  
Pedro L. Moro, M.D., Titilope Oduyebo, M.D., Lakshmi Panagiotakopoulos, M.D.,  
Paige L. Marquez, M.S.P.H., Christine K. Olson, M.D., Ruiling Liu, Ph.D.,  
Karen T. Chang, Ph.D., Sascha R. Ellington, Ph.D., Veronica K. Burkel, M.P.H.,  
Ashley N. Smoots, M.P.H., Caitlin J. Green, M.P.H., Charles Licata, Ph.D.,  
Bicheng C. Zhang, M.S., Meghna Alimchandani, M.D., Adamma Mba-Jonas, M.D.,  
Stacey W. Martin, M.S., Julianne M. Gee, M.P.H., and Dana M. Meaney-Delman, M.D.,  
for the CDC v-safe COVID-19 Pregnancy Registry Team\*

April 21, 2021



**Table 1. Characteristics of Persons Who Identified as Pregnant in the V-safe Surveillance System and Received an mRNA Covid-19 Vaccine.\***

Characteristic	Pfizer–BioNTech Vaccine	Moderna Vaccine	Total
Total	19,252 (53.9)	16,439 (46.1)	35,691 (100)
Age at first vaccine dose			
16–19 yr	23 (0.1)	36 (0.2)	59 (0.2)
20–24 yr	469 (2.4)	525 (3.2)	994 (2.8)
25–34 yr	11,913 (61.9)	9,960 (60.6)	21,873 (61.3)
35–44 yr	6,002 (31.2)	5,011 (30.5)	11,013 (30.9)
45–54 yr	845 (4.4)	907 (5.5)	1,752 (4.9)
Pregnancy status			
Pregnant at time of vaccination	16,522 (85.8)	14,365 (87.4)	30,887 (86.5)
Positive pregnancy test after vaccination	2,730 (14.2)	2,074 (12.6)	4,804 (13.5)
Race and ethnic group†			
Participants with available data	14,320	13,232	27,552
Non-Hispanic White	10,915 (76.2)	9,982 (75.4)	20,897 (75.8)
Hispanic	1,289 (9.0)	1,364 (10.3)	2,653 (9.6)
Non-Hispanic Asian	972 (6.8)	762 (5.8)	1,734 (6.3)
Non-Hispanic Black	371 (2.6)	338 (2.6)	709 (2.6)
Non-Hispanic multiple races	315 (2.2)	292 (2.2)	607 (2.2)
Non-Hispanic other race	76 (0.5)	56 (0.4)	132 (0.5)
Non-Hispanic American Indian or Alaska Native	40 (0.3)	54 (0.4)	94 (0.3)
Non-Hispanic Native Hawaiian or other Pacific Islander	33 (0.2)	31 (0.2)	64 (0.2)
Unknown race or unknown ethnic group	309 (2.2)	353 (2.7)	662 (2.4)



**Figure 1. Most Frequent Local and Systemic Reactions Reported in the V-safe Surveillance System on the Day after mRNA Covid-19 Vaccination.**

Shown are solicited reactions in pregnant persons and nonpregnant women 16 to 54 years of age who received a messenger RNA (mRNA) coronavirus disease 2019 (Covid-19) vaccine — BNT162b2 (Pfizer–BioNTech) or mRNA-1273 (Moderna) — from December 14, 2020, to February 28, 2021. The percentage of respondents was calculated among those who completed a day 1 survey, with the top events shown of injection-site pain (pain), fatigue or tiredness (fatigue), headache, muscle or body aches (myalgia), chills, and fever or felt feverish (fever).



## V-safe pregnancy registry

- **V-safe** participants who report pregnancy following COVID-19 vaccination are actively contacted to enroll in pregnancy registry\*
- Participants are contacted once per trimester, after delivery, and when the infant is 3 months old†
- Outcomes of interest include miscarriage and still birth, pregnancy complications, maternal intensive care unit admission, adverse birth outcomes, neonatal death, infant hospitalizations, and birth defects

**Table 3. Characteristics of V-safe Pregnancy Registry Participants.\***

Characteristic	Pfizer–BioNTech Vaccine	Moderna Vaccine	Total
	<i>number (percent)</i>		
Total	2136 (54.0)	1822 (46.0)	3958 (100)
Timing of first eligible dose			
Periconception: within 30 days before last menstrual period	55 (2.6)	37 (2.0)	92 (2.3)
First trimester: <14 wk	615 (28.8)	517 (28.4)	1132 (28.6)
Second trimester: ≥14 and <28 wk	932 (43.6)	782 (42.9)	1714 (43.3)
Third trimester: ≥28 wk	533 (25.0)	486 (26.7)	1019 (25.7)
Missing data	1 (<0.1)	0	1 (<0.1)
Covid-19 infection during pregnancy			
No Covid-19 infection	2084 (97.6)	1779 (97.6)	3863 (97.6)
Before vaccination	32 (1.5)	24 (1.3)	56 (1.4)
≤14 days after first eligible dose of vaccination	3 (0.1)	7 (0.4)	10 (0.3)
>14 days after first eligible dose of vaccination	9 (0.4)	3 (0.2)	12 (0.3)
Missing data	8 (0.4)	9 (0.5)	17 (0.4)

**Table 4. Pregnancy Loss and Neonatal Outcomes in Published Studies and V-safe Pregnancy Registry Participants.**

Participant-Reported Outcome	Published Incidence*	V-safe Pregnancy Registry†
	%	no./total no. (%)
Pregnancy loss among participants with a completed pregnancy		
Spontaneous abortion: <20 wk <sup>15-17</sup>	10–26	104/827 (12.6)‡
Stillbirth: ≥ 20 wk <sup>18-20</sup>	<1	1/725 (0.1)§
Neonatal outcome among live-born infants		
Preterm birth: <37 wk <sup>21,22</sup>	8–15	60/636 (9.4)¶
Small size for gestational age <sup>23,24</sup>	3.5	23/724 (3.2)
Congenital anomalies <sup>25**</sup>	3	16/724 (2.2)
Neonatal death <sup>26††</sup>	<1	0/724

**827 Completed pregnancies**

# Limitations

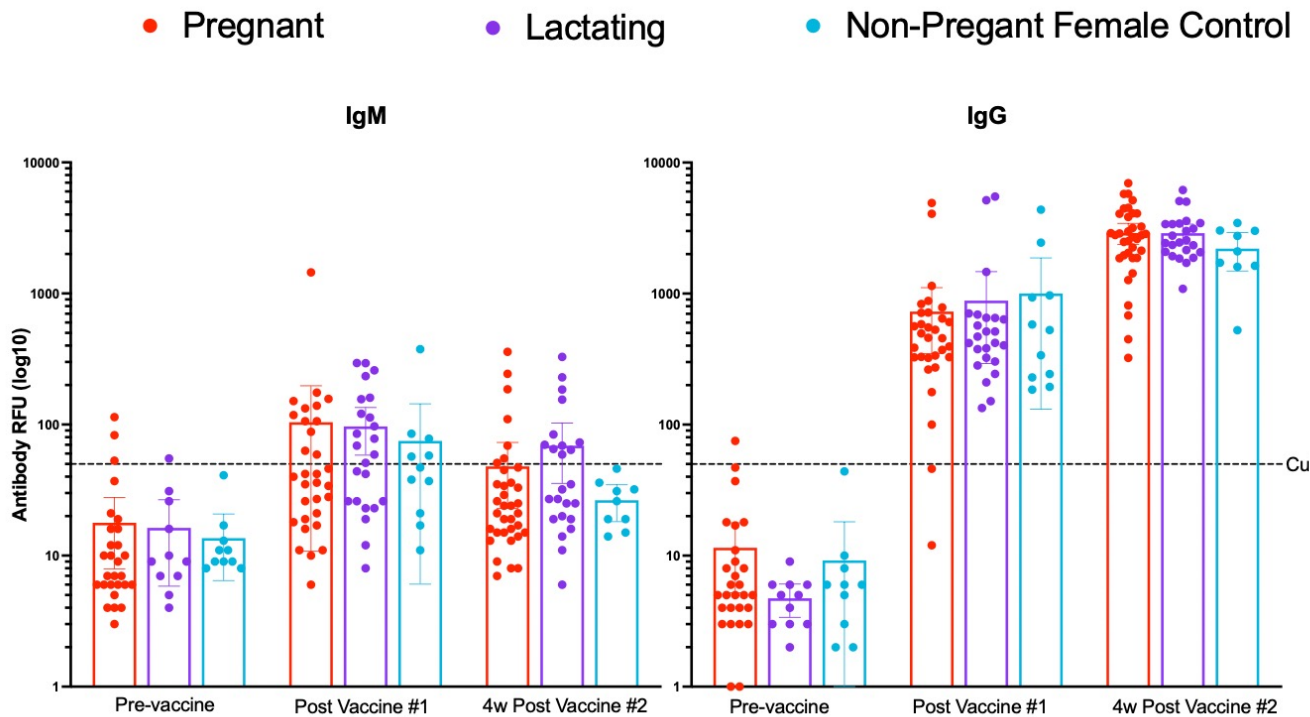
- Dec 14, 2020-Feb 28, 2021-> just 11 weeks
- Early vaccinees-> all HCW, 75% White
  - population-wide comparison may not be appropriate)
- Only 827 completed pregnancies-->mostly 3rd trimester vaccinations

# Strengths

- Largest study to date
- Prospective data collection, phone interviews for registry
- Very good symptomatology data
- Continuing to collect data

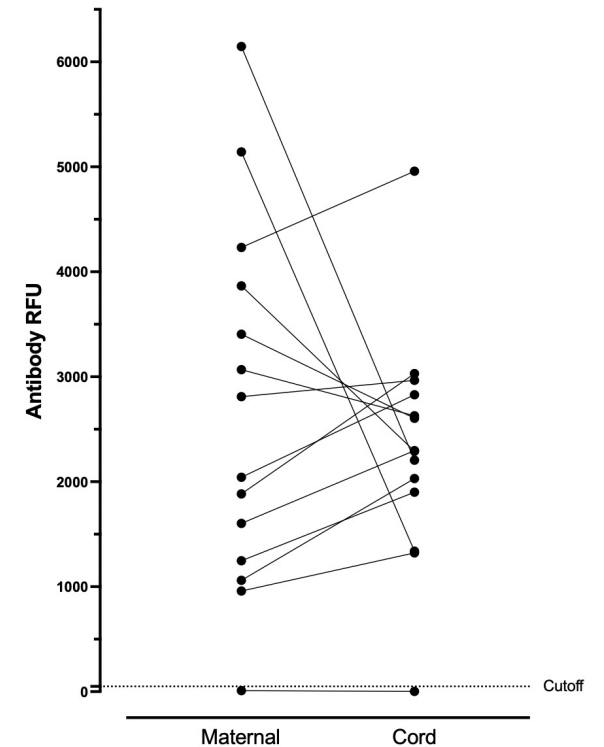
# COVIPAL Study (COVID-19 Vaccines in Pregnancy and Lactation)

IgM and IgG response in pregnant and lactating individuals similar to non-pregnant volunteers



Infants born to vaccinated mothers have IgG in cord blood

Maternal and Cord Plasma IgG at Delivery



# Robust antibody response is generated in pregnancy

ORIGINAL RESEARCH: OBSTETRICS | ARTICLES IN PRESS

## COVID-19 vaccine response in pregnant and lactating women: a cohort study

Kathryn J. Gray, MD PhD • Evan A. Bordt, PhD • Caroline Atyeo, BS • ... Michal A. Elovitz, MD • Galit Alter, PhD • Andrea G. Edlow, MD, MSc • Show all authors • Show footnotes

Open Access • Published: March 25, 2021 • DOI: <https://doi.org/10.1016/j.ajog.2021.03.038>    

RESEARCH LETTER | ARTICLES IN PRESS

## Cord Blood Antibodies following Maternal COVID-19 Vaccination During Pregnancy

Leena B. MITHAL, MD MSCI • Sebastian OTERO, BA • Elisheva D. SHANES, MD • Jeffery A. GOLDSTEIN, MD PhD • Emily S. MILLER, MD MPH

Published: March 31, 2021 • DOI: <https://doi.org/10.1016/j.ajog.2021.03.038>    

RESEARCH LETTER

## Antibody Response to Coronavirus Disease 2019 (COVID-19) Messenger RNA Vaccination in Pregnant Women and Transplacental Passage Into Cord Blood

Prabhu, Malavika MD; Murphy, Elisabeth A. PhD; Sukhu, Ashley C. BS; Yee, Jim BS; Singh, Sunidhi BA; Eng, Dorothy BA, BS; Zhao, Zhen PhD; Riley, Laura E. MD; Yang, Yawei J. MD, PhD

[Author Information](#) 

Obstetrics & Gynecology: April 28, 2021 - Volume Latest Articles - Issue - 10.1097/AOG.0000000000004438

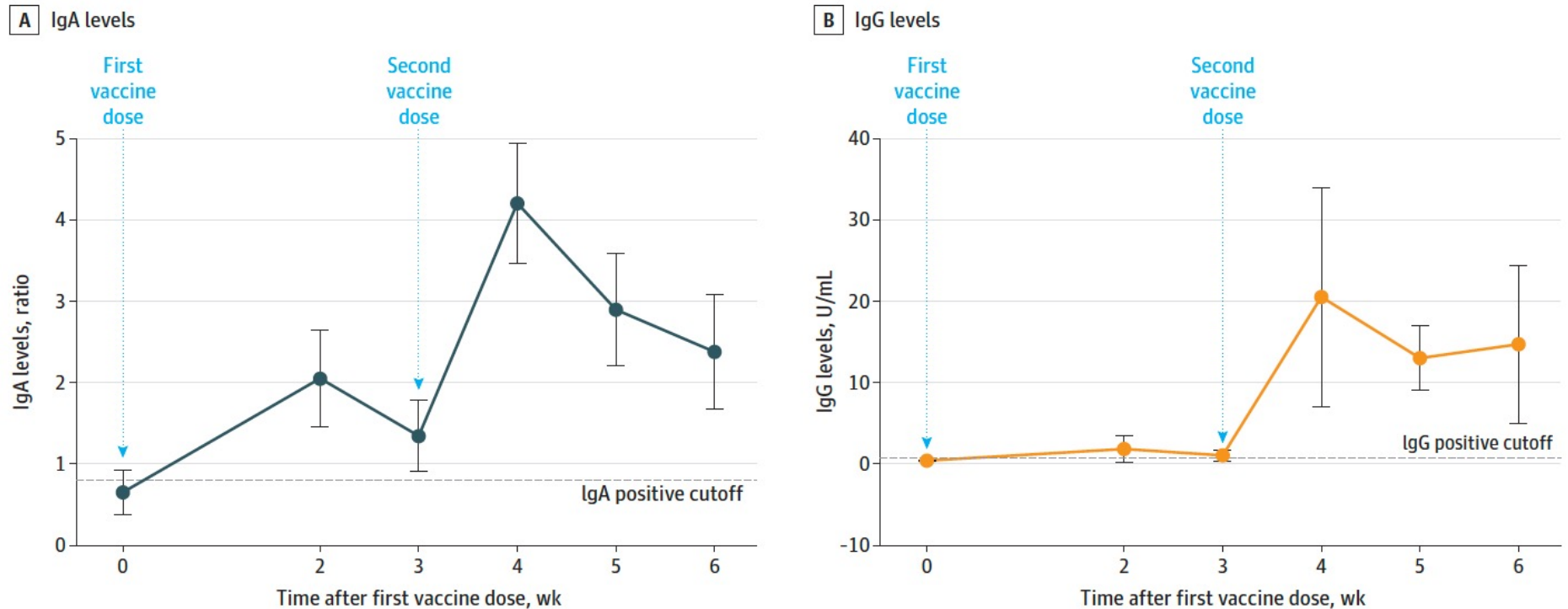
doi: 10.1097/AOG.0000000000004438

And antibodies are transferred to the baby!  
- (if vaccinated at least 2-3 weeks before delivery)



# Antibodies are secreted into breastmilk after vaccination

Figure. Changes in Levels of IgA and IgG in Breast Milk Over Time



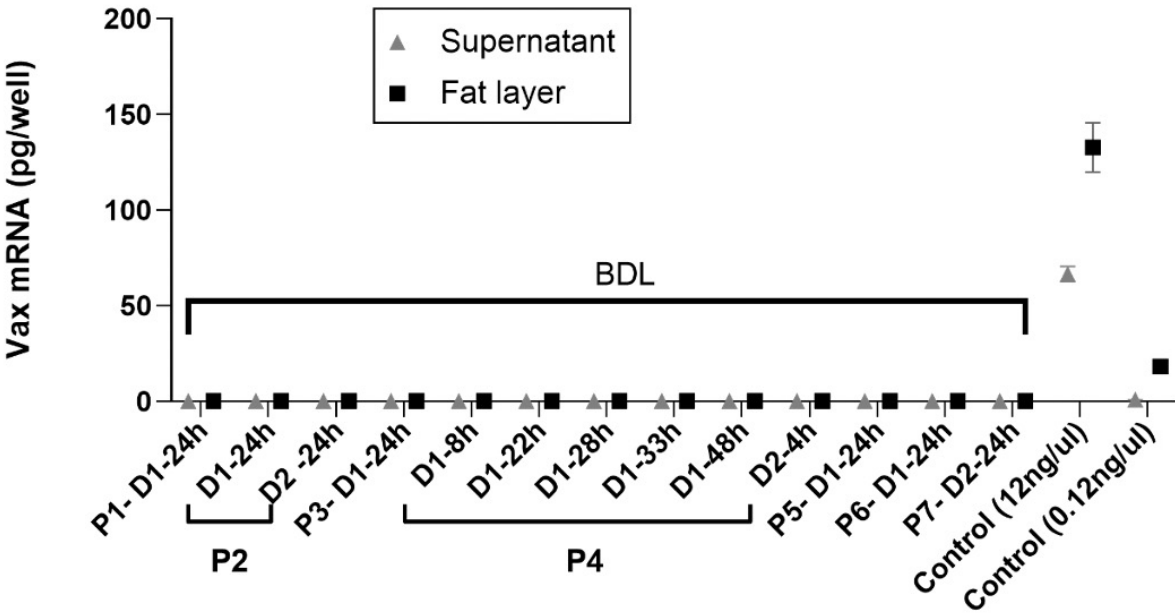
A, All the comparisons between time points are  $P < .001$ . B, The comparison point at week 4 is  $P = .004$ ; at week 5,  $P < .001$ ; and at week 6,  $P = .005$ .

Data points represent means; error bars, 95% CIs.

# mRNAs from COVID-19 BTN162b2 and mRNA-1273 vaccines are not detected in human milk

Yarden Golan, Ph.D.<sup>1</sup>, Mary Prahl, M.D.<sup>2</sup>, Arianna Cassidy, M.D.<sup>3</sup>, Christine Y. Lin<sup>3</sup>, Nadav Ahituv, Ph.D.<sup>1</sup>, Valerie J. Flaherman, M.D., M.P.H.<sup>2</sup>, Stephanie L. Gaw, M.D., Ph.D.<sup>3</sup>

C





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NEWS / Pfizer and BioNTech Commence Global Clinical Trial to Evaluate COVID-19 Vaccine in Pregnant Women

## PFIZER AND BIONTECH COMMENCE GLOBAL CLINICAL TRIAL TO EVALUATE COVID-19 VACCINE IN PREGNANT WOMEN

Thursday, February 18, 2021 - 01:30pm EST

- Double blind RCT of 4000 pregnancies
- International (>60 US sites)
- 24-34 weeks GA
- Participants unblinded at delivery
- Infants followed for 1 year

Started in March 2021 → expect results in Winter 2021

# How do I consider risks/benefits?

## Get the vaccine!

- Pregnancy and lactation is a risk factor for severe disease.
- The vaccine works based on early antibody data.
- Reduce transmission to friends/family.
- I can pass on to my baby (in utero and in milk)
- Early safety data indicates overall safety.



## Don't get the vaccine!

- I have no risk of getting COVID-19.
- I am allergic.
- I want to wait for more data.

**For the majority- PLEASE GET THE VACCINE!**

Questions?