COVID VACCINE AND FERTILITY

- NO IMPACT ON FERTILITY OBSERVED
- LONG TERM SIDE EFFECTS HIGHLY UNLIKELY
- PREGNANT WOMEN LIKELY TO TRANSFER ANTIBODIES TO UNBORN CHILD

During the Pfizer vaccine studies, 23 women volunteers became pregnant, and the only one who suffered a pregnancy loss was in the placebo group

Where did the fertility rumor begin?

December 2020, 2 physicians wrote a letter to the European equivalent of the FDA:

- Claiming that the spike protein is similar in structure to a placenta protein, and vaccine would cause a woman to make antibodies to the placenta
- There is no evidence that this is true
- SARS-CoV-2 spike protein and syncytin-1 protein have one sequence of 4 amino acids in common
  - That's out of 538-amino acids in the syncytin-1 protein and
  - 1273-amino acids in the SARS-CoV-2 spike protein

In the same letter they made other claims that never happened

- "Pfizer/BioNTech mRNA vaccine [has] polyethylene glycol…Seventy percent of people make antibodies to PEG and most do not know it…many could have allergic, potentially deadly, reactions to a PEG-containing vaccine“
  - **This has not happened**
- "Pfizer/BioNTech is also inserting a [bioluminescent] ingredient derived from a marine invertebrate, mNeonGreen, into its vaccine.”
  - **This is not true. The vaccine does not glow in the dark**

- **There is no evidence that the vaccines affects fertility**
- **There IS evidence that COVID-19 disease impacts fertility in women and in men**

Safety in Pregnancy

- There is no live virus in the vaccine
- Pregnant women are at higher risk of severe COVID-19 disease including miscarriage
- The Society for Fetal and Maternal Medicine and American College of Obstetrics and Gynecology recommend that pregnant women be offered SARS-CoV-2 vaccine

https://www.smfm.org/covidclinical

https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/03/novel-coronavirus-2019

CDC has systems in place to look for vaccine side effects: VAERS and V-SAFE

VAERS is the nation's early warning system for vaccine safety

CDC + FDA

VAERS

Vaccine Adverse Event Reporting System

co-managed by CDC and FDA

http://vaers.hhs.gov

V-SAFE has a special pregnancy module

1. Text message check-ins from CDC (daily 1st week; weekly thru 6 weeks; then 3, 6, and 12 months)

vaccine recipient completes web survey*

Vaccine recipients

v-safe℠ after vaccination health checker

2. Clinically important health impact reported

✓ received medical care

Call center

3. **V-safe** call center conducts active telephone follow-up on a clinically important event and takes a VAERS report if appropriate

4. Pregnancy registry team conducts outreach to assess eligibility for registry and obtain consent for enrollment and follow-up

Call center

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 stillbirth, pregnancy complications, maternal intensive care unit admission, adverse birth outcomes, neonatal death, infant hospitalizations, and birth defects

* Must be registered in **v-safe** and have been pregnant at the time of COVID-19 vaccine receipt or within 30 days of vaccination; enrollment may discontinue when sufficient enrollment numbers are achieved

† Phone surveys are conducted along with maternal and infant medical record review

V-SAFE participants

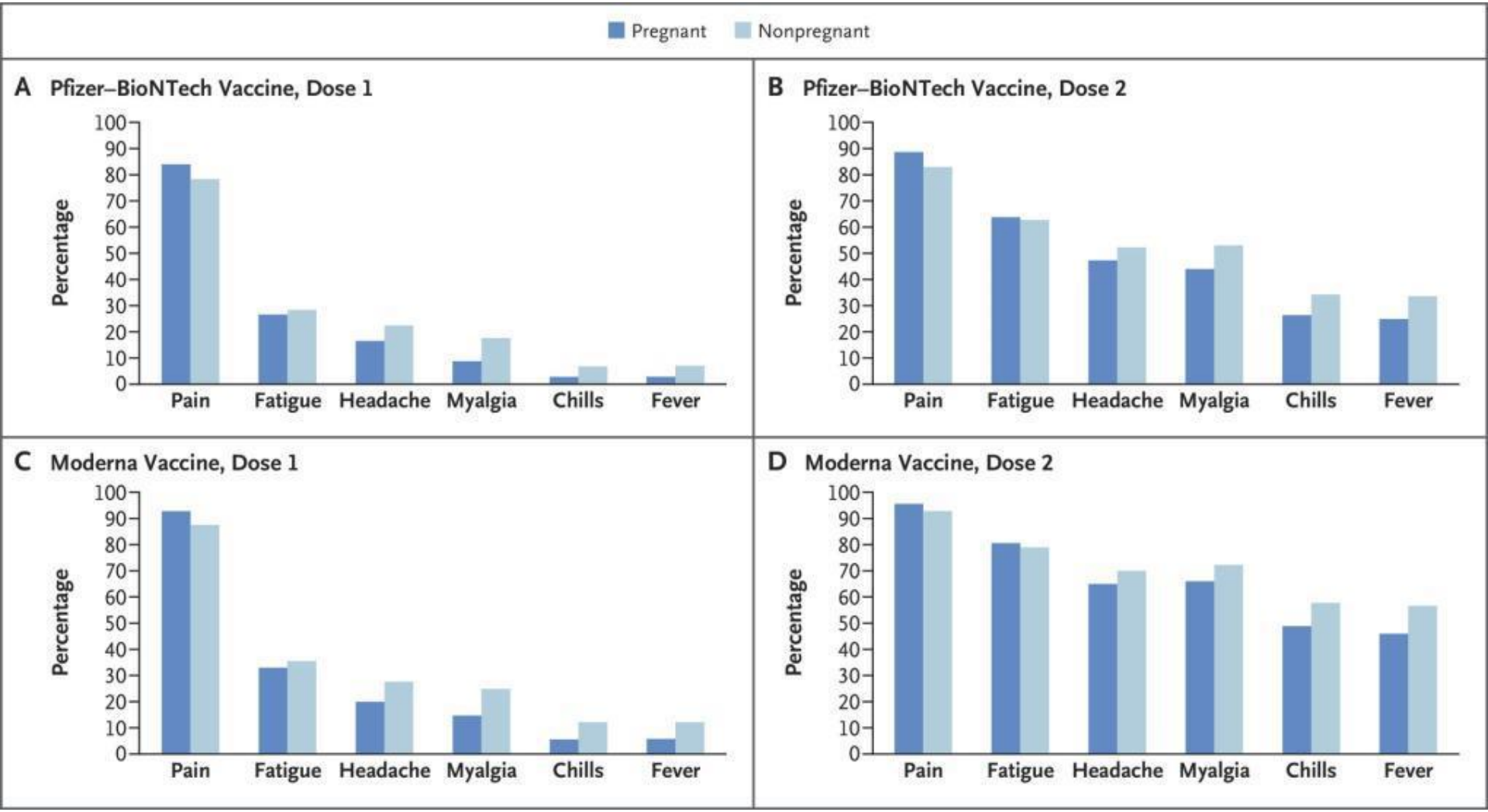
Table 1. Characteristics of Persons Who Identified as Pregnant in the V-safe Surveillance System and Received an mRNA Covid-19 Vaccine.*

Characteristic	Pfizer–BioNTech Vaccine	Moderna Vaccine	Total
		number (percent)	
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)

- >35,000 women
- Ages 16-54
- Included variety of race/ethnicities
- Pregnant when vaccinated or got pregnant shortly after vaccine

https://www.nejm.org/doi/full/10.1056/NEJMoa2104983

Symptoms after vaccination similar to what non-pregnant women experience



Results

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[15-17]	10–26	104/827 (12.6)‡
Stillbirth: ≥ 20 wk[18-20]	<1	1/725 (0.1)§
Neonatal outcome among live-born infants		
Preterm birth: <37 wk[21,22]	8–15	60/636 (9.4)¶
Small size for gestational age[23,24]‖	3.5	23/724 (3.2)
Congenital anomalies[25]**	3	16/724 (2.2)
Neonatal death[26]††	<1	0/724

- **No increase in miscarriage, still birth, premature birth, small babies, birth defects, or newborn death**

https://www.nejm.org/doi/full/10.1056/NEJMoa2104983

In contrast, there are many studies showing increased risk of severe COVID disease in pregnancy

https://www.cdc.gov/mmwr/volumes/69/wr/mm6944e2.htm

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7838012/

https://www.cdc.gov/mmwr/volumes/69/wr/mm6944e3.htm

https://jamanetwork.com/journals/jama/fullarticle/2772773

Summary of many studies of COVID-19 disease and pregnancy outcomes

Table 1: Summary of pooled results using random-effects models

Outcome	No. of studies	No. of participants	No. of events	Mean difference (95% CI)	OR (95% CI)	Heterogeneity, %
Patients with COVID-19 versus those without COVID-19						
Preeclampsia	13	424 344	28 326		1.33 (1.03 to 1.73)	31
Gestational diabetes	13	425 890	40 567		1.03 (0.76 to 1.39)	54
Fetal distress	3	874	47		1.50 (0.64 to 3.53)	8
Stillbirth	6	413 122	1366		2.11 (1.14 to 3.90)	24
Chorioamnionitis or intra-amniotic infection	5	4368	433		0.85 (0.57 to 1.26)	0
Admission to the ICU	5	409 737	2012		4.78 (2.03 to 11.25)	76
Cesarean delivery	22	429 366	121 650		1.00 (0.82 to 1.23)	78
Postpartum hemorrhage	5	2981	355		0.89 (0.52 to 1.53)	55
Preterm birth	18	425 357	25 071		1.82 (1.38 to 2.39)	64
Neonatal sex, male	5	11 985	6369		0.97 (0.71 to 1.33)	9
Gestational age at birth, wk	13	4197		−0.24 (−0.49 to 0.00)		61
Birth weight, g	13	2973		−68.96 (−130.22 to −7.69)		29
Low birth weight	2	1054	678		2.32 (0.26 to 21.07)	85
Admission to the NICU	10	5675	785		3.69 (1.39 to 9.82)	94
Neonatal death	5	2838			1.10 (0.41 to 2.95)	0

- >2 times higher risk of stillbirth
- >3 ½ times higher risk of baby going to Neonatal ICU
- >4 ¾ times risk of mother going to the ICU
- COVID is a bad disease in pregnancy

https://www.cmaj.ca/content/cmaj/193/16/E540.full.pdf

Male fertility

- COVID vaccines have no live virus
- Study in Journal of the American Medical Association (JAMA): 45 healthy men
- Measured sperm concentration, movement, and total count before and after 2 doses of COVID vaccine
- **No difference**

JAMA. Published online June 17, 2021.
doi:10.1001/jama.2021.9976

Consider mumps

- Mumps is a virus that can cause infertility
- Mumps doesn't just cause swelling of the salivary glands, it affects the testicles too
- MMR vaccine prevents mumps, protects against infertility

Consider COVID-19 disease

- Just as mumps can affect fertility, there is evidence that COVID-19 disease can too
- The virus that causes COVID-19 disease can cause inflammation of the testicles
- The MMR and COVID-19 vaccines do NOT cause infertility
- The MMR and COVID-19 vaccines DO prevent infections that can cause infertility

Evidence that COVID-19 disease affects male fertility

- Review of 28 studies published Dec 2019 – Jan 2021
- Receptor that the virus bind to (ACE-2 receptor) is present cells of the testes and prostate
  - Present in higher amounts in younger men
- Men who had moderate COVID-19 illness had lower sperm counts, motility, and concentration compared to men who never had COVID

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8190708/

COVID-19 and male fertility

- SARS, a closely related virus that infected people in 2003 caused testicular inflammation and sperm abnormalities
- Several studies show evidence of changes in male hormone COVID-19 disease
- International Federation of Fertility Societies, European Society of Human Reproduction and Embryology, and the American Society for Reproductive Medicine all recommend vaccination against COVID-19

https://pubmed.ncbi.nlm.nih.gov/33941061/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7689309/
https://academic.oup.com/biolreprod/article/74/2/410/2667029
https://onlinelibrary.wiley.com/doi/10.1111/j.1439-0272.2007.00794.x

Many studies show testicular dysfunction with prior COVID-19 infection

Testicular dysfunction		Number of cases	References
Clinical manifestations	viral orchitis recorded in 6 patients; no virus detected in the semen	34	[11]
	seminiferous cellular damage was observed in the specimens from 12 patients died from COVID-19; no virus detected in testes in 11 deceased patients, but 1 was positive	12	[13]
	decreased levels of total and free testosterone; increased serum level of LH was detected	31	[14]
	significant reduction in the serum testosterone level in 113 patients (51.1%) with severe COVID-19	221	[15]
	moderate decrease in the testosterone levels; LH level was higher; testosterone: LH level and FSH: LH ratio were lower	119	[16]
	LH and FSH levels were elevated; both testosterone and dihydrotestosterone levels decreased	35	[17]
	SARS-CoV-2 RNA was not detected in 12 semen samples and testicular biopsy	12	[23]
	six patients (15.8%) had positive SARS-CoV-2	38	[22]
	no virus was detected in 34 semen samples	34	[24]
Infection via ACE2 receptor	ACE2 and TMPRSS2 expression detected mainly in seminiferous duct cells, spermatogonia, Leydig cells, primordial germ cells, and Sertoli cells		[7, 27, 28-33]
Inflammatory response and persistent fever	cytokines could cause orchitis in patients by inducing inflammatory response		[5, 33, 36, 37]
	hyper-inflammatory conditions with persistent fever affect testis function		[39-43]
Drug-related testicular injury	glucocorticoids and stress cause testes injury; ribavirin reduced testosterone levels and inhibited spermatogenesis		[22, 45]
	lopinavir/ritonavir could inhibit spermatogenesis		[46]
	chloroquine phosphate affects spermatogenesis and epididymal function		[47]

COVID-19 and erectile dysfunction (ED)

- COVID-19 causes blood vessel dysfunction
- Online survey 100 men, Italy, April-May 2020
- ED significantly higher among men with prior COVID (28% vs 9.33%), independent of age, BMI, and self-reported psychological factors

	COVID+ (*n* = 25)	COVID- (*n* = 75)	*p*-value
Age (years)	39.00 [29.00, 45.00]	42.00 [32.50, 49.00]	0.142 [a]
BMI (kg/m^2)	22.65 [20.83, 23.74]	22.74 [20.98, 24.53]	0.266 [a]
GAD−7 score	4.00 [2.00, 6.00]	4.00 [2.00, 5.00]	0.741 [a]
PHQ−9 score	5.00 [3.00, 6.00]	4.00 [2.00, 5.00]	0.873 [a]
Erectile dysfunction	7 (28%)	7 (9.33%)	**0.027** [b]

https://onlinelibrary.wiley.com/doi/10.1111/andr.13003

Weigh benefits and risks