

Message

From: Markowitz, Lauri (CDC/DDID/NCIRD/DVD) [REDACTED]
Sent: 3/22/2021 3:36:27 PM
To: Anderson, Steven [REDACTED]; Bell, Beth [REDACTED]; Beresnev, Tatiana H (NIH) [REDACTED]; Broder, Karen R (CDC) [REDACTED]; Calvert, Geoffrey M (CDC) [REDACTED]; Clark, Matthew (IHS) [REDACTED]; Clark, Thomas A (CDC) [REDACTED]; Cohn, Amanda C (CDC) [REDACTED]; Collins, Limone [REDACTED]; Cunningham, Fran [REDACTED]; Daley, Matt [REDACTED]; DeStefano, Frank (CDC) [REDACTED]; Dooling, Kathleen L (CDC) [REDACTED]; Edwards, Kathy [REDACTED]; Farizo, Karen [REDACTED]; Forshee, Richard [REDACTED]; Gee, Julianne M (CDC) [REDACTED]; Hamburger, Tanya (CDC) [REDACTED]; Helfand, Rita (CDC) [REDACTED]; Hiers, Susan G (CDC) [REDACTED]; Hopkins, Bob [REDACTED]; Jackson, Lisa [REDACTED]; Kelman, Jeffrey A (CMS) [REDACTED]; Kulldorf, Martin [REDACTED]; Lee, Grace [REDACTED]; MacNeil, Jessica R (CDC) [REDACTED]; Markowitz, Lauri (CDC) [REDACTED]; Marquez, Paige L (CDC) [REDACTED]; Mbaeyi, Sarah A (CDC) [REDACTED]; Myers, Tanya R (CDC) [REDACTED]; Nair, Narayan [REDACTED]; Oliver, Sara E (CDC) [REDACTED]; Patricia Whitley-Williams [REDACTED]; Riley, Laura [REDACTED]; Rubin, Mary (HRSA) [REDACTED]; Schechter, Robert [REDACTED]; Shanley, Edwin (CDC) [REDACTED]; Shay, David K (CDC) [REDACTED]; Shimabukuro, Tom (CDC) [REDACTED]; Sotir, Mark J (CDC) [REDACTED]; Steinberg, Judith L (OS) [REDACTED]; Su, John (CDC) [REDACTED]; Talbot, Keipp [REDACTED]; Wasley, Annemarie (CDC) [REDACTED]; Weintraub, Eric S (CDC) [REDACTED]; Wharton, Melinda (CDC) [REDACTED]; Wong, Hui-Lee [REDACTED]; Woo, Jared M (CDC) [REDACTED]; Young, Mardia A (CDC) [REDACTED]
CC: Moro, Pedro L (CDC) [REDACTED]; Ellington, Sascha R (CDC) [REDACTED]; Kim, Shin Y (CDC) [REDACTED]; Meaney-Delman, Dana Marie (CDC) [REDACTED]; Oduyebo, Titilope (CDC) [REDACTED]; OLSEN, CHRISTIAN (CDC) [REDACTED]; Brenna Hughes, MD [REDACTED]; Denise Jamieson, MD [REDACTED]; Kevin Ault [REDACTED]; Richard Beigi, MD [REDACTED]
Subject: [EXTERNAL] VaST - Agenda for March 22 (1:30 - 2:30 pm EDT) and presentations - CONFIDENTIAL
Attachments: VAST_VaxSafety_VAERS_PREGNANCY_MARCH22_PM.pdf; VaST vsafe 3_22_2021 pregnancy_v2.pdf; COVID-19Vaccine_Pregnancy_VAST_MAR222021.pdf; Meeting with ACIP Vaccines Safety Technical Sub-Group Final draft 20 March 2020_pdf.pdf; 2021_03_22 VaST Meeting Agenda.docx

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear all,

This email includes the VaST agenda for today as well as 4 presentations.

Agenda:

Data from AdVac® vector vaccines (Richard Nettles, Janssen)
VAERS (Pedro Moro, CDC)
v-safe (Tanya Myers, CDC)
v-safe pregnancy registry (Shin Kim, CDC)

The VaST call link information should be on your calendars (or you will receive it soon).

Reminder - all VaST documents and communications are confidential.

Lauri Markowitz and Melinda Wharton

*Lauri Markowitz, MD
VaST Co-Lead
Division of Viral Diseases*



COVID-19 maternal vaccine safety update - VAERS

December 14, 2020 – March 16, 2021

Vaccine Safety Technical subgroup

March 22, 2021

**Pedro L. Moro, MD, MPH
Immunization Safety Office**

Outline

- Characteristics of pregnancy reports
- Most common signs and symptoms reported
- Pregnancy and neonatal-specific conditions reported
- Characteristics of spontaneous abortion reports
- Racial and ethnic characteristics of reports
- Data mining findings
- Summary

Characteristics of VAERS COVID-19 vaccine pregnancy reports submitted to VAERS*

Characteristic	All	Pfizer-BioNTech	Moderna	Janssen
Number of reports	345**	191	148	5
Serious† reports	68 (19.7)	44 (23.0)	23 (15.5)	0
Pregnancy-specific reports	108 (31.3)	69 (36.1)	38 (25.7)	0
Maternal age in years, median (range)	33 (16–51)	33 (22–51)	33 (16–50)	35 (30–39)
Gestational age in weeks at time of vaccination when reported, median (range)	13 (1–38)	12 (1–38)	15 (1–36)	24 (17–31)
Trimester of pregnancy at time of vaccination	n (%)			
First (0–13 weeks)	128/256 (50.0)	82/153 (53.6)	46/100 (46)	0
Second (14–27 weeks)	78/256 (30.4)	43/153 (28.1)	33/100 (33)	2
Third (28+ weeks)	50/256 (19.5)	28/153 (18.3)	21/100 (21)	1

*Reports received and processed through March 16, 2021; **Brand unknown in one report

†Based on the Code of Federal Regulations if one of the following is reported: death, life-threatening illness, hospitalization or prolongation of hospitalization, permanent disability, congenital anomaly or birth defect

Most common signs and symptoms among pregnant persons following COVID-19 vaccination reported to VAERS

All COVID-19 vaccines (n=237)		Pfizer-BioNTech COVID-19 vaccine (n=122)		Moderna COVID-19 vaccine (n=110)		Janssen COVID-19 vaccine (n=5)	
Adverse event†	N (%)	Adverse event†	N (%)	Adverse event†	N (%)	Adverse event†	N (%)
FATIGUE	65 (27.4)	FATIGUE	36 (29.5)	FATIGUE	27 (25.0)	HEADACHE	3 (60)
HEADACHE	60 (25.3)	HEADACHE	33 (27.0)	HEADACHE	24 (21.8)	PYREXIA	3 (60)
CHILLS	46 (19.4)	CHILLS	30 (24.6)	PAIN IN EXTREMITY	24 (21.8)	NAUSEA	2 (40)
PAIN IN EXTREMITY	40 (16.9)	PAIN	22 (18.0)	NAUSEA	19 (17.3)	MYALGIA	2 (40)
PAIN	40 (16.9)	NAUSEA	17 (13.9)	PAIN	18 (16.4)	FATIGUE	2 (40)
NAUSEA	38 (16.0)	PYREXIA	17 (13.9)	CHILLS	16 (14.5)	OROPHARYNGEAL PAIN	1 (20)
PYREXIA	35 (14.8)	PAIN IN EXTREMITY	16 (13.1)	INJECTION SITE ERYTHEMA	15 (13.6)	FLUSHING	1 (20)
DIZZINESS	26 (10.9)	DIZZINESS	15 (12.3)	PYREXIA	15 (13.6)	MUSCLE TIGHTNESS	1 (20)
INJECTION SITE PAIN	25 (10.5)	INJECTION SITE PAIN	14 (11.4)	INJECTION SITE PRURITUS	12 (10.9)	LOSS OF CONSCIOUSNESS	1 (20)
INJECTION SITE ERYTHEMA	17 (7.2)	VOMITING	11 (9.0)	DIZZINESS	10 (9.1)	INJECTION SITE PAIN	1 (20)

* Reports received and processed through March 16, 2021; †Adverse events are not mutually exclusive

Pregnancy and neonatal specific conditions among pregnant persons following COVID-19 vaccination reported to VAERS*

Characteristic	All	Pfizer-BioNTech	Moderna	Janssen
Total reports	108	69	38	0
Spontaneous abortion/miscarriage	75 [†]	52	22	0
Vaginal bleeding	6	1	5	0
Preterm delivery	5	4	1	0
Stillbirth	3	2	1	0
Preeclampsia	3	2	1	0
Premature rupture of membranes	3	2	1	0
Fetal hydrops	2	0	2	0
Neonatal death	2	2	0	0
Other ^a	9	4	5	0

*Reports received and processed through March 16, 2021

[†] For one report of spontaneous abortion brand of vaccine unknown

^aOther reports include: for Pfizer one report each of shortened cervix, painful contractions, periventricular leukomalacia, placental abruption; for other Moderna one each of calcified placenta, leakage of amniotic fluid, gestational diabetes, large for gestational age, gestational hypertension

Characteristics of spontaneous abortion reports (n=75)

Characteristic	
Pfizer: 52 Moderna: 22 Unknown brand: 1 Janssen: 0	
Maternal age in years, median (range)	32 (20-43)
Age $\geq$ 35 years	21
Onset interval of symptoms in days, median (range)	6 (0-61)
Onset of symptoms: ▪ within 7 days in 40 ▪ within 9-13 days in 9 ▪ $\geq$ 14 days in 23	
Gestational age (n=63) when vaccinated in weeks, median (range)	6 (1-16)
Gestational age at onset < 12 weeks	53
Gestational age at onset $\geq$ 12 weeks	10

Racial and ethnic characteristics of COVID-19 vaccine pregnancy reports submitted to VAERS*

Race/ethnicity	All**	Pfizer-BioNTech	Moderna	Janssen
White	235	126	106	3
Asian	28	17	10	1
Black/African-American	11	5	6	0
Multiracial	13	8	5	0
American Indian/Alaskan native	3	3	0	0
Native Hawaiian or other Pacific Islander	1	0	1	0
Other	6	1	4	1
Missing or unknown	48	31	16	0
Hispanic	24	8	14	1
Non-Hispanic	244	133	108	3
Missing or unknown	77	50	26	1

*Reports received and processed through March 16, 2021; **Brand unknown in one report

Data mining analysis

- Empirical Bayesian data mining conducted by FDA did not detect any disproportionality alerts for any pregnancy/neonatal-specific or non-pregnancy-specific adverse events for any COVID-19 vaccine in women aged 16-54 years

Summary

- ❑ Most common signs and symptoms reported were systemic and local reactions similar to non-pregnant women in VAERS
- ❑ Most common pregnancy-specific condition was spontaneous abortion:
 - No disproportionality: comparable to other maternal vaccines in VAERS
 - Miscarriage relatively frequent in pregnancy
- ❑ Safety profile of Covid-19 vaccine reports in pregnant persons in VAERS is reassuring

QUESTIONS?

Thank you

For more information, contact CDC

1-800-CDC-1172 (1-800-455-1172)

 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

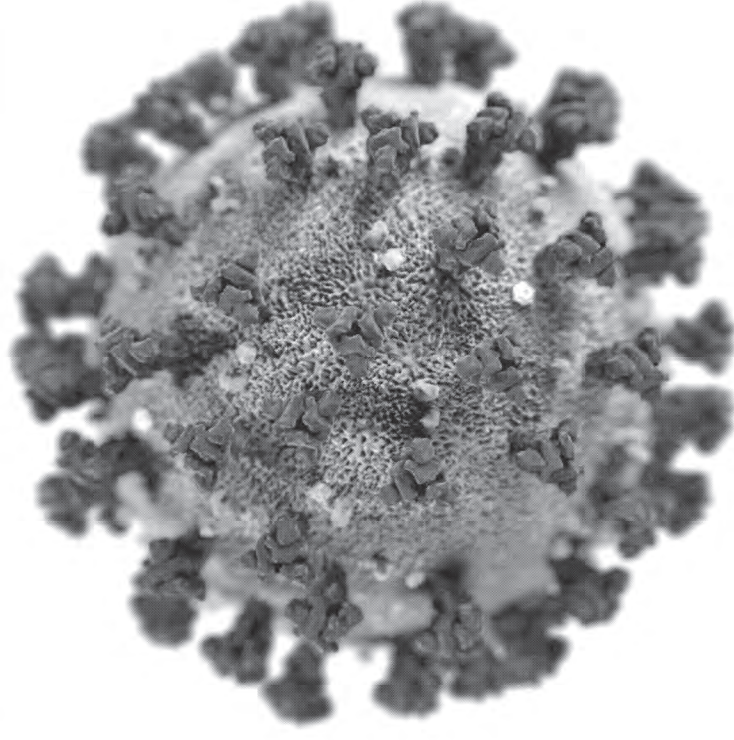


PSICOVID_00010521

Update: Pregnancies in v-safe

Tanya Myers, PhD, MSc

March 22, 2021



Outline

- Overview of v-safe
- Basic demographics of pregnancies in v-safe
- Reactogenicity reported on day 1
- Current findings and next steps

6:59 PM
v-safe-call-center-screening.ung

Symptom Check

Have you had any of these symptoms today where you got the shot (injection site)? *

Select all that apply.

☐ Pain
☐ Redness
☐ Swelling
☐ Itching
☐ None

Have you experienced any of these symptoms today? *

Select all that apply.

☐ Chills
☐ Headache
☐ Joint pains

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

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

vaccine recipient completes web survey

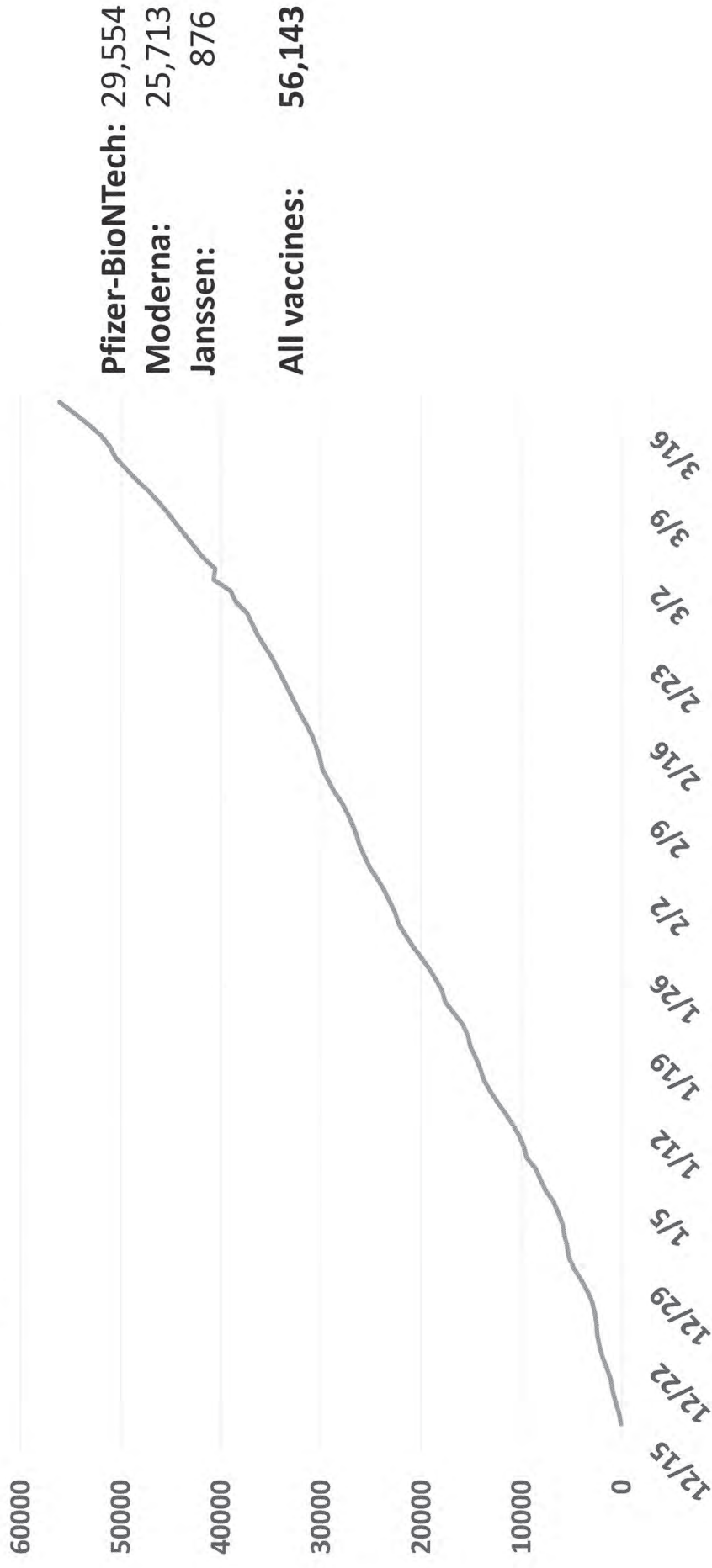


4. pregnancy registry team conducts outreach to assess eligibility for registry and obtain consent for enrollment and follow-up

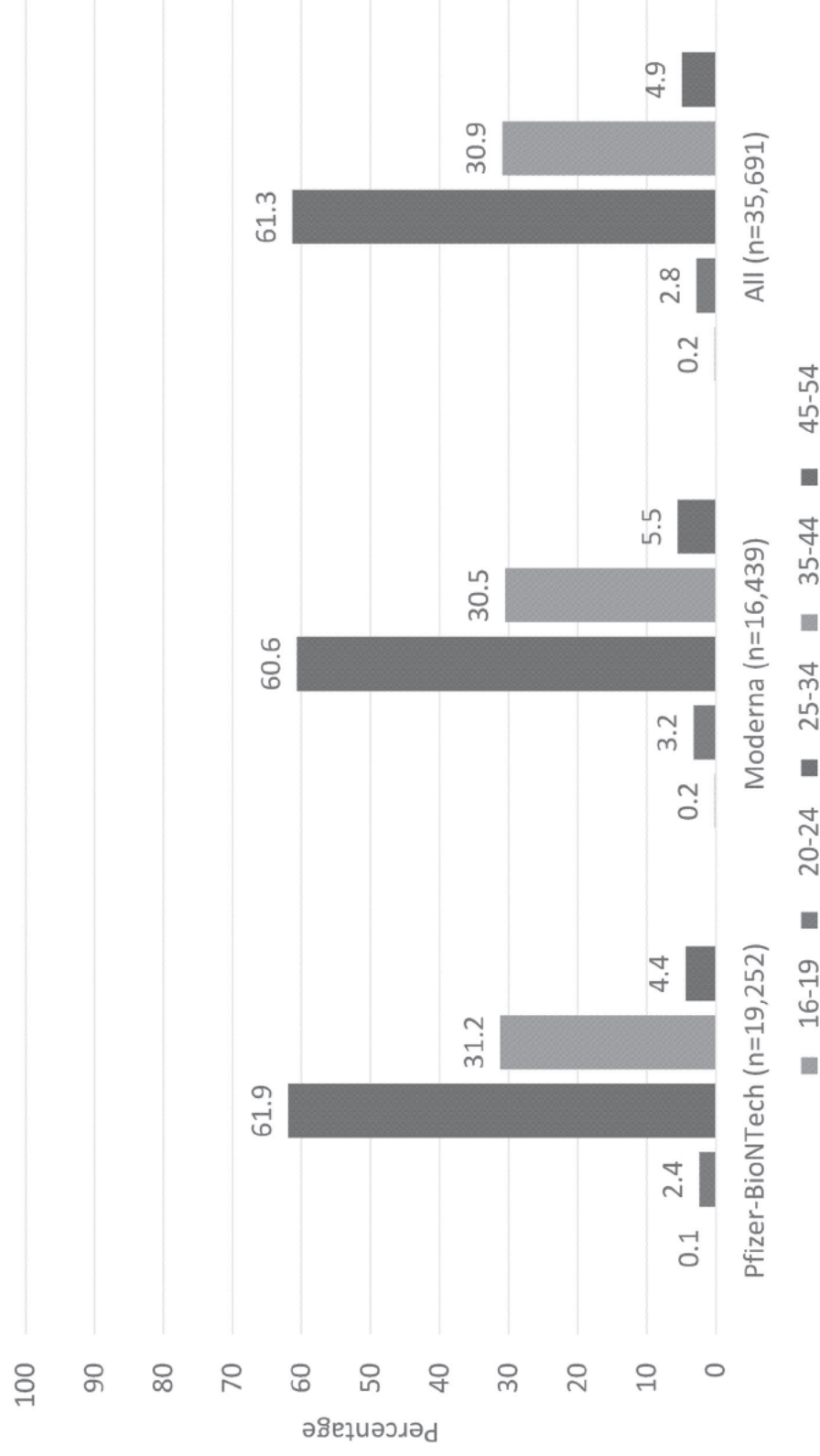
Call center



Pregnancies recorded in v-safe, 3/19/2021

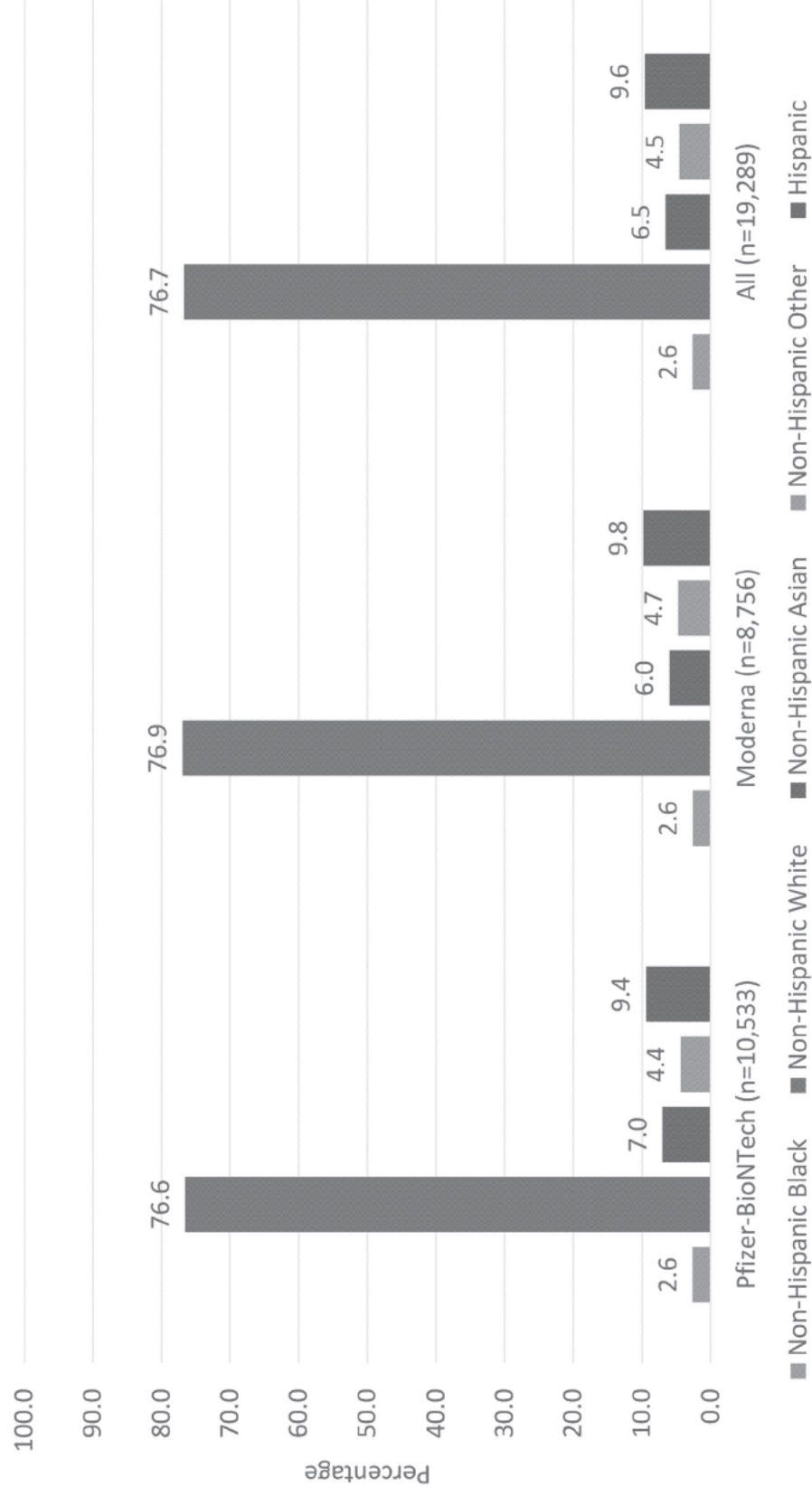


Pregnancies reported in v-safe, by age at 1st dose^a



^a v-safe data reporting through 2/28/2021

Pregnancies reported in v-safe, by race/ethnicity



^a v-safe data reporting through 2/28/2021, race/ethnicity data capture in >50%

Solicited local and systemic reactions

- Have you had a fever or felt feverish?

Do you know your highest temperature reading from today?

- Have you had any of these symptoms at or near the injection site?

pain

swelling

redness

itching

- Have you experienced any of these symptoms?

chills

fatigue or tiredness

abdominal pain

headache

nausea

rash (not at site)

joint pain

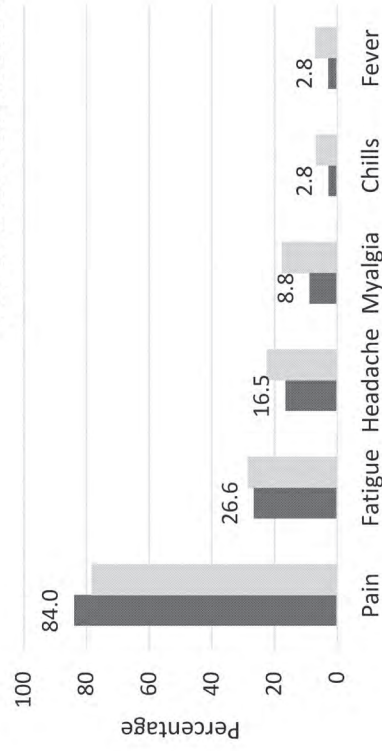
vomiting

muscle or body aches

diarrhea

Comparison of solicited reactions in pregnant and non-pregnant v-safe participants, day 1 after vaccine, December 14, 2020 - February 28, 2021

Pfizer-BioNTech dose 1

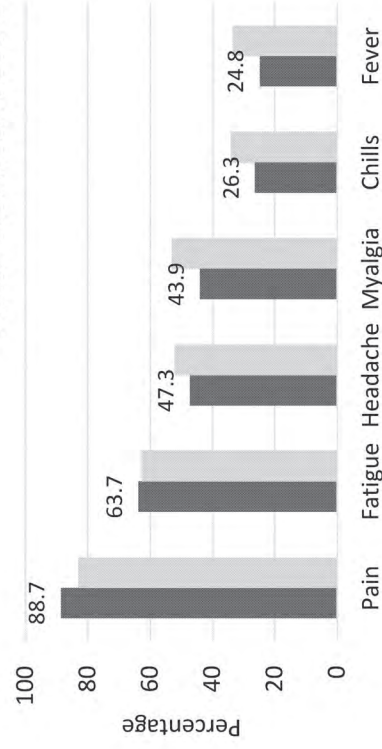


Moderna dose 1

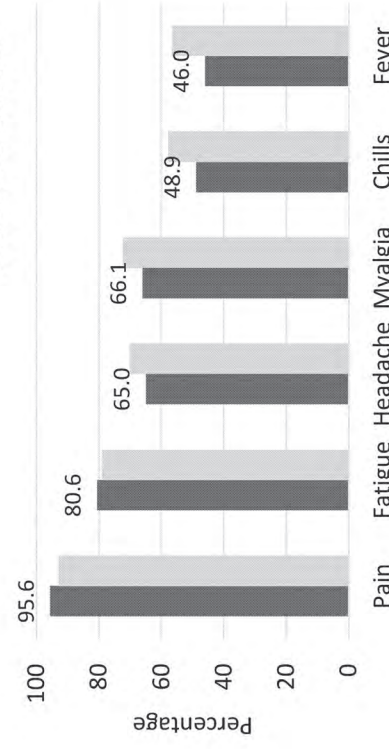


■ Pregnant persons
■ Non-pregnant women

Pfizer-BioNTech dose 2

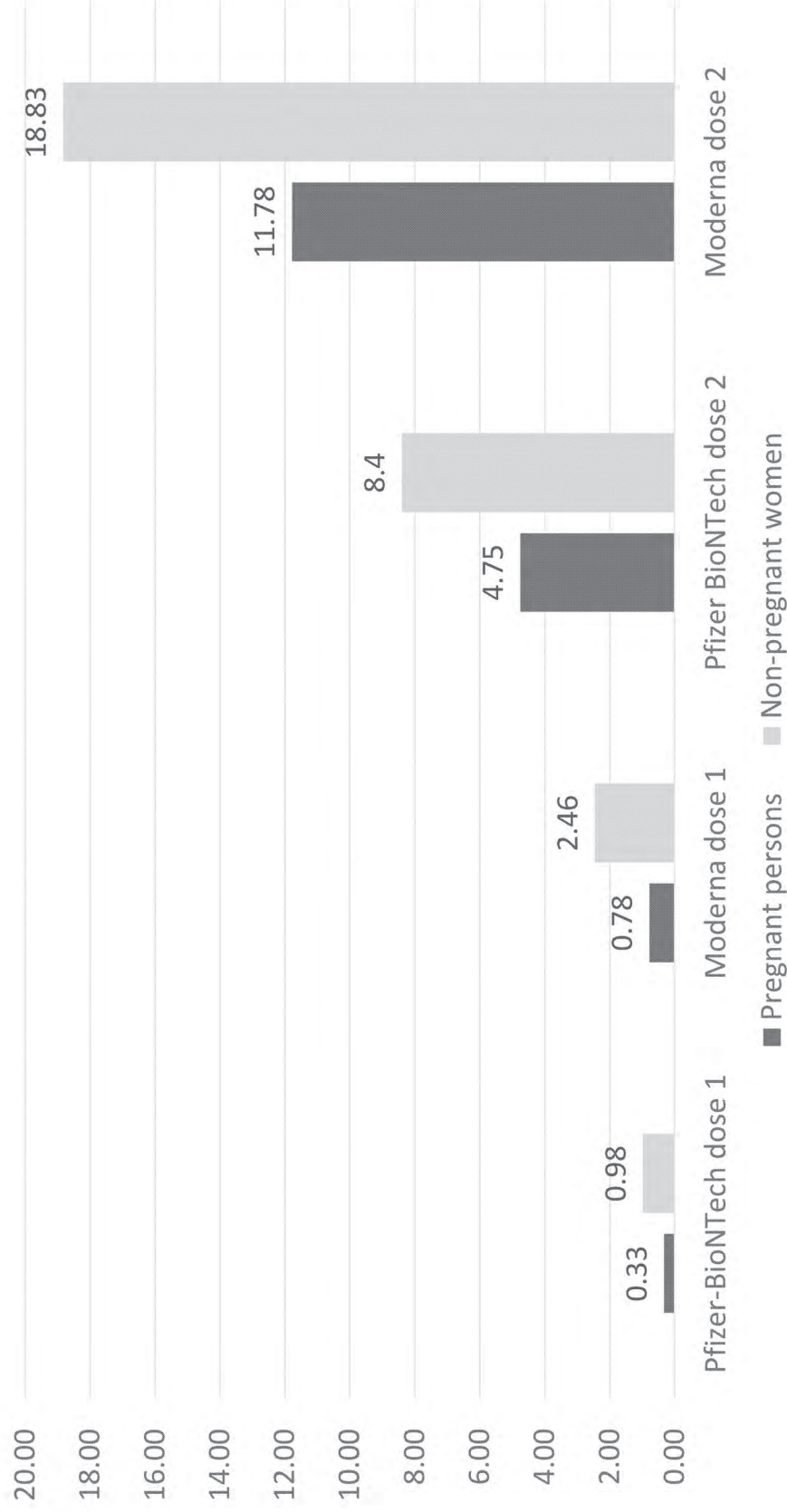


Moderna dose 2



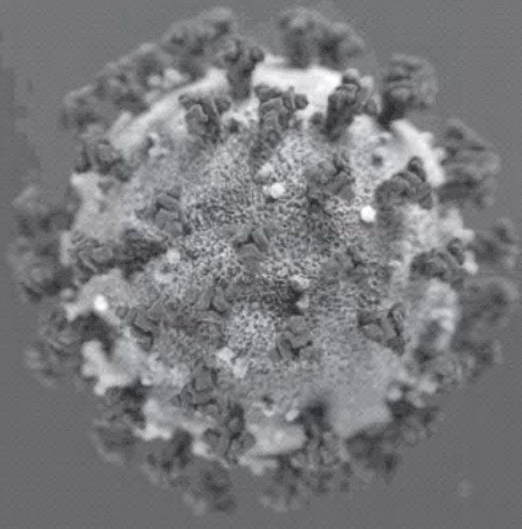
■ Non-pregnant women

Reported fever $\geq 38^{\circ}\text{C}$ on day 1 after mRNA vaccines in pregnant and non-pregnant v-safe participants, December 14, 2020 - February 28, 2021



Current findings and next steps

- Pregnant participants reported more reactogenicity after dose 2 of both mRNA vaccines (similar to findings for all v-safe participants)
- Injection pain reported more frequently in pregnant participants as compared to non-pregnant women, other solicited local and systemic reactions reported less frequently or similarly
- Fever $\geq 38^{\circ}\text{C}$ was reported less frequently in those identified as pregnant in v-safe as compared to non-pregnant women
- Next pregnancy session: first look at Janssen vaccine



For more information, contact CDC


 www.cdc.gov

Thank you

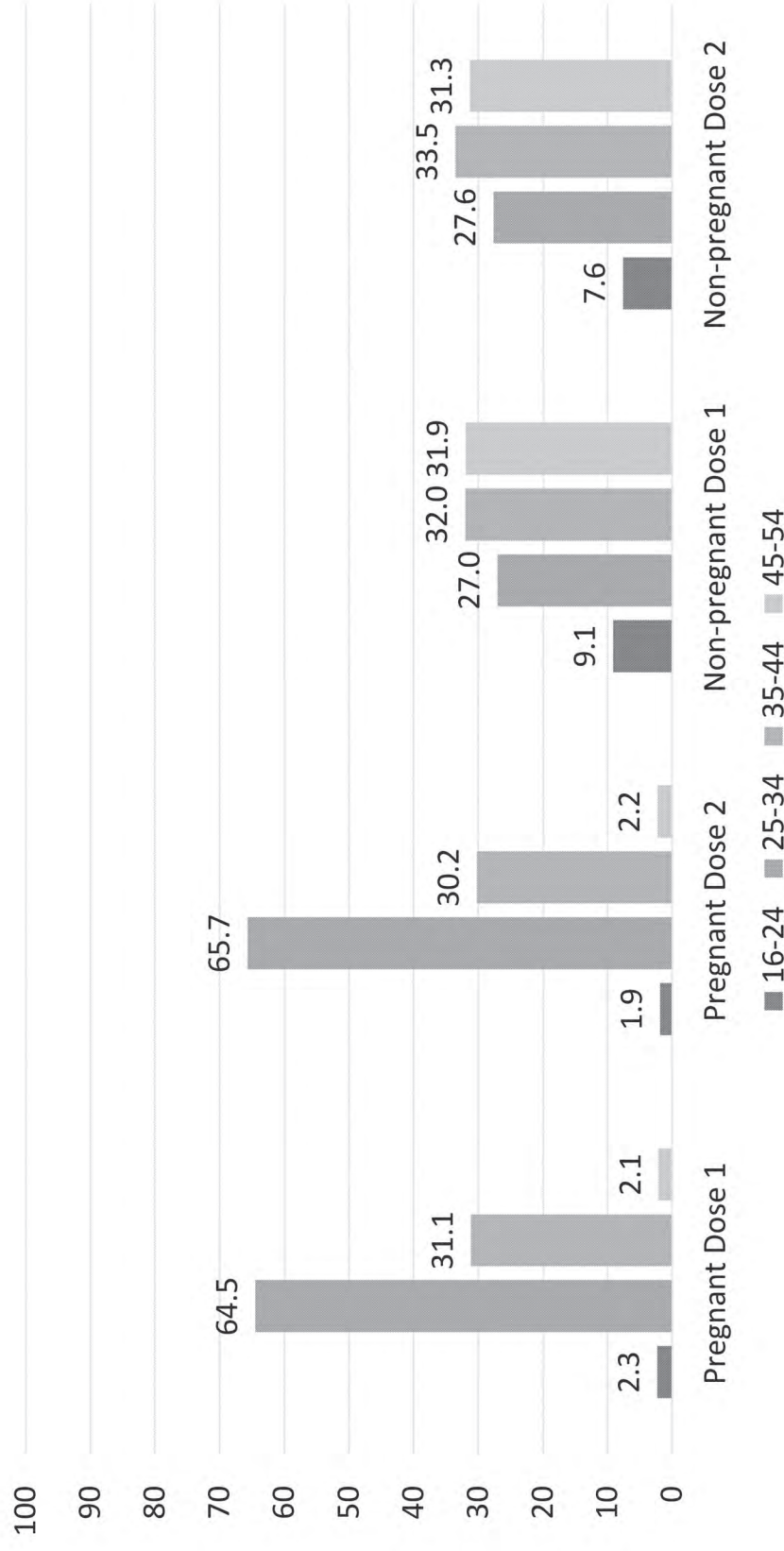
The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



PSICOVID_00010532

Backup Slides

Age distribution in pregnant persons and non-pregnant women (16-54 years), day 1 survey respondents



Centers for Disease Control and Prevention



V-Safe Pregnancy Registry

Shin Kim, MPH
Sascha Ellington, PhD
Co-leads v-safe Pregnancy Registry
Vaccine Task Force
Centers for Disease Control and Prevention

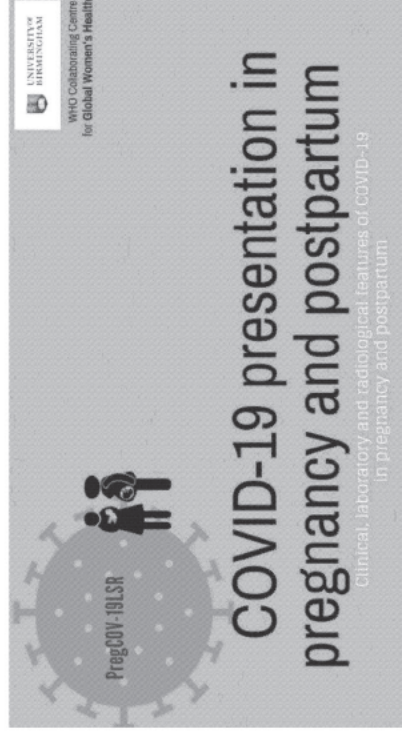
March 22, 2021

Outline

- Background: COVID-19 in Pregnancy
- Number of pregnant persons enrolled to date by vaccine and geographic distribution
- NEW: v-safe follow-up survey
- Description of pregnant participants and pregnancy outcomes
- Next steps

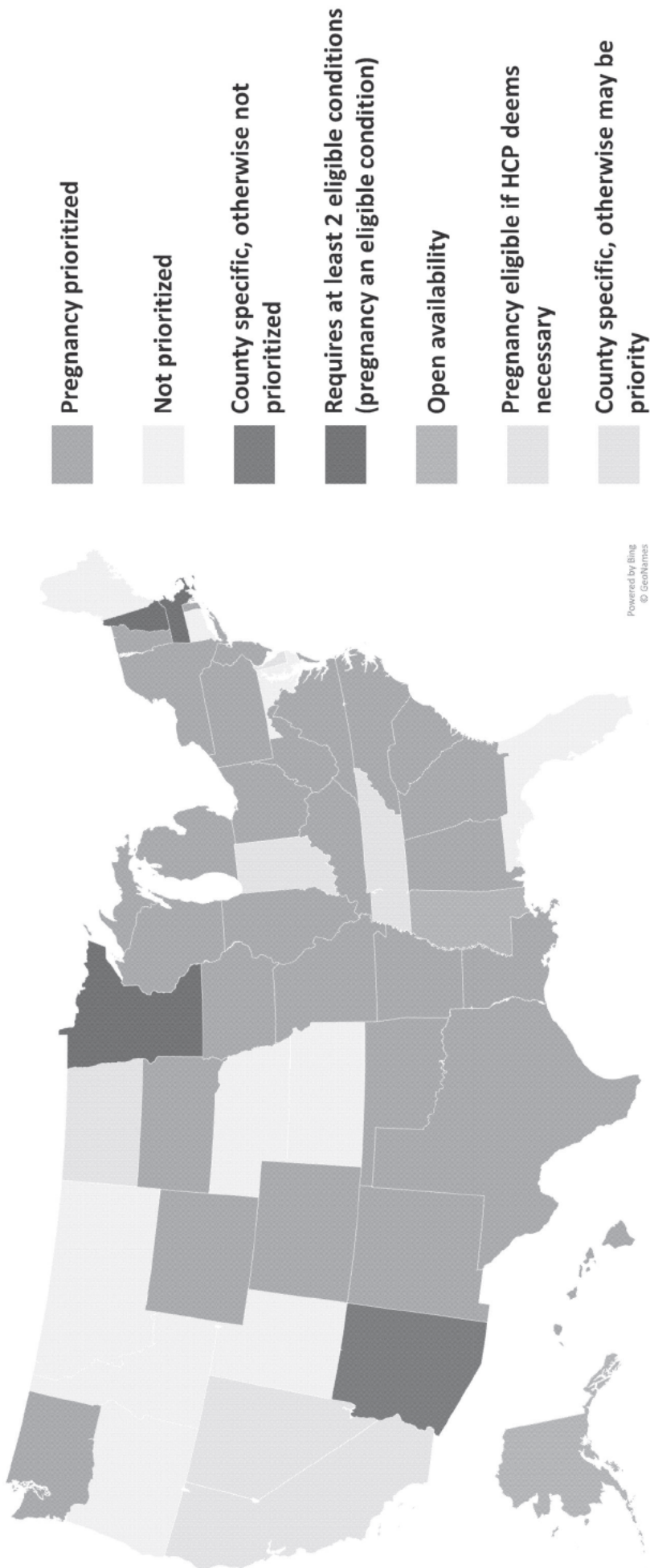
COVID-19 in Pregnancy

- Fever and cough most common occurring in about 40% of pregnant people with COVID-19
- Compared to non-pregnant people, pregnant people are at increased risk of severe illness from COVID-19 and death
- COVID-19 associated with pregnancy complications and maternal death
 - Admission to ICU (OR=2.85, 95% CI: 1.08-7.52)
 - Preterm birth (OR=1.47, 95% CI: 1.14-1.91)
 - Maternal death (OR=2.85, 95% CI: 1.08-7.52)
- Effects on fetus and neonate
 - Stillbirth (OR=2.84, 95% CI: 1.25-6.45)
 - Neonatal intensive care unit (OR=4.89, 95% CI: 1.87 to 12.81)



Allotey J, Stallings E, Bonet M et al. Update to living systematic review on covid-19 in pregnancy. BMJ 2021; March 10 <https://www.bmj.com/content/bmj.m3320.full.pdf>
Zambrano LD, Ellington S, Strid P, et al. Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status — United States, January 22–October 3, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1641–1647. DOI: <http://dx.doi.org/10.15585/mmwr.mm6944e3>

States Prioritizing Pregnancy for COVID-19 Vaccinations



As of March 17, 2021

v-safe and pregnancy registry (As of 3/19/2021; 5 AM ET)

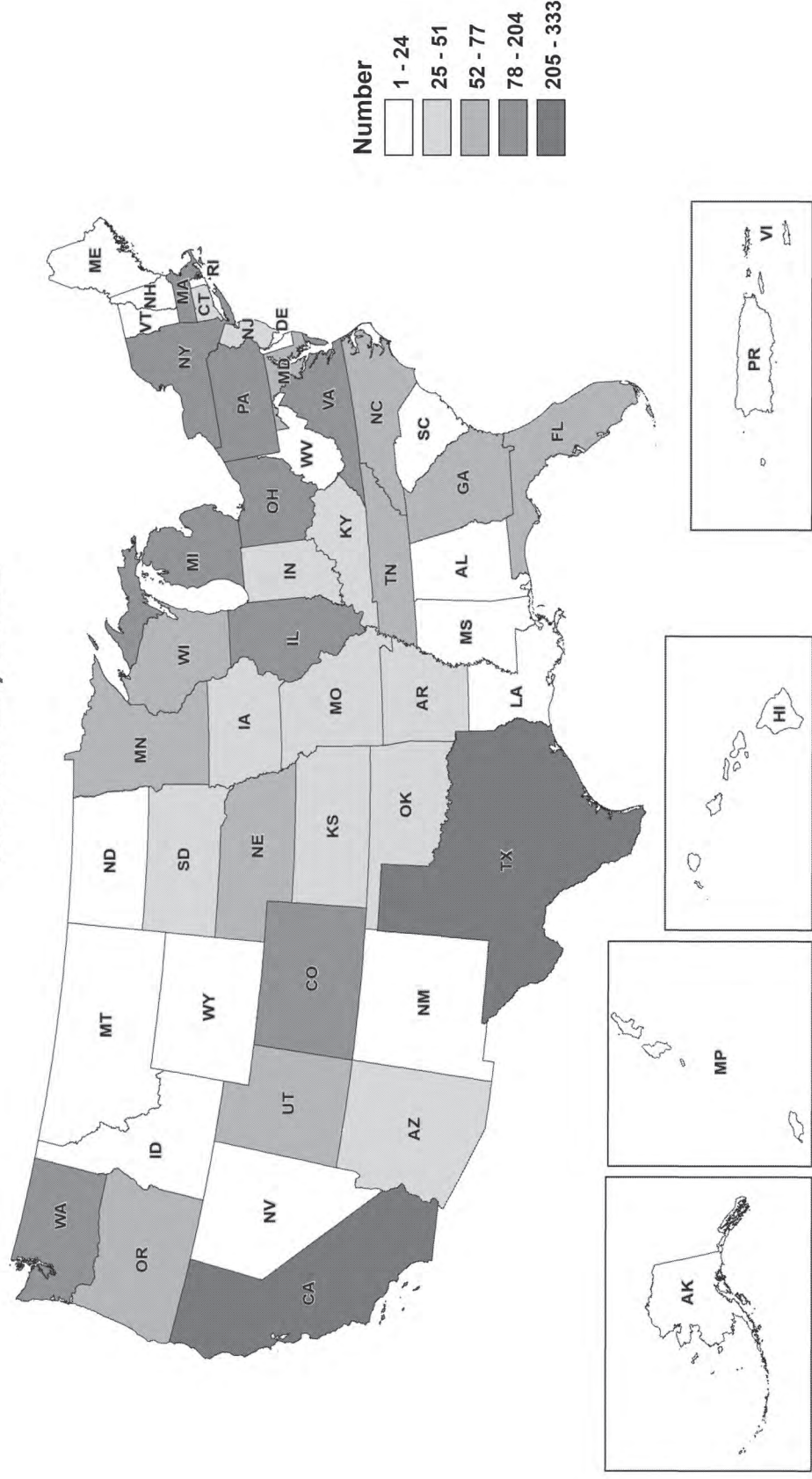
	All Vaccines N	Pfizer- BioNTech N	Moderna N	Janssen N
Potential pregnancies in v-safe	56,079	29,554	25,713	812
Pregnancy registry				
Enrolled	3523	1926	1597	--
Not Eligible ^a	202	109	93	--
Refused/Declined ^b	58	39	19	--
Unreachable ^c	627	391	236	--

^a Eligibility assessment determines whether vaccination was during pregnancy or within 30 days of last menstrual period

^b Refused indicates those for whom eligibility could not be fully assessed because participant chose not to engage with pregnancy registry team; declined indicates those who were eligible to participate but chose not to enroll

^c Unreachable indicates those that were not reached after at least 2 attempted calls 3-days apart or due to language barriers (updated weekly)

V-Safe Pregnancy Registry Enrolled Participants, March 17, 2021



NEW v-safe follow-up survey

Pregnancy Question[^]:

Dose 1: Initial survey, Day 21, 42^{^^}

Dose 2: Initial survey, Day 21, 42, Month 3, 6, 12^{^^}

NEW Follow-up survey

Question 1: Pregnancy status

Question 2: Permission to contact

Question 3: Availability

[^]Will be asked of all non-male sex v-safe participants (i.e., female, unknown, prefer not to say)

^{^^}Question will be hidden if vaccine recipient answers "yes" to a prior pregnancy status question for the respective dose

 v-safe Pregnancy Registry

Introduction text about the Pregnancy Registry.

Pregnancy Status

Please choose which of the following scenarios best describes you *

☐ Pregnant at time of vaccination

☐ Pregnant after vaccination

☐ Not pregnant at or since vaccination

Permission to Contact

Please select your choice below *

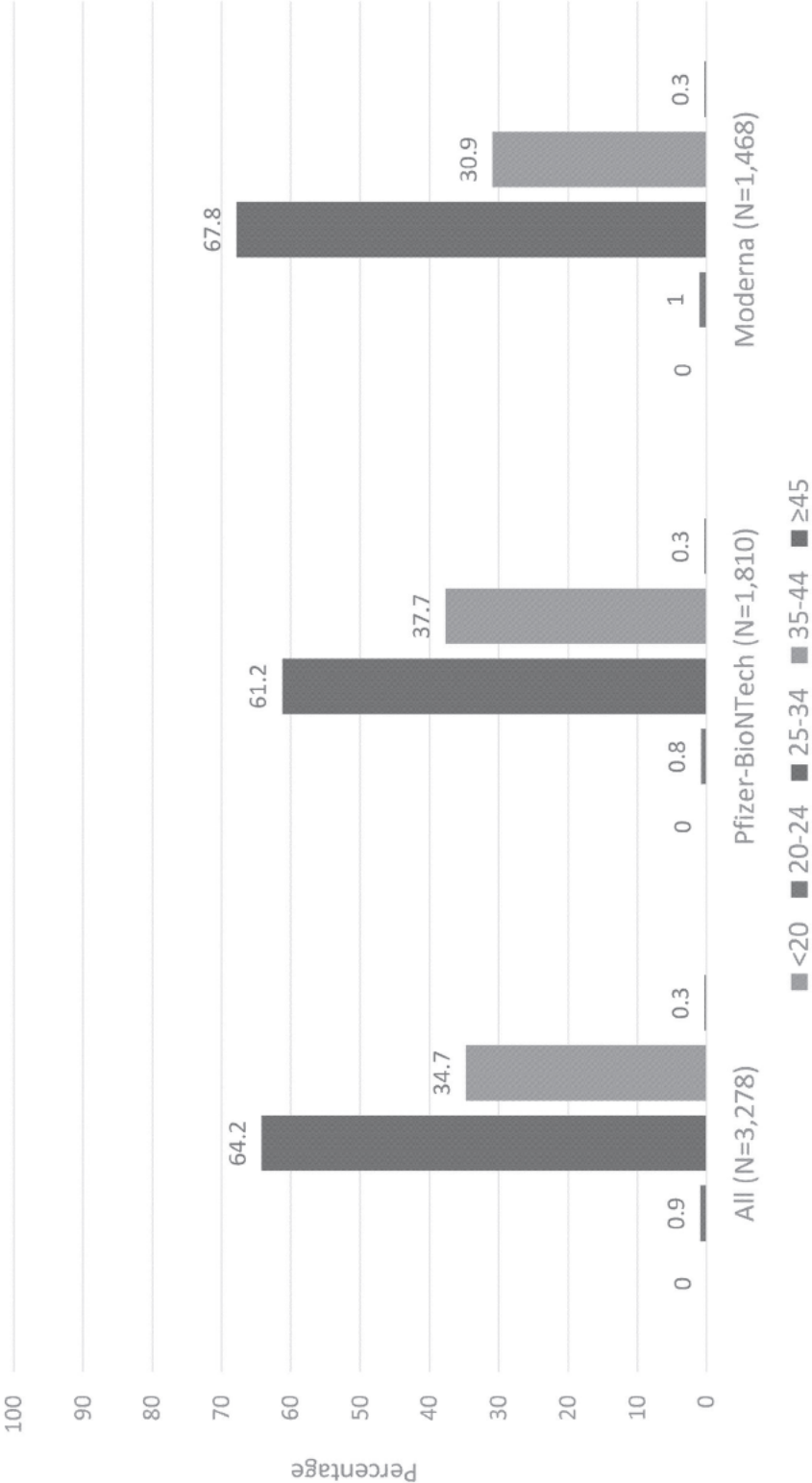
☐ Yes, I would like someone to contact me so that I can learn more about the CDC's v-safe pregnancy registry

☐ No, Please do not call me, I do not want to participate

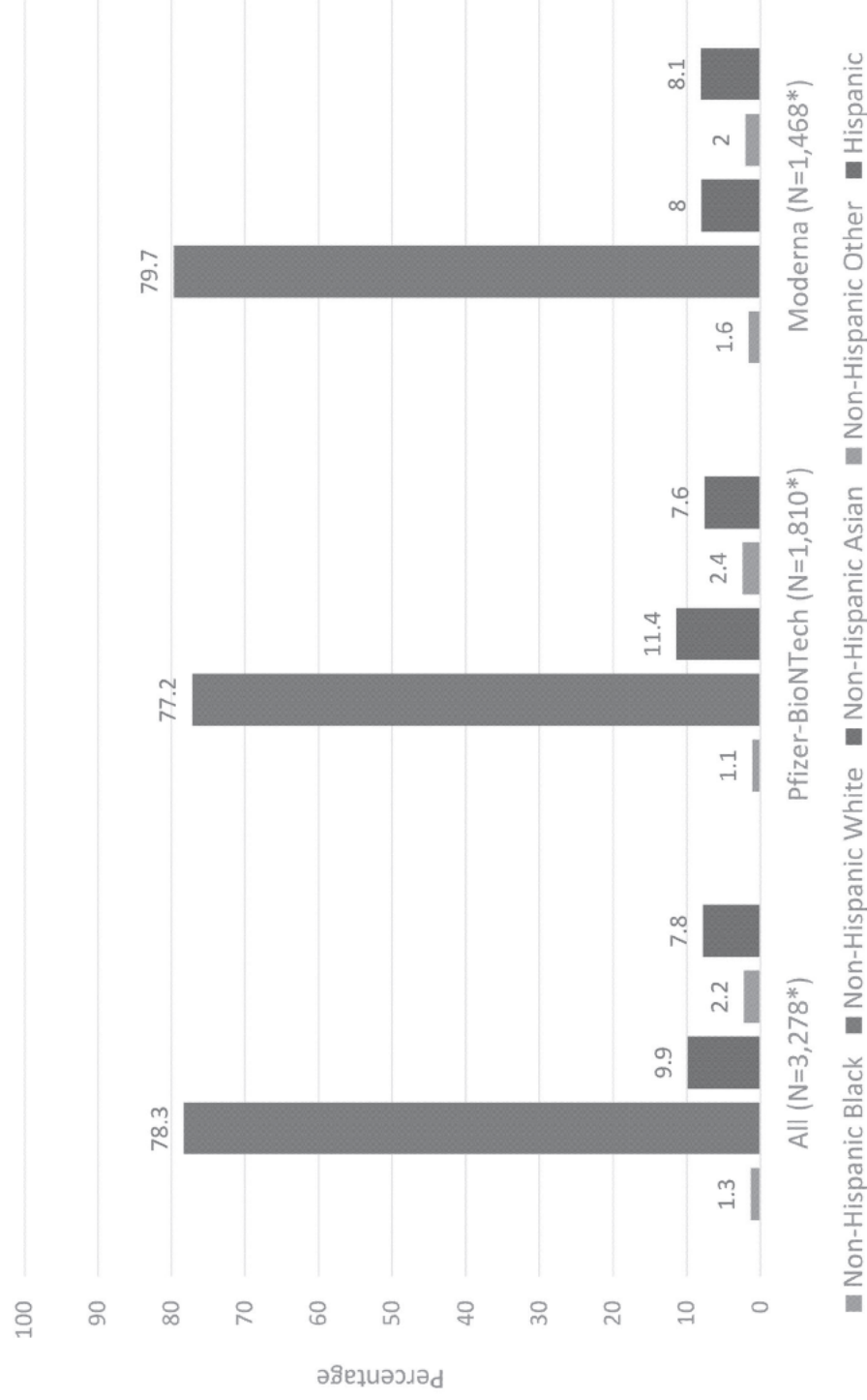


Registry Participant Characteristics and Pregnancy Outcomes: enrolled as of 03/16/2021 at 8:15am

Registry Participant Characteristic: Age at 1st Eligible Vaccine Dose



Registry Participant Characteristic: Race/Ethnicity



*Missing/Declined N=14 (All), N=5 (Pfizer), N=9 (Moderna)

Self-Reported Vaccine Priority Group[^]

	Vaccine manufacturer					
	All		Pfizer-BioNTech		Moderna	
	n	%	n	%	N	%
Self-Reported Vaccine priority group[^]						
Healthcare personnel only	2,978	90.8	1,659	91.7	1,319	89.9
Non-healthcare essential worker only	42	1.3	17	0.9	25	1.7
Medical condition other than pregnancy only	9	0.3	3	0.2	6	0.4
Pregnancy only	6	0.2	3	0.2	3	0.2
Healthcare personnel and non-healthcare essential worker	23	0.7	11	0.6	12	0.8
Healthcare personnel and medical condition	159	4.9	94	5.2	65	4.4
Healthcare personnel and pregnancy	1	0.0	0	0.0	1	0.1
Healthcare personnel and other	8	0.2	4	0.2	4	0.3
Non-hc essential worker and medical condition	2	0.1	0	0.0	2	0.1
Non-hc essential worker and pregnancy	1	0.0	0	0.0	1	0.1
Non-hc essential worker and other	1	0.0	0	0.0	1	0.1
Medical condition and pregnancy	1	0.0	1	0.1	0	0.0
Medical condition and other	2	0.1	1	0.1	1	0.1

[^]Military, state/federal government employee categorized as non-healthcare essential worker

COVID-19 Infection During Pregnancy

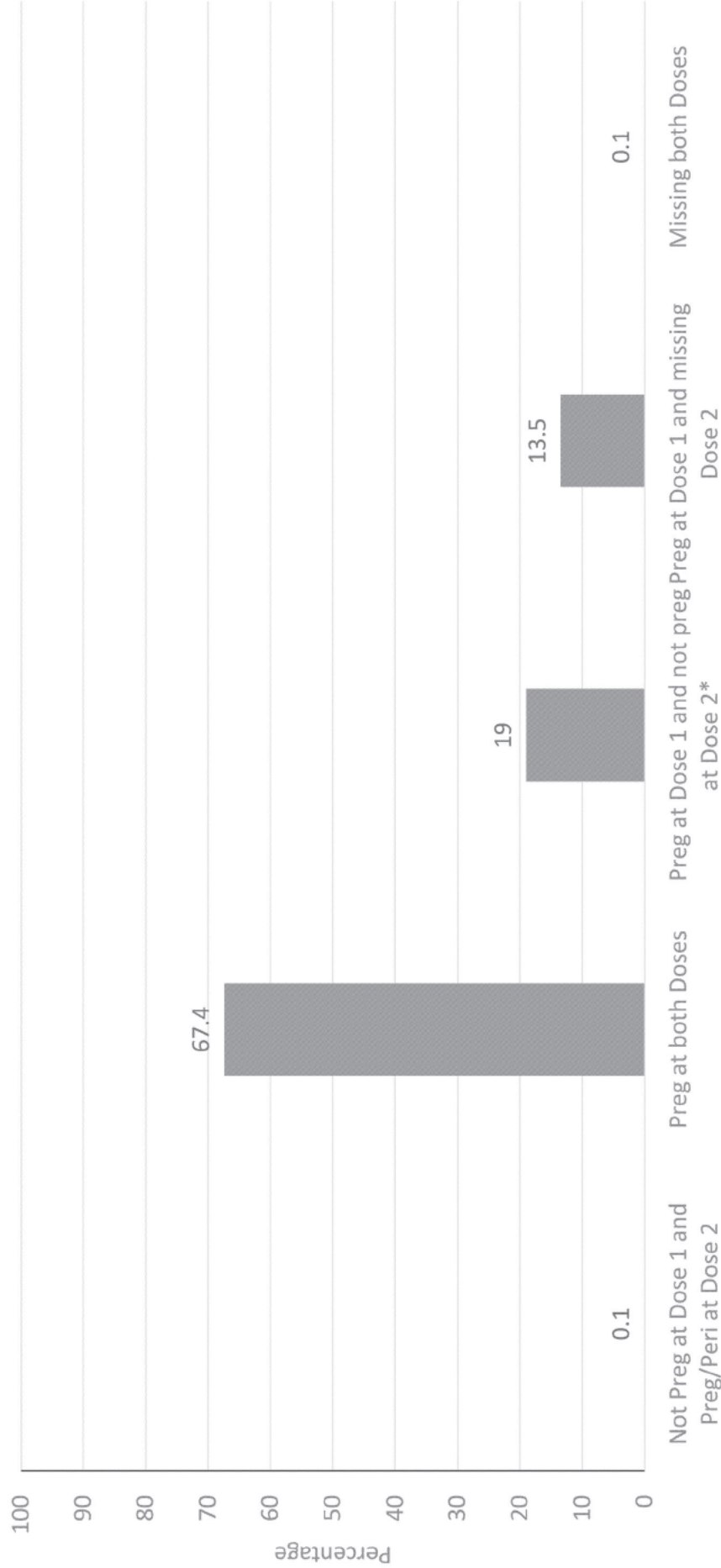
		Dose 1				Dose 2			
		All		Pfizer-BioNTech		Moderna		All	
Characteristics		n	%	n	%	n	%	n	%
COVID-19 infection during pregnancy relative to timing of vaccine dose									
No COVID		3,201	97.7	1,764	97.5	1,437	97.9	3,201	97.7
Prior to vaccination		46	1.4	30	1.7	16	1.1	38	1.2
Within 14 days of vaccine		7	0.2	3	0.2	4	0.3	2	0.1
After 14 days of vaccine		9	0.3	6	0.3	3	0.2	21	0.6
Missing		15	0.5	7	0.4	8	0.5	16	0.5

*Three participants with two eligible pregnancies

Timing of 1st Eligible Vaccine Dose

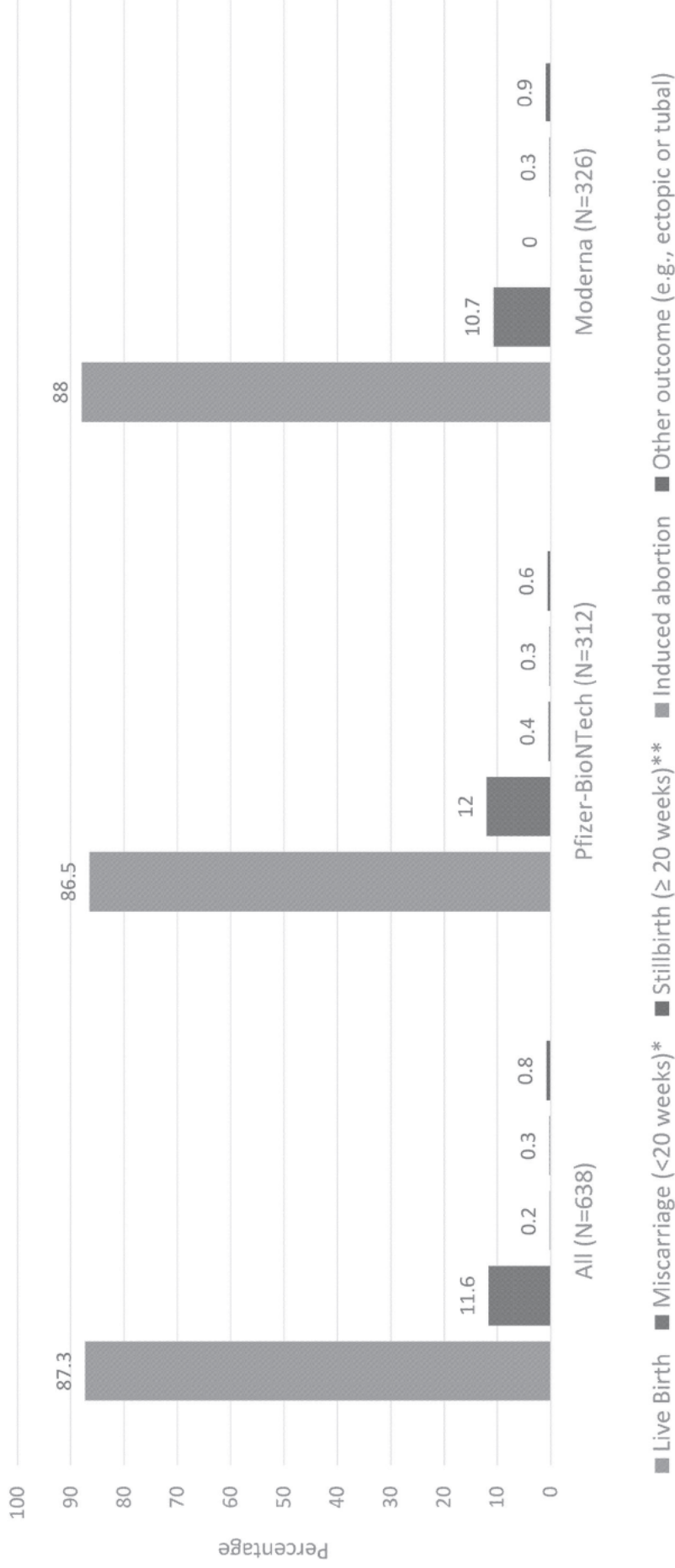
		Vaccine manufacturer					
		All		Pfizer-BioNTech		Moderna	
		n	%	n	%	n	%
	Periconception (within 30 days)	16	0.5	9	0.5	7	0.5
	First trimester (<14 weeks)	920	28.1	505	27.9	415	28.3
	Second trimester (≥14 and <28 weeks)	1,463	44.6	816	45.1	647	44.1
	Third trimester (≥28 weeks)	877	26.8	478	26.4	399	27.2
	Missing	2	0.1	2	0.1	0	0.0

Pregnancy Status by Dose 1 and Dose 2



*Among n=623 (19%), 10.3% resulted in a pregnancy loss

Pregnancy Outcome Among Completed Pregnancies



* Miscarriage <13 weeks is 94.4% of All miscarriage <20 weeks

**Stillbirth denominator is total live born infants + stillbirth (n=568)

Neonatal Outcomes of Interest Among Live Born Infants (n=567*)

Outcomes	Background rate	Self-reported vsafe Registry Overall
Preterm birth (<37 weeks)	8-15%	9.4%
Major congenital anomalies^^	3%	2.3%
Small for gestational age###	3-7%	3.5%
Admitted to NICU	9%	3.4%
Neonatal death	<1%	0.0%

*n=562 third trimester, n=5 second trimester

^^Birth defect diagnosed after delivery only, v-safe all self-reported (n=19); Includes only major congenital anomalies in accordance with the Metropolitan Atlanta Congenital Defects Program Birth defect list

(<https://www.cdc.gov/nccd/dd/birthdefects/macdp.html#:~:text=Since%20MACDP%20began%20tracking%20birth,clinical%20review%20of%20abstracted%20records>); all pregnancies with major congenital anomalies were exposed to COVID-19 vaccines in the third trimester of pregnancy

###Birthweight below the 10th percentile for gestational age and sex using INTERGROWTH-21st Century growth standards

Summary of Findings

- Among pregnant participants who received a vaccine between 12/14/2020 through 02/16/2021, majority were:
 - Between ages 25-44 years old
 - Non-Hispanic White
 - Healthcare personnel
 - Second trimester
 - No COVID-19 infection in pregnancy
 - Live birth
- Most neonatal outcomes are among those with third trimester vaccine (except n=5)
 - Currently do not have 1st and 2nd trimester outcome data as pregnancies are ongoing
 - First live birth outcome expected for 2nd trimester on 3/12 and 1st trimester on 06/19
- Pregnancy and neonatal outcomes of interest are all within background rates

Next Steps-data analysis and upcoming public reporting

- Data Analysis
 - Include Janssen participants next month
 - Oversample by periconception/1st trimester exposure, race/ethnicity, and geography
- Upcoming Public Reporting
 - Disseminate information in peer-reviewed publication (Target NEJM) on: “Preliminary findings of mRNA COVID-19 vaccine safety in pregnant persons, United States – December 2020-February 2021” (in CDC clearance along with a CDC Director commentary on COVID-19 and Pregnancy (Target OBGYN))
 - Communication plan in development
 - WHO presentation: April 6, 2021 on US strategies to vaccinate pregnant women
 - Meeting with Mother-To-Baby Registry

*Infant outcomes require at least 9 months to a year for women vaccinated in the 1st trimester

Discussion

What would we need to strengthen vaccine recommendations for pregnant people:

- Larger numbers of women
- Greater racial, ethnic and occupational diversity
- Medical record abstraction
- Maternal and infant outcomes following 1st and 2nd trimester vaccination

For more information, contact CDC



www.cdc.gov



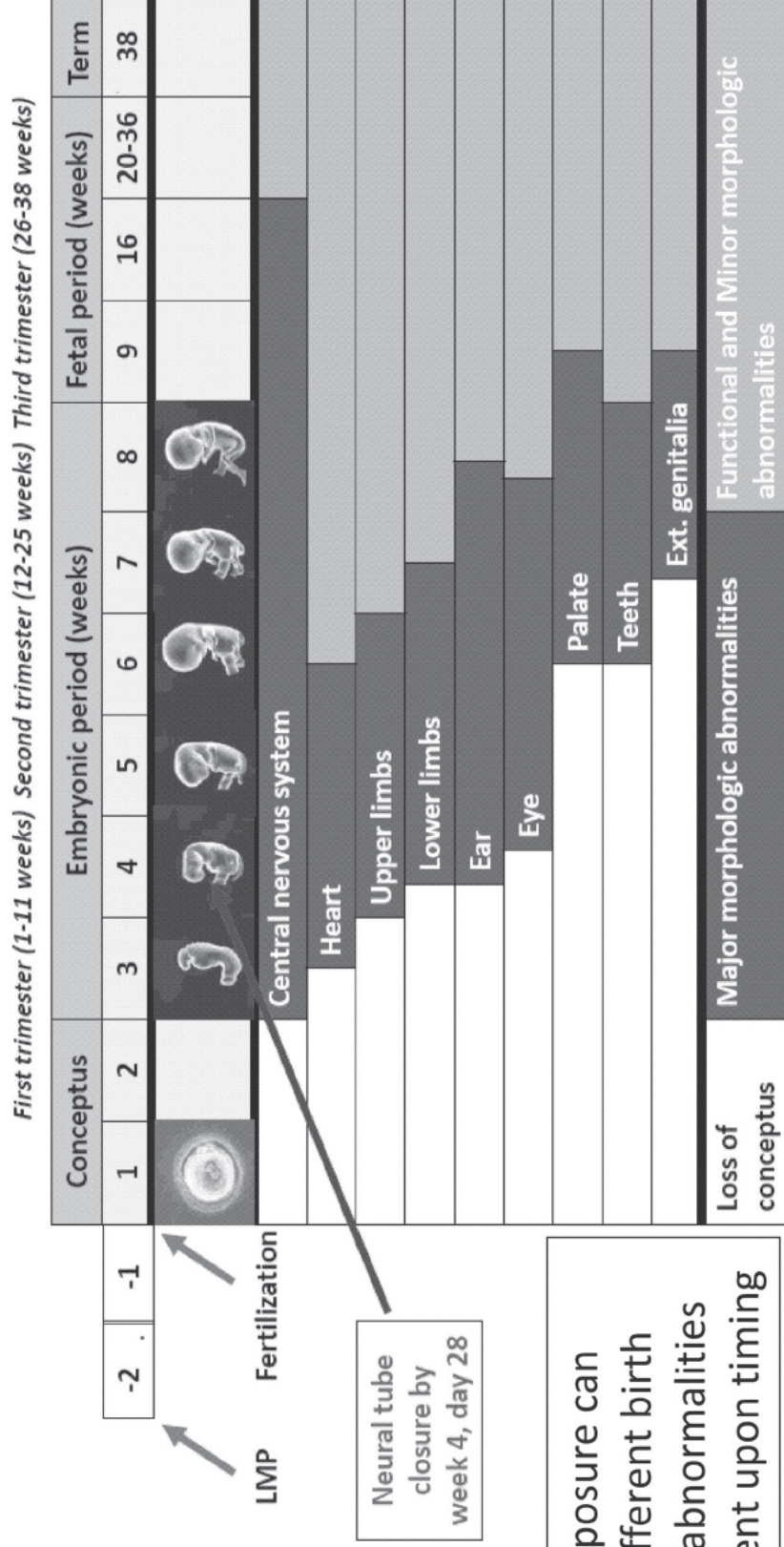
The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



PSICOVID_00010554

Critical Periods of Fetal Development

Human Developmental Timeline



Systematic Review and Meta-analyses: Fever in Pregnancy and Neural Tube Defects in the Offspring (Dreier 2014): Results – case-control studies

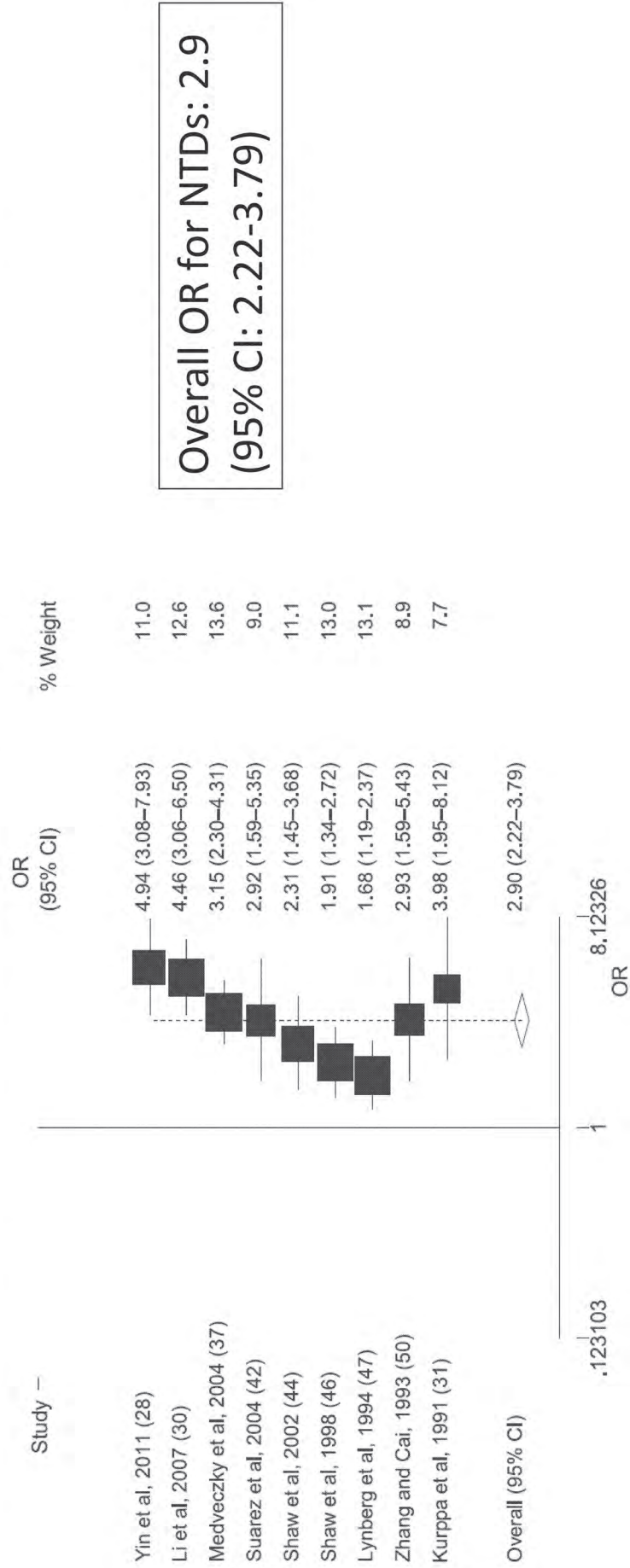


FIGURE 2 Forest plot of case-control studies considering maternal fever and risk of neural tube defects in the offspring.

Systematic Review and Meta-analyses: Fever in Pregnancy and Heart Defects in the Offspring (Dreier 2014): Results – case-control studies

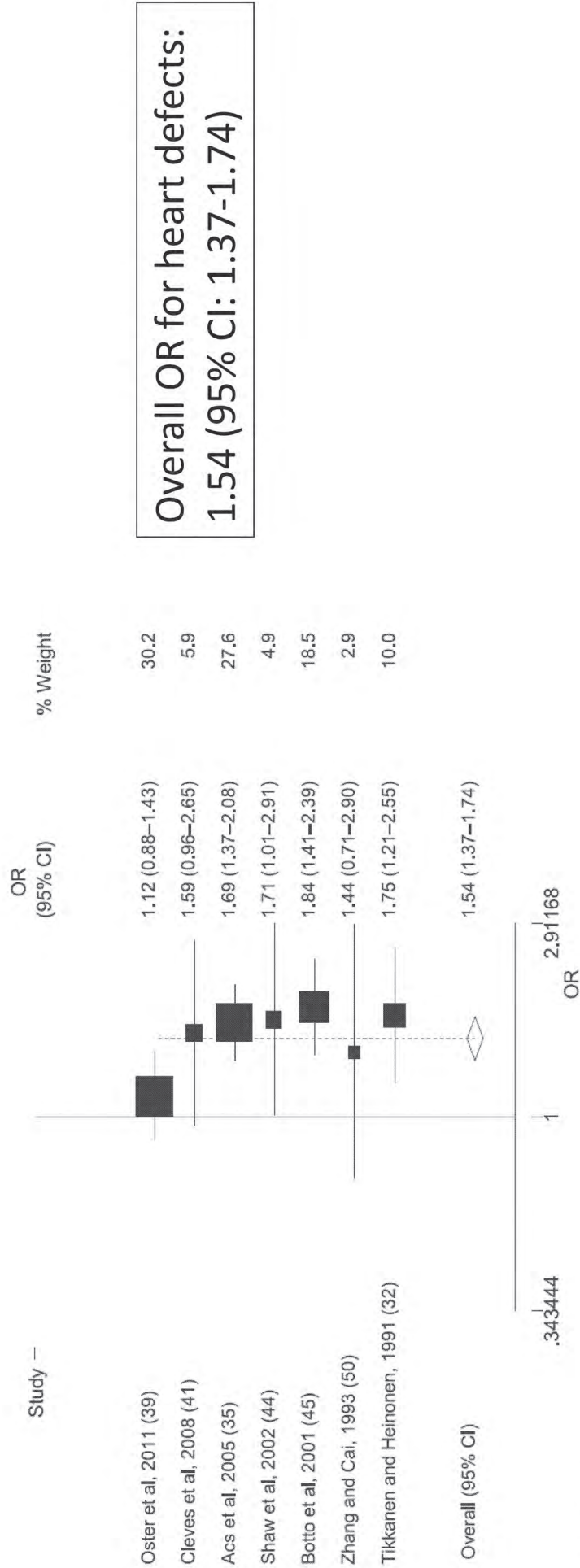


FIGURE 3 Forest plot of case-control studies considering maternal fever and risk of heart defects in the offspring.

Systematic Review and Meta-analyses: Fever in Pregnancy and Oral Clefts in the Offspring (Dreier 2014): Results – case-control studies

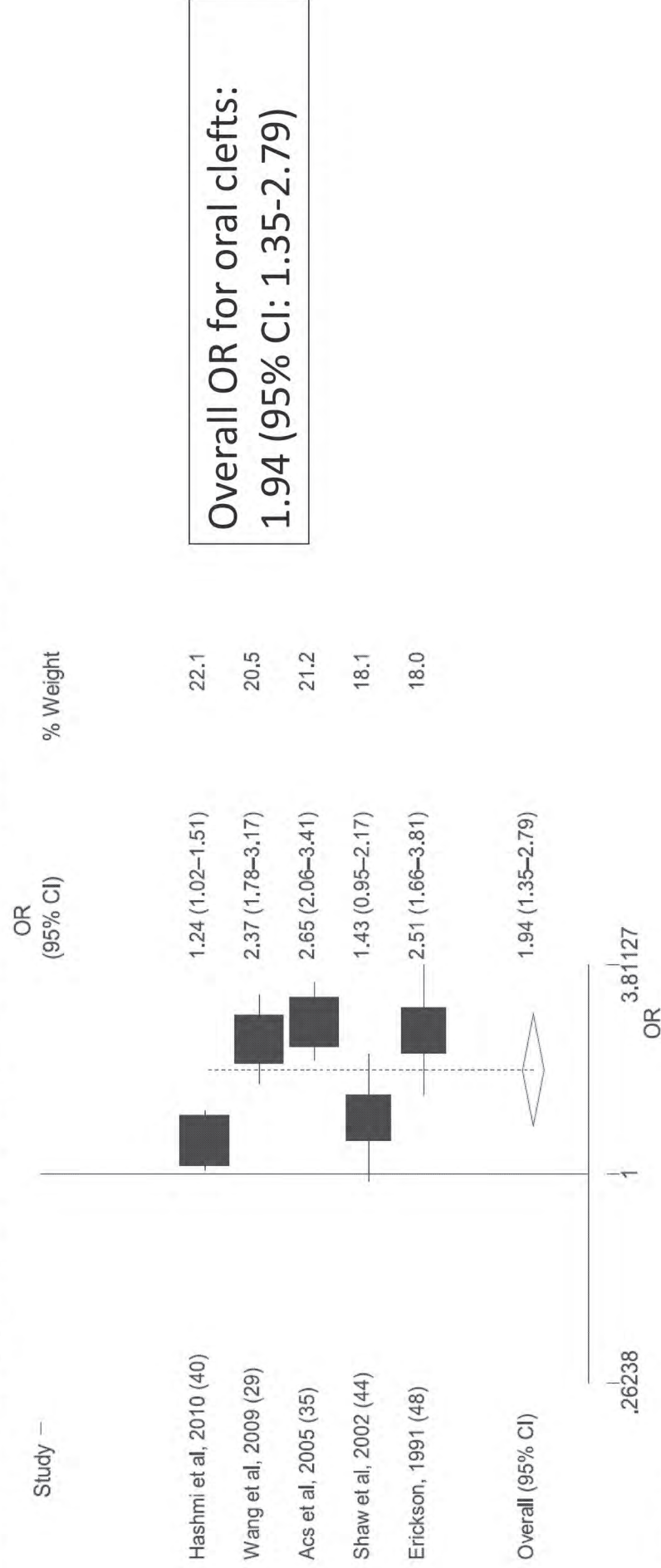


FIGURE 4 Forest plot of case-control studies considering maternal fever and risk of oral clefts in the offspring.

Systematic Review and Meta-analyses: Fever in Pregnancy and Health Impacts in the Offspring (Dreier 2014): Level of Fever

TABLE 3 Effect of Fever During Pregnancy According to Level of Fever

Ref.	Author	Outcome	Low Fever			High Fever			Effect of High Fever
			Definition	Estimate	95% CI	Definition	Estimate	95% CI	
Pregnancy outcomes									
7	Andersen et al, 2002	Fetal death	≤38.9°C	aHR = 0.7	0.5–1.0	>39.0°C	aHR = 0.9	0.6–1.2	No effect
24	Chambers et al, 1998 ^a	Spontaneous abortion	<38.9°C or <24 h	RR = 0.9	0.5–1.8	≥38.9°C and ≥24 h	RR = 1.1	0.6–2.1	No effect
Birth defects									
40	Hashmi et al, 2010	Oral clefts	<38.5°C	aOR = 1.1	0.7–1.8	≥38.5°C	aOR = 1.3	0.8–2.1	No effect
41	Cleves et al, 2008 ^b	Congenital heart defects	<38.3°C	—	—	>38.3°C	—	—	No effect
24	Chambers et al, 1998 ^a	Digital anomalies	<38.9°C or <24 h	RR = 3.1	0.7–13.5	≥38.9°C and ≥24 h	RR = 6.5	2.2–19.8	↑ risk
		Palpebral fissures	<38.9°C or <24 h	RR = 2.6	0.5–8.6	≥38.9°C and ≥24 h	RR = 3.4	1.1–10.9	
		Cleft vulva	<38.9°C or <24 h	RR = 2.5	0.3–21.5	≥38.9°C and ≥24 h	RR = 8.7	2.1–35.1	
		Ear anomalies	<38.9°C or <24 h	RR = 1.4	0.2–10.1	≥38.9°C and ≥24 h	RR = 2.9	0.7–12.4	
Developmental deficits									
16	Atladóttir et al, 2012	Infantile autism	<38.5°C	aHR = 1.3	0.7–2.3	≥38.5°C	aHR = 1.3	0.9–1.8	No effect
		Autism spectrum disorders	<38.5°C	aHR = 1.1	0.8–1.6	≥38.5°C	aHR = 1.0	0.8–1.2	
17	Sun et al, 2011	Epilepsy	37.0–37.9°C	aIRR = 0.5	0.1–2.0	38.5–38.9°C	aIRR = 1.0	0.7–1.4	No effect
			38.0–38.4°C	aIRR = 1.2	0.8–1.8	39.0–39.5°C	aIRR = 1.2	0.9–1.7	
						>39.5°C	aIRR = 1.2	0.8–1.8	

aHR, adjusted hazard ratio; aIRR, adjusted incidence rate ratio; RR, relative risk.

^a Estimates are calculated based on numbers presented in the original article.

^b No estimates provided; only conclusion.

Systematic Review and Meta-analyses: Fever in Pregnancy and Health Impacts in the Offspring (Dreier 2014): Use of Antipyretic Agents

TABLE 4 Effect of Fever During Pregnancy With or Without Use of Antipyretic Agents

Ref.	Author	Outcome	Fever Without Antipyretics		Fever With Antipyretics		Effect of Antipyretic Use
			aOR	95% CI	aOR	95% CI	
Birth defects							
30	Li et al, 2007	Neural tube defects	4.0	2.5–6.5	13.9	3.0–63.6	↑ risk
35	Acs et al, 2005	Neural tube defects	2.7	1.8–4.0	0.7	0.3–1.6	↓ risk ^a
42	Suarez et al, 2004	Neural tube defects	3.9	1.5–10.0	2.4	1.1–5.4	↓ risk
46	Shaw et al, 1998 ^b	Neural tube defects	2.9	1.8–4.8	1.3	0.8–2.2	↓ risk ^a
39	Oster et al, 2011	Right-sided obstructive defects	2.4	1.3–4.3	1.5	0.9–2.4	↓ risk
35	Acs et al, 2005	Heart defects	1.7	1.3–2.2	1.4	0.9–2.1	↓ risk
40	Hashmi et al, 2010	Oral clefts	1.8	1.2–2.8	1.1	0.9–1.5	↓ risk ^a
35	Acs et al, 2005	Cleft lip ± palate	3.3	2.4–4.7	1.4	0.8–2.5	↓ risk ^a
34	Czeizel et al, 2007	Multiple congenital abnormalities	2.2	1.7–2.9	1.6	0.9–2.9	↓ risk
36	Vogt et al, 2005	Congenital cataract	11.1	5.3–23.3	0.6	0.1–4.0	↓ risk ^a
Developmental deficits							
38	Zerbo et al, 2013	Autism spectrum disorders	2.6	1.3–5.0	1.3	0.6–2.8	↓ risk
		Developmental delay	2.7	1.2–6.3	2.1	0.8–5.4	↓ risk

aOR, adjusted odds ratio.

^a Significant differences between risk estimates for fever exposure with or without antipyretic use.

^b Estimates are calculated based on numbers presented in the original article (crude estimates).

A black and white photograph of two hikers with backpacks reaching the peak of a mountain. They are holding hands and raising their arms in triumph. The background shows a vast, hazy landscape with distant mountains and a bright sun or moon low on the horizon.

Meeting with ACIP Vaccines Safety Technical Sub-Group (VaST)

22 March 2021

Melinda, Tree of Life

Melinda's artwork reflects her journey living with HIV.

Janssen Participants

Rick Nettles, US Medical Affairs, Infectious Diseases and Vaccines
Cynthia Robinson, Medical Leader
Luis Anaya Velarde, Medical Safety
Min Wang, Medical Safety
Macaya Douguilh, clinical Development and Medical Affairs, Vaccines
Nina Ahmad, US Medical Affairs, Infectious Diseases and Vaccines
Roy van Heesbeen, Clinical Development, Vaccines
Valerie Oriol Mathieu, Global Medical Affairs, Vaccines

The contents of these slides are confidential and are not be copied, modified or redistributed.

Agenda

AdVac® vector introduction

Pregnancy Cases Reported in AdVac® vaccine programs

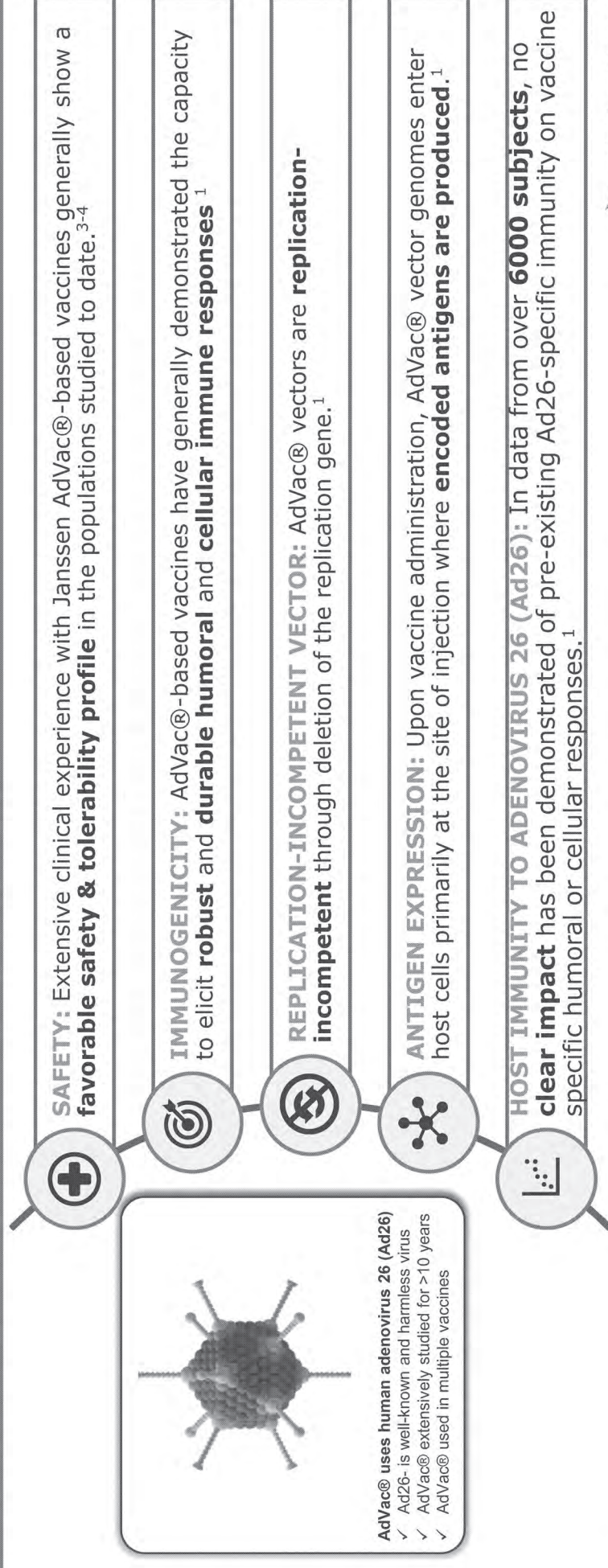
Details on Ebola vaccine program

Details on COVID-19 vaccine program

Conclusions

Janssen uses a replication-incompetent AdVac® vector for several of its vaccines

- Expedited new vaccine development and allows for rapid at-scale manufacturing.
- Deployed in Janssen's COVID-19 Vaccine (FDA, EMA, and WHO emergency / conditional use authorization)¹ and Ebola Vaccine (EMA approved)²
- Several investigational vaccines including HIV, RSV, and Zika.



SOURCES: [1] COVID-19 Vaccine Approvals in FDA; EMA; WHO; [2] Ebola Vaccine Approval in EMA; [3] Custers et al. Vaccine. 2021; [4] Data on File

*ADCC: Antibody dependent cellular cytotoxicity; **ADCP**: Antibody dependent complement deposition; **Th1**: Type-1 T-helper cells.

Clinical Experience with Janssen Advac® based vaccines

Millions of subjects vaccinated to date

- >50 completed and ongoing studies using Ad26-based vaccines
 - RSV, HIV, Ebola, Malaria, Filo, Zika, HPV, COVID-19 vaccine programs
- Government-lead Ebola vaccination program in Rwanda (UMURINZI)
- Start of COVID-19 vaccine rollout: HCWs in South Africa and US (EUA)
- Ad26 dose levels tested: 1×10^9 up to 1.6×10^{11} vp



Adults



Elderly



HIV+ adults



Pregnant & breastfeeding women



Children (1-17 years of age)



Infants (4-11 months of age)

Generally well tolerated in studied populations
Adverse events mostly mild-moderate of rapid onset and short duration

No significant safety issues have been identified in the current adenoviral safety database

Countries:

Argentina, Australia, Belgium, Brazil, Burkina Faso, Canada, Chili, Colombia, Côte d'Ivoire, DRC, Finland, France, Germany, Guinea, Japan, Kenya, Liberia, Malawi, Mali, Mexico, Mozambique, The Netherlands, Nigeria, Peru, Poland, Rwanda, Senegal, Sierra Leone, South Africa, Spain, Sweden, Tanzania, Thailand, Uganda, UK, USA, Zambia, Zimbabwe

Agenda

AdVac® vector introduction

Pregnancy Cases Reported in AdVac® vaccine programs

Details on Ebola vaccine program

Details on COVID-19 vaccine program

Conclusions

Significant Pregnancy Experience Across AdVac® Vaccine Programs

- Extraction from Global Medical Safety (GMS) database as of 31 Dec 2020
- Safety review of adenovirus type 26 (Ad26) vectored vaccines exposure during pregnancy from ongoing and completed clinical trials as well as post-authorization vaccination campaign
- COVID-19 vaccine, Ebola vaccine, HIV vaccine, Filovirus vaccine, HPV vaccine, RSV vaccine, and Zika vaccine
- Of these 47 studies/campaign, pregnancy cases were reported in 22 studies, 4 of which are still blinded



1,631 pregnancies:

- 1,522 reported exposure to Ebola vaccine or placebo in Ebola program
- 101 reported exposure to HIV vaccine or placebo in HIV program
- 8 reported exposure to COVID-19 vaccine or placebo in COVID-19 program

Vaccine Exposure During All Pregnancy Trimesters in AdVac® Vaccine Programs

Vaccine	Exposure within 3 months prior to conception	1 st Trimester	2 nd Trimester	3 rd trimester	Unknown	Total
EBL	418	265	239	266	334	1522
HIV	43	10	3	1	44	101
COV	3	5	-	-	-	8
Total	464	280	242	267	378	1631

Most exposure to vaccine occurred prior to conception or during the first trimester

Timing of vaccine exposure during pregnancy dependent on accurate reporting of LMP or EDD* which is frequently not reported or inaccurate*

[1] Data on File. Global Medical Safety Contribution for the Cumulative Review of Pregnancy Cases Reported in the Janssen Adenoviral 26 Vectored Vaccine Programs. 23 January 2021

*LMP: Last Menstrual Period, EDD: Estimated Date of Delivery

Pregnancy outcomes in Advac® Vaccine Programs

1,631 pregnancies

939 pregnancies had final outcomes reported

781 healthy baby

158 other outcomes including:

Pregnancy stopped

102 spontaneous abortions + 2 abortion incomplete

9 elective abortions + 6 induced abortions

1 abortion and 1 termination (reason unknown)

3 ectopic pregnancies

Death (fetal)

19 stillbirths

7 intrauterine deaths

Neonatal outcomes

5 premature babies/labor

3 congenital malformations (lingula frenulum, cleft lip and evisceration on exomphalos)

243 pregnancies ongoing

449 pregnancy outcomes unknown/not reported

Pregnancy Outcome by Trimester: Ebola Vaccine Experience*

Outcome		Exposure within 3 months prior to conception	1 st Trimester	2 nd Trimester	3 rd trimester	Time of exposure unknown	Total
Live birth	Healthy baby	64	120	169	205	188	746
	Premature	0	0	1	0	1	2
	Congenital malformation	0	0	1	1	1	3
Fetal death	Still birth	1	7	7	2	1	18
	Intrauterine death	2	1	1	0	0	4
	Spontaneous abortion	49	22	2	0	15	88
Pregnancy stopped	Incomplete abortion	1	0	0	0	1	2
	Abortion	0	0	0	0	1	1
	Ectopic pregnancy	0	1	0	0	1	2
	Elective abortion	3	1	0	0	1	5
	Induced abortion	0	1	0	0	5	6
	Termination	0	1	0	0	0	1
		114	30	26	21	22	213
Continuing / Ongoing		184	81	32	37	97	431
Unknown / Not reported							
Total		418	265	239	266	334	1522

- Significant experience with Ad26.ZEBOV throughout pregnancy
- Outcome data by trimester available in 44% of all reported pregnancies; follow-up of continuing/ongoing and unknown/not reported outcomes is ongoing
- Most pregnancies resulted in healthy baby regardless of when vaccine exposure occurred
- As expected, spontaneous abortion was the most commonly reported abnormal pregnancy outcome (5.8%) which is within the expected background rates (10-30%; Alves and Rapp, 2020)

Summary of Pregnancy Experience in AdVac® Vaccine Programs

- Significant experience/exposure to Ad26-based vaccines throughout pregnancy
 - Most experience comes from the Ebola vaccine in African studies / vaccination campaigns
- No safety concerns related to vaccine exposure during pregnancy observed
 - Most pregnancies result in healthy baby, regardless of which trimester vaccine exposure occurred
 - Spontaneous abortions in first trimester are the most commonly reported adverse outcome but not at a greater rate compared to reported background rates
- Follow-up of 'not reported/unknown' cases continues along with routine pharmacovigilance activities

[1] Data on File. Global Medical Safety Contribution for the Cumulative Review of Pregnancy Cases Reported in the Janssen Adenoviral 26 Vectored Vaccine Programs. 23 January 2021

Agenda

AdVac® vector introduction

Pregnancy Cases Reported in AdVac® vaccine programs

Details on Ebola vaccine program

Details on COVID-19 vaccine program

Conclusions

EBL3010*: Safety, reactogenicity and immunogenicity in pregnant women in Rwanda

- **Sponsor:** Janssen; CHFR and Emory University in close collaboration
- **Funder:** CEPI; Janssen
- **Location:** District hospitals near Western Border close to Goma, DRC
- **Study design:**
 - Women found to be pregnant in the UMURINZI vaccination campaign and pregnant women in the areas targeted by the UMURINZI campaign
 - Open label Randomised controlled design: 1,000 women in active arm, and 1,000 in control arm (control group will receive vaccine ~3 months after delivery)
- **Objectives:**
 - **Assess safety in healthy pregnant women (focus on adverse maternal and foetal outcomes in line with GAIA guidelines)**
 - Assess immunogenicity in healthy pregnant women (subset of 300)
 - Assess background incidence of adverse maternal and foetal outcomes (control group)
- **Immunological assessments:**
 - FANG ELISA, Q2 Solutions laboratory (USA)
- **Study Start: Nov 2020**
- **Enrollment: 180 randomized to group A (vaccination during pregnancy) 202 randomized to group B (vaccination upon completion; 23 babies born to mothers who received vaccine and 23 babies born in control group**
- **Three Groups: Group A receives vaccine during pregnancy, Group B receives vaccine once pregnancy is completed and Group C are 500 pregnant women from UMURINZI for safety only**

Data on file as of March 2021

*NCT: NCT04556526

Open label randomized clinical trial to evaluate the safety, reactogenicity and immunogenicity of a 2-dose Ebola vaccine regimen of Ad26.ZEBOV followed by MVA-BN-Filo in healthy pregnant women in Rwanda

Adverse maternal/fetal outcomes in EBL3010

Arm	Outcome	START DATE	SAE?	Dose 1 date	Dose 2 date
Group A	Pathways to Preterm Birth	2020-12-14	No	2020-10-09	2020-12-04
Group B	Pathways to Preterm Birth	2020-12-24	Yes	NA	NA
Group B	Pathways to Preterm Birth	2021-02-02	No	NA	NA
Group B	Pathways to Preterm Birth	2021-02-03	No	NA	NA

Adverse maternal/fetal outcome from group A considered NOT related to vaccine

Data on file as of March 2021
group A (vaccination during pregnancy)
group B (vaccination upon completion)

Adverse neonatal outcomes in EBL 3010

Arm	Infant outcome	START DATE	Relationship to study treatment	Dose 1 date	Dose 2 date
Group A	Premature baby 33 to 36 weeks	2020-12-14	Not related	2020-10-09	2020-12-04
Group A	Small for gestational age	2021-01-23	Not related	2020-10-23	2020-12-18
Group A	Small for gestational age	2021-01-28	Not related	2020-10-30	2020-12-23
Group A	Small for gestational age	2021-02-28	Not related	2020-11-17	2021-01-12
Group A	Small for gestational age	2021-02-27	Not related	2020-11-30	2021-01-25
Group A	Small for gestational age	2021-03-05	Not related	2020-12-01	2021-01-26

Group B	Small for gestational age	2020-12-27	NA	NA	NA
Group B	Small for gestational age	2020-12-30	NA	NA	NA
Group B	Small for gestational age	2021-01-29	NA	NA	NA
Group B	Low birth weight baby	2021-01-29	NA	NA	NA
Group B	Premature baby	2020-12-24	NA	NA	NA
Group B	Low birth weight baby	2020-12-24	NA	NA	NA
Group B	Premature baby death	2020-12-28	NA	NA	NA
Group B	Premature baby 33 to 36 weeks	2021-02-02	NA	NA	NA
Group B	Premature baby 33 to 36 weeks	2021-02-03	NA	NA	NA

Data on file as of March 2021
group A (vaccination during pregnancy)
group B (vaccination upon completion)

Preliminary Summary of Safety in EBL3010

- SAE reports evenly divided into pregnancy-related SAEs and non-pregnancy related SAEs
 - Only 1 SAE considered related to vaccine: vomiting
- One adverse maternal outcome reported in vaccine group, not related to vaccine
- ‘Small for gestational age’ was most frequently reported adverse fetal outcome in active and control groups
 - Value of the concurrent control group
- Reactogenicity: Overall comparatively low frequency of reactogenicity complaints
 - Most frequent local AE: pain/tenderness
 - Most frequent systemic AE: headache and fatigue
- No Safety signals so far
- Good overall retention- 100%; no loss to follow to-date

Agenda

AdVac® vector introduction

Pregnancy Cases Reported in AdVac® vaccine programs

Details on Ebola vaccine program

Details on COVID-19 vaccine program

Conclusions

COVID-19 Pregnancy Experience

- Pregnant women were excluded from Phase 1 and 2 and pivotal Phase 3 trials
- A total of 16 spontaneous pregnancies have been reported in ongoing studies
- No safety concerns identified from analysis of this data

Patient ID	Treatment	LMP	EDD	Exposure date	Period of exposure	Outcome
3002988	Placebo	24-Oct-20	31-Jul-21	4-Nov-20	Pre-natal	Incomplete abortion
3003779	Placebo	28-Oct-20	4-Aug-21	11-Nov-20	1st Trimester	Ongoing
3008226	Placebo	28-Oct-20	4-Aug-21	12-Nov-20	1st Trimester	Elective abortion
3004787	Placebo	16-Oct-20	23-Jul-21	8-Nov-20	Pre-natal	Elective abortion
3020464	Ad26.COV2.S 5x10 ¹⁰ vp	27-Oct-20	3-Aug-21	20-Nov-20	1st Trimester	Ongoing
3016462	Ad26.COV2.S 5x10 ¹⁰ vp	23-Oct-20	30-Jul-21	18-Nov-20	1st Trimester	Spontaneous abortion
3001279	Ad26.COV2.S 5x10 ¹⁰ vp	29-Oct-20	5-Aug-21	10-Oct-20	Pre-natal	Ongoing
3046432	Ad26.COV2.S 5x10 ¹⁰ vp	23-Nov-20	31-Aug-21	11-Dec-20	1st Trimester	Ectopic pregnancy
3004818		18-Nov-20	27-Aug-21	9-Nov-20	N/A (partur exposure)	Ongoing
3012281		4-Dec-20	9-Sep-21	17-Nov-20	Pre-natal	Ongoing
3004382		14-Dec-20	20-Sep-21	17-Nov-20	Pre-natal	Ongoing
3019673		7-Nov-20	14-Aug-21	UNK N/A (partur exposure)		Ongoing
3006331		16-Nov-20	28-Aug-21	UNK 1st Trimester		Ongoing
3003721		14-Dec-20	20-Sep-21	12-Nov-20	Pre-natal	Ongoing

Data on file as of March 2021

COVID-19 Clinical Development Plan for Pregnant Women

- Pregnancy is listed as an **area of missing information** for Ad26.COV2.S

Additional pharmacovigilance activities:

- COV2004*: open label study, safety and efficacy in ± 400 pregnant women and their offspring
- Pregnancy registry** (not-Janssen sponsored): worldwide pregnancy registry (C-VIPER)

Data on file as of March 2021

* NCT04765384

** NCT04705116

Agenda

AdVac® vector introduction

Pregnancy Cases Reported in AdVac® vaccine programs

Details on Ebola vaccine program

Details on COVID-19 vaccine program

Conclusions

Conclusions

- AdVac® has been used in Janssen's COVID-19 Vaccine (FDA EUA) and Ebola Vaccine (EMA approved), as well as several investigational vaccines including HIV, RSV, and Zika
- Extensive clinical experience with Janssen AdVac®-based vaccines –Ad26-based vaccines generally show a favorable safety & tolerability profile in the populations studied to date
- Extraction from Global Medical Safety (GMS) database as of 31 Dec 2020 did not show any concern based on 1,631 pregnancies
- The Ebola vaccine, approved by the EU, is the most extensively evaluated in pregnant women with no safety concern
 - Most pregnancies resulted in healthy baby regardless of when vaccine exposure occurred.
- The COVID-19 vaccine did not show any safety concern in a small number of pregnant women so far. Additional studies are on their way.
- Janssen continues to monitor pregnancies in clinical trials, registries and other programs

THANK YOU FOR YOUR ATTENTION

Confidential - Property of Janssen
SIMIT congress – Dec 2020

VaST Agenda – March 22, 2021

Open session
1:30 - 2:30

Pregnancy focused session

Data from AdVac® vector vaccines (Richard Nettles, Janssen)

VAERS (Pedro Moro, CDC)

v-safe (Tanya Myers, CDC)

v-safe pregnancy registry (Shin Kim, CDC)

DRAFT

VaST meeting notes

March 22, 2021

Confidential

Presentation slides were distributed; presentations are only briefly summarized in meeting notes. Chat notes not answered verbally on the call are available but have not been incorporated into the minutes.

Participants

Expert consultant members: Beth Bell, Mat Daley, Kathy Edwards, Bob Hopkins (Co-Chair), Lisa Jackson, Martin Kulldorf, Grace Lee (Co-Chair), Veronica McNally, Laura Riley, Rob Schechter, Keipp Talbot

Ex officio and liaison members: Tatiana Beresnev, Matthew Clark, Limone Collins, Karen Farizo, Jeff Kelman, Mary Rubin, Hui Lee Wong

CDC: Karen Broder, Tom Clark, Frank DeStefano, Kathleen Dooling, Shin Kim, Julianne Gee, Rita Hefland, Nicole Lindsey, Jessica MacNeil, Lauri Markowitz (CDC Co-lead), Dana Meaney Delman, Pedro Moro, Tanya R. Myers, Titilope Oduyebo, Sara Oliver, Eddie Shanley, David Shay, Tom Shimabukuro, John Su, Melinda Wharton (CDC Co-lead), Jared Woo

Technical SMEs: Steve Anderson, Kevin Ault, Richard Beigi, Fran Cunningham, Richard Forshee, Brenna Hughes, Denise Jamieson, Narayan Nair

Janssen: Richard Nettles, Valerie Oriol Matheieu, Nina Ahmad, Luis Anaya, Roy van Heesbeen, Cynthia Robinson, Min Wang

Agenda

- Administrative issues
- AdVac® vector vaccines and pregnancy (Janssen)
- v-safe (Tanya Myers, CDC)
- v-safe pregnancy registry (Shin Kim, CDC)
- VAERS (Pedro Moro, CDC)

Administrative issues and announcements - Co-chairs and Co-leads

- Reminders about COI and confidentiality
- Doses distributed: 156,734,555; Doses administered: 124,481,412 (last updated: March 21)
 - Doses distributed: Pfizer-BioNTech: 76,983,855; Moderna: 75,496,800; J&J/Janssen 4,253,900
 - Doses administered: Pfizer-BioNTech: 62,529,418; Moderna: 59,518,840; J&J/Janssen: 2,298,614; Unknown: 134,540
 - First doses: 81,415,769; Fully vaccinated: 44,141,228

These data are posted on the CDC website and are updated regularly ([HYPERLINK "https://covid.cdc.gov/covid-data-tracker/" \l "vaccinations).%E2%80%AF" \h]

AdVac® vector vaccines and pregnancy - Rick Nettles, Cynthia Robinson, Luis Anaya (Janssen)

Dr. Nettles, Robinson, and Luis Anaya presented on pregnancies in AdVac® vector Ebola and COVID-19 vaccine programs. AdVac® based vaccines have been administered to millions of patients to date, and no significant safety issues have been identified in the current adenoviral safety database. There were 1,631 pregnancies reported exposures to Ebola (n = 1,522), HIV (n = 101), and COVID-19 (n = 8) AdVac® vaccine or placebo. Of the 1,631 pregnancies reported, 939 pregnancies had final outcomes reported that include 781 healthy baby reports and 158 other outcomes that include pregnancy stopped, fetal death, and neonatal outcomes.

Dr. Robinson presented on safety, reactogenicity and, immunogenicity of the Ebola vaccine in pregnant women in Rwanda. There are no safety signals to date.

Dr. Anaya reviewed the 16 pregnancy experiences that have occurred in their COVID-19 clinical trials. Pregnant women were excluded from the clinical trials, so all pregnancies that were reported were 'spontaneous'. There were no safety concerns to date.

Questions and discussion:

- Were the malformations described?
 - There were 3 congenital malformations - lingula frenulum, cleft lip and evisceration on exomphalos.
- What is the baseline stillbirth rates at the enrolling trial sites?
 - From Rwanda, there are no background rates on abortions, stillbirths. The majority of pregnancy data come from Democratic Republic of Congo (DRC) and this study was uncontrolled; there are no background rates on either abortions or stillbirths in that country either.
- What is the timing and expected availability of further trial data regarding pregnancy?
 - Rwandan study should complete enrollment by end-of-year 2021. Data would probably not be available until 2023 because of the wait time for pregnancies. Interim data could be presented when available, but the timeline is to be determined.
 - DRC is cleaning and data should be locked by September 2021. The data would be available to present at the end of 2022.
- How are small for gestational age (SGA) and low birthweight defined?
 - They used definitions put out by GAIA group.
 - OBs are blinded to treatment assignment.
- Is there meaningful difference between Ebola vs COVID-19 vaccines other than antigen (Ebola vs COVID-19)?
 - There are small differences, but they are largely similar.
- Have any pregnant woman received a second dose of any of the Janssen vaccines?
 - None of the pregnant women received a second dose of a Janssen vaccine.
- Janssen to send study protocol to Lauri

VAERS pregnancy data – Pedro Moro (CDC)

Dr. Moro provided an update on VAERS pregnancy data. There were 345 pregnancy reports, 68 serious reports and 108 pregnancy-specific reports. The most common report was spontaneous abortion (n = 75) where the median maternal age was 32 and the majority (71%) had a gestational age of less than 12

weeks. There was no disproportionality of spontaneous abortions when compared to other maternal vaccinations in VAERS. The most common signs and symptoms reported were systemic and local reactions, similar those for non-pregnant women in VAERS.

Questions and discussion:

- Were there any congenital anomalies reported?
 - There were 2 fetal hydrops.
- Different cut-offs can be used to possibly detect directional signals to provide more insight if proportional ratios or comparison between Pfizer and Moderna are not available.
 - The CDC will check with the FDA to provide more information on the proportional ratios.
- For miscarriages, are there any data on whether the pregnant woman had had an ultrasound?
 - It is helpful when reporting pregnancy data. The risk of miscarriage goes down significantly after documentation of fetal heart rate.
 - VAERS can follow-up with pregnancy reports, but VSD will have better information.

v-safe pregnancy data - Tanya Myers (CDC)

Dr. Myers provided an overview of how v-safe collects and summarizes pregnancy data. There were 56,143 pregnancies recorded (Pfizer-BioNTech: 29,554; Moderna: 25,713; Janssen: 876) as of March 19th. Approximately 90% of women were between 25 and 44 years across all vaccines. Most pregnancies were in Non-Hispanic Whites (76%), followed by Hispanics (9.6%), Asians (6.5%), Non-Hispanic Other (4.5%), and Non-Hispanic Blacks (2.6%) across Pfizer-BioNTech and Moderna vaccines. Pregnant participants reported more reactogenicity after dose 2 of both mRNA vaccines, which is similar to findings for all v-safe participants.

Questions and discussion:

- Does v-safe have information on the duration of fever?
 - The survey does not have features to look into onset/duration.
- Are these comparisons adjusted for any other variables?
 - Currently, v-safe is only descriptive.
- Are there any details on why it seems to be different by vaccine manufacturer? Is it about the age of pregnant women, or other reasons (e.g. HCP vs. non-HCP)?
 - It will be helpful to look at this in the future.

v-safe pregnancy registry – Shin Kim (CDC)

Ms. Kim provided updates on the v-safe pregnancy registry data, which covers only Pfizer-BioNTech and Moderna, but the registry is currently adding enrollees for Janssen. There were 3,523 pregnant persons enrolled (Pfizer-BioNTech: 1,926; Moderna: 1,597) in the v-safe pregnancy registry as of March 19. A new component of the registry was added to allow further follow-up. As expected, the majority of women are between the ages 25 and 44 years. The majority of enrollees are Non-Hispanic White (78.3%), followed by Non-Hispanic Asians (9.9%), Hispanic (7.8%), Non-Hispanic Other (2.2%), and Non-Hispanic Black (1.3%). All pregnancy and neonatal outcomes of interest were within background rates.

Questions and discussion:

- First trimester exposures that report ongoing pregnancies is reassuring. The combination of VAERS and v-safe data shows thousands of pregnancies without congenital anomalies or pregnancy risk. The lack of events with the number of pregnancies is promising.

Overall issues:

- What are the plans to communicate the data presented to the public?
 - Communication is expected to be done through the county health depts, OB/GYNs, and jurisdictions. A publication is planned for the NEJM.
- Can BEST or DoD provide pregnancy information?
- Follow-up with FDA for empirical based data mining.
- Janssen can join another call when more data are more available.

Papers

- *Reactogenicity following receipt of mRNA-based COVID-19 vaccines* (scheduled for publication in JAMA this week)
- *Preliminary findings of mRNA COVID-19 vaccine safety in pregnant persons, United States — December 2020–February 2021* (under review at NEJM)
- *U.S. Population-Based Background Incidence Rates of Medical Conditions for Use in Safety Assessment of COVID-19 Vaccines* (under review at Vaccine)
- *Safety of the Janssen COVID-19 vaccine — United States, March 2021* (MMWR planned)
- *Rapid Cycle Analysis (RCA) to monitor the safety of COVID-19 vaccines in near real-time within the Vaccine Safety Datalink* (in process)



Processes and procedures for evaluating reports of death to VAERS following COVID-19 vaccination

**Tom Shimabukuro, MD, MPH, MBA
CDC COVID-19 Vaccine Task Force
Vaccine Safety Team**

References

- https://www.cdc.gov/nchs/data/misc/hb_cod.pdf
- https://www.cdc.gov/nchs/data/dvs/blue_form.pdf
- https://www.cdc.gov/nchs/data/dvs/red_form.pdf
- <https://www.cdc.gov/phlp/publications/coroner/investigations.html>
- <https://www.thename.org/assets/docs/NAME%20Autopsy%20Protocol%20for%20Deaths%20after%20COVID-19%20vaccination.pdf>
- <https://vaers.hhs.gov/reportevent.html>
- <https://www.cdc.gov/nchs/data/databriefs/db395-H.pdf>

Certification of death

Certification

- The registration of deaths is a state function supported by individual state laws and regulations
- Cause of death is determined by the certifying physician, coroner, medical examiner
 - Coroners may be elected or appointed and may not have a medical background or medical training
 - Most medical examiners are trained in forensic pathology
- Cause of death is the opinion of certifying official
- In most cases, the physician who pronounces death also certifies death
- The death certificate is the legal document that officially records the cause, date, and place of death

Cause-of-death – Background, Examples, and Common Problems

Accurate cause of death information is important

- to the public health community in evaluating and improving the health of all citizens, and
- often to the family, now and in the future, and to the person settling the decedent's estate.

The cause-of-death section consists of two parts. Part I is for reporting a chain of events leading directly to death, with the immediate cause of death (the final disease, injury, or complication directly causing death) on line a and the underlying cause of death (the disease or injury that initiated the chain of events that led directly and inevitably to death) on the lowest used line. Part II is for reporting all other significant diseases, conditions, or injuries that contributed to death but which did not result in the underlying cause of death given in Part I. The cause-of-death information should be YOUR best medical OPINION. A condition can be listed as "probable" even if it has not been definitively diagnosed.

Examples of properly completed medical certifications

CAUSE OF DEATH (See instructions and examples)			Approximate interval: Onset to death
32. PART I. Enter the <u>chain of events</u> —diseases, injuries, or complications—that directly caused the death. DO NOT enter terminal events such as cardiac arrest, respiratory arrest, or ventricular fibrillation without showing the etiology. DO NOT ABBREVIATE. Enter only one cause on a line. Add additional lines if necessary.			
IMMEDIATE CAUSE (Final disease or condition -----> resulting in death)	a. <u>Rupture of myocardium</u> Due to (or as a consequence of):		<u>Minutes</u>
Sequentially list conditions, if any, leading to the cause listed on line a. Enter the UNDERLYING CAUSE (disease or injury that initiated the events resulting in death) LAST	b. <u>Acute myocardial infarction</u> Due to (or as a consequence of):		<u>6 days</u>
	c. <u>Coronary artery thrombosis</u> Due to (or as a consequence of):		<u>5 years</u>
	d. <u>Atherosclerotic coronary artery disease</u>		<u>7 years</u>
PART II. Enter other <u>significant conditions contributing to death</u> but not resulting in the underlying cause given in PART I <u>Diabetes, Chronic obstructive pulmonary disease, smoking</u>			33. WAS AN AUTOPSY PERFORMED? ☒ Yes ☐ No
			34. WERE AUTOPSY FINDINGS AVAILABLE TO COMPLETE THE CAUSE OF DEATH? ☒ Yes ☐ No
35. DID TOBACCO USE CONTRIBUTE TO DEATH? ☒ Yes ☐ Probably ☐ No ☐ Unknown	36. IF FEMALE: ☒ Not pregnant within past year ☐ Pregnant at time of death ☐ Not pregnant, but pregnant within 42 days of death ☐ Not pregnant, but pregnant 43 days to 1 year before death ☐ Unknown if pregnant within the past year	37. MANNER OF DEATH ☒ Natural ☐ Homicide ☐ Accident ☐ Pending investigation ☐ Suicide ☐ Could not be determined	

<https://www.cdc.gov/nchs/data/dvs/death11-03final-acc.pdf>

PSICOID_00010593

Autopsy

- Usually done by physicians who are pathologists
- Conducted to determine the cause and manner of death
- Not all deaths get autopsies
 - Forensic autopsy to investigate suspicious, unusual, or unnatural deaths (part of a medicolegal death investigation through a medical examiner or coroner office*)
 - Clinical autopsy to advance the understanding of disease
- Findings are included in an autopsy report (may take weeks or longer for final report)
- An autopsy report may contradict the death certificate
 - In this case, the death certificate may be amended, but the process may differ by jurisdiction and certifier

* <https://www.cdc.gov/phlp/publications/coroner/investigations.html>

Evaluation of deaths following COVID-19 vaccination

PSICOVID_0001059

Types of CDC death evaluations

- 'Top down'
 - VAERS receives a report of a death following COVID-19 vaccination; no prior CDC knowledge
 - Main purpose of an evaluation is to confirm the cause of death through collection of official records and other records
- 'Bottom up'
 - State or local health officials, healthcare providers, ME, or coroner notify CDC of a death following COVID-19 vaccination
 - May trigger CDC technical assistance to state/local officials in establishing cause of death and providing communication support
 - or
 - CDC may simply facilitate reporting of the death to VAERS

VAERS contractor actions for COVID-19 vaccines*

- Expedites processing of report (day of report)
- Contacts reporter for additional information (medical records, death certificate, etc.)
 - For autopsy cases, autopsy report is requested
- Notifies state vaccine safety coordinator of the death and provides a copy of initial report
- Posts report and accompanying records on the secure VAERS VPN
- Includes initial report in the daily extract to CDC and FDA
- Makes multiple attempts, if necessary, to collect records

* Mainly applicable to 'top down' evaluations

CDC ISO actions for COVID-19 vaccines^{*,†}

- Upon notification of death report through VAERS, an ISO data manager assigns the review to an individual clinician reviewer
 - Reviewers may include CDC physicians, physician assistants, nurses, PharmDs, and others with experience reviewing medical records
- Reviewers use the initial report and records in the VAERS VPN to extract and input information into the COVID-19 AESI abstraction database
 - Provide impressions when only initial report is available
 - Update the abstraction database as records become available
- If reviewer determines death is unusual, unexpected, or suspicious, she/he can alert the VAERS team lead for rapid follow-up and/or for discussion on the CDC-FDA coordination call

* Mainly applicable to 'top down' evaluations; † FDA physicians also review every VAERS COVID-19 vaccine death report

PSICOVID_00010598

‘Bottom up’ death notification

- If CDC is directly or indirectly informed of a possible unusual, unexpected, or suspicious death following a COVID-19 vaccination, CDC will:
 - Work with the HCP or state or local health officials to get the death reported to VAERS so report processing and formal record collection can commence
 - Determine if technical assistance is appropriate and wanted
 - Coordinate internally (i.e., ISO, Infectious Disease Pathology Branch [IDPB], CISA) to assist the state and/or local health department, medical examiner/coroner, or healthcare facility on the investigation of the death*
 - guidance on specimen collection
 - assistance with clinical case and autopsy findings review
 - analysis of autopsy specimens
 - advice on public health communications

* This may also occur in a ‘top down’ situation

‘Bottom up’ death notification (cont.)

- The purpose of these activities is to provide assistance and guidance to state and local officials in establishing the cause of death, assessing whether vaccination may have contributed to the death, and providing communication support when needed
 - CDC does not make cause of death determinations

Partnership

- Infectious Disease Pathology Branch, ISO, and NCHS have worked with the Natl Assoc of Medical Examiners who have developed a protocol for investigation and autopsy of deaths occurring after COVID-19 vaccination, which emphasizes importance of autopsy, reporting to VAERS, etc.
 - <https://www.thename.org/assets/docs/NAME%20Autopsy%20Protocol%20for%20Deaths%20after%20COVID-19%20vaccination.pdf>

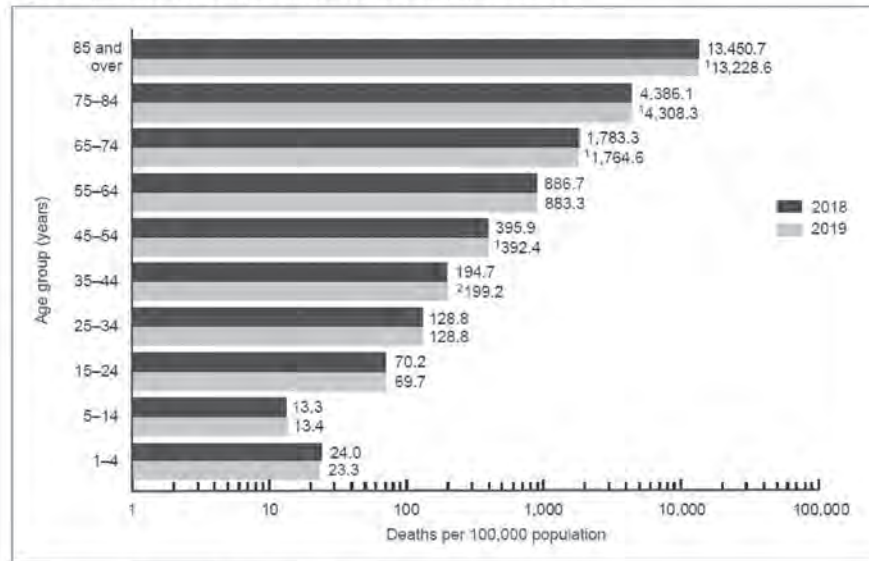
Analysis

- Surveillance
 - Individual death report review by CDC and FDA reviewers and discussion of unusual or unexpected deaths and additional evaluation
 - Reviewing non-death reports for outcomes of interest related to deaths (e.g., ITP)
 - Evaluating reports for conditions associated with death from other information sources (e.g., CVST – based on reports from Europe associated with AZ vaccine)
 - Comparison of counts and reporting rates to background rates
 - Comparing causes of death in reports to causes of death in the population based on vital statistics
 - Disproportionality analysis using empirical Bayesian data mining (FDA)
 - Enhanced surveillance of conditions that may lead to death (e.g., AMI, stroke, PE, serious acute demyelinating diseases, etc.)

Analysis

- Individual case investigation (typically 'bottom up')
 - Limited to technical assistance to state and local partners, usually on complex death cases where there is suspicion of possible vaccine association
 - IDPB helps with guidance on specimen collection, clinical case and autopsy findings review, and analysis of autopsy specimens
 - CISA provides consultation to healthcare providers or health departments about living patients, but will continue to assist if patient dies while case is under review; CISA may also consult on death cases in collaboration with the VAERS team and IDPB
 - The purpose of these activities is to provide assistance and guidance to state and local officials in establishing the cause of death and assessing whether vaccination may have contributed to the death
 - CDC does not make cause of death determinations

Figure 3. Death rates for ages 1 year and over: United States, 2018 and 2019



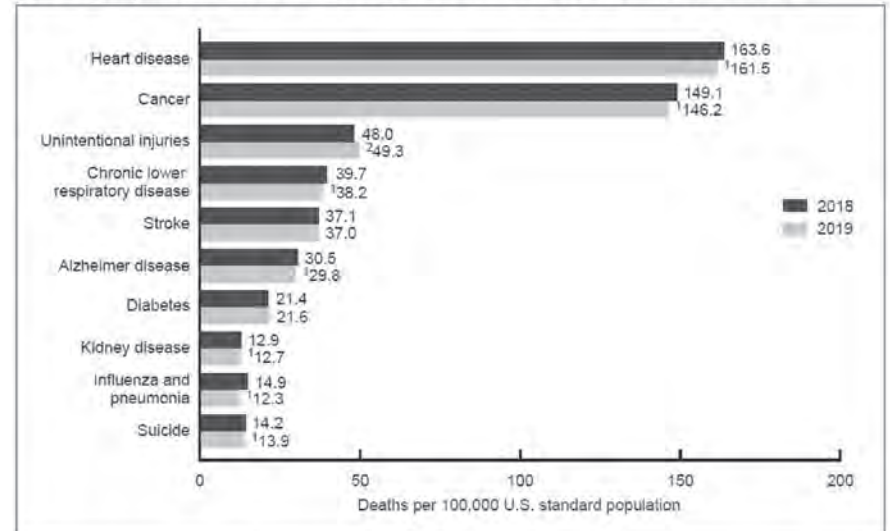
¹Statistically significant decrease in age-specific death rate from 2018 to 2019 ($p < 0.05$).

²Statistically significant increase in age-specific death rate from 2018 to 2019 ($p < 0.05$).

NOTES: Rates are plotted on a logarithmic scale. Access data table for Figure 3 at: <https://www.cdc.gov/nchs/data/databriefs/db395-tables-508.pdf#5>.

SOURCE: National Center for Health Statistics, National Vital Statistics System, Mortality.

Figure 4. Age-adjusted death rates for the 10 leading causes of death in 2019: United States, 2018 and 2019



¹Statistically significant decrease in age-adjusted death rate from 2018 to 2019 ($p < 0.05$).

²Statistically significant increase in age-adjusted death rate from 2018 to 2019 ($p < 0.05$).

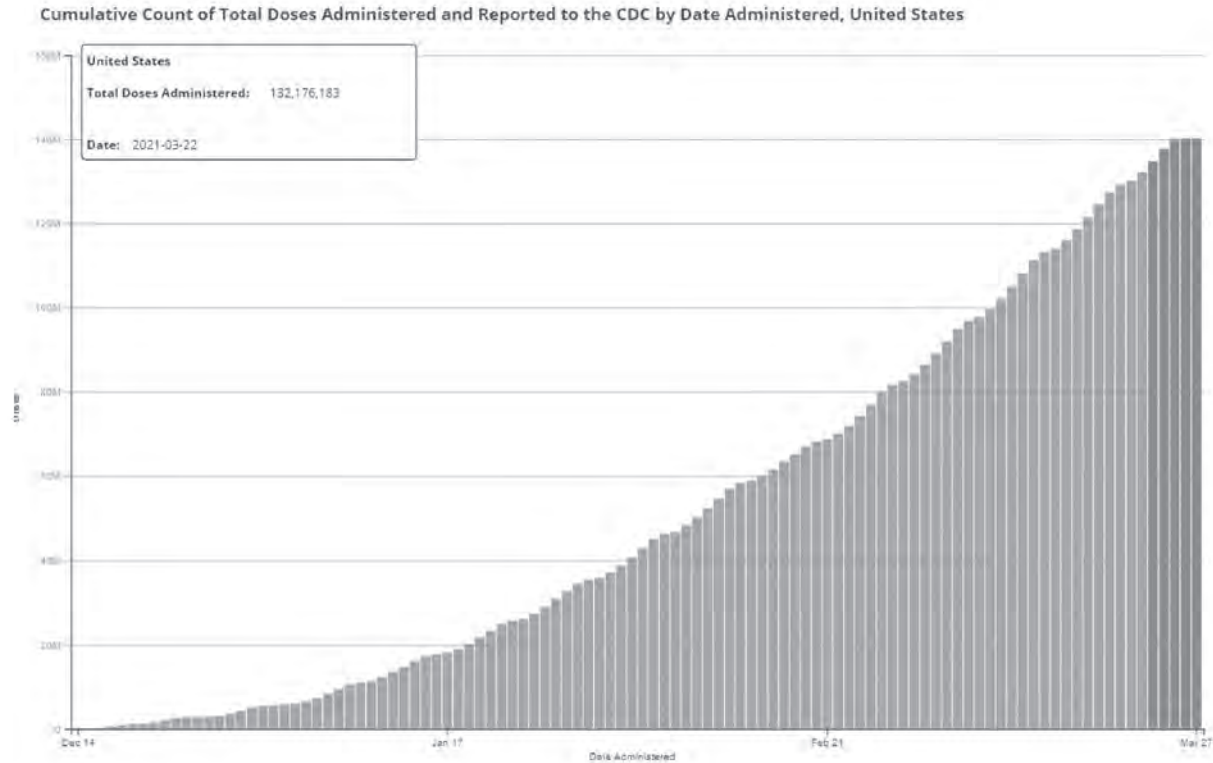
NOTES: A total of 2,854,838 resident deaths were registered in the United States in 2019. The 10 leading causes of death accounted for 73.4% of all deaths in the United States in 2019. Causes of death are ranked according to number of deaths. Rankings for 2018 data are not shown. Data table for Figure 4 includes the number of deaths for leading causes. Access data table for Figure 4 at: <https://www.cdc.gov/nchs/data/databriefs/db395-tables-508.pdf#4>.

SOURCE: National Center for Health Statistics, National Vital Statistics System, Mortality.

- 2,854,838 resident deaths registered in the United States in 2019
 - 7,821 deaths per day
- 10 leading causes of death accounted for 73.4% of all deaths

<https://www.cdc.gov/nchs/data/databriefs/db395-H.pdf>

PSICOID_00010604



- 132 million COVID-19 vaccines have been given through March 22
 - ~1900 deaths reported to VAERS through March 22

<https://covid.cdc.gov/covid-data-tracker/#vaccination-trends>

PSICOID_00010605

Challenges

- Timing of death report submission to VAERS (early is better)
- Heterogeneity of reports (quality and completeness)
 - An autopsy report or death certificate is the final record for VAERS
 - Medical records are helpful in the absence of an autopsy report or death certificate
 - Some deaths reports only include the initial VAERS report; follow-up is not successful
 - Includes incomplete reports, hearsay reports, misclassified reports
- Lags for record availability and incomplete records
- Limitations of death certificates in general

Questions

PSICOVID_0001060

Vaccine Safety Datalink

Mortality and Vaccination with COVID-19 Vaccines

Stan Xu, PhD
Kaiser Permanente Southern California

DEPARTMENT OF RESEARCH & EVALUATION

 KAISER PERMANENTE®

PSICOVID_00010608

Mortality and Vaccination with COVID-19 Vaccines

- **Lead Site:** Kaiser Permanente Southern California
- **KPSC Team Members:**
 - **Investigators:** Stan Xu, Hung Fu Tseng, Lei Qian, Lina Sy
 - **Data Analysts:** Runxin Huang, Sungching Glenn
 - **Project Manager/Coordinator:** Denison Ryan, Kerresa Morrisette
- **VSD Collaborators:** HealthPartners, Kaiser Permanente Colorado, Kaiser Permanente Washington, Marshfield Clinic, Kaiser Permanente Northern California, Kaiser Permanente Northwest, the Centers for Disease Control and Prevention
- **Aim:** To assess mortality risk after receiving COVID-19 vaccines among members enrolled in collaborating Vaccine Safety Datalink (VSD) sites.

Outline

Study population, exposure, and outcome

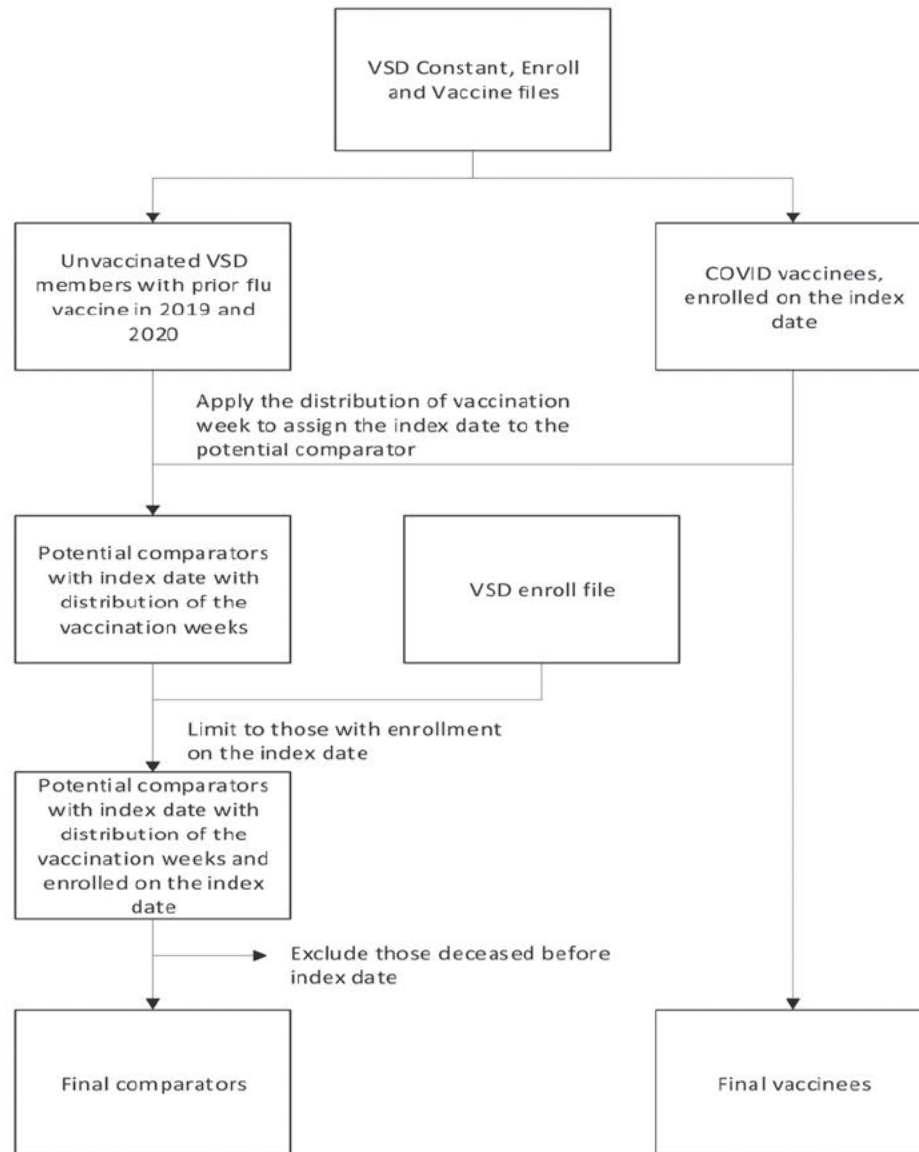
Analytic Plan

Preliminary results based on a single site

Study population, exposure, and outcome

- **Study Population:** All members enrolled in HealthPartners, Kaiser Permanente Colorado, Kaiser Permanente Washington, Marshfield Clinic, Kaiser Permanente Northern California, Kaiser Permanente Northwest, and Kaiser Permanente Southern California
- **Study Period:** December 2020 – December 2023
- **Exposure:** Vaccination with COVID-19 vaccines
 - **Vaccinees:** those who were vaccinated with COVID-19 vaccines
 - **Comparators:** those who received influenza vaccines in the last two years but did not receive COVID-19 vaccines
- **Outcome:** All deaths except COVID-19 related deaths for primary analyses; all cause deaths for sensitivity analyses

Algorithm for identifying vaccinees and comparators



Rationales for assigning index dates to comparators using the distribution of vaccination dates among vaccinees

1. It makes the follow-up duration comparable between vaccinees and comparators
2. It helps control for temporal factors such as seasonality and secular trends
3. Death data lag will be non-differential between vaccinees and comparators

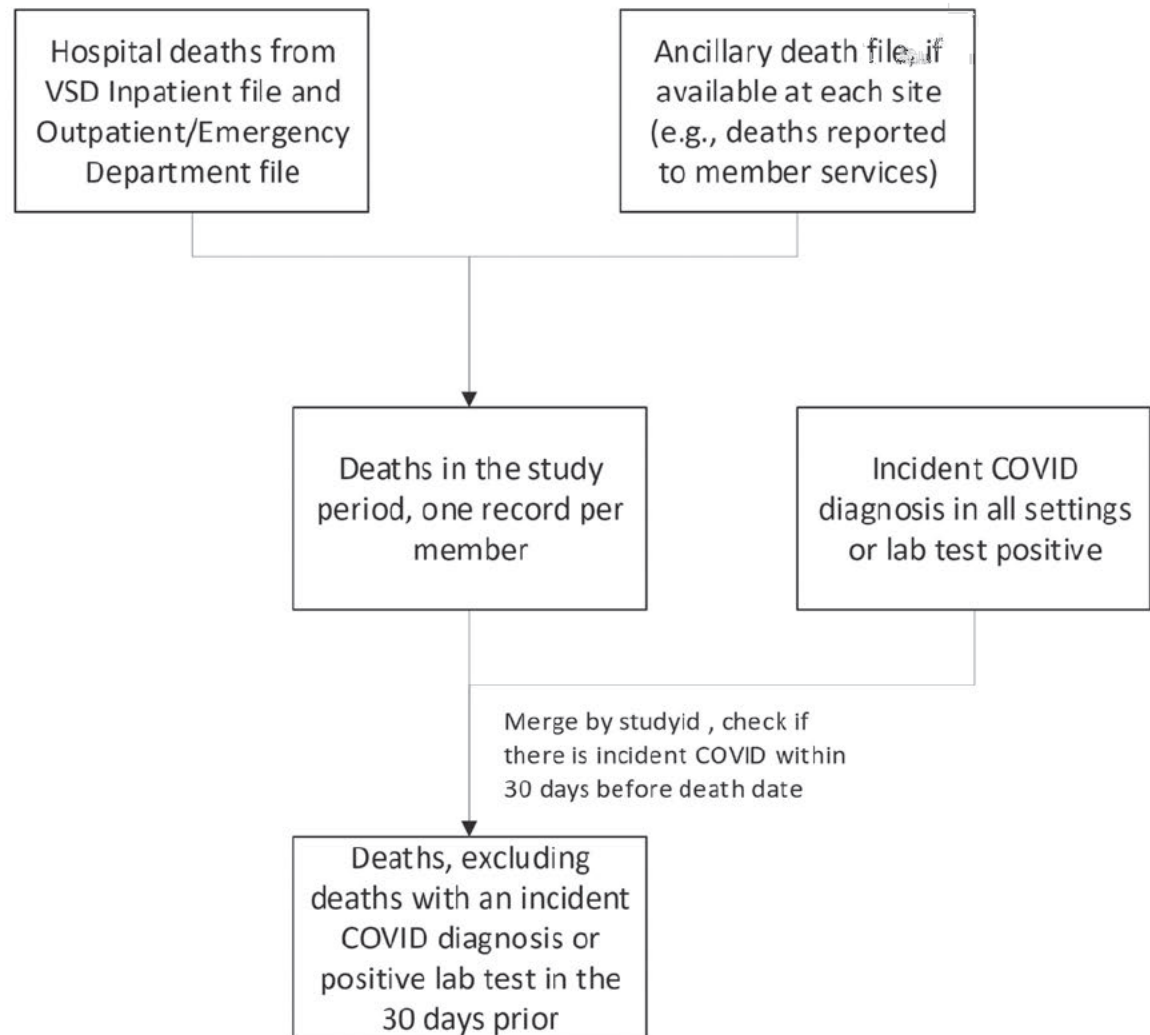
Vaccination frequencies among vaccinees
during Week 49 of 2020 to Week 8 of 2021
(single site data)

Week of first vaccination date	Sunday of the week	Frequency	Percent
20W49	12/6/2020	22	0.0
20W50	12/13/2020	10020	2.3
20W51	12/20/2020	20626	4.7
20W52	12/27/2020	20082	4.6
21W01	1/3/2021	23690	5.4
21W02	1/10/2021	34016	7.7
21W03	1/17/2021	53316	12.1
21W04	1/24/2021	68127	15.5
21W05	1/31/2021	69056	15.7
21W06	2/7/2021	56260	12.8
21W07	2/14/2021	45299	10.3
21W08	2/21/2021	39909	9.1

Assigned index date frequencies among
comparators during Week 49 of 2020 to Week 8
of 2021 (single site data)

Week of index date	Sunday of the week	Frequency	Percent
20W49	12/6/2020	131	0.0
20W50	12/13/2020	61583	2.3
20W51	12/20/2020	126898	4.6
20W52	12/27/2020	123185	4.6
21W01	1/3/2021	144330	5.4
21W02	1/10/2021	206756	7.7
21W03	1/17/2021	323409	12.1
21W04	1/24/2021	412693	15.5
21W05	1/31/2021	418043	15.7
21W06	2/7/2021	338902	12.7
21W07	2/14/2021	273849	10.3
21W08	2/21/2021	240784	9.0

Algorithm for identifying death



Analytic Plan

- Monthly mortality rates by vaccine type, dosage, age, sex, and race/ethnicity
- Semi-annual interim analyses involving propensity score adjustment and survival analyses
- Sensitivity analyses including all deaths

Mortality rates and preliminary results based on a single site

- Vaccinees were vaccinated with Pfizer COVID-19 vaccine or Moderna COVID-19 vaccine before February 27, 2021.
- For the first dose among vaccinees person-time was counted from the 1st vaccination to the end of follow-up (March 20, 2021 for this preliminary report), death date, 2nd vaccination date, or disenrollment, whichever occurred first.
- For the second dose among vaccinees person-time was counted from the 2nd vaccination to the end of follow-up (March 20, 2021 for this preliminary report), death date, or disenrollment, whichever occurred first.
- For comparators person-time was counted from the index date to the end of follow-up (March 20, 2021 for this preliminary report), death date, or disenrollment, whichever occurred first.
- Mortality rate per 100 person-years was calculated as

$$100 \times \frac{\text{number of deaths}}{\text{person years}}$$

overall and by age, sex, and race/ethnicity

Mortality rates per 100 person-years among those who received either mRNA vaccine and comparators by age, sex, and race/ethnicity

	Vaccinees*								
	Dose 1			Dose 2			Comparators		
	N	Number of deaths [‡]	Mortality rate per 100 person-years	N	Number of deaths [‡]	Mortality rate per 100 person-years	N	Number of deaths [‡]	Mortality rate per 100 person-years
Overall	440,369	231	0.7	192,569	103	0.7	2,054,578	1,665	1.0
Age (in years)									
16-17	190	0	0.0	74	0	0.0	77,266	0	0.0
18-44	94,987	1	0.0	58,209	1	0.0	894,059	46	0.1
45-64	94,262	4	0.1	57,263	1	0.0	716,525	256	0.4
65-74	106,128	44	0.6	22,987	13	0.7	265,647	384	1.8
75+	144,802	182	1.7	54,036	88	2.2	101,081	979	12.1
Sex									
Female	265,079	92	0.5	121,123	51	0.5	1,135,200	782	0.9
Male	175,290	139	1.1	71,446	52	0.9	919,378	883	1.2
Race/ethnicity									
Hispanic	115,974	41	0.5	48,306	23	0.6	790,991	451	0.7
Non-Hispanic White	174,491	122	0.9	70,346	51	0.9	660,367	803	1.5
Non-Hispanic Asian	69,467	25	0.5	38,181	12	0.4	228,687	135	0.7
Non-Hispanic Black	33,982	33	1.3	12,525	11	1.1	139,679	197	1.7
Multiple/Other/UNK	46,455	10	0.3	23,211	6	0.3	234,854	79	0.4

*vaccinated with COVID-19 vaccines before February 27th

‡number of deaths as of March 20th

COVID-19 related deaths excluded

% of Patients with Inpatient visits, ED visits, and Charlson comorbidity index one year prior to the index date among vaccinees and comparators by age group

	Vaccinees			Comparators		
Age groups	45-64	65-74	75+	45-64	65-74	75+
Had inpatient visits one year prior to the index date (%)	3.0	6.2	8.9	3.7	5.6	12.1
Had ED visits one year prior to the index date (%)	15.2	18.4	25.8	14.5	16.7	29.4
CCI, mean (SD)	1.4 (0.7)	1.9 (1.2)	2.3 (1.3)	1.4 (0.8)	1.8 (1.1)	2.4 (1.4)

CCI: Charlson comorbidity index

Next Steps

- Collaborating VSD sites to obtain IRB approval.
- To develop Distributed Data Model (DDM) programs and distribute the programs to collaborating sites
- To create monthly mortality tables using data from all collaborating sites
- To prepare semi-annual interim analyses

Questions/Discussion

Back up slides

Mortality rates by vaccine

Include all deaths

KPSC mortality versus US mortality

Influenza vaccination among COVID-19 vaccinees

Mortality rates per 100 person-years among those who received Pfizer COVID-19 vaccine and comparators by age, sex, and race/ethnicity

	Vaccinees*								
	Dose 1			Dose 2			Comparators		
	N	Number of deaths [‡]	Mortality rate per 100 person-years	N	Number of deaths [‡]	Mortality rate per 100 person-years	N	Number of deaths [‡]	Mortality rate per 100 person-years
Overall	219,570	124	0.8	105,919	59	0.7	2,054,578	1,665	1.0
Age (in years)									
16-17	178	0	0.0	72	0	0.0	77,266	0	0.0
18-44	48,777	1	0.0	32,448	0	0.0	894,059	46	0.1
45-64	49,036	3	0.1	32,342	0	0.0	716,525	256	0.4
65-74	58,495	27	0.6	12,030	7	0.7	265,647	384	1.8
75+	63,084	93	2.1	29,027	52	2.3	101,081	979	12.1
Sex									
Female	132,136	57	0.6	66,193	35	0.7	1,135,200	782	0.9
Male	87,434	67	1.1	39,726	24	0.8	919,378	883	1.2
Race/ethnicity									
Hispanic	57,319	22	0.6	25,495	11	0.5	790,991	451	0.7
Non-Hispanic White	82,854	68	1.2	37,489	35	1.2	660,367	803	1.5
Non-Hispanic Asian	37,631	13	0.5	22,809	7	0.4	228,687	135	0.7
Non-Hispanic Black	17,362	17	1.4	6,746	2	0.4	139,679	197	1.7
Multiple/Other/UNK	24,404	4	0.2	13,380	4	0.4	234,854	79	0.4

*vaccinated with COVID-19 vaccines before February 27th

‡number of deaths as of March 20th

COVID-19 related deaths excluded

Mortality rates per 100 person-years among those who received Moderna COVID-19 vaccine and comparators by age, sex, and race/ethnicity

	Vaccinees*								
	Dose 1			Dose 2			Comparators		
	N	Number of deaths [‡]	Mortality rate per 100 person-years	N	Number of deaths [‡]	Mortality rate per 100 person-years	N	Number of deaths [‡]	Mortality rate per 100 person-years
Overall	220,799	107	0.6	86,650	44	0.7	2,054,578	1,665	1.0
Age (in years)									
16-17	12	0	0.0	2	0	0.0	77,266	0	0.0
18-44	46,210	0	0.0	25,761	1	0.0	894,059	46	0.1
45-64	45,226	1	0.0	24,921	1	0.1	716,525	256	0.4
65-74	47,633	17	0.5	10,957	6	0.7	265,647	384	1.8
75+	81,718	89	1.4	25,009	36	2.0	101,081	979	12.1
Sex									
Female	132,943	35	0.3	54,930	16	0.4	1,135,200	782	0.9
Male	87,856	72	1.0	31,720	28	1.2	919,378	883	1.2
Race/ethnicity									
Hispanic	58,655	19	0.4	22,811	12	0.7	790,991	451	0.7
Non-Hispanic White	91,637	54	0.7	32,857	16	0.6	660,367	803	1.5
Non-Hispanic Asian	31,836	12	0.5	15,372	5	0.4	228,687	135	0.7
Non-Hispanic Black	16,620	16	1.2	5,779	9	2.1	139,679	197	1.7
Multiple/Other/UNK	22,051	6	0.3	9,831	2	0.3	234,854	79	0.4

*vaccinated with COVID-19 vaccines before February 27th

‡number of deaths as of March 20th

COVID-19 related deaths excluded

Mortality rates per 100 person-years among those who received Pfizer COVID-19 vaccine and comparators by age, sex, and race/ethnicity

	Vaccinees*								
	Dose 1			Dose 2			Comparators		
	N	Number of deaths [‡]	Mortality rate per 100 person-years	N	Number of deaths [‡]	Mortality rate per 100 person-years	N	Number of deaths [‡]	Mortality rate per 100 person-years
Overall	219,570	154	1.0	105,919	59	0.7	2,054,578	2,458	1.5
Age (in years)									
16-17	178	0	0.0	72	0	0.0	77,266	0	0.0
18-44	48,777	1	0.0	32,448	0	0.0	894,059	61	0.1
45-64	49,036	3	0.1	32,342	0	0.0	716,525	400	0.7
65-74	58,495	30	0.7	12,030	7	0.7	265,647	613	2.9
75+	63,084	120	2.7	29,027	52	2.3	101,081	1,384	17.1
Sex									
Female	132,136	72	0.8	66,193	35	0.7	1,135,200	1,067	1.2
Male	87,434	82	1.4	39,726	24	0.8	919,378	1,391	1.9
Race/ethnicity									
Hispanic	57,319	29	0.7	25,495	11	0.5	790,991	838	1.3
Non-Hispanic White	82,854	87	1.5	37,489	35	1.2	660,367	1,040	2.0
Non-Hispanic Asian	37,631	15	0.6	22,809	7	0.4	228,687	217	1.2
Non-Hispanic Black	17,362	18	1.5	6,746	2	0.4	139,679	251	2.2
Multiple/Other/UNK	24,404	5	0.3	13,380	4	0.4	234,854	112	0.6

*vaccinated with COVID-19 vaccines before February 27th

‡number of deaths as of March 20th

COVID-19 related deaths included

Mortality rates per 100 person-years among those who received Moderna COVID-19 vaccine and comparators by age, sex, and race/ethnicity

	Vaccinees*								
	Dose 1			Dose 2			Comparators		
	N	Number of deaths [‡]	Mortality rate per 100 person-years	N	Number of deaths [‡]	Mortality rate per 100 person-years	N	Number of deaths [‡]	Mortality rate per 100 person-years
Overall	220,799	125	0.7	86,650	45	0.7	2,054,578	2,458	1.5
Age (in years)									
16-17	12	0	0.0	2	0	0.0	77,266	0	0.0
18-44	46,210	0	0.0	25,761	1	0.0	894,059	61	0.1
45-64	45,226	1	0.0	24,921	1	0.1	716,525	400	0.7
65-74	47,633	20	0.5	10,957	6	0.7	265,647	613	2.9
75+	81,718	104	1.6	25,009	37	2.1	101,081	1,384	17.1
Sex									
Female	132,943	43	0.4	54,930	17	0.4	1,135,200	1,067	1.2
Male	87,856	82	1.2	31,720	28	1.2	919,378	1,391	1.9
Race/ethnicity									
Hispanic	58,655	29	0.6	22,811	13	0.7	790,991	838	1.3
Non-Hispanic White	91,637	58	0.8	32,857	16	0.6	660,367	1,040	2.0
Non-Hispanic Asian	31,836	15	0.6	15,372	5	0.4	228,687	217	1.2
Non-Hispanic Black	16,620	17	1.3	5,779	9	2.1	139,679	251	2.2
Multiple/Other/UNK	22,051	6	0.3	9,831	2	0.3	234,854	112	0.6

*vaccinated with COVID-19 vaccines before February 27th

‡number of deaths as of March 20th

COVID-19 related deaths included

Table 2. Mortality rates per 100 person-years among those who received either mRNA vaccine and comparators by age, sex, and race/ethnicity

	Vaccinees*								
	Dose 1			Dose 2			Comparators		
	N	Number of deaths [‡]	Mortality rate per 100 person-years	N	Number of deaths [‡]	Mortality rate per 100 person-years	N	Number of deaths [‡]	Mortality rate per 100 person-years
Overall	440,369	279	0.9	192,569	104	0.7	2,054,578	2,458	1.5
Age (in years)									
16-17	190	0	0.0	74	0	0.0	77,266	0	0.0
18-44	94,987	1	0.0	58,209	1	0.0	894,059	61	0.1
45-64	94,262	4	0.1	57,263	1	0.0	716,525	400	0.7
65-74	106,128	50	0.6	22,987	13	0.7	265,647	613	2.9
75+	144,802	224	2.0	54,036	89	2.2	101,081	1,384	17.1
Sex									
Female	265,079	115	0.6	121,123	52	0.5	1,135,200	1,067	1.2
Male	175,290	164	1.3	71,446	52	0.9	919,378	1,391	1.9
Race/ethnicity									
Hispanic	115,974	58	0.7	48,306	24	0.6	790,991	838	1.3
Non-Hispanic White	174,491	145	1.1	70,346	51	0.9	660,367	1,040	2.0
Non-Hispanic Asian	69,467	30	0.6	38,181	12	0.4	228,687	217	1.2
Non-Hispanic Black	33,982	35	1.4	12,525	11	1.1	139,679	251	2.2
Multiple/Other/UNK	46,455	11	0.3	23,211	6	0.3	234,854	112	0.6

*vaccinated with COVID-19 vaccines before February 27th

[‡]number of deaths as of March 20th

COVID-19 related deaths included

KPSC members with at least one day of enrollment in January of 2019, 2020, or 2021 and having influenza vaccine within 2 years prior to index date

Age (in years)	2019		2020		2021	
	Number of deaths	Mortality per 100 person-years	Number of deaths	Mortality per 100 person-years	Number of deaths	Mortality per 100 person-years
16-17	2	0.04	0	0.00	1	0.02
18-44	31	0.05	33	0.05	49	0.07
45-54	52	0.19	50	0.17	63	0.21
55-64	130	0.42	183	0.57	212	0.64
65-74	370	1.39	395	1.42	492	1.70
75-84	508	3.89	564	4.09	561	3.90
85+	585	12.75	724	15.02	635	12.79

*Includes deaths within 30 days following index date
2021 COVID-19 related deaths were excluded

2019 U.S. national mortality

Age (in years)	2019	
	Number of death	Mortality rate per 100 person-years
15-24	29,771	0.07
25-34	59,178	0.13
35-44	82,996	0.20
45-54	160,393	0.39
55-64	374,937	0.88
65-74	555,559	1.76
75-84	688,027	4.31
85+	873,746	13.23

Source: <https://www.cdc.gov/nchs/data/databriefs/db395-tables-508.pdf#page=3>

94% of COVID-19 vaccinees had influenza vaccines in the last two years

All actively enrolled members during 12/6/2020 – 1/29/2021

	Had COVID-19 vaccine in the period of interest				All	
	Yes		No			
	#	%	#	%	#	%
Had well visit in the period of interest						
Yes	1,742	1	41,772	1	43,514	1
No	127,303	99	4,366,462	99	4,493,765	99
Had any encounter within 1 year prior						
Yes	121,035	94	3,483,545	79	3,604,580	79
No	8,010	6	924,689	21	932,699	21
Had encounter within 2 years prior						
Yes	126,360	98	3,939,730	89	4,066,090	90
No	2,685	2	468,504	11	471,189	10
Had well visit within 2 years prior						
Yes	34,071	26	1,484,407	34	1,518,478	33
No	94,974	74	2,923,827	66	3,018,801	67
Had flu vaccine within 2 years prior						
Yes	121,128	94	2,680,131	61	2,801,259	62
No	7,917	6	1,728,103	39	1,736,20	38
All	129,045	100	4,408,234	100	4,537,279	100

*Period of interest: 12/6/2020 – 1/29/2021

Well visit ICD-10 codes: Z0000, Z0001, Z0012



BROWN
School of Public Health

Vaccine Safety Monitoring among Residents of 284 Genesis Skilled Nursing Facilities

Barbara Bardenheier, PhD, MPH, MA
March 29, 2021

This research was supported, in part, by a grant from the National Institute on Aging [3U54AG063546-02S5] with supplemental funding from the Centers for Disease Control and Prevention under an inter-agency agreement.



BROWN
School of Public Health

PSICOID_00010629

Background

- Genesis is a nursing home chain with 30K residents
 - **Skilled Nursing Facilities (284 Facilities)**
- COVID-19 vaccination began on December 18
- This study assessed adverse event (AE) rates
 - First dose from December 18, 2020 – January 3, 2021 (n=8,553)
 - Second dose from January 8 – February 20, 2021 (n=8,371)



Methods

- Vaccinated residents followed for 15 days (7 days for mortality and hospital transfers)
 - Early vaccinating facilities (n=147) started vaccinating Dec 18, 2020
- Comparator group includes yet-to-be vaccinated residents followed during same time period
 - Later vaccinating facilities (n=137)
 - Identified by facilities that vaccinated at least 15 days prior
 - Same unvaccinated comparator group used to compare following first and second dose of vaccine



Methods

Late Vaccinating Facilities linked to Early Vaccinating Facilities



147 Facilities started vaccinating between December 18, 2020 and January 3, 2021. The 137 late-vaccinating facilities began vaccinating at least 15 days afterward, on January 4 and were the unvaccinated comparator group (including residents who were in those facilities on the date of their linked vaccinating facilities). For example, in strata 1, vaccinated residents were in facilities that started vaccinating on December 18, 2020 and unvaccinated residents were in the facilities that did not start vaccinating until January 4, 2021 *who were in those facilities on December 18, 2020* and all were followed for 15 days, from December 18-January 3. This ensured the comparator group was unvaccinated and followed during the same time period as the vaccinated residents.



BROWN
School of Public Health

PSICOVID_00010632

Methods

- Assessed the same list of AEs as that used by the Vaccine Safety Datalink

- Acute Disseminated Encephalomyelitis (ADEM)
- Acute Myocardial Infarction (AMI)
- Acute Respiratory Distress Syndrome (ARDS)
- Anaphylaxis
- Appendicitis
- Bell's Palsy
- Convulsions/Seizures
- Disseminated Intravascular Coagulation
- Encephalitis/Myelitis/Encephalomyelitis/Encephalopathy
- Guillain-Barré syndrome (GBS)
- Thrombotic thrombocytopenic purpura (TTP)
- Immune thrombocytopenia (ITP)
- Multisystem Inflammatory Syndrome in Adults (MIS-A)
- Myocarditis / pericarditis
- Narcolepsy and cataplexy
- Stroke, hemorrhagic
- Stroke, ischemic
- Transverse myelitis (TM)
- Venous thromboembolism (VTE)
- Pulmonary Embolism (PE)
- Death

Results: Unadjusted

	Vaccinating Facilities (n=147)				Yet-to-vaccinate facilities (n=137)	
	First Dose (n=8,553 residents)		Second Dose (n=8,371 residents)		Unvaccinated (n=11,072 residents)	
	n	Cases per 100,000 residents	n	Cases per 100,000 residents	n	Cases per 100,000 residents
Acute Myocardial Infarction (AMI)	0	-	1	12 (2, 68)	0	-
Bell's Palsy	1	12 (2, 66)	0	-	0	-
Stroke, ischemic	1	12 (2, 66)	0	-	0	-
Venous thromboembolism	2	23 (6, 85)	0	-	1	9 (2, 51)
Pulmonary Embolism (PE)	1	12 (2, 66)	0	-	1	9 (2, 51)
Death	32	374 (265, 528)	44	526 (392, 705)	126	1138 (957, 1353)
Hospital Transfer	128	1497 (1260, 1777)	84	1003 (811, 1241)	179	1617 (1398, 1869)



Note: Residents with a positive COVID-19 test within 20 days of vaccination (since they should not have been vaccinated) or start date, or who were treated with monoclonal antibodies within 90 days of vaccination or start date were excluded.

BROWN
School of Public Health

PSICOVID_00010634

Results: Adjusted Risk Ratios

	First Dose vs unvaccinated	Second Dose vs first dose	Second dose vs unvaccinated
	Adjusted Risk Ratio 95%CI	Adjusted Risk Ratio 95%CI	Adjusted Risk Ratio 95%CI
Acute Myocardial Infarction (AMI)	-	-	-
Bell's Palsy	-	-	-
Stroke, ischemic	-	-	-
Venous thromboembolism	2.41 (0.22, 26.3)	-	-
Pulmonary Embolism (PE)	1.14 (0.07, 18.0)	-	-
Death	0.34 (0.22, 0.54)	1.51 (0.96, 2.38)	0.49 (0.34, 0.71)
Hospital Transfer	0.95 (0.72, 1.24)	0.66 (0.51, 0.86)	0.57 (0.43, 0.75)

Note: Residents with a positive COVID-19 test within 20 days of vaccination (since they should not have been vaccinated) or start date, or who were on monoclonal antibodies within 90 days of vaccination or start date were excluded.

We used inverse probability weighting to adjust for probability of vaccination. Variables included age, sex, race and ethnicity, diabetes, COPD, kidney disease, hypertension, coronary heart disease, dementia, cognitive function, physical function and history of congestive heart failure.

Significant differences are bolded.



BROWN
School of Public Health

PSICOID_00010635

Discussion

- No significant safety signals for residents after COVID-19 vaccination
- Lower mortality among the vaccinated is likely due to healthy vaccinee effect
- Fewer hospital transfers among those receiving the second dose of vaccine than those receiving one or no doses
 - Those still in the facility able to receive the second dose were less likely to die or be transferred to the hospital
- Although there were AE cases observed among the vaccinated individuals that were not observed among the unvaccinated individuals, too few were observed to generate sufficiently precise estimates or determine that risk of events was increased due to vaccination.





BROWN
School of Public Health

ACKNOWLEDGMENTS

Vincent Mor
Richard Feifer
Carolyn Blackman
Stefan Gravenstein
Denine Hastings
Elizabeth White
Chris Santostefano
Neil Sarkar
Kevin McConeghy
Jeff Hiris
Aman Nanda



BROWN
School of Public Health

PSICOVID_00010637



FDA VAERS Data Mining

Bethany Baer, MD

Medical Officer, Division of Epidemiology
Center for Biologics Evaluation and Research, FDA

ACIP Vaccine Safety Team Meeting
March 29, 2021



Disclaimer

My comments are an informal communication and represent my own best judgment. These comments do not bind or obligate the US FDA.

FDA VAERS Data Mining



- Goal of data mining: identify any adverse events that are disproportionally reported for one vaccine compared to other vaccines
- Vaccine + adverse event (AE) = vaccine-AE pair
- Compare the number of reports of an adverse event after a vaccine with number of reports for that adverse event after all vaccines in VAERS



Empiric Bayes Geometric Mean (EBGM)

- Statistical model fit to the entire VAERS database uses Multi-item Gamma Poisson Shrinker (MGPS) algorithm to account for instability with small numbers*
- The model produces the Empiric Bayes Geometric Mean (EBGM)
- EBGM is calculated using observed to expected vaccine-AE pair ratios

*Szarfman A, Tonning JM, Doraiswamy PM. Pharmacovigilance in the 21st century: new systematic tools for an old problem. *Pharmacotherapy*. 2004 Sep;24(9):1099-104. doi: 10.1592/phco.24.13.1099.38090. PMID: 15460169.



Adjustments

- EBGGM statistic is adjusted for potential confounders:
 - Age – Six age groupings + unknown age
 - Infant (0-23.9 mos), child (2-8.9 yrs), teen (9-18.9 yrs), adult1 (19-44.9 yrs), adult2 (45-64.9 yrs), adult3 (≥ 65 yrs)
 - Gender
 - Year Received
- Data mining conducted using Empirica Signal software by Oracle



EB05 Threshold

- Technically, any EBGM value above one indicates disproportional reporting
- 90% Confidence Interval around the EBGM with EB05 signifying the lower 5% bound and EB95 signifying the upper 5% bound.
- Standard Threshold: $EB05 \geq 2$



Different Assessments

- FDA analyses include an overall score for all reports
- Additional assessments include EB05 scores for the following subgroups:
 - US reports
 - US Age groups
 - US Gender
 - US Serious and fatal reports
- Data mining results reviewed at different intervals based on length of time vaccine has been licensed and number of VAERS reports received for the product
- Currently reviewing data mining runs weekly for COVID-19 vaccines



Limitations

- Hypothesis generating tool only
 - An elevated EB05 score is not necessarily a safety signal
- Absence of disproportionality does not confirm the absence of a safety signal
- Passive reporting of VAERS database
 - Impacted by stimulated reporting
 - Underreporting
 - Incomplete or variable reporting
 - Unverified reports



Limitations (cont.)

- Potential statistical interaction with concomitant vaccines
- Confounding by indication
- MedDRA constraints – Based on coding hierarchy
 - Preferred Terms may not best capture a pathophysiologic process



Evaluation of a Data Mining Finding

- Case series review - look for patterns, consider possible explanations
- Characterize the finding:
 - unexpected?
 - clinically significant?
 - serious?
- Other Epidemiologic methods
 - Active surveillance
 - Potential for formal pharmacoepidemiologic study in a different database – e.g., CMS, VSD, Sentinel



Questions?

Message

From: Markowitz, Lauri (CDC/DDID/NCIRD/DVD) [REDACTED]
Sent: 4/22/2021 7:21:49 PM
To: Anderson, Steven [REDACTED]; Beresnev, Tatiana H (NIH) [REDACTED]; Broder, Karen R (CDC) [REDACTED]; Calvert, Geoffrey M (CDC) [REDACTED]; Clark, Matthew (IHS) [REDACTED]; Clark, Thomas A (CDC) [REDACTED]; Cohn, Amanda C (CDC) [REDACTED]; Collins, Limone [REDACTED]; Cunningham, Fran [REDACTED]; Daley, Matt [REDACTED]; DeStefano, Frank (CDC) [REDACTED]; Edwards, Kathy [REDACTED]; Farizo, Karen [REDACTED]; Forshee, Richard [REDACTED]; Gee, Julianne M (CDC) [REDACTED]; Helfand, Rita (CDC) [REDACTED]; Hiers, Susan G (CDC) [REDACTED]; Hopkins, Bob [REDACTED]; Jackson, Lisa [REDACTED]; Kelman, Jeffrey A (CMS) [REDACTED]; LaPorte, Kathleen (CDC) [REDACTED]; Lee, Grace [REDACTED]; MacNeil, Jessica R (CDC) [REDACTED]; Markowitz, Lauri (CDC) [REDACTED]; Marquez, Paige L (CDC) [REDACTED]; Mbaeyi, Sarah A (CDC) [REDACTED]; Mullen, Jennifer (CDC) [REDACTED]; Myers, Tanya R (CDC) [REDACTED]; Nair, Narayan [REDACTED]; Oliver, Sara E (CDC) [REDACTED]; Patricia Whitley-Williams [REDACTED]; Riley, Laura [REDACTED]; Rubin, Mary (HRSA) [REDACTED]; Schechter, Robert [REDACTED]; Shanley, Edwin (CDC) [REDACTED]; Shay, David K (CDC) [REDACTED]; Shimabukuro, Tom (CDC) [REDACTED]; Sotir, Mark J (CDC) [REDACTED]; Steinberg, Judith L (OS) [REDACTED]; Su, John (CDC) [REDACTED]; Talbot, Keipp [REDACTED]; Wasley, Annemarie (CDC) [REDACTED]; Weintraub, Eric S (CDC) [REDACTED]; Wharton, Melinda (CDC) [REDACTED]; Wong, Hui-Lee [REDACTED]; Woo, Jared M (CDC) [REDACTED]; Young, Mardia A (CDC) [REDACTED]
Subject: [EXTERNAL] VaST - Draft minutes and report from April 19 (CONFIDENTIAL)
Attachments: 2021-04-19 - VaST Report Data Table DRAFT.docx; 2021_04_19_VaST minutes_draftv2.docx

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear VaST members and attendees,

Attached are the draft minutes and summary report from the call this week. Please let us know if there are any corrections or comments.

The next VaST call is April 26, 1:30 – 3:00 pm EDT.

The agenda will focus on maternal immunization for the first half, followed by further data on TTS.

Lauri Markowitz and Melinda Wharton

*Lauri Markowitz, MD
VaST Co-Lead
Division of Viral Diseases
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention*

Message

From: Markowitz, Lauri (CDC/DDID/NCIRD/DVD) [REDACTED]
Sent: 4/26/2021 3:23:35 PM
To: Anderson, Steven [REDACTED]; Beresnev, Tatiana H (NIH) [REDACTED]; Broder, Karen R (CDC) [REDACTED]; Calvert, Geoffrey M (CDC) [REDACTED]; Clark, Matthew (IHS) [REDACTED]; Clark, Thomas A (CDC) [REDACTED]; Cohn, Amanda C (CDC) [REDACTED]; Collins, Limone [REDACTED]; Cunningham, Fran [REDACTED]; Daley, Matt [REDACTED]; DeStefano, Frank (CDC) [REDACTED]; Edwards, Kathy [REDACTED]; Farizo, Karen [REDACTED]; Forshee, Richard [REDACTED]; Gee, Julianne M (CDC) [REDACTED]; Helfand, Rita (CDC) [REDACTED]; Hiers, Susan G (CDC) [REDACTED]; Hopkins, Bob [REDACTED]; Jackson, Lisa [REDACTED]; Jennifer Nelson [REDACTED]; Kelman, Jeffrey A (CMS) [REDACTED]; LaPorte, Kathleen (CDC) [REDACTED]; Lee, Grace [REDACTED]; MacNeil, Jessica R (CDC) [REDACTED]; Markowitz, Lauri (CDC) [REDACTED]; Marquez, Paige L (CDC) [REDACTED]; Mbaeyi, Sarah A (CDC) [REDACTED]; Mullen, Jennifer (CDC) [REDACTED]; Myers, Tanya R (CDC) [REDACTED]; Nair, Narayan [REDACTED]; Oliver, Sara E (CDC) [REDACTED]; Patricia Whitley-Williams [REDACTED]; Riley, Laura [REDACTED]; Rubin, Mary (HRSA) [REDACTED]; Schechter, Robert [REDACTED]; Shanley, Edwin (CDC) [REDACTED]; Shay, David K (CDC) [REDACTED]; Shimabukuro, Tom (CDC) [REDACTED]; Sotir, Mark J (CDC) [REDACTED]; Steinberg, Judith L (OS) [REDACTED]; Su, John (CDC) [REDACTED]; Talbot, Keipp [REDACTED]; Wasley, Annemarie (CDC) [REDACTED]; Weintraub, Eric S (CDC) [REDACTED]; Wharton, Melinda (CDC) [REDACTED]; Wong, Hui-Lee [REDACTED]; Woo, Jared M (CDC) [REDACTED]; Young, Mardia A (CDC) [REDACTED]
Subject: [EXTERNAL] VaST - Agenda for April 26 (1:30 - 3 pm ET) and presentations - CONFIDENTIAL
Attachments: VaST vsafe 4_26_2021_pregnancy.pdf; VaST 26-registry Apr 2021.pdf; VAST_VaxSafety_VAERS_PREGNANCY_April26.pdf; VSD studies on COVID vaccine and pregnancy for VaST 042620_clean.pdf; VaST general update vsafe 4_26_2021.pdf; 2021_04_26 VaST Meeting Agenda.docx

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear all,

This email includes the VaST agenda for today as well as slides for the call.
The maternal immunization portion is 1:30 to 2:30 pm, followed by a focus on TTS from 2:30 to 3:00 pm.

The VaST call information should be on your calendars.
Reminder - all VaST documents and communications are confidential.

Lauri Markowitz and Melinda Wharton

Lauri Markowitz, MD
VaST Co-Lead
Division of Viral Diseases
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention



Update from v-safe team: Preliminary reporting from pregnant Janssen COVID-19 vaccine recipients

Tanya Myers, PhD, MSc
v-safe Team Lead

Vaccine Safety Technical Subgroup
April 26, 2021

Outline

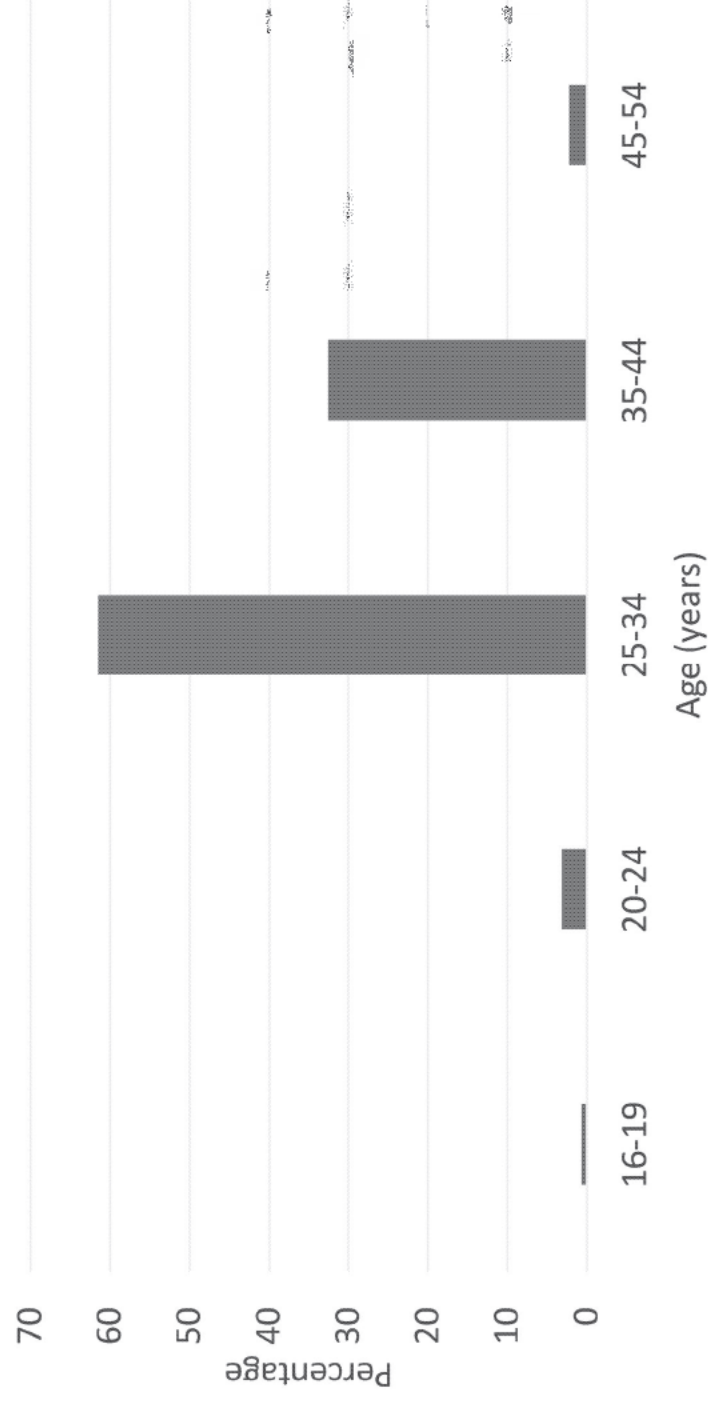
- Pregnancies reporting to v-safe after Janssen COVID-19 vaccine
- Reactogenicity reported on day 1

Pregnancies reported to v-safe after Janssen COVID-19 vaccine

Among participants at 16 -54 at 1 st dose	Number	%
Eligible for pregnancy questions*	148,353	--
Total identified as potential pregnancy	3,118	2.1
Pregnant at time of vaccination	2,944	2.0
Positive pregnancy test after vaccination	174	0.1

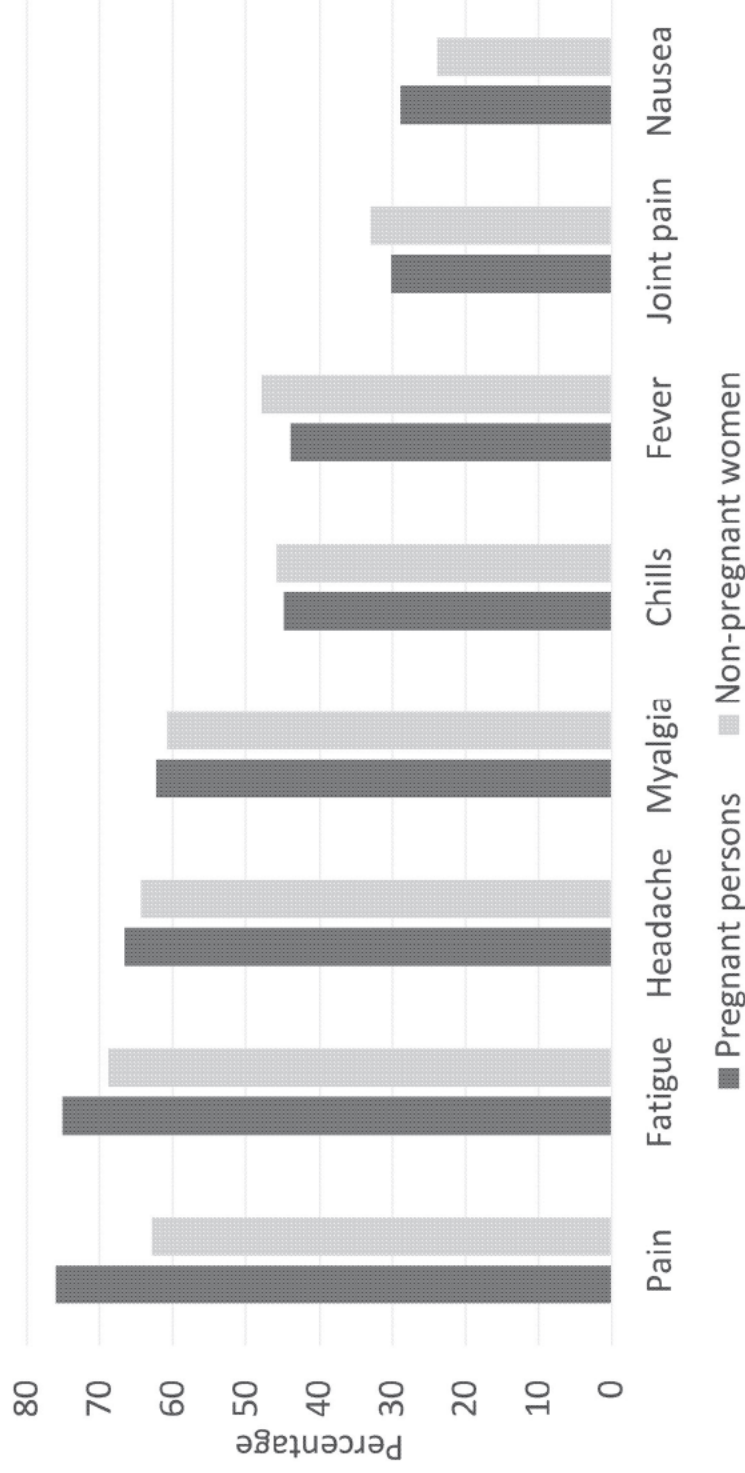
*data through April 19, 2021 at 5 am ET; participants who selected sex as female, other or prefer not to say were eligible for pregnancy questions

Age of pregnant Janssen COVID-19 vaccine recipients* in v-safe



*data through April 19, 2021 at 5 am ET

Comparison of solicited reactions in pregnant and non-pregnant v-safe participants*, day 1 after vaccine



*data through April 19, 2021 at 5 am ET

For more information, contact CDC

  www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



PSICOVID_00010656

Centers for Disease Control and Prevention



V-Safe Pregnancy Registry

Sascha Ellington, PhD

Shin Kim, MPH

Co-leads v-safe Pregnancy Registry

Vaccine Task Force

Centers for Disease Control and Prevention

April 26, 2021

Outline

- Number of pregnant persons enrolled to date
- NEW: v-safe follow-up survey
- Description of pregnant participants and pregnancy outcomes
- Next steps

v-safe and pregnancy registry (As of 4/26/2021; 5 AM ET)

	All Vaccines N	Pfizer- BioNTech N	Moderna N	Janssen N
Potential pregnancies in v-safe	100,599	55,724	41,423	3,452
Pregnancy registry				
Enrolled	4,711	2,376	2,073	262
Not Eligible ^a	3,267	1,527	1,721	19
Refused/Declined ^b	2,776	1,513	1,246	17
Unreachable ^c	1,876	879	872	125

^a Eligibility assessment determines whether vaccination was during pregnancy or within 30 days of last menstrual period

^b Refused indicates those for whom eligibility could not be fully assessed because participant chose not to engage with pregnancy registry team; declined indicates those who were eligible to participate but chose not to enroll

^c Unreachable indicates those that were not reached after 2 attempted calls 3-days apart or due to language barriers

NEW v-safe follow-up survey

Pregnancy Question[^]:

Dose 1: Initial survey, Day 21, 42^{^^}

Dose 2: Initial survey, Day 21, 42, Month 3, 6, 12^{^^}

NEW Follow-up survey

Question 1: Pregnancy status

Question 2: Permission to contact

Question 3: Availability

[^]Will be asked of all non-male sex v-safe participants (i.e., female, unknown, prefer not to say)

^{^^}Question will be hidden if vaccine recipient answers "yes" to a prior pregnancy status question for the respective dose

 v-safe Pregnancy Registry

Introduction text about the Pregnancy Registry.

Pregnancy Status

Please choose which of the following scenarios best describes you *

☐ Pregnant at time of vaccination

☐ Pregnant after vaccination

☐ Not pregnant at or since vaccination

Permission to Contact

Please select your choice below *

☐ Yes, I would like someone to contact me so that I can learn more about the CDC's v-safe pregnancy registry

☐ No, Please do not call me, I do not want to participate



NEW: v-safe follow-up survey results (as of 4/18/2021)

	All Vaccines N	Pfizer- BioNTech N	Moderna N	Janssen N
Completed surveys ^a	30,854	17,910	12,798	146
	N (%)	N (%)	N (%)	N (%)
Pregnant	26,250 (85%)	15,672 (88%)	10,439 (82%)	139 (95%)
Pregnant after vaccination	1,761 (6%)	901 (5%)	860 (7%)	0 (0%)
Not Pregnant	2,843 (9%)	1,337 (7%)	1,499 (12%)	7 (5%)
Willing to be contacted ^b	25,376 (91%)	15,135 (91%)	10,112 (89%)	129 (93%)

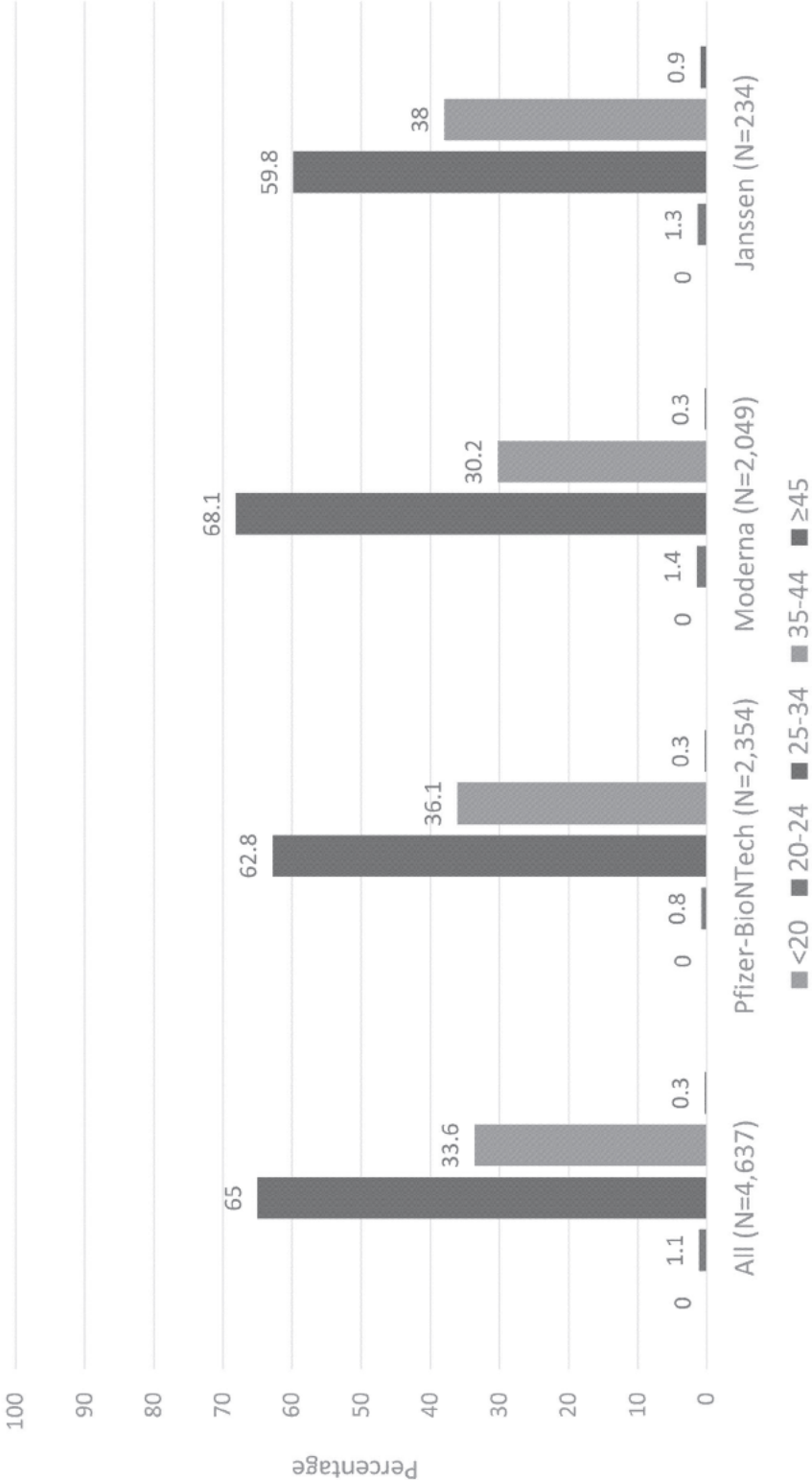
^a Excludes 3 participants whose preferred language was not English or Spanish

^b Percentage among those who are pregnant at or after vaccination

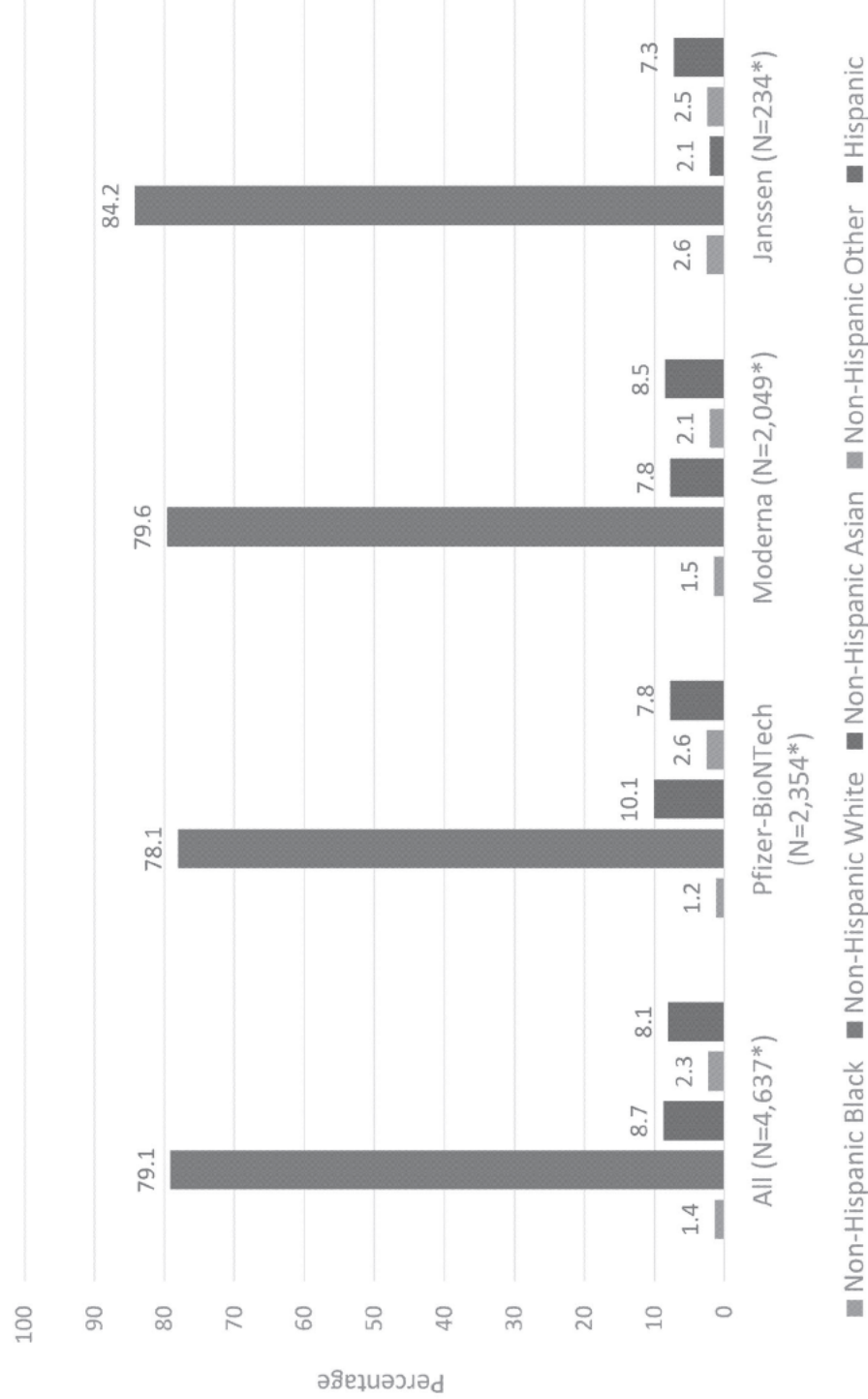


Registry Participant Characteristics and Pregnancy Outcomes: enrolled as of 04/20/2021 at 8:15am

Registry Participant Characteristic: Age at 1st Eligible Vaccine Dose (N=4,637)



Registry Participant Characteristic: Race/Ethnicity



*Missing/Declined N=18 (All), N=5 (Pfizer), N=10 (Moderna), N=3 (Janssen)

Self-Reported Vaccine Priority Group[^]

	Vaccine manufacturer						
	Pfizer- BioNTech						Janssen-J&J
	All		All	Moderna			All
	N=4,637	N=2,354	N=2,049	N=2,049			N=234
Self-reported vaccine priority group^	N	%	n	%	n	%	n
Healthcare worker*	4,082	88.0	2,190	93.0	1,847	90.1	45
Non-healthcare essential worker*	235	5.1	80	3.4	101	4.9	54
Medical condition other than pregnancy only	40	0.9	12	0.5	10	0.5	18
Pregnancy only	82	1.8	20	0.8	20	1.0	42
Other only	19	0.4	7	0.3	7	0.3	5
No to all options (including other)	151	3.3	37	1.6	52	2.5	62
Missing	21	0.5	6	0.3	8	0.4	7

[^]Military, state/federal government employee categorized as non-healthcare essential worker

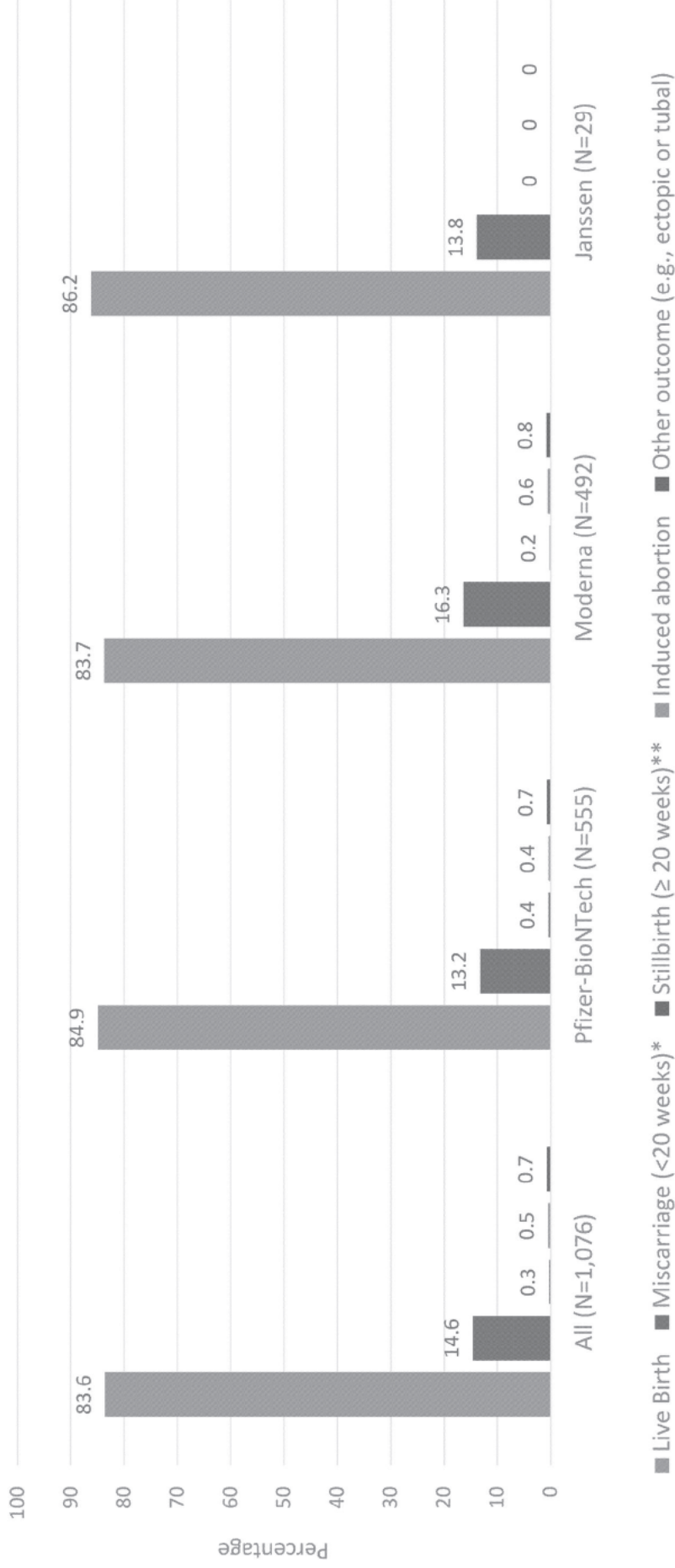
*Includes respondents who selected other categories

Timing of first eligible COVID-19 dose among v-safe pregnancy registry participants

Among 4,637 pregnancies



Pregnancy Outcome Among Completed Pregnancies



* Miscarriage <13 weeks is 93.6% of All miscarriage <20 weeks

**Stillbirth denominator is total live born infants + stillbirth (n=917)

Outcomes by Trimester of Vaccination

Characteristics	All n %	Trimester at first eligible vaccine dose							
		Pre-pregnancy		1st trimester		2nd trimester		3rd trimester	
Total Completed Pregnancies*		n	%	n	%	n	%	n	%
Live births	1076	47	4.4	124	11.5	24	2.2	880	81.8
Spontaneous abortion	900	0	0.0	0	0.0	20	83.3	880	100.0
Induced abortion*	160	42	89.4	116	93.5	2	8.3	NA	NA
Other (e.g. ectopic or tubal)	5	2	4.3	2	1.6	0	0.0	0	0.0
Stillbirths**	8	3	6.4	5	4.0	NA	NA	NA	NA
	3	0	0	1	0.8	2	8.3	0	0.0
Live born infants	914					21	2.3	893	97.7
Preterm***	69		8.6			10	47.6	59	7.5
Small for gestational age	25		2.7			0	0.0	25	2.8
Major birth defect****	23		2			1	0	22	2
Admitted to NICU	98		10.7			9	42.9	89	10.0
Neonatal or infant death	0		0.0			0	0.0	0	0.0

*One induced abortion missing trimester of vaccination

**Stillbirths among liveborn infants and stillborn infants

***Preterm birth among infants born to mothers vaccinated before 37 weeks gestation

****Birth defect: reviewed and categorized by clinical team and SMEs

Neonatal Outcomes of Interest Among Live Born Infants (n=914*)

Outcomes	Background rate	Self-reported v-safe Registry Overall
Preterm birth (<37 weeks)	8-15%	8.6%
Major congenital anomalies^^	3%	2.2%
Small for gestational age^^^	3-7%	2.7%
Admitted to NICU	9%	10.7%
Neonatal death	<1%	0.0%

*n=893 third trimester, n=21 second trimester

^^Birth defect diagnosed after delivery only, v-safe all self-reported (n=19); Includes only major congenital anomalies in accordance with the Metropolitan Atlanta Congenital Defects Program Birth defect list

(<https://www.cdc.gov/ncbddd/birthdefects/macdp.html#:~:text=Since%20MACDP%20began%20tracking%20birth,clinical%20review%20of%20abstracted%20records>); all pregnancies with major congenital anomalies were exposed to COVID-19 vaccines in the third trimester of pregnancy

^^^Birthweight below the 10th percentile for gestational age and sex using INTERGROWTH-21st Century growth standards

Summary of Findings

- Among Janssen pregnant participants who received a vaccine between 12/14/2020 through 03/27/2021, majority were:
 - Between ages 25-44 years old
 - Non-Hispanic White
 - Not a healthcare personnel
 - Second trimester
 - No COVID-19 infection in pregnancy
 - Live birth
- Most neonatal outcomes are among those with third trimester vaccine (except n=21)
- Pregnancy and neonatal outcomes of interest are all within background rates

Next Steps-data analysis and upcoming public reporting

- Data Analysis
 - Medical record abstraction training and prioritization
 - Subsequent calls of enrolled participants
- Upcoming Public Reporting
 - 4/26: ASTHO/HRSA Maternal and Child Health COVID-19 National Partners Convening (Titi)



COVID-19 maternal vaccine safety update - VAERS

December 14, 2020 – April 17, 2021

Vaccine Safety Technical subgroup

April 26, 2021

**Pedro L. Moro, MD, MPH
Immunization Safety Office**

Outline

- Characteristics of pregnancy reports
- Most common signs and symptoms reported
- Pregnancy and neonatal-specific conditions reported
- Fetal-infant conditions
- Maternal and infant deaths
- Thromboembolic events in pregnancy
- Data mining findings
- Racial and ethnic characteristics of reports
- Summary

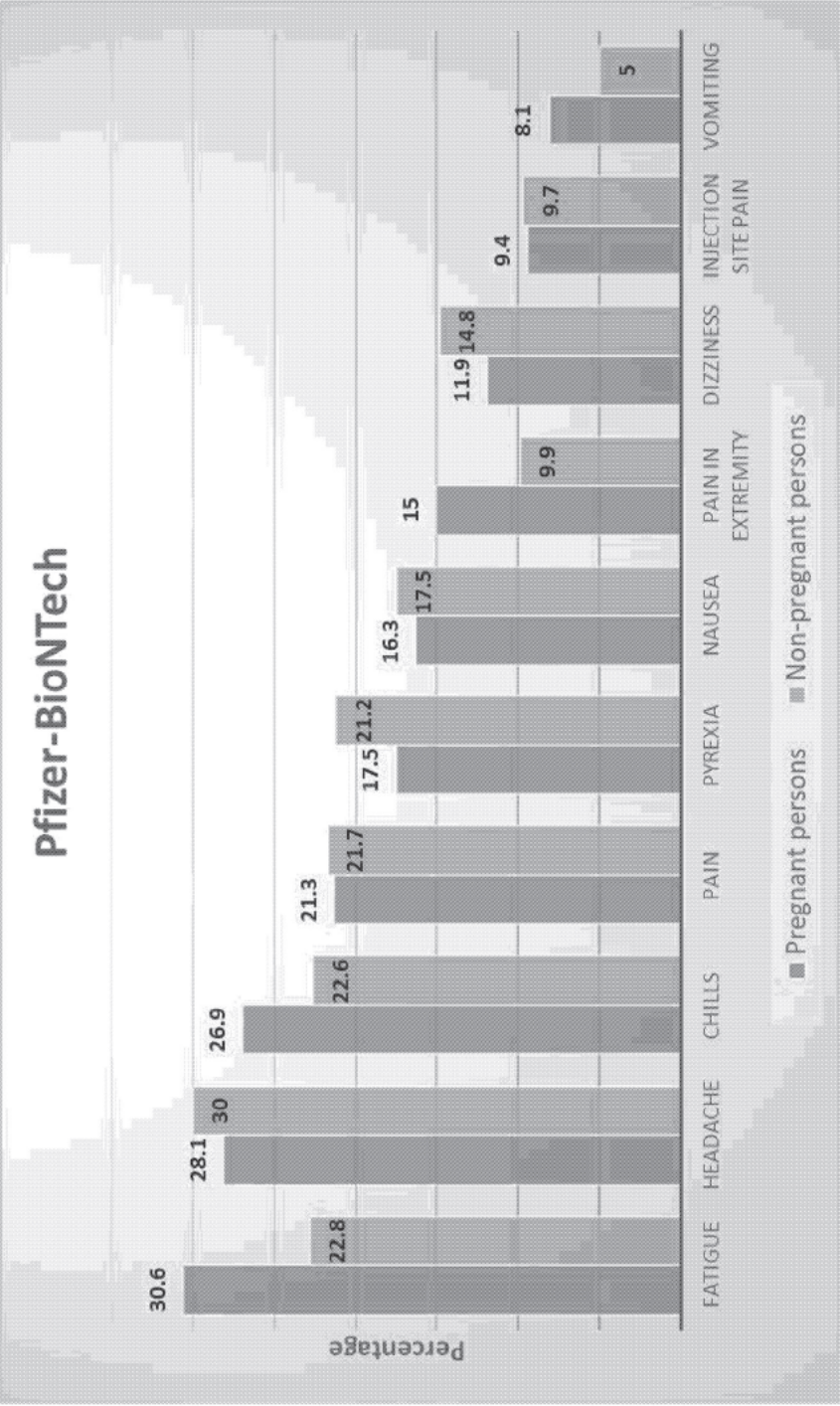
Characteristics of VAERS COVID-19 vaccine pregnancy reports submitted to VAERS*

Characteristic	Pfizer-BioNTech			
	All	Moderna	Janssen	
Number of reports	541**	257	207	76
Serious† reports	109 (20.1)	65 (23.0)	39 (15.5)	4 (5.3)
Maternal deaths	2 (0.4)	1 (0.4)	1 (0.5)	0
Pregnancy-specific reports	167 (30.9)	97 (36.1)	61 (25.7)	8 (10.5)
Maternal age in years, median (range)	33 (16–51)	33 (22–51)	33 (16–50)	33 (22–51)
Gestational age in weeks at time of vaccination when reported, median (range)	15 (1–39)	13 (1–39)	15 (1–37)	19 (2–39)
Trimester of pregnancy at time of vaccination		n (%)		
First (0–13 weeks)	185/405 (45.7)	102/201 (50.7)	66/144 (45.8)	17/60 (28.3)
Second (14–27 weeks)	127/405 (31.4)	59/201 (29.4)	46/144 (31.9)	22/60 (36.7)
Third (28+ weeks)	93/405 (22.9)	40/201 (19.9)	32/144 (22.2)	21/60 (35.0)

*Reports received and processed through April 17, 2021; **Brand unknown in one report

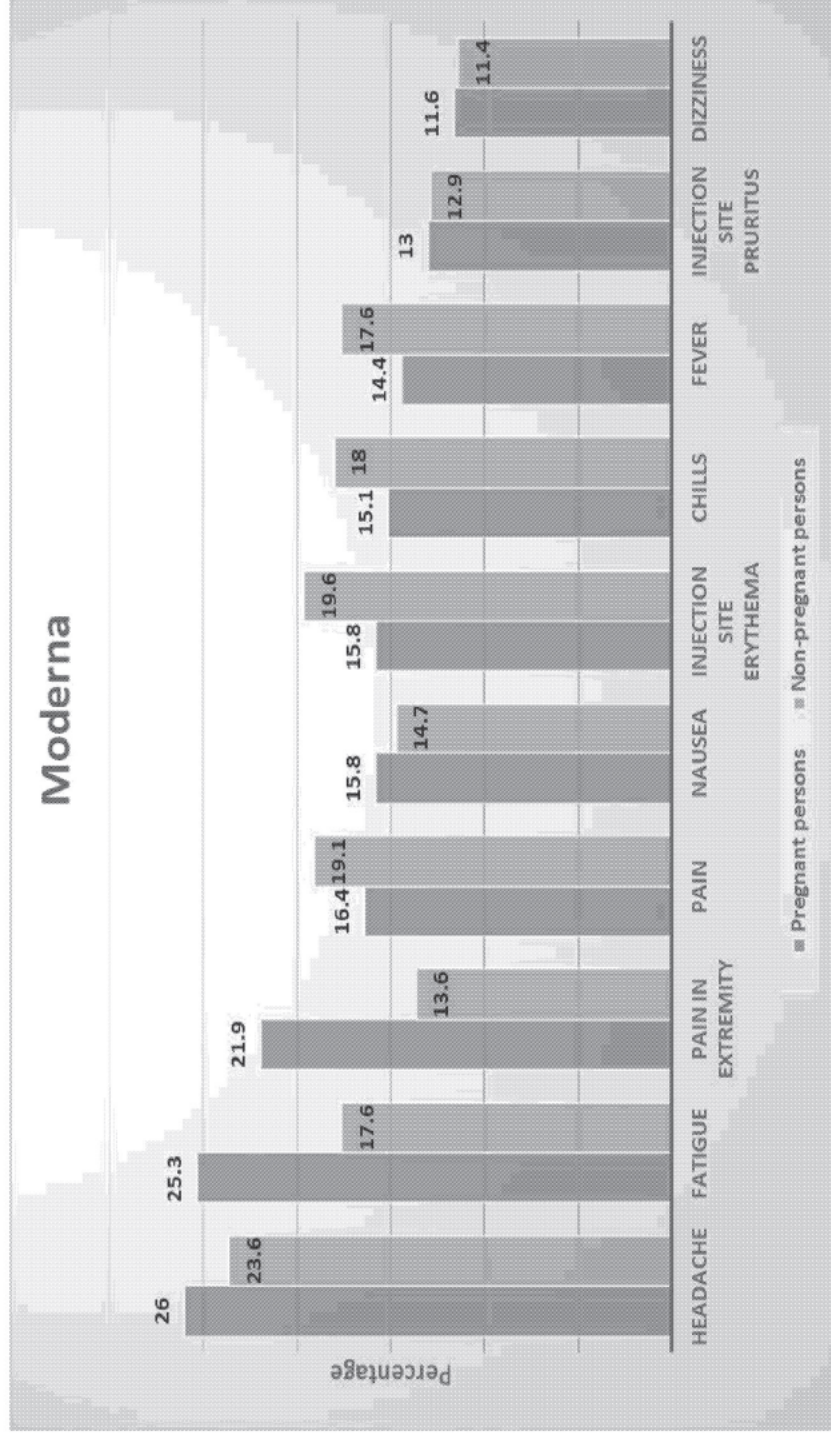
†Based on the Code of Federal Regulations if one of the following is reported: death, life-threatening illness, hospitalization or prolongation of hospitalization, permanent disability, congenital anomaly or birth defect

Most common signs and symptoms among pregnant and non-pregnant persons following COVID-19 (Pfizer-BioNTech) vaccination, VAERS



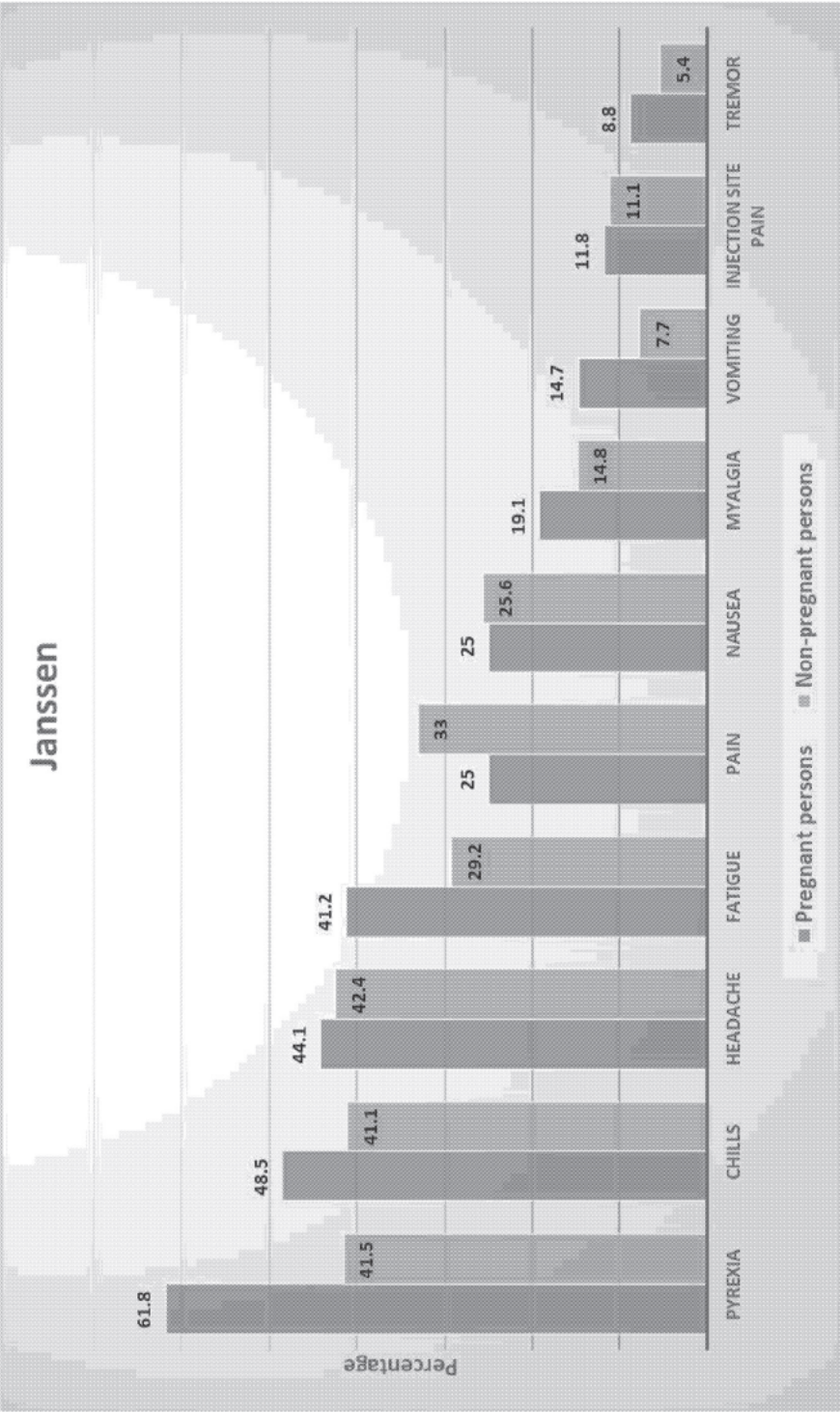
* Reports received and processed through April 17, 2021; † Adverse events are not mutually exclusive

Most common signs and symptoms among pregnant and non-pregnant persons following COVID-19 (Moderna) vaccination, VAERS



* Reports received and processed through April 17, 2021; † Adverse events are not mutually exclusive

Most common signs and symptoms among pregnant and non-pregnant persons following COVID-19 (Janssen) vaccination, VAERS



* Reports received and processed through April 17, 2021; [†] Adverse events are not mutually exclusive

Pregnancy and neonatal specific conditions among pregnant persons following COVID-19 vaccination reported to VAERS*

Characteristic	All	Pfizer-		
		BioNTech	Moderna	Janssen
Total reports	167	97	61	8
Spontaneous abortion/miscarriage	108 [†]	66	36	5
Vaginal bleeding	11	2	6	2
Preterm delivery	11	8	3	0
Preeclampsia	5	3	2	0
Premature rupture of membranes	5	3	2	0
Stillbirth	3	2	1	0
Neonatal deaths	3	3	0	0
Gestational hypertension	2	0	2	0
Other ^a	20	10	9	1

*Reports received and processed through April 17, 2021

[†] For one report of spontaneous abortion brand of vaccine unknown

^a Other reports include: for Pfizer one report each of shortened cervix, , painful contractions, placental abruption, rupture of membranes, infant seizures/ischemic brain injury, reduced fetal movement, micrognathia/absent femurs and underdeveloped/missing lower extremities, contractions/abdominal pain, eroded skin lower legs, and premature closure of ductus arteriosus; for Moderna one each of hydrops, calcified placenta, leakage of amniotic fluid, gestational diabetes, large for gestational age, skeletal dysplasia, placental abruption, and intrauterine growth retardation; for Janssen one report of gestational thrombocytopenia

Fetal-Infant conditions (n=12)

Adverse event	Vaccine
Neonatal death—preterm birth at 22 weeks	Pfizer-BioNTech
Neonatal death—preterm birth at 20 weeks	Pfizer-BioNTech
Neonatal death—preterm birth at 20 weeks	Pfizer-BioNTech
Skeletal dysplasia/cystic hygromælective termination (Ega 9w)	Pfizer-BioNTech
Severe micrognathia, absent femurs and underdeveloped/missing lower extremities (Ega 3w)	Pfizer-BioNTech
Fetal cystic hygroma—spontaneous abortion	Pfizer-BioNTech
Premature closure of ductus arteriosus, severe pulmonary hypertension (Ega 27w)	Pfizer-BioNTech
Fetal hydrops (n=2) Ega 27w]	Moderna
Infant seizures/ischemic brain injury	Pfizer-BioNTech
Preterm infant/injured brain tissue	Pfizer-BioNTech
Large for gestational age	Moderna

Maternal and Neonatal deaths

Maternal deaths (n=2)

- 1) 38 yearold, received Pfizer Covid-19 vaccine at 39 weeks gestation. History of gestational diabetes on insulin a hemochromatosis and low lying placenta. Fourteen days after vaccination presented maternal cardiac arrest terminal fetal bradycardia, emergency esection. Likely amniotic fluid embolism and disseminated intravascular coagulation.
- 2) 35 yearold received the Moderna Covid-19 vaccine at 37 weeks. Eight day later she went into labor and was progressing appropriately but she had sudden onset ofoughing followed by loss of consciousnessEmergency esection performed. Patient expired despite resuscitative efforts.

Neonatal deaths (n=3)

- 1) Person received dose 2 of PfizerBioNTechvaccine one day prior to delivery; onset of preterm labor symptoms began 2 days before dose 2 and birth occurred 32 hours after dose 2 22 weeks. Reported symptoms following receipt of dose 2 were muscle aches and chills
- 2) Person received dose 1 of PfizerBioNTechand 18 days later presented to ER with contractions and leaking fluid (no vaginal bleeding). Pregnancy had been uncomplicated. She had a history of a past~~action~~ction. Case was considered too pre-viable to attempt resuscitation. She delivered a male infant 20 weeks, 0lbs, 12 ozapgars2, 2
- 3) Person received PfizerBioNTechvaccine at20 weeks. Anatomy scan around time of vaccination was normal. Two prior pregnancies both healthy and carried full term in 2017 and 2019. Five days after vaccination patient presented spontaneous preterm labor and preterm birth of female infant who died an hour and a half after birth. Labs came back normal, no signs of infection, placenta pathology came back normal.

Thromboembolic events in pregnancy reported to VAERS

Adverse event	Age (years)	Gestational age At vaccination	Vaccine
Pulmonary embolism/superficial venous thrombosis	42	24 weeks	Moderna
Maternal death: amniotic fluid embolism and disseminated intravascular coagulation	38	39 weeks	Pfizer-BioNTech
Maternal death: Pulmonary embolism associated with death	42	27 weeks	Pfizer-BioNTech
Maternal death: thrombosis 4 weeks post-partum resulting in death	Unknown	Unknown	Janssen

Data mining analysis

- Empirical Bayesian data mining conducted by FDA (lock point 4/16/2021) did not detect any disproportionality alerts for any pregnancy/neonatal-specific or non-pregnancy-specific adverse events for any COVID-19 vaccine in women aged 15-54 years

Racial and ethnic characteristics of COVID-19 vaccine pregnancy reports submitted to VAERS*

Race/ethnicity	All**	Pfizer-		
		BioNTech	Moderna	Janssen
Total reports	541	257	207	76
White	390	176	153	61
Asian	35	20	13	2
Black/African-American	14	6	8	0
Multiracial	20	10	7	3
American Indian/Alaskan native	3	3	0	0
Native Hawaiian or other Pacific Islander	3	0	1	2
Other	10	1	6	3
Missing or unknown	66	41	19	5
Hispanic	39	13	17	8
Non-Hispanic	386	175	149	62
Missing or unknown	116	69	41	6

*Reports received and processed through April 17, 2021; **Brand unknown in one report

Summary

- ❑ Most common signs and symptoms reported were systemic and local reactions similar to non-pregnant women in VAERS
- ❑ Most common pregnancy-specific condition was spontaneous abortion:
 - Comparable to other maternal vaccines in VAERS
 - Miscarriage relatively frequent in pregnancy
- ❑ No disproportional reporting for any adverse event after the three Covid-19 vaccines
- ❑ Safety profile of Covid-19 vaccine reports in pregnant persons in VAERS appears to be reassuring

Acknowledgments

- FDA
 - Meghna Alimchandani
 - Adamma Mba-Jonas

Thank you

For more information, contact CDC



www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



PSICOVID_00010686

Safety of COVID-19 Vaccination in Pregnancy, Interim Data from the Vaccine Safety Datalink

Elyse Kharbanda, MD, MPH
HealthPartners Institute

ACIP COVID-19 Vaccines Safety Technical
Workgroup Meeting

April 26, 2021

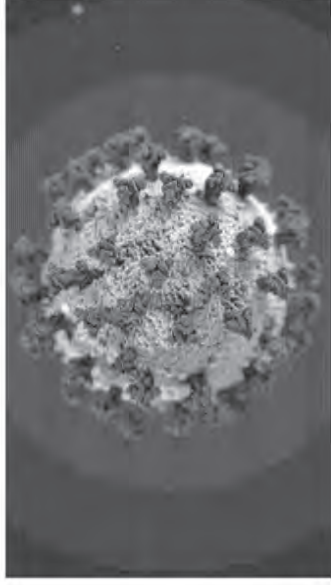


Overview of VSD maternal vaccination surveillance

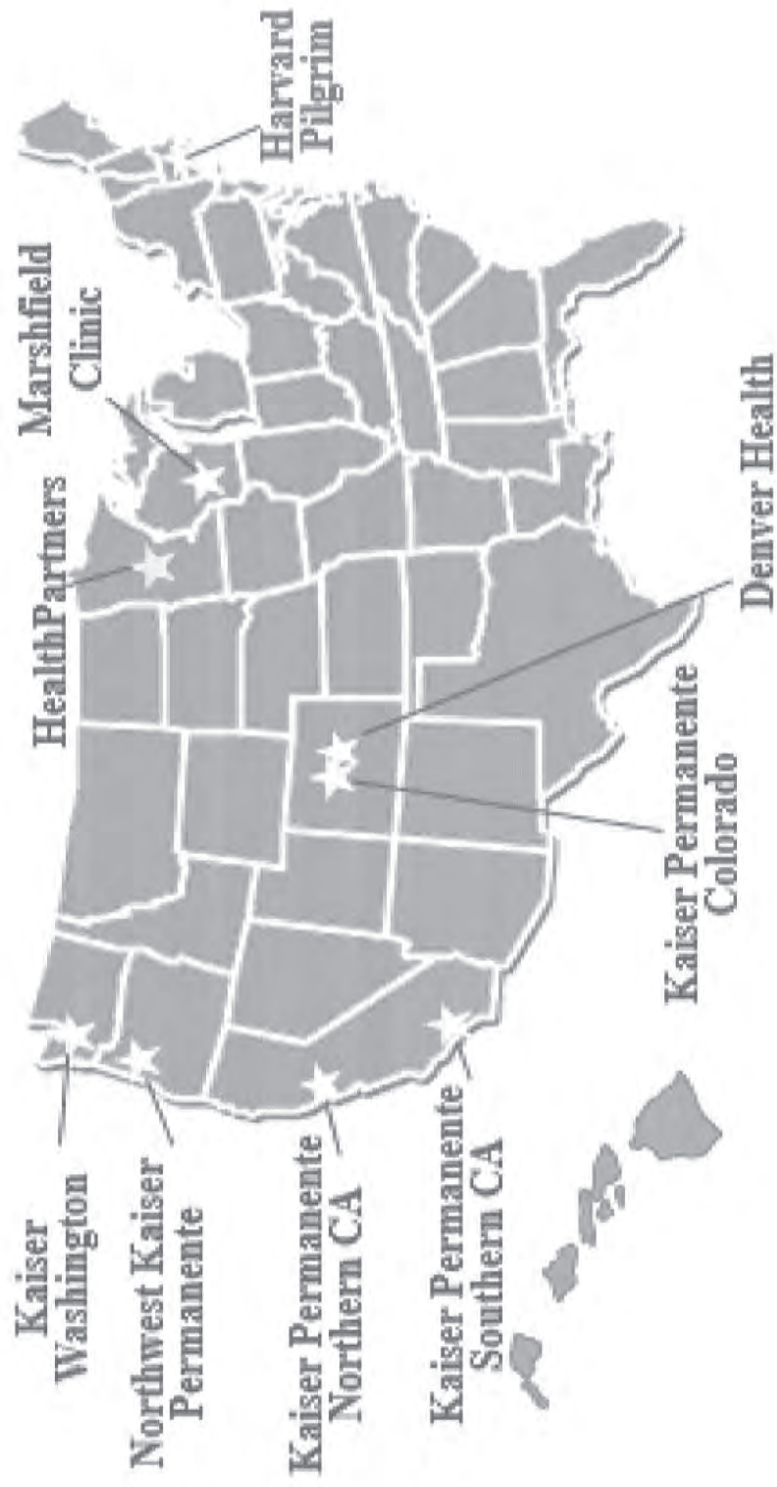
- To evaluate the safety of COVID-19 vaccine administered during pregnancy for a range of maternal and infant outcomes:
 - Spontaneous abortion (SAB)
 - Stillbirth
 - Acute (0-21 and 0-42 day) vaccine safety outcomes
 - Pregnancy complications (eg, preeclampsia)
 - Birth outcomes (eg, preterm birth)
 - Infant morbidity
 - Infant mortality
 - Birth defects
 - Infant growth and development in first year of life

Presentation today

- Interim safety data from
 - SAB near-real time surveillance
 - Stillbirth surveillance
 - Acute event surveillance (0-21 days)
- Next steps for VSD studies on COVID-19 vaccine safety in pregnancy



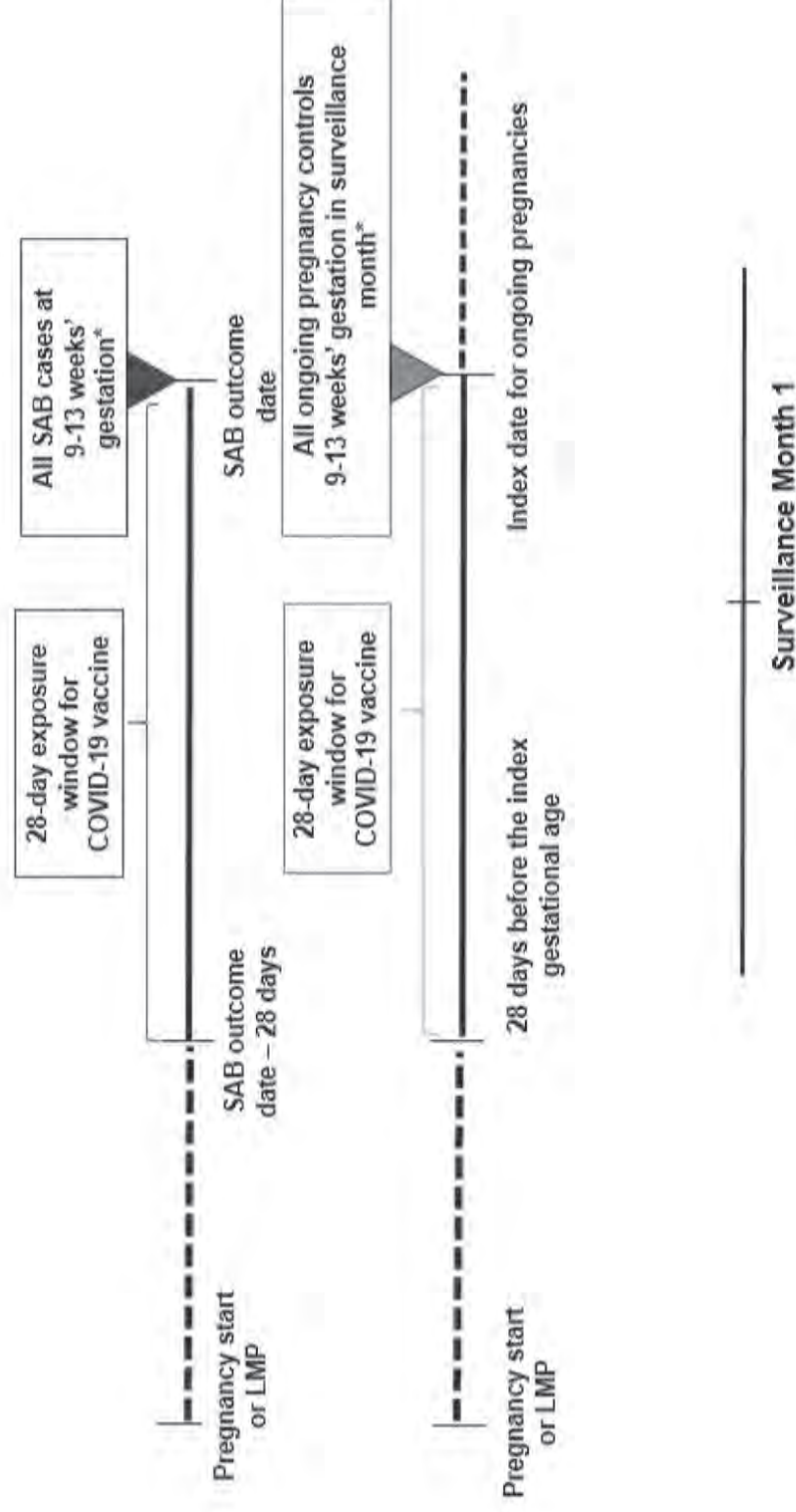
Vaccine Safety Datalink (VSD) sites



COVID-19 vaccine in pregnancy and spontaneous abortion (SAB) near-real time surveillance

- Using a validated algorithm, applied to automated electronic health data, to conduct near-real time case-control surveillance
- Every 4 weeks we identify SABs and ongoing pregnancies <20 weeks stratified by gestational age groups, maternal age, receipt of prenatal care
- Using GEE, odds of exposure to COVID-19 vaccine in 28 days prior to SAB compared to odds of exposure to COVID-19 vaccine among ongoing pregnancies in 28 days prior to index date
- Pregnancy outcomes and pregnancy dating not chart confirmed

SAB-control surveillance – example for SABs and ongoing pregnancies between 9-13 weeks' gestation, during first surveillance period



*Use exact gestational age dating if available; if only estimated gestational age available, assign index gestational age of 8, 12, 16 weeks for gestational age groups ≤8, 9-13, 15-19 weeks, respectively

Interim results, 12/15/20-3/8/21 for 7 VSD sites, 28,564 pregnancies <20 weeks' gestation Baseline characteristics for SAB surveillance

Pregnancy Episodes 12/15/20 - 3/8/21	Ongoing		SAB		All	
	N	%	N	%	N	%
All	25,409	100.0	3155	100.0	28,564	100.0
Maternal Age						
16-24 years	3189	12.6	293	9.3	3482	12.2
25-34 years	16139	63.5	1573	49.9	17712	62.0
35-49 years	6081	23.9	1289	40.9	7370	25.8
Race/ethnicity						
Asian	4566	18.0	583	18.5	5149	18.0
Black, non-Hispanic	1783	7.0	262	8.3	2045	7.2
Hispanic	5668	22.3	677	21.5	6345	22.2
Unknown / Other	2672	10.5	330	10.5	3002	10.5
White, non-Hispanic	10720	42.2	1303	41.3	12023	42.1

Interim results, 12/15/20-3/8/21 for 7 VSD sites, 48,742 pregnancy-months of surveillance

	All pregnancies			Ongoing pregnancies			Spontaneous abortions		
	N	COVID vaccine n	COVID vaccine %	N	COVID vaccine n	COVID vaccine %	N	COVID vaccine n	COVID vaccine %
All pregnancy months*	48,742	1947	4.0	45,587	1808	4.0	3155	139	4.4
By gestational age strata									
6-8 weeks	5811	274	4.7	5019	237	4.7	792	37	4.7
9-13 weeks	19,860	769	3.9	17,797	681	3.8	2063	88	4.3
14-19 weeks	23,071	904	3.9	22,771	890	3.9	300	14	4.7

*Individual pregnancies may be contribute data for more than one month of surveillance
Pregnancies <20 weeks' gestation included

Interim analyses, SAB surveillance 12/15/20-3/8/21, 7 VSD sites

	aOR (95% CI)	p-value
All pregnancy months	0.98 (0.82 - 1.17)	0.81
By gestational age strata		
6-8 weeks	0.87 (0.61 - 1.22)	0.41
9-13 weeks	1.02 (0.81 - 1.28)	0.89
14-19 weeks	1.06 (0.62 – 1.80)	0.84

aOR = adjusted odds ratio; SAB= spontaneous abortion

aORs for SABs outcome during monthly surveillance

GEE models adjusted for gestational age group, study month, site, maternal age group, number of antenatal visits, and race/ethnicity and accounted for repeated ongoing pregnancies

Stillbirth surveillance – 8 VSD sites

- Potential stillbirth cases with COVID-19 vaccine exposures identified monthly from automated algorithm
- To increase sensitivity, including diagnosed stillbirths and SABs at 18-19 weeks' gestation
- Case accrual began in December 2020
- All potential cases chart reviewed by sites
- All potential cases then adjudicated by Yale OB team – Drs. Lipkind, Reddy, Sheth and Greenberg
- For confirmed stillbirths, using adjudicated date and gestational age at fetal demise, evaluated timing of COVID-19 vaccine exposures

Stillbirth surveillance – 8 VSD sites December 2020 – March 2021 Interim results based on April data pull

Outcome date	Stillbirths or SABs at 18 or 19 weeks' gestation* (N)	Stillbirths or SABs at 18 or 19 weeks' gestation with COVID-19 vaccine* (N)	Excluded** (N)	Confirmed stillbirths with COVID-19 vaccine exposure during pregnancy (N)
December 2020	49	0	.	0
January 2021	102	3	3	0
February 2021	88	6	5	1
March 2021	67	6	3	3
December 2020- March 2021	306	15	11	4***

*Based on automated pregnancy algorithm

**Exclusions due to outcome not a stillbirth (SAB, n=10), (ongoing pregnancy, n=1)

*** Of 4 confirmed stillbirths, 3 had a presumed non-vaccine related etiology for the stillbirth

- Acute adverse events, within 21 days of maternal vaccination, 7 VSD sites
- Vaccines administered from 12/15/20 – 3/14/21
 - Ongoing pregnancies or ending in SAB, stillbirth or live birth
 - Outcomes identified primarily from diagnoses, applied algorithms similar to VSD RCA
 - Severe vaccine safety outcomes (eg, VTE, PE, anaphylaxis)
 - Other outcomes of interest (eg, medically attended fever, lymphadenitis, urticaria)
 - Algorithms exclude if alternative etiology, prior diagnosis

Acute adverse events
(0-21 days) following
maternal COVID-19
vaccination, interim
results:

Baseline
characteristics of
population, 7 VSD
sites

	N	%
All	10,022	100.00
Pregnancy outcome		
Live birth	862	8.6
Ongoing	8750	87.3
Spontaneous abortion	407	4.1
Stillbirth	3	0.03
Age group (years)		
16-24	343	3.4
25-29	1758	17.5
30-34	4349	43.4
35-39	2976	29.7
40-49	596	6.0
Race ethnicity		
Asian	2347	23.4
Black, non-Hispanic	267	2.7
Hispanic	1518	15.2
Other/unknown	893	8.9
White, non-Hispanic	4997	49.9
Vaccine type		
Janssen	403	4.0
Moderna	4076	40.7
Pfizer	5541	55.3
Covid-19 doses received during pregnancy		
1	7463	74.5
2	2559	25.5

Interim results: Acute events following COVID-19 vaccination, 12/15/20 – 3/14/2021, 7 VSD sites, of 12,475 doses in pregnancy

Acute events	N	Events per 10,000 vaccines
1-7 days following vaccination		
Fever	4	3.2
Lymphadenitis / lymphadenopathy / arm pain	10	8.0
Malaise / fatigue / complication following immunization NOS	17	13.6
Rash / urticaria / allergy / serum reaction to vaccine	9	7.2
1-21 days following vaccination		
Appendicitis	1	0.8
Venous thromboembolism	1	0.8

Summary and next steps

- Interim evaluation of maternal COVID-19 vaccination in pregnancy have found no concerning safety signals to date
- Acute safety events to be evaluated for first 6 months of vaccination, with rates compared to matched, unvaccinated pregnant women
- SAB and stillbirth surveillance to continue and planning for retrospective case-control study, with all cases chart reviewed and adjudicated
- Maternal complications, birth outcomes, birth defects, infant morbidity, mortality, growth and development to be evaluated using a retrospective cohort

Our Team

HealthPartners

- Elyse Kharbanda, Project Director
- Malini DeSilva
- Gabriela Vazquez-Benitez
- Leslie Kuckler
- Jingyi Zhu
- Jacob Haapala
- Sunita Thapa
- Sheryl Kane
- Nicole Trower

Yale University

- Heather Lipkind, Co-Project Director for IUFD
- Uma Reddy,
- Sangini Sheth,
- Victoria Greenberg,

Kaiser Northwest

- Kimberly Vesco



HealthPartners[®] Institute

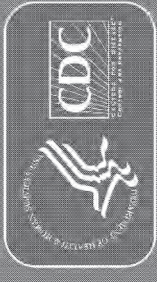


CDC

- Anne Hause
- Mike McNeil
- Eric Weintraub

Other VSD sites

- Nicola Klein
- Matt Daley
- Darios Getahun
- Stephanie Irving
- Michael Jackson
- Joshua Williams
- Simon Hambidge
- Jim Donahue



Update from v-safe team

Tanya Myers, PhD, MSc
v-safe Team Lead

Vaccine Safety Technical Subgroup
April 26, 2021

Outline

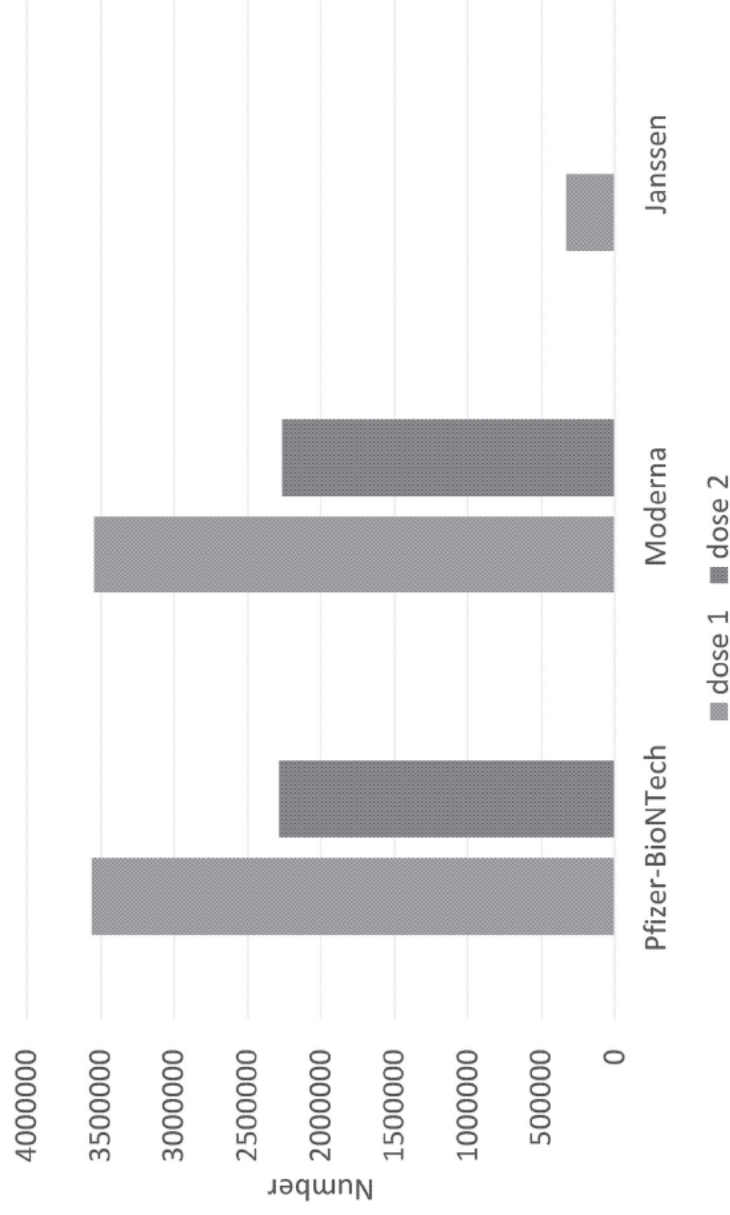
- Operational updates
- Current participation for all vaccines
- Focus on Janssen COVID-19 vaccine

Operational updates

- Additional languages added to v-safe platform
 - Spanish, Chinese, Vietnamese, Korean
- Reconfiguration to permit unusual dose completion patterns
 - Pfizer-BioNTech/Moderna 1st dose, Janssen 2nd dose
- Assessment of changes required for utilization in younger ages
 - Parental/guardian consent and contact information

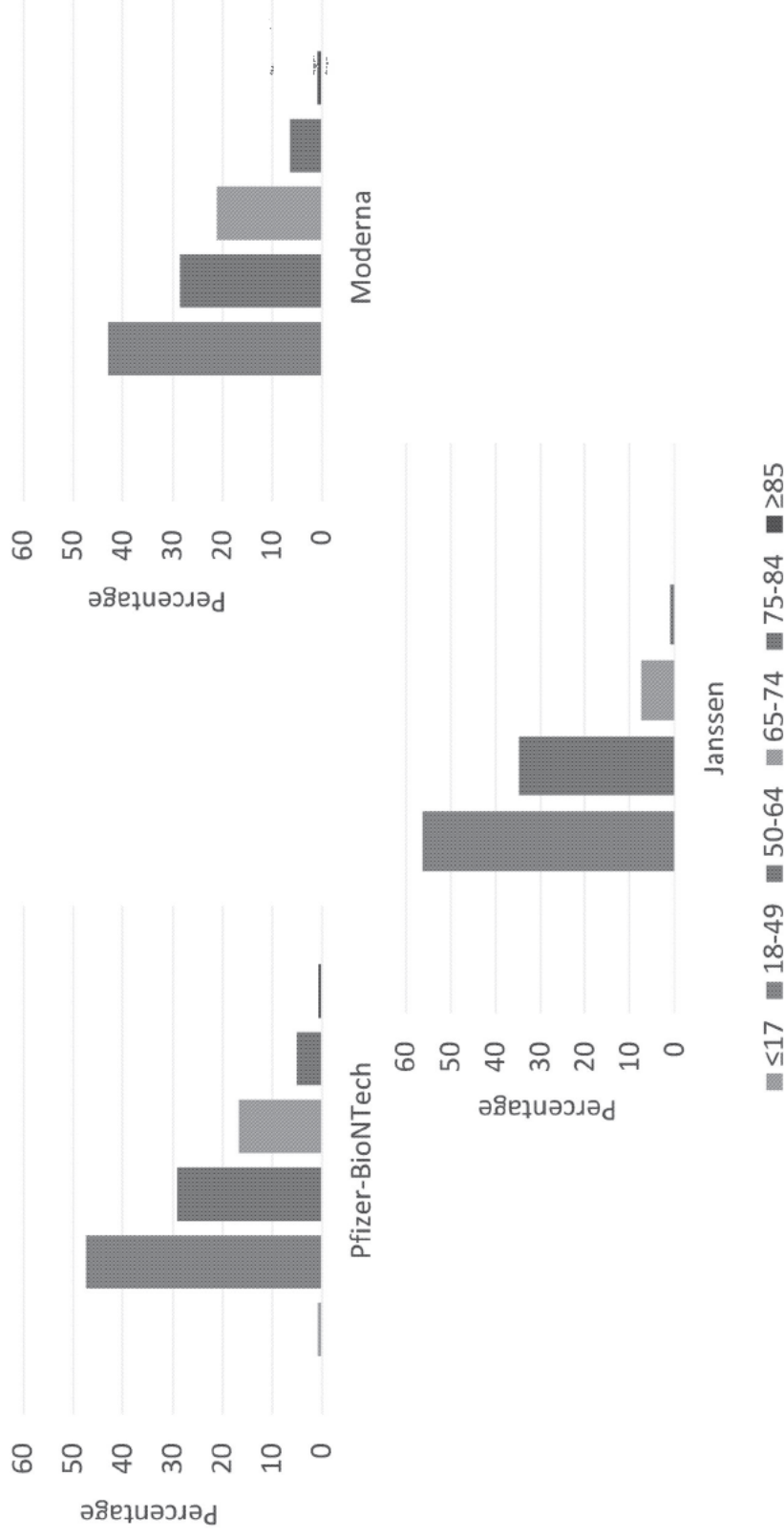
</

Manufacturer and dose for active v-safe participants*



*active indicates completion of at least one health survey by April 12, 2021 at 5 am ET

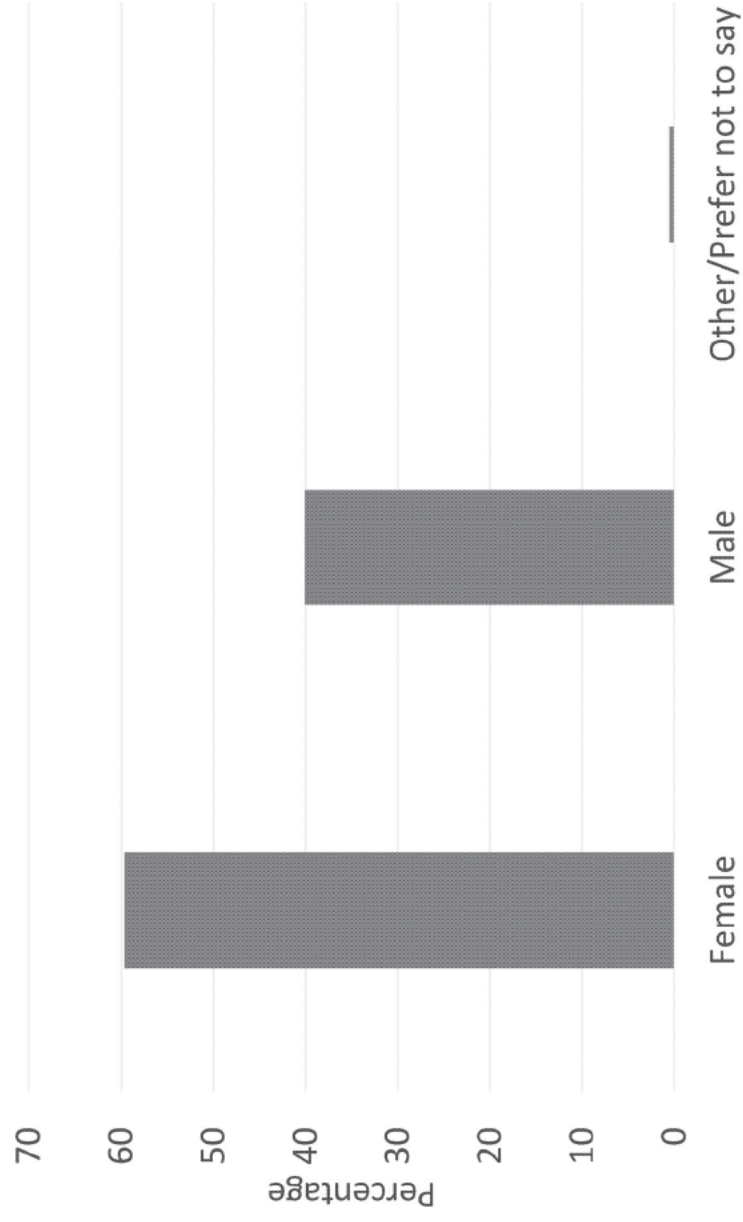
Age at first dose for active v-safe participants*



*active indicates completion of at least one health survey by April 12, 2021 at 5 am ET

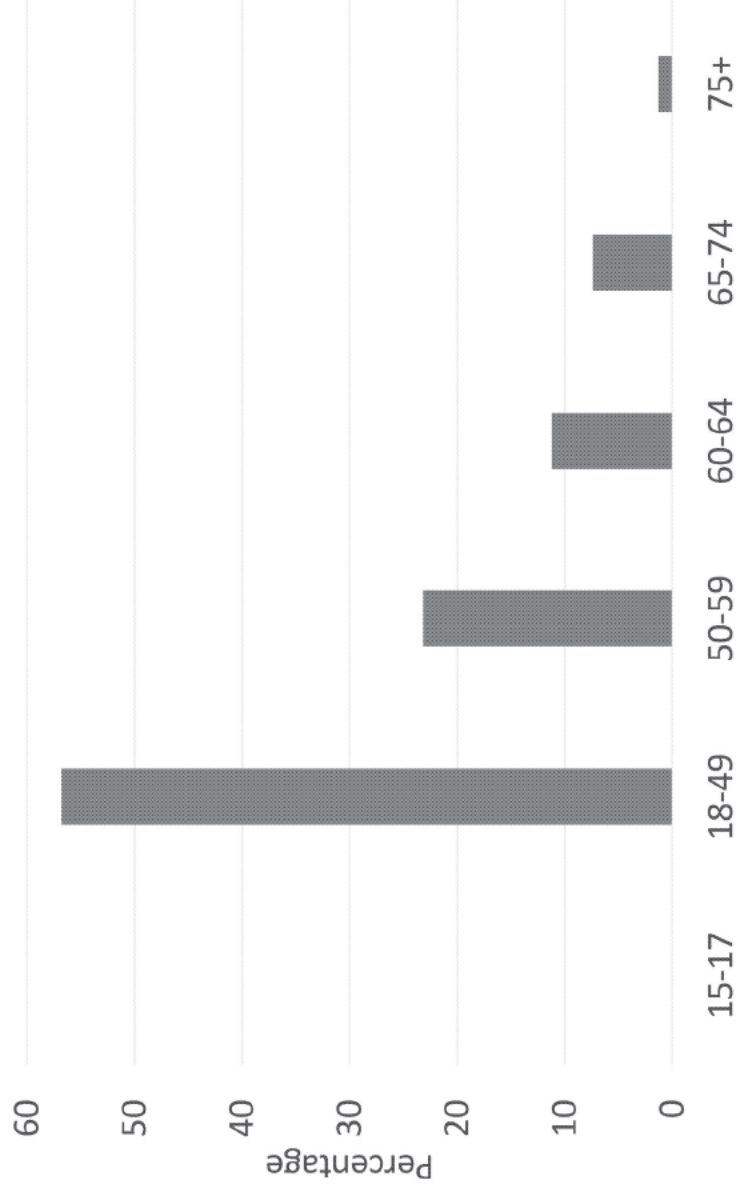
Reports in v-safe from Janssen recipients

Sex of Janssen recipients* in v-safe



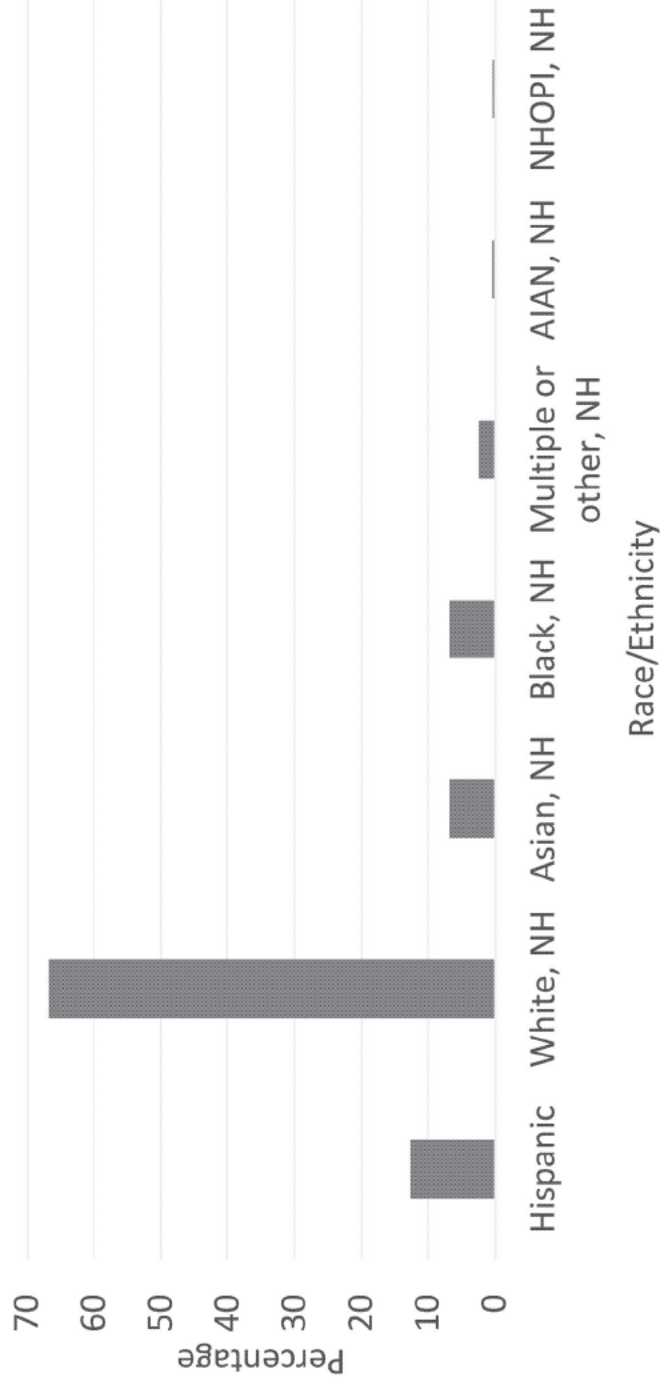
*vaccinated by April 12, 2021 at 5 am ET and completing at least one health survey in days 0-7

Age of Janssen recipients* in v-safe



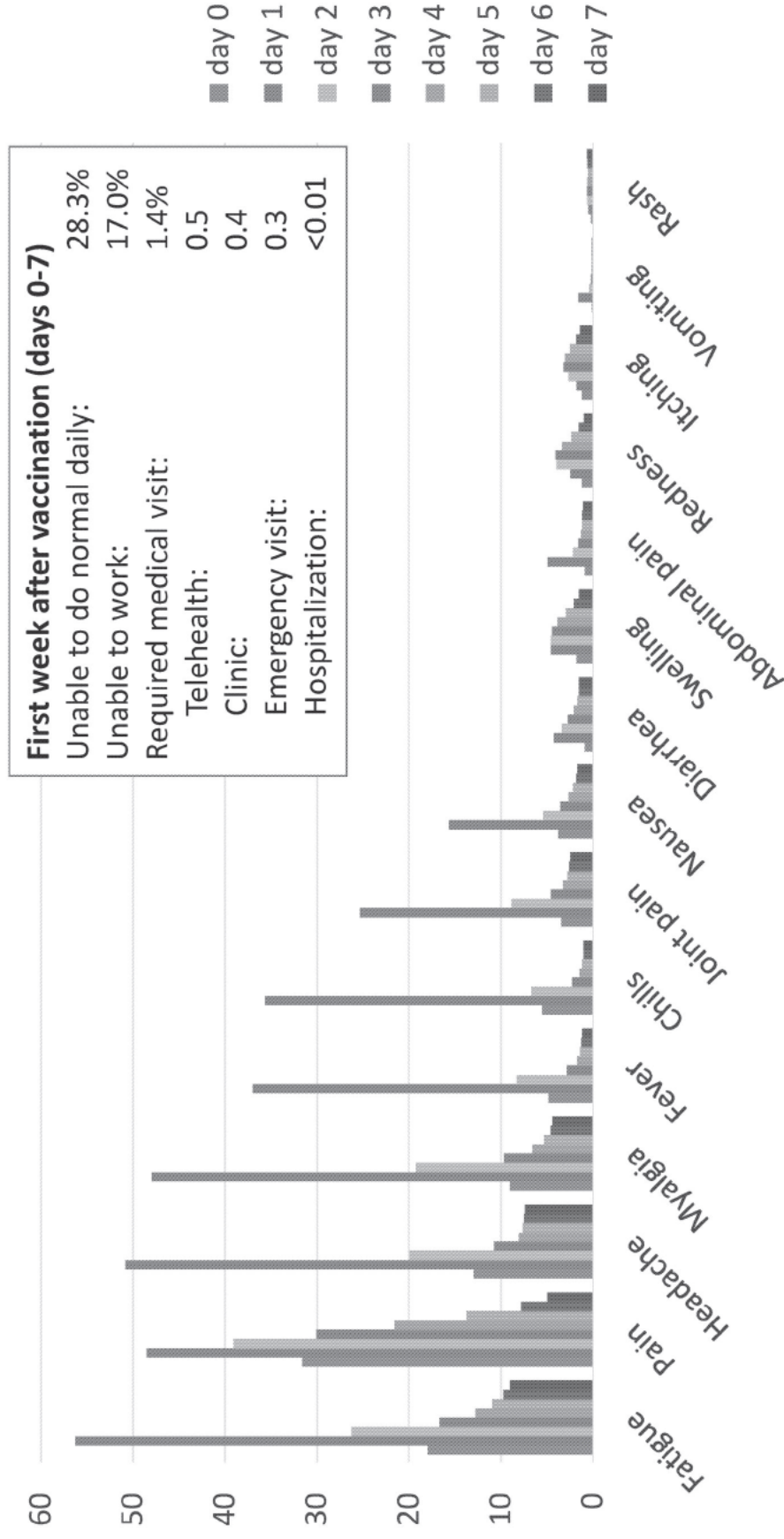
*vaccinated by April 12, 2021 at 5 am ET and completing at least one health survey in days 0-7

Race and ethnicity of Janssen recipients* in v-safe



*vaccinated by April 12, 2021 at 5 am ET and completing at least one health survey in days 0-7
 Race and/or ethnicity was unknown for 4.8% of participants
 NH=non-Hispanic, AIAN=American Indian or Alaska Native, NHOPI=Native Hawaiian or Other Pacific Islander

Solicited reactogenicity day 0-7 after Janssen COVID-19 vaccine



Hospitalizations* reported to v-safe, select non-solicited events

Type of event (total)	Self-reported event	Number
Cardiac	Atrial fibrillation/accelerated heart rate	11
	Heart attack	9
	Chest pain	6
Vascular	Stroke or stroke-like symptoms	19
	Blood clots	14
	High blood pressure/hypertension	11
	Pulmonary embolism	7
	CVST (1 with thrombocytopenia)	3
	DVT	3
	TIA	3
	Low blood pressure or blood pressure unspecified	3
	Brain hemorrhage or brain aneurysm	2
	Unspecified/undiagnosed, ↑ D-dimer or treatment with blood thinner	2

*From 370 Janssen recipients who reported hospitalization on any health survey as of April 20, 5 am ET

Hospitalizations* reported to v-safe, select non-solicited events

Type of event	Self-reported event	Number
Gastrointestinal	Appendicitis or appendectomy	13
	Intestinal blockage	7
	Pancreatitis or pancreatic disorder	5
	Gastrointestinal bleed or bloody stool	5
Neurologic	Seizures	9
	Headache or migraine	9
	Dizziness or vertigo	3
	Numbness or tingling	3
	Nerve pain or radiculopathy	2
	GBS	1
	Bell's palsy	1
	3 rd nerve palsy	1

*From 370 Janssen recipients who reported hospitalization on any health survey as of April 20, 5 am ET

Hospitalizations* reported to v-safe, select non-solicited events

Type of event	Self-reported event	Number
Immunologic	Allergic reaction	5
	Anaphylaxis	1
	Immune thrombocytopenia	1
Infection	COVID or possible COVID	8
	Pneumonia (no mention of COVID)	5
	Fever	3
	Shingles	2
Other	Shortness of breath or difficulty breathing	6
	Diabetic ketoacidosis	3
	Enlarged or swollen lymph node	3
	Systemic inflammatory response syndrome	1
Death	Death - cause unspecified	2

*From 370 Janssen recipients who reported hospitalization on any health survey as of April 20, 5 am ET

Hospitalizations* reported to v-safe, select non-solicited events

Type of event	Self-reported event	Number
Obstetric	Childbirth	4
	Preterm delivery	3
	Preterm labor	1
	Induced delivery due to HELLP	1
	Spotting during pregnancy	1
	Stillbirth	1
Gynecologic	Abnormal menstruation	1
	Hysterectomy	1
	Ovarian cyst/torsion	1

*From 370 Janssen recipients who reported hospitalization on any health survey as of April 20, 5 am ET

For more information, contact CDC



www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



PSICOVID_00010718

VaST Agenda – April 26, 2021

Open session

1:30 - 3:00

Maternal immunization section

1:30-1:35 - Announcements

1:35-1:40 - v-safe (Tanya Myers, CDC) 5 min

1:40-1:50 - v-safe registry (Sascha Ellington, CDC) 10 min

1:50-1:55 - Discussion 5 min

1:55-2:05 - VAERS (Pedro Moro, CDC) 10 min

2:05-2:10 - Discussion 5 min

2:10-2:20 - VSD (Elyse Kharbanda, Health Partners) 10 min

2:20-2:30 - Discussion 10 min

TTS session

2:30-2:40 - v-safe (Tanya Myers, CDC) 10 min

2:40-2:50 - Agency updates, data and plans (all) 10 min

2:50-3:00 - Discussion 10 min