

Message

From: Markowitz, Lauri (CDC/DDID/NCIRD/DVD) [REDACTED]
Sent: 2/22/2021 3:19:27 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]; Kuldorf, Martin [REDACTED]; Lee, Grace [REDACTED]; MacNeil, Jessica R (CDC) [REDACTED]; Markowitz, Lauri (CDC) [REDACTED]; Marquez, Paige L (CDC) [REDACTED]; Martin, Stacey (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]; Wharton, Melinda (CDC) [REDACTED]; Wong, Hui-Lee [REDACTED]; Woo, Jared M (CDC) [REDACTED]; Young, Mardia A (CDC) [REDACTED]
CC: Olson, Christine K (CDC) [REDACTED]; Moro, Pedro L (CDC) [REDACTED]; Brenna Hughes, MD [REDACTED]; Denise Jamieson, MD [REDACTED]; Kim, Shin Y (CDC) [REDACTED]; Meaney-Delman, Dana Marie (CDC) [REDACTED]; Oduyebo, Titilope (CDC) [REDACTED]; Richard Beigi, MD [REDACTED]
Subject: [EXTERNAL] VaST - Agenda for February 22 (1:30 - 3 pm ET) and presentations - CONFIDENTIAL
Attachments: 2021_02_22_VaST agenda.docx; VAERS for VaST 22 Feb 2021 mod1 .pdf; VSD RCA Covid-19 vax - update VaST - 02-22-2021_final.pdf; COVID-19Vaccine_Pregnancy_VAST_Feb22_02122021 JG.pdf; VaST vsafe 2_22_2021 pregnancyv3.pdf; VAERS for Pregnancy VaST 22 Feb 2021.pdf; ACIP_VaxSafety_Shimabukuro_3-1-2021_DRAFT.pdf

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Dear all,

This email includes the VaST agenda for today as well as 6 presentations. The focus of the call will be maternal immunization.

Of note, the attached presentation for the ACIP meeting next week (ACIP_VaxSafety_Shimabukuro) is a draft based on the planned presentation for VRBPAC this week; this likely will be expanded for ACIP.

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
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

VaST Agenda – February 22, 2021

Open session

1:30-3:00

Introduction/administrative issues	Co-leads and chairs
VAERS	John Su (CDC)
VSD	Nicky Klein (KPNC)
Pregnancy focused session	
v-safe	Tanya Myers (CDC)
v-safe pregnancy registry	Shin Kim (CDC)
VAERS	John Su (CDC)
Dry runs for ACIP meeting	Tom Shimabukuro (CDC) and Grace Lee (VaST)



Update on Reports to the Vaccine Adverse Event Reporting System (VAERS) after COVID-19 Vaccines, Including Anaphylaxis -- Dec 14, 2020 – Feb 19, 2021

John R. Su, MD, PhD, MPH

Feb 22, 2021

Reports to VAERS after COVID-19 Vaccines*

VAERS COVID19 Vaccine Reports
Initial domestic reports only, VAERS reports as of February 19, 2021 at 3PM

COVID19 Vaccine	Total N	Death N(%)	Serious ^b Non-Death N(%)	Non-Serious N(%)	Age in years Median (Range)	Female N(%)	Vsafe N(%)	Onset interval in days ^c Median (Range)
ALL COVID19	19,573	980 (5.0)	2,701 (13.8)	15,892 (81.2)	45 (0,105)	14,573 (74.5)	518(2.6)	0 (0,47)
MODERNA	7,092	478 (6.7)	1,215 (17.1)	5,399 (76.1)	46 (0,103)	5,268 (74.3)	55(0.8)	1 (0,42)
PFIZER-BIONTEC	12,444	493 (4.0)	1,475 (11.9)	10,476 (84.2)	45 (0,105)	9,282 (74.6)	463(3.7)	0 (0,47)
UNKNOWN	37	9 (24.3)	11 (29.7)	17 (45.9)	50 (19,94)	23 (62.2)		1 (0,18)
MULTIPLE	5	1 (20.0)	2 (40.0)	2 (40.0)	43 (39,87)	5 (100.0)		5 (0,31)

*processed as of Feb 19, 2021, 3 p.m.

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Reports to VAERS after COVID-19 Vaccines (cont'd)

- Most frequently reported symptoms – overall (N = 19,573)*

Obs	PT_NAME	count	percent
1	HEADACHE	4101	21.0%
2	FATIGUE	3011	15.4%
3	PYREXIA	2998	15.3%
4	CHILLS	2910	14.9%
5	PAIN	2739	14.0%
6	DIZZINESS	2695	13.8%
7	NAUSEA	2638	13.5%
8	INJECTION SITE PAIN	1899	9.70%
9	PAIN IN EXTREMITY	1714	8.76%
10	DYSPNOEA	1567	8.01%

*processed as of Feb 19, 2021, 3 p.m.

Reports to VAERS after COVID-19 Vaccines (cont'd)

- Dose number by manufacturer* (n = 16,759)

Dose No.	Manufacturer		Total
	Pfizer/BioNTech	Moderna	
1	9,565 (90.9%)	5,737 (92.1%)	15,302 (91.3%)
2	962 (9.1%)	495 (7.9%)	1,457 (8.7%)
Total	10,527 (100%)	6,232 (100%)	16,759 (100%)

* as of Feb 19, 2021; of 16,759 reports with data on dose number available; stratification by manufacturer pending

Reports to VAERS after COVID-19 Vaccines (cont'd)

- Most frequently reported adverse event – by dose number (n = 16,771)*

Dose 1 (n = 15,310)

Rank	Adverse event**	n (%)
1	Headache	3,225 (21.1)
2	Fatigue	2,373 (15.5)
3	Chills	2,228 (14.6)
4	Dizziness	2,223 (14.5)
5	Fever	2,208 (14.4)

Dose 2 (n=1,461)

Rank	Adverse event**	n (%)
1	Fever	328 (22.5)
2	Headache	288 (19.7)
3	Chills	268 (18.3)
4	Pain	239 (16.4)
5	Fatigue	226 (15.5)

* as of Feb 12, 2021; of 16,771 reports with dose number data available; stratification by manufacturer pending

** not mutually exclusive

Reports to VAERS after COVID-19 Vaccines (cont'd)

- Most commonly reported adverse events of special interest (as of Feb 12, 2021):
 - COVID-19 disease after vaccination (1,142)
 - Death (808)
 - Anaphylaxis (278; 71 confirmed*)
 - Pregnancy during or after vaccination (222)

* Via interview with health care provider and/or record review

**Cases of
anaphylaxis
identified in
VAERS to date**

	Pfizer/ BioNTech	Moderna	Total reports
Confirmed reports	51	20	71
Brighton Level 1	22 (43%)	11 (55%)	33 (46%)
Brighton Level 2	26 (51%)	8 (40%)	34 (48%)
Brighton Level 3	3 (6%)	1 (5%)	4 (6%)
States/territories ²	24	11	29
Female	47 (92%)	19 (95%)	66 (93%)
Male	4 (8%)	1 (5%)	5 (7%)
Median age (range)	40 (27–63)	42 (24–63)	40 (24–63)
Hx of allergies	38 (75%)	17 (85%)	55 (77%)
Hx of anaphylaxis	17 (33%)	5 (25%)	22 (31%)

Deaths after COVID-19 vaccines

- Total reports processed as of Feb 19, 2021: **980**
 - Reports among residents of long term care facilities (LTCFs): **470**
 - Substantial (e.g., approx. 1/3) in hospice care or DNR/DNI orders
 - Available data on cause of death reflects underlying comorbidities of the patients
 - Reports not known to be residents of LTCFs: **510***
 - Available data on cause of death often reflects cardiovascular causes

* Reflects updated data on residency status

Summary

- 19,573 reports processed by VAERS after COVID-19 vaccines
 - Abstraction of AESIs on going
- 71 reports of anaphylaxis
 - Mostly with history of allergies; onset mostly within 30 minutes
- 980 reports of death
 - Proportion by LTCF, sex comparable between available vaccines
 - 470 among LTCF, 510 not known to be among LTCF
 - Where known, cause of death often cardiovascular in nature

Acknowledgements

- VAERS Team
- GDIT (VAERS contractor)
- Clinical Immunization Safety Assessment (CISA) Project
- VTF Safety Team leadership
- State, local partners

For more information, contact CDC

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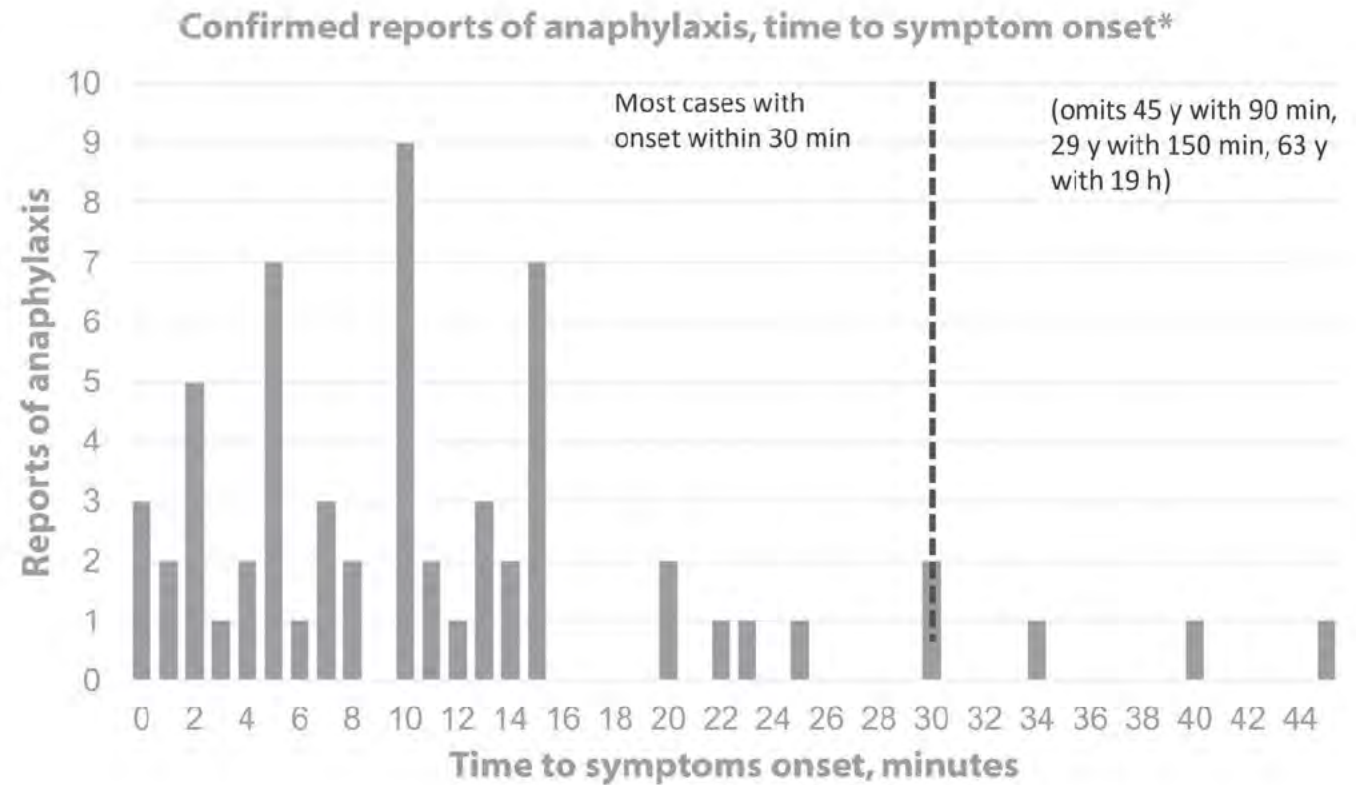
TTY: [REDACTED] www.cdc.gov

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.



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Anaphylaxis – time to onset



- Most cases (57/67, 85%) with time to onset within 30 minutes

Rapid Cycle Analysis (RCA) to Monitor the Safety of COVID-19 Vaccines in Near Real-Time within the Vaccine Safety Datalink

Nicola Klein, MD, PhD

Kaiser Permanente Vaccine Study Center
Kaiser Permanente Northern California
Marshfield Clinic Research Institute

Eric S. Weintraub

Vaccine Safety Datalink – Immunization Safety Office, CDC

 KAISER PERMANENTE
VACCINE STUDY CENTER



Marshfield Clinic[®]
Research Institute

Vaccine Uptake (Through 2/13/21)

VSD COVID-19 Vaccine Totals

Total Doses
Administered

829,657

+216,949
since last week

Total Doses
Admin per 100K

7,670

+2,033
since last week

People Initiating
Vaccination

629,523

+140,516
since last week

Series
Completed

200,134

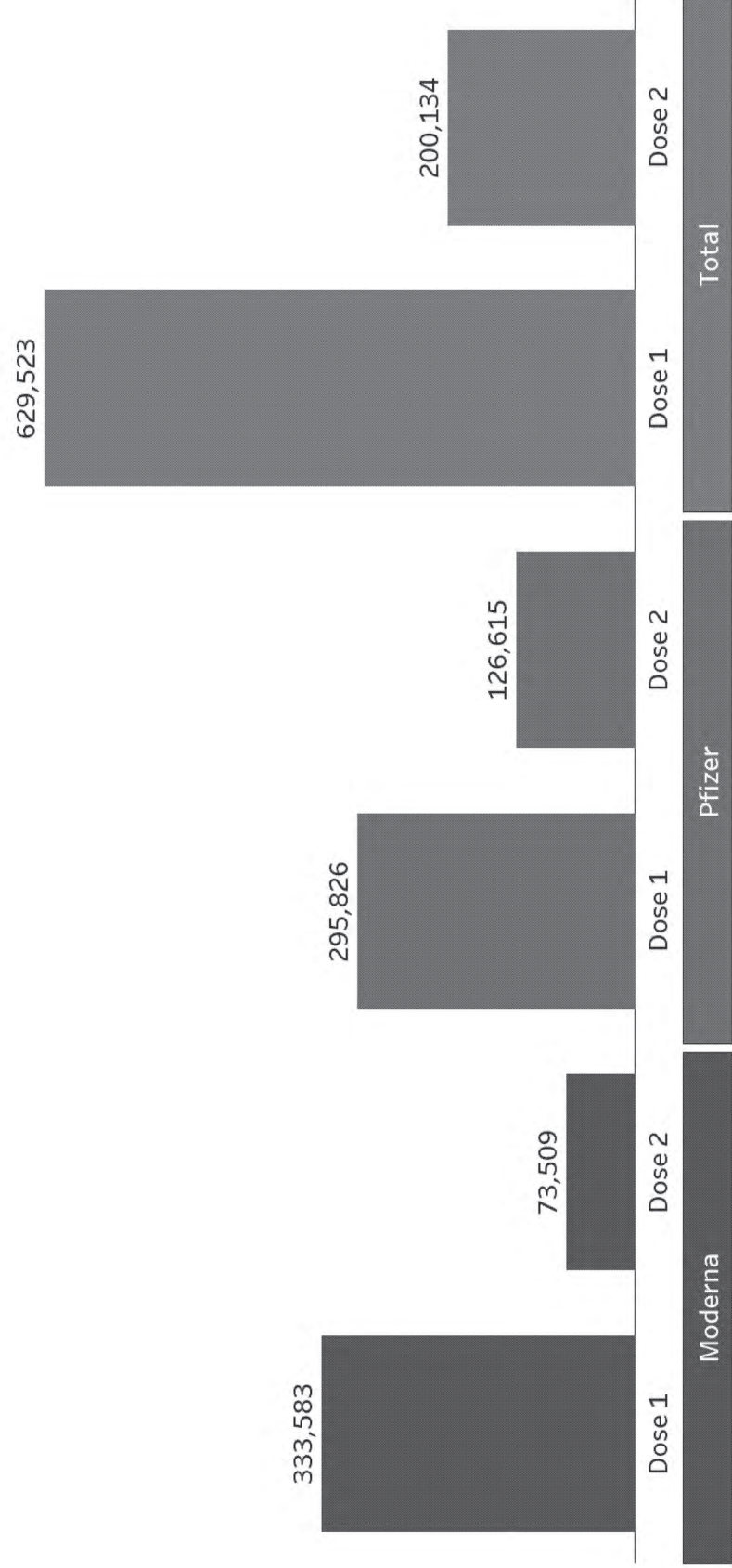
+76,433
since last week

To date, **5.8%** of VSD population
received Dose 1 of COVID-19 vaccine

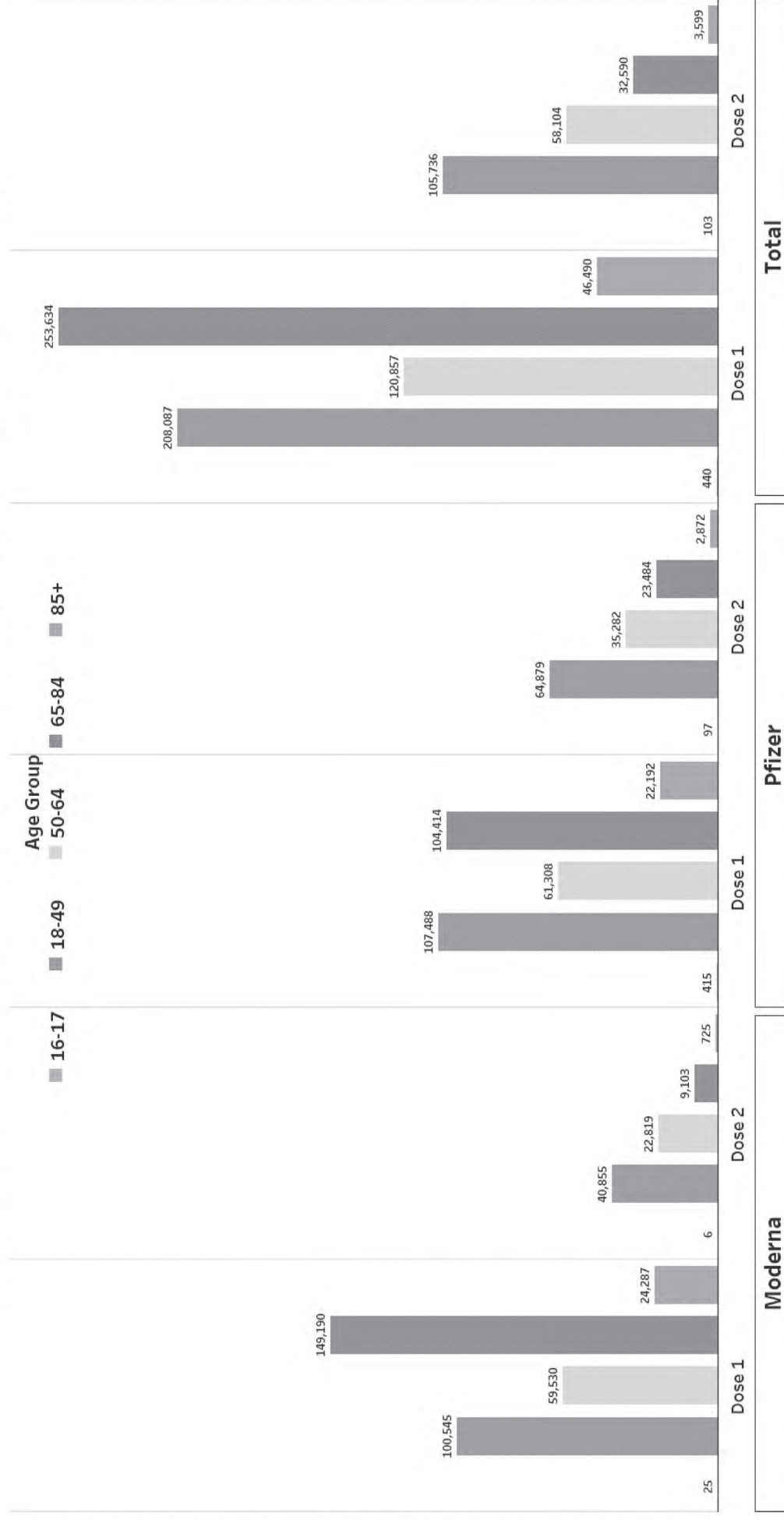
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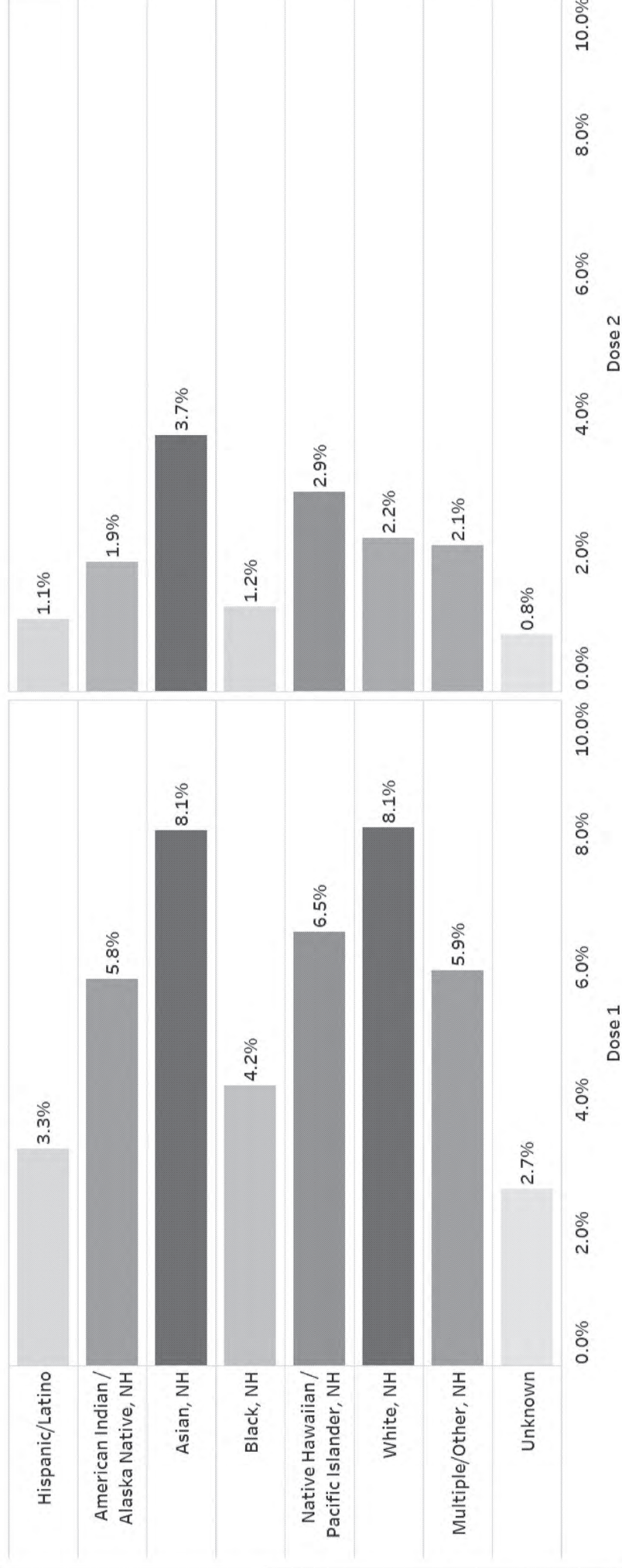
VSD COVID-19 Vaccine Totals



COVID-19 Vaccine Totals by Age Group



COVID-19 Vaccine Coverage by Race



Analysis (Data Through 2/13/21)

VSD RCA COVID-19 Outcome Summary

#	VSD Outcomes	Abbreviation	Signal (Y/N)
1	Acute disseminated encephalomyelitis (settings = E, I)	ADEM	N
2	Acute myocardial infarction (settings = E, I)	AMI	N
3	Acute respiratory distress syndrome (settings = E, I)	ARDS	N/A
4	Anaphylaxis (settings = E, I)	ANAPH	N/A
5	Appendicitis (settings = E, I)	APPND	N
6	Bell's palsy (settings = E, I, O)	BP	N
7	Convulsions / seizures (settings = E, I)	SZ	N
8	Disseminated intravascular coagulation (settings = E, I)	DIC	N
9	Encephalitis / myelitis / encephalomyelitis (settings = E, I)	ENCEPH	N
10	Guillain-Barré syndrome (settings = E, I)	GBS	N
11	Thrombotic thrombocytopenic purpura (settings = E, I)	TTP	N
12	Immune thrombocytopenia (settings = E, I, O)	ITP	N
13	Kawasaki disease (settings = E, I)	KD	N
14	Multisystem Inflammatory Syndrome in Children & Adults (MIS-C, MIS-A) (settings = E, I)	MISC	N/A
15	Myocarditis / pericarditis (settings = E, I)	MYOC	N
16	Narcolepsy and cataplexy (settings = E, I, O)	NARC	N/A
17	Stroke, hemorrhagic (settings = E, I)	HSTK	N
18	Stroke, ischemic (settings = E, I)	ISTK	N
19	Transverse myelitis (settings = E, I)	TM	N
20	Venous thromboembolism (settings = E, I, O)	VTE	N
21	Pulmonary embolism (subset of VTE) (settings = E, I)	PE	N

Abbreviations: E = ED; I = Inpt; O = Outpt

VSD COVID-19 RCA Planned Analyses

For Risk Intervals 1-21 & 1-42 Days

Analytic Methods	Moderna			Pfizer			mRNA-Vaccines Combined		
	Dose 1	Dose 2	Dose 1 & Dose 2 Combined	Dose 1	Dose 2	Dose 1 & Dose 2 Combined	Dose 1	Dose 2	Dose 1 & Dose 2 Combined
Vaccinated Concurrent Comparators	✓	✓	✓	✓	✓	✓	✓	✓	✓
Unvaccinated Concurrent Comparators	✓	✓	✓	✓	✓	✓	✓	✓	✓
Historical Background rates	✓	✓	✓	✓	✓	✓	✓	✓	✓
Historical Well care visits	✓	✓	✓	✓	✓	✓	✓	✓	✓

Analysis

- Poisson regression will be used to model outcome incidence observed during the risk interval in comparison with incidence expected (under H_0)
- Sequential Analysis is the Vaccinated Comparator
 - Significant Threshold is a 1-Sided P-Value < 0.0048
- Models are adjusted for:
 - Calendar day
 - Age in categories
 - Race
 - Site
 - Sex

Primary Analyses: Vaccinated Comparison “Sequential Analysis”

See Slide 30 for Visual Explanation of the Analysis

Outcome events in 21-day risk interval after either dose of any mRNA vaccine

Compared with outcome events in vaccinated comparators on the same calendar days

Outcome Event	Events in Risk Interval	Events in Comparison Interval ³	Adjusted Expected Interval ⁴	Adjusted Events Risk Rate Ratio ⁴	Weekly Analysis ¹			Sequential Test ²	
					95% Confidence Interval	2-Sided P-Value	1-sided P-value	Signal	
Acute myocardial infarction	21	2	30.8	0.68	0.17 - 4.59	0.596	0.834	No	
Appendicitis	25	7	53.5	0.47	0.19 - 1.26	0.124	0.966	No	
Bell's palsy	17	2	23.1	0.74	0.18 - 4.94	0.658	0.809	No	
Disseminated intravascular coagulation	1	0	.	.	0.00 - ne	0.969	0.969	No	
Immune thrombocytopenia	1	0	.	.	0.00 - ne	0.998	0.998	No	
Myocarditis / pericarditis	2	0	.	.	0.00 - ne	0.963	0.963	No	
Narcolepsy	2	0	n/a	n/a	n/a	n/a	n/a	n/a	
Seizures	10	1	9.4	1.06	0.15 - 25.69	0.969	0.718	No	
Stroke, hemorrhagic	7	0	.	.	0.10 - ne	0.660	0.660	No	
Stroke, ischemic	37	3	43.5	0.85	0.26 - 3.90	0.769	0.741	No	
Venous thromboembolism	23	1	12.4	1.86	0.32 - 40.78	0.621	0.468	No	
Pulmonary embolism (subset of VTE)	19	0	.	.	0.46 - ne	0.225	0.225	No	

¹**Weekly analyses** include all data to date, but confidence intervals and p-values do not account for the multiple chances for a false positive signal during surveillance.

²**Sequential test** requires 1-sided $p < 0.0048$ for a signal. This keeps the probability of a false positive signal (due to chance alone) below 0.05 in 2 years of surveillance.

³**Comparison interval** is 22–42 days after either dose.

⁴**Adjusted** for VSD site, 5-year age group, sex, race/ethnicity, and calendar date. ne=not estimable

Unvaccinated Comparison

See Slide 31 for Visual Explanation of the Analysis

Outcomes events in the 21-day risk interval after either dose of any mRNA vaccine

Compared with outcome events in unvaccinated comparators on the same calendar days

Outcome Event						Weekly Analyses ¹			
	Events in Risk Interval	Events in Unvaccinated	Adjusted Expected Events in Risk Interval ²	Adjusted Rate Ratio ²	Lower 95% Conf Limit	Upper 95% Conf Limit	2-Sided P-Value		
ARDS	0	29	.	n/a	n/a	n/a	n/a		
Acute disseminated encephalomyelitis	0	1	.	0.00	0.00	342.51	0.947		
Acute myocardial infarction	23	867	26.0	0.88	0.56	1.33	0.589		
Appendicitis	31	1270	23.6	1.31	0.92	1.88	0.139		
Bell's palsy	21	906	20.3	1.03	0.65	1.58	0.859		
Disseminated intravascular coagulation	1	51	1.1	0.92	0.04	4.97	0.969		
Encephalitis / myelitis / encephalomyelitis	1	15	0.1	9.27	0.37	68.43	0.133		
Guillain-Barré syndrome	1	32	0.6	1.67	0.08	9.47	0.593		
Immune thrombocytopenia	1	52	1.0	0.96	0.04	5.30	0.940		
Kawasaki disease	0	4	.	0.00	0.00	24391.56	1.000		
Multisystem Inflammatory Syndrome in Children	0	23	.	n/a	n/a	n/a	n/a		
Myocarditis / pericarditis	2	78	2.1	0.97	0.15	3.51	0.962		
Narcolepsy	2	26	0.9	n/a	n/a	n/a	n/a		
Pulmonary embolism (subset of VTE)	20	771	21.0	0.95	0.59	1.47	0.852		
Seizures	10	510	9.6	1.05	0.52	1.91	0.856		
Stroke, hemorrhagic	8	374	10.0	0.80	0.36	1.56	0.558		
Stroke, ischemic	41	1376	38.8	1.06	0.77	1.45	0.727		
Thrombotic thrombocytopenic purpura	0	11	.	0.00	0.00	18.48	0.807		
Transverse myelitis	0	6	.	0.00	0.00	114.43	0.963		
Venous thromboembolism	26	943	26.3	0.99	0.65	1.46	0.980		

¹**Weekly analyses** include all data to date, but confidence intervals and p-values do not account for the multiple chances for a false positive signal during surveillance.

²**Adjusted** for VSD site, 5-year age group, sex, race/ethnicity, and calendar date.

Outcomes events in the 42-day risk interval after either dose of any mRNA vaccine

Compared with outcome events in unvaccinated comparators on the same calendar days

Outcome Event	Weekly Analyses ¹				Adjusted Rate Ratio ²	Adjusted Expected Events in Risk Interval ²	Events in Unvaccinated	Events in Risk Interval	Lower 95% Conf Limit	Upper 95% Conf Limit	2-Sided P-Value
	Events in Risk Interval	Events in Unvaccinated	Adjusted Expected Events in Risk Interval ²	Adjusted Rate Ratio ²							
ARDS	0	29	.	n/a	n/a				n/a	n/a	n/a
Acute disseminated encephalomyelitis	0	1	.	0.00	0.00				0.00	217.87	0.920
Acute myocardial infarction	25	867	28.1	0.89	0.89				0.58	1.32	0.598
Appendicitis	38	1276	26.7	1.42	1.42				1.03	1.97	0.035
Bell's palsy	23	907	22.9	1.00	1.00				0.64	1.51	0.960
Disseminated intravascular coagulation	1	51	1.2	0.83	0.83				0.04	4.53	0.957
Encephalitis / myelitis / encephalomyelitis	1	15	0.1	8.15	8.15				0.30	63.95	0.159
Guillain-Barré syndrome	1	32	0.6	1.64	1.64				0.08	9.31	0.601
Immune thrombocytopenia	1	52	1.1	0.91	0.91				0.04	5.03	0.978
Kawasaki disease	0	4	.	0.00	0.00				0.00	24391.56	1.000
Multisystem Inflammatory Syndrome in Children	0	23	.	n/a	n/a				n/a	n/a	n/a
Myocarditis / pericarditis	2	78	2.3	0.88	0.88				0.14	3.20	0.941
Narcolepsy	2	26	1.1	n/a	n/a				n/a	n/a	n/a
Pulmonary embolism (subset of VTE)	20	771	22.7	0.88	0.88				0.54	1.37	0.609
Seizures	11	513	10.6	1.04	1.04				0.54	1.85	0.870
Stroke, hemorrhagic	8	374	10.8	0.74	0.74				0.34	1.46	0.432
Stroke, ischemic	44	1376	41.4	1.06	1.06				0.78	1.44	0.693
Thrombotic thrombocytopenic purpura	0	11	.	0.00	0.00				0.00	17.60	0.798
Transverse myelitis	0	6	.	0.00	0.00				0.00	107.58	0.960
Venous thromboembolism	27	943	29.1	0.93	0.93				0.61	1.36	0.735

¹**Weekly analyses** include all data to date, but confidence intervals and p-values do not account for the multiple chances for a false positive signal during surveillance.

²**Adjusted** for VSD site, 5-year age group, sex, race/ethnicity, and calendar date.

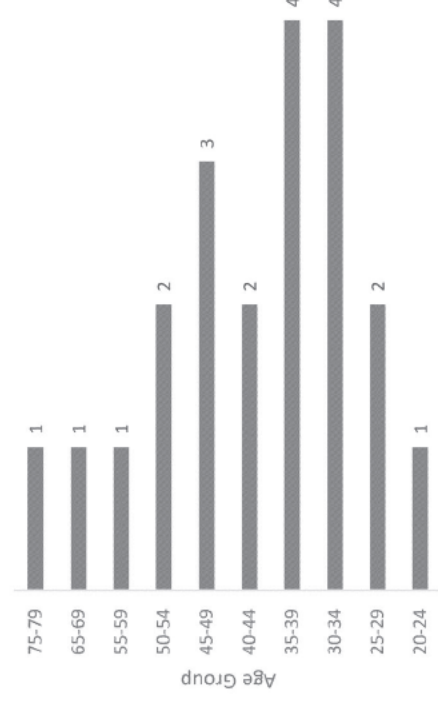
Anaphylaxis Automated Summary

21

Automated cases identified following dose 1 for days 0-1



- Age in years ranged from 20 – 79, with the 17 of the cases between ages 25-54



Anaphylaxis Chart Review Summary

- Chart review completed for 13/21 cases*
- 12/13 (92%) cases confirmed as post-vaccination anaphylaxis

	Pfizer (n=8)	Moderna (n=4)
Age in years, median (range)	38 (27-55)	44 (36-50)
Female sex	8 (100%)	4 (100%)
Minutes to symptom onset, median (range)	10 (0-29)	17 (7-30)
Prior history of allergies	5 (63%)	2 (50%)
Prior history of anaphylaxis	2 (25%)	0
First dose	8 (100%)	4 (100%)
Brighton Collaboration case definition level		
1	4 (50%)	4 (100%)
2	2 (25%)	0
3	2 (25%)	0
No. first doses	295,826	333,583
No. confirmed cases (95% CI) per million first doses	27.0 (11.7-53.3)	12.0 (3.3-30.7)

*Full review not completed until 30 days after the event

GBS Summary

- 1 automated case identified on day 2 following dose 1
- Outcome was miscoded
- Determined not to be GBS on chart review

Summary

- Continue to monitor vaccine uptake within the VSD.
 - Monitor by race, sex and high-risk conditions
- No signals identified to date.

Next Steps

- Vaccinated concurrent comparators:

- Will continue this analysis as additional informative comparator follow-up becomes available

- For each outcome

- Dose specific analyses
 - Product specific analyses
 - Analyses for 2 risk intervals – 1-21 & 1-42 days

- Historical Comparators

- General age comparable background rates
 - Rates following well care visits among those that received influenza vaccine in the past 18 months
 - Planning to start in latter half of March

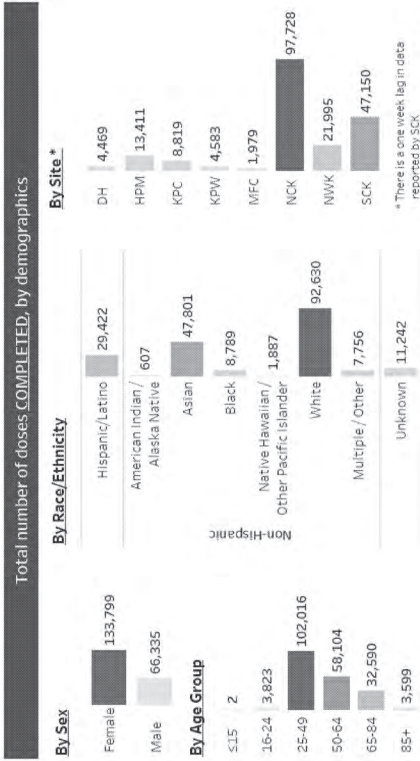
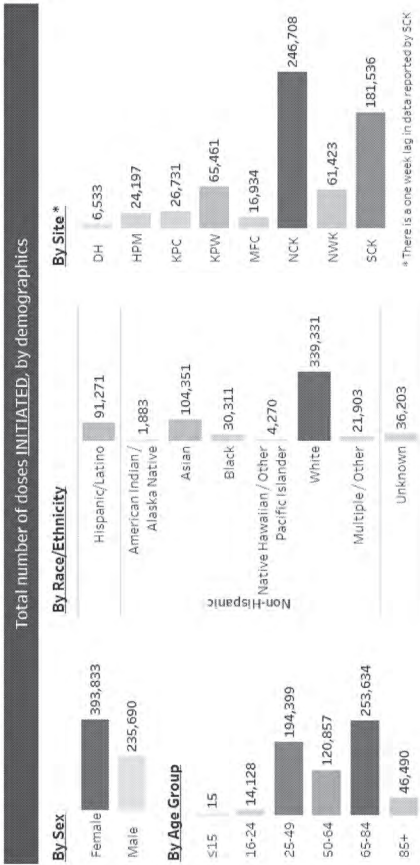
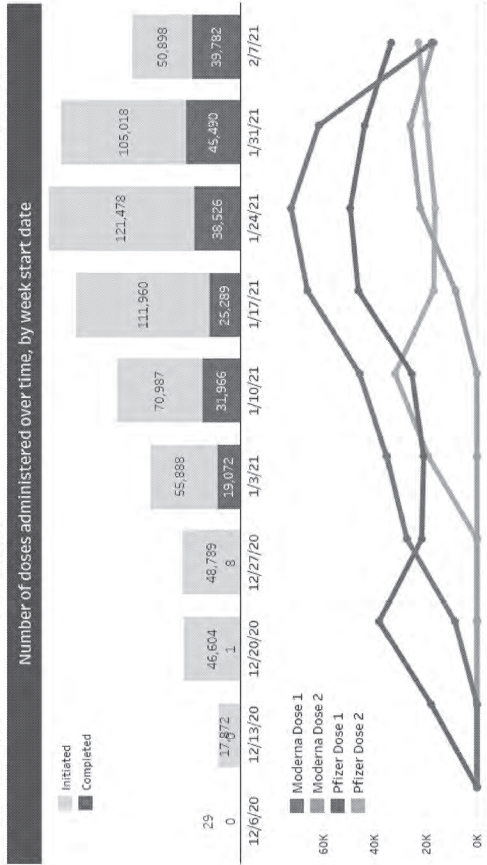
Extra Slides

Vaccine Safety Datalink (VSD) Weekly COVID-19 Vaccine Summary: February 16, 2021 *

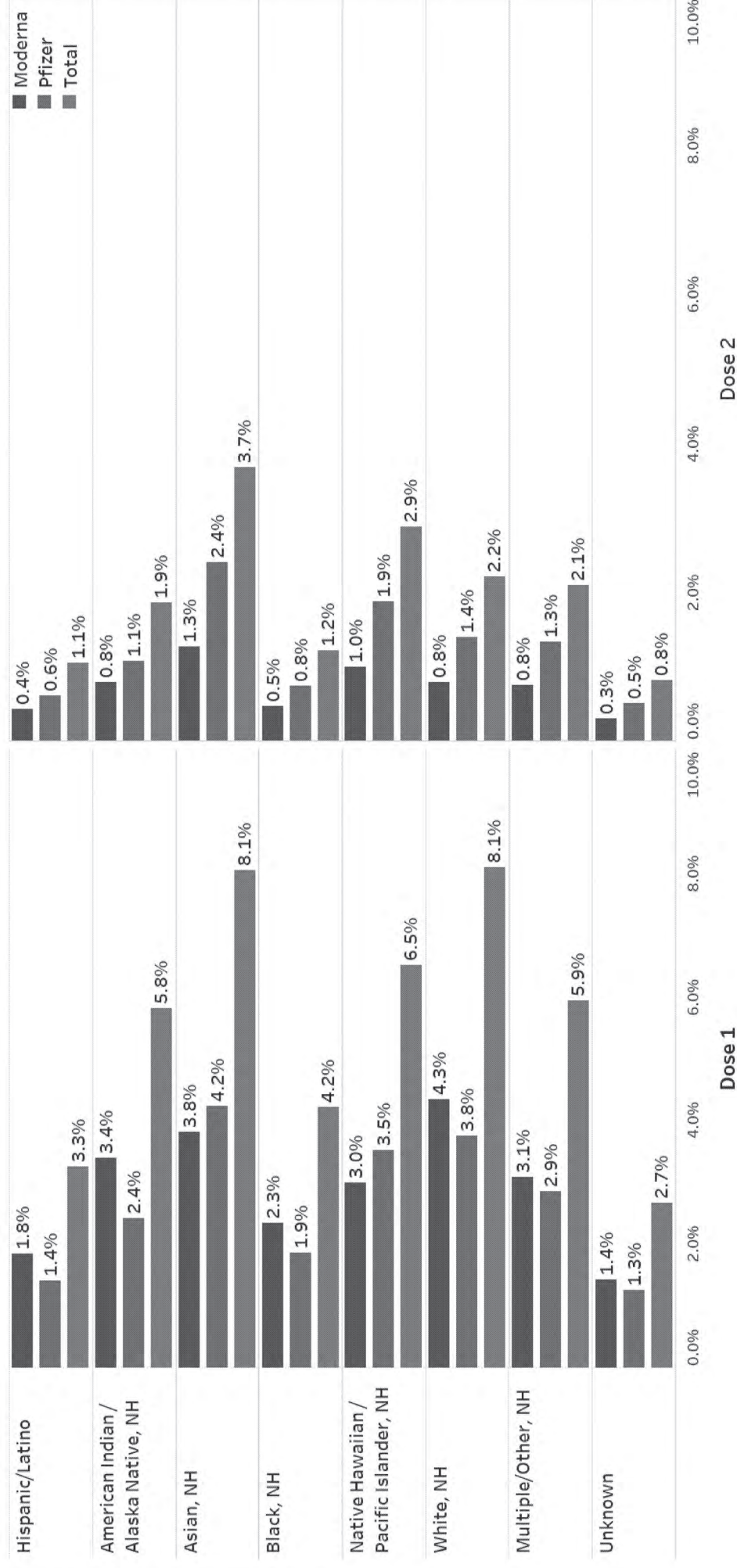
* Visualization published on February 16, 2021. Data current as of previous Saturday.

Total Doses Administered	Total Doses Admin per 100K	# People Initiating Vaccination	Series Completed
829,657	7,670	629,523	200,134
+216,949 since last week	+2,033 since last week	+140,516 since last week	+76,433 since last week

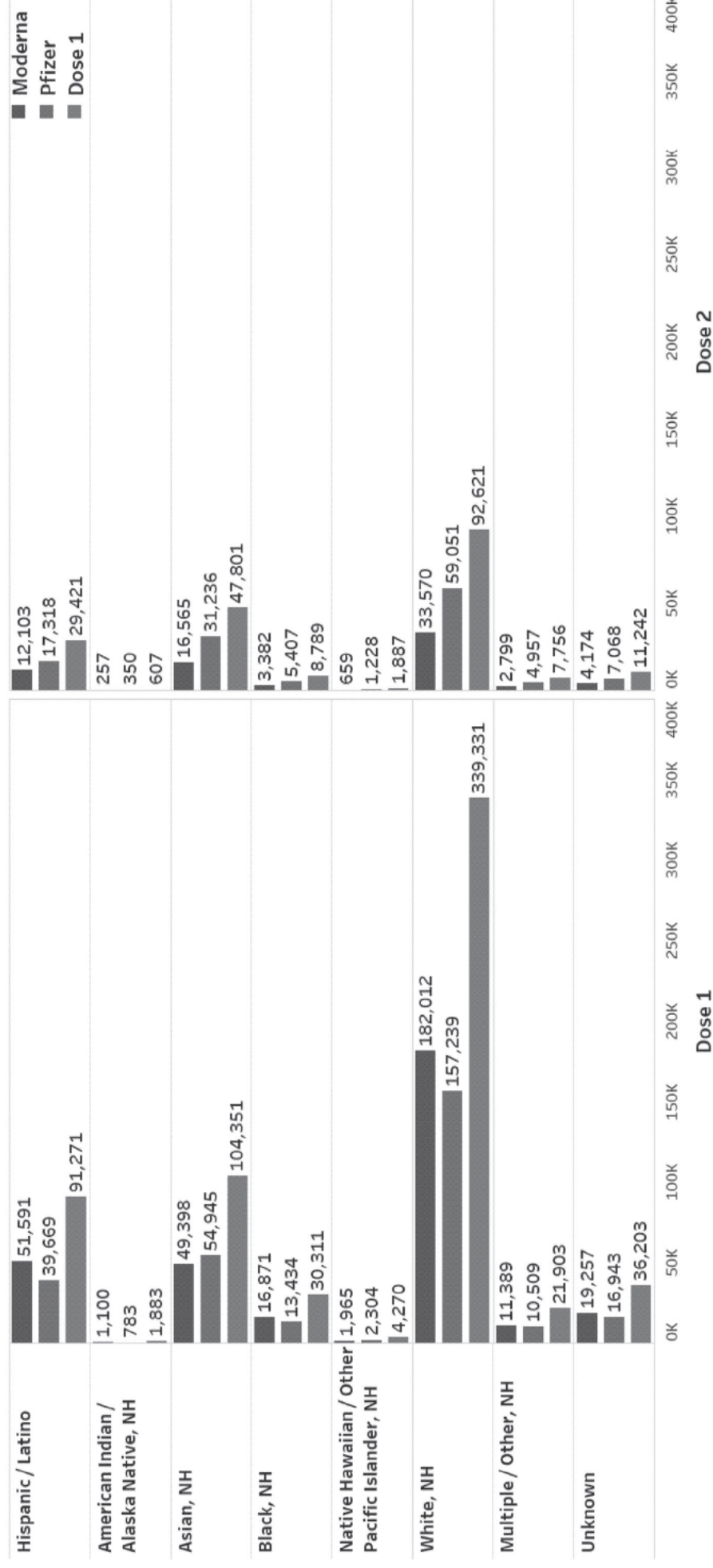
No signals have been observed to date.



COVID-19 Vaccine Coverage by Race



COVID-19 Vaccine Totals by Race



COVID-19 Vaccine Totals by Sex, High Risk Status, History of COVID-19 Disease, & Simultaneous Vaccinations

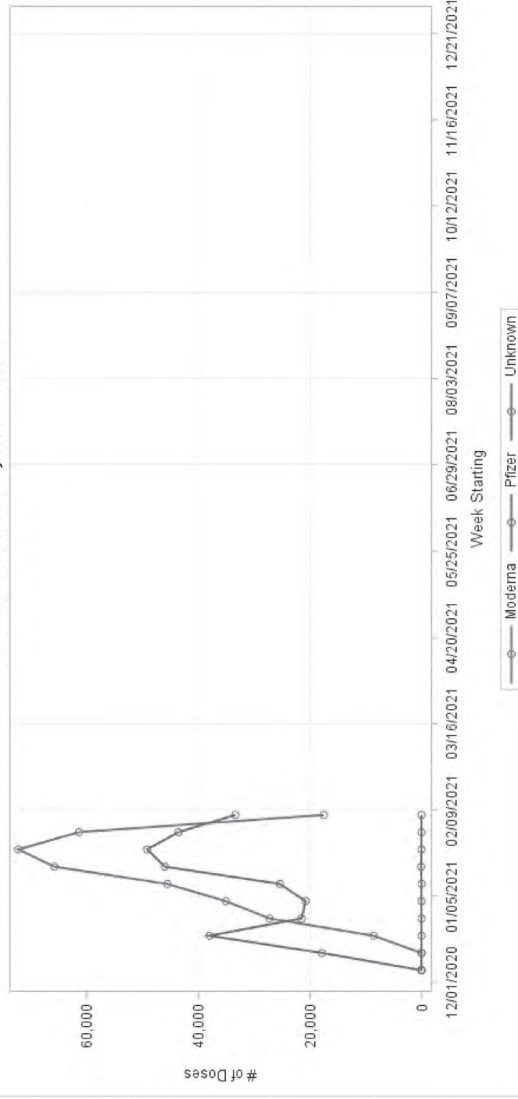
Category	Variable	Moderna		Pfizer		Totals			Coverage %		
		Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2	Total Doses	Denominator	Dose 1	Series Completed
Sex	Female	207,985	50,520	185,775	83,270	393,833	133,799	527,632	5,556,392	7.09	2.41
	Male	125,598	22,989	110,051	43,345	235,690	66,335	302,025	5,260,877	4.48	1.26
High Risk	No	151,267	48,635	147,760	80,050	299,093	128,691	427,784	7,994,428	3.74	1.61
	Yes	182,316	24,874	148,066	46,565	330,430	71,443	401,873	2,822,841	11.71	2.53
History of COVID-19 Disease	No	321,139	70,317	282,207	120,251	603,457	190,578	794,035	10,077,576	5.99	1.89
	Yes	12,444	3,192	13,619	6,364	26,066	9,556	35,622	739,693	3.52	1.29
Simultaneous Vaccines	No	333,525	73,509	295,767	126,604	629,406	200,123	829,529	.	.	.
	Yes	58	0	59	11	117	11	128	.	.	.
Total		333,583	73,509	295,826	126,615	629,523	200,134	829,657	10,817,269	5.82	1.85

COVID-19 Vaccine Totals by Age Groups*

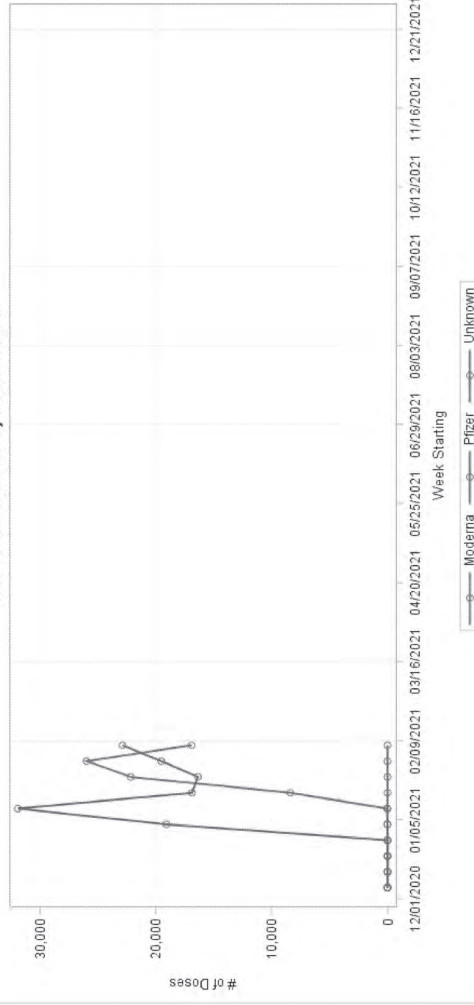
	Moderna		Pfizer		Totals		Coverage %			
Age	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2	Total Doses	Denominator	Dose 1	Series Completed
16	8	2	177	39	185	41	226	137463	0.13	0.03
17	17	4	238	58	255	62	317	139507	0.18	0.04
18	338	45	347	94	686	139	825	135683	0.51	0.10
19	482	57	474	157	956	214	1170	133952	0.71	0.16
20-24	6109	1191	5934	2176	12046	3367	15413	713801	1.69	0.47
25-29	12044	3798	11911	5913	23959	9712	33671	758114	3.16	1.28
30-34	17945	7167	18424	11010	36378	18177	54555	831331	4.38	2.19
35-39	21235	9311	22996	14742	44240	24053	68293	807594	5.48	2.98
40-44	21365	9790	23668	15382	45049	25173	70222	742228	6.07	3.39
45-49	21027	9496	23734	15405	44773	24901	69674	702713	6.37	3.54
50-54	20585	8598	22207	13677	42801	22275	65076	729487	5.87	3.05
55-59	19759	7603	20456	11634	40221	19238	59459	739727	5.44	2.60
60-64	19186	6618	18645	9971	37835	16591	54426	716170	5.28	2.32
65-69	30750	3361	21741	8534	52498	11896	64394	563510	9.32	2.11
70-74	37253	2960	21219	7008	58481	9968	68449	455664	12.83	2.19
75-79	50814	1805	37215	5132	88040	6938	94978	242618	36.29	2.86
80-84	30373	977	24239	2810	54615	3788	58403	151620	36.02	2.50
85-89	16020	450	14030	1623	30055	2074	32129	90074	33.37	2.30
90+	8267	275	8162	1249	16435	1525	17960	56563	29.06	2.70
Total	333,583	73,509	295,826	126,615	629,523	200,134	829,657	10,817,269	5.82	1.85

COVID-19 Vaccine Totals by Week

VSD COVID-19 Doses by Week - Dose 1

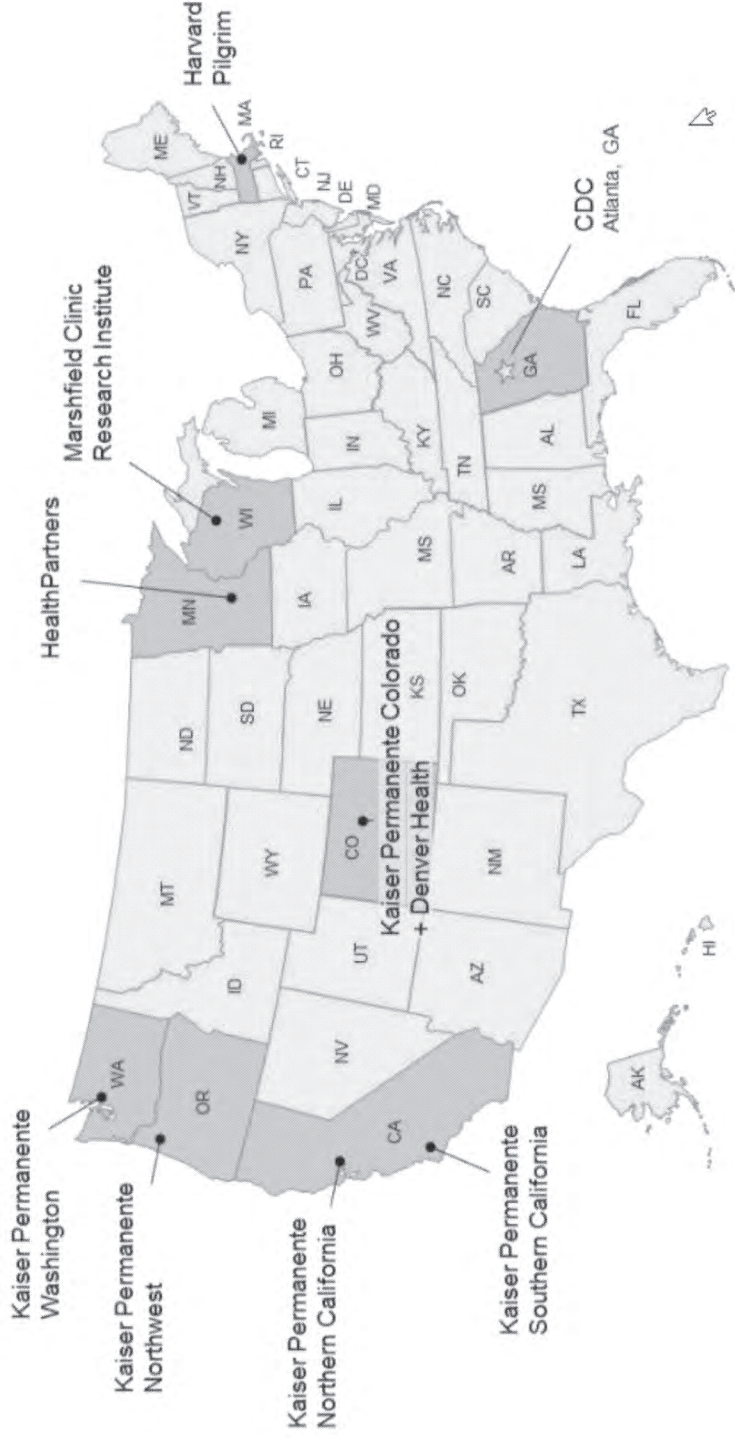


VSD COVID-19 Doses by Week - Dose 2



The Vaccine Safety Datalink (VSD)

Participating VSD Healthcare Organizations



- Established in 1990
- Collaborative project between CDC and Nine Integrated Health Care Organizations

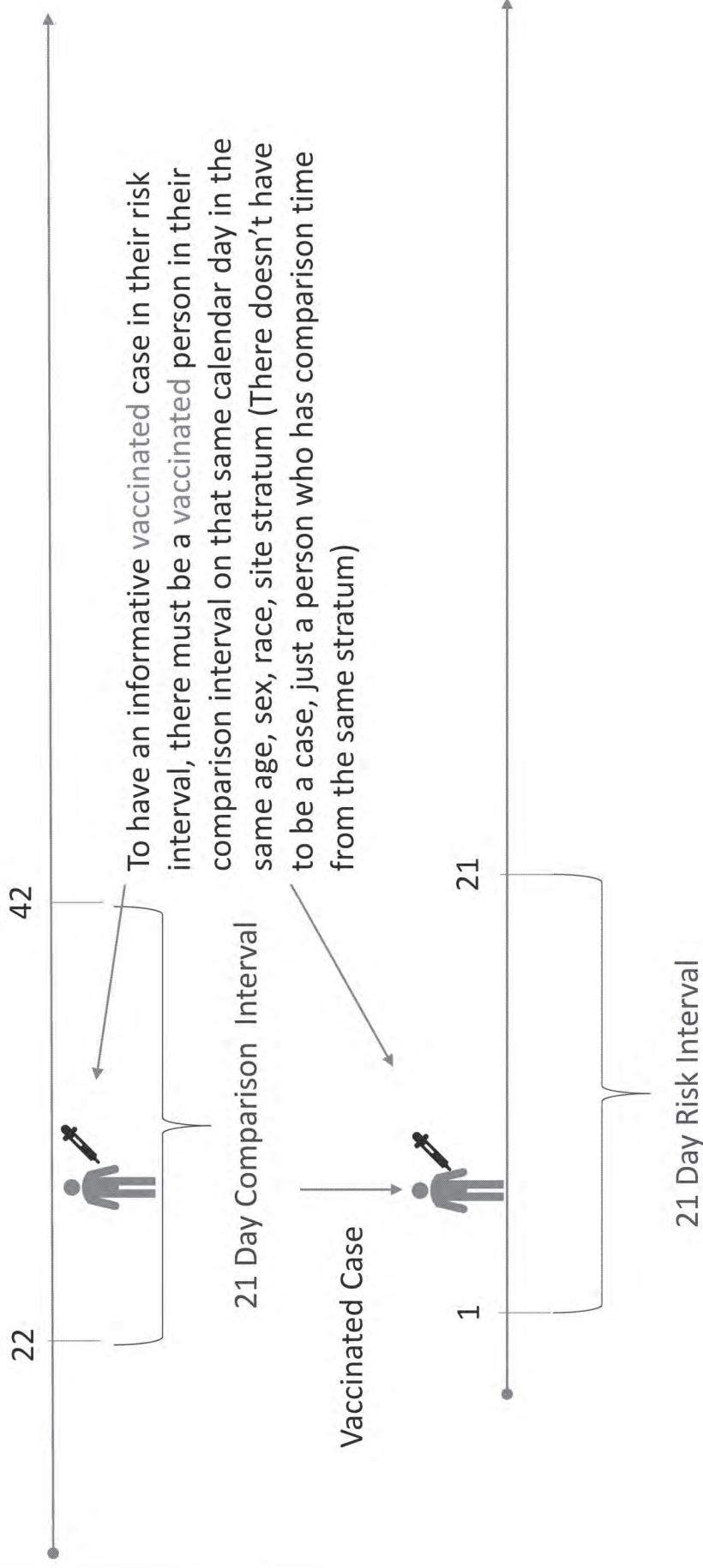
VSD Rapid Cycle Analysis

The specific aims:

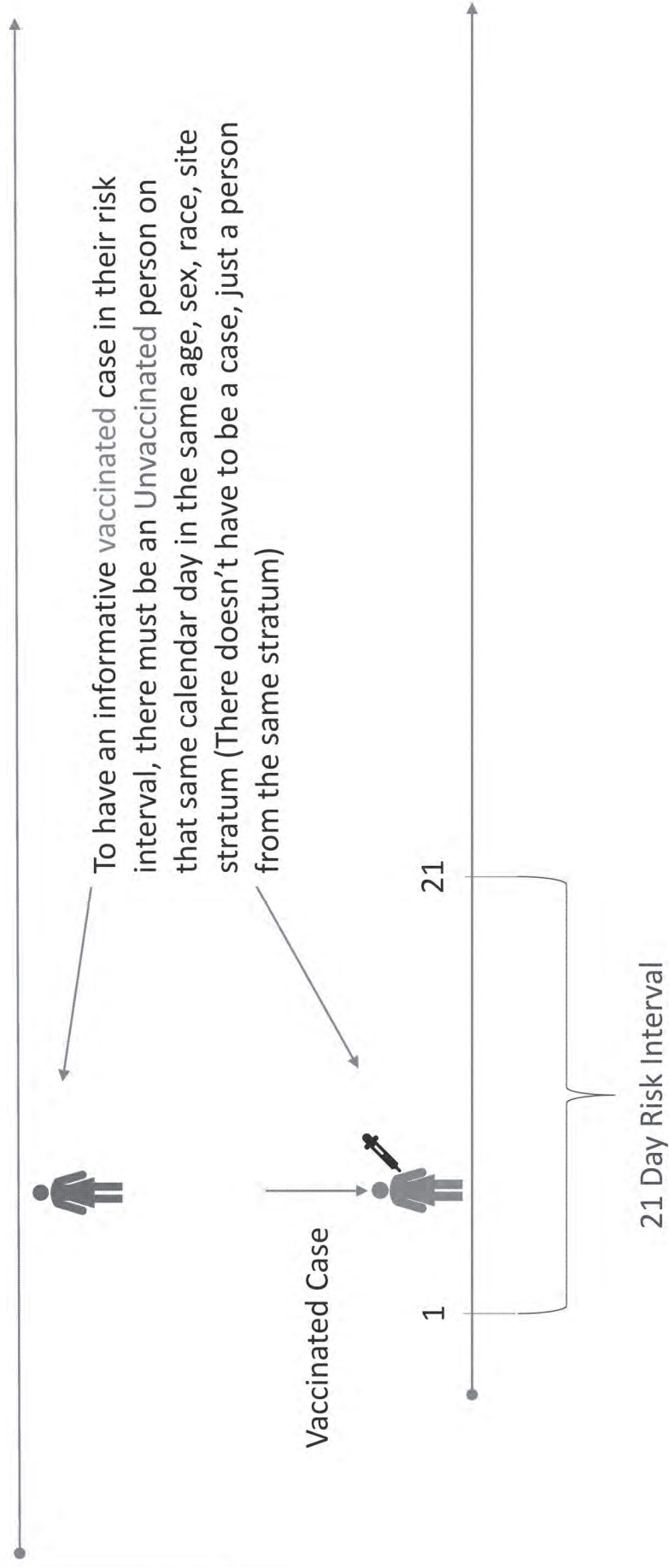
- To monitor the safety of COVID-19 vaccines weekly using pre-specified outcomes of interest among VSD members.
- To describe the uptake of COVID-19 vaccines over time among eligible VSD members overall and in strata by age, site, and race/ethnicity.

Project Period: Sept 2020 – August 2023 (3 years)

Vaccinated Comparison



Unvaccinated Comparison



VSD RCA COVID-19 Outcomes

#	VSD Outcomes	Abbreviation	Risk Window (days)	Chart Review	Monitoring Only	Exclude if COVID-19 in the Prior X Days
1	Acute disseminated encephalomyelitis (settings = E, I)	ADEM	1-21, 1-42	Yes		
2	Acute myocardial infarction (settings = E, I)	AMI	1-21, 1-42			30 days
3	Acute respiratory distress syndrome (settings = E, I)	ARDS	1-21, 1-42		Yes	42 days
4	Anaphylaxis (settings = E, I)	ANAPH	0-1	Yes	Yes	
5	Appendicitis (settings = E, I)	APPND	1-21, 1-42			
6	Bell's palsy (settings = E, I, O)	BP	1-21, 1-42			30 days
7	Convulsions / seizures (settings = E, I)	SZ	1-21, 1-42 (day 0 included for children)			30 days
8	Disseminated intravascular coagulation (settings = E, I)	DIC	1-21, 1-42			42 days
9	Encephalitis / myelitis / encephalomyelitis (settings = E, I)	ENCEPH	1-21, 1-42			30 days
10	Guillain-Barré syndrome (settings = E, I)	GBS	1-21, 1-42	Yes		
11	Thrombotic thrombocytopenic purpura (settings = E, I)	TTP	1-21, 1-42			30 days
12	Immune thrombocytopenia (settings = E, I, O)	ITP	1-21, 1-42			30 days
13	Kawasaki disease (settings = E, I)	KD	1-21, 1-42			
14	Multisystem Inflammatory Syndrome in Children & Adults (MIS-C, MIS-A) (settings = E, I)	MISC			Yes	
15	Myocarditis / pericarditis (settings = E, I)	MYOC	1-21, 1-42			30 days
16	Narcolepsy and cataplexy (settings = E, I, O)	NARC			Yes	
17	Stroke, hemorrhagic (settings = E, I)	HSTK	1-21, 1-42			30 days
18	Stroke, ischemic (settings = E, I)	ISTK	1-21, 1-42			30 days
19	Transverse myelitis (settings = E, I)	TM	1-21, 1-42	Yes		
20	Venous thromboembolism (settings = E, I, O)	VTE	1-21, 1-42			30 days
21	Pulmonary embolism (subset of VTE) (settings = E, I)	PE	1-21, 1-42			30 days
	Notes: specific settings for code search is noted below (E = ED; I = Inpt; O = Outpt)					

Analytic Strategies: Aim 1

The number of events observed in the risk interval will be compared to the number expected, with the expected derived from 3 types of comparators, the first of which will be primary when available:

- vaccinated concurrent comparators in a comparison interval after COVID-19 vaccination.
 - On each day, outcome incidence in the vaccinees who are in their risk interval will be compared to outcome incidence in vaccinees who are concurrently—on the same calendar date—in their comparison interval.
 - Analyses will be stratified in risk sets anchored to the calendar dates of outcome events.
 - Analyses will be stratified by age group, sex, race/ethnicity, and VSD site, as well as by calendar date.
- Unvaccinated concurrent comparators in a comparison interval after COVID-19 vaccination.
 - On each day, outcome incidence in the vaccinees who are in their risk interval will be compared to outcome incidence in Unvaccinated individuals who are concurrently—on the same calendar date—at risk.
 - Analyses will be stratified in risk sets anchored to the calendar dates of outcome events.
 - Analyses will be stratified by age group, sex, race/ethnicity, and VSD site, as well as by calendar date.
- self-controls in a comparison interval after COVID-19 vaccination.
 - Among the vaccinees who had an outcome event in either the risk interval or the comparison interval, we compare outcome incidence in the risk interval with outcome incidence in the comparison interval.

Quick medical record review of cases

Outcome	Dose	Sex	Age	Vaccine	Symptom Onset after vaccination	Days after vaccination	Notes
Appendicitis	1	F	60-64	Pfizer	Y	13	Path report confirmed acute appendicitis, Appendectomy
	1	F	45-49	Moderna	Y	6	Confirmed
	1	F	55-59	Moderna	Y	10	Confirmed
	1	M	30-34	Pfizer	Y	15	Path report confirmed acute appendicitis, Appendectomy
	1	F	60-64	Pfizer	Y	1	Path report confirmed acute appendicitis, Appendectomy, 2 nd dose of vaccine given
	2	F	55-59	Pfizer	Y	4	Confirmed
	1	M	35-39	Moderna		5	
	1	F	55-59	Pfizer		11	
	1	F	80-84	Moderna		4	

Quick medical record review of cases*

Outcome	Sex	Age	Vaccine	Symptom Onset after vaccination	Days after vaccination	Notes
Appendicitis	F	60-64	Pfizer	Y	13	Path report confirmed acute appendicitis, Appendectomy
	F	45-49	Moderna	Y	6	confirmed
	F	55-59	Moderna	Y	10	confirmed
	M	30-34	Pfizer	Y	15	Path report confirmed acute appendicitis, Appendectomy
	F	60-64	Pfizer	Y	1	Path report confirmed acute appendicitis, Appendectomy, 2 nd dose of vaccine given
Bell's Palsy	F	35-39	Pfizer	Y	2	Neuro confirmation of Bell's Palsy
	M	45-49	Moderna	N	NA	Chart review showed that symptom onset started before vaccination
Stroke, hemorrhagic	F	45-49	Pfizer	Y	4	Hospitalized for 3 days, continued to improve during hospitalization. Released in stable condition.
VTE	F	50-54	Pfizer	N	NA	Chart review showed that symptom onset started 3 weeks before vaccination

* As of 01/16/21

35

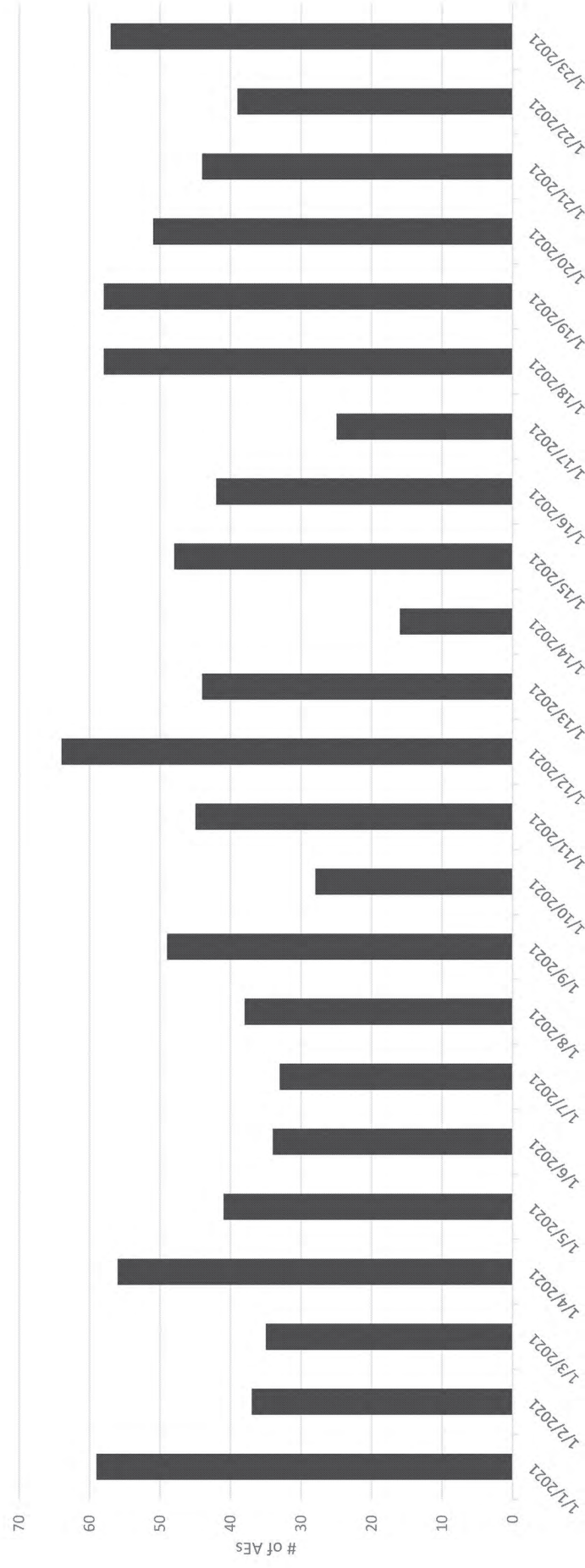
PSICOVID_00010206

Analytic Strategies: Aim 1

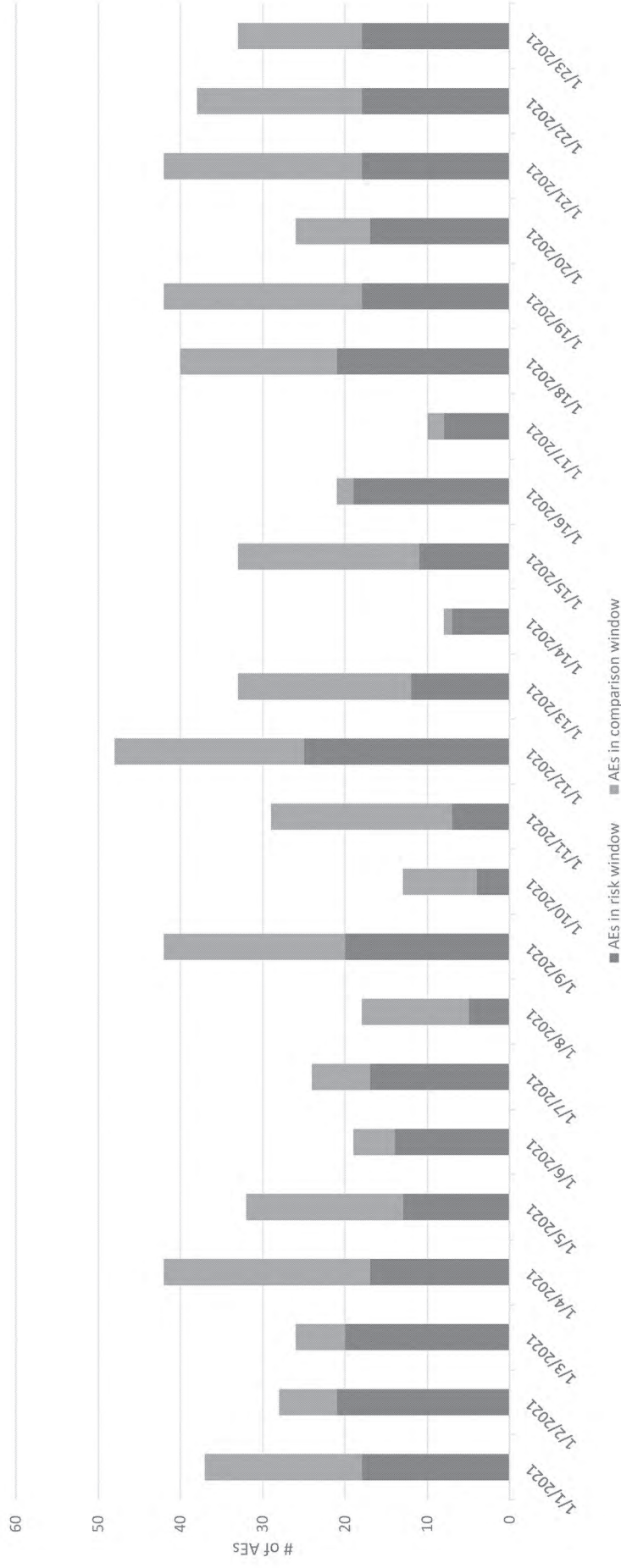
Design	Advantages	Limitations
Primary		
Concurrent Vaccinated	- Not confounded by time-stable co-morbidities, propensities to use health services, or demographics - Follow-up in the comparison interval is on the same calendar dates as follow-up time in the risk interval - Avoids bias that can arise from day-to-day variation in health services - Reduces bias that can arise from data lags	- Transient difficulty finding appropriate comparators soon after a new risk group becomes eligible for vaccine
Unvaccinated concurrent	- Well-adjusted for calendar time	- Bias from comorbidities, demographics, and propensities that may be associated with both the outcome and vaccination status
Supplemental		
Self-Control	- Not confounded by time-stable co-morbidities, propensities to use health services, or demographics as the same vaccinees are contributing person time to both the risk and the comparison intervals	- Bias from differences between risk and comparison intervals in calendar time - Analyses are less timely and can only include vaccinees for whom the control window is complete and for whom the data have settled

- Primary design will be vaccinated concurrent comparators
- If vaccinated concurrent comparators are unavailable, the primary analyses will use Unvaccinated concurrent comparators

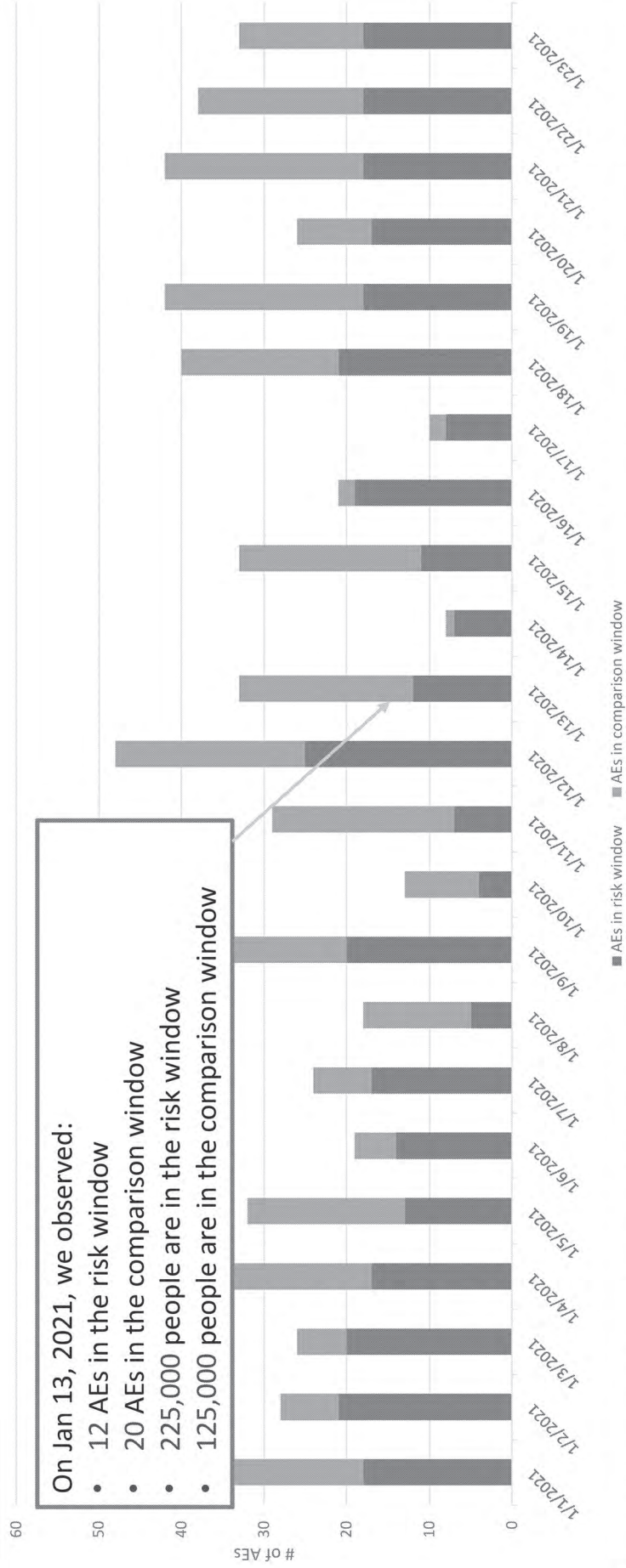
Total # of Events on Each Day



Did the event occur in a risk or comparison interval?



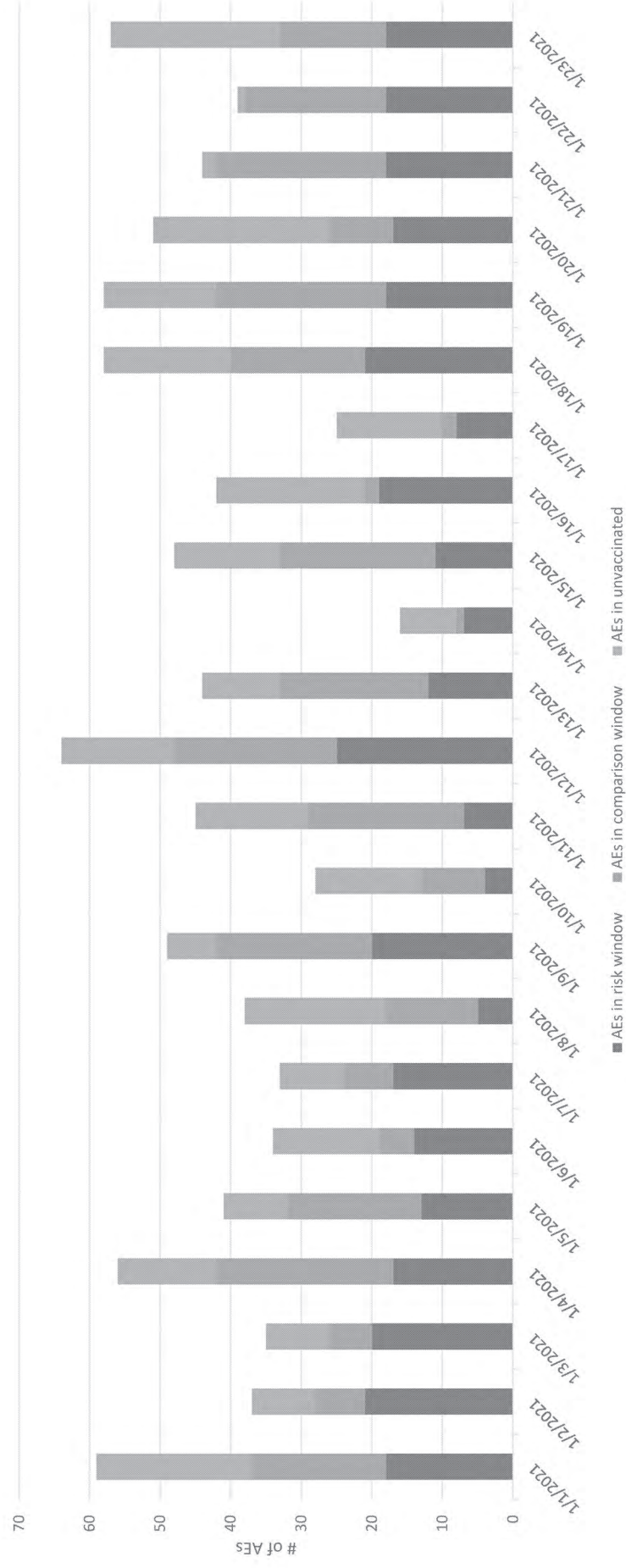
Vaccinated Concurrent Comparator Analyses



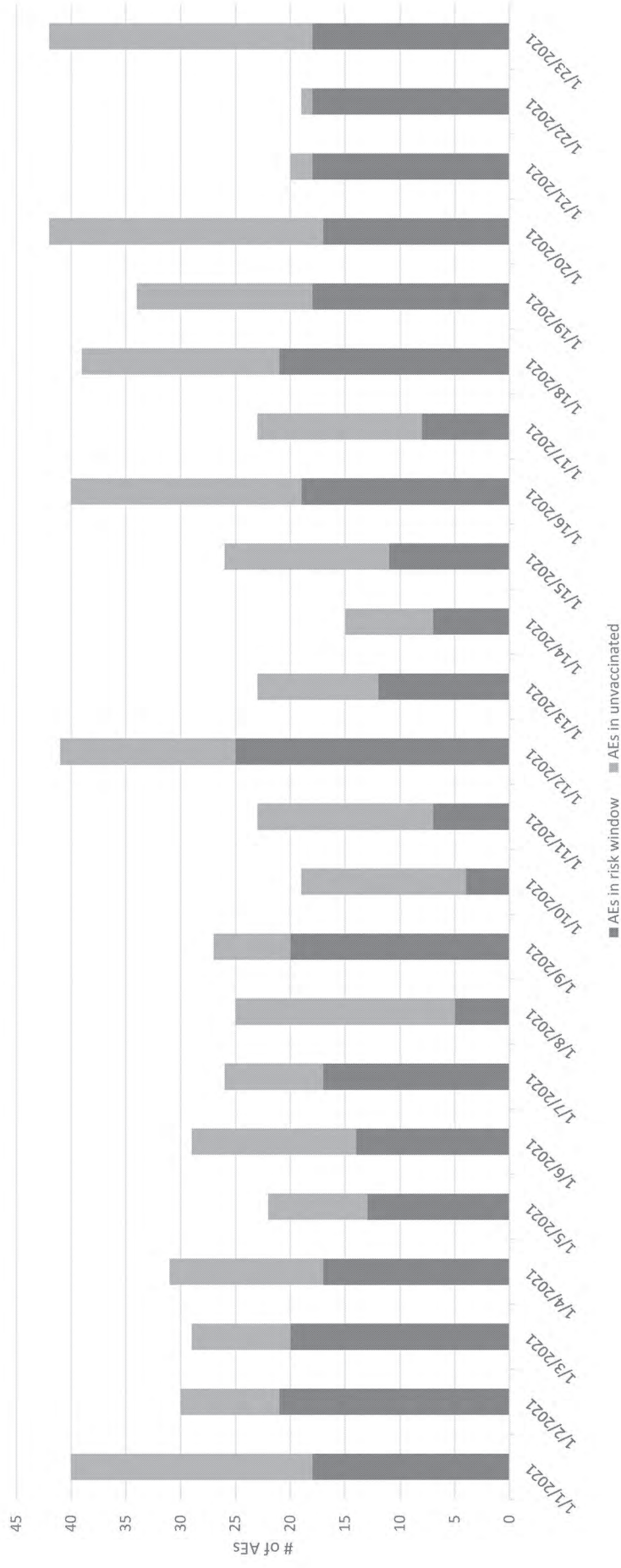
Looking at the data each day in this way, we inherently adjust for variations that occur on different days (e.g., a holiday, every Monday, or a weekend).

At each analysis, we compute a summary rate ratio (risk vs comparison) with all the data available to date. This rate ratio is adjusted for calendar time by day.

Did the event occur in a risk or comparison interval or Unvaccinated?



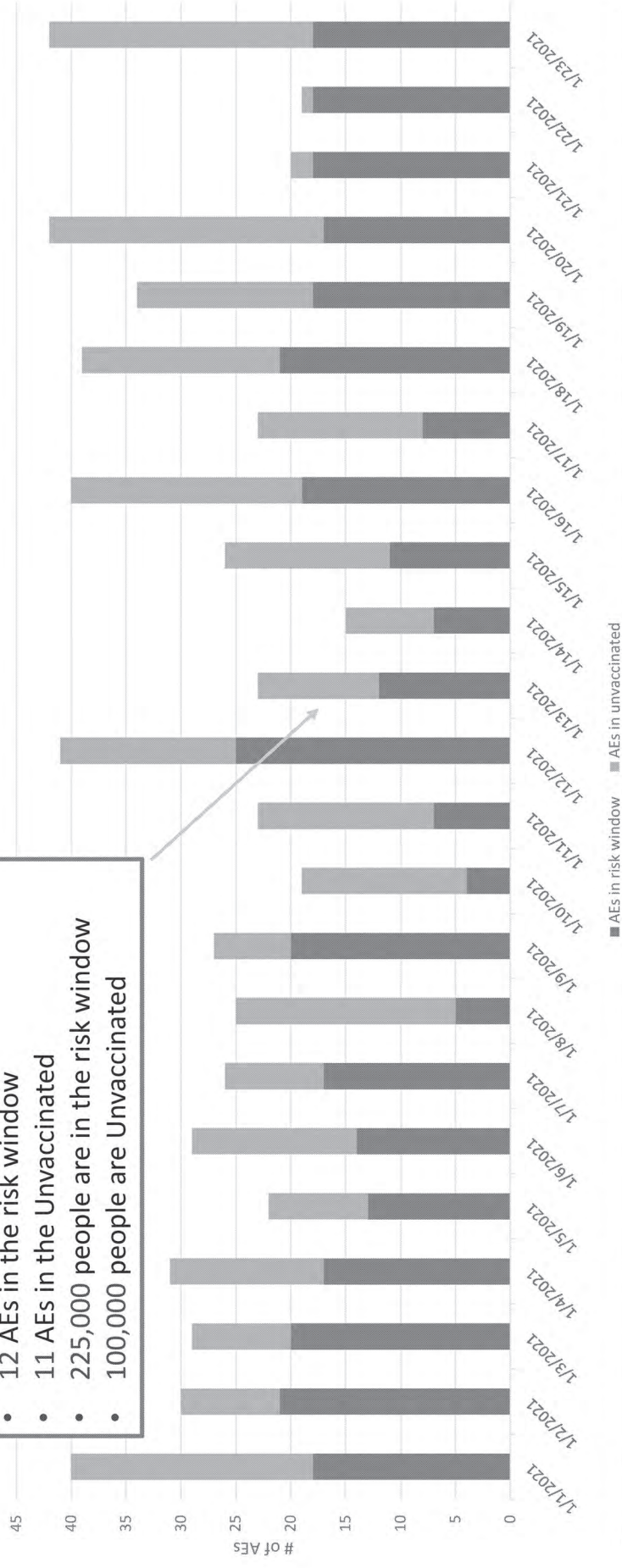
Did the event occur in a risk interval or in the Unvaccinated?



Unvaccinated Concurrent Comparator Analyses

On Jan 13, 2021, we observed:

- 12 AEs in the risk window
- 11 AEs in the Unvaccinated
- 225,000 people are in the risk window
- 100,000 people are Unvaccinated

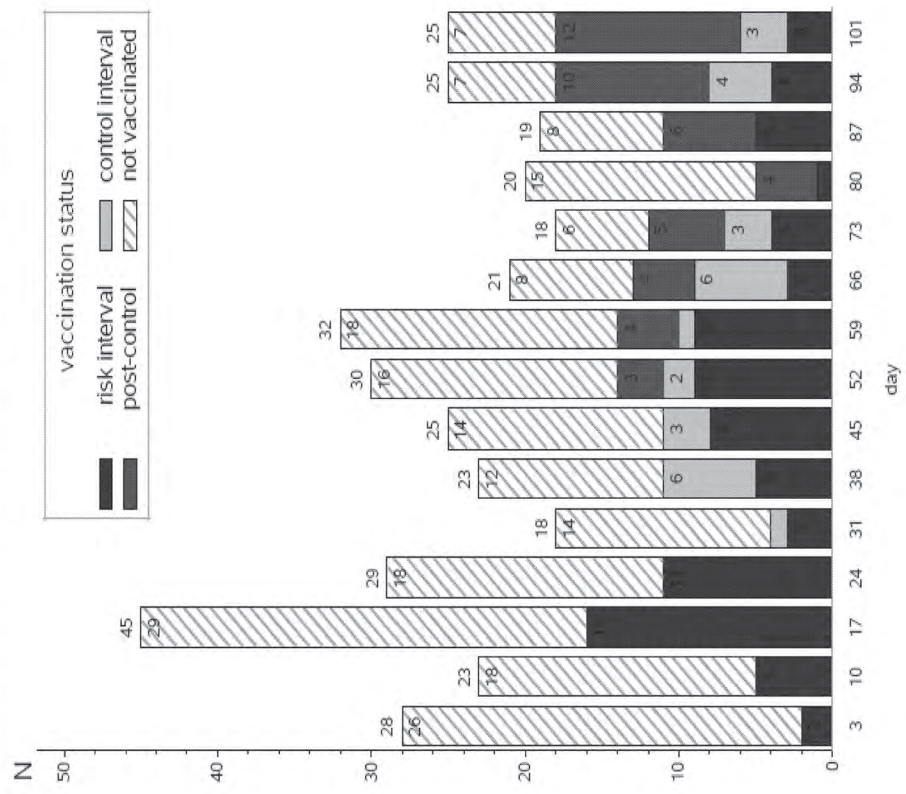


At each analysis, we compute a summary rate ratio (risk vs Unvaccinated) with all the data available to date. This rate ratio is adjusted for calendar time by day

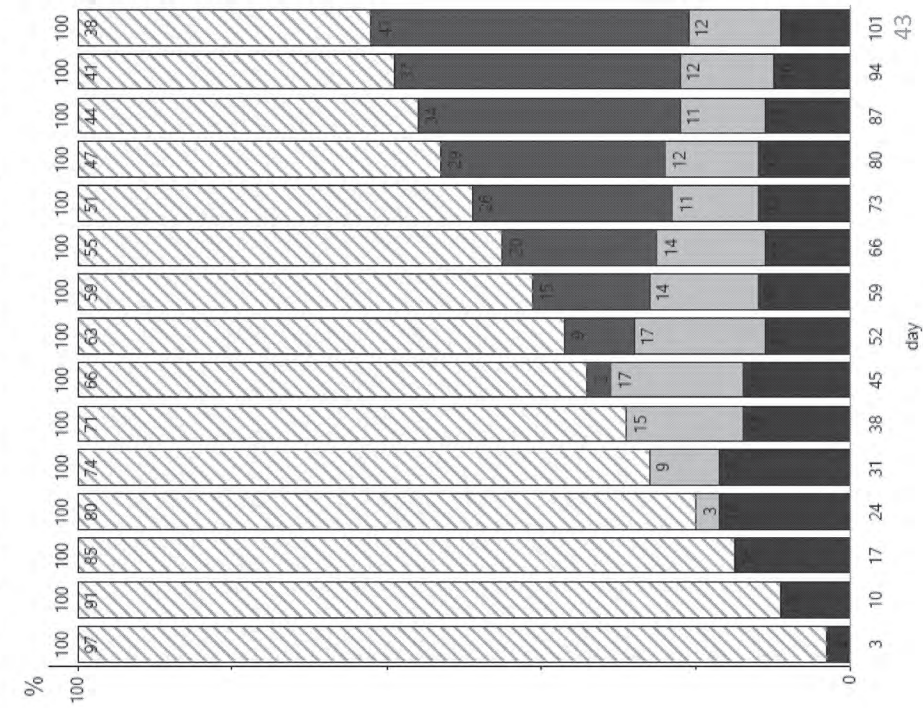
Looking at the data each day in this way, we inherently adjust for variations that occur on different days (e.g., a holiday, every Monday, or a weekend).

All AEs and follow-up in the population by vaccination status and day

All AEs in the population on selected days by vaccination status



Distribution of the population on selected days by vaccination status



Rate Ratio Estimates

Poisson regression will be used to model outcome incidence observed during the risk interval in comparison with incidence expected (under H_0)

- Estimates of the rate ratio (RR) will be reported with nominal 95% confidence intervals rather than confidence intervals that are widened to correspond with the threshold of the sequential tests.
- Trends in outcome incidence over calendar time and time-since-vaccination, and heterogeneity across subgroups will be tracked.
- Supplementary analyses will disaggregate the risk interval (days 1-7, days 8-15, etc.), comparing risk interval weeks with each other and with the incidence expected (under H_0) from our primary comparator. We'll also look at whether incidence varies across the weeks of the comparison interval.

Sequential Tests

- For each outcome, the primary analysis each week will include a sequential test of the one-sided null hypothesis that the vaccine does not increase risk in the risk interval.
- The threshold for a signal is pre-specified by an alpha-spending plan that keeps the overall chance of a Type 1 error below 0.05 for 2 years (104 weekly analyses).
 - With a Pocock style plan, the 2-sided p-value required for a signal at a weekly analysis is 0.0096, amounting to a 1-sided p-value of 0.0048.
- The criteria for signaling are not criteria for “stopping”.
 - After a signal, weekly updates will continue as we add analyses to evaluate the signal.
- The multiplicity of different hypotheses tested will be taken into consideration informally.
 - Our sequential testing adjusts for the multiplicity of weekly looks at each hypothesis, but we will not adjust formally for the multiplicity of hypotheses.

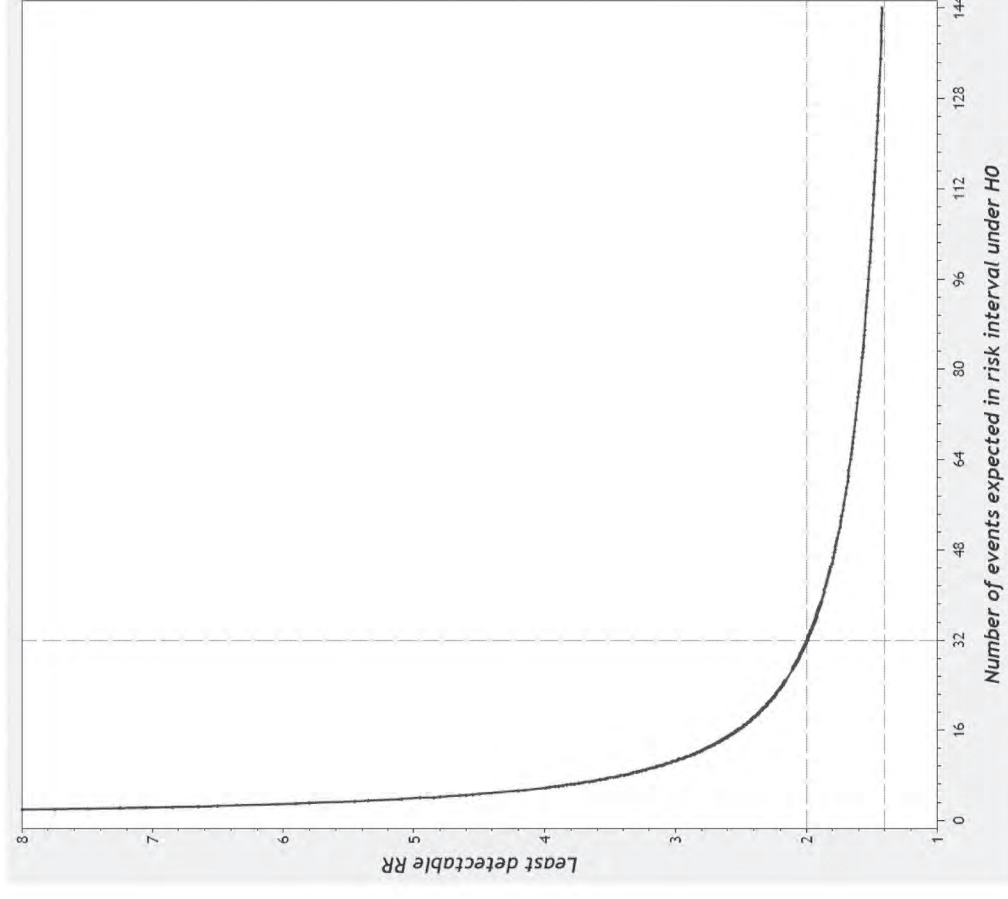
Power (Aim 1)

Power of planned analyses comparing observed outcomes vs expected outcomes in a risk interval—where the expected is based on vaccinees in a comparison interval.

- The magnitude of the rate ratio (RR) detectable with 80% power will decrease as the number of outcomes expected in the risk interval (under H_0) increases.
- If our alpha-spending plan sets the threshold for a signal at 2-sided $p=0.0096$ (amounting to 1-sided $p=0.0048$) then $RR = 2.0$ is detectable when **32** outcomes are expected in the risk interval.
 - RRs of 5, 4, 3, and 1.5 are detectable when 4, 6, 11, and 110 AEs, respectively, are expected in risk interval.
- If E denotes the background rate (outcomes expected per 100,000 person-years under H_0) then an RR of 2.0 is detectable when the number of person-days in the risk interval is:

$$32/E \times 365,000$$

- For example, if the background rate is 32 per 100,000 person years, then an RR of 2 is detectable when 365,000 person days are in the risk interval, which we'd have if 1.74 million vaccinees are each observed 21 days.



Relative risk detectable with 80% power, comparing AEs in risk v. comparison intervals of equal length, By the N of events expected in risk interval under the H_0 that the vaccine is safe.

Time-to-signal by the rate ratio and the N of events expected weekly under H0

- This table reports on the time-to-signal in 5 million simulations of safety surveillance in each of 12 scenarios, defined by:
 - 3 levels of the rate ratio: 1.5, 2, and 3, and
 - 4 levels of outcome incidence expected under H0: 1, 5, 20, or 100 outcome events per week.
- The top row of each panel indicates when the chance of detecting the panel's RR exceeds 50, 80 and 95% for an AE with expected incidence of only 1 per week
 - The top row of the top panel shows time-to-signal if the true RR=1.5 for an outcome so rare that under H0 we expect only 1 AE per week. (An example of such an outcome would be TTP if we have about 500,000 VSD vaccinees per week)
 - For this infrequent outcome (1 AE/week), the chance of detecting RR=1.5 exceeds 50% by the 55th week and exceeds 80% by the 101st week. It won't ever exceed 95%.
 - For this infrequent outcome, the chance of detecting RR=3.0 exceeds 50% by week 7, 80% by week 11, 95% by week 17.
- Similarly, the 2nd row of each panel indicates when the chance of detecting the RR exceeds 50, 80 and 95% for an AE with expected incidence of 5/week (perhaps Bell's Palsy). The chance of detecting RR=2 passes 50% by week 4, 80% by week 7, 95% by week 11.

For simplicity, expected incidence (under H0) was constant in each scenario.

		Week when chance of signal passes:		
		50%	80%	95%
Rate Ratio	AEs/week expected in risk interval			
1.5	1 (TTP)	55	101	
	5 (Bells P.)	12	22	33
	20 (seizure)	4	6	9
	100 (AMI)	1	2	2
2	1 (TTP)	19	32	49
	5 (Bells P.)	4	7	11
	20 (seizure)	2	2	3
	100 (AMI)	1	1	1
3	1 (TTP)	7	11	17
	5 (Bells P.)	2	3	4
	20 (seizure)	1	1	1
	100 (AMI)	1	1	1

Signal Follow-up

- If the criteria for a signal are met, we will already have the supplemental comparators (i.e., Unvaccinated concurrent and self-control) available for context and interpretation of results.
- Further analyses of the potential vaccine-outcome association may be undertaken, such as:
 - Chart review (especially of outcomes during the risk interval)
 - Evaluate for clustering of outcomes if they appear during brief sub-intervals within the risk interval
 - Evaluate for clustering in subgroups defined by:
 - age
 - sex
 - race/ethnicity
 - VSD site
 - prior COVID-19 disease

Chart Review

- We will conduct routine chart review for selected rare outcomes (e.g., GBS, ADEM, TM, anaphylaxis) shortly after a case is detected and prior to analysis.
- If the criteria for a signal are met, further analyses of the potential vaccine-outcome association may be undertaken through chart review.
- In collaboration with MCRI and CDC, with feedback from participating VSD sites, we will design, test, validate, and manage all chart reviews across the participating sites.

Study Design: Aim 2

Aim 2: To describe the uptake of COVID-19 vaccines over time among eligible VSD members overall, and in strata by age, sex, race/ethnicity, and VSD site.

- After a COVID-19 vaccine becomes routinely available in the VSD, we will monitor vaccine coverage overall, and in strata defined by age group, sex, race/ethnicity, and VSD site.
- Surveillance of vaccine coverage will be updated weekly.
 - For each week during the study period, we will tabulate the number of doses delivered, the cumulative number of doses, and vaccine coverage.
 - If different vaccines are in use in the VSD population, we will monitor vaccine coverage separately for each type of vaccine, and for all COVID-19 vaccines combined.

Vaccine Safety Datalink (VSD)

- VSD consists of electronic health data from each participating site
 - Demographic data: sex, age, race, and service area
 - Vaccine data: type of vaccine, vaccination date, and vaccination site
 - Medical record: includes all healthcare utilization (outpatient, emergency department, and hospitalizations)
- The total 2020 VSD population is ~12.4 million people (3.8% of the total U.S. population).
 - 2,483,518 children (<18 YOA)
 - 9,916,888 adults (18+ YOA)
 - 2019 birth cohort was 105,586

Vaccine Safety Datalink

- Active surveillance: newly licensed vaccines
- Evaluate vaccine safety:
 - of new recommendations for existing vaccines
 - for vaccines in high-risk populations, particularly pregnant women (+ other groups)
 - changes to the vaccine schedule
- Develop new methodologies for vaccine safety assessment
- Test hypotheses noted by signals from VAERS, clinical trials, and other platforms

Importance of Rapid Cycle Analysis in Vaccine Safety

- Rare adverse events may be impossible to detect in pre-licensure studies
- Reports to passive surveillance systems (e.g., the Vaccine Adverse Event Reporting System) often need rapid surveillance/follow-up
- Traditional cohort or case control studies are not well suited for rapid signal detection
 - Studies can take months to years using traditional approaches

Rapid Cycle Analysis in VSD

- Rapid Cycle Analysis (RCA) allows VSD to detect adverse events following vaccination in near real-time so the public can be informed quickly of possible risks.
- VSD has used RCA to monitor safety of many vaccines including:
 - DTaP-IPV/Hib
 - DTaP-IPV
 - Human papillomavirus (4 valent and 9 valent)
 - Influenza
 - Rotavirus
 - Meningococcal conjugate
 - Measles, mumps, rubella, and varicella (MMRV)
 - Tetanus, Diphtheria, Pertussis (Tdap)
 - Recombinant zoster vaccine

Data

- Sites that participate in VSD produce weekly dynamic data files (DDF) that capture information on demographics, immunizations, and ICD-coded diagnoses assigned by health care providers in outpatient, emergency, or hospital encounters.
- The DDF will be used as the primary data source for both Aims 1 and 2, including identifying and following vaccine recipients for outcomes of interest.

Covariates

- Selected covariates including age, sex, site, race/ethnicity and calendar time will be considered *a priori* and will be used as stratification variables.
- Additional covariates may be considered with CDC and the VSD RCA working group as appropriate.

Historical Comparator Analysis

General Analytic Approach

- MFC will use historical comparators
- Most appropriate for infrequent or rare outcomes
- Using historical data accumulated over multiple years provides more stable estimates and greater statistical power, which potentially leads to earlier detection of a safety signal
- Ideally, the historical period starts October 1, 2015 (the start of ICD-10 coding) and ends December 31, 2019 to avoid the influence of the pandemic in the early part of 2020
- Limitation: Secular trends in disease or in diagnostic or coding practices may lead to either false signaling or failure to identify a true signal

Sequential Analysis using MaxSPRT and CMaxSPRT

- Near real-time surveillance based on weekly aggregate data
- Sequential analysis to detect signals, but maintaining a pre-defined type I error rate
- Poisson-based MaxSPRT, developed by VSD researchers (Kulldorff, et al.)
- Compare observed number of events to expected number based on the historical background rates
 - Expected counts based on the incidence rate expected during the risk window multiplied by the number of vaccines administered
 - Reject H_0 of no excess risk if log-likelihood ratio exceeds a critical value → **statistical signal**
- Critical values based on probability of a false positive (e.g. $\alpha=0.05$) and planned length of surveillance, defined in terms of expected counts under the null hypothesis
- Use conditional MaxSPRT (CMaxSPRT) when the number of historical cases is small and background rates are unstable

Historical Comparator Groups

- General VSD population (age comparable)
 - Used to estimate general background person-time rates
 - Rates multiplied by vaccine counts to produce expected (prorated to length of post-vax window)
- Other comparator group(s) defined by care-seeking behavior and/or comparator vaccine visits*
 - Well visits (e.g., ICD10: Z00.00, Z00.01)
 - Non-COVID vaccination (e.g., Td, Tdap, pneumococcal, influenza)
 - Compute number events in post-visit risk windows
- Some combination of well visits and vaccination visits in the historical period?
 - For example, well visit and a flu vaccine in the previous 18 months
- Compare different groups to vaccinated group using baseline covariates

Centers for Disease Control and Prevention



V-Safe Pregnancy Registry

Vaccine Task Force
Centers for Disease Control and Prevention

February 22, 2021

Outline

- How and when we identify pregnant persons through v-safe
- Number of pregnant persons enrolled to date by vaccine
- Description of pregnant participants and pregnancy outcomes
- Data analysis, reporting plans, and next steps

Pregnancy Question*

Dose 1:

Initial survey (can be administered up to day 42 post vaccination):

Were you pregnant at the time of your COVID-19 vaccination?

Yes/No/Don't know

Day 21, 42 (if participant does not receive/register 2nd dose information)**

Since your last COVID-19 vaccination, have you had a home or laboratory pregnancy test that was positive? Yes/No

*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



Pregnancy Questions*

- Dose 2:
 - Initial survey (this could occur as early as 21 or 28 days following first dose vaccination depending on manufacturer):
 - **Were you pregnant at the time of your 2nd COVID-19 vaccination?**
Yes/No/Don't know
 - Day 21, 42**
 - **Since your last COVID-19 vaccination, have you had a home or laboratory pregnancy test that was positive? Yes/No**
 - 3, 6, 12 month** (will be asked after dose 1 if no dose 2 is administered):
 - **Since your last COVID-19 vaccination, have you had a home or laboratory pregnancy test that was positive? Yes/No**

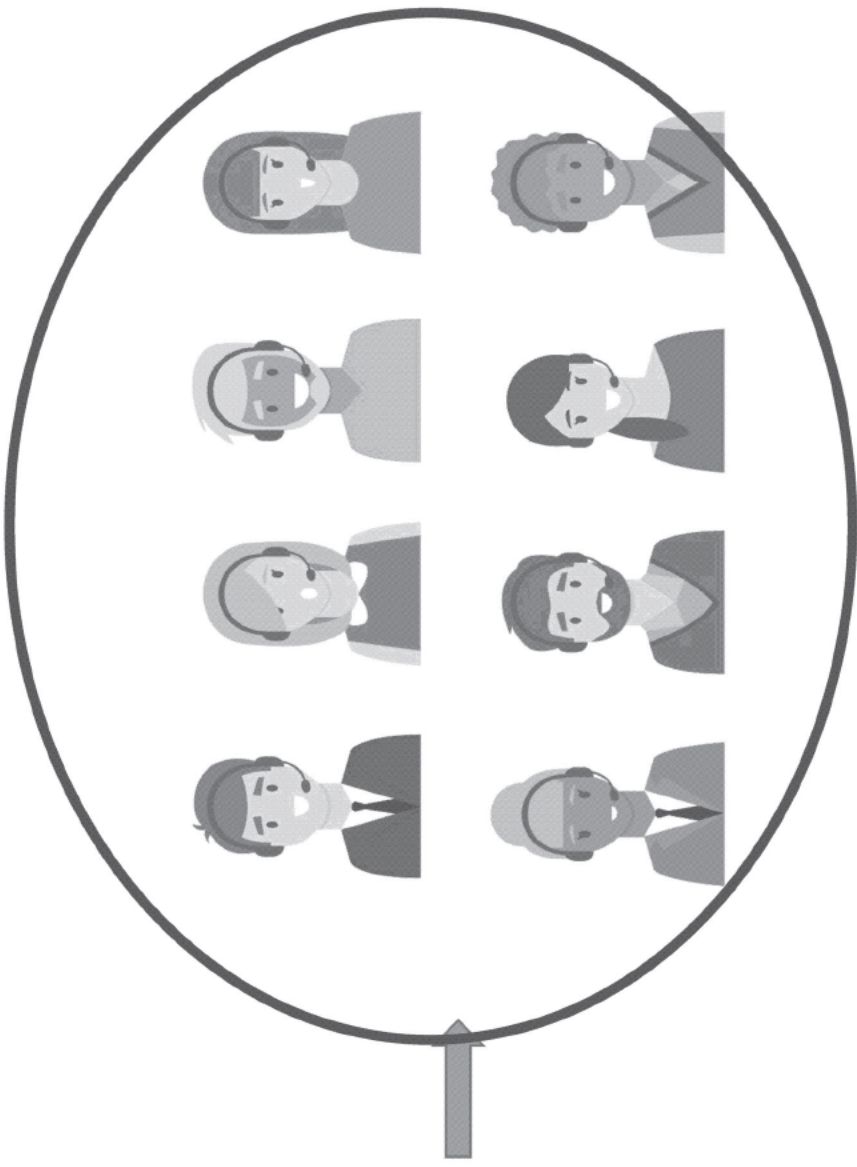
*Will be asked of all non-male sex v-safe participants (i.e., female, unknown, prefer not to say)

**Question will be hidden if vaccine recipient answers “yes” to a prior pregnancy status question for the respective dose





Yes **No** **Unknown**



COVID-19 Vaccine Pregnancy Registry



If a person reports:

- ✓ Pregnant at time of vaccination (initial survey for each dose)
- ✓ Had a positive pregnancy test since vaccination (Day 21, 42 of each dose and monthly surveys)



COVID-19 Vaccine Pregnancy Registry:

- Once each trimester during pregnancy
- Once after delivery
- Once after the infant is 3 months old.



Medical records requested:

- At conclusion of pregnancy
- After first 3 months of infant's life



Data flow:

- Person self-identify pregnancy
- Two data sources to manage eligibility and interviews
 - Eligibility: Access
 - Interviews of enrolled participants: REDCap

v-safe and pregnancy registry: 2/19/2021, 5 am ET

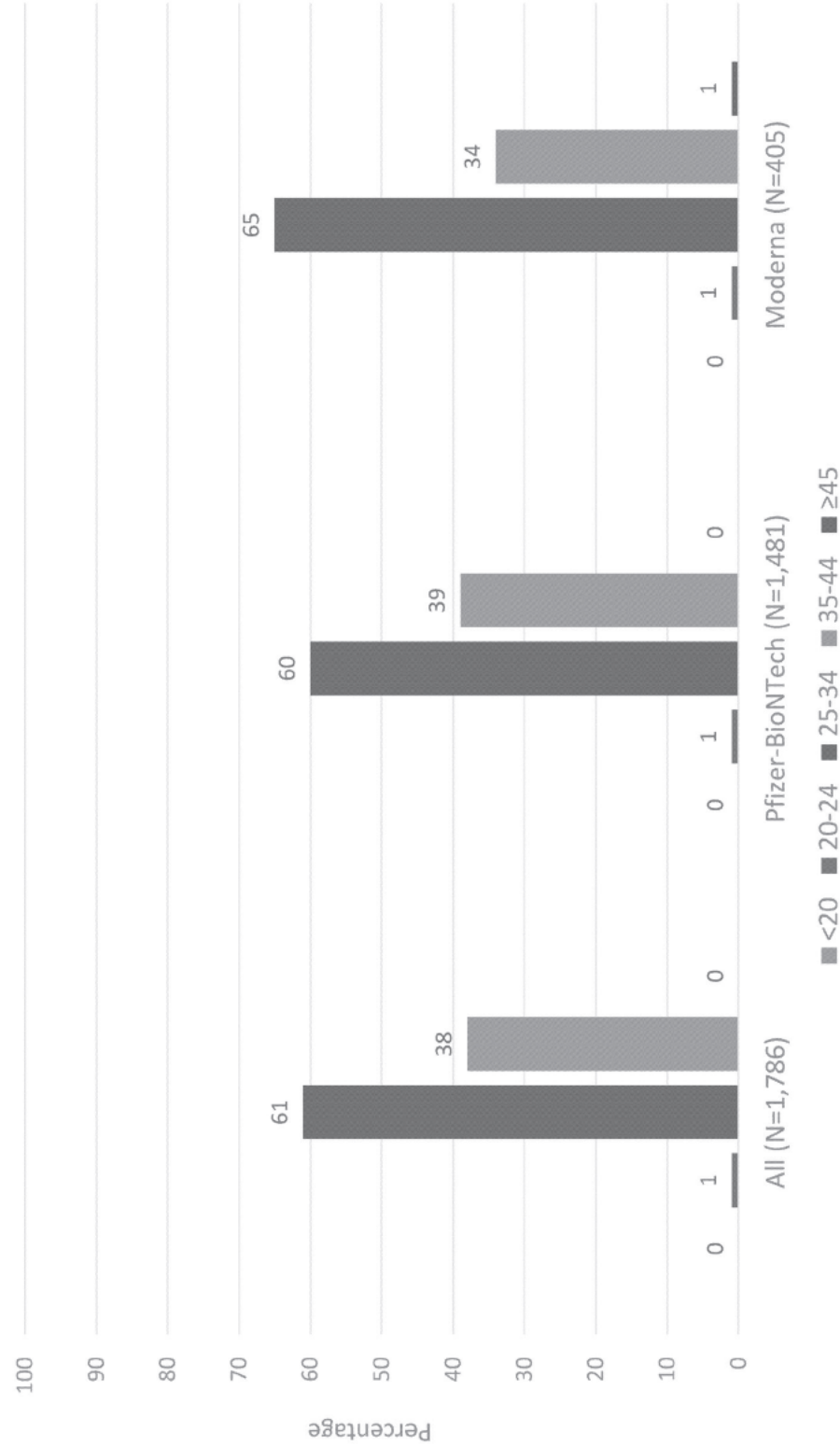
	All Vaccines N	Pfizer-BioNTech N	Moderna N
Potential pregnancies in v-safe	32,120	16,857	15,263
Pregnancy registry			
Enrolled	1815	1491	324
Not Eligible ^a	103	83	20
Refused/Declined ^b	31	26	5

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

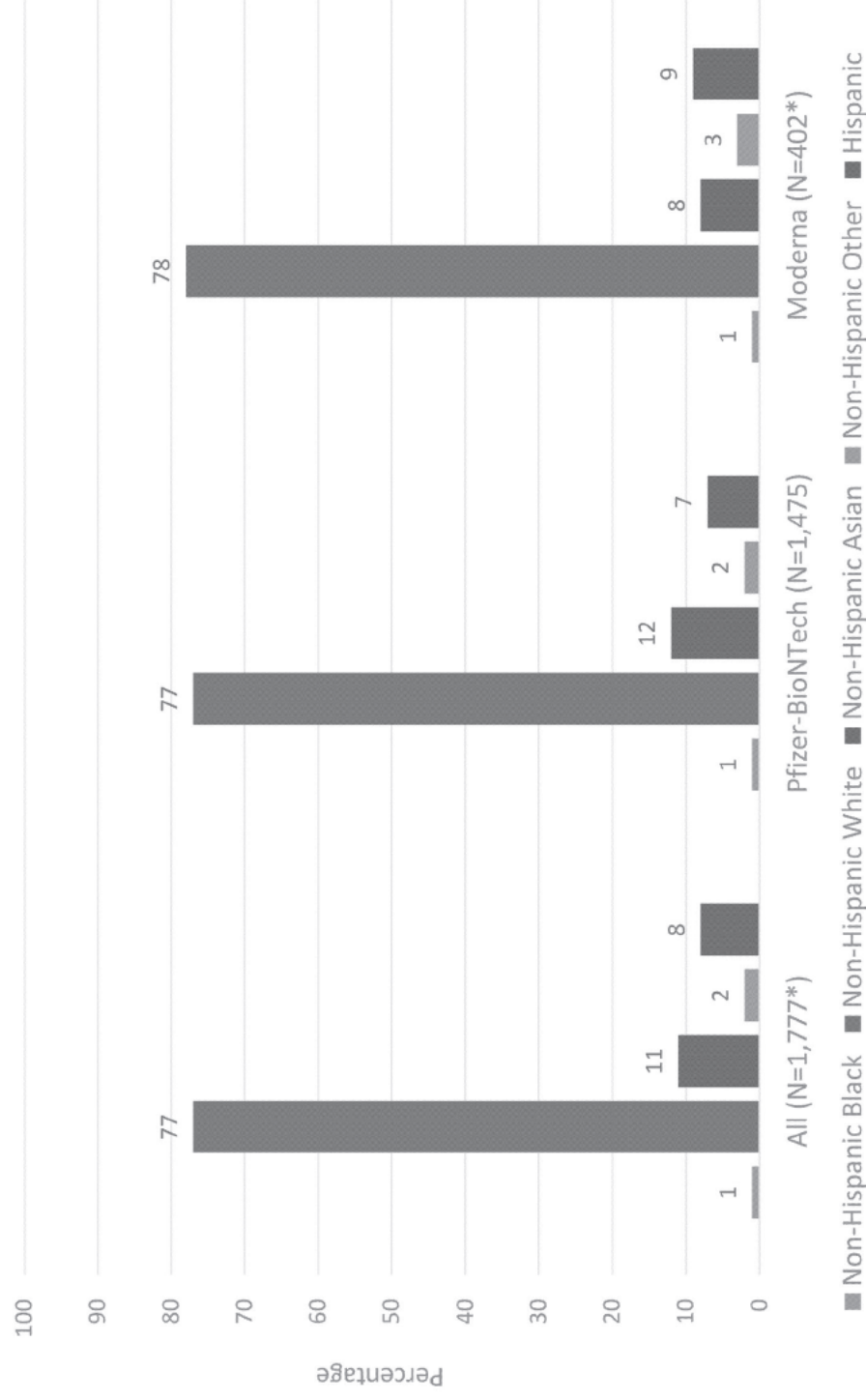
^b Refused indicates those for whom eligibility could not be fully assessed because participant chose not to engage with pregnancy registry team; declined indicates those who were eligible to participate but chose not to enroll

Registry Participant Characteristics and Pregnancy Outcomes: enrolled as of 02/18/2021 at 3:00pm

Registry Participant Characteristic: Age at 1st Vaccine Dose



Registry Participant Characteristic: Race/Ethnicity



*Missing N=9 (All), N=6 (Pfizer), N=3 (Moderna)

Registry enrollment by group and product received

		Vaccine manufacturer					
		All		Pfizer-BioNTech		Moderna	
		n	%	n	%	n	%
Self-Reported Vaccine priority group^							
	Healthcare worker only	1,648	92	1,372	93	276	90
	Non-healthcare essential worker only	11	1	8	1	3	1
	Medical condition other than pregnancy only	1	0	1	0	0	0
	Healthcare worker and Non-healthcare essential worker	12	1	9	1	3	1
	Healthcare worker and Medical condition	100	6	80	5	20	7
	Missing	14	1	11	1	3	1
Timing of 1st vaccine dose							
	Pre-pregnancy (within 30 days)	3	0	2	0	1	0
	First trimester (<14 weeks)	505	28	410	28	95	31
	Second trimester (>=14 and <28 weeks)	817	46	686	46	131	43
	Third trimester (>=28 weeks)	453	25	377	25	76	25
	Missing	8	0	6	0	2	1

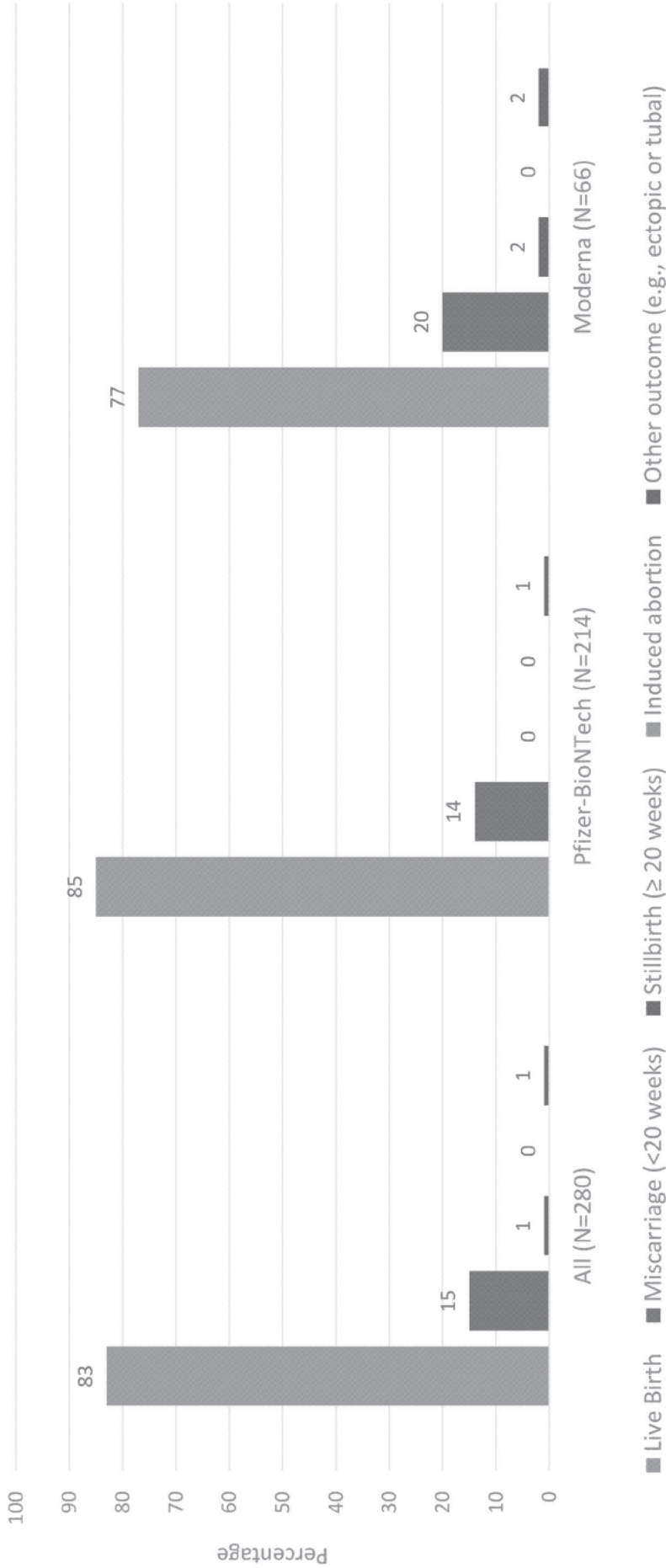
[^]Military, state/federal government employee categorized as non-healthcare essential worker

COVID-19 Infection and Fever During Pregnancy

		Vaccine manufacturer					
		All		Pfizer-BioNTech		Moderna	
		n	%	n	%	n	%
COVID-19 infection relative to timing of 1st vaccine dose							
	No COVID	1,742	98	1,444	98	298	98
	COVID diagnosed before vaccine	28	2	26	2	2	1
	COVID within 14 days of vaccine	3	0	1	0	2	1
	COVID after 14 days of vaccine	5	0	4	0	1	0
	Missing	8	0	6	0	2	1
Fever relative to timing of 1st vaccine dose#							
	No fever	1,689	95	1,410	95	279	91
	Fever diagnosed before vaccine	7	0	6	0	1	0
	Fever within 7 days of vaccine	2	0	1	0	1	0
	Fever after 7 days of vaccine	75	4	56	4	19	6
	Missing	13	1	8	1	5	2

#One participant with fever after 7 days of vaccine in addition to within 7 days of vaccine

Pregnancy Outcome



Pregnancy and Neonatal Outcomes of Interest

Outcomes	Background rate	vsafe Registry Overall
Pregnancy Complications		
Gestational diabetes	7-14%	10%
Preeclampsia or Gestational Hypertension **	10-15%	15%
Eclampsia	0.27%	0%
Intrauterine Growth Restriction	3-7%	1%
Neonatal		
Preterm birth	10.1%	10%
Congenital anomalies^^	3% overall birth defects	4%
Small for gestational age^^	3-7%	4%
Neonatal death	0.38%	0%

**Pre-eclampsia or gestational hypertension diagnosed during pregnancy and/or during delivery

^^Birth defect diagnosed after delivery only

##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 01/06/2021:
 - Between ages 25-44 years old
 - Non-Hispanic White
 - Healthcare workers
 - Second trimester
 - No COVID-19 infection in pregnancy
 - No fever in pregnancy
 - Live birth
- Pregnancy and neonatal outcomes of interest are all within background rates

Data Analysis, Interpretation and Reporting Plans

- Data analysis and interpretation
 - Daily reports of # pregnant women enrolled; will be included in VaST summary
 - Weekly reports of demographic variables, pregnancy characteristics, outcomes of interest available*
 - Monthly reports reviewing medical record data with interview data
 - Clinical review with internal and external experts
 - Power calculations to understand required sample size
 - Longitudinal follow up of infant outcomes planned through 3 months of age for infant
- Upcoming public reporting
 - Presentations at ACIP meeting (03/01) and VRBPAC meeting (2/26)
 - Publication in MMWR for data through 02/16/2021

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

Next Steps

- Contracts for v-safe pregnancy registry
 - Interim contract to start 03/01 (Period of Performance: 6 months)
 - Medical record request and abstraction
 - Long term contract to start early May (Period of Performance: 3 years)
 - Call center
 - Medical record request and abstraction
 - Analysis

For more information, contact CDC

TTY: [REDACTED] 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.

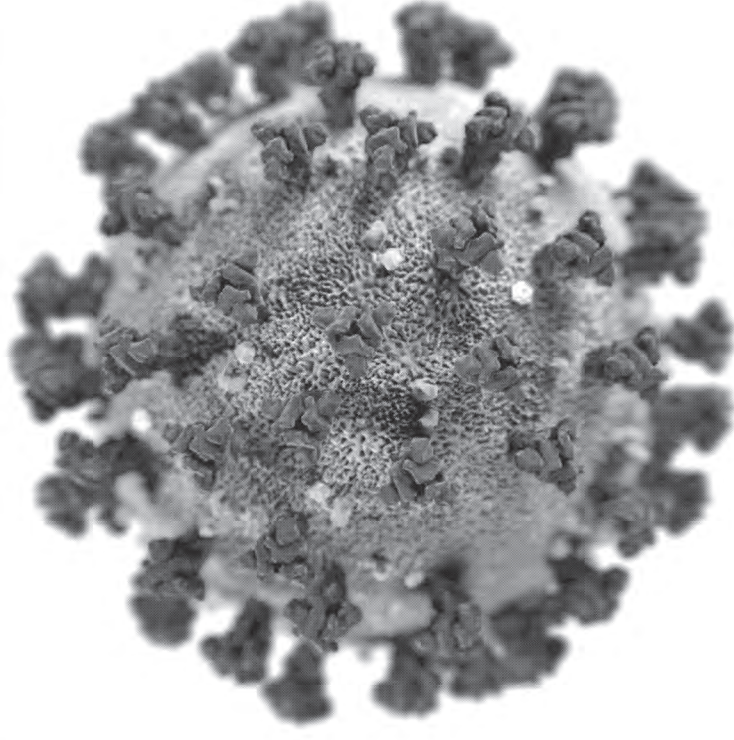


PSICOVID_00010249

Pregnancies in v-safe

Tanya Myers, PhD, MSc

February 22, 2021



Outline

- Overview of v-safe and current dataset
- Basic demographics of pregnancies in v-safe
- Reported health events and reactivity in pregnancies
- Conclusions and further work

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



Pregnancy Question*

Dose 1:

Initial survey (can be administered up to day 42 post vaccination):

Were you pregnant at the time of your COVID-19 vaccination?

Yes/No/Don't know

Day 21, 42 (if participant does not receive/register 2nd dose information)**

Since your last COVID-19 vaccination, have you had a home or laboratory pregnancy test that was positive? Yes/No

*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



Pregnancy Questions*

- Dose 2:
 - Initial survey (this could occur as early as 21 or 28 days following first dose vaccination depending on manufacturer):
 - Were you pregnant at the time of your 2nd COVID-19 vaccination?
Yes/No/Don't know
- Day 21, 42**
 - Since your last COVID-19 vaccination, have you had a home or laboratory pregnancy test that was positive? Yes/No
- 3, 6, 12 month** (will be asked after dose 1 if no dose 2 is administered):
 - Since your last COVID-19 vaccination, have you had a home or laboratory pregnancy test that was positive? Yes/No

*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



Data structure

- Current dataset: December 14-January 13
- Data available for dose 1 (Pfizer-BioNTech, Moderna) and dose 2 (Pfizer-BioNTech only)
- Vast majority of pregnancies in those who identified as female, very few other/prefer not to say (n=6)

v-safe: demographics of pregnant persons^a

	All		Pfizer-BioNTech		Moderna	
	N	%	N	%	N	%
All	10,507	100	6,383	100	4,124	100
Age at 1 st vaccine dose (years)						
16-19	9	0.1	4	0.1	5	0.1
20-24	210	2.0	100	1.6	110	2.7
25-34	6,735	64.1	4,056	63.5	2,679	65.0
35-44	3,265	31.1	2,055	32.2	1,210	29.3
45-54	288	2.7	168	2.6	120	2.9
Pregnancy status						
Pregnant at time of vaccine	10,483	99.8	6,359	99.6	4,124	100
Positive pregnancy test after vaccine	24	0.2	24	0.4	---	---

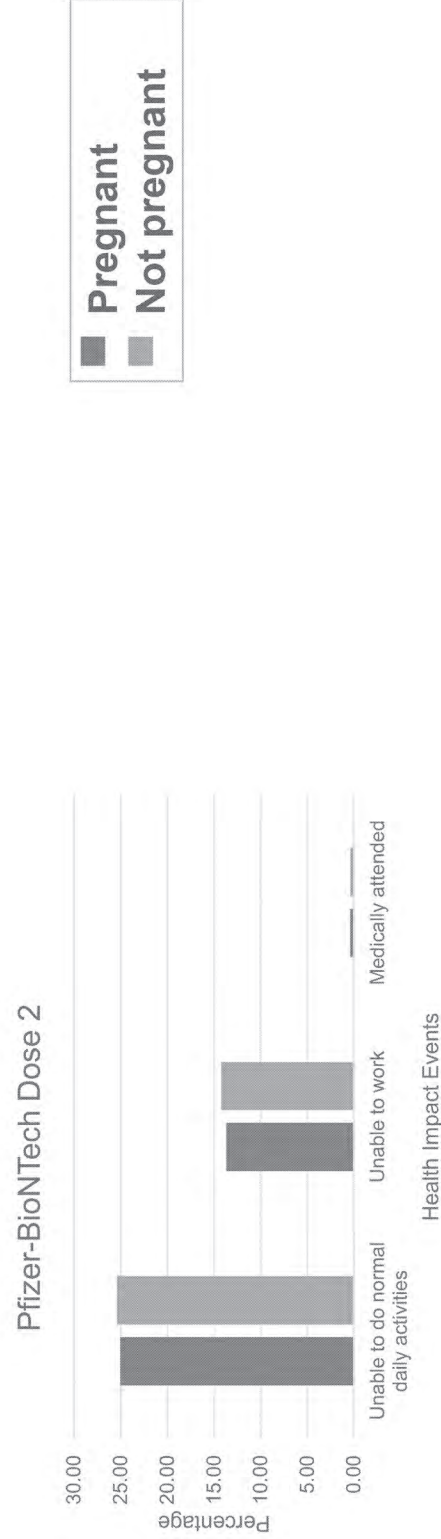
^a pregnant at time of vaccination or positive pregnancy test at day 21 after vaccine and age 16-54 years

v-safe: Day 1 health impacts reported by pregnant women^a

	All		Pfizer-BioNTech		Pfizer-BioNTech		Moderna	
	Doses 1 & 2		Dose 1		Dose 2		Dose 1	
Completed Day 1 survey	N	%	N	%	N	%	N	%
All	7,147	100	3,662	100	1,446	100	2,707	100
Unable to do normal daily activities	618	8.7	102	2.8	362	25.0	158	5.8
Unable to work	296	4.1	42	1.2	198	13.7	60	2.2
Required medical care	20	0.3	9	0.3	6	0.4	5	0.2
Telehealth/virtual/e-mail	6	0.1	1	0.0	4	0.3	1	0.0
Outpatient or urgent care	5	0.1	1	0.0	2	0.1	2	0.1
Emergency room/dept.	8	0.1	6	0.2	---	---	2	0.1
Hospitalization	1	0.0	1	0.0	---	---	---	---

^a pregnant at time of vaccination or positive pregnancy test at day 21 after vaccine and age 16-54 years

v-safe: Day 1 health impacts in women, age 16-54 years



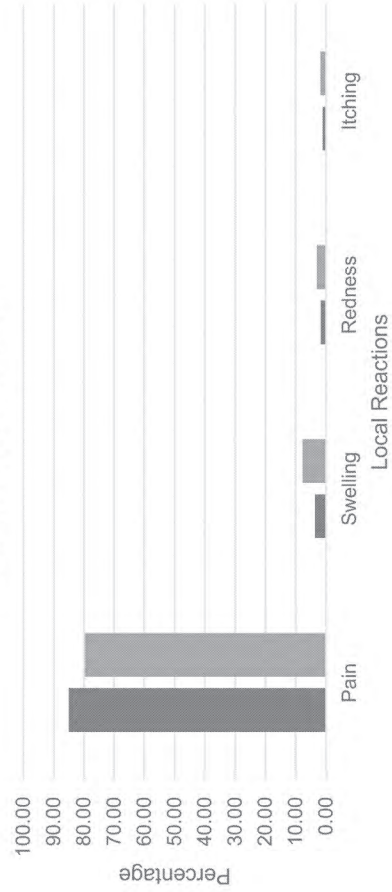
v-safe: Day 1 reactogenicity reported by pregnant women^a

	All		Pfizer-BioNTech		Pfizer-BioNTech		Moderna	
	Doses 1 & 2		Dose 1		Dose 2		Dose 1	
Completed Day 1 survey	N	%	N	%	N	%	N	%
All	7,147	100	3,662	100	1,446	100	2,707	100
Local Reactions								
Pain	6,372	89.6	3,110	84.9	1,317	91.1	2,509	92.7
Swelling	456	6.4	131	3.6	71	4.9	263	9.7
Redness	198	2.8	58	1.6	30	2.1	112	4.1
Itching	101	1.4	40	1.1	18	1.2	45	1.7

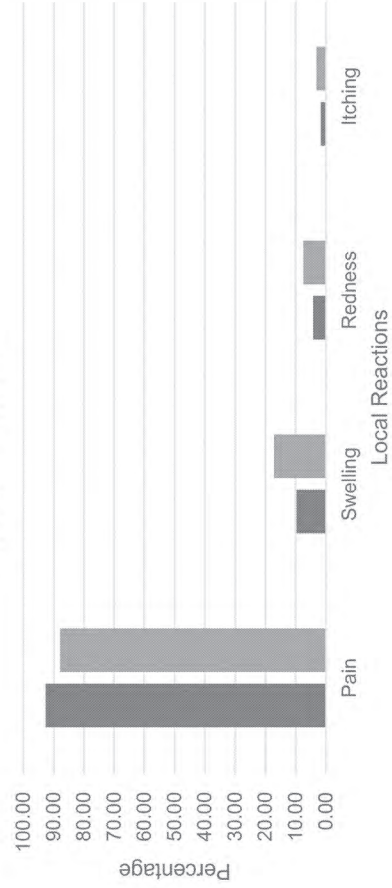
^a pregnant at time of vaccination or positive pregnancy test at day 21 after vaccine and age 16-54 years

v-safe: Day 1 local reactions in women, age 16-54 years

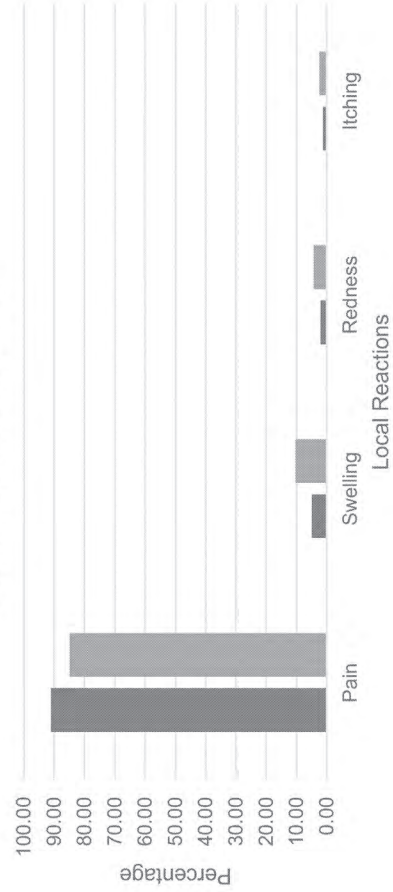
Pfizer-BioNTech Dose 1



Moderna Dose 1



Pfizer-BioNTech Dose 2

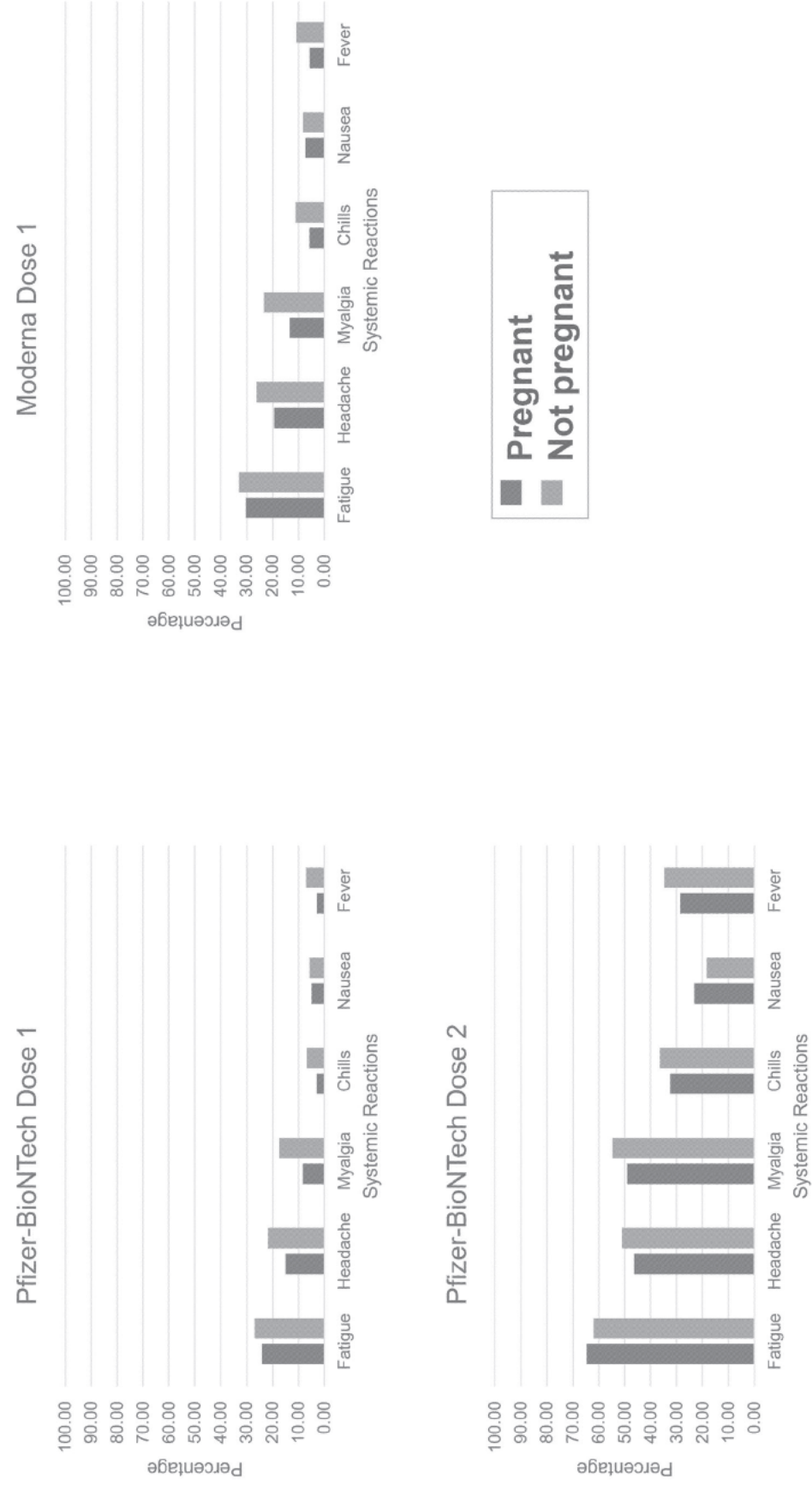


v-safe: Day 1 reactogenicity reported by pregnant women^a

	All		Pfizer-BioNTech		Pfizer-BioNTech		Moderna	
	Doses 1 & 2		Dose 1		Dose 2		Dose 1	
Completed Day 1 survey	N	%	N	%	N	%	N	%
All	7,147	100	3,662	100	1,446	100	2,707	100
Systemic Reactions								
Fatigue	2,511	35.1	880	24.0	936	64.7	821	30.3
Headache	1,694	23.7	546	14.9	669	46.3	528	19.5
Myalgia	1,329	18.6	301	8.2	710	49.1	359	13.3
Chills	723	10.1	105	2.9	470	32.5	157	5.8
Nausea	690	9.7	181	4.9	335	23.2	196	7.2
Fever	655	9.2	99	2.7	413	28.6	153	5.7
Fever ≥ 38C	123	1.7	8	0.2	96	6.6	19	0.7

^a pregnant at time of vaccination or positive pregnancy test at day 21 after vaccine and age 16-54 years

v-safe: Day 1 systemic reactions in women, age 16-54 years



Conclusions and further work

- Similar to previous report for all v-safe participants, pregnant women reported more reactogenicity after dose 2 of Pfizer-BioNTech vaccine
- Pain, fatigue and headache were the most common reported solicited adverse events after either vaccine
- Local and systemic adverse events reported with similar frequencies in pregnant and non-pregnant women
- Upcoming: Moderna dose 2 assessment, MMWR describing safety of COVID-19 vaccine in pregnancy

Backup Slides

v-safe: demographics, pregnant and non-pregnant women^a

	All - Pregnant		All – Non-pregnant	
	N	%	N	%
All	7,147	100	534,376	100
Age at 1 st vaccine dose (years)				
16-19	7	0.1	3,396	0.6
20-24	134	1.9	37,629	7.0
25-34	4,582	64.1	154,609	28.9
35-44	2,239	31.3	177,579	33.2
45-54	185	2.6	161,163	30.2

^a pregnant at time of vaccination or positive pregnancy test at day 21 after vaccine and age 16-54 years, completed day 1 survey

COVID-19 vaccine safety in pregnancy

Characteristics of COVID-19 vaccine pregnancy reports submitted to VAERS* (N=154)



Characteristic	
Maternal age in years, median (range)	16 (24–51)
Gestational age in weeks at time of vaccination when reported, median (range)	13 (2–38)
Trimester of pregnancy at time of vaccination	
First (0-13 weeks)	60/118 (50.8)
Second (14-27 weeks)	36/118 (30.5)
Third (28+ weeks)	22/118 (18.6)
Vaccine	
Pfizer-BioNTech	97 (62.9)
Moderna	56 (36.4)
Unreported	1 (0.6)

* Reports received and processed through Feb 16, 2021

Adverse events in pregnant women following COVID-19 vaccine reported to VAERS* (N=154)



* Reports received and processed through February 16, 2021

† The frequency of clinically recognized early pregnancy loss for women aged 20–30 years is 9–17%, and this rate increases sharply from 20% at age 35 years to 40% at age 40 years and 80% at age 45 years. Reference: ACOG Practice Bulletin No. 200: Early Pregnancy Loss. Obstet Gynecol. 2018;132(5):e197-e207.

Adverse events	n
Pregnancy/neonatal specific conditions	42
Spontaneous abortion/miscarriage [†]	29
Premature rupture of membranes	3
Fetal hydrops	2
Neonatal death in 22 w preterm birth	1
Premature delivery	1
Gestational diabetes	1
Vaginal bleeding	1
Stillbirth	1
Shortened cervix	1
Leakage amniotic fluid	1
Calcified placenta	1
Non-pregnancy specific adverse events (top 10)	112
Headache (31), fatigue (29), chills (21), pain in extremity (17), nausea (15), dizziness (14), pain (14), pyrexia (13), injection site pain (13), injection site erythema (10)	



COVID-19 vaccine safety update

Advisory Committee on Immunization Practices (ACIP)
March 1, 2021

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

DRAFT

Disclaimer

- 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 (CDC) or the U.S. Food and Drug Administration (FDA)
- Mention of a product or company name is for identification purposes only and does not constitute endorsement by the CDC or FDA

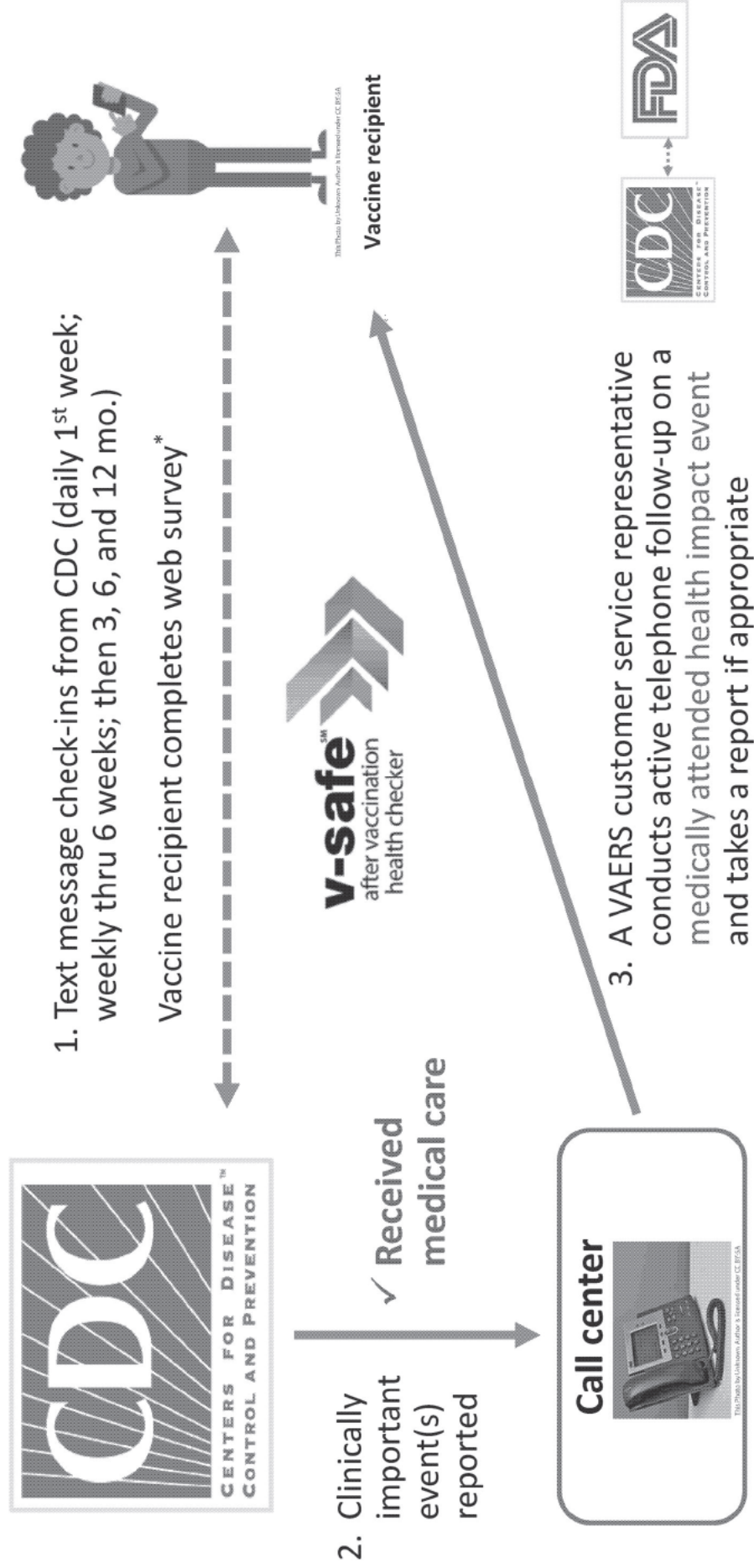
Topics

- V-safe update
- Vaccine Adverse Event Reporting System (VAERS) update
- Vaccine Safety Datalink (VSD) update
- COVID-19 vaccine safety in pregnancy



Use your smartphone to tell CDC about any side effects after getting the COVID-19 vaccine. You'll also get reminders if you need a second vaccine dose.

An illustration of a hand holding a smartphone. The screen of the phone shows the v-safe app interface, which includes the v-safe logo and some text. The background of the illustration is a dark gray chevron shape pointing to the right.



* Selected web surveys capture information on pregnancy status



Centers for Disease Control and Prevention



Early Release / Vol. 70

Morbidity and Mortality Weekly Report

February 19, 2021

First Month of COVID-19 Vaccine Safety Monitoring — United States,
December 14, 2020–January 13, 2021

Early Release

TABLE 2. Percentage of v-safe enrollees who completed at least one survey (N = 1,602,065) with local and systemic reactions reported for day 0–7 and for day 1 after receiving Pfizer-BioNTech and Moderna COVID-19 vaccines — v-safe,* United States, December 14, 2020–January 13, 2021

Local and systemic reaction	Percentage of v-safe enrollees reporting reactions			
	Both vaccines		Pfizer-BioNTech vaccine	
	Day 0–7	Dose 1, day 1	Dose 2, day 1	Dose 1, day 1
Injection site pain	70.9	72.9	79.3	78.1
Fatigue	33.5	21.9	53.5	25.1
Headache	29.5	17.5	43.4	19.9
Myalgia	22.9	14.7	47.2	18.3
Chills	11.6	5.5	30.6	8.4
Fever	11.4	5.8	29.2	8.2
Injection site swelling	10.8	6.2	8.6	12.6
Joint pain	10.4	5.3	23.5	7.3
Nausea	8.9	4.2	14.0	5.5

Abbreviation: COVID-19 = coronavirus disease 2019.

* <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafe.html>

* Gee J, Marquez P, Su J, et al. First Month of COVID-19 Vaccine Safety Monitoring — United States, December 14, 2020–January 13, 2021. MMWR Morb Mortal Wkly Rep. ePub: 19 February 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7008e3>

6

PSICOVID_00010274



Summary of v-safe data

	Pfizer- BioNTech	Moderna	Total
People receiving 1 or more doses in the United States*	28,374,410	26,738,383	55,220,364
Registrants completing at least 1 v-safe health check-in†	1,776,960	2,121,022	3,897,982
Pregnancies reported to v-safe	16,039	14,455	30,494

* COVID Data Tracker as of Feb 16, 2021 (107,571 doses with manufacturer not identified)

† V-safe data as of Feb 16, 2021, 5 am ET

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



VAERS

Vaccine Adverse Event Reporting System

co-managed by
CDC and FDA

<http://vaers.hhs.gov>

VAERS
Vaccine Adverse Event Reporting System
www.vaers.hhs.gov

About VAERS

Report an Adverse Event

VAERS Data

Resources

Submit Follow-Up Information

Have you had a reaction following a vaccination?

1. Contact your healthcare provider.
2. Report an Adverse Event using the VAERS online form or the new downloadable PDF. *New!*

Important: If you are experiencing a medical emergency, seek immediate assistance from a healthcare provider or call 9-1-1. CDC and FDA do not provide individual medical treatment, advice, or diagnosis. If you need individual medical or health care advice, consult a qualified healthcare provider.

¿Ha tenido una reacción después de recibir una vacuna?

1. Contacte a su proveedor de salud.
2. Reporte una reacción adversa utilizando el formulario de VAERS en línea o la nueva versión PDF descargable. *Nuevo!*

What is VAERS?


REPORT AN ADVERSE EVENT
Report significant adverse events after vaccination.


SEARCH VAERS DATA
Download VAERS Data and search the CDC WONDER database.


REVIEW RESOURCES
Find materials, publications, learning tools, and other resources.


SUBMIT FOLLOW-UP INFORMATION
Upload additional information related to VAERS report.


8

PSICOVID_00010276

Vaccine Adverse Event Reporting System (VAERS)

Strengths

- National data
- Rapidly detects safety signals
- Can detect rare adverse events
- Data available to public

Limitations

- Reporting bias
- Inconsistent data quality and completeness of information
- Lack of unvaccinated comparison group
- Not designed to assess causality

- VAERS accepts all reports from everyone regardless of the plausibility of the vaccine causing the event or the clinical seriousness of the event
- As a hypothesis generating system, VAERS identifies potential vaccine safety concerns that can be studied in more robust data systems

U.S. reports to VAERS after COVID-19 vaccines*

Vaccine	N	Non-serious AEs (%)	Serious AEs†§ (%)
Moderna	56,567	54,708 (97)	1,859 (3)
Pfizer-BioNTech	48,196	43,974 (91)	4,222 (9)
Total	104,763	98,682 (94)	6,081 (6)

* Total pre-processed reports received through Feb 16, 2021

† 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

§ Includes 456 reports of death following Moderna COVID-19 vaccine and 510 reports of death following Pfizer-BioNTech COVID-19 vaccine

Most commonly reported adverse events to VAERS after COVID-19 vaccines*

Pfizer-BioNTech COVID-19

Adverse event†	N (%)
Headache	2,322 (20.0)
Fatigue	1,801 (15.5)
Dizziness	1,659 (14.3)
Pyrexia	1,551 (13.4)
Chills	1,508 (13.0)
Nausea	1,482 (12.8)
Pain	1,464 (12.6)
SARS-COV-2 Test Positive	1,002 (8.6)
Injection Site Pain	997 (8.6)
Pain In Extremity	923 (8.0)

Moderna COVID-19 vaccine

Adverse event†	N (%)
Headache	1,353 (23.4)
Pyrexia	1,093 (18.9)
Chills	1,056 (18.3)
Pain	945 (16.3)
Fatigue	888 (15.4)
Nausea	884 (15.3)
Dizziness	792 (13.7)
Injection Site Pain	671 (11.6)
Pain In Extremity	576 (10.0)
Dyspnoea	487 (8.4)

No empirical Bayesian data mining alerts (EB05 ≥ 2) detected for any adverse event-COVID-19 vaccine pairs (most recent [Feb 11, 2021] weekly results)

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

Anaphylaxis following mRNA COVID-19 vaccines

JAMA Insights

Reports of Anaphylaxis After Receipt of mRNA COVID-19 Vaccines in the US—December 14, 2020-January 18, 2021

Tom T. Shimabukuro, MD, MPH, MBA; Matthew Cole, MPH; John R. Su, MD, PhD, MPH

Shimabukuro TT, Cole M, Su JR. Reports of Anaphylaxis After Receipt of mRNA COVID-19 Vaccines in the US-December 14, 2020-January 18, 2021. JAMA. 2021 Feb 12. doi: 10.1001/jama.2021.1967. Epub ahead of print.

Clinical Review & Education

Table. Characteristics of Reported Cases of Anaphylaxis Following Receipt of Pfizer-BioNTech (9 943 247 Doses) and Moderna (7 581 429 Doses) COVID-19 Vaccines—Vaccine Adverse Events Reporting System (VAERS), US, December 14, 2020-January 18, 2021

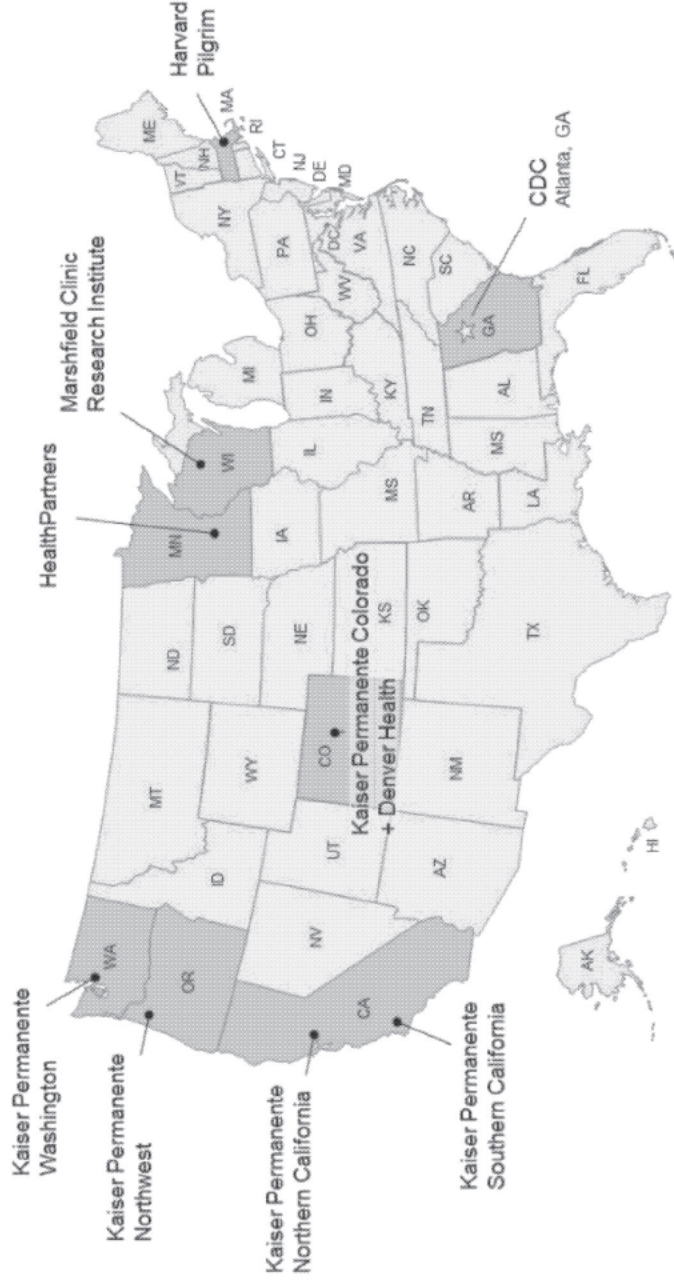
Characteristics	No. (%) of cases	
	Pfizer-BioNTech (n = 47)	Moderna (n = 19)
Age, median (range), y	39 (27–63) ^a	41 (24–63)
Female sex	44 (94)	19 (100)
Minutes to symptom onset, median (range)	10 (<1–1140 [19 h]) ^b	10 (1–45)
Symptom onset, min		
≤15	34 (76) ^b	16 (84)
≤30	40 (89) ^b	17 (89)
Reported history ^c		
Allergies or allergic reactions	36 (77)	16 (84)
Prior anaphylaxis	16 (34)	5 (26)
Vaccine dose		
First	37	17
Second	4	1
Unknown	6	1
Brighton Collaboration case definition level ^d		
1	21 (45)	10 (52)
2	23 (49)	8 (43)
3	3 (6)	1 (5)
Anaphylaxis reporting rate (cases per million doses administered)	4.7	2.5





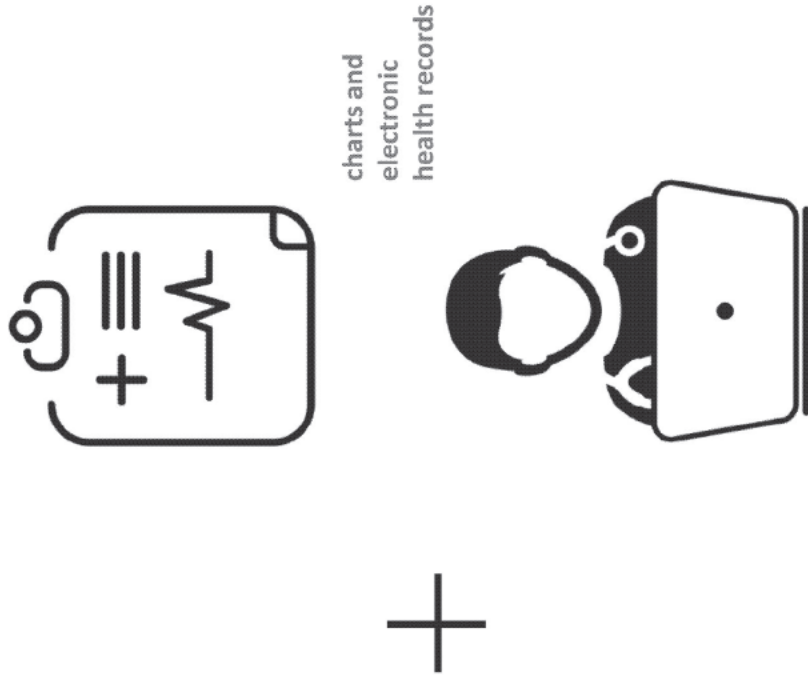
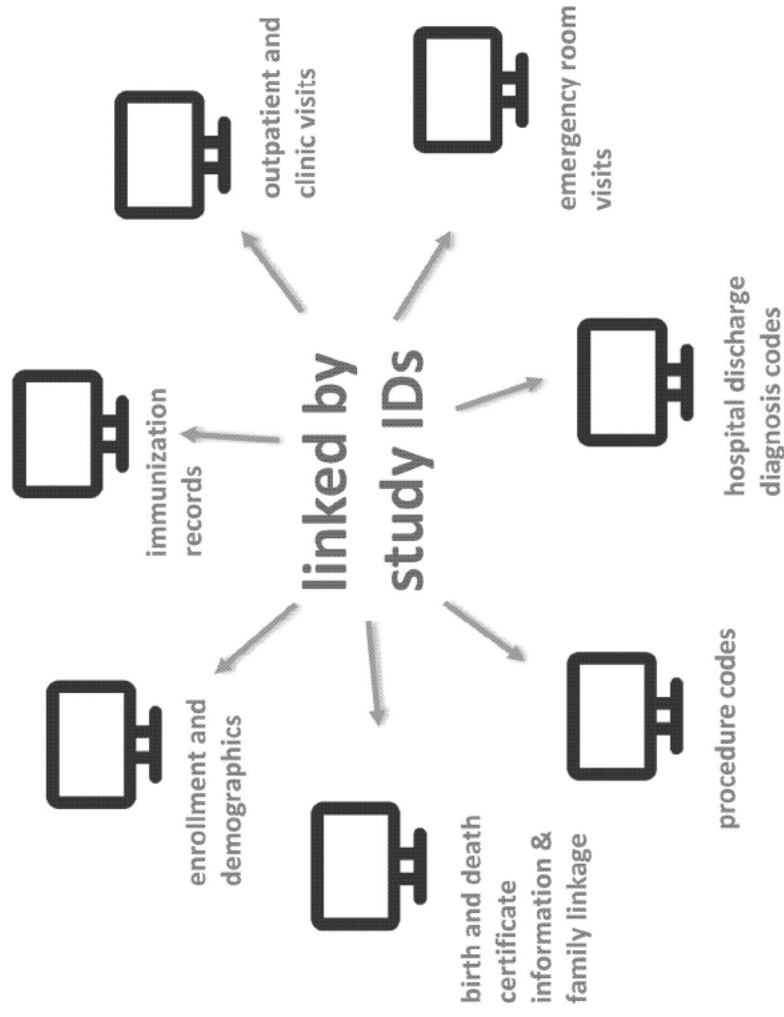
VSD

Vaccine Safety Datalink



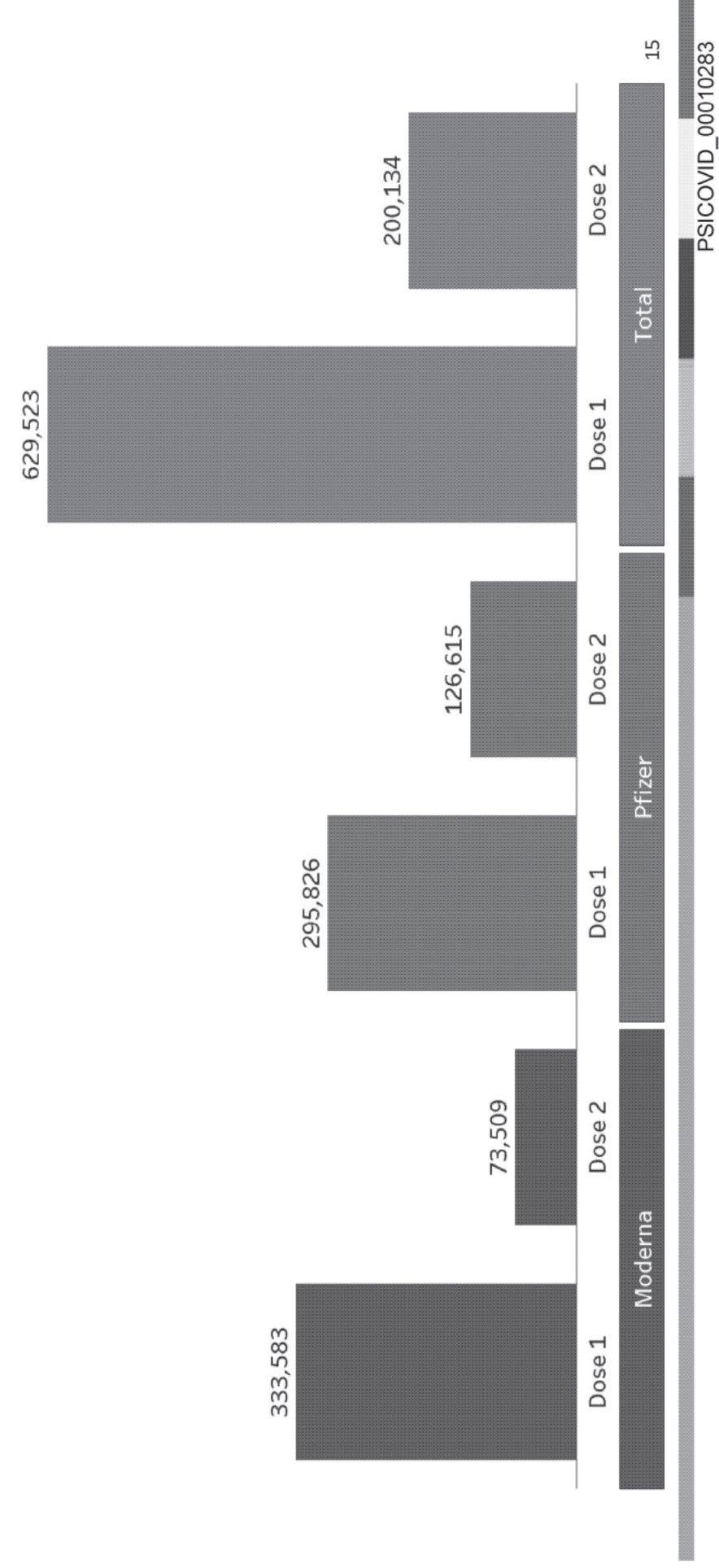
9 participating integrated healthcare organizations
data on over 12 million persons per year

Types of information in VSD

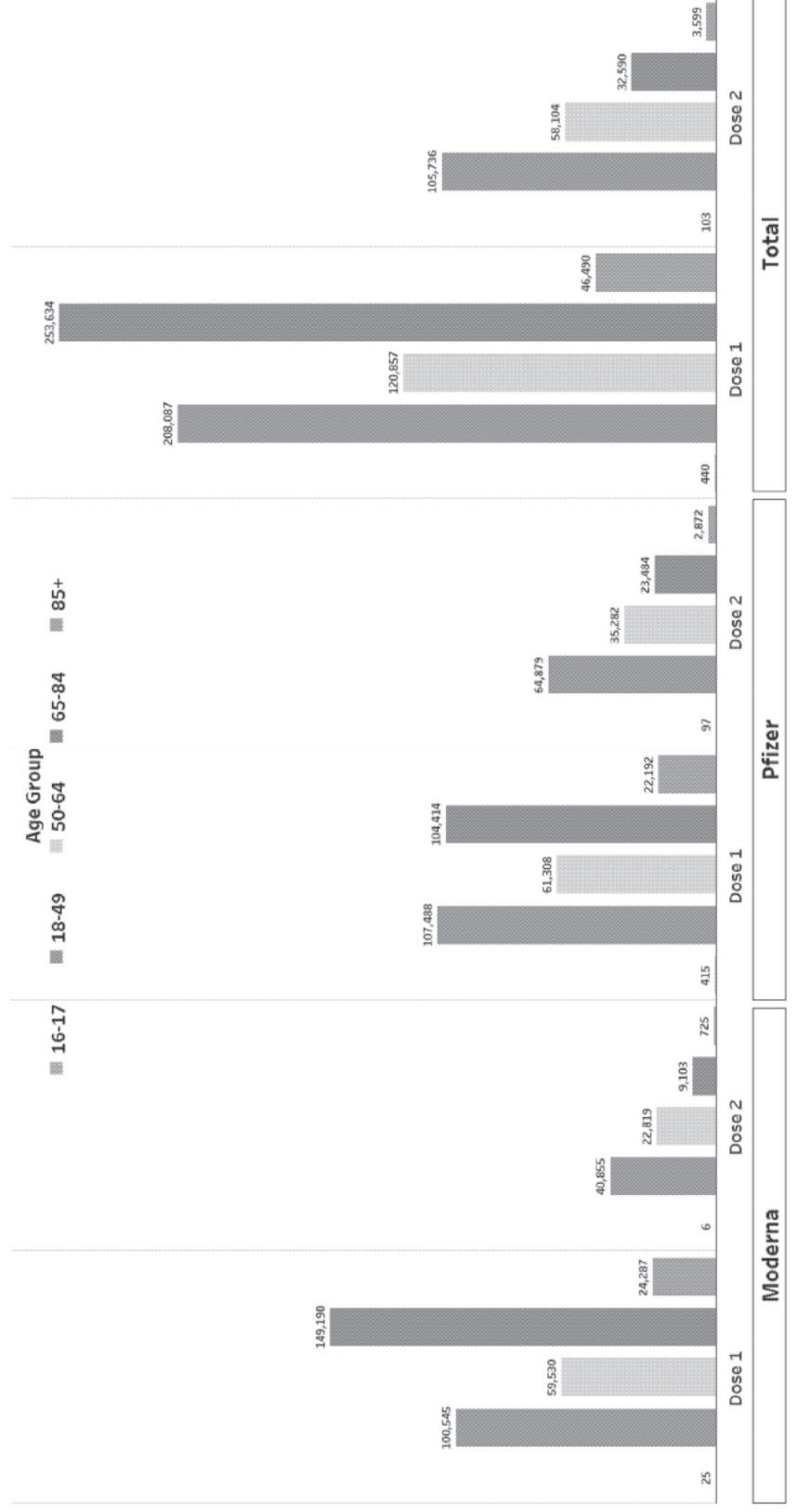


charts and
electronic
health records

VSD COVID-19 vaccine totals through Feb 13, 2021



VSD COVID-19 vaccine totals through Feb 13, 2021



VSD RCA outcomes for COVID-19 vaccines	Concurrent comparator	Risk interval	Events in vaccinated	Adjusted expected events in risk interval	Signal (Y/N)
Acute disseminated encephalomyelitis	Unvaccinated	1-21 days	0	0	N
Acute myocardial infarction	Unvaccinated	1-21 days	23	26.0	N
Acute respiratory distress syndrome	Unvaccinated	1-21 days	0	NA	NA
Anaphylaxis	Unvaccinated	0-1 days	20	NA	NA
Appendicitis	Unvaccinated	1-21 days	31	23.6	N
Bell's palsy	Unvaccinated	1-21 days	21	20.3	N
Convulsions / seizures	Unvaccinated	1-21 days	10	9.6	N
Disseminated intravascular coagulation	Unvaccinated	1-21 days	1	1.1	N
Encephalitis / myelitis / encephalomyelitis	Unvaccinated	1-21 days	1	.1	N
Guillain-Barré syndrome	Unvaccinated	1-21 days	1	.6	N
Thrombotic thrombocytopenic purpura	Unvaccinated	1-21 days	0	0	N
Immune thrombocytopenia	Unvaccinated	1-21 days	1	1	N
Kawasaki disease	Unvaccinated	1-21 days	0	0	N
MIS-C and MIS-A	Unvaccinated	NA	0	NA	NA
Myocarditis / pericarditis	Unvaccinated	1-21 days	2	2.1	N
Narcolepsy and cataplexy	Unvaccinated	NA	2	NA	NA
Stroke, hemorrhagic	Unvaccinated	1-21 days	8	10	N
Stroke, ischemic	Unvaccinated	1-21 days	41	38.8	N
Transverse myelitis	Unvaccinated	1-21 days	0	0	N
Venous thromboembolism	Unvaccinated	1-21 days	26	26.3	N
Pulmonary embolism (subset of VTE)	Unvaccinated	1-21 days	20	21.0	N

- Preliminary results of the VSD unvaccinated concurrent comparator analyses for COVID-19 vaccine safety – after either dose of any mRNA vaccine
- No signals as of February 13, 2021

VSD RCA outcomes for COVID-19 vaccines	Concurrent comparator	Risk interval	Events in Risk Interval	Adjusted expected events in risk interval	Signal (Y/N)
Acute myocardial infarction	Vaccinated	1-21 days	21	30.8	N
Appendicitis	Vaccinated	1-21 days	25	53.5	N
Bell's palsy	Vaccinated	1-21 days	17	23.1	N
Convulsions / seizures	Vaccinated	1-21 days	10	9.4	N
Disseminated intravascular coagulation	Vaccinated	1-21 days	1	0	N
Immune thrombocytopenia	Vaccinated	1-21 days	1	0	N
Myocarditis / pericarditis	Vaccinated	1-21 days	2	0	N
Narcolepsy and cataplexy	Vaccinated	NA	2	NA	NA
Stroke, hemorrhagic	Vaccinated	1-21 days	7	0	N
Stroke, ischemic	Vaccinated	1-21 days	37	43.5	N
Venous thromboembolism	Vaccinated	1-21 days	23	12.4	N
Pulmonary embolism (subset of VTE)	Vaccinated	1-21 days	19	0	N

- Preliminary results of the VSD sequential vaccinated concurrent comparator analyses for COVID-19 vaccine safety – after either dose of any mRNA vaccine
- Only outcomes with events in the risk interval are shown
- No signals as of February 13, 2021

VSD RCA next steps – next analyses

- For each pre-specified outcome the VSD will conduct:
 - Dose specific analyses
 - Product specific analyses
 - Analyses for 2 risk intervals 1-21 & 1-42 days
- The VSD will utilize historical comparators as an additional sequential analysis
 - General age comparable background rates
 - Rates following well care visits among those that received influenza vaccine in past 18 mo.
 - Planning to start in mid-March

COVID-19 vaccine safety in pregnancy

PSICOVID_0001028

Characteristics of COVID-19 vaccine pregnancy reports submitted to VAERS* (N=154)



Characteristic	
Maternal age in years, median (range)	33 (16–51)
Gestational age in weeks at time of vaccination when reported, median (range)	13 (2–38)
Trimester of pregnancy at time of vaccination	
First (0-13 weeks)	60/118 (51)
Second (14-27 weeks)	36/118 (31)
Third (28+ weeks)	22/118 (19)
Vaccine	
Pfizer-BioNTech	97 (63)
Moderna	56 (36)
Unreported	1 (0.6)

* Reports received and processed through Feb 16, 2021

Adverse events in pregnant women following COVID-19 vaccine reported to VAERS* (N=154)



* Reports received and processed through February 16, 2021

† The frequency of clinically recognized early pregnancy loss for women aged 20–30 years is 9–17%, and this rate increases sharply from 20% at age 35 years to 40% at age 40 years and 80% at age 45 years.

Reference: ACOG Practice Bulletin No.

200: Early Pregnancy Loss. Obstet Gynecol. 2018;132(5):e197–e207.

Adverse events	n
Pregnancy/neonatal specific conditions	42
Spontaneous abortion/miscarriage [†]	29
Premature rupture of membranes	3
Fetal hydrops	2
Neonatal death in 22 week preterm birth	1
Premature delivery	1
Gestational diabetes	1
Vaginal bleeding	1
Stillbirth	1
Shortened cervix	1
Leakage amniotic fluid	1
Calcified placenta	1
Non-pregnancy specific adverse events (top 10)	112
Headache (31), fatigue (29), chills (21), pain in extremity (17), nausea (15), dizziness (14), pain (14), pyrexia (13), injection site pain (13), injection site erythema (10)	



V-safe pregnancy registry

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

^a Must be registered in v-safe and have been pregnant at the time of COVID-19 vaccine receipt or within 30 days of vaccination

^b Phone surveys are supplemented with maternal and infant medical records



V-safe pregnancy registry enrollment^a

v-safe participants evaluated (N = 1,949)	
Enrolled	1,815
Not eligible ^b	103
Refused/declined ^c	31

^a Enrollment as of 2/19/2021 8:30am EST

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

^c 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

Other CDC COVID-19 maternal vaccination safety activities

- Vaccine Safety Datalink (VSD)
 - COVID-19 vaccination coverage in pregnancy
 - Fetal death study: miscarriage and stillbirth following COVID-19 vaccination
 - Safety in pregnancy study
 - Acute adverse events in pregnancy, longer term safety assessment of acute adverse events, pregnancy complications and birth outcomes, and infant follow up for the first year of life
- Clinical Immunization Safety Assessment (CISA) Project
 - Prospective observational cohort study
 - Adverse pregnancy and birth outcomes, serious adverse events, local and systemic reactogenicity, infant health outcomes for first 3 months of life

Closing thoughts on COVID-19 vaccine safety (Feb 2021)

- Just over 55 million COVID-19 vaccine doses administered in the United States (Feb 16)
- Reactogenicity profiles of mRNA vaccines in v-safe monitoring are consistent with what was observed in clinical trials
- Systemic and local reactions are most commonly reported to VAERS; anaphylaxis occurs following both vaccines, though rarely; no safety signals for serious adverse events in VAERS
- No safety signals among VSD Rapid Cycle Analysis pre-specified outcomes as of Feb 13
- Most reports to VAERS among pregnant women (73%) involved non-pregnancy specific adverse events (e.g., local and systemic reactions)
- Miscarriage was the most frequently reported pregnancy-specific adverse event to VAERS, but was below expected background rate
- Safety monitoring in pregnant women is ongoing/planned in v-safe, VSD, and CISA

Acknowledgments

We wish to acknowledge the contributions of investigators from the following organizations:

Centers for Disease Control and Prevention

COVID-19 Vaccine Task Force
COVID-19 Vaccine Task Force, Vaccine Safety Team
Immunization Safety Office
Division of Healthcare Quality Promotion
National Center on Birth Defects and Developmental Disabilities
Division of Reproductive Health
Vaccine Safety Datalink
Clinical Immunization Safety Assessment Project
V-safe Team

U.S. Food and Drug Administration

Office of Biostatistics and Epidemiology

Questions

PSICOVID_0001029

Message

From: Markowitz, Lauri (CDC/DDID/NCIRD/DVD) [REDACTED]
Sent: 2/26/2021 9:36:14 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]; Kuldorf, Martin [REDACTED]; Lee, Grace [REDACTED]; MacNeil, Jessica R (CDC) [REDACTED]; Markowitz, Lauri (CDC) [REDACTED]; Marquez, Paige L (CDC) [REDACTED]; Martin, Stacey (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]
Subject: [EXTERNAL] VaST - draft minutes and report from February 22 call (CONFIDENTIAL)
Attachments: 2021-02-22 VaST Meeting Minutes_DRAFT.docx; 2021-02-22 - VaST Report Data Table_DRAFT.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 VaST call this week. Let us know if there are any corrections.

Reminder - all VaST documents and communications are confidential.

There is no VaST call next Monday due to the planned ACIP meeting on February 28 and March 1. The next VaST call is March 8 at 1:30 – 3 pm ET.

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

VaST meeting notes

February 22, 2021

Confidential

DRAFT

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

Participants

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

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

CDC: Karen Broder, Geoff Calvert, Mark Delorey, Frank DeStefano, Kathleen Dooling, Julianne Gee, Tanya Hamburger, Rita Helfand, Susan Hiers, Amelia Jazwa, Shin Kim, Lauri Markowitz (CDC Co-lead), Paige L. Marquez, Stacey Martin, Dana Meaney Delman, Sarah Mbaeyi, Michael McNeil, Pedro Moro, Yi Mu, Tanya R. Myers, Titilope Oduyebo, Sara Oliver, Christine Olson, Eddie Shanley, David Shay, Tom Shimabukuro, Mark Sotir, John Su, Eric Weintraub, Melinda Wharton (CDC Co-lead), Jared Woo, Mardia Young

Technical SMEs: Steve Anderson, Richard Beigi, James Donahue, Bruce Fireman, Richard Forshee, Kristin Goddard, Kayla Hanson, Brenna Hughes, Denise Jamieson, Nicola Klein, Ned Lewis, Narayan Nair, Ousseny Zerbo

Agenda

- Administrative issues and announcements
- VAERS
- VSD
- Pregnancy focused session
 - v-safe
 - v-safety Pregnancy Registry
 - VAERS
- Dry run for ACIP meeting

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

- Reminders about COI and confidentiality
- Tentative dates for next ACIP meetings – February 28 and March 1
- Doses distributed: 75,204,965; Doses administered: 63,090,634 (last updated: February 21)
 - Pfizer-BioNTech: 32,232,422; Moderna: 30,747,615; Unknown: 110,597
 - First doses: 43,628,092; Second doses: 18,865,319

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

[PAGE * MERGEFORMAT]

VAERS – Dr. John Su (CDC)

Dr. Su gave an update from VAERS. There have been 19536 VAERS reports (Moderna: 7092 Pfizer-BioNTech: 12444), including 1287 reports of COVID-19 disease after vaccination and 980 death reports to VAERS. Of the death reports, 470 were from long term care facilities. Where known, the cause of death was often cardiovascular. Dr. Su will give an update on anaphylaxis at the next VaST meeting.

Questions and discussion

1. There was no disproportionality reporting to VAERS.
2. Were there deaths that occurred on the same day as vaccination? Any death occurring the same day after COVID-19 vaccination does not mean that death is related to anaphylaxis. There was further discussion of the death investigations and more will be presented at future VaST calls.

VSD – Dr. Nicky Klein (KPNC)

Dr. Klein presented data from the Vaccine Safety Datalink (VSD). To date, 5.8% of the VSD population has received at least one dose. About 200,000 have received a second dose. Of note, there was an increase in uptake in the 65-84 years age group (targeted). COVID-19 vaccine coverage by race was presented and appears to be diverse. Dr. Klein presented data analyzed through 2/13/21, including sequential analysis for the vaccinated and unvaccinated comparators. No concerns or signals have been identified to date. VSD will continue to monitor vaccine uptake by race, sex, and high-risk conditions.

Pregnancy focused session

Additional SMEs invited to join: Richard Beigi, Brenna Hughes, Denise Jamieson, Dana Meaney Delman, Titilope Oduyebo

Pregnancies in v-safe – Dr. Tanya Meyers (CDC)

Dr. Meyers presented on pregnancies in v-safe, including the basic demographics of pregnancies in v-safe, collected from 12/14/20 to 1/13/21 (N=10,507). For doses 1 and 2, recipients who identified as female were asked questions about pregnancy (Moderna dose 2 is not part of this data set). Among women aged 16 through 54 years, day 1 health outcomes and reactogenicity in those pregnant and not pregnant were similar. Similar to women not pregnant, among pregnant women, there was more reactogenicity after dose 2 than dose 1. Future reports will include a Moderna dose 2 assessment. An MMWR describing safety data for COVID-19 in pregnancy is planned.

Questions and discussion:

1. How was fever defined? Above 100.4° F.
2. Does the survey include a question on medication use? No.

v-safe Pregnancy Registry – Dr. Shin Kim (CDC)

Dr. Kim provided a detailed overview of the v-safe pregnancy registry and how data are received by the registry, building on Dr. Meyers' previous presentation. There are 1,815 enrolled out of 32,120 potential pregnancies in v-safe; the majority, 1491, received the Pfizer-BioNTech vaccine. Efforts to contact appropriate vaccinees are ongoing. Dr. Kim reviewed the registry participant characteristics enrolled as of 2/18/2021, and pregnancy outcomes. Age and race/ethnicity characteristics are driven primarily by the prioritization of healthcare workers to receive the vaccination in the first phase. Pregnancy and neonatal outcomes are all within background rates. The registry findings to date will be presented at the 3/1 ACIP meeting and the 2/26 VRBPAC meeting.

Questions and discussion

1. How is fever defined? Data are based on 38° C.
2. Which congenital anomalies have been reported? How were they defined? The registry will be able to confirm through medical chart abstraction; abstraction is ongoing.
3. Can miscarriage be reported by less than 12 weeks and 12-20 weeks? Yes, this can be done going forward.
4. Pregnancy and neonatal outcomes of interest are all within background rates. Were the background rate of congenital anomalies collected in a similar way or from the literature? These were from the literature.
5. What is the difference between 32,000 potential pregnancies in v-safe and the 1,000 that are enrolled in the registry? Outreach is ongoing.
6. Should there be there oversampling to obtain a more diverse population? The registry seeks to enroll all pregnant women.
7. For pregnancy loss, data should be presented by gestational age; important to look at loss before 12 weeks and also after 18 weeks.

VAERS - COVID-19 vaccine in pregnancy – Dr. John Su (CDC)

Dr. Su presented on the characteristics of COVID-19 vaccine pregnancy reports submitted to VAERS. There were 154 reports. Approximately half were in women in their first trimester when they were vaccinated; 2/3 of the reports were in women who received the Pfizer-BioNTech vaccine. Adverse events were broken down by pregnancy/neonatal specific conditions, such as spontaneous abortion or miscarriage, and symptoms not specific to pregnancy. Most reports were not specific to pregnancy.

Questions and discussion

1. A note was made to revise the maternal age median.

Review for ACIP meeting – Drs. Tom Shimabukuro (CDC) and Grace Lee (VaST)

Dr. Shimabukuro reviewed draft slides for the VRBPAC meeting on Friday 2/26 and the ACIP meeting on Monday 3/1. The slide presentation included information on v-safe, VAERS, VSD, safety and pregnancy updates and the recently published MMWR on the first month of COVID-10 vaccine safety monitoring. CISA update slides will be added. The core slides will be used for VRBPAC and feedback from the VaST call discussion will be incorporated.

Questions and discussion

1. Display slides with background rates for the pregnancy rates (side-by-side).
2. Highlight the slides from v-safe from overall group and pregnancy module, leading with those instead of the VAERS slides.
3. Consider deleting the phrase "fetal death study." It could be perceived as more alarming than intended. Could just specify miscarriage and stillbirth.

Combined Systems Safety Monitoring Report - DRAFT

February 22, 2021

Confidential

VaST meeting and comments:

The VaST session focused on COVID-19 vaccination during pregnancy. Three additional SMEs joined this session. There were also updates from VAERS, v-safe and VSD. Finally, in preparation for the March 1 ACIP meeting, there was a draft COVID-19 vaccine safety presentation. The ACIP presentation will provide brief updates from the basic safety monitoring systems, but focus mainly on data regarding COVID-19 vaccination during pregnancy.

The updates from the VAERS and v-safe did not raise any concerns.

There have been no concerns in VSD with >500K doses administered. For the VSD RCA, there was discussion about presentation of 95% CI and concern about perception of signals where none exist.

The data on maternal immunization were reassuring; VaST as well as the new SMEs who joined the call appreciated seeing the data. There will be broad interest in the data and it is important to present these to ACIP and to prepare an MMWR, as planned.

Regarding preparations for ACIP:

The vaccine in pregnancy data from v-safe and the v-safe registry are of interest and the ACIP presentation from VaST should focus on those rather than data from VAERS.

Data from v-safe should be presented along with the background rates, as was done in the presentation on the VaST call.

When VAERS data are presented, it should be emphasized that the FDA data mining has not raised any concerns. Discussion of serious vs non serious reports should be abbreviated.

When the VSD data are presented, it should be emphasized that there are no concerns identified to date; slides should be simplified as much as possible.

It would be helpful for the VaST co-chair to mention in the introduction what VaST has been reviewing and to briefly summarize the plans for incorporating additional maternal immunization SMEs into monthly sessions.

At future meetings, VaST would like to hear data on neurologic outcomes, including bell's palsy.

VaST discussed some of the data on deaths and what further information would be helpful to review. Some members would like to see additional data on deaths, specifically those occurring on the day of vaccination.

Safety systems are ready to start capturing safety data for a third COVID-19 vaccine.

Table 1. COVID-19 vaccine monitoring systems reviewed by the VaST – Pfizer BioNTech (recommended for use in persons age ≥ 16 years)

Vaccine Safety Program	Outcomes Monitored	Population Monitored	Pfizer BioNTech population captured	Analyses	Selected Results
Passive Surveillance					
Vaccine Adverse Event Reporting System (VAERS) (Data through 2/19/2021)	All health events, adverse events of special interest*	US population	32,232,422 total doses administered	Descriptive	12,444 processed reports overall 1,475 serious non-death reports 493 deaths 97 pregnancy reports
VA ADERS (Data through 2/5/2021)	All health events	VA employees and Veteran patients	749,490 doses administered	Descriptive	4,615 reports overall (98.9% sent to VAERS) 70 serious reports 29 reports of anaphylaxis
Indian Health Services (IHS)**	All health events, adverse events of special interest*				
Active Surveillance					
V-safe (Data through 2/13/2021)		Vaccinees who enroll	1,751,966 persons enrolled 15,543 pregnancies reported at time of vaccination	Descriptive	414 reports overall (all submitted to VAERS) 40 serious reports
V-safe Pregnancy Registry (Data through 2/19/2021)		Vaccinees who enroll	16,857 potential pregnancies	Descriptive	1,491 participants enrolled
Department of Veterans Affairs (VA) Active Surveillance System	Pre-specified health outcomes*	Veteran Patients			
Vaccine Safety Datalink (VSD)** (Data through 2/13/21)	Pre-specified health outcomes*		295,826 first doses administered; 126,615 second doses administered	Descriptive; Sequential analysis will be added when	Preliminary results of few VSD vaccinated and unvaccinated concurrent comparator analyses for COVID-19 vaccine safety. No signals as of February 13

				more data are available	
Defense Medical Surveillance System (DMSS)**	Pre-specified health outcomes*				
Centers for Medicare and Medicaid Services (CMS)**	Pre-specified health outcomes*				
BEST initiative**	Pre-specified health outcomes*				
Vaccine Trials (Manufacturer)					See GRADE tables https://www.cdc.gov/vaccines/acip/recs/grade/covid-19-pfizer-biontech-vaccine.html

*See Table 3. for the complete list of health outcomes

**Data are currently being processed and will be reported when received

Table 2. COVID-19 vaccine monitoring systems reviewed by the VaST – Moderna (recommended for use in persons age ≥ 18 years)

Vaccine Safety Program	Outcomes Monitored	Population Monitored	Moderna population captured	Analyses	Selected Results
Passive Surveillance					
Vaccine Adverse Event Reporting System (VAERS) (Data through 2/19/2021)	All health events, adverse events of special interest*	US population	30,747,615 total doses administered	Descriptive	7,092 processed reports overall 1,215 serious non-death reports 478 deaths 56 pregnancy reports
VA ADERS (Data through 2/5/2021)	All health events	VA employees and Veteran patients	817,520 doses administered	Descriptive	12,161 reports overall (98.5% sent to VAERS)* 97 serious reports 18 reports of anaphylaxis
Indian Health Services (IHS)**	All health events, adverse events of special interest*				
Active Surveillance					
V-safe (Data through 2/13/2021)		Vaccinees who enroll	2,075,806 persons enrolled 13,688 pregnancies reported at time of vaccination	Descriptive	41 reports overall 16 serious reports
V-safe Pregnancy Registry (Data through 2/19/2021)		Vaccinees who enroll	15,263 potential pregnancies	Descriptive	324 participants enrolled
Department of Veterans Affairs (VA) Active Surveillance System	Pre-specified health outcomes*	Veteran Patients			
Vaccine Safety Datalink (VSD)** (Data through 2/13/2021)	Pre-specified health outcomes*		333,583 first doses administered; 73,509 second doses administered	Descriptive; Sequential analysis will be added when	Preliminary results of VSD few vaccinated and unvaccinated concurrent comparator analyses for COVID-19 vaccine safety. No signals as of February 13

Table 3. Health systems and pre-specified health outcomes

	VAERS	VSD	VA*	DMSS*	CMS*	BEST*
Acute disseminated encephalomyelitis (ADEM)	X ^{1,2}	X	X			
Acute myocardial infarction	X	X	X		X	X
Anaphylaxis	X	X	X		X	X
Appendicitis	X	X	X		X	X
Acute respiratory distress syndrome (ARDS)		X	X			
Arthritis and arthralgia (not osteoarthritis or traumatic arthritis)	X ¹	X				
Ataxia	X ^{1,2}					
Autoimmune disease	X ¹					
Bell's palsy	X	X	X		X	X
Chronic inflammatory demyelinating polyneuropathy (CIDP)	X ^{1,2}					
COVID-19	X					
Death	X					
Disseminated intravascular coagulation (DIC)	X	X	X		X	X
Encephalitis	X	X	X			
Encephalomyelitis	X ^{1,2}	X	X		X	X
Encephalopathy	X ^{1,2}	X	X			
Guillain-Barré syndrome (GBS)	X	X	X		X	X
Immune thrombocytopenic purpura (ITP)		X	X		X	X
Kawasaki disease	X	X				X
Meningitis	X ^{1,2}	X	X			
Meningoencephalitis	X ^{1,2}	X	X			
Multiple sclerosis (MS)	X ^{1,2}					
Multisystem Inflammatory Syndrome in Adults (MIS-A)	X	X ³	X		X	X
Multisystem Inflammatory Syndrome in Children (MIS-C)	X	X ³				X
Myelitis	X ^{1,2}	X	X			
Myocarditis / pericarditis	X	X	X		X	X
Narcolepsy / cataplexy	X	X	X		X	X ⁴
Non-anaphylactic allergic reactions	X ¹					

Optic neuritis (ON)	X ^{1,2}					
Seizures / convulsions (convulsion is now an LLT under PT seizure)	X	X				X
Stroke	X	X			X	X
Thrombocytopenia	X					
Transverse myelitis (TM)	X	X			X	X
Vaccination during pregnancy/adverse pregnancy outcomes	X					X
Venous thromboembolism (VTE)	X	X				-
Pulmonary embolism	-	-			X	X
Deep vein thrombosis	-	-			X	X

¹Health outcomes are counted, but adverse event reports are not abstracted

²Diagnoses are grouped and reported as "Other clinically serious neurologic AEs" in VAERS

³Health outcomes are counted, and no sequential analysis is conducted

⁴Only includes narcolepsy

*TBD

Message

From: Markowitz, Lauri (CDC/DDID/NCIRD/DVD) [REDACTED]
Sent: 3/1/2021 2:08:00 AM
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]; Kuldorf, Martin [REDACTED]; Lee, Grace [REDACTED]; MacNeil, Jessica R (CDC) [REDACTED]; Markowitz, Lauri (CDC) [REDACTED]; Marquez, Paige L (CDC) [REDACTED]; Martin, Stacey (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]
Subject: [EXTERNAL] Vaccine safety slides for March 1st ACIP meeting and key messages – confidential for now
Attachments: ACIP_VaxSafety_Shimabukuro_3-1-2021.pdf; ACIP 03-01-2021_Lee VaST Intro Final.pdf; ACIP 03-01-2021_Lee VaST conclusions Final.pdf; Key Messages_VRBPAAC ACIP_Feb 2021.pdf

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 three presentations for the vaccine safety session tomorrow at ACIP. These will be posted on the ACIP website tomorrow but are confidential for now.

In addition, we are sending the key messages written by the CDC Vaccine Evaluation Communications Team related to the CDC vaccine safety presentation (made at VRBPAC last week and at ACIP tomorrow).

As a reminder (from VaST documents):

"VaST members may be approached by the media. Members should have CDC approval to speak as a VaST member on ACIP or VaST matters. All information and discussions within the VaST, not presented at an open ACIP meeting, are confidential.

Members who receive requests for information from the press about VaST or ACIP should forward these to the ACIP secretariat and the VaST co-chairs. The ACIP secretariat or co-chairs will communicate with the press regarding the procedures and activities of VaST. If deemed appropriate, the secretariat may refer the press to a VaST member after gaining approval from that member. See the <https://www.cdc.gov/vaccines/acip/committee/downloads/Policies-Procedures-508.pdf> for additional guidance on interaction with the media."

Lauri Markowitz and Melinda Wharton

Lauri Markowitz, MD

PSICOVID_00010377

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



COVID-19 vaccine safety update

**Advisory Committee on Immunization Practices (ACIP)
March 1, 2021**

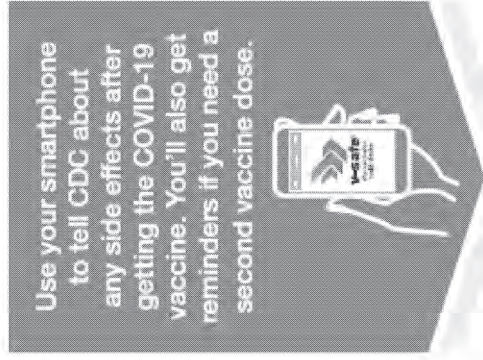
**Tom Shimabukuro, MD, MPH, MBA
CDC COVID-19 Vaccine Task Force
Vaccine Safety Team**

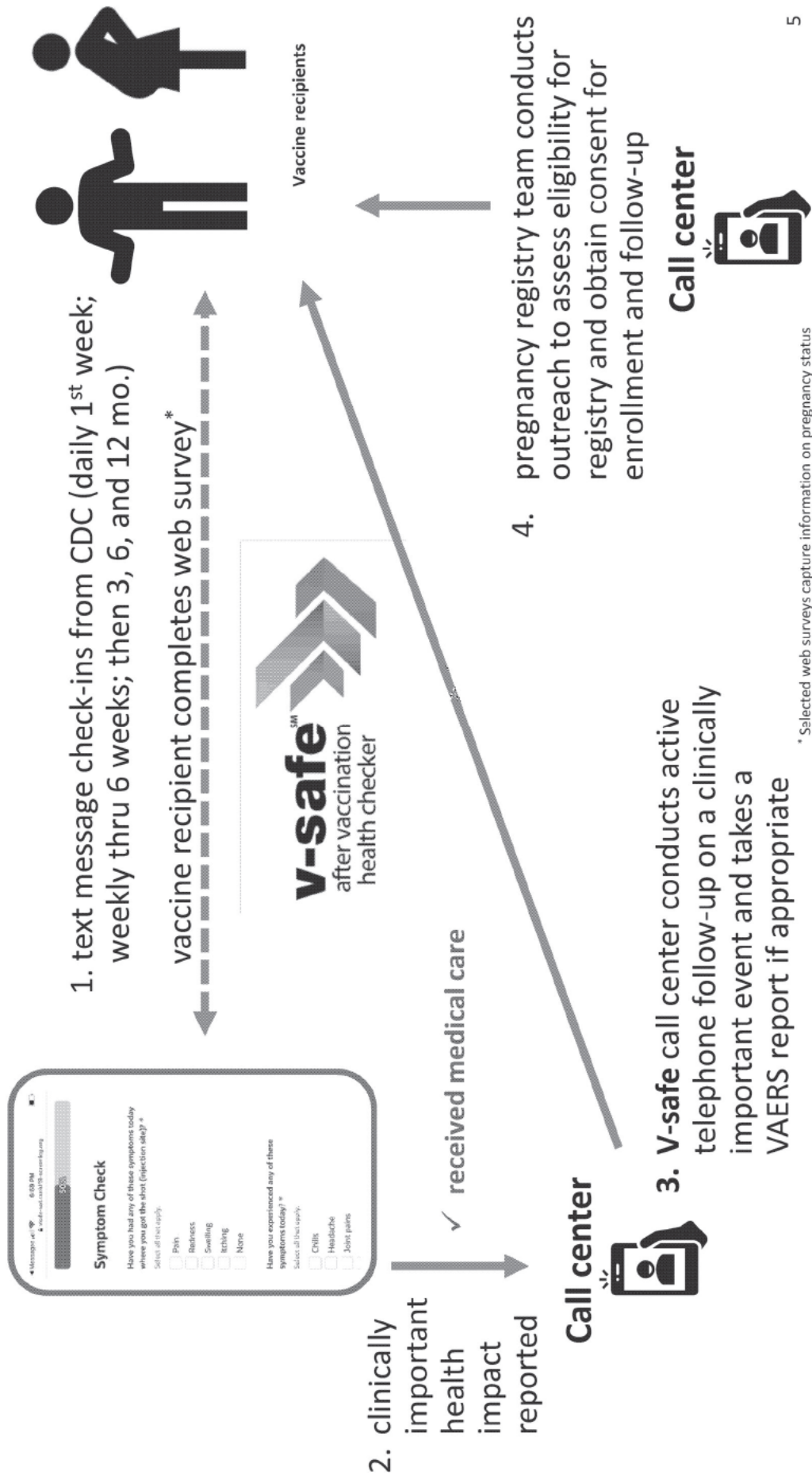
Disclaimer

- 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 (CDC) or the U.S. Food and Drug Administration (FDA).
- Mention of a product or company name is for identification purposes only and does not constitute endorsement by CDC or FDA.

Topics

- V-safe update
- Vaccine Adverse Event Reporting System (VAERS) update
- Vaccine Safety Datalink (VSD) update
- Clinical Immunization Safety Assessment (CISA) Project update
- COVID-19 vaccine safety in pregnancy





* Selected web surveys capture information on pregnancy status



Summary of v-safe data as of February 16, 2021

	Pfizer- BioNTech	Moderna	Total
People receiving 1 or more doses in the United States*	28,374,410	26,738,383	55,220,364
Registrants completing at least 1 v-safe health check-in	1,776,960	2,121,022	3,897,982
Pregnancies reported to v-safe†	16,039	14,455	30,494

* COVID Data Tracker as of Feb 16, 2021 (107,571 doses with manufacturer not identified)

† Self-reported during a v-safe health check-in



Centers for Disease Control and Prevention



Early Release / Vol. 70

Morbidity and Mortality Weekly Report
February 19, 2021

First Month of COVID-19 Vaccine Safety Monitoring — United States,
December 14, 2020–January 13, 2021

Early Release

TABLE 2. Percentage of v-safe enrollees who completed at least one survey (N = 1,602,065) with local and systemic reactions reported for day 0–7 and for day 1 after receiving Pfizer-BioNTech and Moderna COVID-19 vaccines — v-safe,* United States, December 14, 2020–January 13, 2021

Local and systemic reaction	Percentage of v-safe enrollees reporting reactions			
	Both vaccines		Pfizer-BioNTech vaccine	
	Day 0–7		Dose 1, day 1	Dose 2, day 1
Injection site pain	70.9	72.9	79.3	78.1
Fatigue	33.5	21.9	53.5	25.1
Headache	29.5	17.5	43.4	19.9
Myalgia	22.9	14.7	47.2	18.3
Chills	11.6	5.5	30.6	8.4
Fever	11.4	5.8	29.2	8.2
Injection site swelling	10.8	6.2	8.6	12.6
Joint pain	10.4	5.3	23.5	7.3
Nausea	8.9	4.2	14.0	5.5

Abbreviation: COVID-19 = coronavirus disease 2019.

* <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafe.html>



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Early Release / Vol. 70

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* <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafe.html>

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



VAERS

Vaccine Adverse Event Reporting System

co-managed by
CDC and FDA

<http://vaers.hhs.gov>

The screenshot shows the VAERS Vaccine Adverse Event Reporting System homepage. At the top, the VAERS logo is followed by the text "Vaccine Adverse Event Reporting System" and the URL "www.vaers.hhs.gov". Below this is a navigation bar with links: "About VAERS", "Report an Adverse Event", "VAERS Data", "Resources", and "Submit Follow-Up Information". The main content area is divided into several sections. On the left, there is a section titled "Have you had a reaction following a vaccination?" with two numbered steps: "1. Contact your healthcare provider." and "2. Report an Adverse Event using the VAERS online form or the new downloadable PDF. *New!*". Below this is an "Important" note: "If you are experiencing a medical emergency, seek immediate assistance from a healthcare provider or call 9-1-1. CDC and FDA do not provide individual medical treatment, advice, or diagnosis. If you need individual medical or health care advice, consult a qualified healthcare provider." To the right of this is a large image of a family (a man, a woman, and two children) with the text "What is VAERS?". Below the family image is a section titled "¿Ha tenido una reacción después de recibir una vacuna?" with two numbered steps: "1. Contacte a su proveedor de salud" and "2. Reporte una reacción adversa utilizando el formulario de VAERS en línea o la nueva versión PDF descargable. *Nuevo!*". On the far right, there are four smaller sections: "REPORT AN ADVERSE EVENT" (Report significant adverse events after vaccination), "SEARCH VAERS DATA" (Download VAERS Data and search the CDC WONDER database), "REVIEW RESOURCES" (Find materials, publications, learning tools, and other resources), and "SUBMIT FOLLOW-UP INFORMATION" (Upload additional information related to VAERS reports).

Vaccine Adverse Event Reporting System (VAERS)

Strengths

- National data
- Rapidly detects safety signals
- Can detect rare adverse events
- Data available to public

Limitations

- Reporting bias
- Inconsistent data quality and completeness of information
- Lack of unvaccinated comparison group
- Not designed to assess causality

- VAERS accepts all reports from everyone regardless of the plausibility of the vaccine causing the event or the clinical seriousness of the event
- As a hypothesis-generating system, VAERS identifies potential vaccine safety concerns that can be studied in more robust data systems

U.S. reports to VAERS after COVID-19 vaccines through February 16, 2021*

Vaccine	N	Non-serious AEs (%)	Serious AEs ^{†§} (%)
Moderna	56,567	54,708 (97)	1,859 (3)
Pfizer-BioNTech	48,196	43,974 (91)	4,222 (9)
Total	104,763	98,682 (94)	6,081 (6)

* Total pre-processed reports (reports received and classified as serious or non-serious)

[†] 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 commonly reported serious adverse events include: death (456 reports of death following Moderna vaccine and 510 following Pfizer-BioNTech vaccine), dyspnoea, pyrexia, SARS-CoV-2 test negative, nausea, headache, dizziness, fatigue, asthenia, pain

Most commonly reported adverse events to VAERS after COVID-19 vaccines through February 16, 2021*

Pfizer-BioNTech

Adverse event [†]	N (%)
Headache	2,322 (20.0)
Fatigue	1,801 (15.5)
Dizziness	1,659 (14.3)
Pyrexia	1,551 (13.4)
Chills	1,508 (13.0)
Nausea	1,482 (12.8)
Pain	1,464 (12.6)
SARS-CoV-2 Test Positive	1,002 (8.6)
Injection Site Pain	997 (8.6)
Pain in Extremity	923 (8.0)

Moderna

Adverse event [†]	N (%)
Headache	1,353 (23.4)
Pyrexia	1,093 (18.9)
Chills	1,056 (18.3)
Pain	945 (16.3)
Fatigue	888 (15.4)
Nausea	884 (15.3)
Dizziness	792 (13.7)
Injection Site Pain	671 (11.6)
Pain in Extremity	576 (10.0)
Dyspnoea	487 (8.4)

- No empirical Bayesian data mining alerts (EB05 ≥2) detected for any adverse event-COVID-19 vaccine pairs (most recent weekly results)

* For reports received and processed (coded, redacted, and quality assurance performed)
[†]Adverse events are not mutually exclusive

Anaphylaxis following mRNA COVID-19 vaccines

JAMA Insights

Reports of Anaphylaxis After Receipt of mRNA COVID-19 Vaccines in the US—December 14, 2020-January 18, 2021

Tom T. Shimabukuro, MD, MPH, MBA; Matthew Cole, MPH; John R. Su, MD, PhD, MPH

Shimabukuro TT, Cole M, Su JR. Reports of Anaphylaxis After Receipt of mRNA COVID-19 Vaccines in the US—December 14, 2020-January 18, 2021. JAMA. 2021 Feb 12. doi: 10.1001/jama.2021.1967. Epub ahead of print.

Clinical Review & Education

Pfizer-BioNTech Moderna

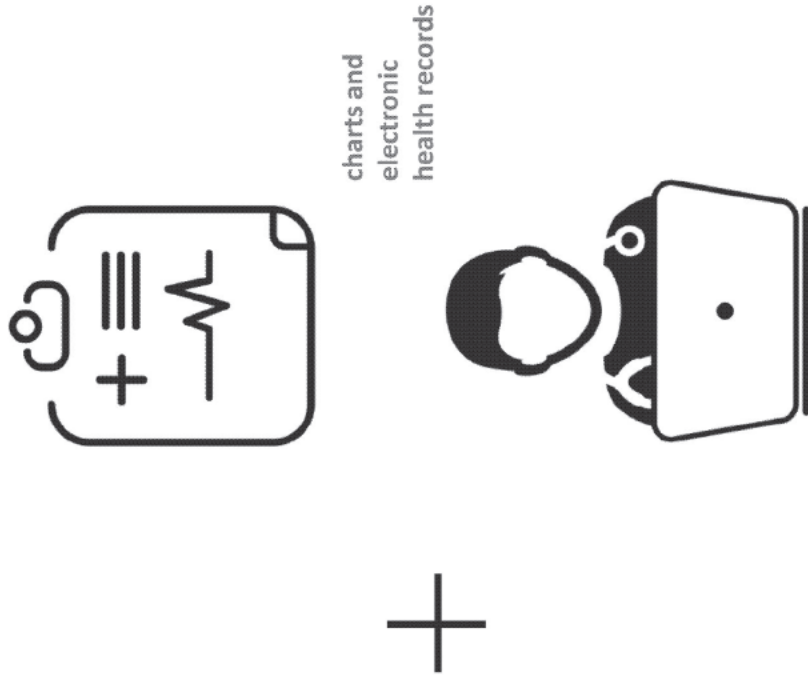
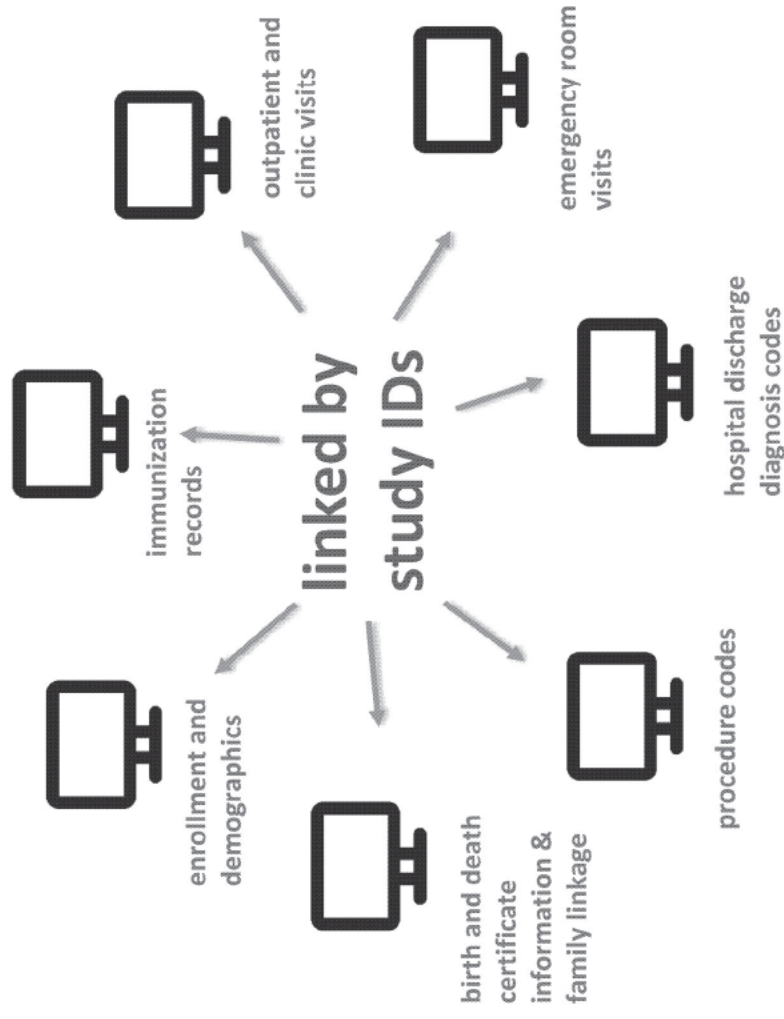
Anaphylaxis reporting rate (cases per million doses administered)	4.7	2.5
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Table. Characteristics of Reported Cases of Anaphylaxis Following Receipt of Pfizer-BioNTech (9 943 247 Doses) and Moderna (7 581 429 Doses) COVID-19 Vaccines—Vaccine Adverse Events Reporting System (VAERS), US, December 14, 2020-January 18, 2021

Characteristics	No. (%) of cases Pfizer-BioNTech (n = 47)	Moderna (n = 19)
Age, median (range), y	39 (27-63) ^a	41 (24-63)
Female sex	44 (94)	19 (100)
Minutes to symptom onset, median (range)	10 (<1-1140 [19 n]) ^a	10 (1-45)
Symptom onset, min		
≤15	34 (76) ^b	16 (84)
≤30	40 (89) ^b	17 (89)
Reported history ^c		
Allergies or allergic reactions	36 (77)	16 (84)
Prior anaphylaxis	16 (34)	5 (26)
Vaccine dose		
First	37	17
Second	4	1
Unknown	6	1
Brighton Collaboration case definition level ^d		
1	21 (45)	10 (52)
2	23 (49)	8 (43)
3	3 (6)	1 (5)
Anaphylaxis reporting rate (cases per million doses administered)	4.7	2.5



Types of information in VSD



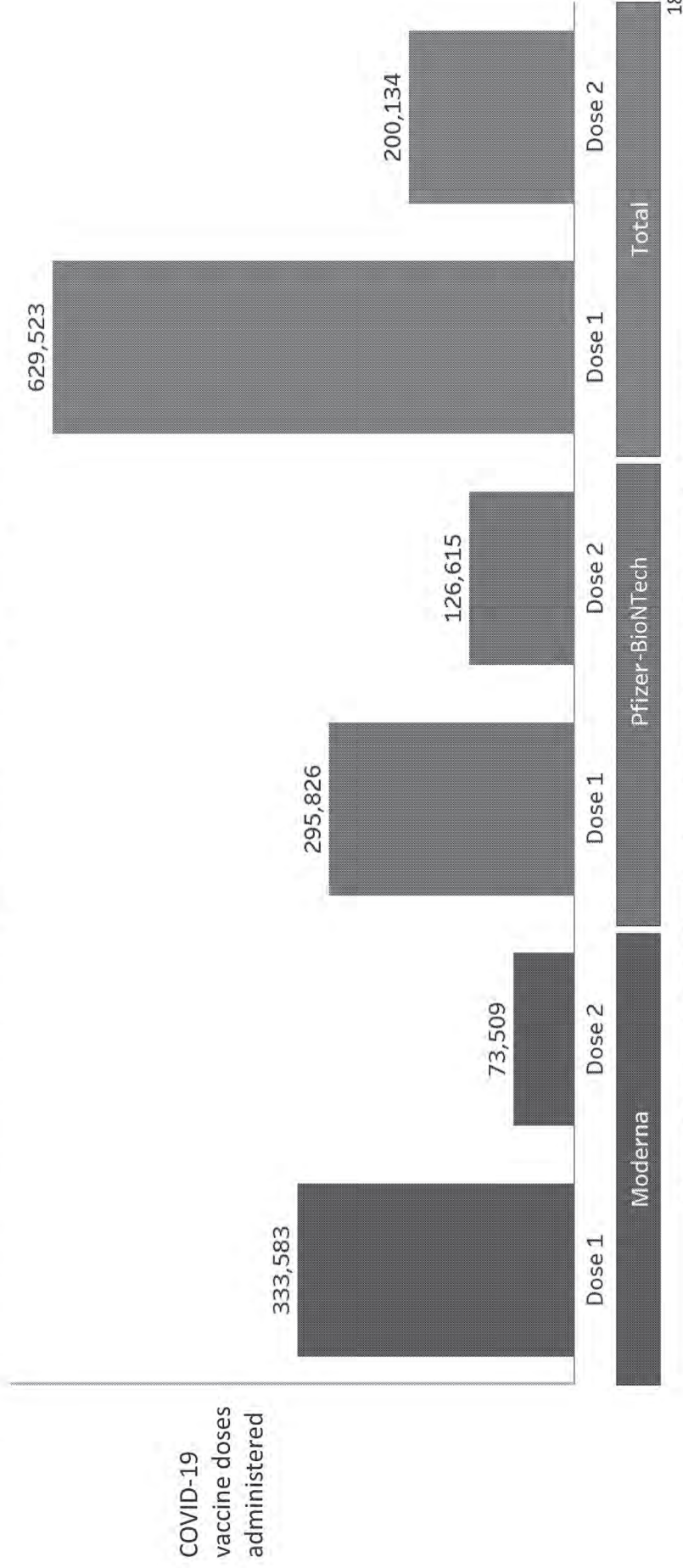
VSD Rapid Cycle Analysis (RCA) for COVID-19 vaccines

- Data are refreshed weekly
- Outcomes monitored are pre-specified (i.e., identified in advance)
- Includes methods to adjust for sequential testing
- A surveillance activity, not the same as an epidemiologic study
- Designed to detect statistically significant associations and statistical signals (values above specified statistical thresholds)
- When a statistically significant association or signal occurs, assessment involves a series of checks and evaluations
- Chart-confirmation of diagnoses to confirm or exclude cases as true incident cases is a key part of statistical signal assessment

VSD RCA for COVID-19 vaccines

- Analyses
 - Unvaccinated concurrent comparators (currently being conducted)
 - Vaccinated concurrent comparators (currently being conducted)
 - Self-controlled risk interval (planned)
 - Historical comparators (planned)

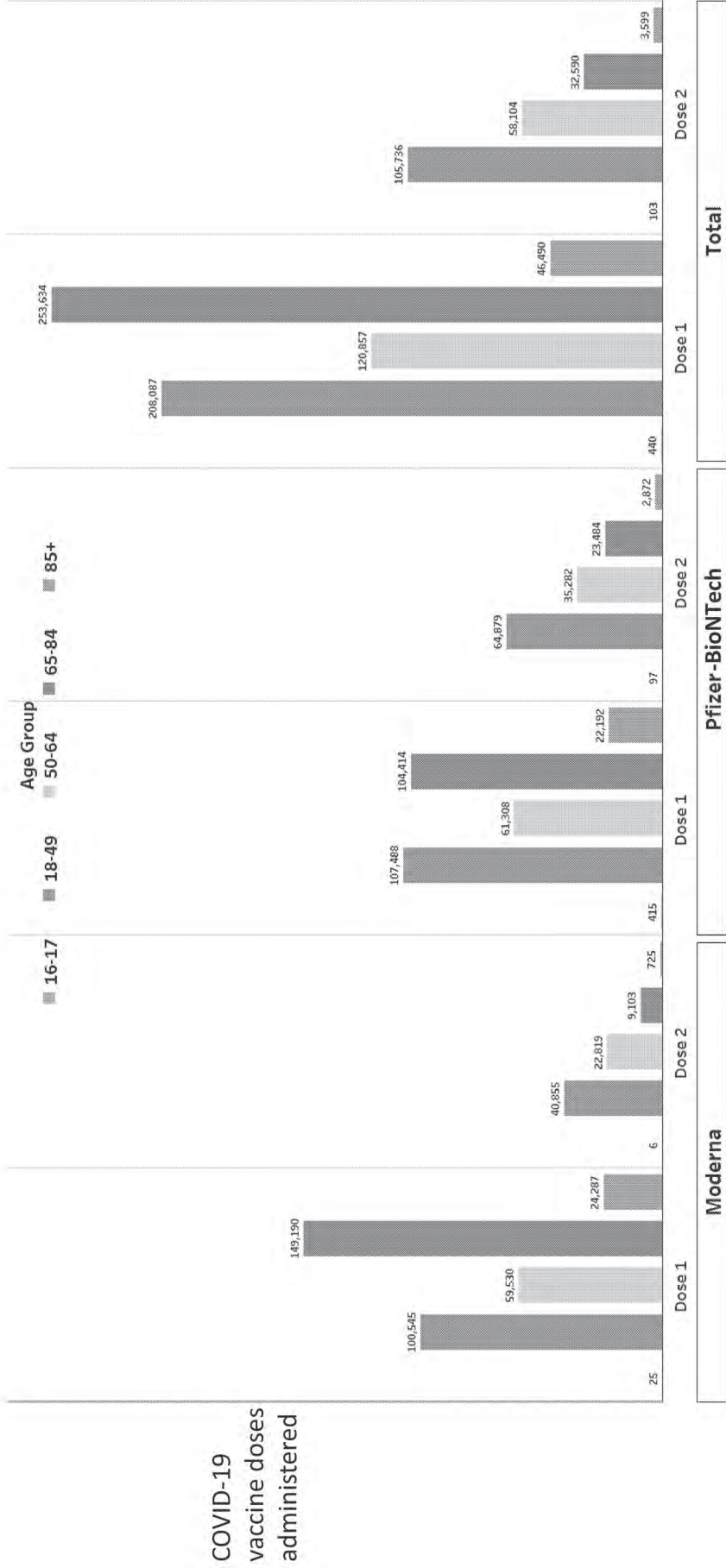
VSD COVID-19 vaccine doses administered by manufacturer through February 13, 2021*



* Source: VSD participating integrated healthcare organizations; total includes a small number of unknown vaccine type

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VSD COVID-19 vaccine doses administered by manufacturer, age group, and dose number through February 13, 2021*



* Source: VSD participating integrated healthcare organizations; total includes a small number of unknown vaccine type

Preliminary results of the VSD **unvaccinated concurrent comparator** analysis for COVID-19 vaccine safety after either dose of any mRNA vaccine as of February 13, 2021

VSD Rapid Cycle Analysis prespecified outcomes for COVID-19 vaccines	Concurrent comparator analysis	Risk interval	Events in vaccinated	Adjusted expected events in risk interval
Acute disseminated encephalomyelitis	Unvaccinated	1-21 days	0	0
Acute myocardial infarction	Unvaccinated	1-21 days	23	26.0
Acute respiratory distress syndrome	Unvaccinated	N/A	0	N/A
Anaphylaxis	Unvaccinated	0-1 days	20	N/A
Appendicitis	Unvaccinated	1-21 days	31	23.6
Bell's palsy	Unvaccinated	1-21 days	21	20.3
Convulsions/seizures	Unvaccinated	1-21 days	10	9.6
Disseminated intravascular coagulation	Unvaccinated	1-21 days	1	1.1
Encephalitis/myelitis/encephalomyelitis	Unvaccinated	1-21 days	1	.1
Guillain-Barré syndrome	Unvaccinated	1-21 days	1	.6
Thrombotic thrombocytopenic purpura	Unvaccinated	1-21 days	0	0
Immune thrombocytopenia	Unvaccinated	1-21 days	1	1
Kawasaki disease	Unvaccinated	1-21 days	0	0
MIS-C and MIS-A	Unvaccinated	N/A	0	N/A
Myocarditis/pericarditis	Unvaccinated	1-21 days	2	2.1
Narcolepsy and cataplexy	Unvaccinated	N/A	2	N/A
Stroke, hemorrhagic	Unvaccinated	1-21 days	8	10
Stroke, ischemic	Unvaccinated	1-21 days	41	38.8
Transverse myelitis	Unvaccinated	1-21 days	0	0
Venous thromboembolism	Unvaccinated	1-21 days	26	26.3
Pulmonary embolism (subset of VTE)	Unvaccinated	1-21 days	20	21.0

- No statistically significant increased risks detected for any prespecified outcomes

Preliminary results of the VSD sequential vaccinated concurrent comparator analysis for COVID-19 vaccine safety after either dose of any mRNA vaccine as of February 13, 2021

- No statistical signals detected

VSD Rapid Cycle Analysis prespecified outcomes for COVID-19 vaccines	Concurrent comparator analysis	Risk interval	Events in risk interval	Adjusted expected events in risk interval	Statistical signal (Y/N)
Acute myocardial infarction	Vaccinated	1-21 days	21	30.8	N
Appendicitis	Vaccinated	1-21 days	25	53.5	N
Bell's palsy	Vaccinated	1-21 days	17	23.1	N
Convulsions/seizures	Vaccinated	1-21 days	10	9.4	N
Disseminated intravascular coagulation	Vaccinated	1-21 days	1	0	N
Immune thrombocytopenia	Vaccinated	1-21 days	1	0	N
Myocarditis/pericarditis	Vaccinated	1-21 days	2	0	N
Stroke, hemorrhagic	Vaccinated	1-21 days	7	0	N
Stroke, ischemic	Vaccinated	1-21 days	37	43.5	N
Venous thromboembolism	Vaccinated	1-21 days	23	12.4	N
Pulmonary embolism (subset of VTE)	Vaccinated	1-21 days	19	0	N

* Only includes outcomes with events in the risk window

VSD RCA next steps – next analyses

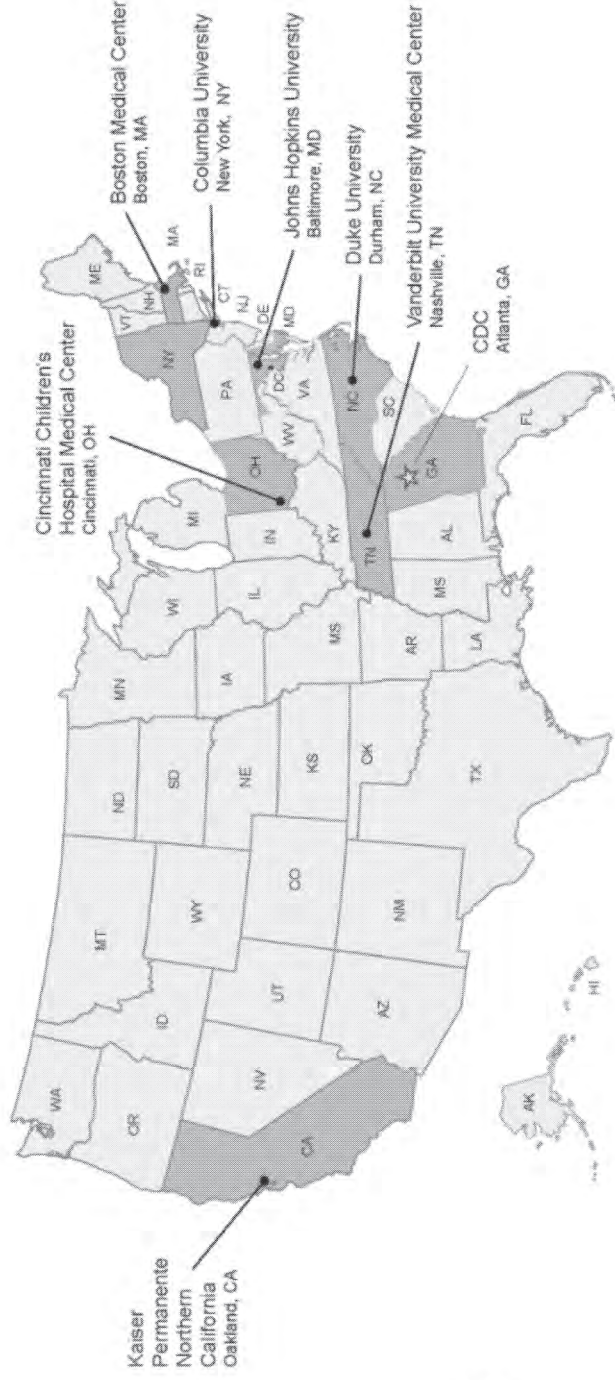
- Dose-specific analyses
- Product-specific analyses
- Analyses for two risk intervals 1-21 and 1-42 days
- Historical comparator analysis



CISA

Clinical Immunization Safety Assessment (CISA) Project

7 participating medical
research centers with
vaccine safety experts



- clinical consult services[†]
- clinical research

[†]More information about clinical consults available at
<http://www.cdc.gov/vaccinesafety/Activities/CISA.html>

CISA Project COVIDvax

- Extension of CDC’s CISA* Project’s clinical consultation service for U.S. healthcare providers and health departments for complex COVID-19 vaccine safety questions/issues that are[†]
 - (1) about an individual patient(s) residing in the United States
 - (2) not readily addressed by CDC or ACIP guidelines
- Vaccine safety subject matter expertise in multiple specialties (e.g., infectious diseases, allergy/immunology, neurology, OB/GYN, pediatrics, geriatrics)
- Requests for a CISA consult about COVID-19 vaccine safety:
 - Contact CDC-INFO: 800-CDC-INFO (800-232-4636) or webform
 - Indicate the request is for a “CDC CISA”* consult (no patient identifiers)

* <https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/cisa/index.html>

† Advice from CDC and CISA is meant to assist in decision-making, rather than provide direct patient management

CISA Project contributions

- Responded to 331 clinical inquiries or consultation requests about COVID-19 vaccine safety (December 14, 2020 through February 10, 2021)
 - Received from 43 states
 - >90% from healthcare provider or health departments
 - Most common topics include anaphylaxis/allergic reactions and nervous system disorders*
- Assisted state health departments with evaluation of complex medical issues pertaining to COVID-19 vaccines safety
- Established CISA Project workgroup with allergy/immunology specialists
 - Provided expert input on anaphylaxis and other allergic reactions to inform clinical considerations for use of COVID-19 vaccines
 - Ongoing work to investigate possible mechanism for anaphylaxis after COVID-19 vaccine, in collaboration with FDA, NIH and other partners

* Includes inquiries about adverse events and for clinical guidance without adverse event

COVID-19 vaccine safety in pregnancy

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Summary of v-safe data as of February 16, 2021

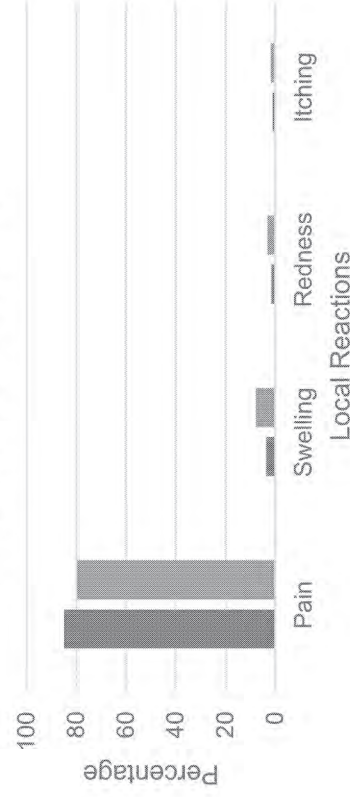
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Pregnancies reported to v-safe†	16,039	14,455	30,494

* COVID Data Tracker as of Feb 16, 2021 (107,571 doses with manufacturer not identified)

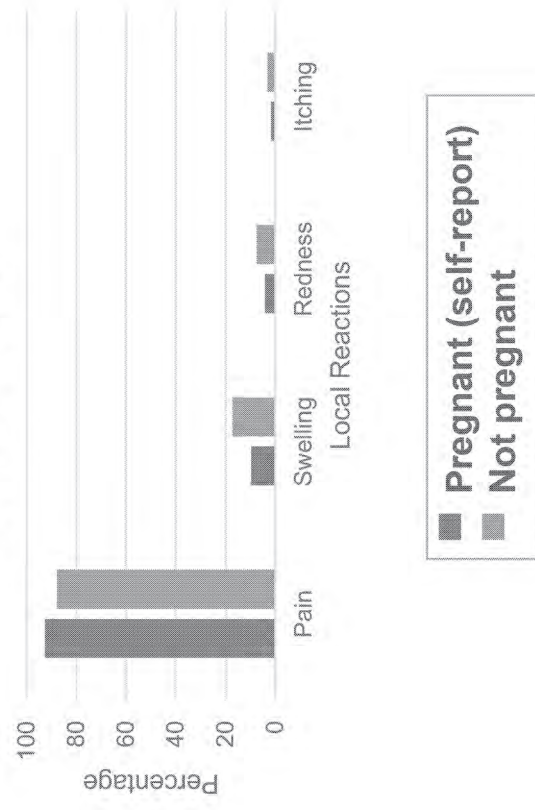
† Self-reported during a v-safe health check-in

V-safe: Day 1 post-vaccination local reactions in pregnant and non-pregnant women aged 16-54 years*

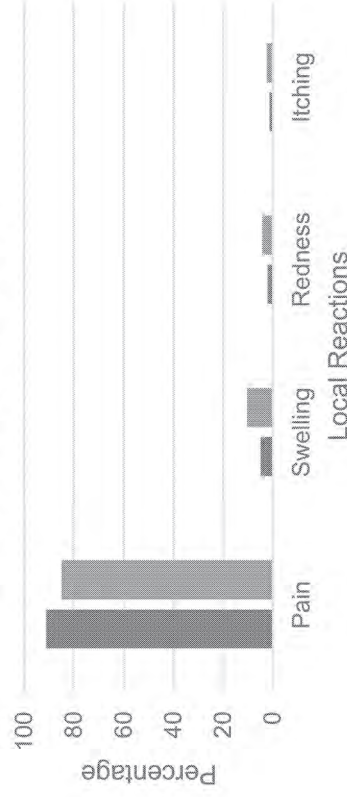
Pfizer-BioNTech Dose 1



Moderna Dose 1



Pfizer-BioNTech Dose 2

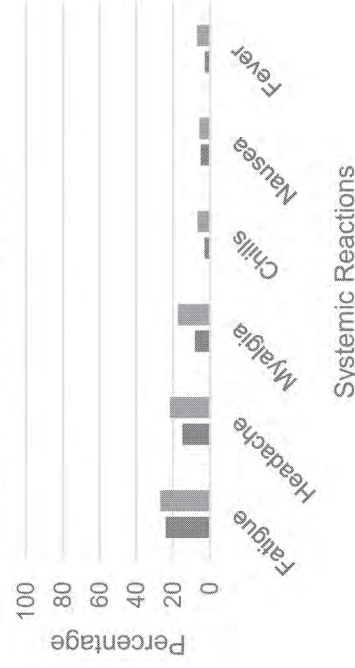


* Source: CDC unpublished v-safe data through January 13, 2021

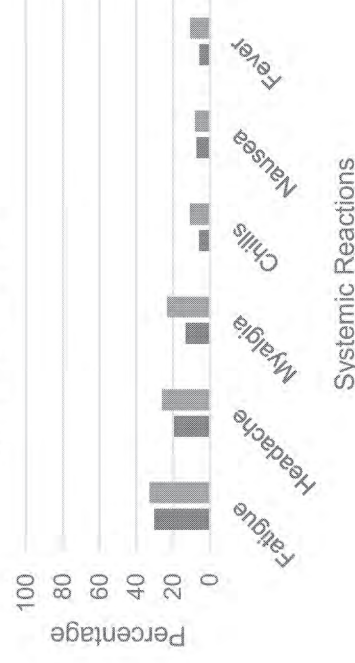
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V-safe: Day 1 post-vaccination local reactions in pregnant and non-pregnant women aged 16-54 years*

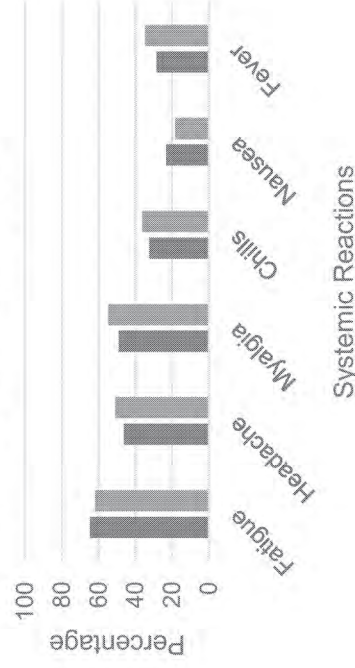
Pfizer-BioNTech Dose 1



Moderna Dose 1



Pfizer-BioNTech Dose 2



Pregnant (self-report)

Not pregnant



* Source: CDC unpublished v-safe data through January 13, 2021

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V-safe pregnancy registry

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

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

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



V-safe pregnancy registry enrollment as of February 19, 2021

Registry participants to date (N = 1,949)	
Enrolled	1,815
Not eligible*	103
Refused/declined†	31

- In the enrolled population, there have been 275 completed pregnancies, including 232 live births
 - Other outcomes include miscarriage, stillbirth, ectopic/tubal, other

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

† 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

V-safe pregnancy registry outcomes of interest in COVID-19 vaccinated pregnant women as of February 18, 2021*

Outcomes	Background rates*	V-safe pregnancy registry overall
Pregnancy outcome		
Miscarriage (<20 weeks)	26%	15% [†]
Stillbirth (≥ 20 weeks)	0.6%	1%
Pregnancy complications		
Gestational diabetes	7-14%	10%
Preeclampsia or gestational hypertension [§]	10-15%	15%
Eclampsia	0.27%	0%
Intrauterine growth restriction	3-7%	1%
Neonatal		
Preterm birth	10.1%	10%
Congenital anomalies [†]	3%	4%
Small for gestational age ⁿ	3-7%	4%
Neonatal death	0.38%	0%

* Sources listed on slide 33; † 93% of these were pregnancy losses <13 weeks of age; § Pre-eclampsia or gestational hypertension diagnosed during pregnancy and/or during delivery; † Congenital anomalies (overall) diagnosed after delivery only; ^ Birthweight below the 10th percentile for gestational age and sex using INTERGROWTH-21st Century growth standards

Sources for pregnancy outcomes and complications and neonatal outcomes background rates

- Miscarriage: <https://www.ncbi.nlm.nih.gov/books/NBK532992/>
- Stillbirth: <https://www.cdc.gov/nchs/data/nvsr/nvsr69-04-508.pdf>
- Gestational diabetes: <https://dmsjournal.biomedcentral.com/articles/10.1186/s13098-019-0406-1>,
[https://www.cdc.gov/pcd/issues/2018/18_0094.htm#:~:text=An%20estimated%201%25%20to%2014,without%20gestational%20diabetes%20\(4\)](https://www.cdc.gov/pcd/issues/2018/18_0094.htm#:~:text=An%20estimated%201%25%20to%2014,without%20gestational%20diabetes%20(4))
- Preeclampsia or gestational hypertension: <https://www.frontiersin.org/articles/10.3389/fcvm.2020.00059/full>,
<https://pubmed.ncbi.nlm.nih.gov/32381164/>
- Eclampsia: CDC Wonder
- Intrauterine growth restriction: <https://pubmed.ncbi.nlm.nih.gov/19404231/>
- Preterm birth: NCHS/Peristats
- Congenital anomalies: <https://www.cdc.gov/ncbddd/birthdefects/data.html>
- Small for gestational age (this has it up to 11%): <https://www.ncbi.nlm.nih.gov/books/NBK563247/>
- Neonatal death: NCHS/Peristats

Characteristics of COVID-19 vaccine pregnancy reports to VAERS through February 16, 2021* (N=154)



Characteristic	
Maternal age in years, median (range)	33 (16–51)
Gestational age in weeks at time of vaccination when reported, median (range)	13 (2–38)
Trimester of pregnancy at time of vaccination	n (%)
First (0-13 weeks)	60/118 (51)
Second (14-27 weeks)	36/118 (31)
Third (28+ weeks)	22/118 (19)
Vaccine	
Pfizer-BioNTech	97 (63)
Moderna	56 (36)
Unreported	1 (0.6)

* Reports received and processed through February 16, 2021

Adverse events in pregnant women following COVID-19 vaccine reported to VAERS through February 16, 2021* (N=154)



* Reports received and processed through February 16, 2021

† Frequency of clinically recognized early pregnancy loss for women aged 20–30 years, 9–17%; age 30, 20%; age 40, 40%; age 45, 80%. ACOG Practice Bulletin No. 200: Early Pregnancy Loss. Obstet Gynecol. 2018;132(5):e197-e207

Adverse events	N (%)
Pregnancy/neonatal specific conditions	42 (27)
Spontaneous abortion/miscarriage [†]	29
Premature rupture of membranes	3
Fetal hydrops	2
Neonatal death in 22-week preterm birth	1
Premature delivery	1
Gestational diabetes	1
Vaginal bleeding	1
Stillbirth	1
Shortened cervix	1
Leakage amniotic fluid	1
Calcified placenta	1
Non-pregnancy specific adverse events (top 10)	112 (73)
Headache (31), fatigue (29), chills (21), pain in extremity (17), nausea (15), dizziness (14), pain (14), pyrexia (13), injection site pain (13), injection site erythema (10)	

Other CDC COVID-19 maternal vaccination safety activities

- Vaccine Safety Datalink (VSD)
 - COVID-19 vaccination coverage in pregnant women
 - Risk of miscarriage and stillbirth following COVID-19 vaccination
 - Safety in pregnancy
 - Acute adverse events in pregnancy, longer-term safety assessment of acute adverse events, pregnancy complications and birth outcomes, and infant follow-up for the first year of life
- Clinical Immunization Safety Assessment (CISA) Project
 - Prospective observational cohort study
 - Adverse pregnancy and birth outcomes, serious adverse events, local and systemic reactogenicity, infant health outcomes for first 3 months of life

Maternal vaccination safety summary

- Pregnant women were not specifically included in pre-authorization clinical trials of COVID-19 vaccines
 - Post-authorization safety monitoring and research are the primary ways to obtain safety data on COVID-19 vaccination during pregnancy
- Substantial numbers of self-reported pregnant persons (>30,000) have registered in **v-safe**
- The reactogenicity profile and adverse events observed among pregnant women in **v-safe** did not indicate any safety problem
- Most (73%) reports to VAERS among pregnant women involved non-pregnancy-specific adverse events (e.g., local and systemic reactions)
- Miscarriage was the most frequently reported pregnancy-specific adverse event to VAERS; numbers are within the known background rates based on presumed COVID-19 vaccine doses administered to pregnant women

Closing thoughts on COVID-19 vaccine safety (Feb 2021)

- 75 million COVID-19 vaccine doses have been administered in the United States through February 28
- Reactogenicity profiles of mRNA vaccines in **v-safe** monitoring are consistent with what was observed in clinical trials, and systemic and local reactions are most commonly reported to VAERS
- Anaphylaxis following both vaccines has been reported to VAERS, though rarely
- No other safety signals for serious adverse events have been detected in VAERS
- No safety concerns have been identified among VSD Rapid Cycle Analysis prespecified outcomes as of February 13
- No unexpected pregnancy or infant outcomes have been observed related to COVID-19 vaccination during pregnancy
- Safety monitoring in pregnant women is ongoing and planned in **v-safe**, VAERS, VSD, and CISA

Acknowledgments

We wish to acknowledge the contributions of investigators from the following organizations:

Centers for Disease Control and Prevention

COVID-19 Vaccine Task Force

COVID-19 Vaccine Task Force, Vaccine Safety Team

Immunization Safety Office

Division of Healthcare Quality Promotion

National Center on Birth Defects and Developmental Disabilities

Division of Reproductive Health

Vaccine Safety Datalink

Clinical Immunization Safety Assessment Project

V-safe Team

U.S. Food and Drug Administration

Office of Biostatistics and Epidemiology

Questions

PSICOVID_0001041

Key Messages

Vaccines and Related Biological Products Advisory Committee (VRBPAC)

Advisory Committee on Immunization Practices (ACIP)

Presentations by Tom Shimabukuro, MD, MPH, MBA

- **V-safe update (as of February 16, 2021)**

- Total doses – 55,220,364
 - Pfizer-BioNTech – 28,374,410 (people receiving 1 or more doses)
 - Moderna – 26,738,383 (people receiving 1 or more doses)
- Total registrants completing at least 1 v-safe health check – 3,897,982
 - Pfizer – 1,776,960
 - Moderna - 2,121,022
- Total pregnancies reported - 30,494
 - Pfizer – 16,039
 - Moderna - 14,455
- Adverse events **dose 1 day 1** (1,602,065 completed at least one survey);

Pfizer: (adverse events dose 1/day 1)	Moderna: (adverse events dose 1/ day 1)
• 73% injection site pain	• 78% injection site pain
• 23% fatigue	• 25% fatigue
• 18% headache	• 20% headache
• 15% myalgia	• 18% myalgia

- Adverse events **dose 2 day 1** (1,602,065 participants)
 - Pfizer (fatigue, headache, myalgia twice as strong)
 - 79% injection site pain
 - 54% fatigue
 - 43% headache
 - 47% myalgia

- **VAERS update (as of February 16, 2021)**

- Total Adverse Events - 104,763
- Total Non-Serious - 98,682 (94%)
 - Moderna: 54,708 (97%); Pfizer: 43,974 (91%)
- Total Serious – 6,081 (6%)
 - Moderna: 1,859 (3%); Pfizer: 4,222 (9%)
- Headache - #1 adverse event reported for both vaccines

- **Anaphylaxis (reported December 14 – January 18)**

- 4.7 cases per million doses of Pfizer
- 2.5 cases per million doses of Moderna

- **VSD update**

- No statistical signals detected

- **COVID-19 vaccine safety in pregnancy**

- V-safe participants enrolled – 1,815

- **v-safe** participants are contacted once per trimester, after delivery and when the infant is three months old
- VAERS – 153 reports of adverse events
 - 97 after Pfizer vaccine
 - 56 after Moderna vaccine
 - Adverse Events:
 - Pregnancy loss (miscarriage and stillbirth) – 29
 - Premature rupture of membranes – 3
 - Fetal hydrops – 2
 - Neonatal death (22-week preterm birth) – 1
- **Conclusion:**
 - Reactogenicity profiles of mRNA vaccines in v-safe monitoring are consistent with what was observed in clinical trials.
 - Systemic and local reactions are most commonly reported to VAERS; anaphylaxis occurs following both vaccines, though rarely; there were no safety signals for serious events found based on reports to VAERS.
 - No safety concerns were identified among VSD Rapid Cycle Analysis prespecified outcomes as of February 13.
 - Most reports to VAERS among pregnant women (73%) involved non-pregnancy-specific adverse events (e.g., local and systemic reactions).
 - Miscarriage was the most frequently reported pregnancy-specific adverse event to VAERS but was below expected background rate.
 - Safety monitoring in pregnant women is ongoing/planned in v-safe, VSD, and CISA.

Message

From: Markowitz, Lauri (CDC/DDID/NCIRD/DVD) [lem2@cdc.gov]
Sent: 3/19/2021 11:05:53 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]
Subject: [EXTERNAL] VaST - Draft minutes and report from March 15 (CONFIDENTIAL)
Attachments: 2021-03-15- VaST Meeting Minutes Draftv2.docx; 2021-03-15 - VaST Report Data Table - DRAFT.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 VaST call this week. Please let us know if there are any corrections or comments.

The next VaST call is March 22, 1:30 – 2:30 pm EDT. (Note the open session is 1 hour instead of 1.5 hours.) This will be the second VaST vaccine in pregnancy focused session.

Draft agenda:

Data from other adenovirus vector vaccines (Janssen)
v-safe (CDC)
v-safe pregnancy registry (CDC)
VAERS (CDC)

Thanks to all,
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