Vaccines and Related Biological Products Advisory Committee Meeting

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COVID-19 vaccine safety update

Vaccines and Related Biological Products Advisory Committee (VRBPAC)
February 26, 2021

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CDC COVID-19 Vaccine Task Force
Vaccine Safety Team

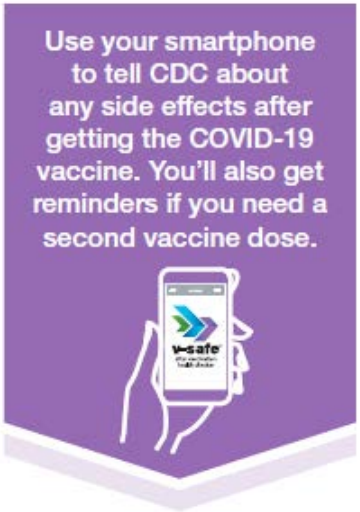
Disclaimer

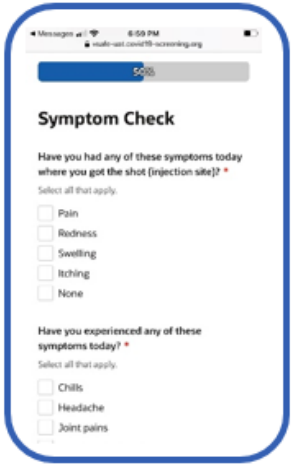
- The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC) or the U.S. Food and Drug Administration (FDA).
- Mention of a product or company name is for identification purposes only 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
- COVID-19 vaccine safety in pregnancy

v-safe[SM] after vaccination health checker





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*

Vaccine recipients

v-safe℠ after vaccination health checker

2. clinically important health impact reported

✓ **received medical care**

Call center

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

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

Call center

* Selected web surveys capture information on pregnancy status

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

v-safe[SM] after vaccination health checker

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 70
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

	Percentage of v-safe enrollees reporting reactions			
	Both vaccines	Pfizer-BioNTech vaccine		Moderna vaccine
Local and systemic reaction	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

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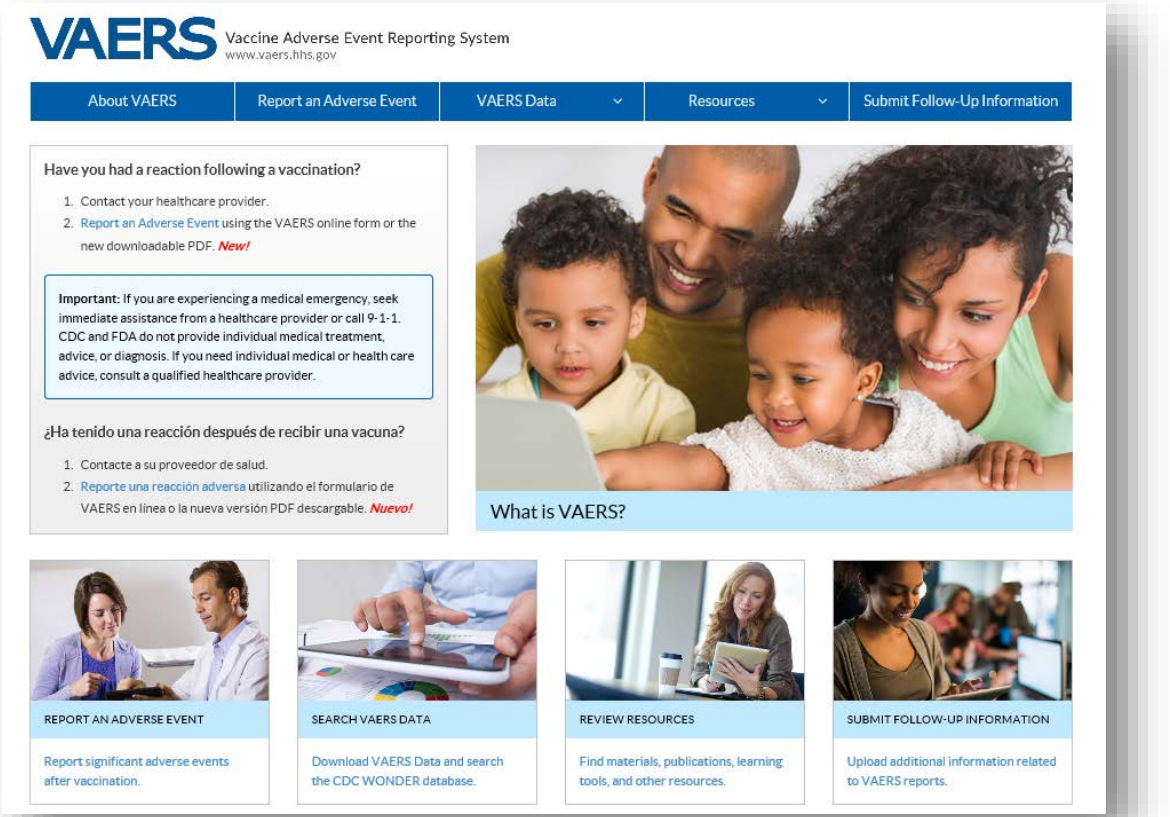
VAERS is the nation's early warning system for vaccine safety

CDC + FDA

VAERS

Vaccine Adverse Event Reporting System



http://vaers.hhs.gov

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 18, 2021] weekly results)

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

Anaphylaxis following mRNA COVID-19 vaccines

Clinical Review & Education

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.

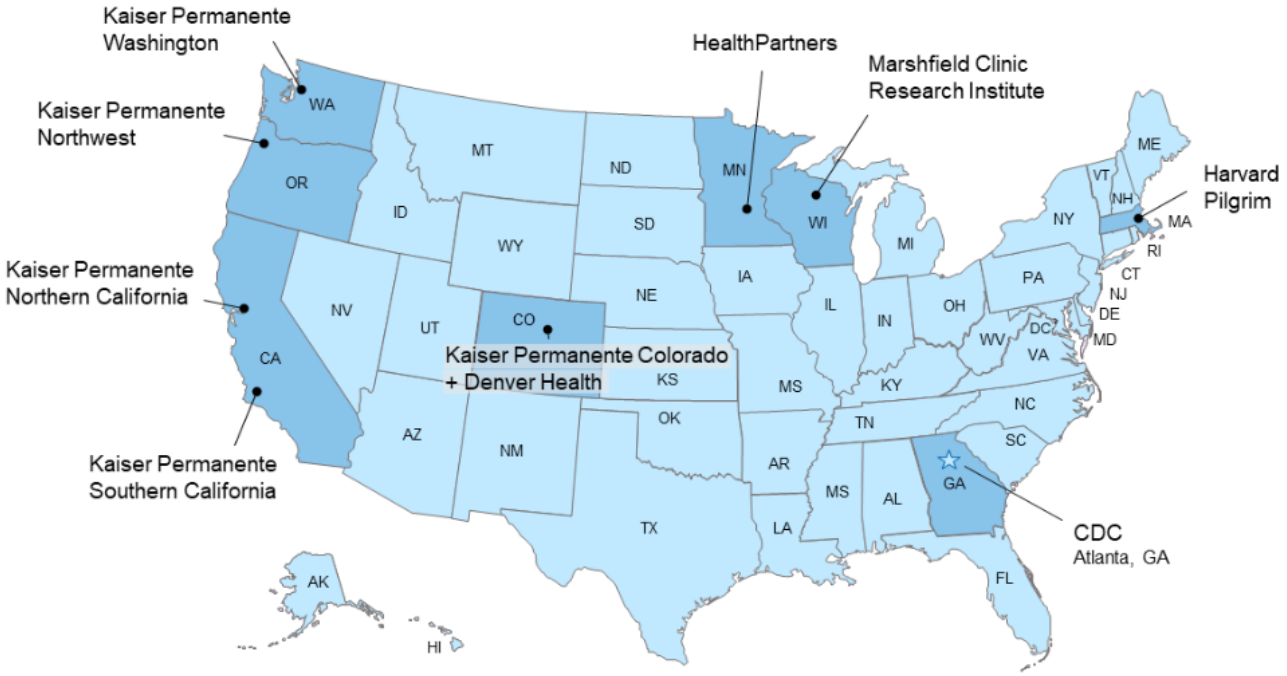
	Pfizer-BioNTech	Moderna
Anaphylaxis reporting rate (cases per million doses administered)	4.7	2.5

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

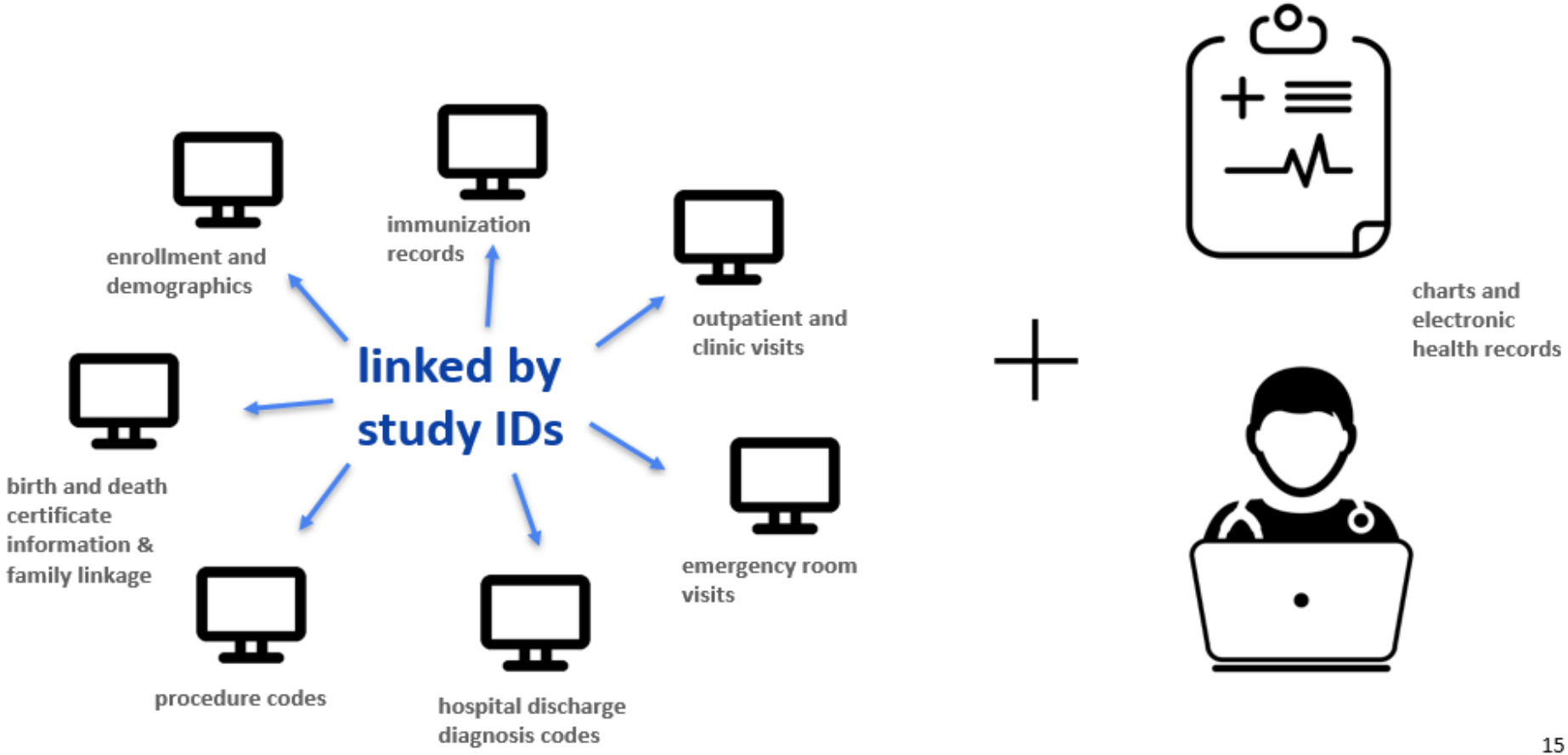
Vaccine Safety Datalink



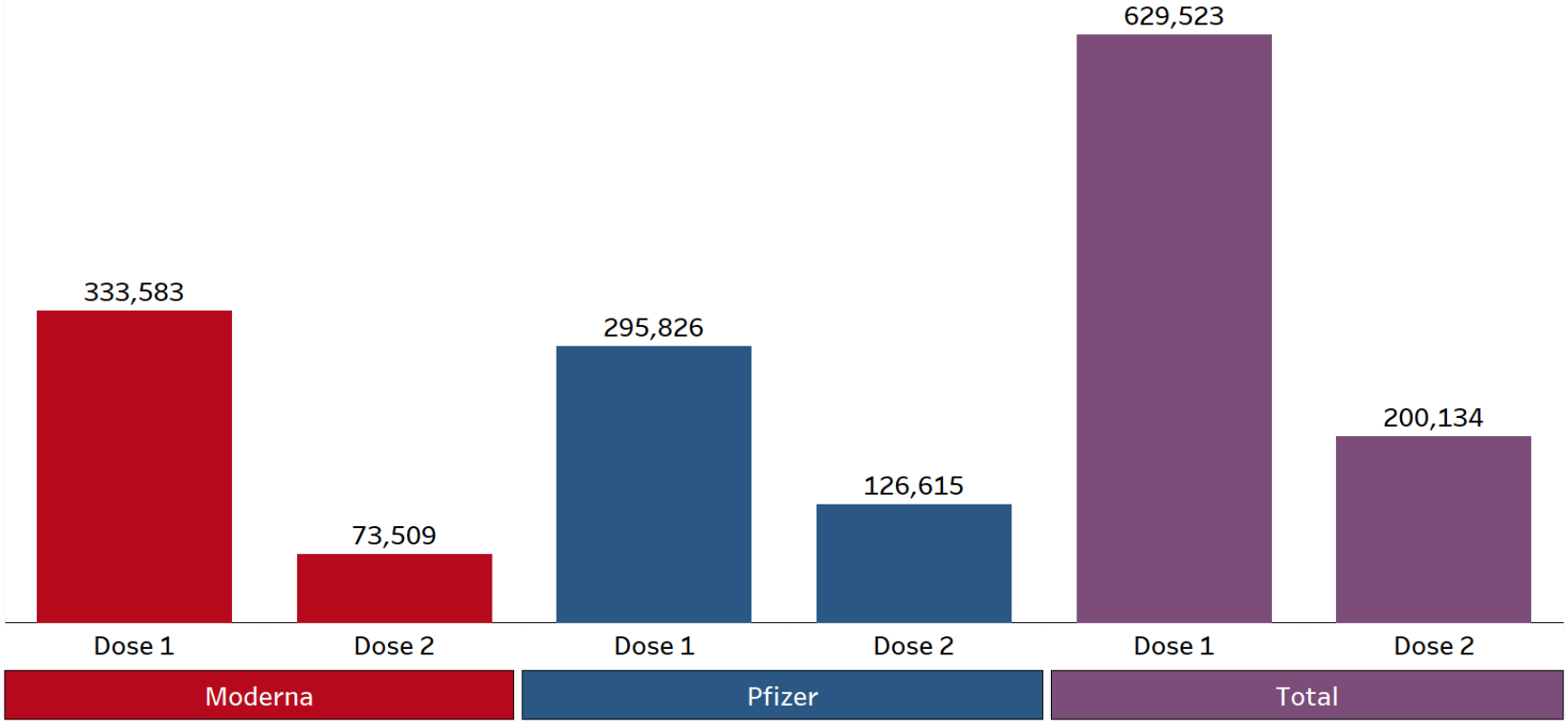
9 participating integrated healthcare organizations

data on over **12 million** persons per year

Types of information in VSD



VSD COVID-19 vaccine doses administered*



* Through February 13, 2021; total includes small number of unknow vaccine type

VSD Rapid Cycle Analysis prespecified outcomes for COVID-19 vaccines	Concurrent comparator	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

Preliminary results of the unvaccinated concurrent comparator analysis for COVID-19 vaccine safety after either dose of any mRNA vaccine

- No statistically significant increased risks detected for any prespecified outcomes*

* As of February 13, 2021

VSD Rapid Cycle Analysis prespecified outcomes for COVID-19 vaccines*	Concurrent comparator	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

Preliminary results of the sequential vaccinated concurrent comparator analysis for COVID-19 vaccine safety after either dose of any mRNA vaccine

- No statistical signals detected†

* Only includes outcomes with events in the risk window
† As of February 13, 2021

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 (expected to start latter half of March)

COVID-19 vaccine safety in pregnancy

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 fetal demise, pregnancy complications, maternal intensive care unit admission, adverse birth outcomes, neonatal death, infant hospitalizations, and major 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
† Phone surveys are conducted along with maternal and infant medical record review

V-safe pregnancy registry enrollment*

V-safe participants to date (N = 1,949)	
Enrolled	1,815
Not eligible†	103
Refused/declined§	31

* Enrollment as of 2/19/2021 8:30am EST
† 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

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	**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 Feb 16, 2021

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

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) 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)	**112 (73)**

* 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*. 2018132(5):e197-e207.

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 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 concerns identified among VSD Rapid Cycle Analysis prespecified 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 the number was not concerning considering 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