Centers for Disease Control and Prevention (CDC) Immunization Safety Office (ISO) Update

Advisory Commission on Childhood Vaccines (ACCV) meeting

March 4, 2021

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Recent Publications

Meningococcal Vaccination: Recommendations of the Advisory Committee on Immunization Practices, United States, 2020

- Mbaeyi SA, et al. *MMWR Recomm Rep.* 2020 Sept;69(No. RR-9):1-41.
- **Summary:** This report compiles and summarizes all recommendations from CDC's Advisory Committee on Immunization Practices (ACIP) for use of meningococcal vaccines in the United States. As a comprehensive summary and update of previously published recommendations, it replaces all previously published reports and policy notes. This report also contains new recommendations for administration of booster doses of serogroup B meningococcal (MenB) vaccine for persons at increased risk for serogroup B meningococcal disease. These guidelines will be updated as needed on the basis of availability of new data or licensure of new meningococcal vaccines.

Available at: https://www.cdc.gov/mmwr/volumes/69/rr/rr6909a1.htm

Safety Surveillance of Bivalent Meningococcal Group B Vaccine, Vaccine Adverse Event Reporting System, 2014-2018

- Duffy J, et al. Open Forum Infect Dis. 2020 Oct 27;7(12):ofaa516.
- **Summary:** In October 2014, MenB-FHbp (Trumenba, Pfizer) became the first meningococcal group B vaccine licensed in the United States. It is approved for use in individuals aged 10-25 years. The adverse events most commonly or disproportionately reported following MenB-FHbp were consistent with those identified in clinical trials as described in the US package insert. This analysis did not identify any new safety issues.

Available at: https://pubmed.ncbi.nlm.nih.gov/33324721/

Safety profile of rotavirus vaccines among individuals aged ≥8 months of age, United States, vaccine adverse event reporting system (VAERS), 2006-2019

- Haber P, et al. Vaccine. 2021 Jan 22;39(4):746-750.
- **Summary:** The Advisory Committee on Immunization Practices (ACIP) currently recommends that RV5 or RV1 immunization be initiated by age 14 weeks and 6 days and completed by 8 months 0 days. This analysis did not identify any unexpected AEs for RV vaccines among individuals aged ≥8 months. Health care providers should adhere to the ACIP recommended schedule and older individuals should apply necessary precautions to prevent potential secondary exposure from vaccinated children.

Available at: https://pubmed.ncbi.nlm.nih.gov/33267969/

Developing algorithms for identifying major structural birth defects using automated electronic health data

- Kharbanda EO, et al. Pharmacoepidemiol Drug Saf. 2021 Feb;30(2):266-274.
- **Summary:** Given the 2015 transition to International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnostic coding, updates to the Vaccine Safety Datalink's previously published algorithms for major structural birth defects (BDs) were necessary. Algorithms can identify infants with selected BDs using automated healthcare data with reasonable accuracy. These updated algorithms can be used in observational studies of maternal vaccine safety and may be adapted for use in other surveillance systems.

Available at: https://pubmed.ncbi.nlm.nih.gov/33219586/

Advisory Committee on Immunization Practices (ACIP)

February 2021 regular meeting topics

Rabies Vaccine

- ACIP voted on a change to the rabies pre-exposure prophylaxis (PrEP) vaccine recommendation
  - ACIP recommends a 2-dose [0, 7 days] intramuscular rabies vaccine series in persons for whom rabies vaccine pre-exposure prophylaxis (PrEP) is indicated
  - ACIP recommends an intramuscular booster dose of rabies vaccine, as an alternative to a titer check, no sooner than day 21 but no later than 3 years after the 2-dose PrEP series for those who have sustained and elevated risk for only recognized rabies exposures (i.e., those in risk category #3 of rabies PrEP recommendations table)

Dengue Vaccine

- ACIP continued to discuss development of recommendations for the CYD-TDV dengue vaccine
- The workgroup will finalize the evidence to recommendations framework
- An ACIP vote on CYD-TDV vaccine recommendations is planned to occur at the ACIP June 2021 meeting

Tick-borne Encephalitis (TBE) Vaccine

- Pfizer has submitted a Biologics License Application (BLA) to the Food and Drug Administration (FDA) for their TBE vaccine
- Licensure possible by 3rd quarter of 2021
- No TBE vaccine previously licensed in the United States
- No existing ACIP TBE vaccine recommendations
- Policy question for TBE vaccine GRADE
  - Should TBE vaccine be recommended for use in persons aged ≥1 year traveling to or residing in TBE risk areas and in laboratory staff working with TBE virus?

Ebola Vaccine

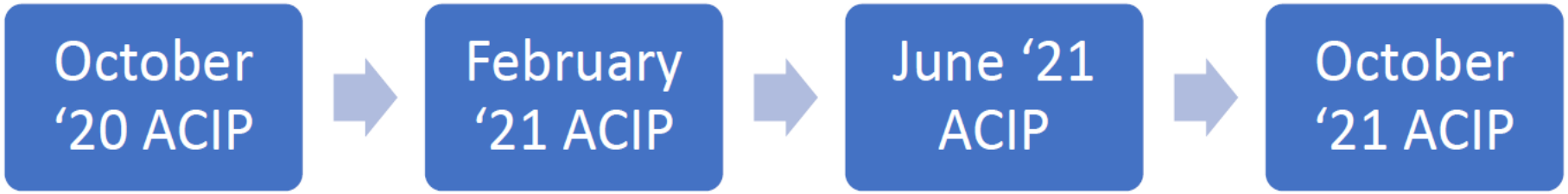
- Use of Ebola Vaccine: Recommendations of the Advisory Committee on Immunization Practices published in MMWR Recommendations and Reports on January 7, 2021
- New Ebola outbreaks identified
  - February 7, 2021, EVD outbreak reported in North Kivu Province, Democratic Republic of Congo
  - Feb 14, 2021, EVD outbreak reported in N'Zerekore Prefecture, Guinea
- ACIP discussed 2 additional U.S. populations at risk for *potential* occupational exposure to Ebola virus (species *Zaire ebolavirus*) for whom potential policy options are under consideration:
  - Healthcare personnel (HCP) at a state designated Ebola Treatment Centers involved in the care and transport of confirmed EVD patients
  - Individuals who work as laboratorians and support staff at Laboratory Research Network (LRN) facilities that handle replication competent Ebola virus (species *Zaire ebolavirus*)

Hepatitis Vaccine

- Proposed Policy Question: Should all unvaccinated adults receive hepatitis B vaccination?
- Alternative PICO for ACIP Committee consideration: Should all unvaccinated adults age 59 years and under receive hepatitis B vaccination?
- Timeline:
  - June 2021
    - GRADE
    - Evidence to Recommendation framework
  - October 2021
    - ACIP Vote

Pneumococcal Vaccine

Anticipated Timeline for Licensure of Higher-Valent Pneumococcal Conjugate Vaccines



Pfizer (PCV20)	Filed to FDA (Oct '20)		Licensure anticipated (June '21*)	
Merck (PCV15)		Filed to FDA (Nov '20)		Licensure anticipated (July 2021**)

Licensure for children anticipated in Q2–Q3 2022 (PCV15) or mid-2023 (PCV20)

Zoster Vaccine

- Recombinant Zoster Vaccine (RZV)
  - 41.3 million doses distributed in U.S. from launch through end of 2020
- Topics discussed:
  - Risk of Guillain-Barré syndrome (GBS) following RZV
  - RZV risk-benefit analysis
  - Introduction of the Evidence to Recommendations Framework for use of RZV in immunocompromised adults

Influenza Vaccine

- U.S. Influenza Activity for the 2020-21 season is low
  - Influenza-like illness (ILI) activity below national and region-specific baselines
  - Cumulative hospitalization rate 0.6/100,000 (lowest since 2005)
- There have been 193.7 million doses of influenza vaccine distributed as of February 12, 2021
- ACIP is conducting a systematic review regarding the relative benefits and harms of different type of influenza vaccine for older adults to be presented later in 2021

Cholera Vaccine

- Policy topic under consideration by work group:
  - Should ACIP cholera vaccine recommendations be expanded to include children and adolescents 2–17 years old?
- ACIP vote planned for October 2021

Orthopoxvirus Vaccine

- Orthopoxviruses species known to infect humans: Variola (Smallpox), Vaccinia (Smallpox Vaccine), Monkeypox, Cowpox, and newly discovered species (e.g., Akhmeta virus, Alaskapox virus)
- JYNNEOS® is a live attenuated non-replicating vaccine approved in 2019 to prevent smallpox and monkeypox disease in adults 18 years or older determined to be at high risk for smallpox or monkeypox infection
- ACIP is considering updating recommendations to include use of JYNNEOS® to prevent Orthopoxviruses in persons at risk for occupational exposure to Orthopoxviruses
- ACIP vote scheduled for October 2021 meeting

COVID-19 vaccines

ACIP held additional emergency meetings

- December 11-12, 2020
- December 19-20, 2020
- January 27, 2021
- February 28 – March 1, 2021

COVID-19 ACIP Vaccine Recommendations

- ACIP has recommended three COVID-19 vaccines
  - Pfizer-BioNTech COVID-19 Vaccine – December 12, 2020
  - Moderna COVID-19 Vaccine – December 19, 2020
  - Janssen COVID-19 Vaccine – February 28, 2021
- Recommendations available at:

  https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html

ACIP Interim Recommendation for Allocation of COVID-19 Vaccine

- On December 1, the Advisory Committee on Immunization Practices (ACIP) recommended that health care personnel and long-term care facility residents be offered COVID-19 vaccination first (Phase 1a).
- On December 20, ACIP updated interim vaccine allocation recommendations.
  - In Phase 1b, COVID-19 vaccine should be offered to persons aged ≥75 years and non–health care frontline essential workers, and in
  - Phase 1c, to persons aged 65–74 years, persons aged 16–64 years with high-risk medical conditions, and essential workers not included in Phase 1b.
  - Federal, state, and local jurisdictions should use this guidance for COVID-19 vaccination program planning and implementation.

Additional COVID-19 topics discussed at ACIP meetings

- Implementation considerations for COVID-19 vaccines
- Clinical considerations for use of COVID-19 vaccines
- Informational updates on
  - AstraZeneca COVID-19 vaccine (AZD1222)
  - Pediatric COVID-19 Clinical Trials
  - COVID-19 Vaccine Safety Update
  - COVID-19 Vaccine Effectiveness Studies
  - Emerging SARS-CoV-2 Variants

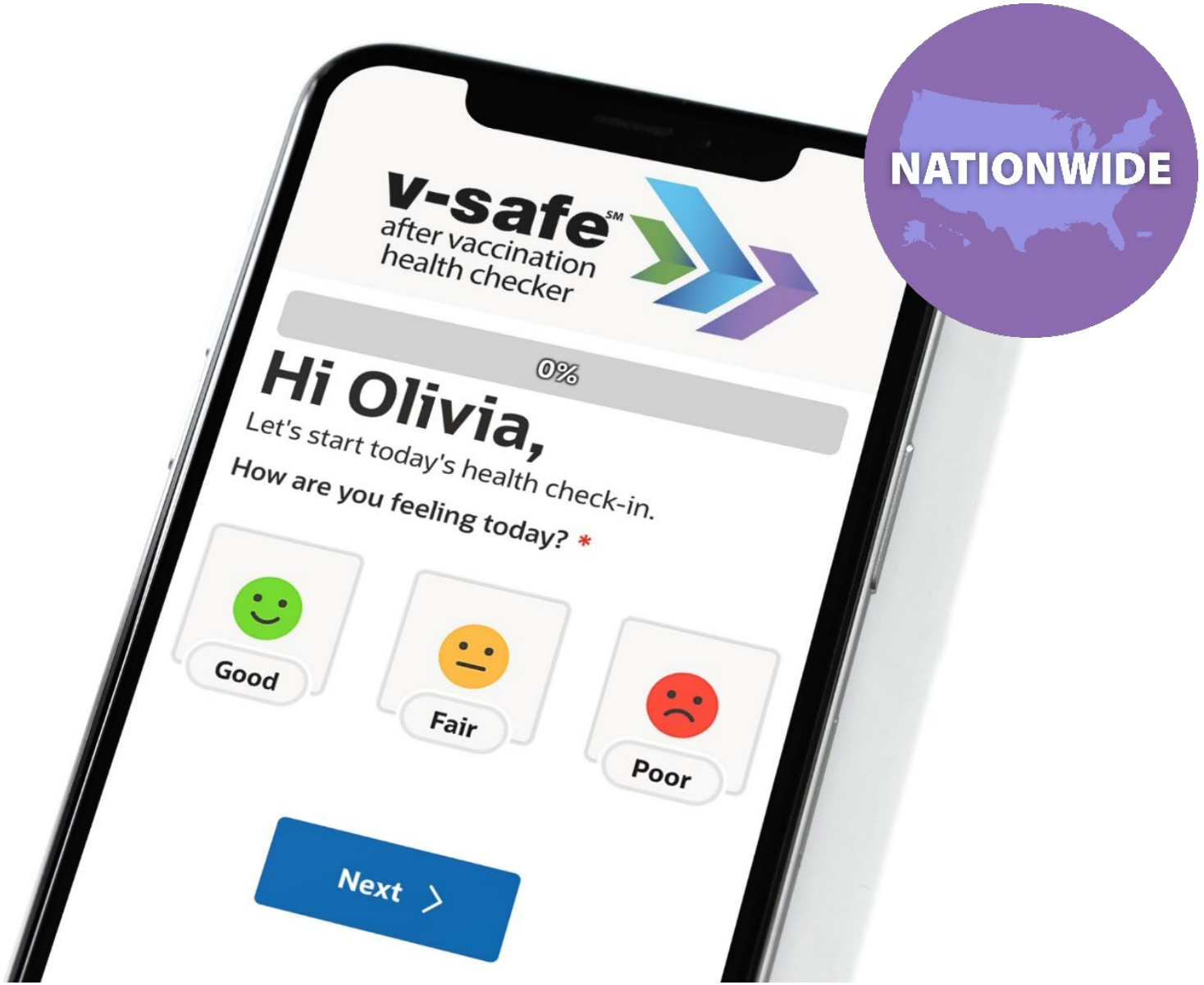
COVID-19 vaccine safety updates presented to ACIP

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

Smartphone-based active safety monitoring

v-safe[SM]
after vaccination
health checker

http://cdc.gov/vsafe



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

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

v-safe℠ 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

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

CDC + FDA

VAERS

Vaccine Adverse Event Reporting System

http://vaers.hhs.gov

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 (reports received and classified as serious or non-serious) 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 vaccine and 510 reports of death following Pfizer-BioNTech vaccine; most commonly reported serious adverse events include: death, dyspnoea, pyrexia, SARS-CoV-2 test negative, nausea, headache, dizziness, fatigue, asthenia, pain

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

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 [Feb 18, 2021] weekly results)

* For reports received and processed (coded, redacted, and quality assurance performed) 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.

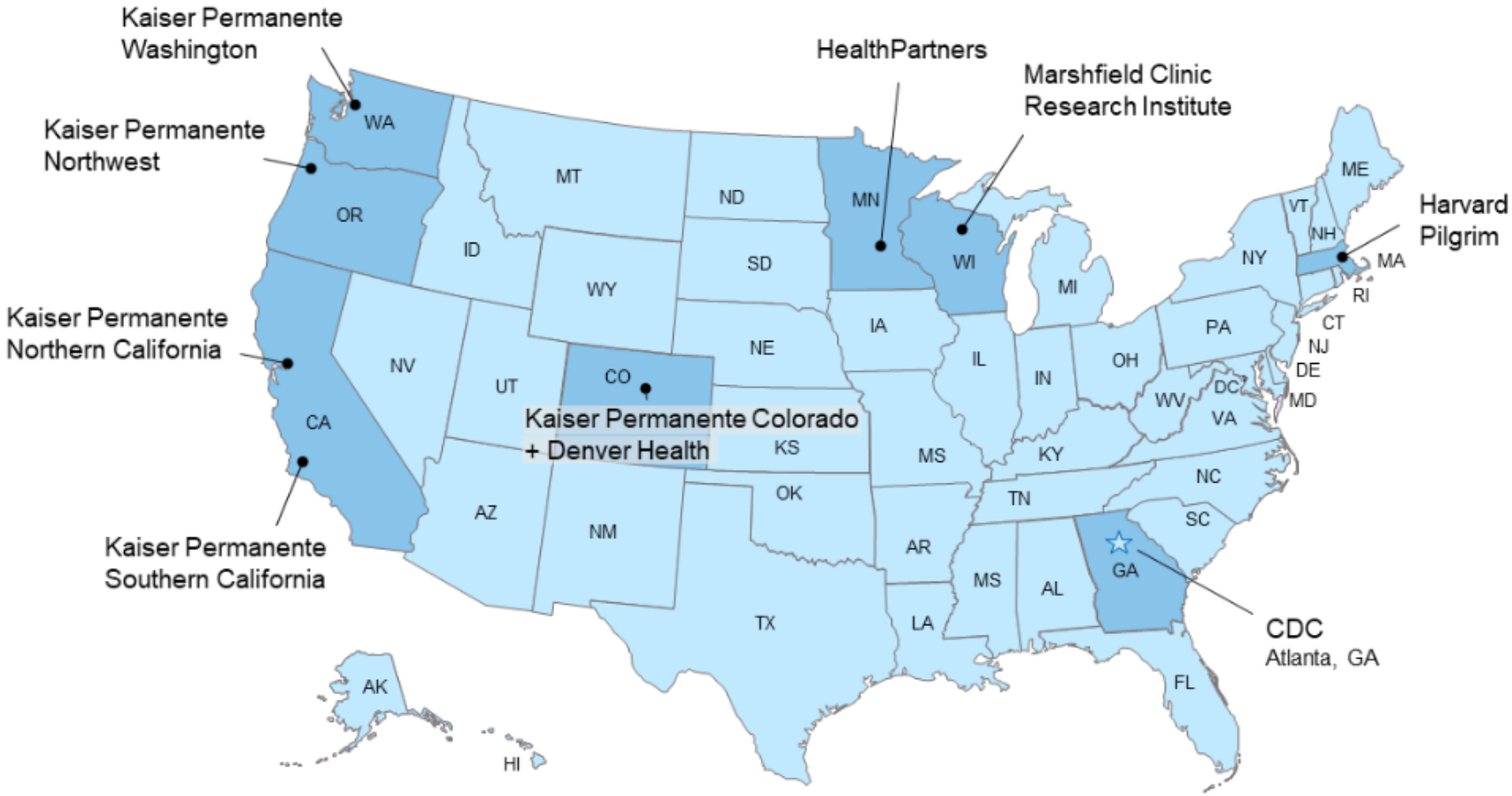
	Pfizer-BioNTech	Moderna
Anaphylaxis reporting rate (cases per million doses administered)	4.7	2.5

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

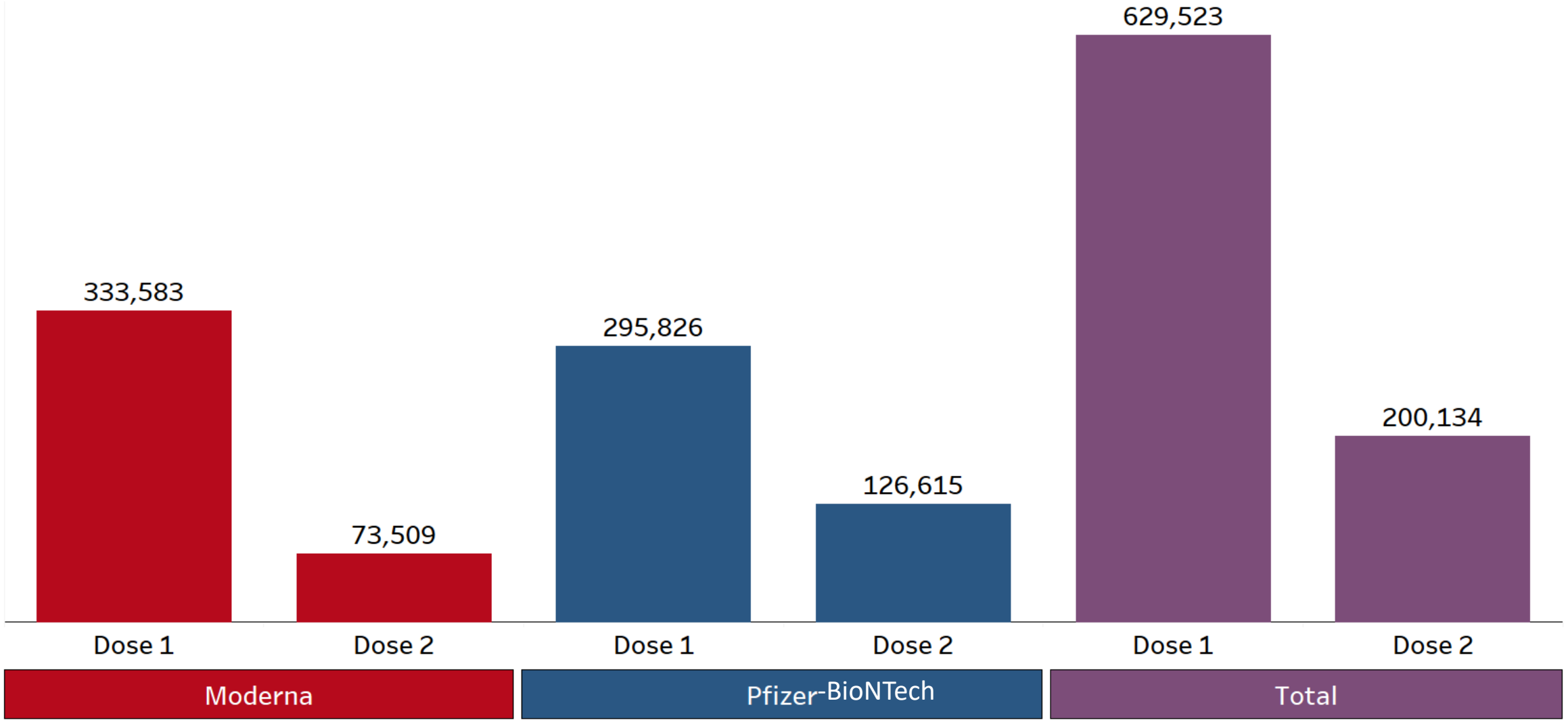
Vaccine Safety Datalink



9 participating integrated healthcare organizations

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

VSD COVID-19 vaccine doses administered*



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

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 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

Preliminary results:

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

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

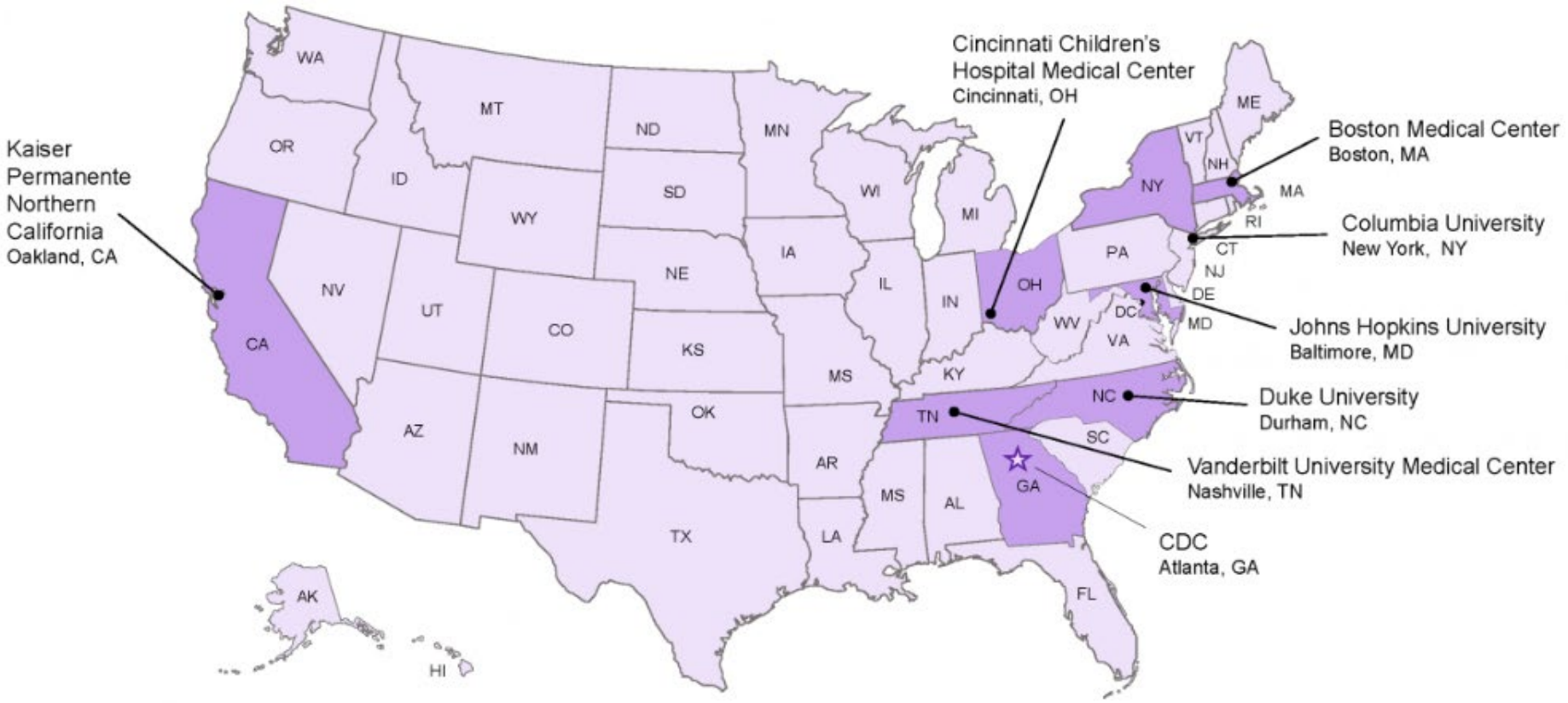
- No statistical signals detected†

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
† As of February 13, 2021

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*
  - Received from 43 states
  - >90% from healthcare provider or health departments
  - Most common topic: anaphylaxis/allergic reactions (34%)†
- Assisted state health departments with evaluation of complex medical issues pertaining to COVID-19 vaccines safety
- CISA Project workgroup with allergy/immunology specialists
  - 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

*Since December 14, 2020 – February 20, 2021

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

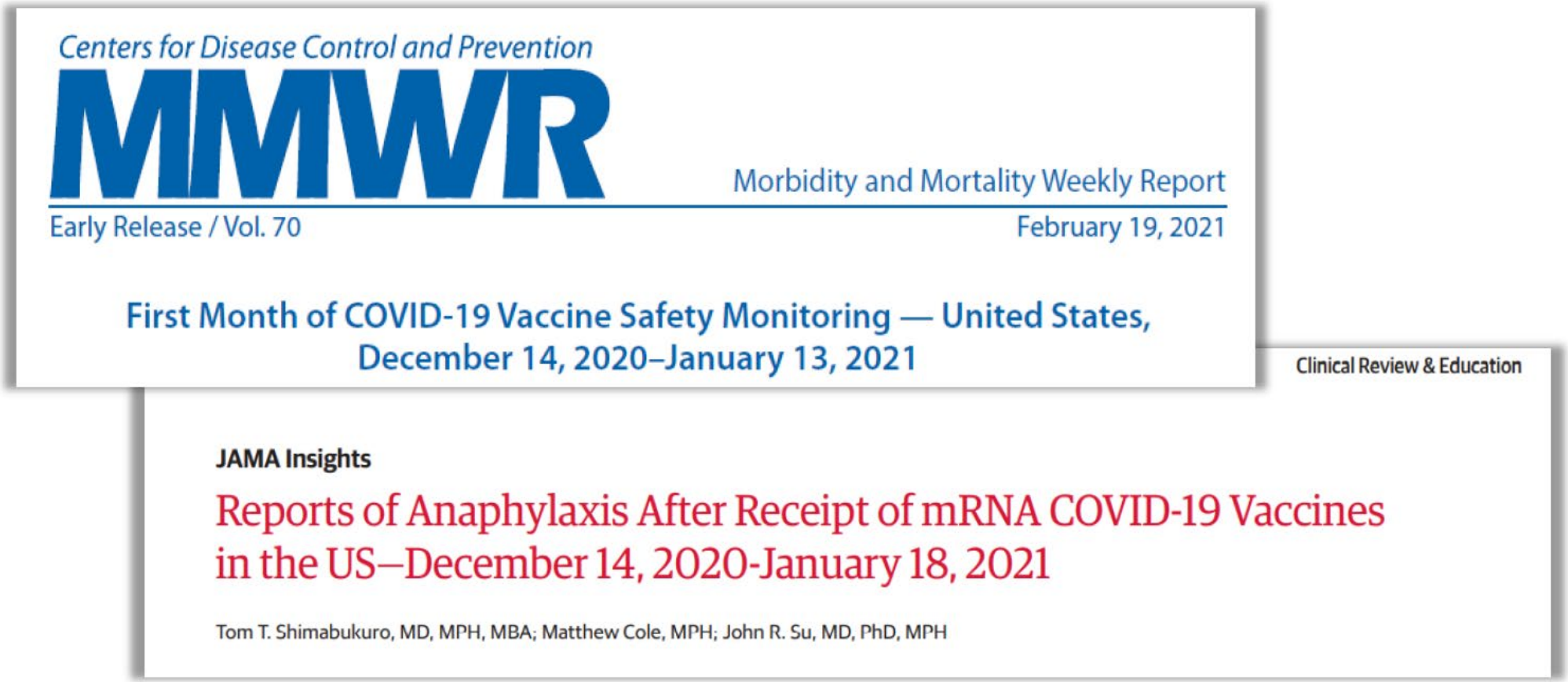
Maternal vaccination safety summary

- 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
- Larger than expected numbers of self-reported pregnant women have registered in v-safe
- The reactogenicity profile and adverse events observed among pregnant women in v-safe did not indicate any safety problems
- 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; 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)

- Just over 55 million COVID-19 vaccine doses administered in the United States through February 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 February 13
- Safety monitoring in pregnant women is ongoing and planned in v-safe, VAERS, VSD, and CISA

COVID-19 vaccine safety publications



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Thank You

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov