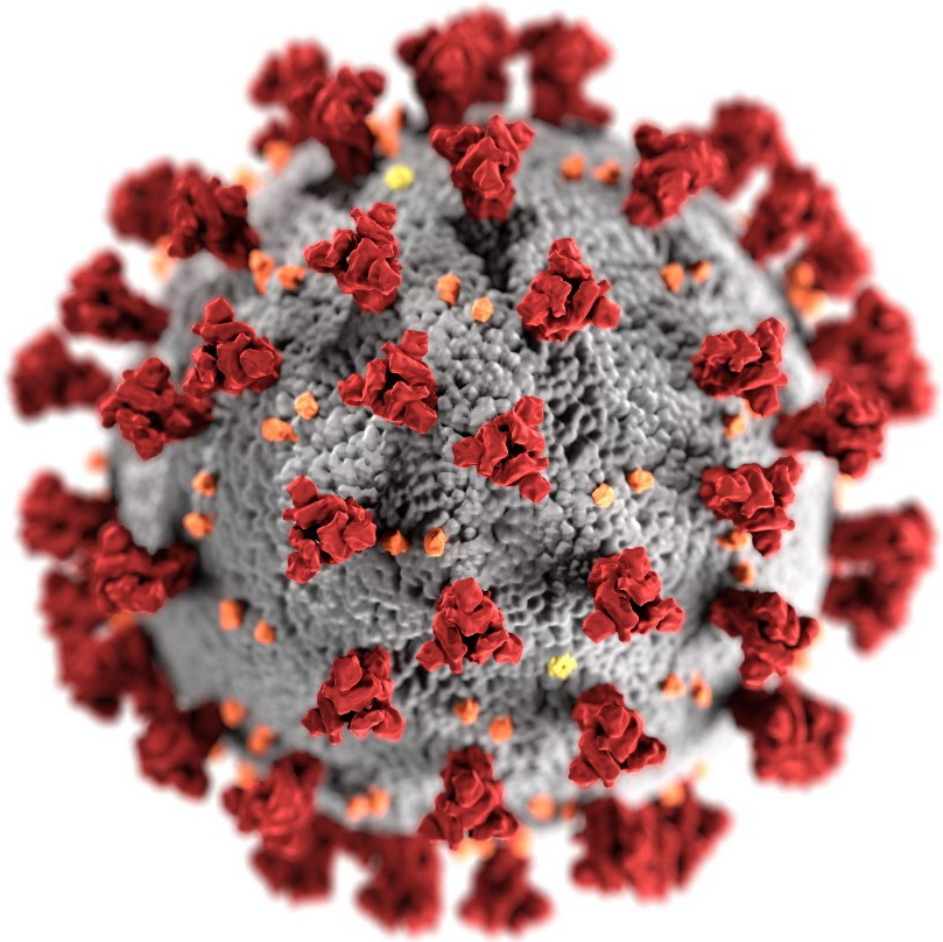
COVID-19 Vaccine Safety Updates

Vaccines and Related Biological Products Advisory Committee (VRBPAC)

June 10, 2021

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



cdc.gov/coronavirus

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

- Early safety data of Pfizer-BioNTech vaccination in persons aged 12–15 years old
- Myocarditis and pericarditis following mRNA vaccination

Early safety data of Pfizer-BioNTech vaccination in persons aged 12–15 years old

Smartphone-based active safety monitoring

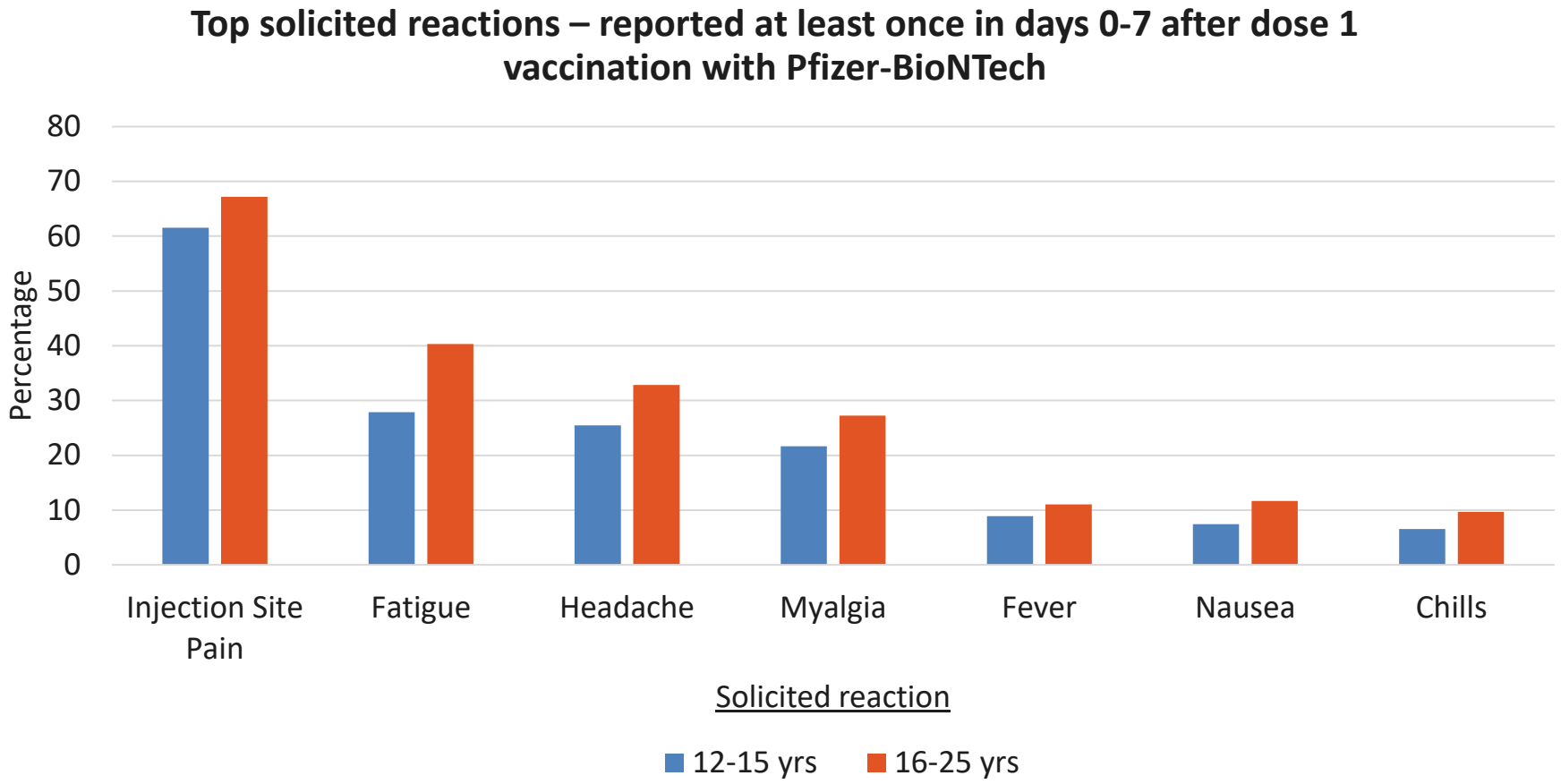
v-safe[SM]
after vaccination
health checker

http://cdc.gov/vsafe

Overview of v-safe monitoring of Pfizer-BioNTech COVID-19 vaccine for younger adolescents

- On May 11, 2021, v-safe age limits expanded to allow registration down to 12 years of age at dose 1
- As of May 31 (5 am), 46,533 persons age 12–15 years were registered and submitted at least one health check-in during days 0–7 after dose 1 Pfizer-BioNTech COVID-19 vaccination

Pfizer-BioNTech monitoring in v-safe: Younger adolescents compared to older adolescents/young adults* (data thru May 31, 2021)



* Includes participants who completed at least one survey in the first week after dose 1 of Pfizer-BioNTech COVID-19 vaccine

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

CDC + FDA

VAERS

Vaccine Adverse Event Reporting System

http://vaers.hhs.gov

VAERS

VAERS accepts all reports from everyone regardless of the plausibility of the vaccine causing the event or the clinical seriousness of the event

key strengths

- Rapidly detects potential safety problems
- Can detect rare adverse events

key limitations

- Inconsistent quality and completeness of information
- Reporting biases
- Generally, cannot determine cause and effect

Reports to VAERS after Pfizer-BioNTech COVID-19 vaccination: persons aged 12–15 years vs. 16–25 years* (data thru May 31, 2021)

Ages	N	Non-serious AEs (%)	Serious AEs‡,§ (%)
12–15 years old	1,497	1,449 (96.8)	48 (3.2)
16–25 years old† (for comparison)	10,095	9,439 (93.5)	656 (6.5)

- 12–15 years old: 3.26 million doses administered (May 10 thru May 31, 2021)
- 16–25 years old: 19.84 million doses administered (December 14, 2020, thru May 31, 2021)

* Data as of June 2, 2021, for reports with vaccination date and receipt date May 10 through May 31, 2021

† Data as of June 2, 2021, for reports with vaccination date and receipt date December 14, 2020, through May 31, 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 0 reports of death in the 12–15-year-old age group and 14 reports of death in the 16–25-year-old age group

Most commonly reported adverse events to VAERS after Pfizer-BioNTech COVID-19 vaccination* (data thru May 31, 2021)

12–15 years old* (N= 1,497)

Adverse event‡	n (%)
Dizziness	416 (27.8)
Syncope	321 (21.4)
Nausea	192 (12.8)
Pallor	150 (10.0)
Loss of consciousness	142 (9.5)
Headache	134 (9.0)
Hyperhidrosis	132 (8.8)
Vomiting	119 (7.9)
Fatigue	79 (5.3)
Fall	77 (5.1)

16–25 years old† (N= 10,095)

(for comparison)

Adverse event‡	n (%)
Dizziness	2,249 (22.3)
Headache	1,798 (17.8)
Pyrexia	1,585 (15.7)
Nausea	1,577 (15.6)
Fatigue	1,367 (13.5)
Chills	1,307 (12.9)
Pain	1,254 (12.4)
Syncope	980 (9.7)
Hyperhidrosis	726 (7.2)
Vomiting	723 (7.2)

- 12–15 years old: 3.26 million doses administered (May 10 thru May 31, 2021)
- 16–25 years old: 19.84 million doses administered (December 14, 2020, thru May 31, 2021)

* Data as of June 2, 2021, for reports with vaccination date and receipt date May 10 through May 31, 2021

† Data as of June 2, 2021, for reports with vaccination date and receipt date December 14, 2020, through May 31, 2021

‡ Adverse events are not mutually exclusive

Myocarditis and pericarditis following mRNA vaccination

Preliminary myocarditis/pericarditis reports to VAERS following mRNA vaccination with dose number documented (data thru May 31, 2021)

Manufacturer	Myocarditis/pericarditis reports after dose 1	Myocarditis/pericarditis reports after dose 2
Pfizer-BioNTech (488 total reports)	116	372
Moderna (301 total report)	100	201
	216 Total reports after dose 1	573 Total reports after dose 2

- Includes total preliminary reports identified through VAERS database searches for reports with myocarditis/pericarditis MedDRA* codes and pre-screened VAERS reports with signs and symptoms consistent with myocarditis/pericarditis (and with dose number documented)
  - Follow-up, medical record review, application of CDC working case definition, and adjudication is ongoing or pending

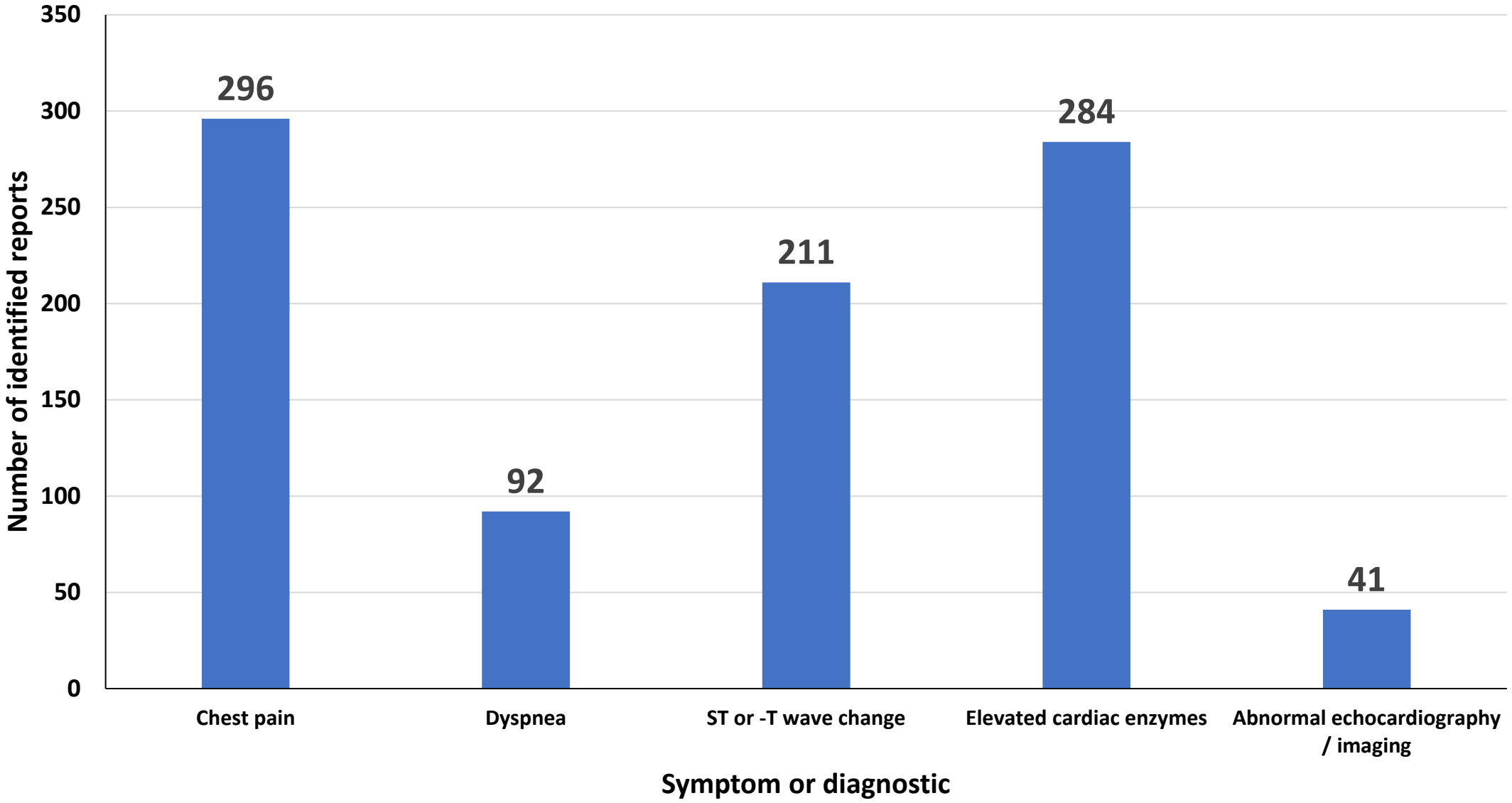
* Medical Dictionary for Regulatory Activities https://www.meddra.org/

Characteristics of preliminary myocarditis/pericarditis reports to VAERS following mRNA vaccination (data thru May 31, 2021)

Characteristics	Dose 1 (n=216)	Dose 2 (n=573)
Median age, years (range)	30 (12–94)	24 (14–87)
Median time to symptom onset, days (range)	3 (0–33)	2 (0–80)
Sex (%)		
Male	140 (65)	455 (79)
Female	73 (34)	113 (20)
Not reported/not available	3 (1)	5 (1)

* Includes total reports identified through VAERS database searches for reports with myocarditis/pericarditis MedDRA codes and pre-screened VAERS reports with signs and symptoms consistent with myocarditis/pericarditis (and with dose number documented); Follow-up, medical record review, application of CDC working case definition, and adjudication is ongoing or pending

Symptoms and diagnostics of preliminary myocarditis/pericarditis reports under review (limited to ≤30 years old) (N=475)



Outcomes of preliminary myocarditis/pericarditis cases reported to VAERS in persons ≤30 years old (N=475) (data thru May 31, 2021)

- 226 (of 475) case reports meet CDC working case definition; follow-up and review are in progress for remaining reports
- 285 (of 475) case reports had known disposition at time of report review
  - 270 discharged; 15 still hospitalized (3 in intensive care unit*)
    - Of 270 discharged
      - 246 (91%) to home
      - 3 to another facility (e.g., rehabilitation facility)
      - 21 did not specify
  - Of 270 discharged, recovery status was known for 221
    - **180 (81%) had full recovery of symptoms**
    - 41 (19%) had ongoing signs or symptoms or unknown status

* One patient with significant comorbidities and BMI>40; one patient with positive stool culture (Campylobacter)

Preliminary myocarditis/pericarditis reports to VAERS following dose 2 mRNA vaccination, Exp. vs. Obs. (data thru May 31, 2021)

Age groups	Doses admin	Crude reporting rate*	Expected†,‡ Myocarditis/ pericarditis cases	Observed† Myocarditis/ pericarditis reports
12–15 yrs	134,041	22.4	0–1	2
16–17 yrs	**2,258,932**	**35.0**	**2–19**	**79**
18–24 yrs	**9,776,719**	**20.6**	**8–83**	**196**
25–39 yrs	26,844,601	5.0	23–228	124
40–49 yrs	19,576,875	3.0	17–166	51
50–64 yrs	36,951,538	1.3	31–314	39
65+ yrs	42,124,078	0.9	36–358	26
NR	—	—	—	11

8.8% of doses admin

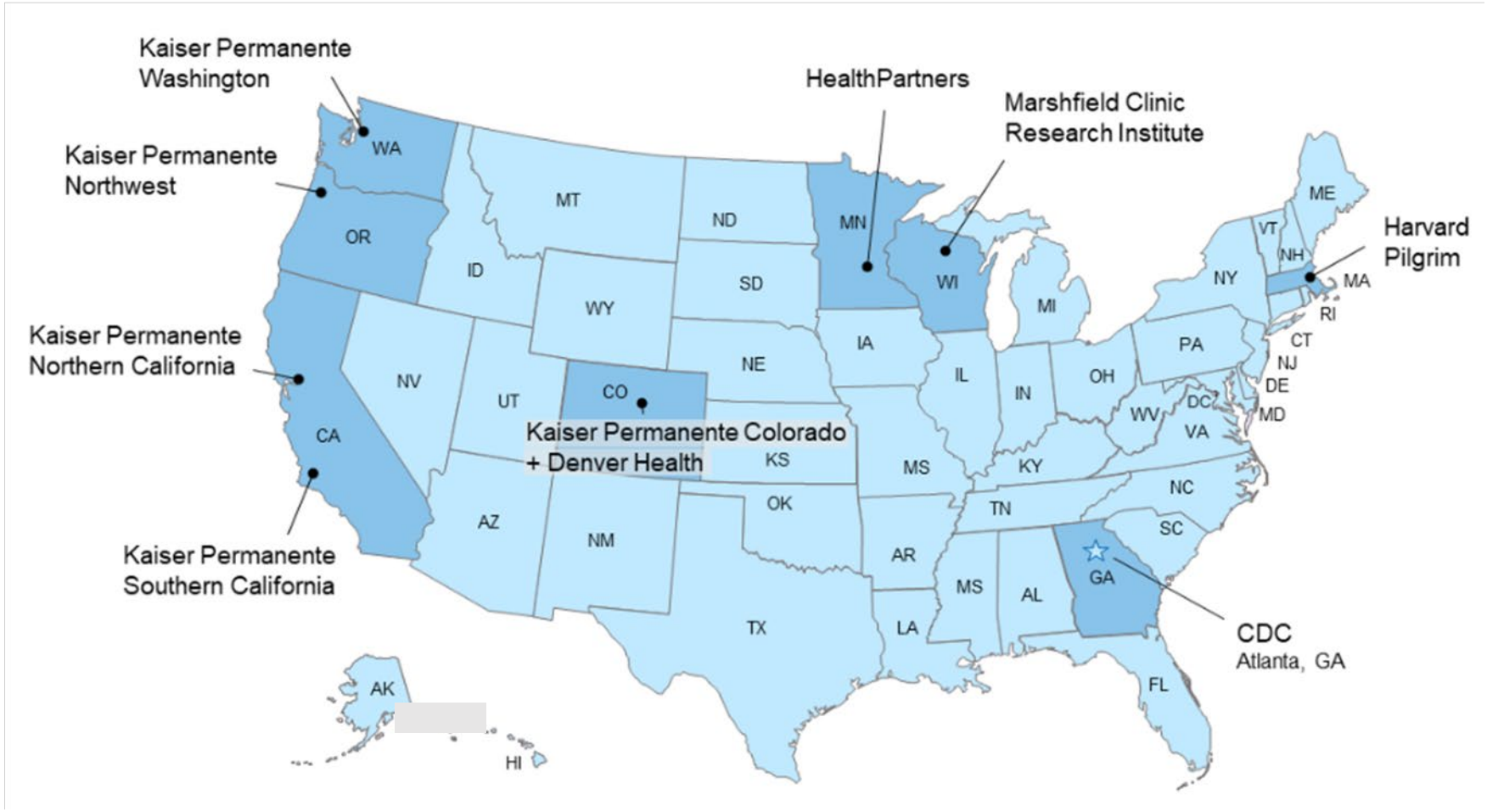
n=277 reports

52.5% of total reports

* Per million doses administered; † Assumes a 31-day post-vaccination observation window; 528 reports with symptom onset within 30 days of vaccination shown; ‡ Based on Gubernot et al. U.S. Population-Based background incidence rates of medical conditions for use in safety assessment of COVID-19 vaccines. Vaccine. 2021 May 14:S0264-410X(21)00578-8.

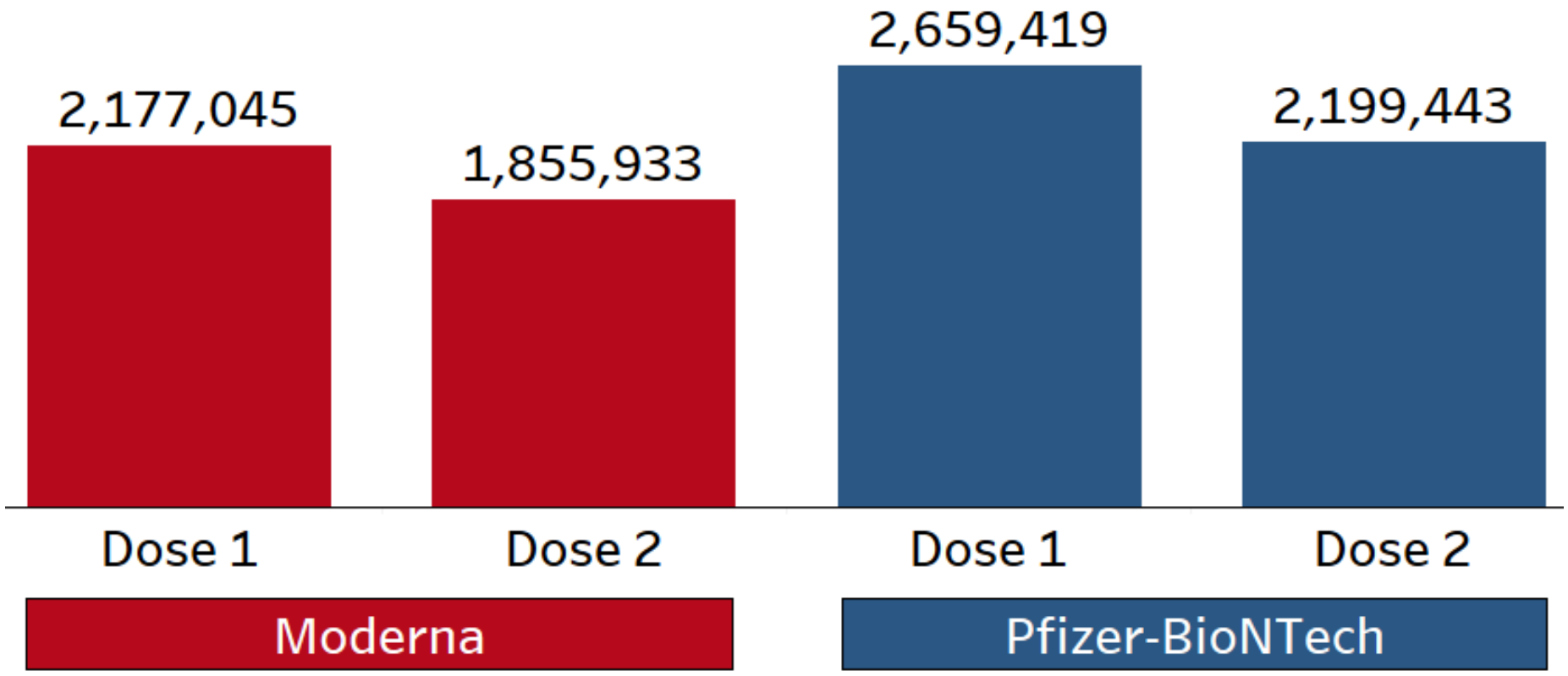
VSD

Vaccine Safety Datalink



- **9** participating integrated healthcare organizations
- Data on over **12 million** persons per year

COVID-19 vaccine doses administered in the VSD
(thru May 29, 2021)



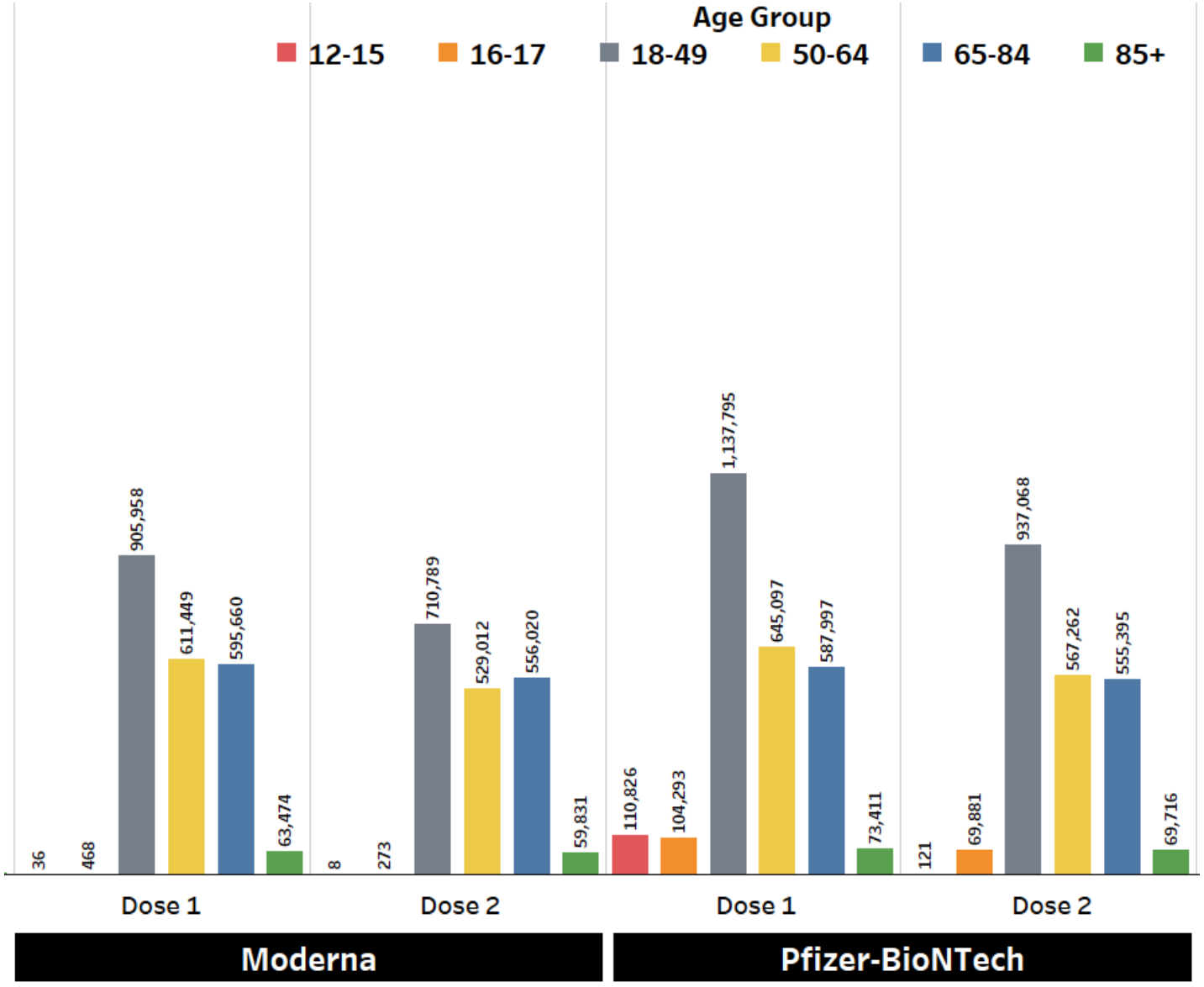
4,032,978
total doses

4,858,862
total doses

COVID-19 vaccine doses administered by age group in the VSD
(thru May 29, 2021)

Pfizer-BioNTech doses

- 12–15-year-olds
  - 110,826 first doses
  - 121 second doses
- 16–17-year-olds
  - 104,293 first doses
  - 69,881 second doses



Outcome events in the VSD in 21-day risk interval after either dose of any mRNA vaccine compared with outcome events in vaccinated comparators on the same calendar days

(thru May 29, 2021)

Pre-specified outcome event	Events in risk interval	Adj Rate Ratio*	95% CI	Signal
Acute disseminated encephalomyelitis	2	.	0.07– .	no
Acute myocardial infarction	560	1.00	0.86–1.17	no
Appendicitis	608	0.82	0.71–0.95	no
Bell's palsy	454	1.02	0.85–1.21	no
Cerebral venous sinus thrombosis	4	1.07	0.17–9.36	no
Disseminated intravascular coagulation	26	0.62	0.33–1.19	no
Encephalitis / myelitis / encephalomyelitis	15	1.06	0.38–3.41	no
Guillain-Barré syndrome	10	0.63	0.20–2.14	no
Stroke, hemorrhagic	224	0.89	0.70–1.14	no
Stroke, ischemic	944	0.97	0.86–1.10	no
Immune thrombocytopenia	43	1.04	0.58–1.92	no
Kawasaki disease	0	0.00	0.00–6.53	no
Myocarditis / pericarditis	**60**	**0.94**	**0.59–1.52**	**no**
Seizures	233	1.01	0.79–1.31	no
Transverse myelitis	2	0.50	0.04–15.32	no
Thrombotic thrombocytopenic purpura	5	2.04	0.33–17.36	no
Thrombosis with thrombocytopenia syndrome (TTS)	60	0.76	0.49–1.18	no
Venous thromboembolism	530	1.06	0.90–1.25	no
Pulmonary embolism	459	1.00	0.84–1.19	no

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

Myocarditis/pericarditis events in VSD in 16-39-year-olds in the 21-day risk interval compared with outcome events in vaccinated comparators on the same calendar days

(thru May 29, 2021)

Vaccine (dose #)	Events in risk interval	Adj Rate Ratio*	95% CI
Pfizer-BioNTech (both doses)	8	0.49	0.15–1.81
Pfizer-BioNTech (dose 1)	1	0.12	0–1.06
Pfizer-BioNTech (dose 2)	7	0.84	0.25–3.01
Moderna (both doses)†	14	4.07	1–27.59
Moderna (dose 1)	3	1.74	0.23–17.27
Moderna (dose 2)	**11**	**ne‡**	**3.61– .**

* Adjusted for VSD site, 5-year age group, sex, race/ethnicity, and calendar date
† Moderna COVID-19 vaccine is not authorized in persons aged <18 years
‡ ne=not estimable

Myocarditis/pericarditis incidence in VSD in 21-day risk interval, ages 16-39 years old (data thru May 29, 2021)

Vaccine(s) (dose #)	Cases	Doses admin	Rate per million doses (95% CI)
mRNA (both doses)	22	2,546,874	8.6 (5.4–13.1)
mRNA (dose 1)	4	1,428,872	2.8 (0.8–7.2)
mRNA (dose 2)	18	1,118,002	16.1 (9.5–25.4)
Pfizer-BioNTech (dose 1)	1	846,765	1.2 (0.0–6.6)
Pfizer-BioNTech (dose 2)	7	671,899	10.4 (4.2–21.5)
Moderna (dose 1)	3	582,107	5.2 (1.1–15.1)
Moderna (dose 2)	11	446,103	24.7 (12.3–44.1)

Summary

Summary (as of May 31, 2021)

- Initial safety findings from Pfizer-BioNTech COVID-19 vaccination of 12-15-year-olds from v-safe and VAERS surveillance are consistent with results from pre-authorization clinical trials
- Analysis of VAERS preliminary reports of myocarditis/pericarditis is in progress, including follow-up to obtain medical records, complete reviews, apply CDC working case definition, and adjudicate cases
- Preliminary findings suggest:
  - Median age of reported patients is younger and median time to symptom onset is shorter among those who developed symptoms after dose 2 vs. dose 1
  - Predominance of male patients in younger age groups, especially after dose 2
  - Observed reports > expected cases after dose 2 (16–24 years of age)
  - Limited outcome data suggest most patients (at least 81%) had full recovery of symptoms
- Early VSD data also suggest more cases after dose 2 vs. dose 1; rate ~16 cases per million 2nd doses
- ACIP meeting scheduled for June 18, 2021: update data, further evaluate myocarditis following mRNA COVID-19 vaccination, and assess benefit-risk balance

CDC educational materials*

Myocarditis and Pericarditis Following mRNA COVID-19 Vaccination

Updated May 27, 2021 Languages Print

What You Need to Know

- More than 165 million people have received at least one dose of COVID-19 vaccine in the United States, and CDC continues to monitor the safety of COVID-19 vaccines for any health problems that happen after vaccination.
- Since April 2021, there have been increased reports to the Vaccine Adverse Event Reporting System (VAERS) of cases of inflammation of the heart—called myocarditis and pericarditis—happening after mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna) in the United States.
- These reports are rare, given the number of vaccine doses administered, and have been reported after mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna), particularly in adolescents and young adults.
- CDC and its partners are actively monitoring these reports, by reviewing data and medical records, to learn more about what happened and to see if there is any relationship to COVID-19 vaccination.
- Most patients who received care responded well to medicine and rest and quickly felt better.

Clinical Considerations: Myocarditis and Pericarditis after Receipt of mRNA COVID-19 Vaccines Among Adolescents and Young Adults

Summary

Since April 2021, increased cases of myocarditis and pericarditis have been reported in the United States after mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna), particularly in adolescents and young adults. There has not been a similar reporting pattern observed after receipt of the Janssen COVID-19 Vaccine (Johnson & Johnson).

In most cases, patients who presented for medical care have responded well to medications and rest and had prompt improvement of symptoms. Reported cases have occurred predominantly in male adolescents and young adults 16 years of age and older. Onset was typically within several days after mRNA COVID-19 vaccination, and cases have occurred more often after the second dose than the first dose. CDC and its partners are investigating these reports of myocarditis and pericarditis following mRNA COVID-19 vaccination.

CDC continues to recommend COVID-19 vaccination for everyone 12 years of age and older given the risk of COVID-19 illness and related, possibly severe complications, such as long-term health problems, hospitalization, and even death.

* CDC: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myocarditis.html and https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html

Acknowledgments

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

Centers for Disease Control and Prevention

COVID-19 Vaccine Task Force
Vaccine Safety Team
Immunization Safety Office
Division of Healthcare Quality Promotion
Clinical Immunization Safety Assessment Project
Vaccine Safety Datalink

Food and Drug Administration

Center for Biologics Evaluation and Research

CDC vaccine safety monitoring

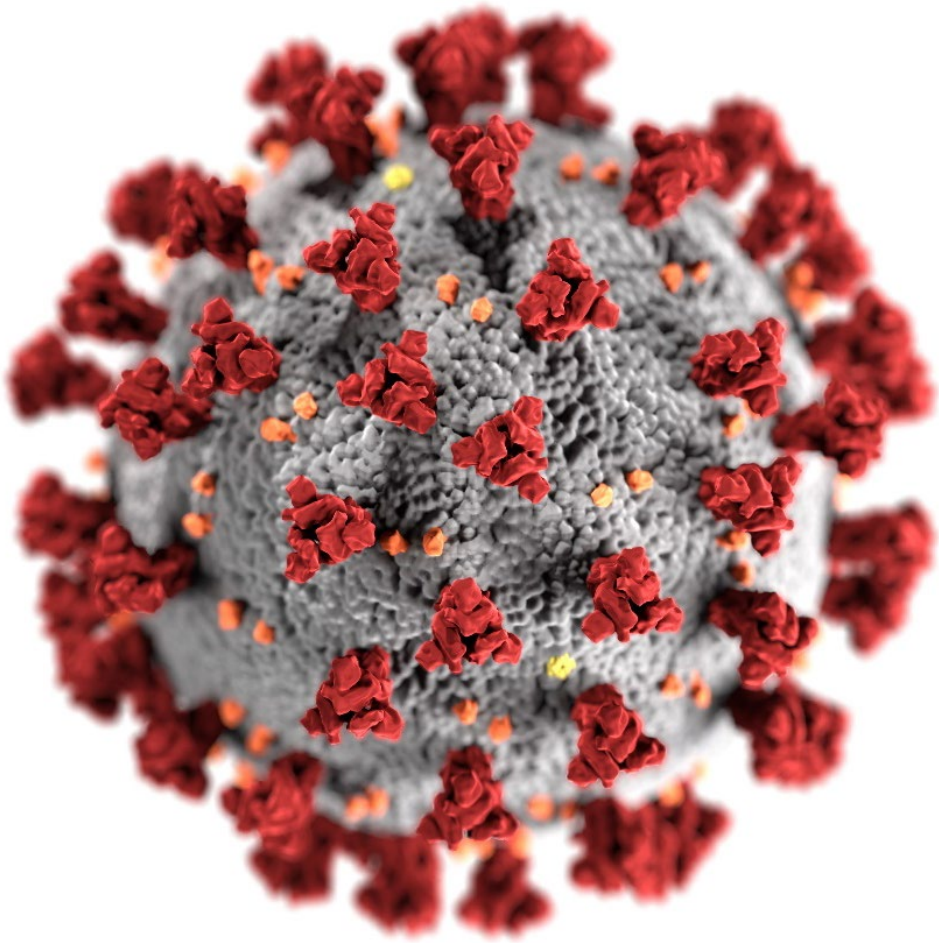
- Authorized COVID-19 vaccines are being administered under **the most intensive vaccine safety monitoring effort in U.S. history**
- Strong, complementary systems are in place—both new and established

v-safe	VAERS	VSD	CISA Project

Full list of U.S. COVID-19 vaccine safety monitoring systems

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety.html

Thank you!



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

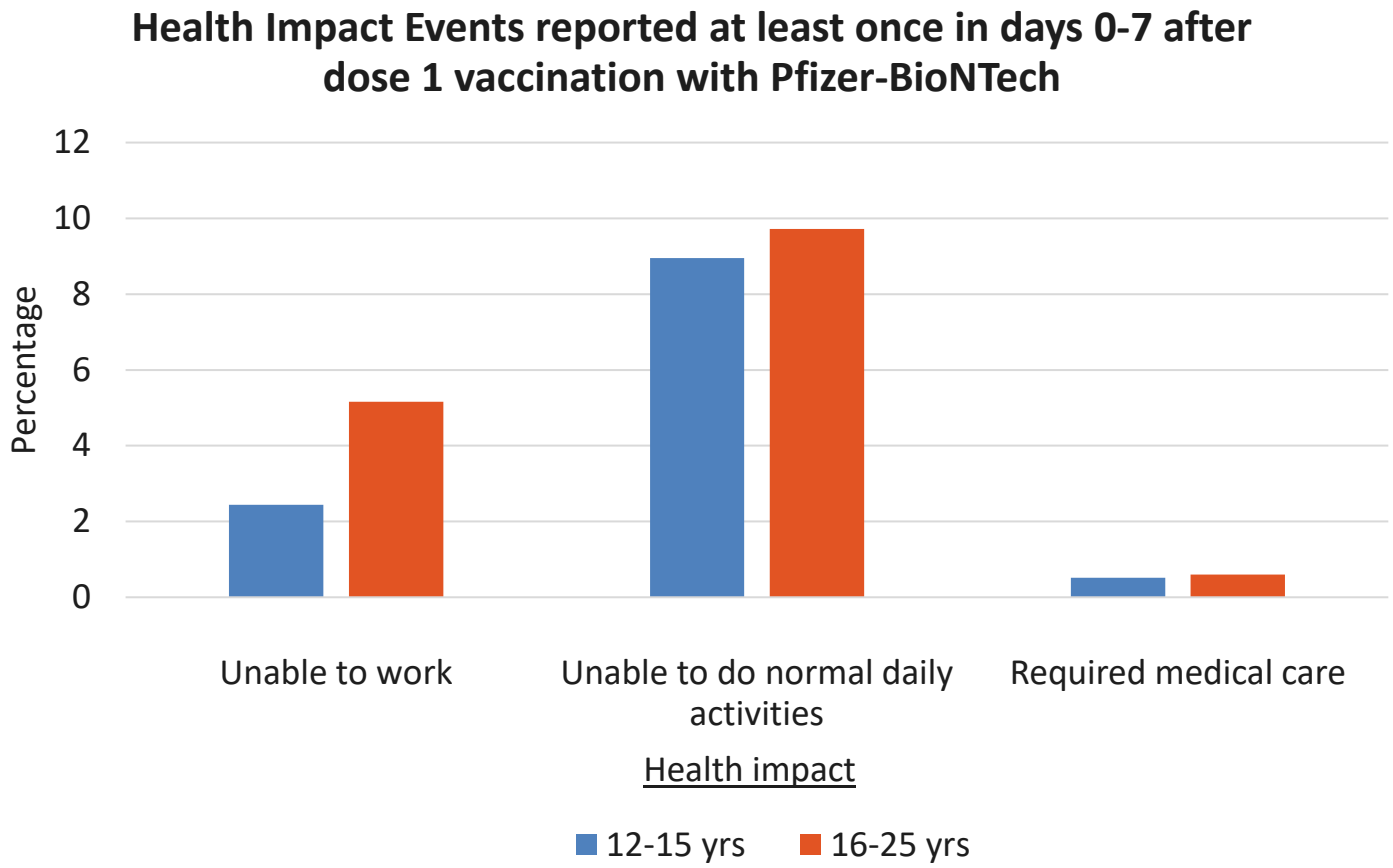
The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Timeline: U.S. adolescent COVID-19 vaccination

- December 2020: FDA issues Emergency Use Authorizations (EUAs) for two COVID-19 vaccines*
  - Pfizer-BioNTech COVID-19 vaccine for persons aged ≥16 years
  - Moderna COVID-19 vaccine for persons aged ≥18 years
- December 2020: CDC publishes ACIP interim recommendations for use of Pfizer-BioNTech and Moderna COVID-19 vaccines for age groups indicated in EUAs†
- February 2021: FDA issues EUA for Janssen COVID-19 vaccines for persons aged ≥18 years*
- March 2021: CDC published ACIP interim recommendations for use of Janssen COVID-19 vaccine for age group indicated in EUA†
- May 2021:
  - FDA expanded the EUA for the Pfizer-BioNTech COVID-19 vaccine to include adolescents aged 12–15 years*
  - ACIP publishes interim recommendations for use of the Pfizer-BioNTech COVID-19 vaccine in adolescents aged 12–15 years†

* FDA: COVID-19 Vaccines https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines
† CDC: COVID-19 ACIP Vaccine Recommendations https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html

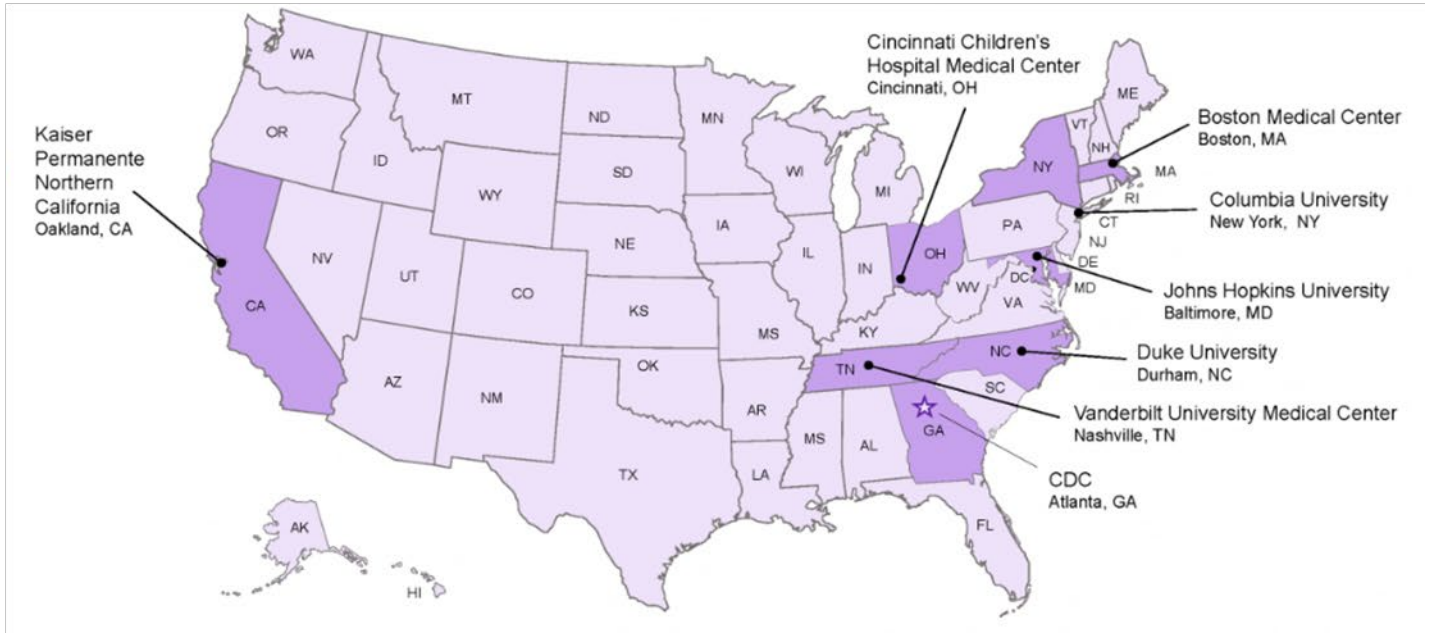
Pfizer-BioNTech monitoring in v-safe: Younger adolescents compared to older adolescents/young adults* (data thru May 31, 2021)



* Includes participants who completed at least one survey in the first week after dose 1 of Pfizer-BioNTech COVID-19 vaccine

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

CDC working case definition for acute myocarditis

Acute Myocarditis

Clinical myocarditis

Probable Case

Presence of at least 1 new or worsening of the following clinical symptoms:

- chest pain/pressure/discomfort
- dyspnea/shortness of breath/pain with breathing, or
- palpitations

OR, infants and children <12 years of age may instead present with at least 2 of:

- irritability
- vomiting
- poor feeding
- tachypnea
- lethargy

AND

At least 1 new finding of:

- troponin level above upper limit of normal (any type of troponin),
- abnormal electrocardiogram (ECG or EKG) or rhythm monitoring findings consistent with myocarditis*, or
- abnormal cardiac function or wall motion abnormalities on echocardiogram or cardiac magnetic resonance imaging (cMRI).†

AND

- No other identifiable cause of the symptoms and findings

Confirmed Case

Presence of at least 1 new or worsening of the following clinical symptoms:

- chest pain/pressure/discomfort
- dyspnea/shortness of breath/pain with breathing, or
- palpitations

OR, infants and children <12 years of age may instead present with at least 2 of:

- irritability
- vomiting
- poor feeding
- tachypnea
- lethargy

AND

Troponin level above upper limit of normal (any type of troponin)

AND

At least one new finding of:

- Histopathologic confirmation of myocarditis§, or
- cMRI findings consistent with myocarditis¶

AND

- No other identifiable cause of the symptoms and findings

CDC working case definition for acute pericarditis

Presence of at least TWO new or worsening of the following clinical features:

- acute chest pain*
- pericardial rub on exam,
- new ST-elevation or PR-depression on EKG, or
- new or worsening pericardial effusion on echocardiogram or MRI

*typically described as pain made worse by lying down, deep inspiration, or cough and relieved by sitting up or leaning forward, although other types of chest pain may occur.

Notes:

1. Autopsy cases may be classified as pericarditis on basis of meeting histopathologic criteria of the pericardium