CDC/IDSA COVID-19 Clinician Call

June 26, 2021

Welcome & Introduction

Dana Wollins, DrPH, MGC
Vice President, Clinical Affairs & Guidelines
IDSA

- 69th in a series of weekly calls, initiated by CDC as a forum for information sharing among frontline clinicians caring for patients with COVID-19
- The views and opinions expressed here are those of the presenters and do not necessarily reflect the official policy or position of the CDC or IDSA. Involvement of CDC and IDSA should not be viewed as endorsement of any entity or individual involved.
- This webinar is being recorded and can be found online at www.idsociety.org/cliniciancalls.

TODAY'S CALL:

Myocarditis after COVID-19 mRNA Vaccine

Plus Vaccine Q&A

Myocarditis and Myopericarditis after COVID-19 Vaccination: A Case Series

Judith A. Guzman-Cottrill, DO

Professor of Pediatrics, Division of Infectious Diseases
Oregon Health & Science University School of Medicine

Overview of Myocarditis and Pericarditis

Matt Oster, MD, MPH

Director, Children's Cardiac Outcomes Research Program
Sibley Heart Center Cardiology, Children's Healthcare of Atlanta
Medical Officer, CDC Center on Birth Defects & Developmental Disabilities
Centers for Disease Control and Prevention, COVID-19 Response

COVID-19 Vaccine Safety Updates

Tom Shimabukuro, MD, MPH, MBA

Captain, U.S. Public Health Service
Deputy Director, Immunization Safety Office
Centers for Disease Control and Prevention

COVID-19 mRNA Vaccines in Adolescents and Young Adults: Benefit-Risk Discussion

Amanda Cohn, MD

Chief Medical Officer, COVID-19 Task Force
Chief Medical Officer, National Center for Immunization & Respiratory Diseases
Captain, U.S. Public Health Service
Centers for Disease Control and Prevention

Question?
Use the “Q&A” Button

Comment?
Use the “Chat” Button

Myocarditis and Myopericarditis after COVID-19 Vaccination: A Case Series

CDC/IDSA COVID-19 Clinician Call
June 26, 2021

Judy Guzman-Cottrill, DO
Professor of Pediatrics
Division of Infectious Diseases
Oregon Health & Science University
Portland, Oregon

Objectives

1. Briefly discuss recent case series in the journal Pediatrics summarizing 7 adolescents who developed myocarditis after receipt of mRNA COVID-19 vaccination.
2. Discuss why this case series was important to quickly publish

Conflict disclosure

- No financial conflicts of interest
- Pediatric infectious disease physician
- Mother of a 16-year-old boy who is fully vaccinated against COVID, and a 13-year-old girl who received dose #2 last week

Prepublication Release

PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Symptomatic Acute Myocarditis in Seven Adolescents Following Pfizer-BioNTech COVID-19 Vaccination

Mayme Marshall, MD, Ian D. Ferguson, MD, Paul Lewis, MD, MPH, Preeti Jaggi, MD, Christina Gagliardo, MD, James Steward Collins, MD, Robin Shaughnessy, MD, Rachel Caron, BA, Cristina Fuss, MD, Kathleen Jo E. Corbin, MD, MHS, Leonard Emuren, MBBS, PhD, Erin Faherty, MD, E. Kevin Hall, MD, Cecilia Di Pentima, MD, MPH, Matthew E. Oste, MD, MPH, Elijah Paintsil, MD, Saira Siddiqui, MD, Donna M. Timchak, MD, Judith A. Guzman-Cottrill, DO

Released online, ahead of print June 4, 2021

My Co-Authors (5 hospitals)

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- **Spectrum Health, Grand Rapids, MI**
  - Adult Interventional Cardiology

Introduction

- The FDA EUA for Pfizer-BioNTech COVID-19 mRNA vaccine was revised to include children 12 years of age and older on 5/10/2021
- Around that same time, media and case reports suggested a possible correlation of COVID-19 mRNA vaccination and myocarditis:
  - United States military
  - Israeli cohort, identified a male predominance
  - 56-year-old man with previous COVID-19
  - 39-year-old man with no history of COVID-19
- Our case series includes 7 healthy male adolescents with acute symptomatic myocarditis, all within four days after the second dose of Pfizer-BioNTech COVID-19 vaccine in April or May, 2021

Demographics, Symptoms

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Age (years)	16	19	17	18	17	16	14
Sex	M	M	M	M	M	M	M
Weight (kg)	68	68	71	69	64	71	92
BMI	24	19	21	21	19	22	28
Exposure to COVID-19	No	No	No	No	No	No	No
Post-vaccine symptom onset (days)	2	3	2	2	4	3	2
Hospital LOS (days)	6	2	2	4	5	3	4
ICU LOS (days)	4	None	None	4	5	2	2
Chest pain	X	X	X	X	X	X	X
Other pain	Arm	Myalgias	Arm		Bilateral arm, abdominal		
Fever	X	X		X	X		X
Fatigue	X	X		X			
Other	N/V, HA	Weakness	Bilateral arm numbness paresthesia	N	Palpitations, shortness of breath, N/V, anorexia	Shortness of breath	Shortness of breath

Diagnostics: Time of Admission

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Troponin	2.59ng/mL (I)	232ng/L (T)	5.55ng/mL (I)	1.09ng/mL (T)	3.2ng/mL (T)	0.66ng/mL (T)	22.1ng/mL (I)
BNP	428 pg/mL	--	376 pg/mL	--	978 pcg/mL	149 pcg/mL	108 pcg/mL
WBC (1000/cu mm)	6.97	8.69	11.8	12.6	16.3	5.0	8.11
ALC (1000/cu mm)	1.69	1.39	2.13	2.3	4.1	1.4	1.05
ANC (1000/cu mm)	4.65	5.93	7.46	9.5	9.8	2.8	4.73
Plt (1000/cu mm)	198	208	231	236	297	189	208
AST (u/L)	54	29	41	82	150	59	87
ALT (u/L)	30	14	33	20	46	22	38
Ferritin (ug/L)	70	--	90	103	347	65	84
CRP (mg/dL, nl < 1.0)	0.99	6.7	2.5	12.7	18.1	1.5	7.7
ESR (mm/hr)	18	13	6	40	38	3	10

Diagnostics: Other Findings

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
COVID-19 PCR	Neg	Neg	Neg	Neg	Neg	Neg	Neg
COVID-19 spike Ab	--	--	Pos	Pos	Pos	Pos	--
COVID-19 nucleocapsid Ab	Neg	--	Neg	Neg	Neg	Neg	Neg
Resp pathogen panel PCR*	Neg	Neg	Neg	Neg	Neg	Neg	Neg
Adenovirus	Neg sPCR	--	Neg serology	Neg sPCR	Neg sPCR	--	Neg sPCR
Enterovirus	Neg sPCR	--	Neg serology	Neg sPCR	Neg sPCR	Neg sPCR	Neg sPCR
CMV	Neg sPCR	--	Neg serology	Neg sPCR	Neg sPCR	Neg sPCR	Neg serology
EBV	--	--	Neg serology	Neg sPCR	Neg sPCR	Neg IgM Pos IgG	Neg serology
Other diagnostics			Neg Parvovirus, *Bartonella*, and Lyme serology		Neg Parvovirus and *Bartonella* serology, HHV-6 sPCR	Neg Lyme serology, *Mycoplasma* and Parvovirus sPCR	Neg Parvovirus IgM, pos Parvovirus IgG, neg *Mycoplasma* PCR (throat swab)

*Respiratory Panel includes PCR for Adenovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Metapneumovirus (human), Rhinovirus/Enterovirus, Influenza A, Influenza B, Parainfluenza 1, Parainfluenza 2, Parainfluenza 3, Parainfluenza 4, Respiratory Syncytial Virus, Bordetella parapertussis, Bordetella pertussis, Chlamydophila pneumonia, Myocoplasma pneumonia.

Diagnostics: Cardiographics

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Echocardiogram	Normal	Normal	Borderline basal lateral and basal posterior strain	Normal	Normal	Normal	Mildly depressed RV and LV function
ECG	AV dissociation with junction escape rhythm, ST elevation	ST elevation (diffuse)	ST elevation (diffuse), T wave abnormality	ST elevation	Sinus bradycardia, T wave abnormality	ST elevation (diffuse)	ST elevation, low voltage of extremity leads
Cardiac MRI	LGE, myocardial edema, axillary adenopathy	LGE, myocardial edema	LGE, myocardial edema	Myocardial edema, hyperemia, mild mitral regurgitation	LGE, no myocardial edema	LGE, diffuse myocardial edema	LGE, myocardial edema, hyperemia

LGE: Late gadolinium enhancement

Summary of Therapeutics

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Oxygen	None	None	None	None	None	None	LFNC - comfort
Vasoactive medications or Inotropic support	None	None	None	None	None	None	None
Anti-inflammatory agents and other relevant medications	NSAID (ketorolac) IVIG Methylprednisolone Prednisone Famotidine	NSAID (ketorolac) Colchicine Aspirin	NSAID (ibuprofen) Famotidine	NSAID (ibuprofen) IVIG Methylprednisolone Prednisone	NSAID (ibuprofen) IVIG Methylprednisolone Prednisone Aspirin	IVIG Prednisone	NSAID (ketorolac, naproxen) Famotidine Furosemide

Our Discussion

- Temporal relationship of clinical myocarditis following second Pfizer-BioNTech COVID-19 vaccine in adolescent males aged 14-19 years of age
- No patient had acute COVID-19 infection
- 4 patients had detectable SARS-CoV-2 spike antibodies (component of vaccine)
- 6/6 patients had negative SARS-CoV-2 nucleocapsid antibody (suggesting no prior SARS-CoV-2 infection)
- None of our patients were critically ill, and all responded quickly to treatment; however, all patients required hospitalization for cardiac monitoring
- Findings consistent with a known male preponderance of myocarditis

Limitations

- Compiled cases through personal communications between colleagues rather than a systematic surveillance system
- Alternative etiologies including idiopathic and other infectious etiologies were not thoroughly excluded
- There was not a systematic diagnostic evaluation for possible etiologies
- Cardiac biopsy was not performed on any patients

Objective #2

Why was this important to quickly publish?

- Our patients' presentations were all so similar, we were concerned this might be a very early safety signal – this was a way to amplify our concerns
- Early recognition of chest pain, elevated troponin, and ECG abnormalities following COVID-19 vaccination may prevent invasive procedures (i.e., cardiac catheterization)
- To recommend that these patients undergo a comprehensive workup to exclude other causes
- All authors concluded that the benefits of vaccination significantly exceed possible risks, and we encourage following the guidance of the CDC ACIP
- To highlight importance of promptly reporting all cases to VAERS

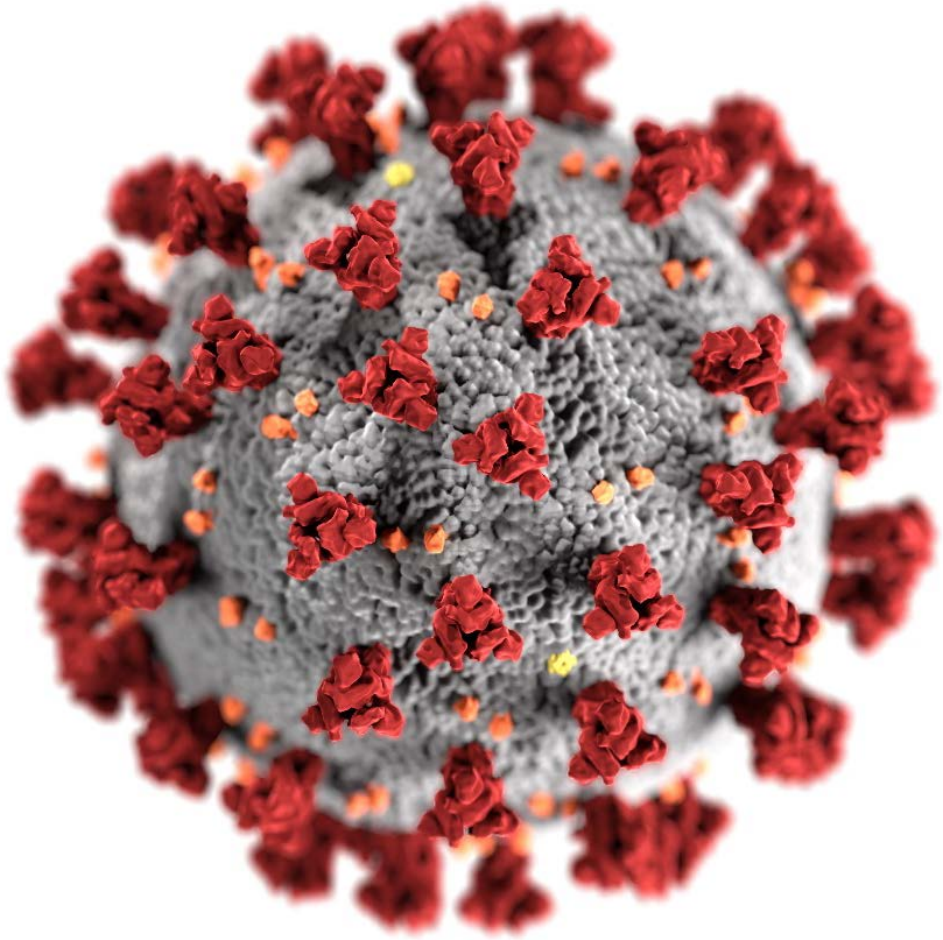
Thank You

Overview of Myocarditis and Pericarditis

IDSA

June 26, 2021

Matthew Oster, MD, MPH
CDC COVID-19 Vaccine Task Force



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Disclaimer

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- Mention of a product or company name is for identification purposes only and does not constitute endorsement by CDC

Myocarditis diagnosis

Probable

1. Symptoms
   - Chest pain/pressure/discomfort
   - Dyspnea/shortness of breath
   - Palpitations
2. Abnormal testing
   - Elevated troponin
   - Electrocardiogram (ECG or EKG) findings
   - Decreased function on echo or MRI
   - MRI findings consistent with myocarditis
3. No other identified cause

Confirmed

1. Symptoms
   - Chest pain/pressure/discomfort
   - Dyspnea/shortness of breath
   - Palpitations
2. Abnormal testing
   - Biopsy
   - Elevated Troponin AND MRI findings consistent with myocarditis
3. No other identified cause

Cases with individuals who lack the listed symptoms but who meet other criteria may be classified as subclinical myocarditis (probable or confirmed)

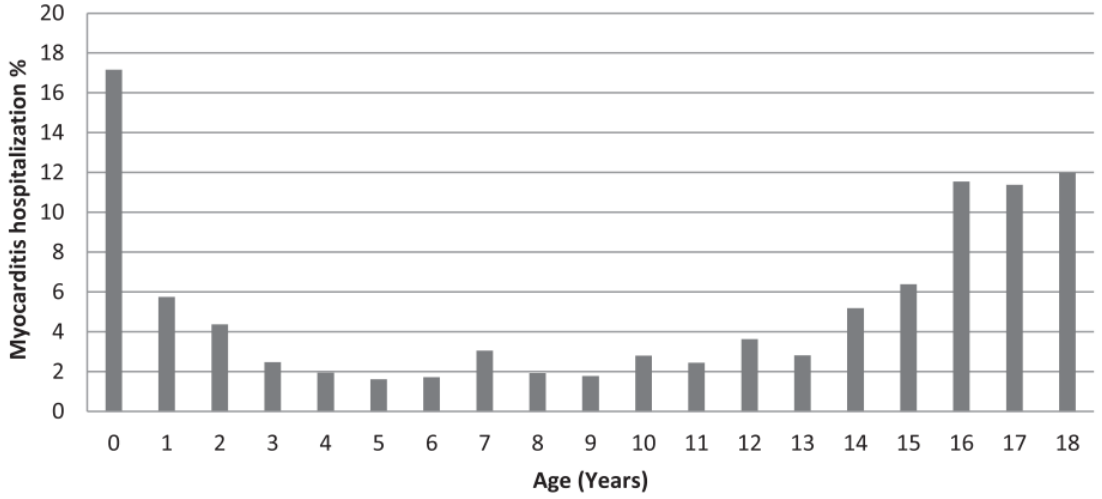
Pericarditis diagnosis

- Must have 2 of:
  - Chest pain
  - Pericardial rub audible by stethoscope
  - Abnormal ECG findings (New ST-elevation or PR-depression)
  - Pericardial effusion on echocardiogram or MRI

Adler et al. *Eur Heart J*. 2015.

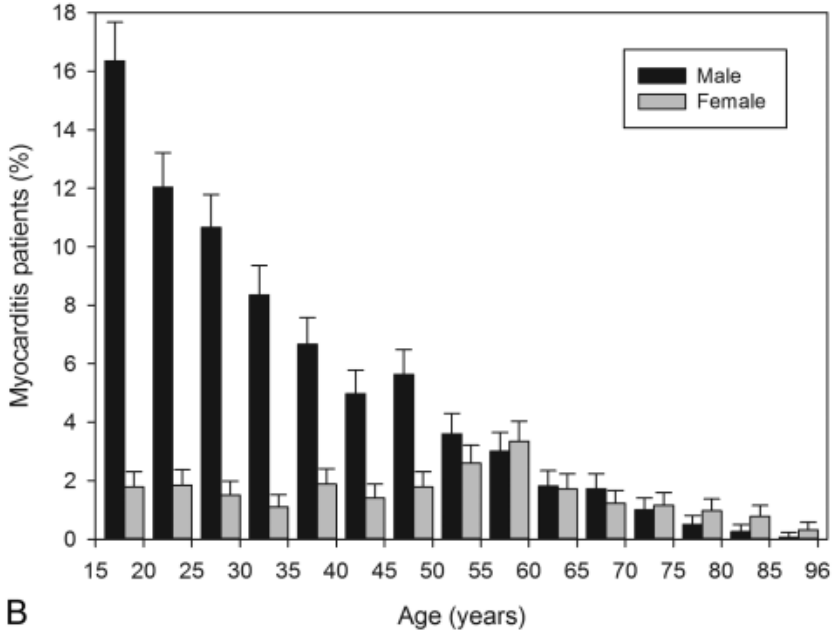
Epidemiology of myocarditis

- Children
  - Annual incidence 0.8 per 100,000
    - In 15-18yo, 1.8 per 100,000 in 2015-2016
  - 66% male
  - Median LOS 6.1 days



Vasudeva et al. *American J Cardiology.* 2021.

- Adults
  - Gradual decrease in incidence with age
  - 76% male



Kyto et al. *Heart*. 2013.

Causes of traditional myocarditis

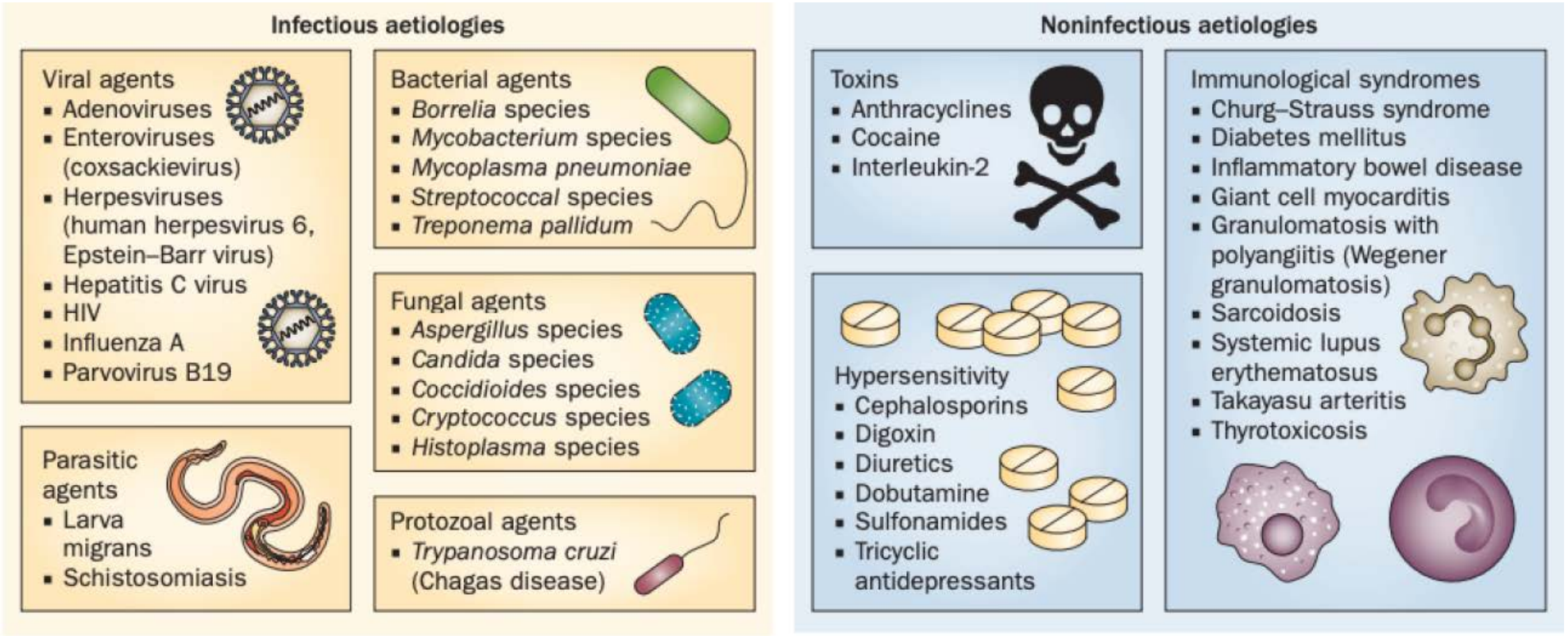
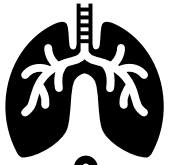


Figure 1 | Common causes of myocarditis. Viral infection is the most common aetiology, but several other aetiologies of myocarditis have also been implicated.

Treatment: Supportive Care



Oxygen supplementation, even if for comfort

- Intubation in severe cases

Fluid resuscitation

Heart Failure management

- Diuretics
- Afterload reduction
- Beta blockers (use in acute setting controversial)
- Inotropes
- Anti-arrhymic medications

Mechanical circulatory support

- Extracorporeal Membrane Oxygenation (ECMO)
- Ventricular Assist Device (VAD)

Transplant

Treatment: Anti-inflammatory

- Non-steroidal Anti-inflammatory Drugs (NSAIDs)
  - Mice studies shown to worsen myocardial injury in myocarditis due to coxsackievirus
  - Still often used for mild cases, particularly when concern for pericarditis
- Intravenous Immunoglobulin (IVIG)
  - Also controversial, as studies have failed to show benefit, particularly in children
  - Still, often used in many hospitals
- Glucocorticoids
  - No good data to support their use, yet still commonly used
  - Exception is in giant cell myocarditis (rare)

Activity Restrictions

- Risk of sudden death
  - 5-10% of sudden death in adolescents and young adults attributable to myocarditis (typically not previously diagnosed)
- Guidelines from American Heart Association and American College of Cardiology

1. Before returning to competitive sports, athletes who initially present with an acute clinical syndrome consistent with myocarditis should undergo a resting echocardiogram, 24-hour Holter monitoring, and an exercise ECG no less than 3 to 6 months after the initial illness *(Class I; Level of Evidence C)*.
2. It is reasonable that athletes resume training and competition if all of the following criteria are met *(Class IIa; Level of Evidence C)*:
   a. Ventricular systolic function has returned to the normal range.
   b. Serum markers of myocardial injury, inflammation, and heart failure have normalized.
   c. Clinically relevant arrhythmias such as frequent or complex repetitive forms of ventricular or supraventricular ectopic activity are absent on Holter monitor and graded exercise ECGs.

   At present, it is unresolved whether resolution of myocarditis-related LGE should be required to permit return to competitive sports.
3. Athletes with probable or definite myocarditis should not participate in competitive sports while active inflammation is present. This recommendation is independent of age, gender, and LV function *(Class III; Level of Evidence C)*.

Maron et al. *JACC.* 2015
Burns et al. *J Peds X.* 2020.

Outcomes of Classic Myocarditis in Children

- Mortality: 4-7% during acute illness
- Heart Transplant: 4-9%
- Risk factors for worse outcomes in those with known myocarditis
  - Late gadolinium enhancement on cardiac MRI
  - Tachyarrhythmias
  - Younger age
  - Severely decreased function on echocardiogram
    - Higher BNP
    - ECMO, VAD, vasoactive medication use

Ghelani et al. *Circ Cardiovasc Qual Outcomes.* 2012
Butts et al. *Pediatric Caridology.* 2017
Sachdeva et al. *Am J Cardiol.*2015

Early reports of myocarditis after mRNA COVID-19 vaccine: United States

- Marshall et al – 7 healthy males 14-19yo within 4 days of 2nd mRNA vaccine
  - All with abnormal troponin, ECG, and MRI
  - Treatment with NSAIDs alone in 3, IVIG/steroids in 4
  - All discharged to home after 2-6 days in the hospital (median 4)

- Rosner et al* – 5 males 19-39yo within 4 days of 2nd dose of vaccine, 1 24yo male 7 days after 1st dose
  - All with abnormal troponin and MRI findings, varying ECG findings
  - Treatment with NSAIDs or colchicine in 4, beta-blockers in 2, steroids in 1
  - All discharged to home after 2-4 days in the hospital (median 3)
  - Note: Spike protein antibodies **negative** in patient who presented after 1st dose

Marshall et al. *Pediatrics.* 2021.
Rosner et al. *Circulation 2021*
**Rosner et al. also reported a 28yo with myocarditis after Johnson & Johnson's Janssen COVID-19 vaccine*

Early reports of myocarditis after mRNA COVID-19 vaccine: International

- Larson et al – 8 males 22-56yo (4 in U.S., 4 in Italy); 7 within 4 days of dose 2, 1 with onset 2 days after dose 1 (had hx of prior SARS-CoV-2 infection)
  - All with abnormal troponin, echo, and MRI; 7/8 with abnormal ECG
  - Treatment with NSAIDs or colchicine in 4, steroids in 2, no treatment in 3
  - All discharged home with resolution of symptoms and preserved ejection fraction

- Israeli Ministry of Health - 148 myocarditis cases occurring within 30 days of mRNA vaccine
  - 27 cases out of ~5.4 million first doses
  - 121 cases out of ~5 million second doses
  - Mostly in men aged 16-30 (particularly 16-19)
  - Most were in the hospital up to 4 days
  - 95% of cases considered mild

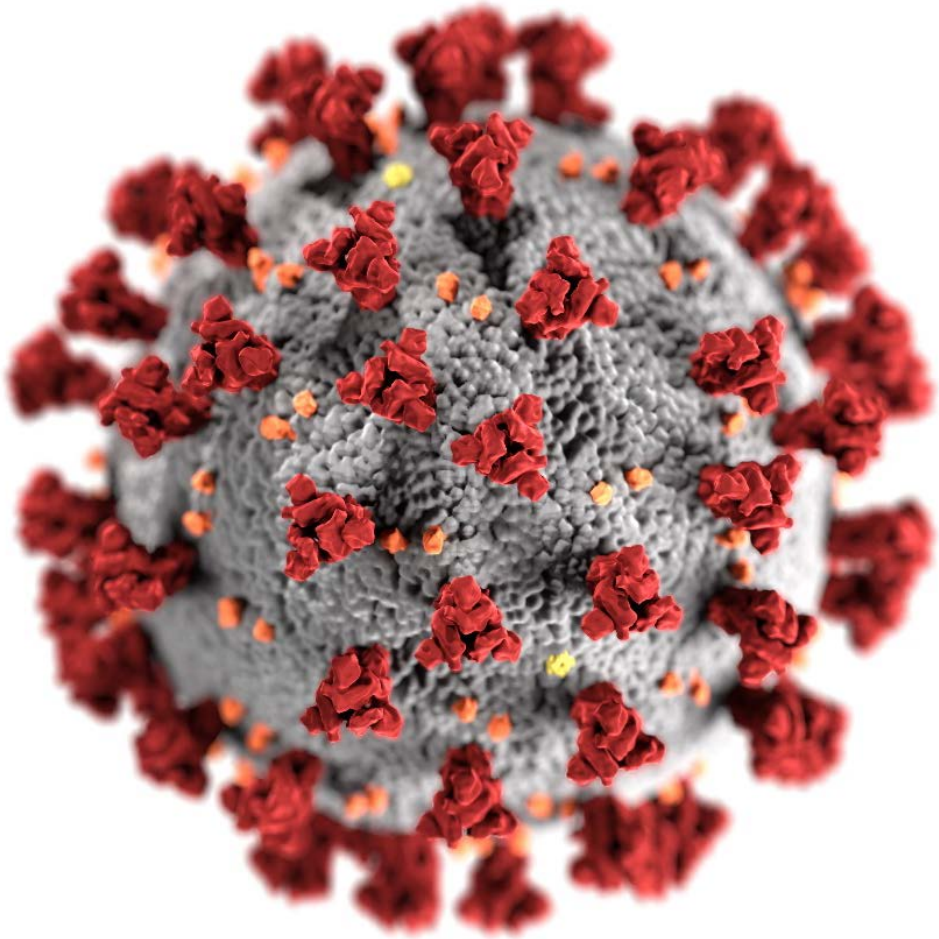
Larson et al. *Circulation*. 2021
https://www.gov.il/en/departments/news/01062021-03

Summary

- Myocarditis is rare, but is not a new disease
- Treatment largely supportive
- Myocarditis after mRNA vaccines:
  - Most commonly males, <30 years old, within a few days after 2nd dose
  - Early data of acute outcomes of myocarditis after mRNA vaccines have been good, but clear evidence of significant inflammation on cMRI
  - No long-term data available yet

Thank you!

Acknowledgments:
- CDC Covid-19 Vaccine Task Force, Vaccine Safety Team
- Clinical Immunization Safety Assessment Project



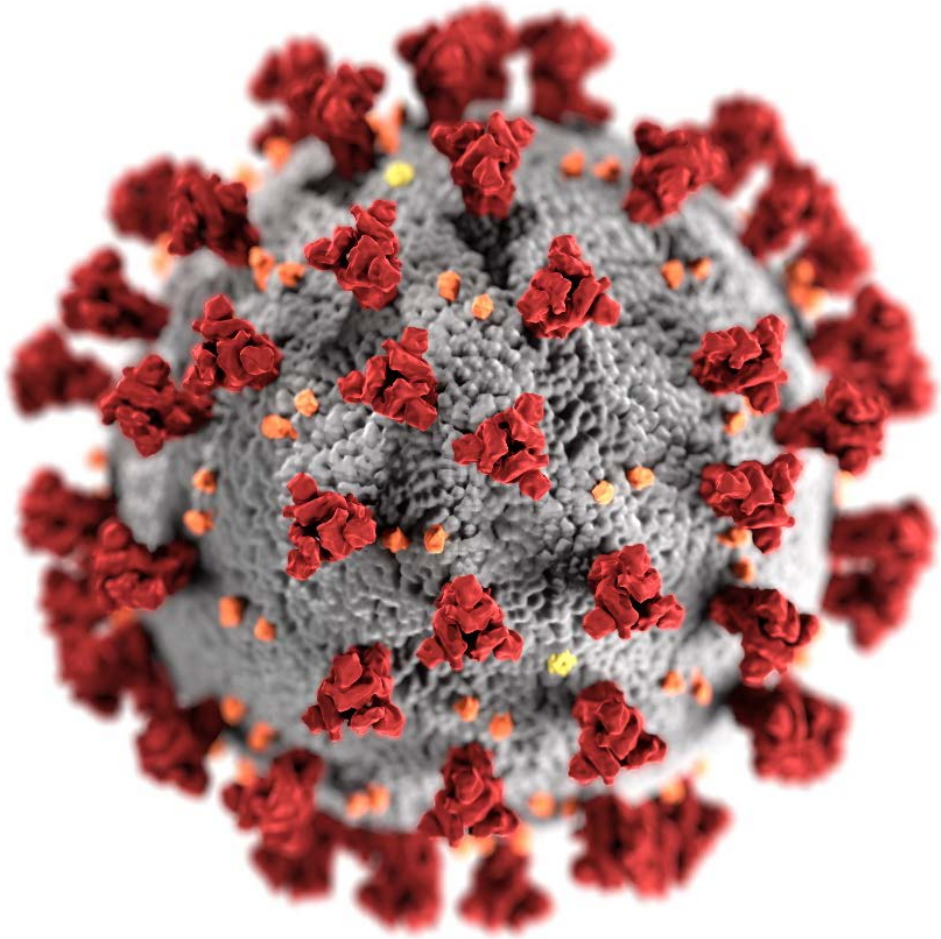
For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

COVID-19 Vaccine safety updates

Infectious Diseases Society of America (IDSA) COVID-19 Clinician Call

June 26, 2021

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



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Myocarditis and pericarditis following mRNA COVID-19 vaccination in the United States

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

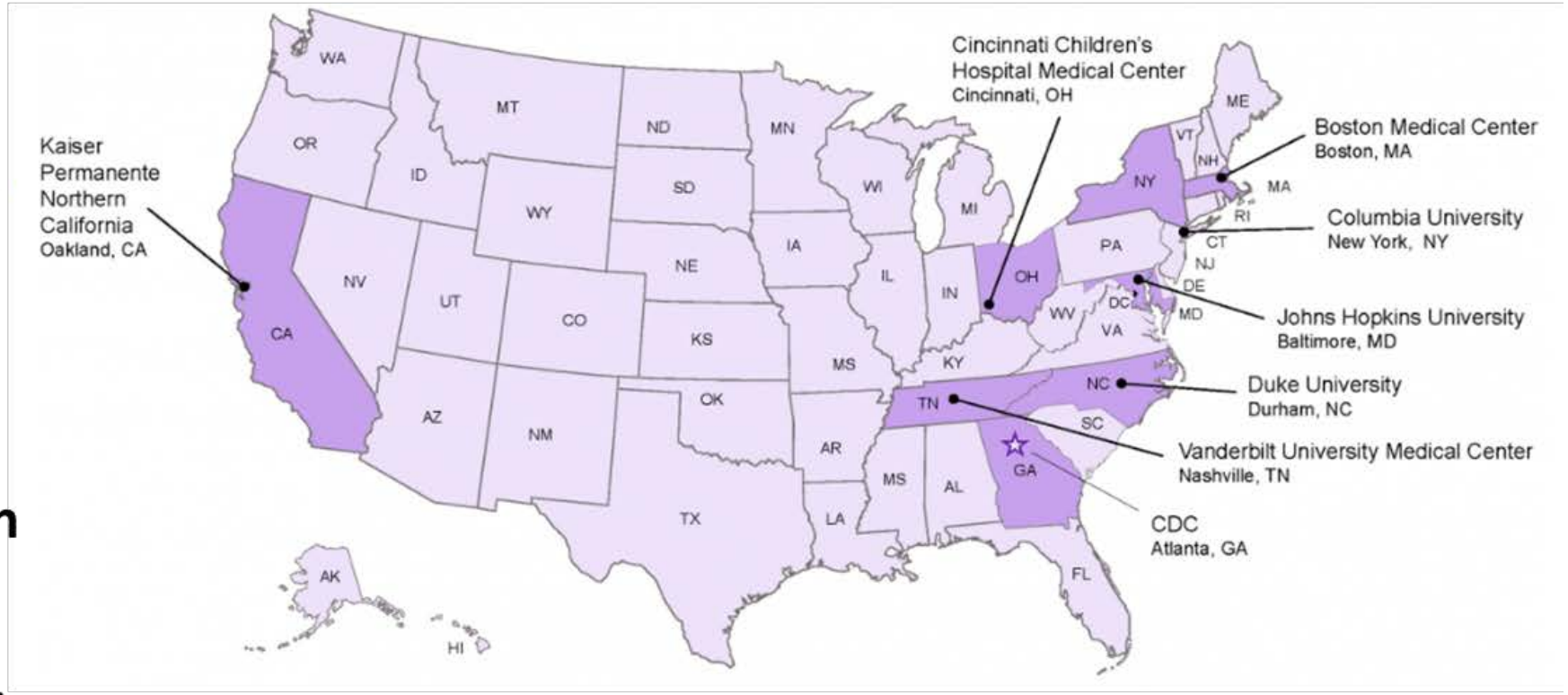
CDC + FDA

Vaccine Adverse Event Reporting System

http://vaers.hhs.gov

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

Preliminary myocarditis/pericarditis reports to VAERS following mRNA COVID-19 vaccination by dose number
(after ~300 million mRNA doses administered, data thru Jun 11, 2021)

Manufacturer	Reports after dose 1	Reports after dose 2	Reports after unknown dose
Pfizer-BioNTech (n=791)	150	563	78
Moderna (n=435)	117	264	54
Total (N=1,226)	**267**	**827**	**132**

- 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
  - 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 COVID-19 vaccination (data thru Jun 11, 2021)

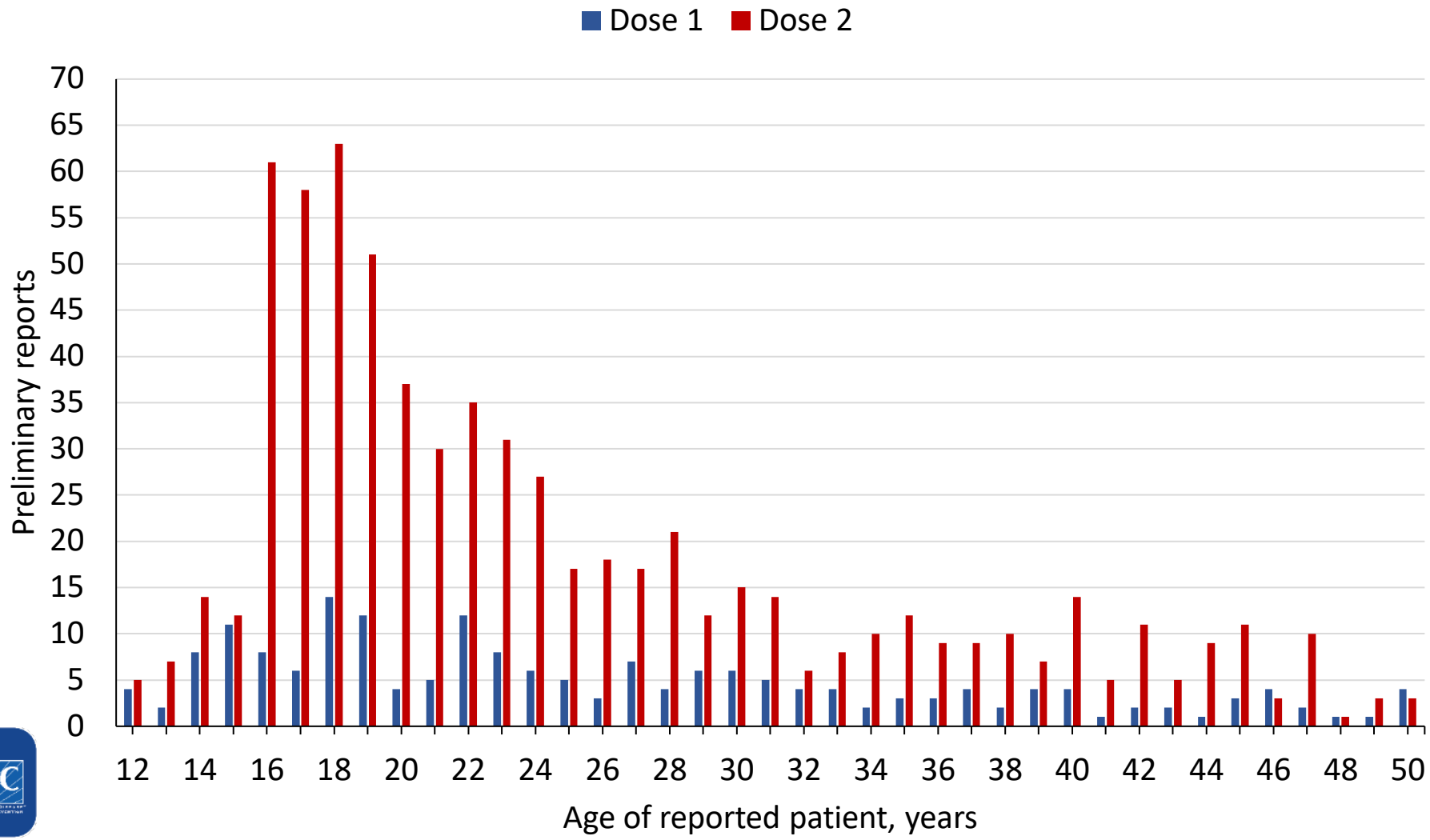
Characteristics	Dose 1 (n=267)	Dose 2 (n=827)
Median age, years (range)	30 (12–94)	24 (12–87)
Median time to symptom onset, days (range)	4 (0–61)†	3 (0–98)†
Sex (%)		
Male	176 (66%)	655 (79%)
Female	88 (33%)	165 (20%)
Not reported/not available	3 (1%)	7 (1%)

* 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

† One report of 179-day onset after dose 1; one report of 151-day onset after dose 2 – included in counts, but not in range

Preliminary reports of myocarditis/pericarditis to VAERS after mRNA COVID-19 vaccination by age and dose number*

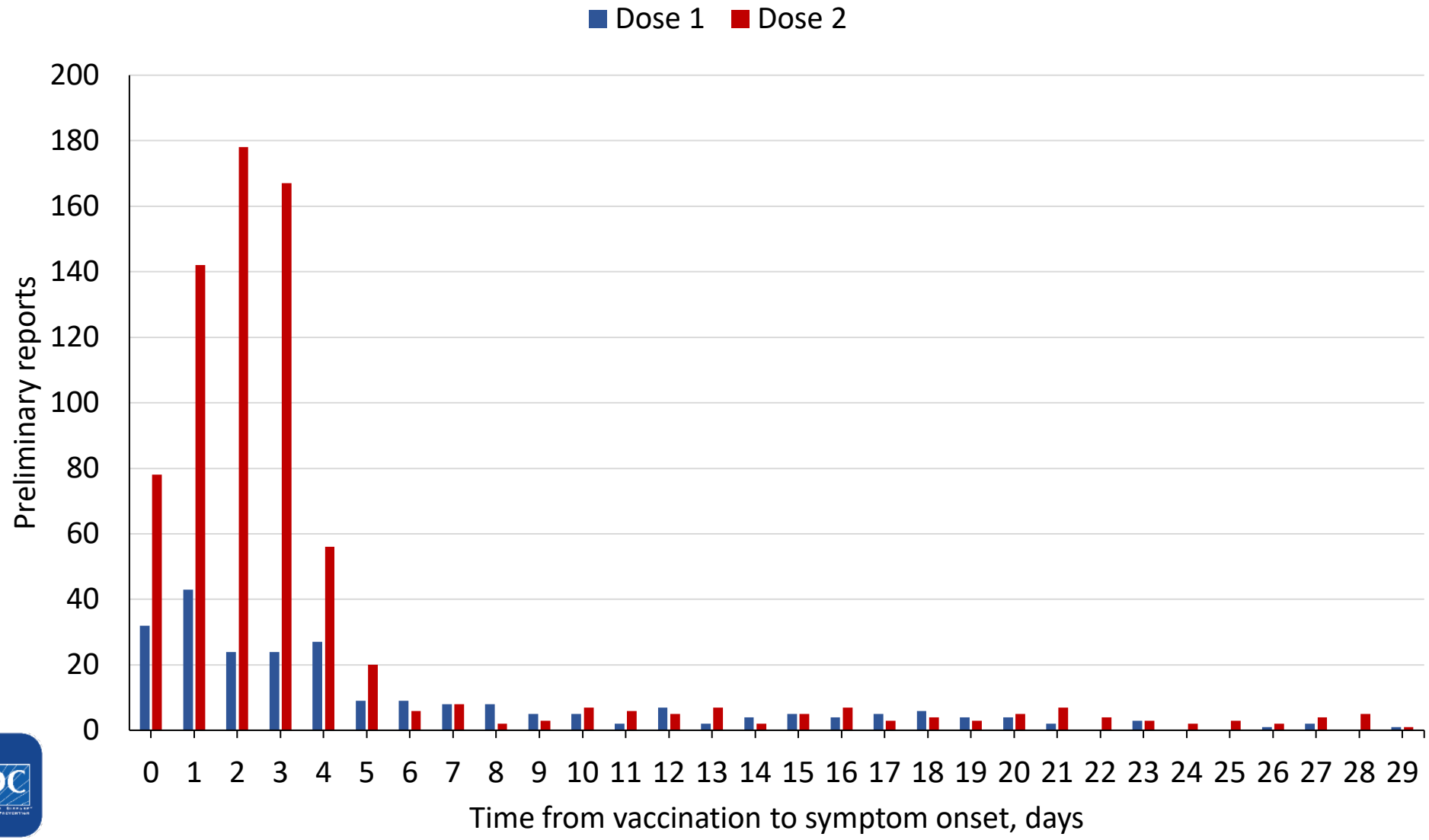
(as of Jun 11, 2021)



* Age truncated at >50yr: Reports of persons >50yr of age include 70 after Dose 1, 119 after Dose 2

Preliminary reports of myocarditis/pericarditis to VAERS after mRNA COVID-19 vaccination by dose number and time to symptom onset*

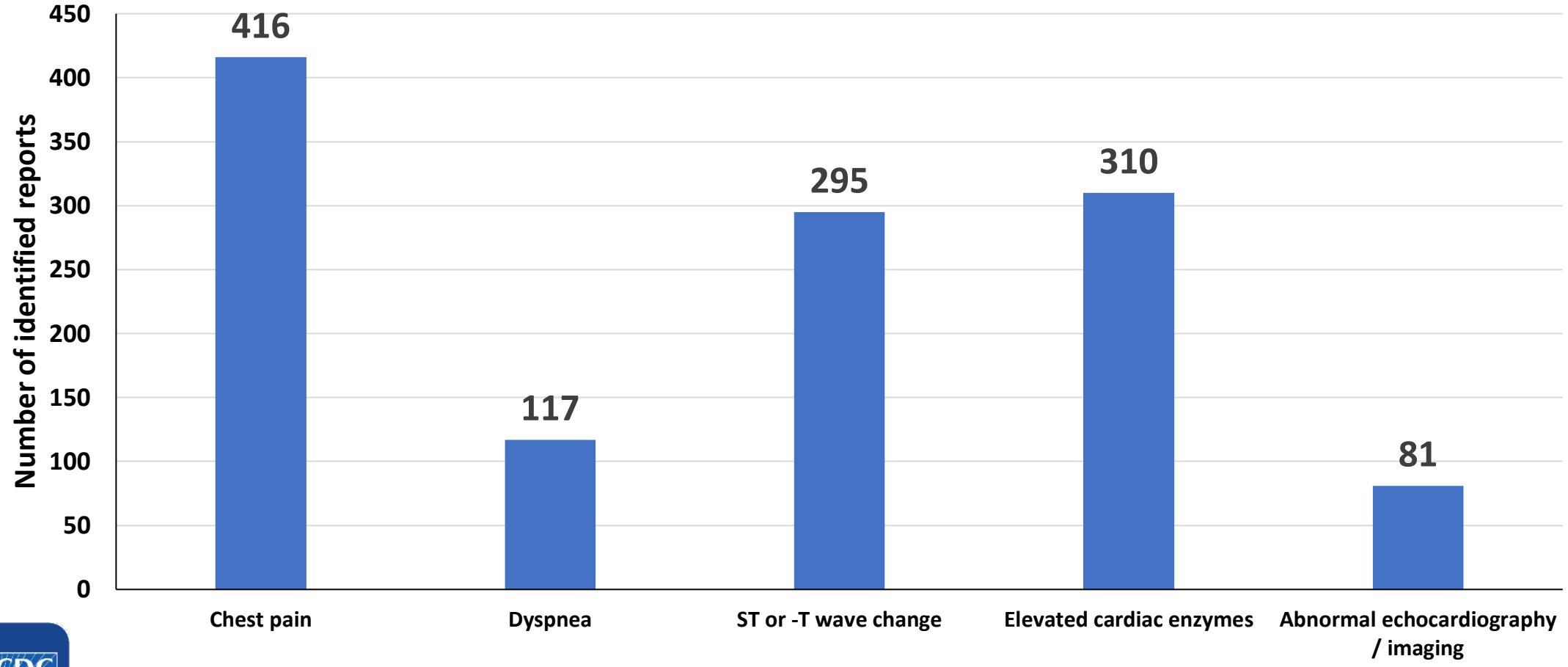
(as of Jun 11, 2021)



* Reports of time to symptom onset truncated at >29 days: Includes 5 reports after Dose 1, 56 after Dose 2

Symptoms and diagnostic findings of preliminary myocarditis/pericarditis reports after mRNA COVID-19 vaccination under review, limited to ≤29 years old (N=484)

(data thru Jun 11, 2021)



Care and outcomes of preliminary myocarditis/pericarditis cases reported to VAERS after mRNA COVID-19 vaccination in persons ≤29 years old (N=484) (data thru Jun 11, 2021)

484 total preliminary reports

- **323** have met CDC working case definition of myocarditis or pericarditis (or both)
- 148 are under review

Of 323 meeting case definition:

- 309 were hospitalized
  - 295 discharged
    - **218 (79%) known to have recovered from symptoms at time of report**
  - 9 still hospitalized (2 in ICU)
  - 5 without outcome data
- 14 were not hospitalized (seen in emergency dept., urgent care, outpatient clinic, not specified)

Preliminary myocarditis/pericarditis reports to VAERS following dose 2 mRNA vaccination, Exp. vs. Obs. using 7-day risk window (data thru Jun 11, 2021)

Age groups	Females			Males		
	Doses admin	Expected*,†	Observed*	Doses admin	Expected*,†	Observed*
12–17 yrs	2,189,726	0–2	**19**	2,039,871	0–4	**128**
18–24 yrs	5,237,262	1–6	**23**	4,337,287	1–8	**219**
25–29 yrs	4,151,975	0–5	**7**	3,625,574	1–7	**59**
30–39 yrs	9,356,296	2–18	11	8,311,301	2–16	**61**
40–49 yrs	9,927,773	2–19	18	8,577,766	2–16	**34**
50–64 yrs	18,696,450	4–36	18	16,255,927	3–31	18
65+ yrs	21,708,975	4–42	10	18,041,547	3–35	11
Not reported	—	—	1	—	—	8

* Assumes a 7-day post-vaccination observation window (i.e., symptom onset from day of vaccination through Day 6 after vaccination)

† 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. Expected counts among females 12–29 years adjusted for lower prevalence relative to males by factor of 1.7 (Fairweather, D. et al, *Curr Probl Cardiol.* 2013;38(1):7-46).

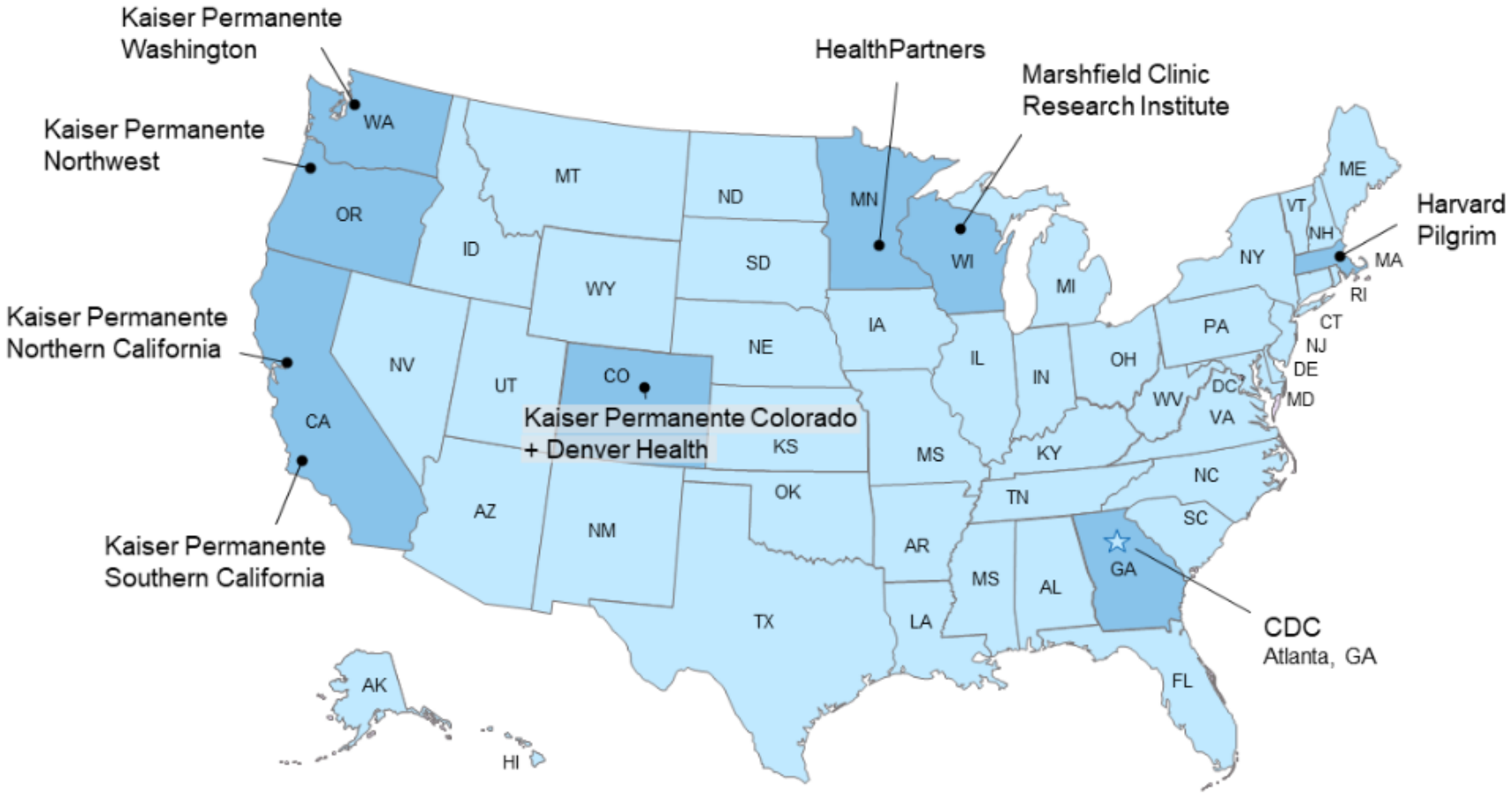
Preliminary myocarditis/pericarditis crude reporting rates to VAERS following mRNA COVID-19 vaccination (data thru Jun 11, 2021)

	Overall reporting rate per million doses			Reporting rate in females per million doses			Reporting rate in males per million doses		
Age groups	All doses	Dose 1	Dose 2	All doses	Dose 1	Dose 2	All doses	Dose 1	Dose 2
12-17 yrs	18.1	5.3	37.0	4.2	1.1	9.1	32.4	9.8	66.7
18-24 yrs	15.9	4.8	28.4	3.6	1.5	5.5	30.7	8.7	56.3
25-29 yrs	6.7	2.5	10.8	2.0	0.8	2.6	12.2	4.5	20.4
30-39 yrs	4.2	1.7	5.6	1.8	1.4	1.8	6.9	2.0	10.0
40-49 yrs	2.7	0.9	3.8	2.0	0.9	2.8	3.5	1.0	5.1
50-64 yrs	1.7	1.0	2.0	1.6	1.0	1.8	1.9	1.0	2.3
65+ yrs	1.1	0.7	1.3	1.1	0.6	1.2	1.2	0.7	1.4

- Myocarditis/pericarditis reports per million mRNA vaccine doses administered by sex and dose number with no restrictions on post-vaccination observation time

VSD

Vaccine Safety Datalink

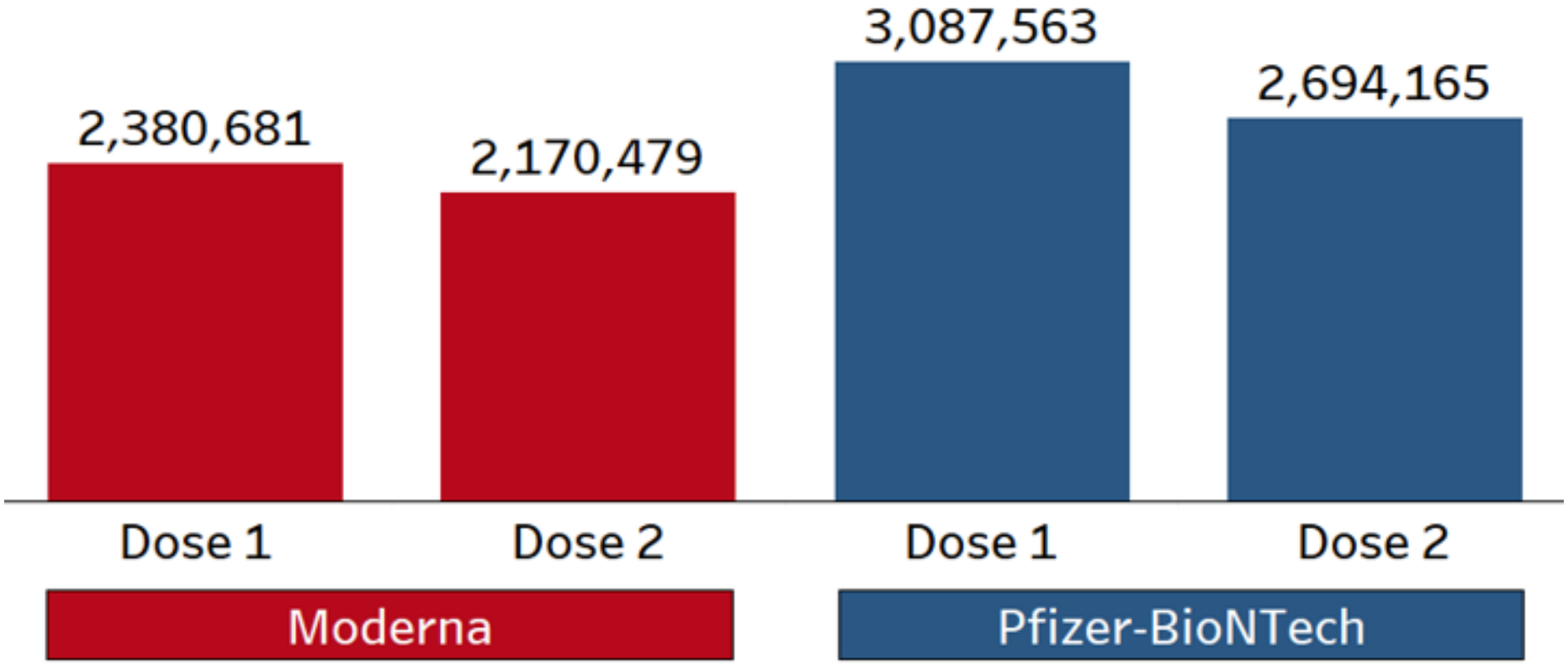


- **9** participating integrated healthcare organizations
- Data on over **12 million** persons per year

VSD Rapid Cycle Analysis (RCA) safety monitoring

- Near real-time sequential (i.e., weekly) monitoring as data become available
- Monitors a limited set of prespecified vaccine safety outcomes
- A public health surveillance activity, not the same as an epidemiologic study
- Designed to detect statistically significant associations and statistical signals (values above specified statistical thresholds), which do not necessarily indicate a safety problem
- Statistical signals detected through RCA require further evaluation

COVID-19 vaccine doses administered in the VSD
(thru Jun 12, 2021)



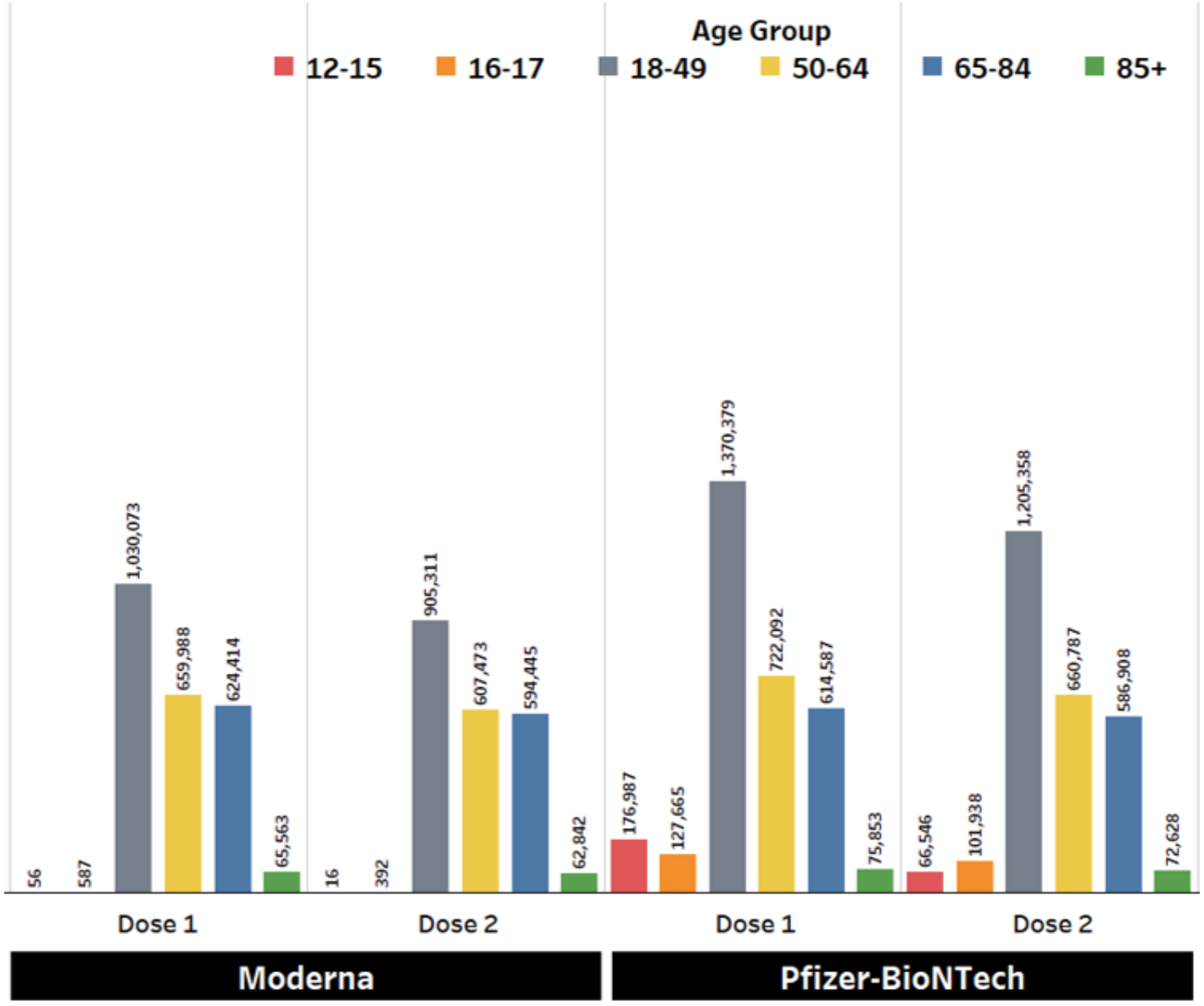
4,551,160
total doses

5,781,728
total doses

COVID-19 vaccine doses administered by age group in the VSD
(thru Jun 12, 2021)

Pfizer-BioNTech doses

- 12–15-year-olds
  - 176,987 first doses
  - 66,546 second doses
- 16–17-year-olds
  - 127,665 first doses
  - 101,938 second doses



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

(thru Jun 12, 2021)

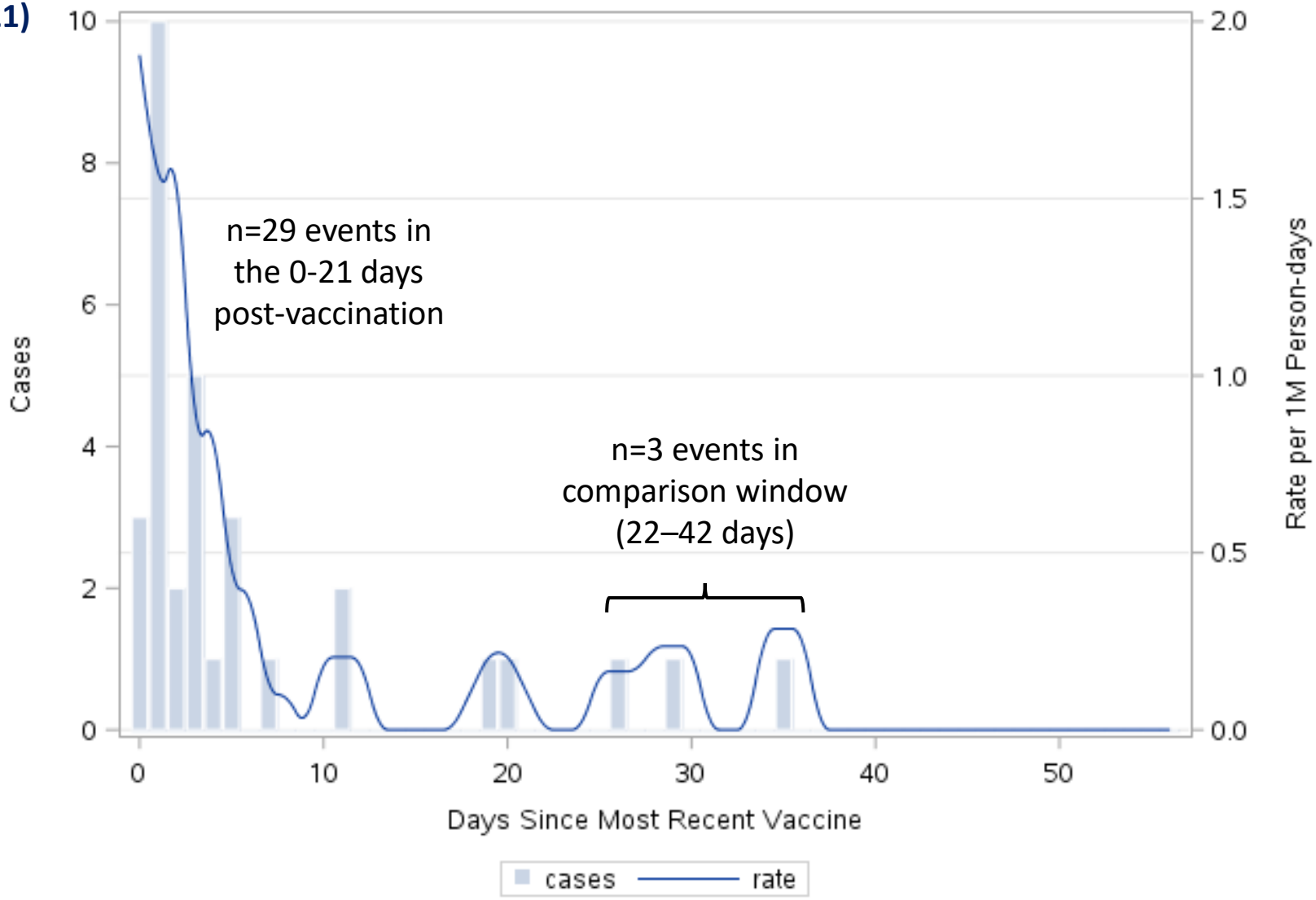
Pre-specified outcome event	Events in risk interval	Adj Rate Ratio*	95% CI	Signal
Acute disseminated encephalomyelitis	2	.	0.07 - ne	no
Acute myocardial infarction	578	0.99	0.85 - 1.15	no
Appendicitis	691	0.80	0.70 - 0.90	no
Bell's palsy	493	0.97	0.83 - 1.15	no
Cerebral venous sinus thrombosis	5	1.15	0.23 - 6.67	no
Disseminated intravascular coagulation	28	0.65	0.35 - 1.20	no
Encephalitis / myelitis / encephalomyelitis	15	0.94	0.35 - 2.77	no
Guillain-Barré syndrome	8	0.57	0.16 - 2.15	no
Stroke, hemorrhagic	227	0.81	0.64 - 1.03	no
Stroke, ischemic	1009	0.98	0.87 - 1.10	no
Immune thrombocytopenia	45	1.03	0.59 - 1.85	no
Kawasaki disease	0	0.00	0.00 - 2.60	no
Myocarditis / pericarditis	75	1.07	0.70 - 1.67	**no**
Seizures	266	1.03	0.82 - 1.30	no
Transverse myelitis	3	1.88	0.17 - 55.81	no
Thrombotic thrombocytopenic purpura	5	1.39	0.27 - 8.02	no
Thrombosis with thrombocytopenia syndrome (TTS)	66	0.79	0.52 - 1.20	no
Venous thromboembolism	579	1.07	0.92 - 1.25	no
Pulmonary embolism	484	0.99	0.84 - 1.18	no

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

Chart confirmed myocarditis/pericarditis cases in VSD by day of symptom onset since most recent mRNA COVID-19 vaccination, 12–39-year-olds

(thru Jun 5, 2021)

- Most likely clusters
  - Days 0–5
  - Days 0–3
  - Days 0–6
- All have a p-value <0.000001
- Parameters for the scan
  - Includes days 0–56
  - Scans all possible windows of length 1–28 days



VSD age-stratified analysis: Chart confirmed myocarditis/pericarditis events in 12–39-year-olds in the 7-day risk interval compared with events in vaccinated comparators on the same calendar days

(thru Jun 5, 2021)

Vaccine (dose #)	Events in risk interval	Adj Rate ratio*	95% CI
Any mRNA (both doses)	22	10.0	2.9–46.5
Any mRNA (dose 1)	4	6.2	0.9–69.8
Any mRNA (dose 2)	18	10.8	3.2–49.0
Pfizer-BioNTech (both doses)	7	2.4	0.4–24.9
Pfizer-BioNTech (dose 1)	0	0	0–20.4
Pfizer-BioNTech (dose 2)	7	6.0	1.1–53.6
Moderna (both doses)†	15	.	6.9–ne
Moderna (dose 1)	4	.	2.1–ne
Moderna (dose 2)	11	.	6.6–ne

* 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, no events in comparison interval (22–42 days after final dose)

Myocarditis/pericarditis chart confirmed rates in VSD in 21-day risk interval, 12–39-year-olds

(thru Jun 5, 2021)

Vaccine(s) (dose #)	Cases	Doses admin	Rate per million doses (95% CI)
mRNA (both doses)	26	3,418,443	8 (5.3–11.8)
mRNA (dose 1)	8	1,879,585	4.4 (1.9–8.8)
mRNA (dose 2)	18	1,538,858	12.6 (7.5–19.9)
Pfizer-BioNTech (dose 1)	3	1,211,080	2.6 (0.5–7.7)
Pfizer-BioNTech (dose 2)	7	958,721	8.0 (3.2–16.5)
Moderna (dose 1)	5	668,505	7.5 (2.4–17.6)
Moderna (dose 2)	11	580,137	19.8 (9.9–35.5)

Care and status of chart confirmed myocarditis/pericarditis cases in VSD within 0–21 days following mRNA COVID-19 vaccination (N=29)*

Care and status	n (%)
Highest level of care received	
Outpatient	1 (3.4)
Emergency department	4 (13.8)
Inpatient hospitalization	22 (75.9)
Intensive care unit (ICU)	2 (5.7)
Median length of hospital stay (days, range)	1 (0–13)
Discharged to home at time of chart review	29 (100)
Follow-up visit noted at time of chart review	27 (93.1)

* 3 of the 29 cases (10.3%) had a history of COVID-19 infection

Follow-up qualitative summary

Current symptoms

- Nearly all follow-up visit notes indicated resolution of symptoms at the time of follow-up
- Of those that had follow-up ECG/echo, lab testing, most had returned to normal or baseline

Ongoing treatment/plan

- Most follow-up visit notes indicate tapering of some medications (NSAIDS, prednisone, etc.)
- Notes indicated maintenance of colchicine and activity limitations for 3–6 months

Myocarditis/pericarditis rates based on ICD-10 coded cases in VSD in 21-day risk interval, ages 12–39 years old

(thru Jun 5, 2021)

Product (dose)	Female cases	Female rates per million doses (95% CI)	Male cases	Male rates per million doses (95% CI)
Any mRNA (both doses)	6	3.2 (1.2–6.9)	26	16.9 (11.0–24.8)
Any mRNA (dose 1)	2	1.9 (0.2–7.0)	4	4.7 (1.3–12.0)
Any mRNA (dose 2)	4	4.7 (1.3–12.0)	22	32.0 (20.1–48.5)
Pfizer-BioNTech (both doses)	1	0.8 (0.0–4.7)	11	11.1 (5.5–19.8)
Pfizer-BioNTech (dose 1)	1	1.5 (0.0–8.5)	1	1.8 (0.0–10.0)
Pfizer-BioNTech (dose 2)	0	. (. – .)	10	23.0 (11.0–42.3)
Moderna (both doses)	5	7.1 (2.3–16.6)	15	27.5 (15.4–45.4)
Moderna (dose 1)	1	2.7 (0.1–14.9)	3	10.2 (2.1–29.9)
Moderna (dose 2)	4	12.2 (3.3–31.2)	12	47.7 (24.6–83.3)

Summary

Summary

- 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 VAERS findings suggest:
  - Median age of reported patients is younger for reports after dose 2 vs. dose 1
  - Symptom onset clusters within the week following vaccination (mostly within 4 days)
  - Predominance of male patients in younger age groups, especially after dose 2
  - Observed reports > expected cases, especially after dose 2 in younger age groups
- Early VSD data for myocarditis/pericarditis in 12–39-year-olds also suggest:
  - More cases after mRNA COVID-19 vaccination with dose 2 vs. dose 1
  - Rate of 12.6 cases per million 2nd doses of any mRNA vaccine in the 21 days following vaccination
    - Rates appear higher in males vs. females
  - Clustering of myocarditis/pericarditis within the week following vaccination (most likely 0–5 days)
- Available outcome data indicate that patients generally recover from symptoms and do well

Next steps for assessing myocarditis/pericarditis following mRNA COVID-19 vaccination

- Continue monitoring in VAERS
  - Follow-up to obtain medical records, conduct case reviews, apply CDC working case definition, and adjudicate case reports
  - Surveillance review focusing on myocarditis and myopericarditis to describe epidemiology and characterize clinical features of cases is in progress
- Continue monitoring and assessment in VSD
  - Quantify risk and characterize clinical features of cases
- Conduct follow-up on vaccine-associated cases to assess longer-term outcomes (i.e., at 3–6 months)

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

How to report an adverse event to VAERS

- Go to vaers.hhs.gov
- Submit a report online
- For help:

  Call 1-800-822-7967

  Email info@VAERS.org

  video instructions https://youtu.be/sbCWhcQADFE

- Please send records to VAERS ASAP if contacted and asked
  - HIPAA permits reporting of protected health information to public health authorities including CDC and FDA

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

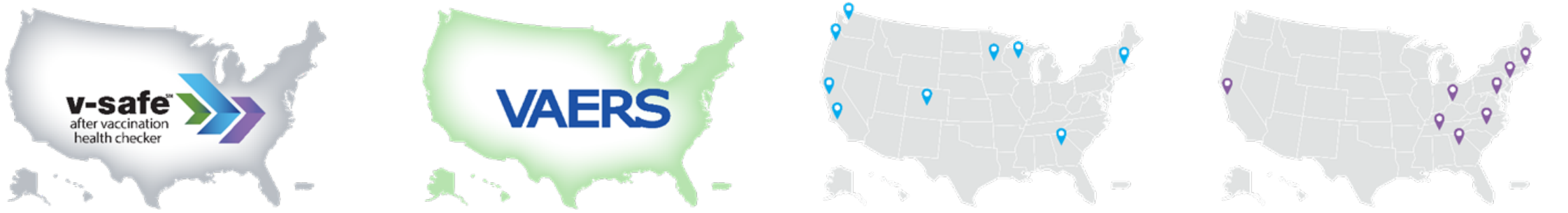
Food and Drug Administration

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

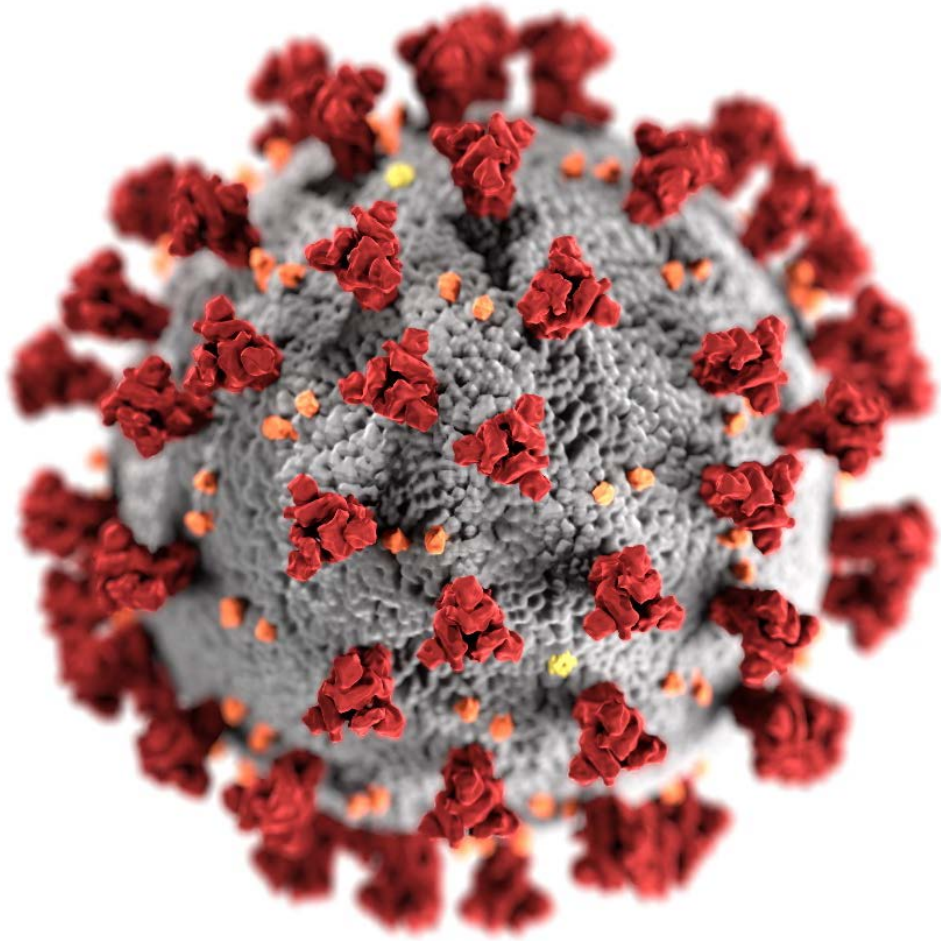
v-safe	VAERS	VSD	CISA Project



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

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

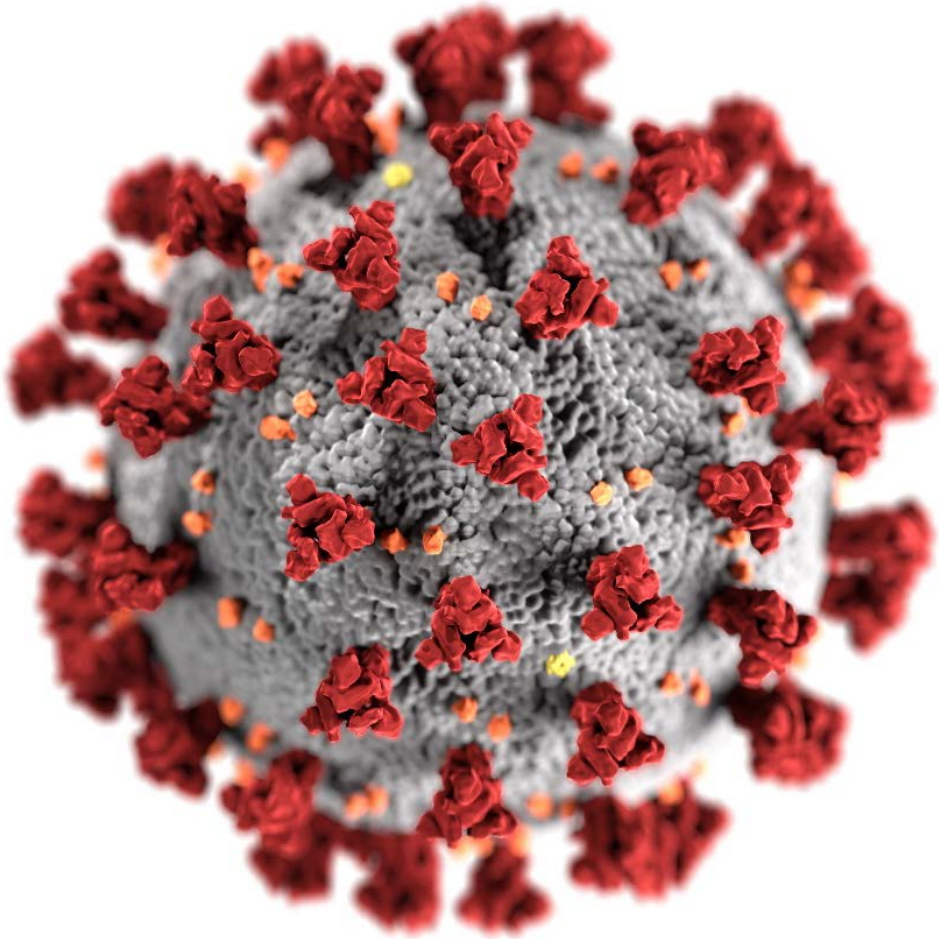
Thank you!



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.

Extra slides



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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†

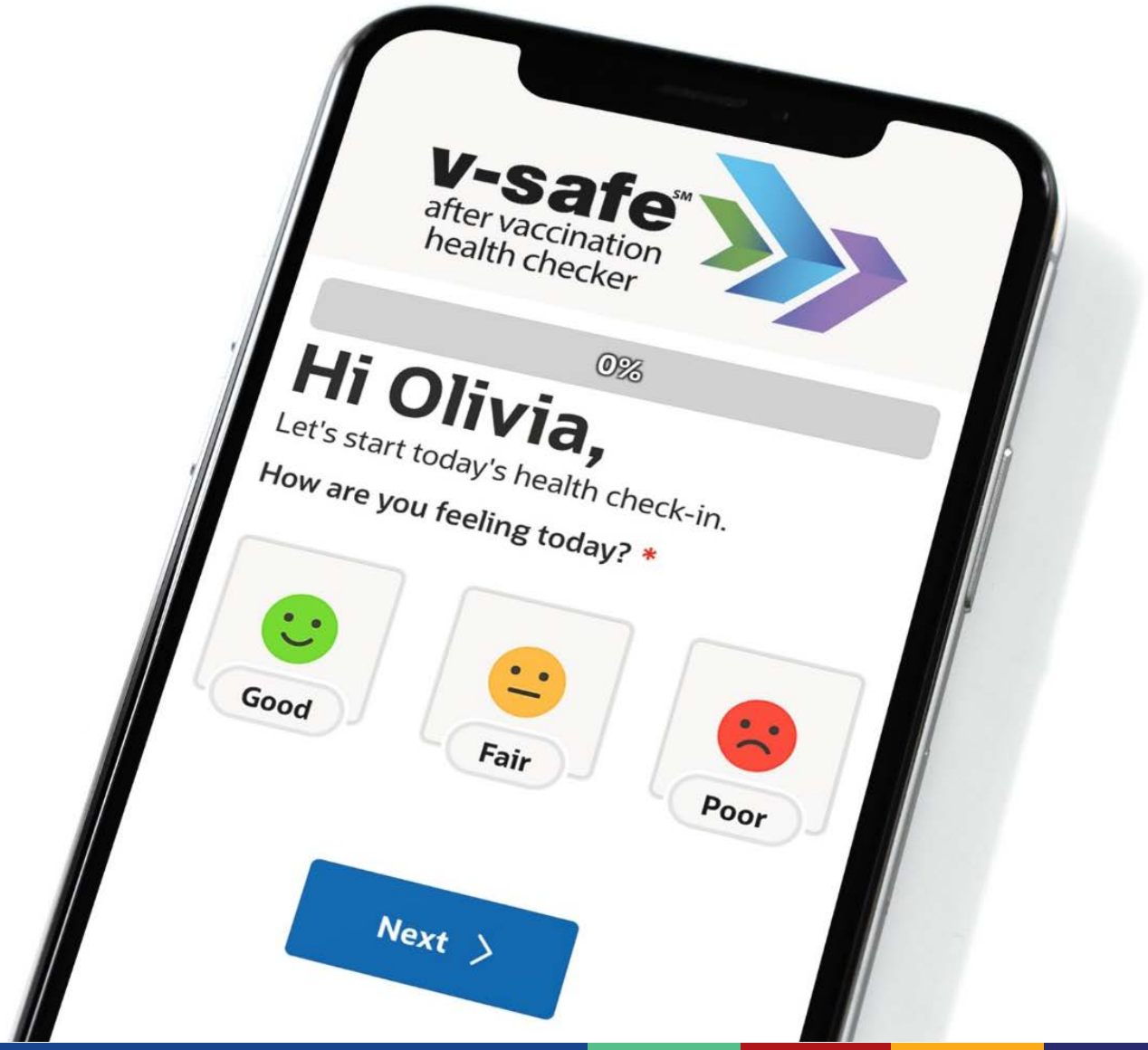
* FDA: COVID-19 Vaccines https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines

† CDC: COVID-19 ACIP Vaccine Recommendations https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html

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



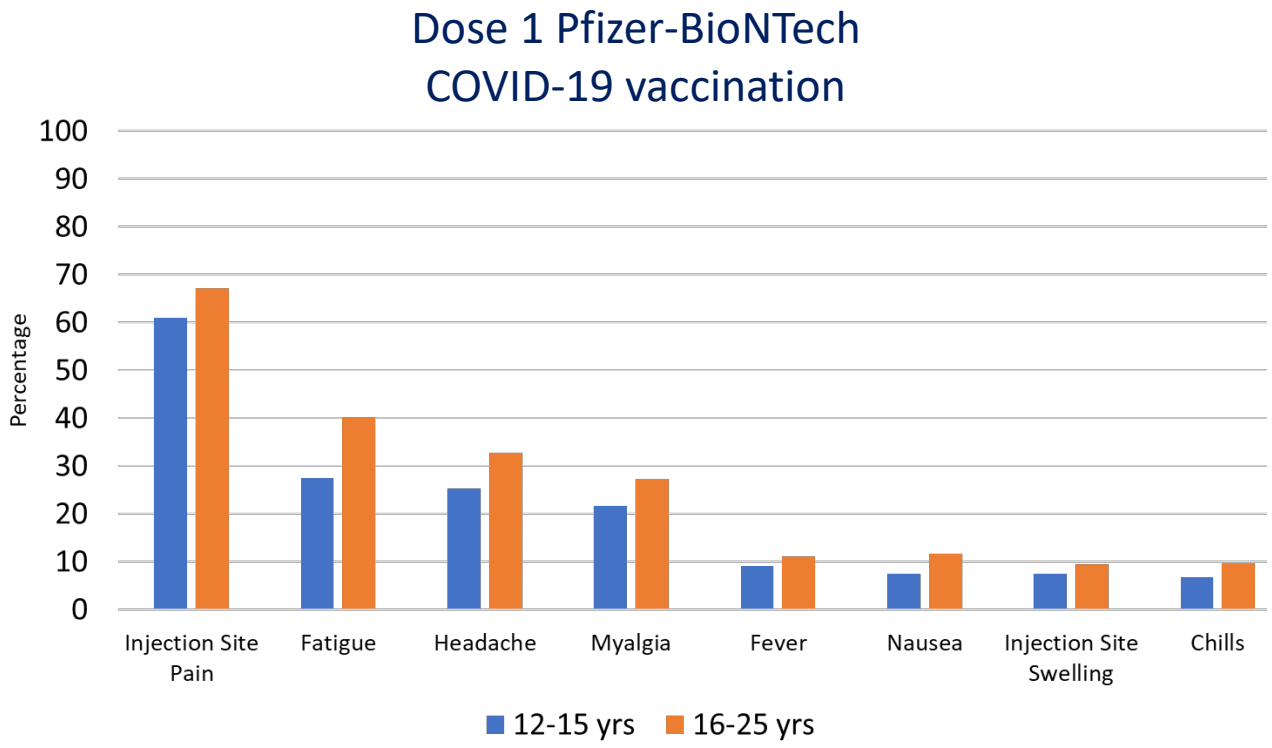
http://cdc.gov/vsafe

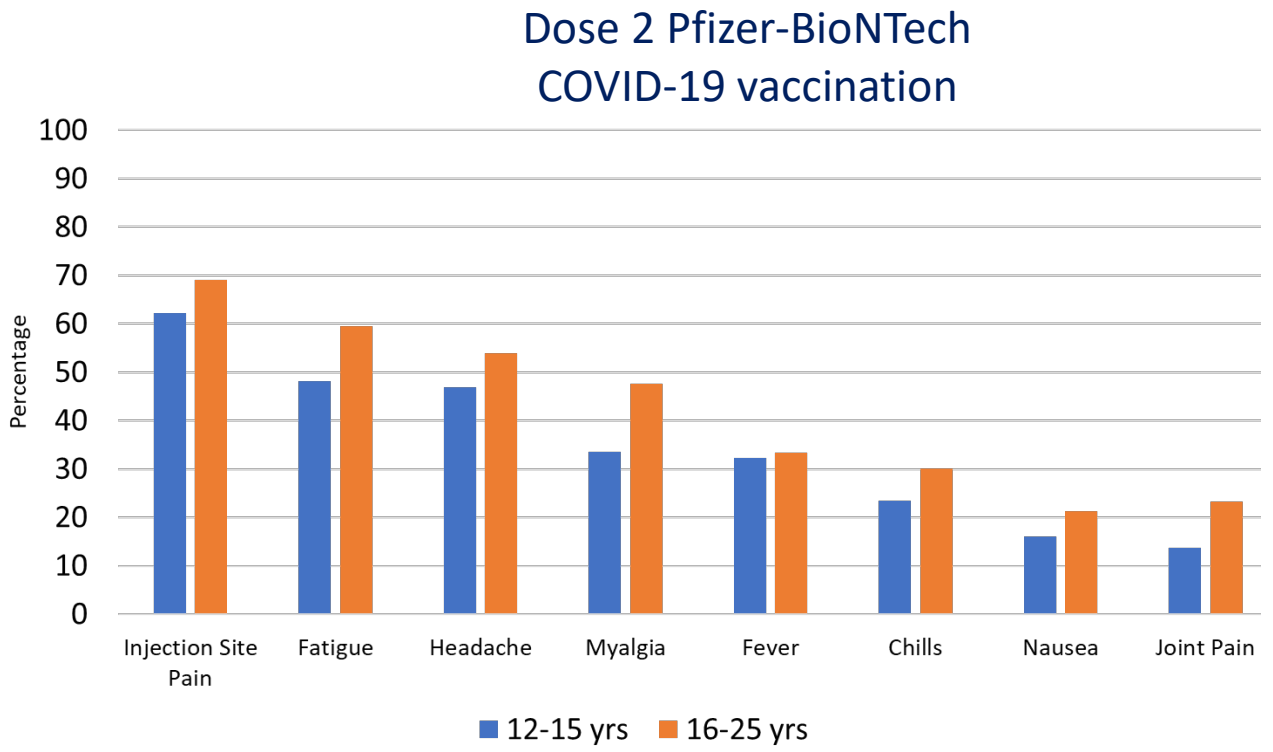
Overview of v-safe monitoring of Pfizer-BioNTech COVID-19 vaccine for younger adolescents

- On May 11, 2021, v-safe age limits expanded to allow registration down to 12 years of age at dose 1
- As of June 13, for persons age 12–15 years after Pfizer-BioNTech COVID-19 vaccination:
  - 57,126 with at least one health check-in during days 0–7 after dose 1
  - 15,988 with at least one health check-in during days 0–7 after dose 2

V-safe: Top solicited reactions reported at least once in days 0–7 after vaccination with Pfizer-BioNTech in 12–15-year-olds vs. 16–25-year-olds*

(data thru Jun 13, 2021)

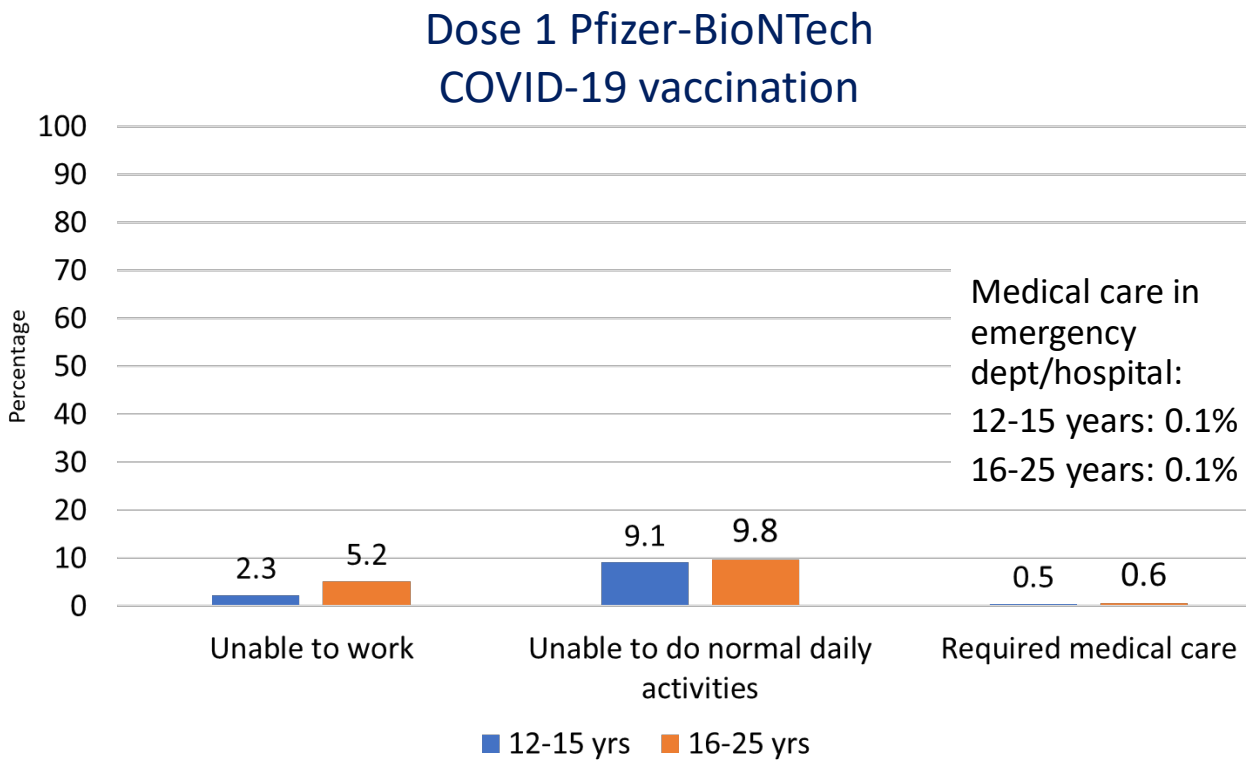


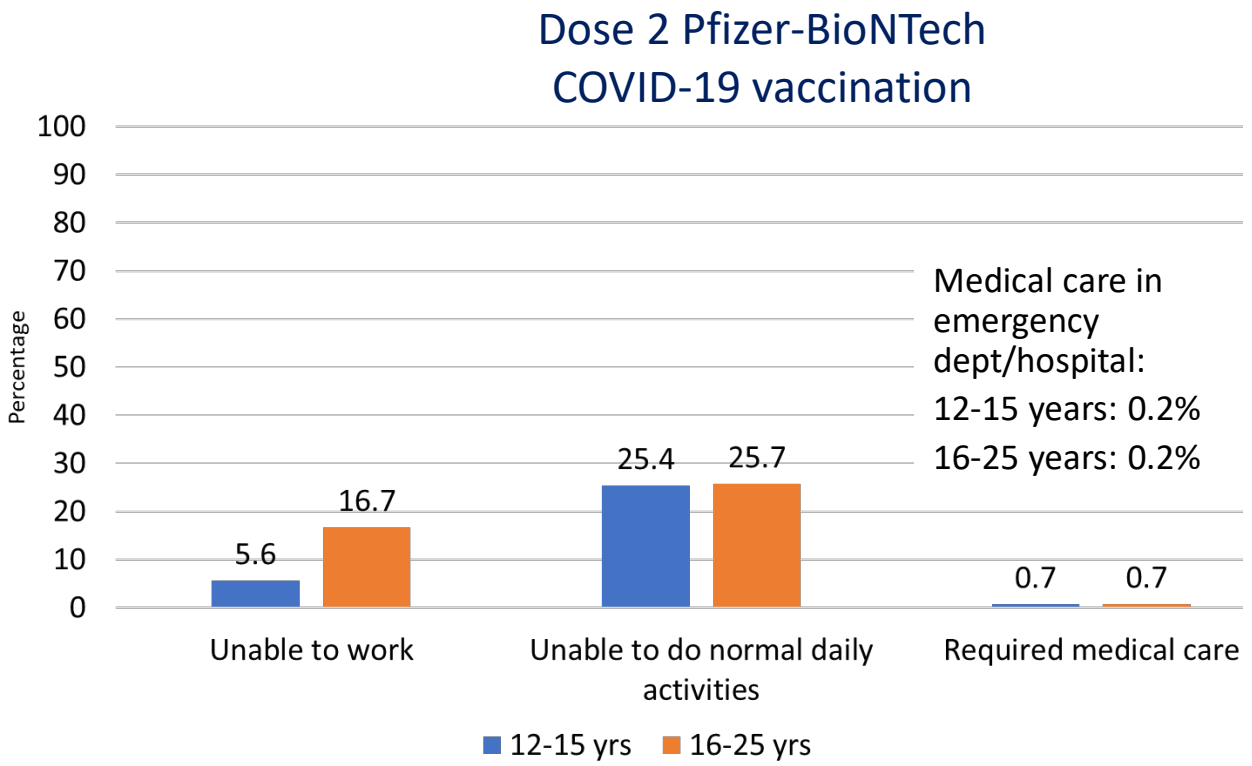


* Includes participants who completed at least one survey in the first week after dose 1 of Pfizer-BioNTech COVID-19 vaccine

V-safe: Health Impact Events reported at least once in days 0-7 after vaccination with Pfizer-BioNTech in 12–15-year-olds vs. 16–25-year-olds*

(data thru Jun 13, 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

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

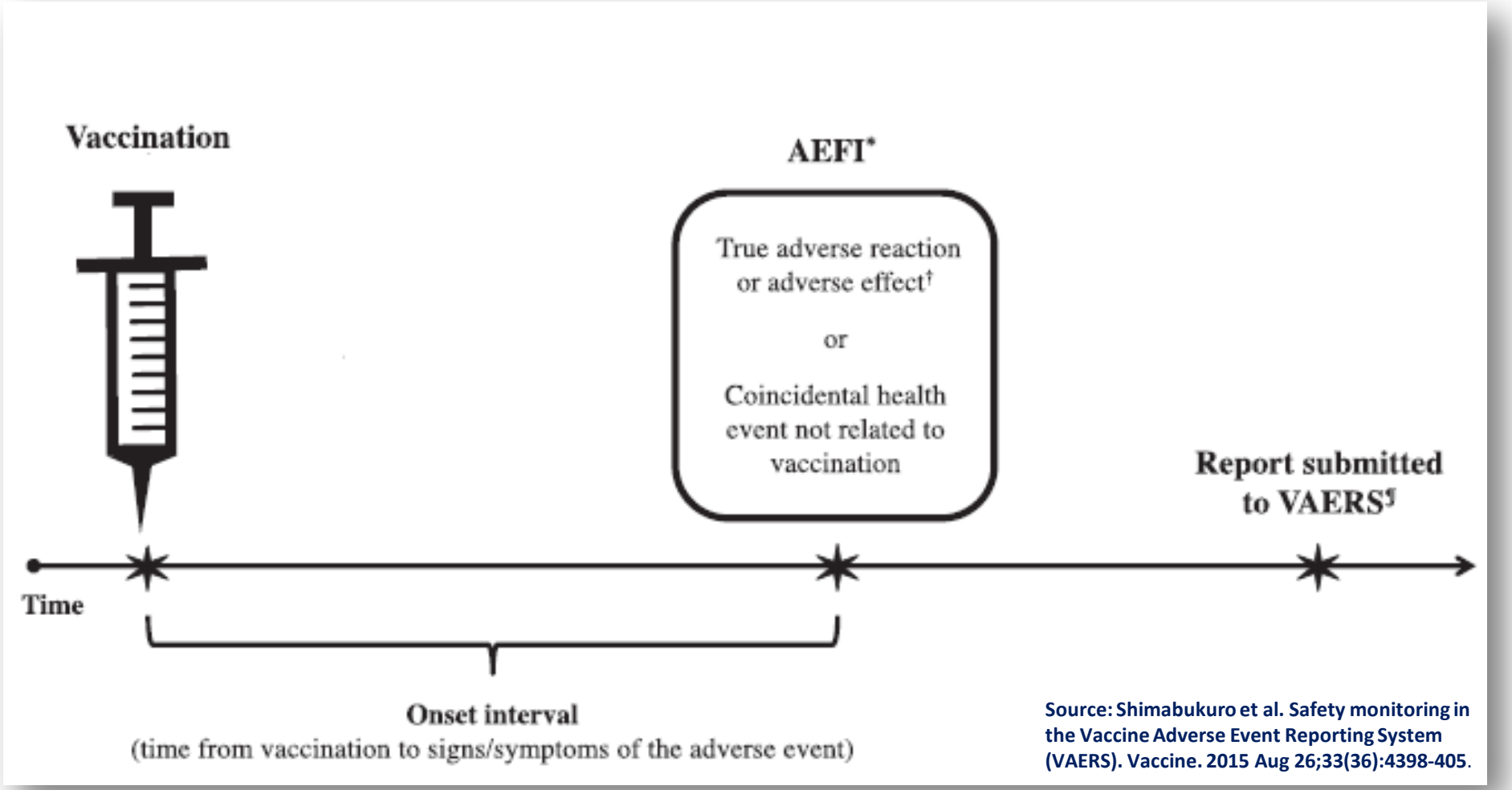
key strengths

- 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

What's in VAERS?



Source: Shimabukuro et al. Safety monitoring in the Vaccine Adverse Event Reporting System (VAERS). Vaccine. 2015 Aug 26;33(36):4398-405.

Does not necessarily mean vaccination caused a health problem

Reports to VAERS after Pfizer-BioNTech COVID-19 vaccination: persons aged 12–15 years vs. 16–25 years* (data thru Jun 11, 2021)

Ages	N	Crude reporting rate (per million doses)	Non-serious adverse events (%)	Serious adverse events‡,§ (%)
12–15 years old	2,540	422	2,396 (94.3)	144 (5.7)
16–25 years old† (for comparison)	12,759	592	11,969 (93.8)	790 (6.2)

- 12–15 years old: ~6.0 million doses administered (May 10 thru June 11, 2021)
- 16–25 years old: ~21.6 million doses administered (December 14, 2020, thru June 11, 2021)

* Data as of June 14, 2021, for reports with vaccination date and receipt date May 10 through June 11, 2021

† Data as of June 14, 2021, for reports with vaccination date and receipt date December 14, 2020, through June 11, 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 1 report of death in the 12–15-year-old age group and 18 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 Jun 11, 2021)

12–15 years old* (N= 2,540)

Adverse event‡	n (%)
Dizziness	618 (24.3)
Syncope	446 (17.6)
Nausea	308 (12.1)
Headache	281 (11.1)
Vomiting	221 (8.7)
Pallor	218 (8.6)
Loss of consciousness	217 (8.5)
Pyrexia (fever)	215 (8.5)
Hyperhidrosis	211 (8.3)
Fatigue	182 (7.2)

16–25 years old† (N= 12,759)

(for comparison)

Adverse event‡	n (%)
Dizziness	2,832 (22.2)
Headache	2,197 (17.2)
Nausea	1,955 (15.3)
Pyrexia (fever)	1,948 (15.3)
Fatigue	1,689 (13.2)
Chills	1,609 (12.6)
Pain	1,560 (12.2)
Syncope	1,257 (9.9)
Hyperhidrosis	946 (7.4)
Vomiting	918 (7.2)

- 12–15 years old: ~6.0 million doses administered (May 10 thru Jun 11, 2021)
- 16–25 years old: ~21.6 million doses administered (December 14, 2020, thru Jun 11, 2021)

* Data as of June 14, 2021, for reports with vaccination date and receipt date May 10 through June 11, 2021

† Data as of June 14, 2021, for reports with vaccination date and receipt date December 14, 2020, through June 11, 2021

‡ Adverse events are not mutually exclusive

CDC working case definition for acute myocarditis

Acute Myocarditis

Clinical myocarditis

Probable Case

Presence of ≥ 1 new or worsening of the following clinical symptoms:

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

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

- irritability
- vomiting
- poor feeding
- tachypnea
- lethargy

AND

≥ 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*
- abnormal cardiac function or wall motion abnormalities on echocardiogram
- cMRI findings consistent with myocarditis†

AND

- No other identifiable cause of the symptoms and findings

Confirmed Case

Presence of ≥ 1 new or worsening of the following clinical symptoms:

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

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

- irritability
- vomiting
- poor feeding
- tachypnea
- lethargy

AND

- Histopathologic confirmation of myocarditis§

OR

- Troponin level above upper limit of normal (any type of troponin), **AND**
- cMRI findings consistent with myocarditis†

AND

- No other identifiable cause of the symptoms and findings

---

*To meet the ECG or rhythm monitoring criterion, must include at least one of:

- ST-segment or T-wave abnormalities
- Paroxysmal or sustained atrial, supraventricular, or ventricular arrhythmias
- AV nodal conduction delays or intraventricular conduction defects

†Using either the original or the revised Lake Louise criteria (Ferreira et al. *J Am Coll Cardiol.* 2018;72:3158-76)
§Using the Dallas criteria (Aretz et al. *Am J Cardiovasc Pathol.* 1987;1:3-14)

Notes:
1. Autopsy cases may be classified as confirmed clinical myocarditis on the basis of meeting histopathologic criteria if no other identifiable cause
2. Cases with individuals who lack the listed symptoms but who meet other criteria may be classified as subclinical myocarditis (probable or confirmed)

CDC working case definition for acute pericarditis

Acute Pericarditis

Presence of ≥2 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

Myopericarditis

This term may be used for patients who meet criteria for both myocarditis and pericarditis.

Preliminary myocarditis/pericarditis reports to VAERS following dose 1 mRNA COVID-19 vaccination, Exp. vs. Obs. using 21-day risk window (data thru Jun 11, 2021)

Age groups	Females			Male		
	Doses admin	Expected*,†	Observed*	Doses admin	Expected*,†	Observed*
12–17 yrs	3,777,097	1–13	4	3,569,239	2–21	**32**
18–24 yrs	6,830,706	2–23	9	5,863,268	3–34	**47**
25–29 yrs	5,198,356	2–18	3	4,685,036	3–27	18
30–39 yrs	11,505,068	7–66	15	10,391,499	6–60	17
40–49 yrs	11,996,507	7–69	9	10,513,258	6–60	8
50–64 yrs	21,957,007	13–126	22	19,270,825	11–111	18
65+ yrs	24,795,212	14–143	13	20,473,779	12–118	15
Not reported	—	—	2	—	—	4

* Assumes a 21-day post-vaccination observation window (i.e., symptom onset from day of vaccination through Day 20 after vaccination)

† 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. Expected counts among females 12–29 years adjusted for lower prevalence relative to males by factor of 1.7 (Fairweather, D. et al, *Curr Probl Cardiol.* 2013;38(1):7-46).

Preliminary myocarditis/pericarditis reports to VAERS following dose 1 mRNA COVID-19 vaccination, Exp. vs. Obs. using 7-day risk window (data thru Jun 11, 2021)

Age groups	Females			Males		
	Doses admin	Expected*,†	Observed*	Doses admin	Expected*,†	Observed*
12–17 yrs	3,777,097	0–4	3	3,569,239	1–7	**27**
18–24 yrs	6,830,706	1–8	6	5,863,268	1–11	**41**
25–29 yrs	5,198,356	1–6	2	4,685,036	1–9	**14**
30–39 yrs	11,505,068	1–13	8	10,391,499	2–20	14
40–49 yrs	11,996,507	1–14	1	10,513,258	2–20	5
50–64 yrs	21,957,007	2–25	16	19,270,825	4–37	10
65+ yrs	24,795,212	2–25	8	20,473,779	4–39	8
Not reported	—	—	2	—	—	2

* Assumes a 7-day post-vaccination observation window (i.e., symptom onset from day of vaccination through Day 6 after vaccination)

† 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. Expected counts among females 12–29 years adjusted for lower prevalence relative to males by factor of 1.7 (Fairweather, D. et al, *Curr Probl Cardiol.* 2013;38(1):7-46).

Preliminary myocarditis/pericarditis reports to VAERS following dose 2 mRNA COVID-19 vaccination, Exp. vs. Obs. using 21-day risk window (data thru Jun 11, 2021)

Age groups	Females			Males		
	Doses admin	Expected*,†	Observed*	Doses admin	Expected*,†	Observed*
12–17 yrs	2,189,726	1–7	**20**	2,039,871	1–12	**132**
18–24 yrs	5,237,262	2–18	**27**	4,337,287	2–25	**233**
25–29 yrs	4,151,975	1–15	11	3,625,574	2–21	**69**
30–39 yrs	9,356,296	5–54	14	8,311,301	5–48	**71**
40–49 yrs	9,927,773	6–57	23	8,577,766	5–49	40
50–64 yrs	18,696,450	11–108	25	16,255,927	9–94	34
65+ yrs	21,708,975	12–125	17	18,041,547	10–104	16
Not reported	—	—	1	—	—	9

* Assumes a 21-day post-vaccination observation window (i.e., symptom onset from day of vaccination through Day 20 after vaccination)

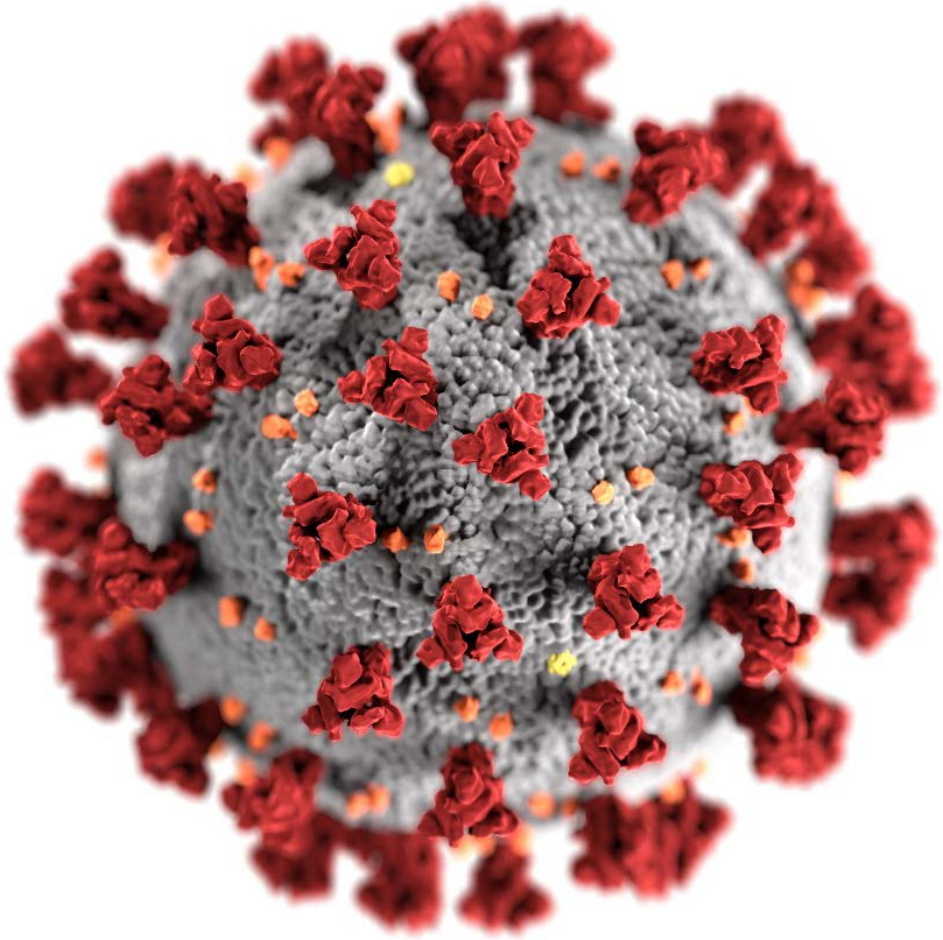
† Based on Gubernot et al. U.S. Population-Based background incidence rates of medical conditions for use in safety assessment of COVID-19 vaccines. Vaccine. 2021 May 14:S0264-410X(21)00578-8. Expected counts among females 12–29 years adjusted for lower prevalence relative to males by factor of 1.7 (Fairweather, D. et al, *Curr Probl Cardiol.* 2013;38(1):7-46).

COVID-19 mRNA vaccines in adolescents and young adults: Benefit-risk discussion

Dr. Megan Wallace and Dr. Sara Oliver

ACIP Meeting

June 23, 2021

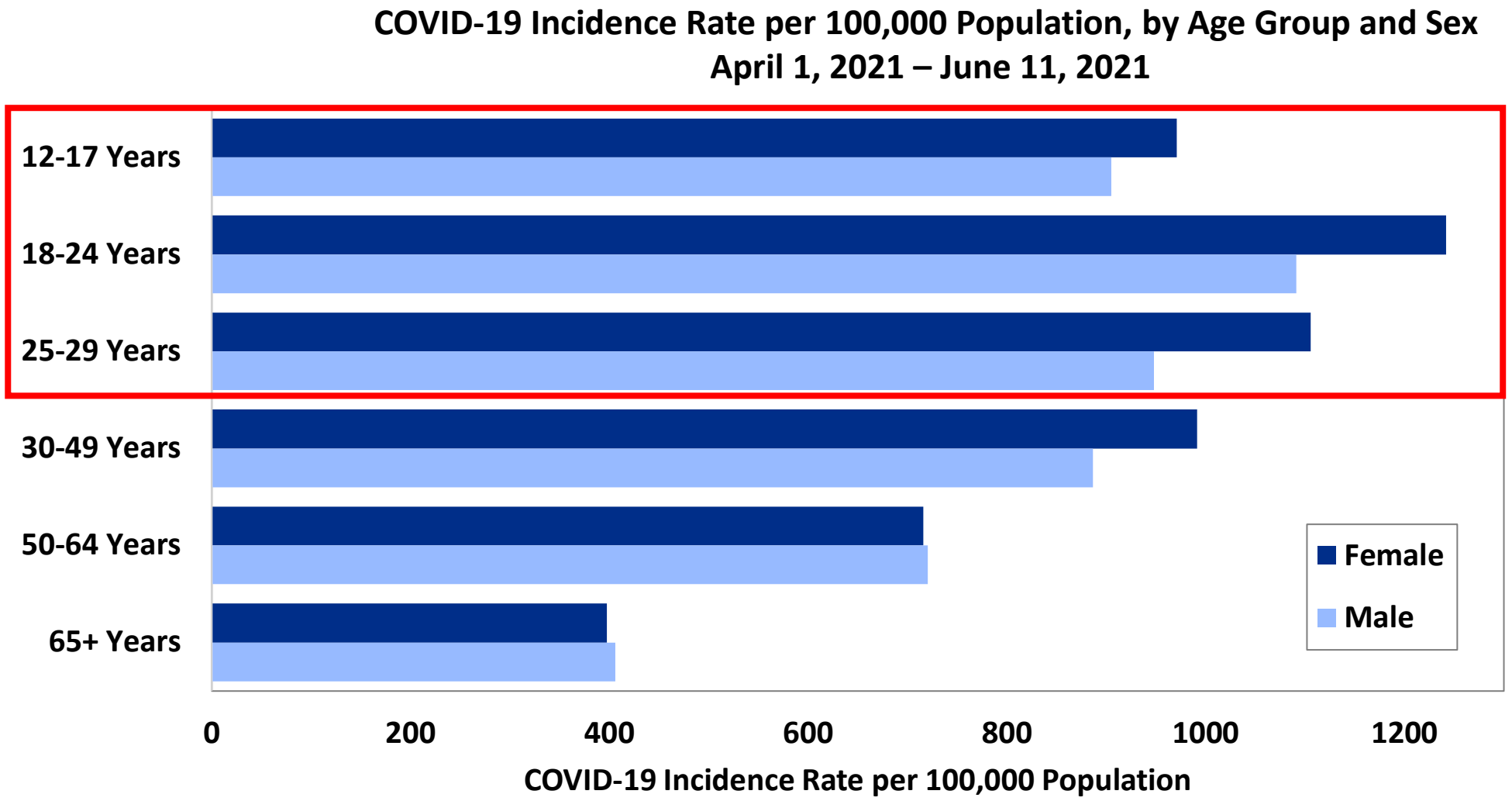


cdc.gov/coronavirus

Current COVID-19 mRNA vaccine policy

- COVID-19 vaccines are recommended for persons 12 years of age and older in the United States under FDA's Emergency Use Authorization

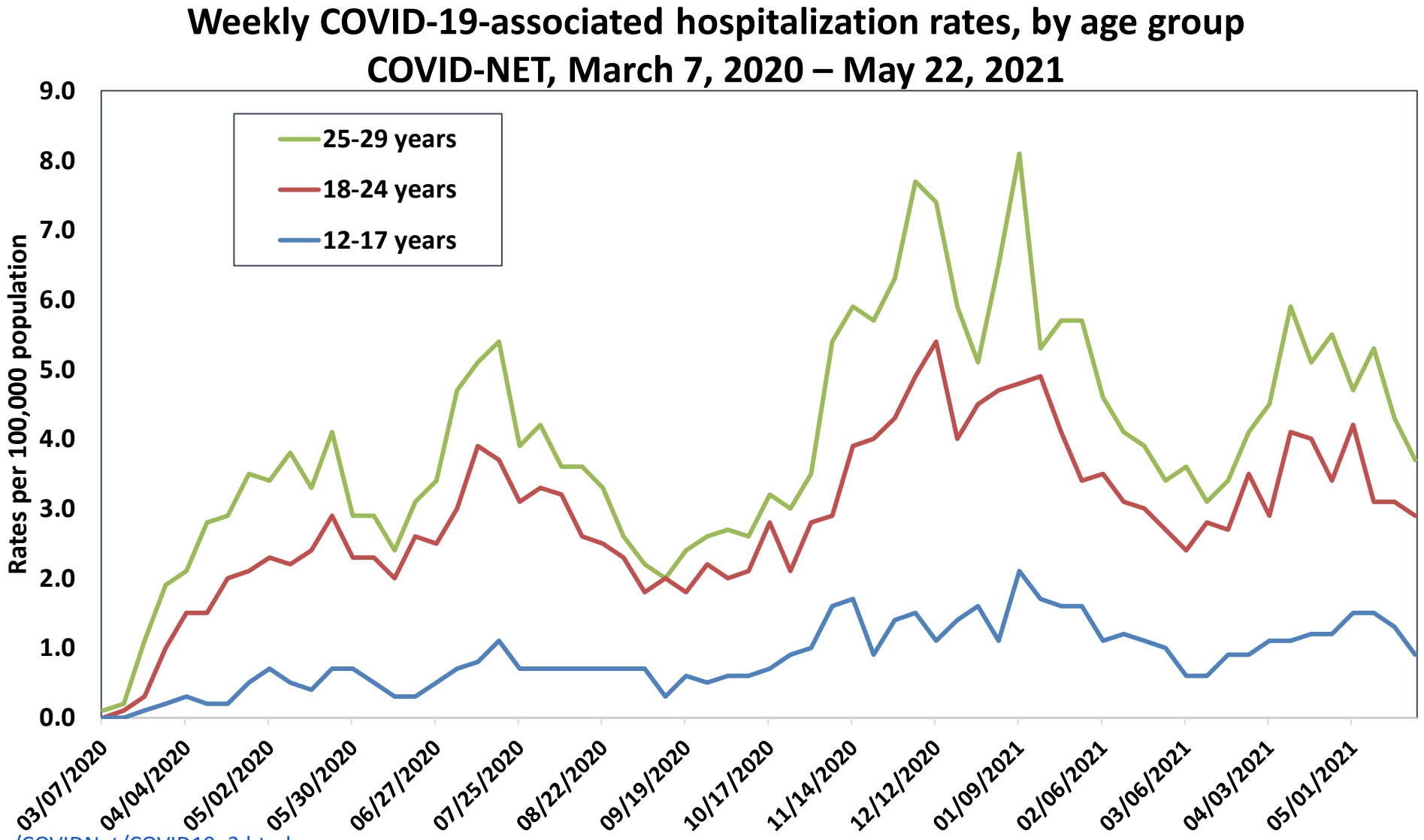
Adolescents and young adults have the highest COVID-19 incidence rates



Since beginning of pandemic **at least 7.7 million** COVID-19 cases have been reported among persons aged 12–29 years

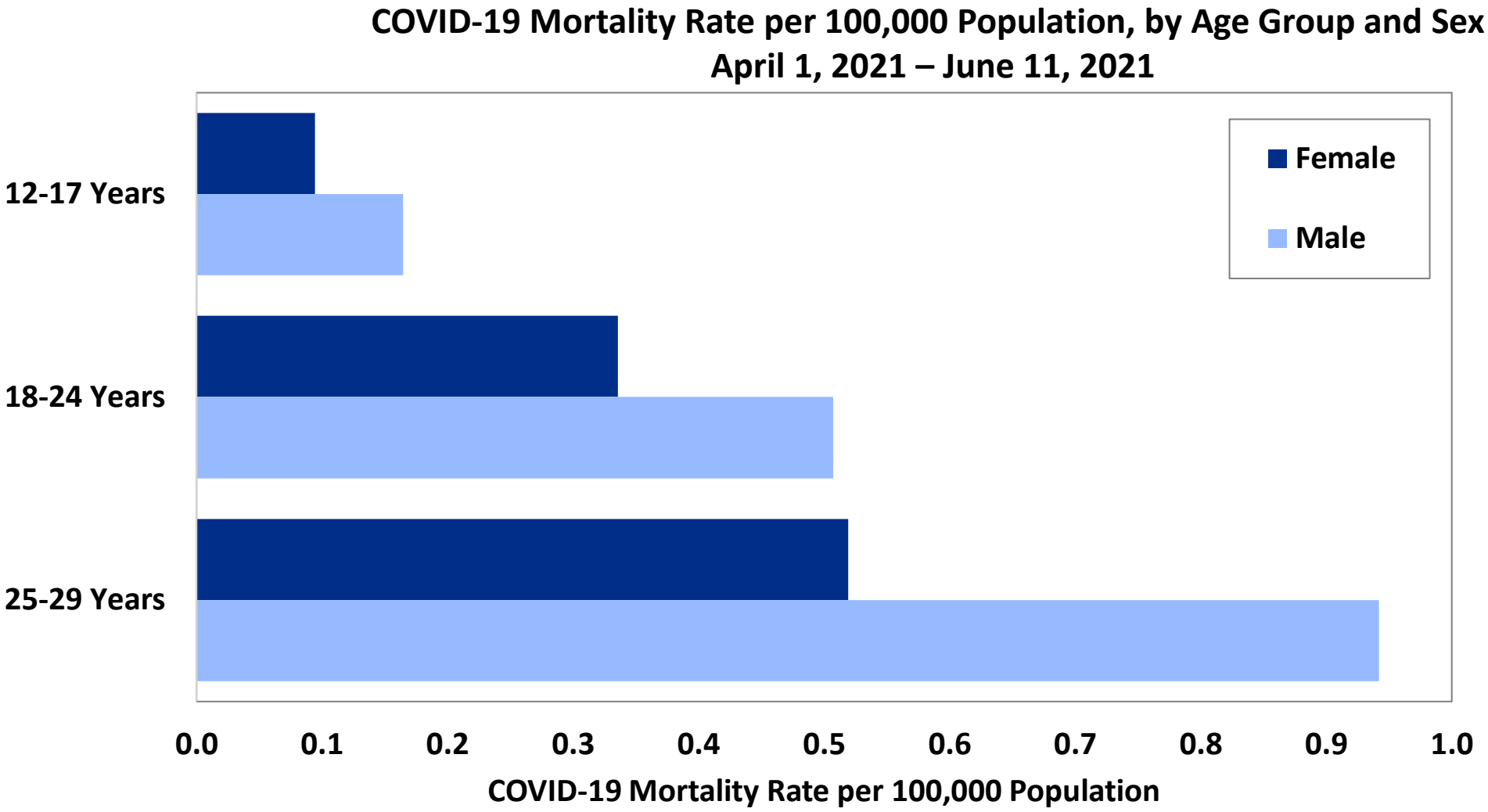
https://covid.cdc.gov/covid-data-tracker/#demographics

COVID-19-associated hospitalization rates have remained stable in adolescents and young adults



https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html

COVID-19-associated deaths continue to occur in adolescents and young adults



Since beginning of pandemic, **2,767** COVID-19 deaths have been reported among persons aged 12-29 years; **316** deaths reported since April 1, 2021

https://covid.cdc.gov/covid-data-tracker/#demographics

Post-COVID conditions can occur after COVID-19

- No standardized definition, but generally **new** or **persisting symptoms** from acute infection or exacerbation of a chronic condition **≥4 weeks after SARS-CoV-2 infection**
- Reported after infections ranging from asymptomatic to severe
- Limited data in adolescents/young adults, but recent cross-sectional studies have shown evidence of new or persisting COVID symptoms in this age group[1,2]
  - Up to one-half of study participants had symptoms 1 month post-diagnosis
  - Symptoms reported include fatigue, insomnia, rhinorrhea, muscle pain, headache, lack of concentration, exercise intolerance, dyspnea, chest pain

[1]Buonsenso et al, Acta Paediatrica (2021)
[2]Walsh-Messinger et al, medRXiv (2020)

Multisystem Inflammatory Syndrome in Children (MIS-C)

- Severe hyperinflammatory syndrome occurring 2–6 weeks after acute SARS-CoV-2 infection among persons <21 years old, resulting in a wide range of manifestations and complications
  - 60%–70% of patients are admitted to intensive care, 1%–2% die[1,2]
- **4,018 MIS-C** cases have been reported to national surveillance as of June 2, 2021[3]
  - Estimated incidence of 1 MIS-C case in 3,200 SARS-CoV-2 infections[4]
  - 36% of cases in persons aged 12–20 years
  - 62% of reported cases have occurred in children who are Hispanic/Latino or Black, Non-Hispanic

1. Feldstein LR, Tenforde MW, Friedman KG, et al. Characteristics and Outcomes of US Children and Adolescents With Multisystem Inflammatory Syndrome in Children (MIS-C) Compared With Severe Acute COVID-19. JAMA. 2021;325(11):1074-1087. doi:10.1001/jama.2021.2091

2. Belay ED, Abrams J, Oster ME, et al. Trends in Geographic and Temporal Distribution of US Children With Multisystem Inflammatory Syndrome During the COVID-19 Pandemic [published online ahead of print, 2021 Apr 6]. JAMA Pediatr. 2021;e210630. doi:10.1001/jamapediatrics.2021.0630

3. Health Department-Reported Cases of Multisystem Inflammatory Syndrome in Children (MIS-C) in the United States. https://www.cdc.gov/mis-c/cases/index.html

4. Payne et al, *JAMA Netw Open.* 2021;4(6):e2116420. doi:10.1001/jamanetworkopen.2021.16420

Myocarditis and COVID-19

- 1597 young athletes with recent SARS-CoV-2 infection had cardiac MRI[1]
  - 37 (**2.3**%) with abnormal MRI findings
  - However, **24** (65%) of 37 had **normal** lab findings and **no symptoms**
  - Another study suggested some MRI findings may be related to remodeling from athletic training[2]
- Retrospective study — children with acute myocarditis treated at a single center from 2018–2020[3]
  - 27 children <18 years of age identified
  - 7/27 (**26**%) had evidence of prior SAR-CoV-2 infection or exposure
    - 6 ultimately diagnosed with MIS-C
  - Individuals with myocarditis/MIS-C related to SARS-CoV-2 had better clinical course
    - None diagnosed with acute fulminant myocarditis
    - Shorter duration of inotropic drug support and ICU stay
    - Did not require mechanical respiratory support

[1]Daniels CJ, et al. *JAMA Cardiol.* Pub online May 27, 2021. doi:10.1001/jamacardio.2021.2065; [2]Clark DE, et al. Circulation; 2021:143(6): [3]Vukomanovic et al. PIDJ;2021:40(5):e173-e178

Summary

- COVID-19 incidence, hospitalization, and mortality rates are decreasing overall
  - Variants continue to spread and scenarios exist in which cases increase in fall
  - Adolescents are growing proportion of cases given vaccine coverage among adults
- Post COVID-19 conditions also impact adolescents and young adults
  - 4,018 MIS-C cases have been reported to national surveillance
- Myocarditis is a disease marked by inflammation of the heart muscle
  - Risk factors include younger age and male sex
  - Can occur with SARS-CoV-2 infection
- Myocarditis after mRNA vaccines noted with highest frequency in males aged 12–29 years following 2nd dose
  - Early outcomes have been encouraging, but no long-term data available yet

COVID-19 mRNA vaccines in adolescents and young adults

Risk after COVID-19 mRNA vaccines in adolescents and young adults

Benefits of COVID-19 mRNA vaccines in adolescents and young adults

Potential harms of the mRNA COVID-19 vaccines:

After dose 2

- 133 million vaccine 2nd doses administered* and 636 reported myocarditis cases as of June 11, 2021
  - Additional potential myocarditis cases under review

	Females			Males		
Age group	**Cases§**	**Doses admin**	**Reporting rate†**	**Cases§**	**Doses admin**	**Reporting rate†**
12-17 years old	19	2,189,726	8.68	128	2,039,871	62.75
18-24 years old	23	5,237,262	4.39	219	4,337,287	50.49
25-29 years old	7	4,151,975	1.69	59	3,625,574	16.27
30-39 years old	11	9,356,296	1.18	61	8,311,301	7.34
40-49 years old	18	9,927,773	1.81	34	8,577,766	3.96
50-64 years old	18	18,696,450	0.96	18	16,255,927	1.11
65+ years old	10	21,708,975	0.46	11	18,041,547	0.61

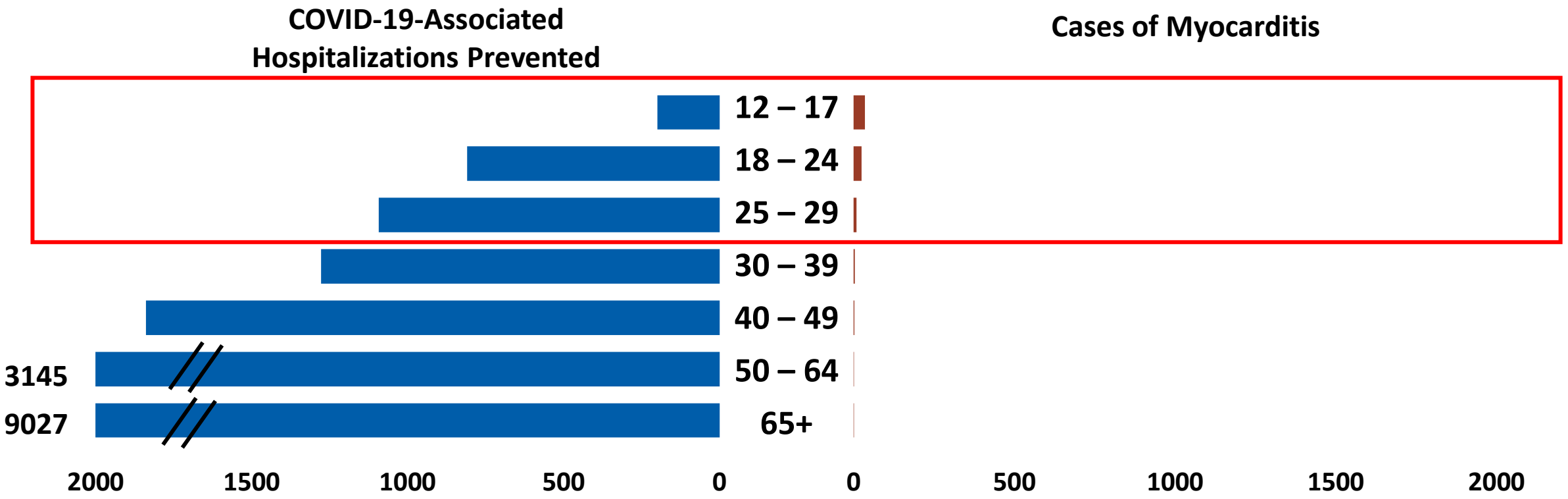
§ Cases reported through VAERS using a 7-day risk window

* Source of doses administered: https://covid.cdc.gov/covid-data-tracker/#vaccinations; Some age- and sex-specific doses administered data were imputed

†Reporting rate = myocarditis cases per 1 million mRNA COVID-19 vaccine doses administered

Benefits and risks after dose 2, by age group

For every **million** doses of mRNA vaccine given with current US exposure risk[1]



[1] Based on hospitalization rates from COVID-NET as of May 22nd. Benefit/Risk calculated over 120 days.

Predicted cases prevented vs. myocarditis cases for every million second dose vaccinations over 120 days

Females 18–24 Years

14,000 COVID-19 cases prevented

1,127 hospitalizations prevented

93 ICU admissions prevented

13 deaths prevented

4–5 myocarditis cases

Males 18–24 Years

12,000 COVID-19 cases prevented

530 hospitalizations prevented

127 ICU admissions prevented

3 deaths prevented

45–56 myocarditis cases

Hospitalizations, ICU admissions and deaths based on data for week of May 22, 2021.

Benefit-risk analyses

Population Level Considerations

- No alternatives to mRNA vaccines for the foreseeable future in adolescents
- Vaccination of students offers an added layer of protection against COVID-19 and can be an important tool to return to 'normal'
- Higher levels of vaccination coverage can lead to less community transmission, which can protect against development and circulation of emerging variants
- Racial and ethnic minority groups have higher rates of COVID-19 and severe disease[1]
  - Potential changes in vaccine policy, or anything that would impact vaccination coverage for adolescents/young adults may disproportionately impact those groups with highest rates of poor COVID-19 outcomes

1. https://covid.cdc.gov/covid-data-tracker/#demographics

Benefit-risk interpretations and limitations

- Direct benefit-risk assessment shows **positive balance** for all age and sex groups
  - Considers individual benefits of vaccination vs. individual risks
  - Benefits are likely an underestimate
    - Analysis was performed using reported rates of cases and hospitalizations
    - Likely represent only a fraction of the true cases that have occurred in the population
  - Still uncertainty in rates of myocarditis after mRNA vaccines
    - Not all cases are verified and crude rates were used
- Balance of risks and benefits **varies** by age and sex
  - Balance could change with increasing or decreasing incidence
- Limited data currently on risk of myocarditis in 12–15 year old population
  - Due to timing of recommendations, limited number of 2nd doses given

Clinical Considerations

COVID-19 mRNA vaccines in adolescents and young adults: Benefit-risk discussion

Work Group Interpretation

- Initial presentations are reassuring; however, continued monitoring of cases, clinical course, and long-term outcomes of myocarditis after mRNA vaccines will be important
- Need to follow the benefit-risk balance as we learn more around myocarditis, as well as updates to epidemiology (cases, variants, etc)
- Currently, the **benefits** still clearly **outweigh** the risks for COVID-19 vaccination in adolescents and young adults

Vaccine considerations in people with a history of myocarditis or pericarditis

Scenario	Recommendation
Pericarditis prior to COVID-19 vaccination	Receive any FDA-authorized COVID-19 vaccine
Pericarditis after 1st dose of an mRNA COVID-19 vaccine but prior to 2nd dose	Proceed with a 2nd dose of mRNA COVID-19 vaccine after resolution of symptoms. Discuss with patient, guardian, and clinical team
Myocarditis prior to COVID-19 vaccination	Receive any FDA-authorized COVID-19 vaccine if heart has recovered
Myocarditis after 1st dose of an mRNA COVID-19 vaccine but prior to 2nd dose	Defer 2nd dose of mRNA COVID-19 vaccine until more information is known However, if heart has recovered, could consider proceeding with 2nd dose under certain circumstances. Discuss with patient, guardian, and clinical team

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- Stephen Hadler
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- Hannah Rosenblum
- COVID-19 Vaccine Task Force
- Vaccine Safety Team
- Immunization team
- Epi Task Force
  - MIS-C unit
  - COVID-NET
- Data, Analytics and Visualization Task Force
- Division of Healthcare Quality Promotion
- Respiratory Viruses Branch

Q&A and Discussion

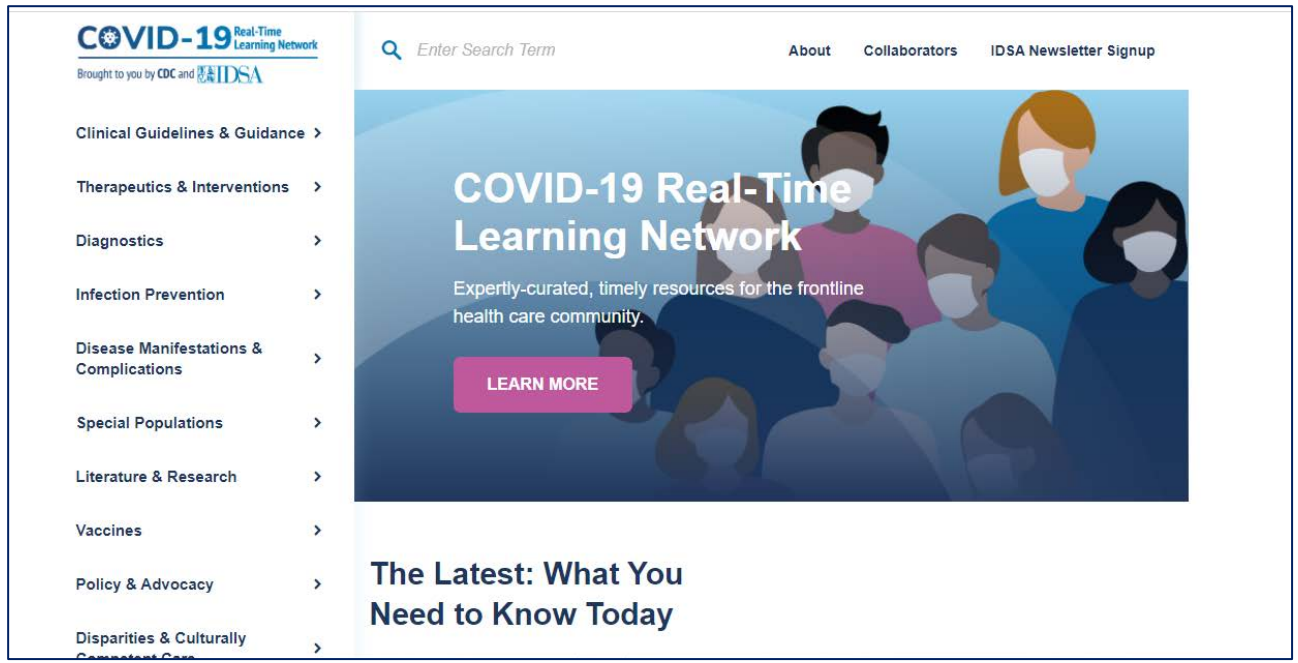
Links and Resources

- Slide 1 – Call recording: www.idsociety.org/cliniciancalls
- Slide 30 - Larson et al. *Circulation*. 2021 https://www.gov.il/en/departments/news/01062021-03
- Slide 36 - VAERS - http://vaers.hhs.gov
- Slide 37 - More information about clinical consults available at https://www.cdc.gov/vaccinesafety/activities/cisa.html
- Slide 38 - CDC Medical Dictionary for Regulatory Activities https://www.meddra.org/
- Slide 59 - https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myocarditis.html
  https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html
- Slide 60 - How to report to VAERS
  VAERS - http://vaers.hhs.gov
  For help: Call 1-800-822-7967
  Email info@VAERS.org
  video instructions https://youtu.be/sbCWhcQADFE
- Slide 62 - https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety.html
- Slide 65 - FDA: 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
- Slide 67 - http://cdc.gov/vsafe
- Slides 83, 85 and 94 - https://covid.cdc.gov/covid-data-tracker/#demographics
- Slide 84 - https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html
- Slide 87 - Health Department-Reported Cases of MIS-C in the United States. https://www.cdc.gov/mis-c/cases/index.html
- Slide 91 - Source of doses administered: https://covid.cdc.gov/covid-data-tracker/#vaccinations
- Slide 102 - https://www.idsociety.org/covid-19-real-time-learning-network/

COVID-19 Real-Time Learning Network

Brought to you by CDC and IDSA

An online community bringing together information and opportunities for discussion on latest research, guidelines, tools and resources from a variety of medical subspecialties around the world.



Specialty Society Collaborators

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Society of Hospital Medicine
Society of Infectious Diseases Pharmacists

www.COVID19LearningNetwork.org
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CDC-IDSA Partnership: Clinical Management Call Support

FOR WHOM?

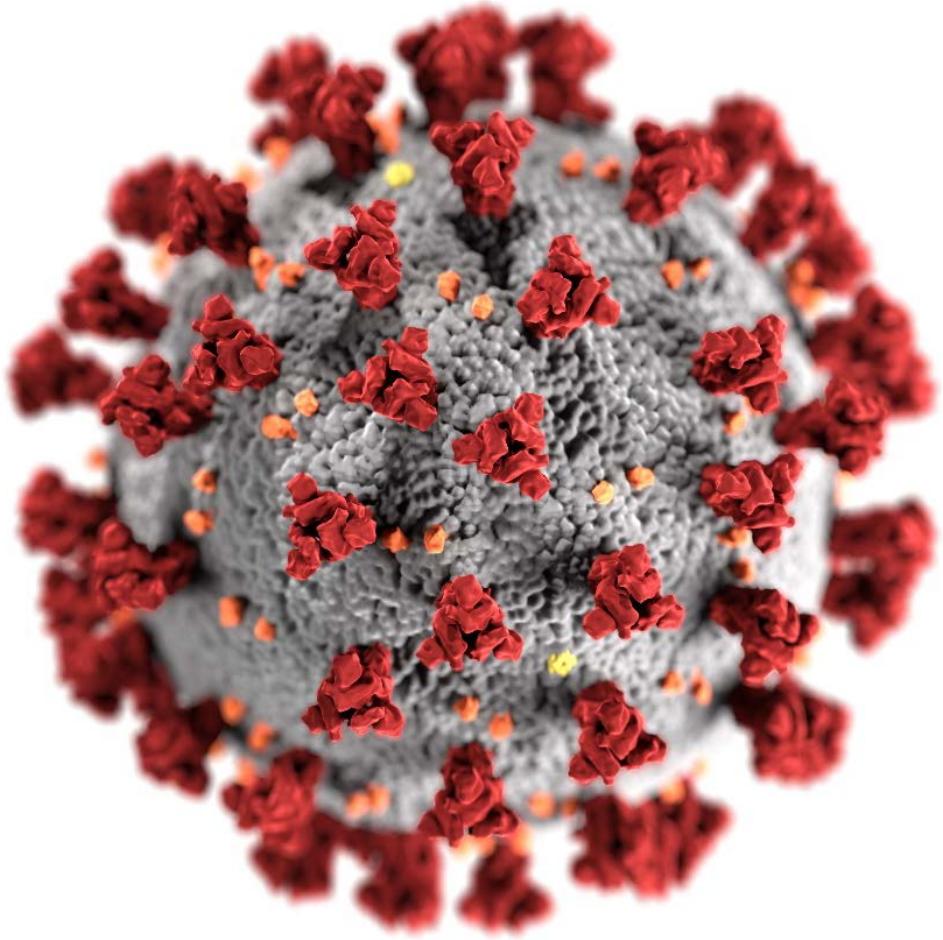
- Clinicians who have questions about the clinical management of COVID-19

WHAT?

- Calls from clinicians will be triaged by CDC to a group of IDSA volunteer clinicians for peer-to-peer support

HOW?

- Clinicians may call the main CDC information line at 800-CDC-INFO (800-232-4636)
- To submit your question in writing, go to www.cdc.gov/cdc-info and click on Contact Form



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Infectious Diseases Society of America

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Virtual Conference

Save the Date
Sept. 29 – Oct. 3, 2021

Attend, Learn & Collaborate.

Advancing Science, Improving Care

Important Dates:

- Registration is Open
- Abstract Submission Deadline – June 9
- Case Submission Deadline – June 9

Continue the conversation on Twitter

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We want to hear from you!

Please complete the post-call survey.

Clinician calls are now twice a month:

Updated Summer Schedule:

July 17

July 31

August 14

August 28

A recording of this call will be posted Monday at **www.idsociety.org/cliniciancalls**

-- library of all past calls available --

Contact Us:

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