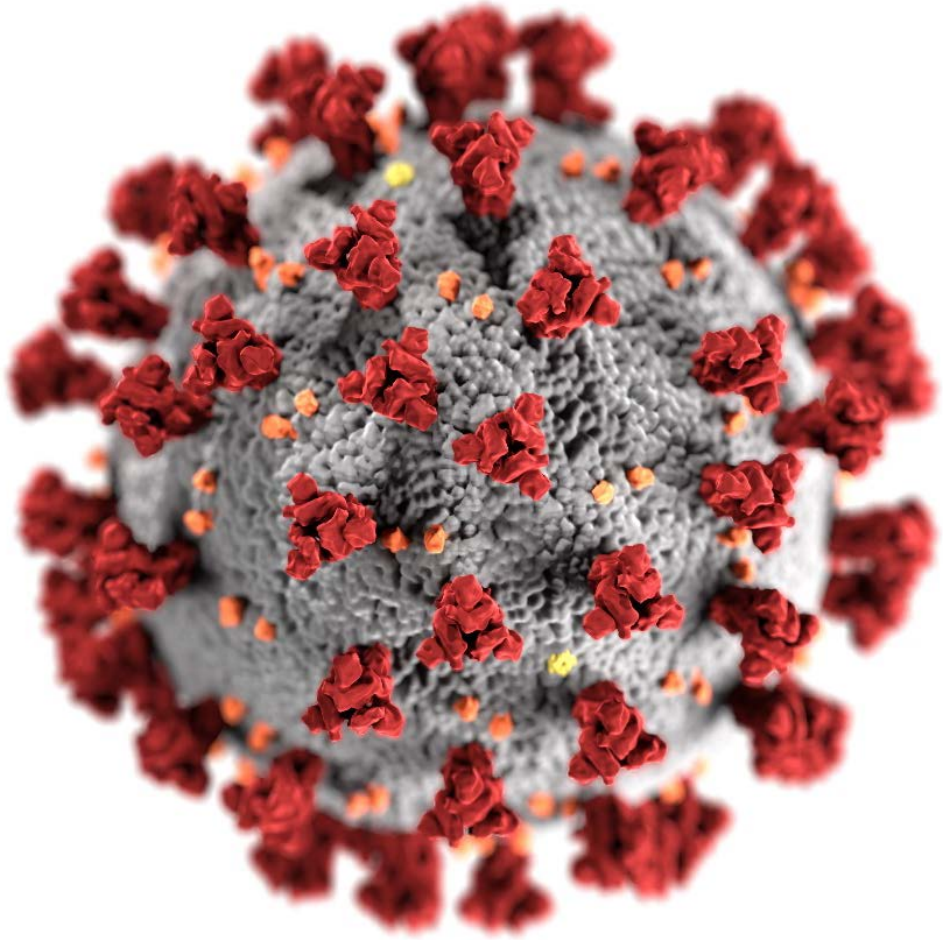
mRNA COVID-19 Vaccine-Associated Myocarditis



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CDC COVID-19 Response, Vaccine Task Force
Pediatric Cardiologist, Children's Healthcare of Atlanta

cdc.gov/coronavirus

Outline

- Cases of myocarditis after COVID-19 vaccine
- Comparing types of myocarditis
- 3-6 month outcomes of myocarditis

Vaccine Adverse Event Reporting System (VAERS): Reporting rates (per 1 million doses administered) of myocarditis after mRNA COVID-19 vaccines, 7-day risk period

- Reporting rates exceed background incidence*

	Pfizer (Males)		Pfizer (Females)	
Ages	**Dose 1**	**Dose 2**	**Dose 1**	**Dose 2**
12-15	**4.2**	**39.9**	0.4	**3.9**
16-17	**5.7**	**69.1**	0.0	**7.9**
18-24	**2.3**	**36.8**	0.2	**2.5**
25-29	1.3	**10.8**	0.2	1.2
30-39	0.5	**5.2**	0.6	0.7
40-49	0.3	**2.0**	0.1	1.1
50-64	0.2	0.3	0.3	0.5
65+	0.2	0.1	0.1	0.3

* An estimated 1–10 cases of myocarditis per 100,000 person years occurs among people in the United States, regardless of vaccination status; adjusted for the 7-day risk period, this estimated background is **0.2 to 1.9 per 1 million person 7-day risk period**

Care and outcomes of preliminary myocarditis cases reported to VAERS after mRNA COVID-19 vaccination in persons aged <30 years (N=1,640)

(data thru Oct 6, 2021)

1,640 total preliminary reports

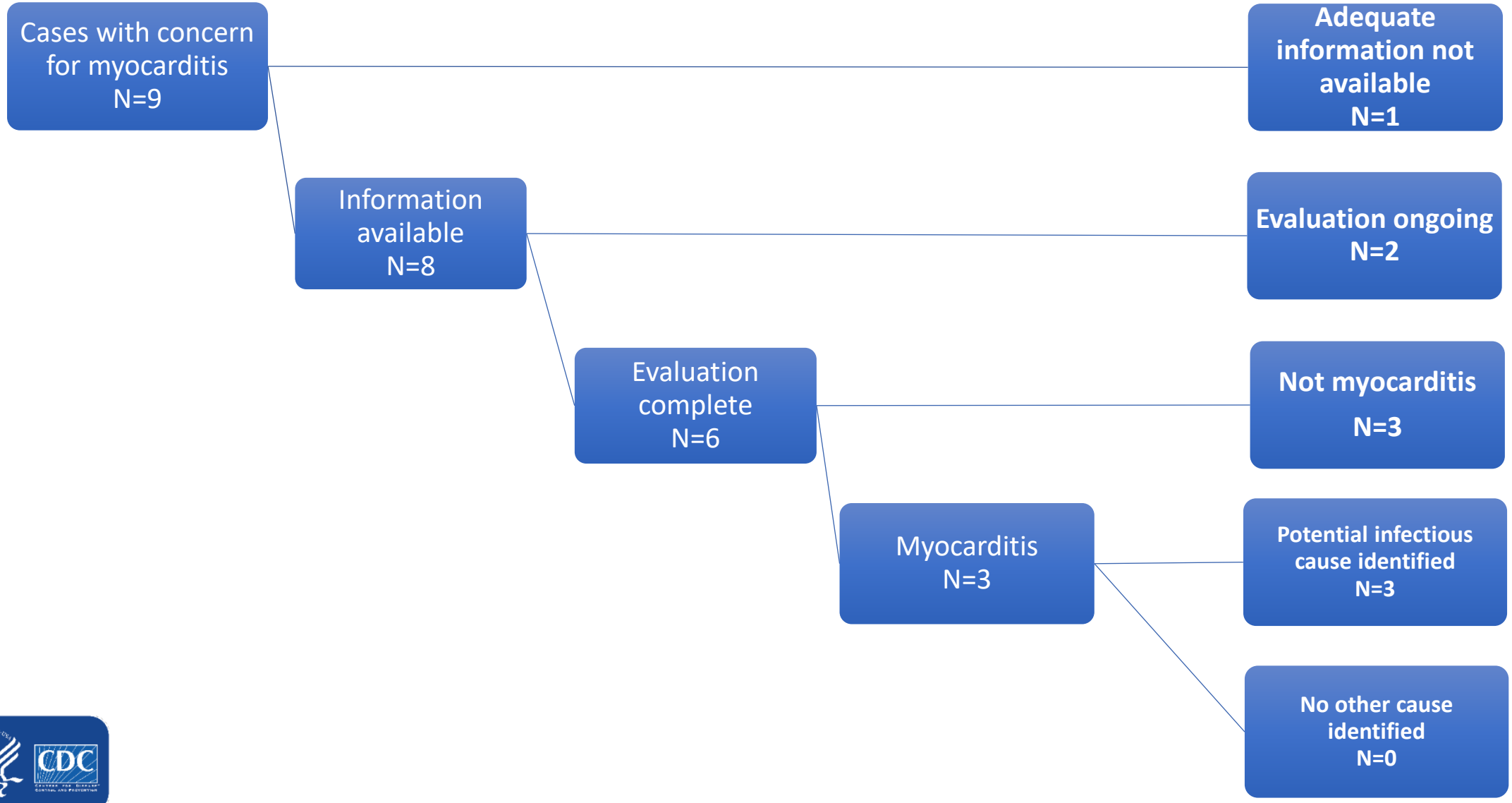
- **877** met CDC case definition* of myocarditis
- 637 under review

Of 877 meeting case definition:

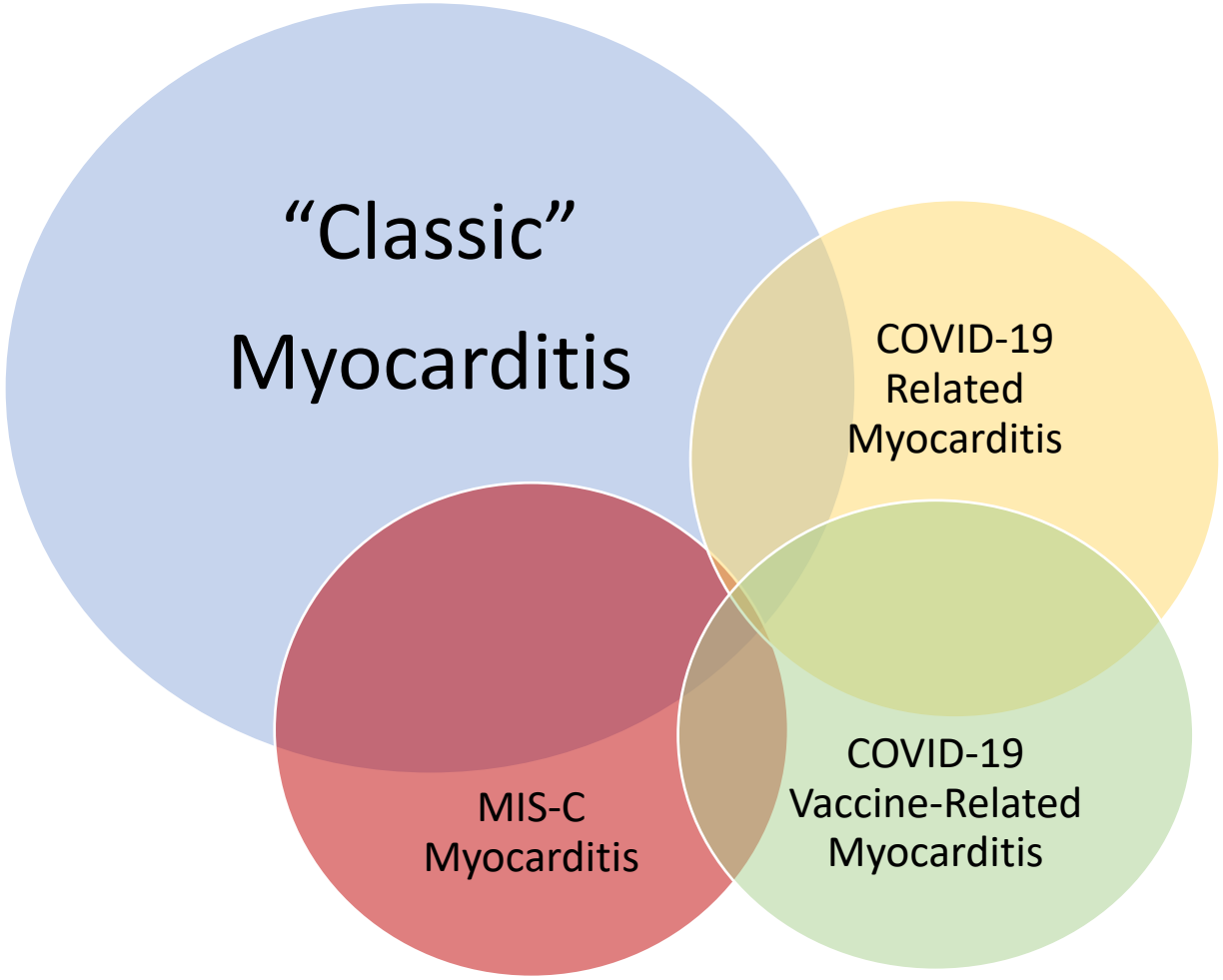
- 829 were hospitalized
  - 789 discharged
    - **607/789 (77%) known to have recovered from symptoms at time of report**
- 34 were not hospitalized (seen in emergency room, urgent care, outpatient clinic, not specified)
- Cardiac MRI abnormal in 72% of cases (223/312)

* Definition available from Gargano JW, Wallace M, Hadler SC, et al. Use of mRNA COVID-19 Vaccine After Reports of Myocarditis Among Vaccine Recipients: Update from the Advisory Committee on Immunization Practices — United States, June 2021. MMWR Morb Mortal Wkly Rep 2021;70:977–982. https://www.cdc.gov/mmwr/volumes/70/wr/pdfs/mm7027e2-H.pdf

Reports of deaths in persons aged <30 years with possible concern for myocarditis in VAERS (among ~86 million doses)



Comparing types of myocarditis



Causes of “classic” myocarditis

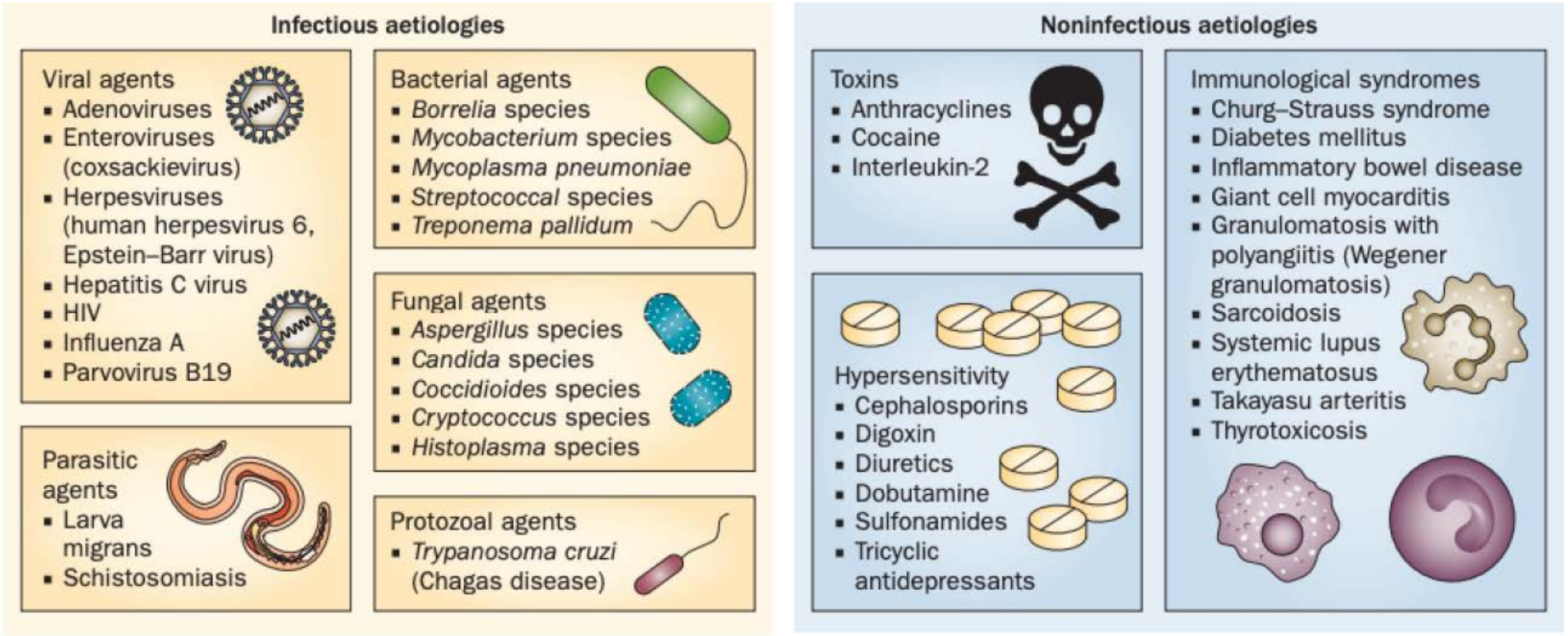
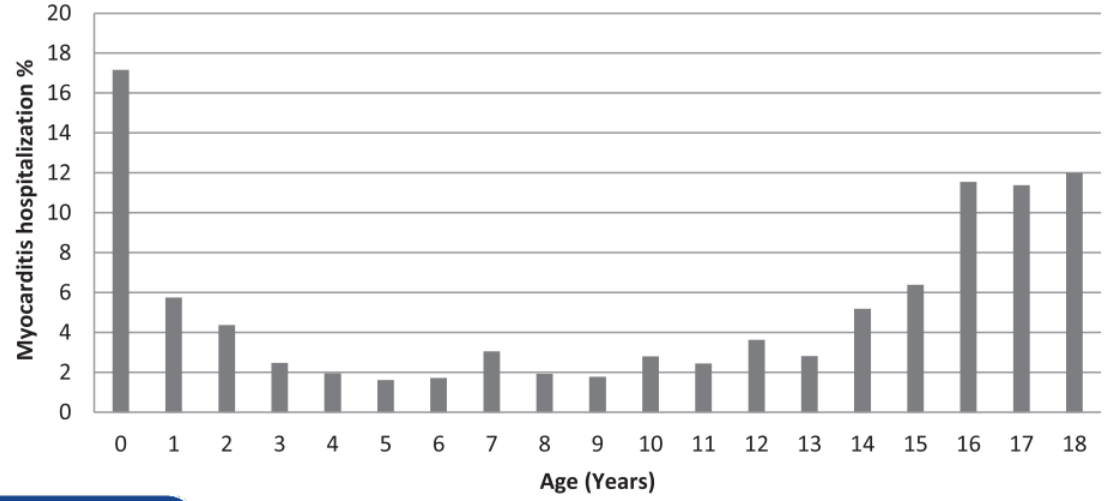


Figure 1 | Common causes of myocarditis. Viral infection is the most common aetiology, but several other aetiologies of myocarditis have also been implicated.

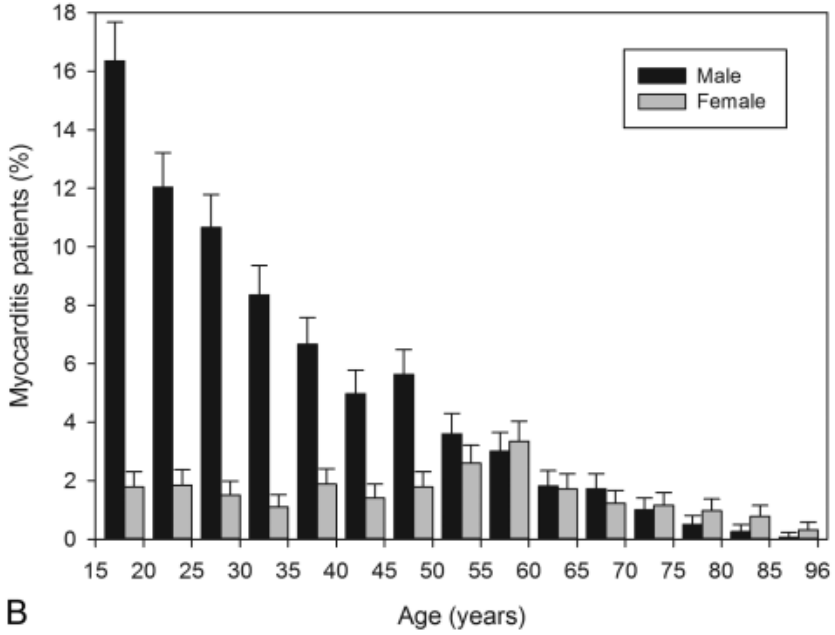
Epidemiology of myocarditis in pre-COVID era

- Children
  - Annual incidence 0.8 per 100,000
    - In persons aged 15-18 years, 1.8 per 100,000 in 2015-2016
  - 66% male
  - Mortality 4-7%, transplant 4-9%



Vasudeva et al. *American J Cardiology.* 2021.
Ghelani et al. *Circ Cardiovasc Qual Outcomes.* 2012
Butts et al. *Pediatric Cardiology.* 2017
Sachdeva et al. *Am J Cardiol.*2015

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



Kyto et al. *Heart*. 2013.

MIS-C myocarditis

JAMA Pediatrics | Original Investigation

Trends in Geographic and Temporal Distribution of US Children With Multisystem Inflammatory Syndrome During the COVID-19 Pandemic

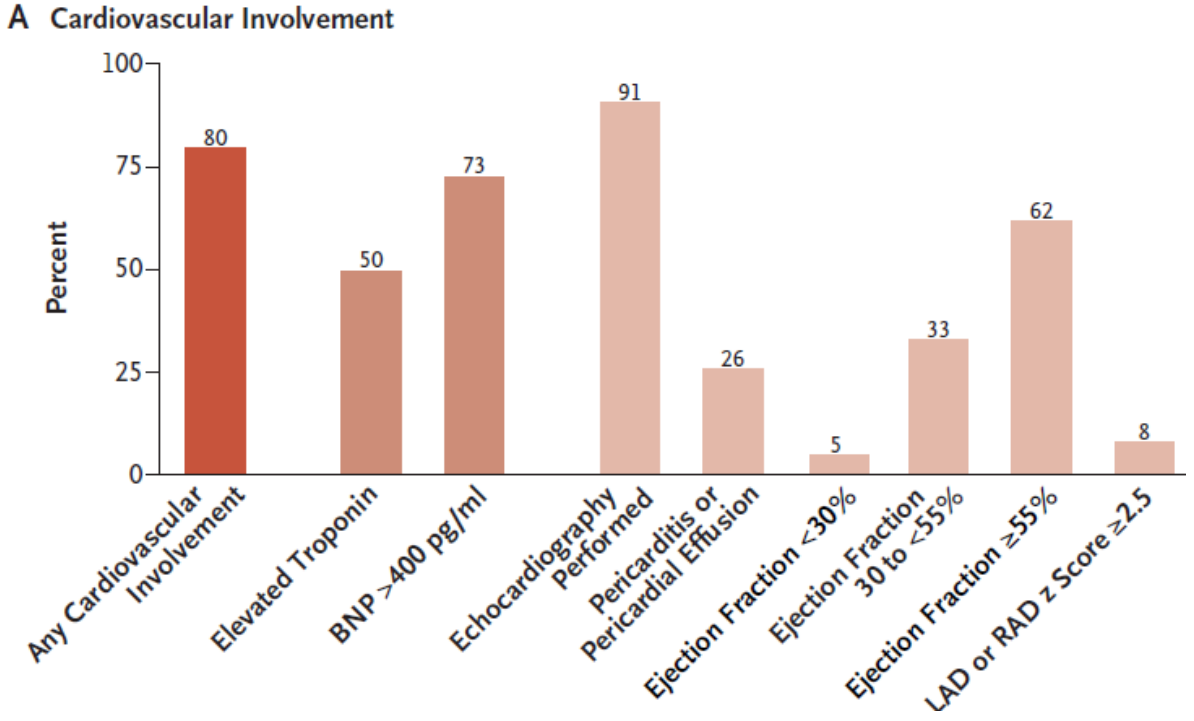
Myocarditis	300 (17.3)

Belay et al. 2021

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Multisystem Inflammatory Syndrome in U.S. Children and Adolescents



Feldstein et al. 2020

COVID-19 myocarditis among pediatric patients

	Myocarditis Diagnosed (%)	Myocarditis NOT Diagnosed (%)
COVID-19 (without MIS-C)	78 (0.02%)	356,721 (99.98%)
MIS-C	203 (8.10%)	2303 (91.90%)

	Myocarditis Diagnosed (%)	Myocarditis NOT Diagnosed (%)
COVID-19 (without MIS-C)	20 (0.08%)	24,144 (99.92%)
MIS-C	172 (9.04%)	1730 (90.96%)

https://www.epic.com/software#Cosmos

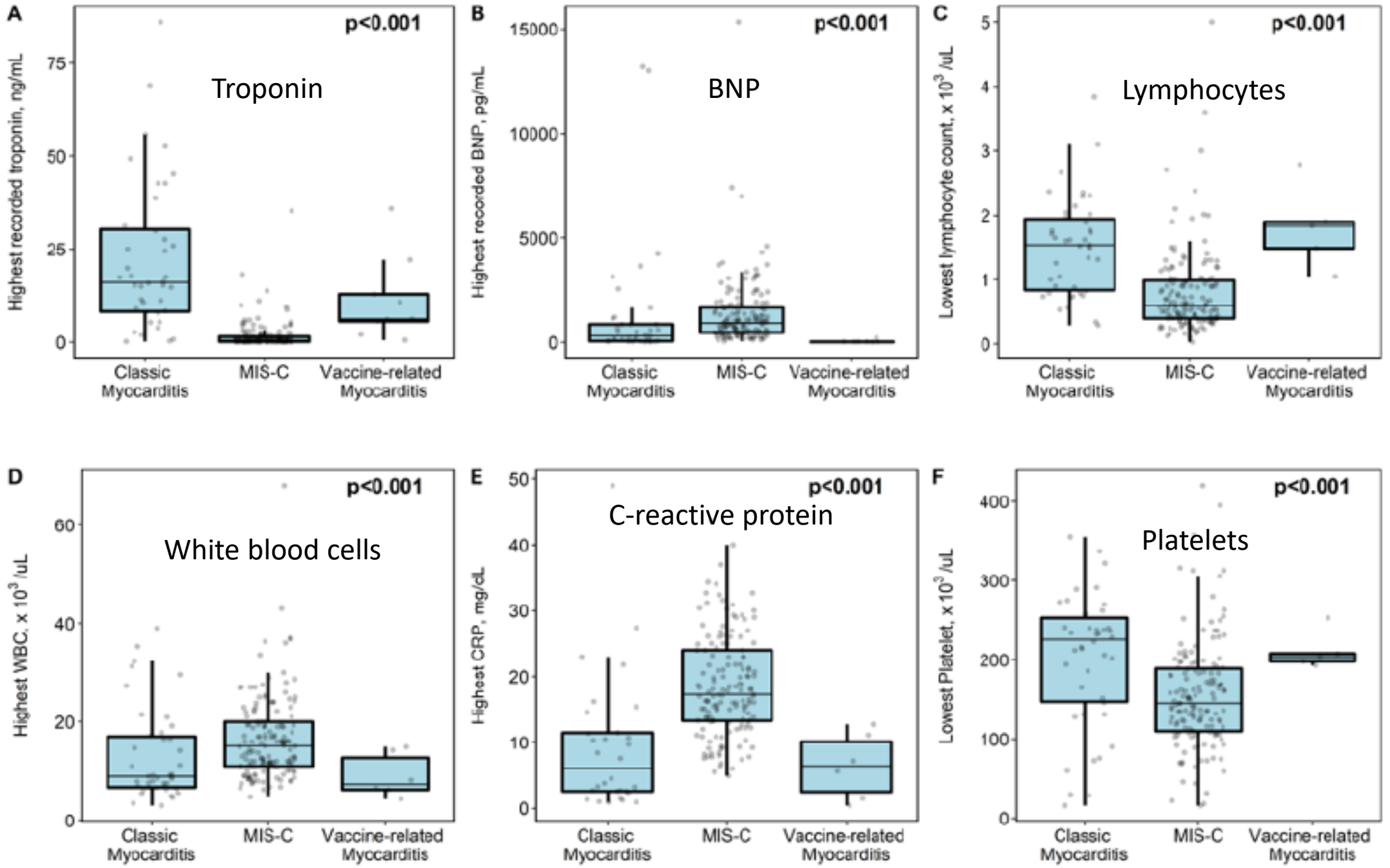
https://www.childrenshospitals.org/phis

Comparing types of myocarditis

Comparison of MIS-C Related Myocarditis, Classic Viral Myocarditis, and COVID-19 Vaccine related Myocarditis in Children

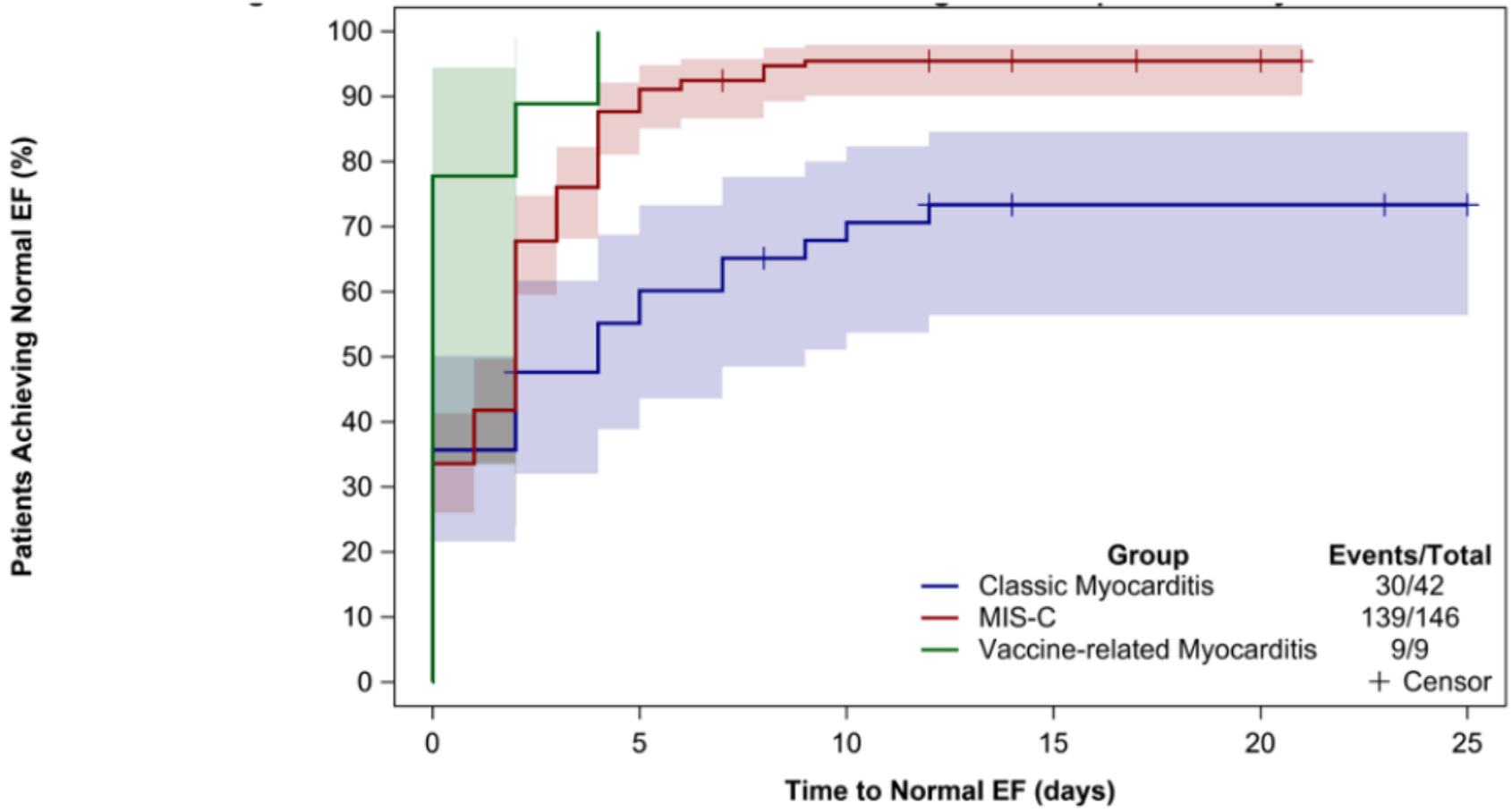
medRxiv

Patel et al. 2021



Patel et al. 2021

Comparing Types of Myocarditis: Time to Normal Ejection Fraction (EF) by Echocardiogram



Patel et al. 2021

Pre-COVID myocarditis outcomes

Contents lists available at ScienceDirect

Cardiovascular Pathology

journal homepage: www.elsevier.com/locate/carpath

Review

Diagnosis, treatment and predictors of prognosis of myocarditis. A narrative review

Picarillo et al. 2021

Variables	Good outcome	Poor outcome
Clinical presentation	• Chest pain [2] • Class NYHA I-II [82]	• Heart Failure at the onset [81] • Class NYHA III-IV [82] • Sustained Ventricular Arrhythmias [51,83] • Acute Kidney Injury [84] • High SOFA [85], APACHE IV [85] and SAPS II [85] admission scores [86]
Electrocardiogram	• Absence of abnormalities [2] • ST elevation with a pericarditis pattern [91]	• Widened QRS and Q waves [56] • Wide QRS-T angle (≥100°) [91] • QTc interval prolongation [10]
Biomarkers	Troponin • Early rise and fast decline [41]	Troponin • Recurrently or persistently abnormal levels [41] BNP • Elevated levels (>4245 pg/mL) [89] • Low levels associated to elevated troponin levels [90]
Echocardiography	• Preserved LV ejection fraction at the onset [2,94] • Normal wall motion [2] • Early improvement or normalization of LV ejection [94,95]	• Increased LV end diastolic diameter [94,95] • Reduced LV ejection fraction (<50%) at the onset [2,9,94] • Persistently reduced LV ejection fraction [94,95] • Left atrium enlargement [94,96] • Worse LV strain and strain rate [98] • Right ventricle dysfunction [1]
Cardiac Magnetic Resonance	• Absence of LGE [81,101] • Decreased LGE over time [81] • LGE in the inferolateral wall [101] • Baseline LV ejection fraction preserved (≥50%) [102]	• Presence of LGE [81] • Persistent LGE over time [81] • Mid-wall LGE in the (antero-) septal segments [101]
Endomyocardial biopsy and immunohistological features		• Invading immune cells and expression of HLA-DR-alpha molecules [82] • Presence of viral genome in patients not treated with anti-viral drugs [103] • Giant-cell myocarditis [41]

Picarillo et al. 2021

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LGE=Late gadolinium enhancement

Picarillo et al. 2021

2015 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.

Vaccine Safety Datalink Confirmed Myocarditis/pericarditis 0-21 Days after Any Dose of mRNA Vaccine by Age Group/Product: 3 month follow-up review of Cases with at least 1 follow-up visit since initial episode

3-month chart review status (not mutually exclusive)	12-17 Year-Olds (Pfizer-BioNTech) N=16	18-39 Year-Olds (Pfizer-BioNTech) N=14	18-39 Year-Olds (Moderna) N=18
Recovered, no medication, without exercise restrictions or symptoms	5 (31%)	6 (43%)	9 (50%)
Still symptomatic	4 (25%)	5 (36%)	3 (17%)
Still on medication (primarily NSAIDS, colchicine)	2 (13%)	4 (29%)	7 (39%)
Still on exercise/physical activity restrictions	7 (44%)	2 (14%)	1 (6%)

3-6 Month Outcomes of Myocarditis after COVID-19 Vaccination

Investigating Long-Term Effects of Myocarditis

How CDC Is Investigating Myocarditis Health Effects after COVID-19 Vaccination

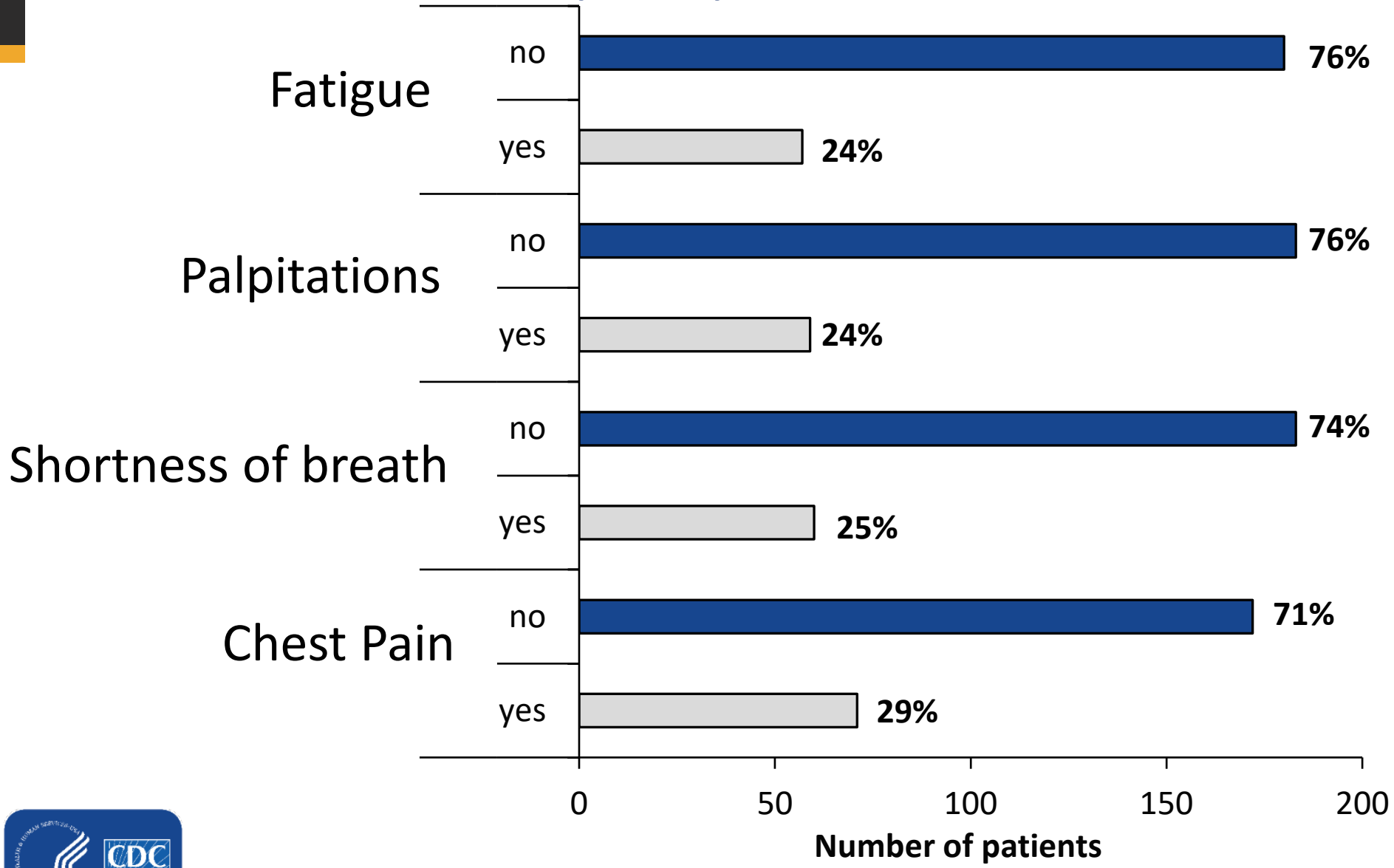
Updated Aug. 20, 2021 Languages Print

What You Need to Know

- CDC is conducting surveys of patients (or their parents or guardians) and healthcare providers to gather information about myocarditis after mRNA COVID-19 vaccination.
- CDC is contacting people who meet the case definition for myocarditis following mRNA COVID-19 vaccination.

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

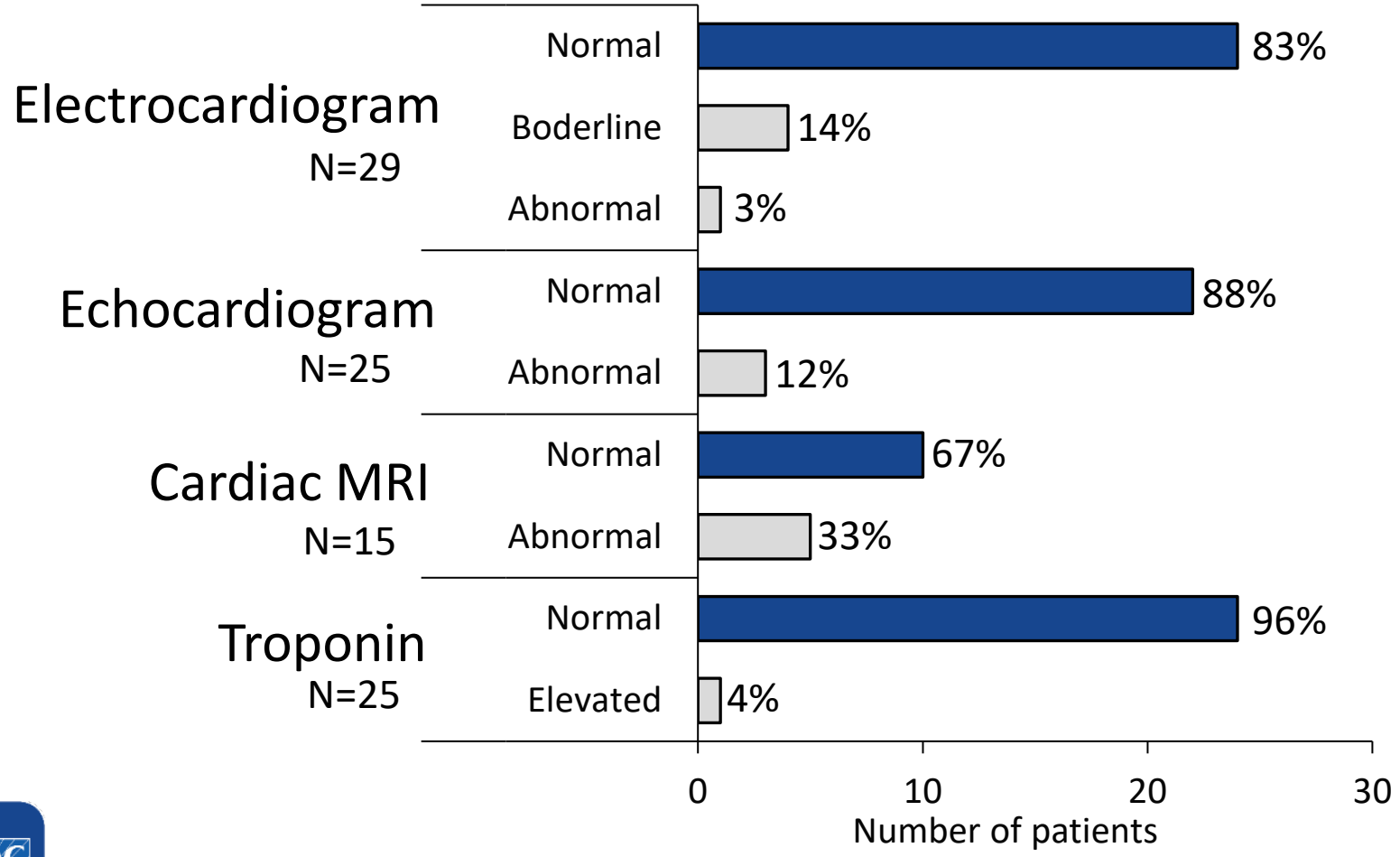
Patient self-report of symptoms within prior 2 weeks at 3-month follow-up of myocarditis after COVID-19 vaccination (N=248)



52% of patients reported no symptoms within prior 2 weeks

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

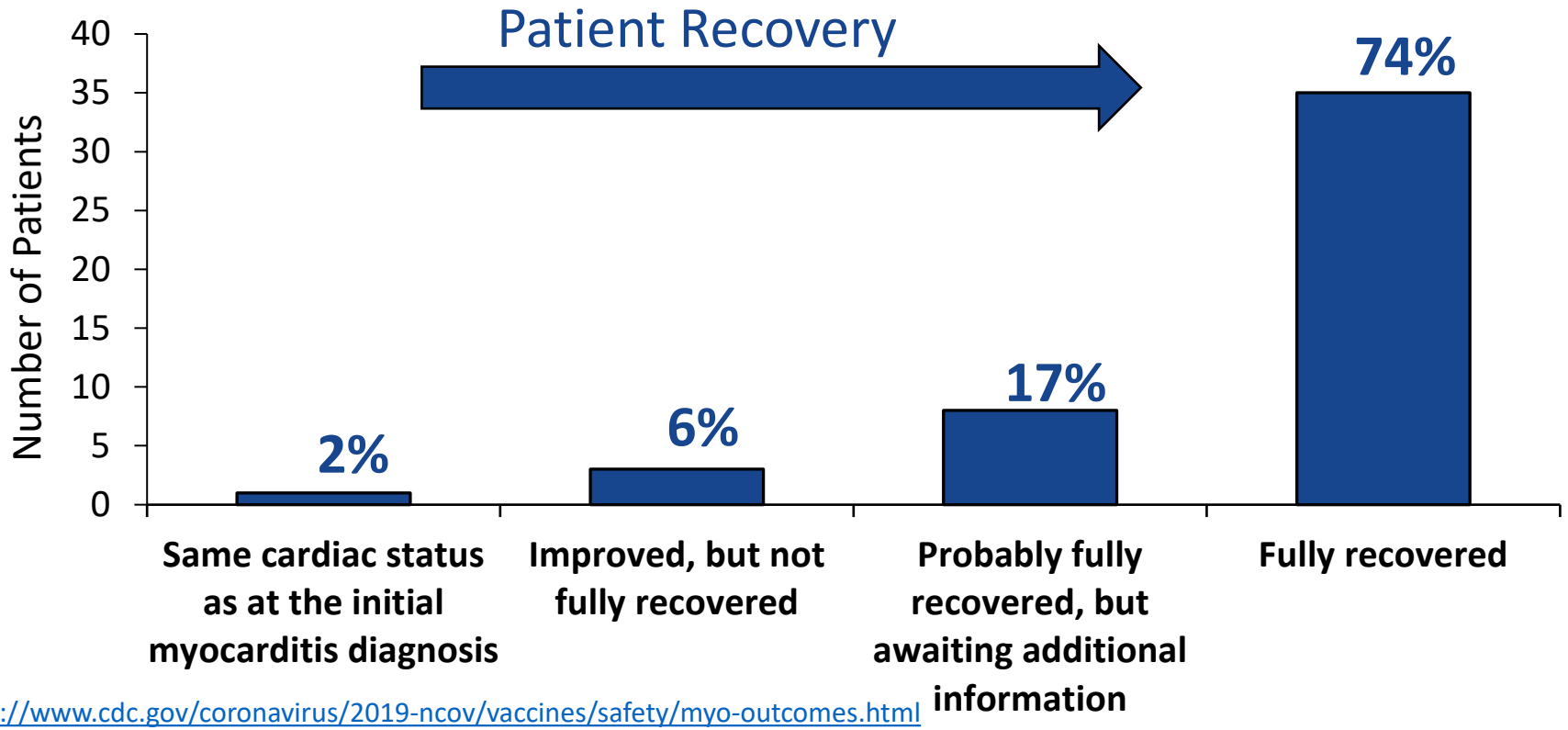
Results of 3-month follow-up cardiac testing in patients with myocarditis after COVID-19 vaccination



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

Cardiologist/healthcare provider assessment of recovery from myocarditis after COVID-19 vaccination by 3 months (n=47)

- 91% of cardiologists or healthcare providers indicated the patient was fully or probably recovered



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Thank you

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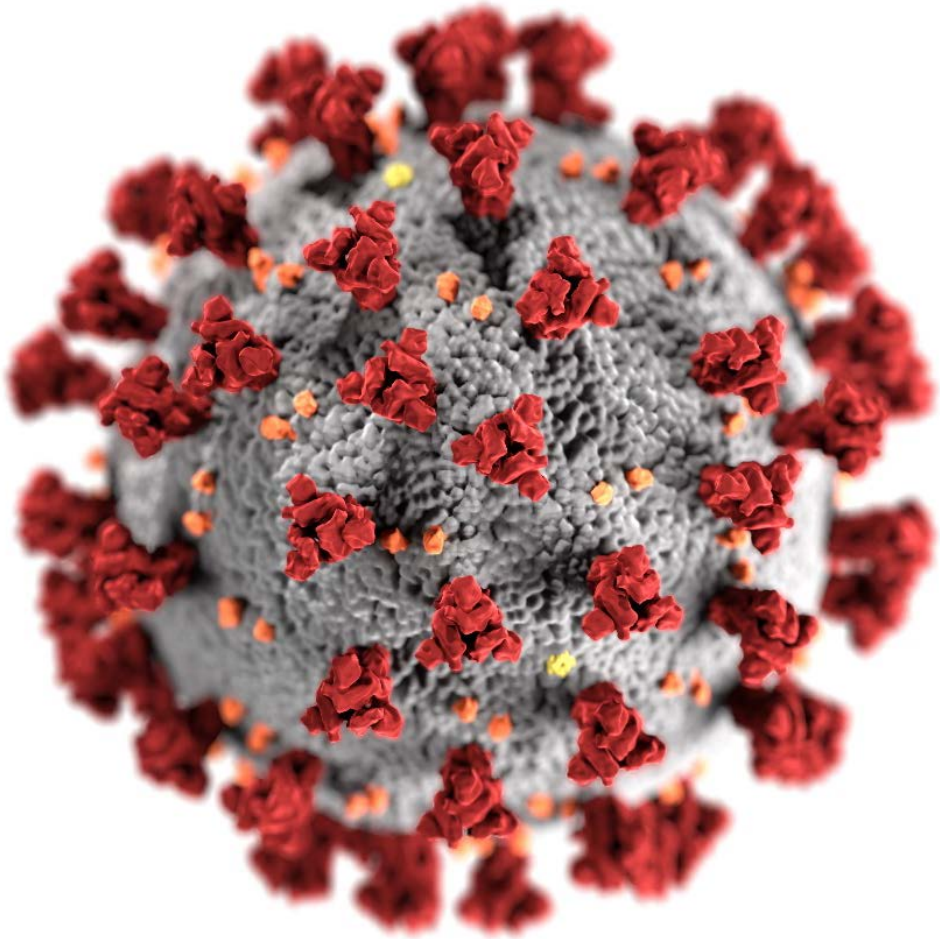
- Clinical Immunization Safety Assessment Project
- Tom Shimabukuro, John Su, CDC Vaccine Task Force
- Nicola Klein, Vaccine Safety Datalink
- Sam Butler, EPIC
- Matt Hall and Cary Thurm, Children's Hospital Association
- CDC team investigating long-term effects of myocarditis



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