

Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods. Medical Dictionary for Regulatory Activities Preferred Terms, Definitions of Myocarditis and Pericarditis, Myocarditis medical review form

The following Medical Dictionary for Regulatory Activities Preferred Terms were used for identification of reports of myocarditis and pericarditis:

Myocarditis:

Autoimmune myocarditis
Coxsackie myocarditis
Cytomegalovirus myocarditis
Enterovirus myocarditis
Eosinophilic myocarditis
Hypersensitivity myocarditis
Immune-mediated myocarditis
Myocarditis
Myocarditis bacterial
Myocarditis helminthic
Myocarditis infectious
Myocarditis meningococcal
Myocarditis mycotic
Myocarditis post infection
Myocarditis septic
Viral myocarditis

Pericarditis:

Atypical mycobacterium pericarditis
Autoimmune pericarditis
Bacterial pericarditis
Coxsackie pericarditis
Cytomegalovirus pericarditis
Pericarditis
Pericarditis adhesive
Pericarditis constrictive
Pericarditis helminthic
Pericarditis infective
Pericarditis mycoplasmal
Pleuropericarditis
Purulent Pericarditis
Viral pericarditis

Acute Myocarditis

Clinical myocarditis

Probable Case

1. 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

2. ≥ 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

3. No other identifiable cause of the symptoms and findings

Confirmed Case

1. 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

2. ≥ 1 new finding of

- Histopathologic confirmation of myocarditis[§]
- cMRI findings consistent with myocarditis[†] in the presence of troponin level above upper limit of normal (any type of troponin)

AND

3. 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)

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.

The following form was used to collect information on suspected cases:

VAERS Adverse Events of Special Interest: Myocarditis medical record review

Record ID _____

Patient Information

Enter all available information as noted in the VAERS report or medical record. If unknown, select unknown.

VAERS ID _____

Is this VAERS ID linked to another VAERS ID

- Yes _____
 No _____

Date VAERS received the report

(MM-DD-YYYY (if unknown enter: 01-01-0000))

State where the VAERS report is coming from

(Please type out the full name)

First Name _____

Last Name _____

Date of birth

(MM-DD-YYYY (if unknown enter: 01-01-0000))

Sex

- Female
 Male
 Unknown

Ethnicity

- Hispanic/Latinx
 Not Hispanic/Latinx
 Unknown

Race
(check all that apply)

- American Indian or Alaska Native
 Asian
 Black
 Native Hawaiian or Other Pacific Islander
 White
 Unknown

Vaccine Information

Enter all available information as noted in the VAERS report or medical record. If unknown, select unknown.

Vaccine Date for Dose 1

(MM-DD-YYYY (if unknown enter: 01-01-0000))

Vaccine Manufacturer for Dose 1

- Pfizer-BioNTech
 Moderna
 J&J/Janssen
 Not reported

Lot Number for Dose 1

Vaccination Date for Dose 2 (if applicable)

(MM-DD-YYYY (if unknown enter: 01-01-0000))

Vaccine Manufacturer for Dose 2

- Pfizer-BioNTech
 Moderna
 J&J/Janssen
 Not reported

Lot Number for Dose 2

Adverse Event of Special Interest

Select AESI(s) for which this VAERS ID was assigned

- Anaphylaxis
 Coagulopathy
 COVID-19
 Death
 GBS
 Kawasaki's Disease
 MIS-A
 MIS-C
 Myocardial Infarction
 Myopericarditis
 Narcolepsy
 Pregnancy
 Seizure
 Stroke
 Transverse Myelitis
 Other

Myocarditis, Pericarditis, and Myopericarditis

Is this case a rule-out based on the initial VAERS report?

- Yes
 No

If yes, enter the reason for rule-out and stop abstraction,

- Miscode of diagnosis
 Miscode of demographic information (i.e. age)
 Other _____

Are medical records available

- Yes
 No

Was the health provider contacted and interviewed?

- Yes
 No

Did a physician diagnose the patient's response as myopericarditis, myocarditis, pericarditis? (e.g. was the VAERS report filed by a physician, or do available medical records state, "Doctor diagnosed...myopericarditis, myocarditis, pericarditis?")

- Yes
 No

What was the physician diagnosis?

- Myopericarditis
 Myocarditis only
 Pericarditis only

Did the patient develop signs and symptoms within 42 days following vaccine administration?

- Yes
 No

Did symptoms occur following dose 1?

- Yes
 No

Did symptoms occur following dose 2?

- Yes
 No

How many days after receipt of their last dose?

((in days))

Did the patient, during the same 42 day period, have upper respiratory illness or flu-like symptoms (fever, cough, malaise, etc.) or have documented illness or signs/symptoms consistent with the following pathogens or illnesses:

- Yes
 No

Adenoviruses
Coxsackieviruses (especially Coxsackievirus B)
Herpesviruses (such as cytomegalovirus, Epstein Barr virus, HHV 6)
Echovirus
Enterovirus
Hepatitis B or C virus
Influenza A or B
Parvovirus B19

Please select all that apply

- Adenoviruses
- Coxsackieviruses (especially Coxsackievirus B)
- Herpesviruses (such as cytomegalovirus, Epstein Barr virus, HHV 6)
- Echovirus
- Enterovirus
- Hepatitis B or C virus
- Influenza A or B
- Parvovirus B19
- Other infection, please specify _____

Did the patient have a history of myocarditis, pericarditis, or myopericarditis?

- Yes
- No

Please specify

- Myopericarditis
- Myocarditis only
- Pericarditis only

Did the patient have a history of any of the following conditions (check all that apply):

- Rheumatoid arthritis
- Scleroderma
- Systemic lupus erythematosus
- Sjogren's syndrome
- Other systemic inflammatory illness

Please specify the other systemic inflammatory illness

Did the patient have a history of exposure to the following (check all that apply):

- Alcohol (e.g. > 2 drinks/day for months or longer, or recent heavy binge drinking)
- Procainamide
- Isoniazid
- Hydralazine
- Anthracycline
- Heavy metals (e.g., mercury, cadmium)
- None of the above/medical history does not indicate a history of exposure

List symptoms present (check all that apply)

- Chest pain/pressure/discomfort
- Dyspnea/shortness of breath/pain with breathing
- Palpitations
- Irritability/fussiness
- Nausea/vomiting
- Poor feeding/loss of appetite
- Tachypnea
- Lethargy
- Pleuritic chest pain without another attributable cause (e.g., pneumonia)
- Pericardial rub
- Conjunctivitis
- Diarrhea
- Fever (highest temp known and duration at presentation)
- Headache
- Rash
- Other (specify)
- None of the above

What is the highest temp known?

What is the duration of the fever at presentation?

((in days))

Please specify the other symptoms that are present:

Diagnostic tests (check all that apply)

- ECG/EKG or other rhythm monitoring
- Imaging (e.g., echocardiography, cMRI) showing depressed left ventricular function
- Any echocardiogram
- Cardiac Magnetic Resonance Imaging (cMRI)
- Cardiac enzymes: peak value for any of the following labs
- Histopathologic evidence of myocardial inflammation (e.g., biopsy or autopsy)
- Histopathologic evidence of pericardial inflammation (e.g., biopsy or autopsy)

What were the results of the imaging test?

- Normal
- Abnormal _____
- Inconclusive _____

ECG/EKG or other rhythm monitoring results details

- ST elevation/ST abnormalities
- T-wave abnormalities/abnormal repolarization
- PR depression without reciprocal ST depression
- Atrial, supraventricular, or ventricular arrhythmia
- Conduction delays or blocks
- AV block 1st degree
- AV block 2nd degree - Type 1
- AV block 2nd degree - Type 2
- AV block 3rd degree
- Frequent atrial or ventricular ectopy

Were any of these EKG findings considered abnormal?

- Yes
- No

Any echocardiogram details

- Decreased left ventricular function
- Pericardial effusion
- Ejection fraction percentage
- Left ventricular strain
- Normal echocardiogram

What was the severity of the decreased left ventricular function?

- Mild
- Moderate
- Severe

How severe was the pericardial effusion?

- Trivial
- Small
- Moderate
- Large

Is the lowest ejection fraction percentage less than 46%?

- Yes
- No

Please list the lowest ejection fraction percentage recorded

((in percent))

Was there ever any left ventricular strain? Yes
 No
 Unknown

Any cMRI details (Please check all that apply) Abnormal cardiac function
 Wall motion abnormality
 Findings consistent with myocarditis (per Lake Louise criteria)
 Normal cMRI

Cardiac enzyme details Troponin I _____
If selected, please enter the values and units. Troponin C _____
 Troponin T _____
 CKMB _____
 BNP _____
 Pro-BNP _____
 CRP _____
 ESR _____

Were any of the Troponin levels noted above elevated? Yes
 No

Were any of these cardiac enzymes tests/assays considered elevated (above the normal range)? Yes
 No

Was the patient hospitalized? Yes
 No

Were there treatments administered during hospitalization for myocarditis? Yes
 No

Please check all the treatments that were received Aspirin
 NSAIDS other than aspirin (e.g. ketorolac/Toradol, ibuprofen/Motrin/Advil, naproxen/Naprosyn/Aleve, colchicine)
 Corticosteroids (e.g. prednisone, methylprednisolone, hydrocortisone)
 IVIG
 Vasoactive medications (e.g. milrinone, epinephrine, norepinephrine, vasopressin, dopamine)
 Diuretics (e.g. furosemide/Lasix, cholorothiazide/Diuril)
 Antiarrhythmics
 Immunomodulators (e.g. anakinra/Kineret, tocilizumab/Actemra, infliximab/Remicade)
 Anticoagulation other than aspirin (Warfarin/Coumadin, Plavix/Clopidogrel)
 Regular/Low flow Nasal cannula oxygen support
 High flow nasal cannula
 Intubation or mechanical ventilation
 Cardioversion/Shock
 ECMO (extracorporeal membrane oxygenation)
 VAD (ventricular assist device)
 Intra-aortic balloon pump
 Heart transplant
 Other _____

Were treatments administered? Yes
 No

Please indicate if the following were administered:

- Aspirin
- Acetaminophen/Tylenol
- Other _____

Disposition

What was the patient's outcome?

- Still hospitalized
- ICU
- Discharged

Where was the patient discharged to?

- Another facility
- Home

Has the patient fully recovered from their symptoms?

- Yes
- No

Please specify what symptoms and/or difficulties the patient still has:

Please describe the patient's disposition

The disposition was last updated on

Does this report meet one of the above case definitions?

- Probable myocarditis
- Confirmed myocarditis
- Pericarditis
- Myopericarditis (probable or confirmed)
- Not a case

Additional impressions

Initial presentation of the case, additional impressions, clarifications, or comments:

If this review is still ongoing/not completed AND your VAERS deployment is ending, please select yes,

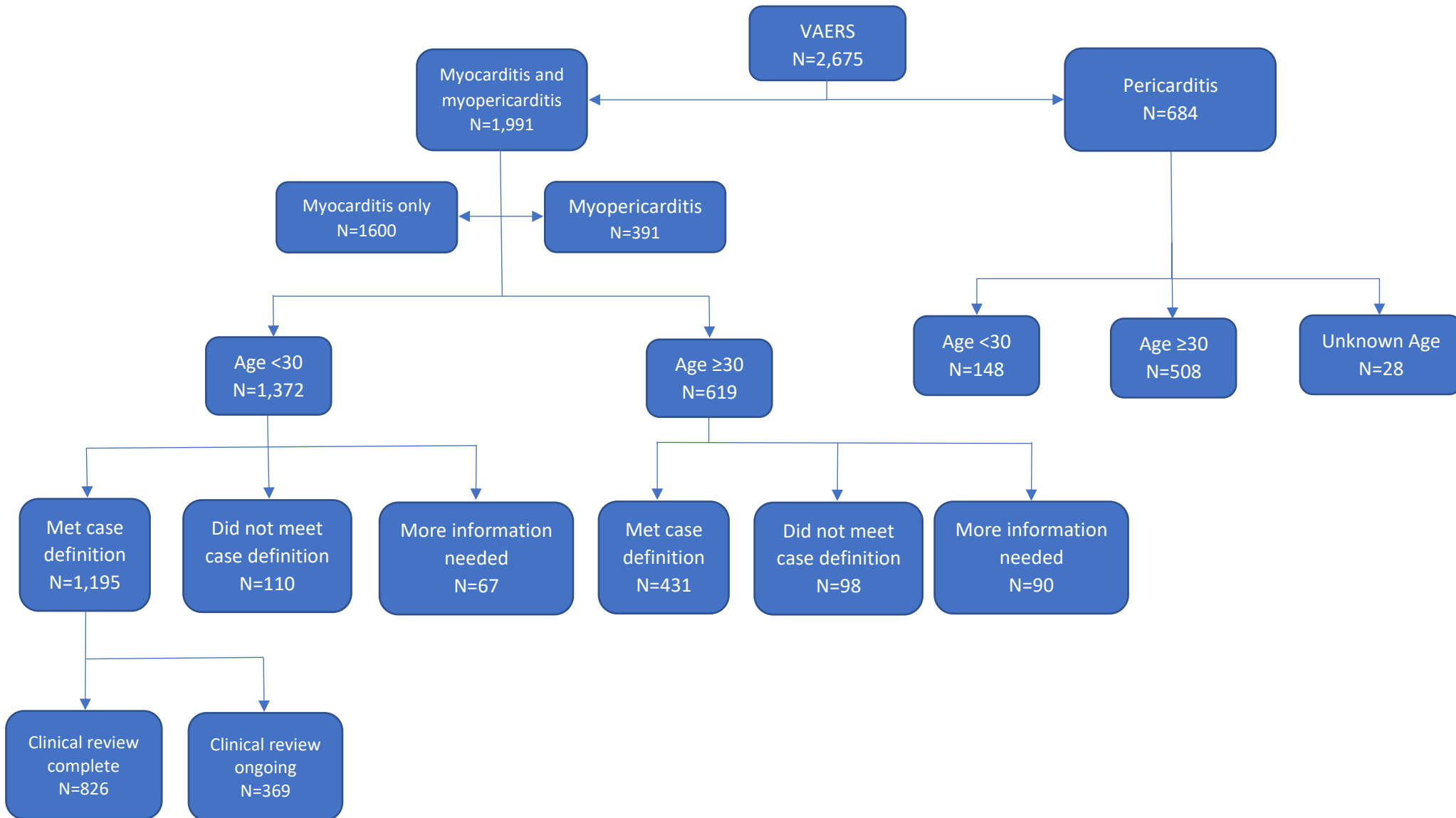
- Yes
- No

If this review is completed, please select no.

Abstraction status

- Awaiting review (abstraction not started yet)
- VAERS report only - the only available record for review is the VAERS report form itself
- Incomplete - other records are available, but insufficient information is available to complete abstraction
- Complete - all data fields for abstraction have been completed, with data from provider interview and/or medical record review
- Not applicable/misclassified

eFigure. Flow diagram of cases of myocarditis and pericarditis reported to Vaccine Adverse Event Reporting System (VAERS) after receiving mRNA-based COVID-19 vaccine, United States, December 14, 2020-August 31, 2021



eTable 1. Characteristics of all myocarditis cases reported to Vaccine Adverse Event Reporting System (VAERS) after mRNA-based COVID-19 vaccination, United States, December 14, 2020–August 31, 2021

	BNT162b2			mRNA-1273			Total
	Dose 1	Dose 2	Dose Unknown	Dose 1	Dose 2	Dose Unknown	
Number of myocarditis reports to VAERS	216	1,066	103	174	390	42	1,991
Doses administered	114,246,837	95,532,396	—	78,158,611	66,163,001	—	354,100,845
Median Age, years (interquartile range (IQR))	22 (16–38)	18 (16–28)	21 (16–33)	32 (24–53)	26 (21–39)	29 (21–39)	22 (17–34)
Median time to symptom onset, days (interquartile range (IQR))	3 (1–8)	2 (1–3)	3 (1–5)	4 (2–9)	3 (1–3)	3 (1–5)	2 (1–4)
Known sex, n (%)	N=215	N=1062	N=101	N=173	N=389	N=41	N=1981
Male	147 (68)	879 (83)	83 (82)	120 (69)	295 (76)	32 (78)	1556 (79)
Female	68 (32)	183 (17)	18 (18)	53 (31)	94 (24)	9 (22)	425 (21)
Known race/ethnicity ^a n (%)	N=191	N=887	N=65	N=133	N=313	N=27	N=1606
American Indian or Alaska Native	2 (1)	5 (1)	0 (0)	2 (2)	1 (<1)	0 (0)	10 (1)
Asian	13 (7)	68 (8)	5 (8)	5 (4)	10 (3)	1 (4)	102 (6)
Black	13 (7)	40 (5)	7 (11)	10 (8)	16 (5)	4 (15)	90 (6)
Hispanic	45 (25)	139 (16)	12 (18)	26 (20)	38 (12)	7 (26)	267 (17)
Multiple	4 (2)	15 (2)	0 (0)	0 (0)	7 (2)	1 (4)	27 (2)
Native Hawaiian or Other Pacific Islander	1 (1)	5 (1)	1 (2)	1 (1)	0 (0)	0 (0)	8 (<1)
Other	0 (0)	7 (1)	0 (0)	0 (0)	1 (<1)	0 (0)	8 (<1)
White	103 (57)	608 (69)	40 (62)	89 (67)	240 (77)	14 (52)	1094 (68)

^a Race categories without ethnicity were either non-Hispanic or had no ethnicity reported.

eTable 2. Characteristics of all pericarditis cases reported to Vaccine Adverse Event Reporting System (VAERS) after mRNA-based COVID-19 vaccination, United States, December 14, 2020–August 31, 2021

	BNT162b2			mRNA-1273			Total
	Dose 1	Dose 2	Dose Unknown	Dose 1	Dose 2	Dose Unknown	
Number of pericarditis reports to VAERS	111	240	68	82	134	49	684
Doses administered	114,246,837	95,532,396	—	78,158,611	66,163,001	—	354,100,845
Median Age, years (interquartile range (IQR))	45 (30–60)	45 (28–60)	41 (25–56)	52 (38–67)	54 (38–66)	56 (40–64)	48 (31–62)
Median time to symptom onset, days (interquartile range (IQR))	4 (1–12)	10 (2–28)	15 (2–33)	6 (2–15)	13 (2–32)	22 (7–66)	8 (2–26)
Known sex, n (%)	N=111	N=238	N=67	N=81	N=134	N=47	N=678
Male	59 (53)	149 (62)	45 (67)	43 (53)	81 (60)	31 (66)	408 (60)
Female	52 (47)	89 (37)	22 (33)	38 (47)	53 (40)	16 (34)	270 (40)
Known race/ethnicity ^a n (%)	N=98	N=210	N=57	N=60	N=110	N=42	N=577
American Indian or Alaska Native	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (0)
Asian	6 (6)	11 (5)	4 (7)	2 (3)	2 (2)	1 (2)	26 (5)
Black	3 (3)	18 (9)	3 (5)	4 (7)	7 (6)	0 (0)	35 (6)
Hispanic	10 (10)	18 (9)	7 (12)	4 (7)	6 (5)	6 (14)	51 (9)
Multiple	2 (2)	6 (3)	1 (2)	0 (0)	2 (2)	0 (0)	11 (2)
Native Hawaiian or Other Pacific Islander	2 (2)	1 (<1)	0 (0)	0 (0)	0 (0)	0 (0)	3 (1)
Other	3 (3)	2 (1)	2 (4)	0 (0)	2 (2)	1 (2)	10 (2)
White	72 (73)	154 (73)	40 (70)	50 (83)	91 (83)	33 (79)	440 (76)

^a Race categories without ethnicity were either non-Hispanic or had no ethnicity reported.

eTable 3. Characteristics of myocarditis cases reported to Vaccine Adverse Event Reporting System after mRNA-based COVID-19 vaccination by case definition status

	Aged <30 years			Aged ≥30 years		
	Met case definition	Did not meet case definition	More information needed	Met case definition	Did not meet case definition	More information needed
Number of reports to VAERS	1,195	110	67	431	98	90
Median time to symptom onset, days (IQR ^a)	2 (1–3)	3 (1–8)	2 (2–4)	3 (2–8)	4 (1–9)	3 (1–8)
Known sex, n (%) ^b	N=1,195	N=103	N=66	N=430	N=97	N=90
Male	1050 (88)	72 (70)	55 (83)	284 (66)	45 (46)	50 (56)
Female	145 (12)	31 (30)	11 (17)	146 (34)	52 (54)	40 (44)
Known race/ethnicity, n (%) ^c	N=969	N=287	N=38	N=361	N=81	N=70
American Indian or Alaska Native	3 (0)	2 (2)	0 (0)	3 (1)	1 (1)	1 (1)
Asian	70 (7)	12 (14)	3 (8)	14 (4)	2 (2)	1 (1)
Black	45 (5)	9 (10)	4 (11)	23 (6)	5 (6)	4 (6)
Hispanic	188 (19)	14 (16)	5 (13)	40 (11)	12 (15)	8 (11)
Multiple	14 (1)	5 (6)	2 (5)	3 (1)	2 (2)	1 (1)
Native Hawaiian or Other Pacific Islander	5 (1)	0 (0)	0 (0)	2 (1)	0 (0)	1 (1)
Other	6 (1)	2 (2)	0 (0)	0 (0)	0 (0)	0 (0)
White	638 (66)	43 (49)	24 (63)	276 (76)	59 (73)	54 (77)

^aInterquartile range

^bFor reports with sex of patient known

^c For reports with race/ethnicity known; race categories without ethnicity were either non-Hispanic or had no ethnicity reported.