

Message

From: Markowitz, Lauri (CDC/DDID/NCIRD/DVD) [REDACTED]
Sent: 4/30/2021 8:50:17 PM
To: Schindelar, Jessica A (CDC) [REDACTED] Anderson, Steven [REDACTED] Beresnev, Tatiana H (NIH) [REDACTED] Broder, Karen R (CDC) [REDACTED] Calvert, Geoffrey M (CDC) [REDACTED] Clark, Matthew (IHS) [REDACTED] Clark, Thomas A (CDC) [REDACTED] Cohn, Amanda C (CDC) [REDACTED] Collins, Limone [REDACTED] Cunningham, Fran [REDACTED] Daley, Matt [REDACTED] DeStefano, Frank (CDC) [REDACTED] Edwards, Kathy [REDACTED] Farizo, Karen [REDACTED] Forshee, Richard [REDACTED] Gee, Julianne M (CDC) [REDACTED] Helfand, Rita (CDC) [REDACTED] Hiers, Susan G (CDC) [REDACTED] Hopkins, Bob [REDACTED] Jackson, Lisa [REDACTED] Kelman, Jeffrey A (CMS) [REDACTED] LaPorte, Kathleen (CDC) [REDACTED] Lee, Grace [REDACTED] MacNeil, Jessica R (CDC) [REDACTED] Markowitz, Lauri (CDC) [REDACTED] Marquez, Paige L (CDC) [REDACTED] Mbaeyi, Sarah A (CDC) [REDACTED] Mullen, Jennifer (CDC) [REDACTED] Myers, Tanya R (CDC) [REDACTED] Nair, Narayan [REDACTED] Oliver, Sara E [REDACTED] Patricia Whitley-Williams [REDACTED] Riley, Laura [REDACTED] Rubin, Mary (HRSA) [REDACTED] Schechter, Robert [REDACTED] Shanley, Edwin (CDC) [REDACTED] Shay, David K (CDC) [REDACTED] Shimabukuro, Tom (CDC) [REDACTED] Sotir, Mark J (CDC) [REDACTED] Steinberg, Judith L (OS) [REDACTED] Su, John (CDC) [REDACTED] Talbot, Keipp [REDACTED] Wasley, Annemarie (CDC) [REDACTED] Weintraub, Eric S (CDC) [REDACTED] Wharton, Melinda (CDC) [REDACTED] Wong, Hui-Lee [REDACTED] Woo, Jared M (CDC) [REDACTED] Young, Mardia A (CDC) [REDACTED]
Subject: [EXTERNAL] VaST - Draft minutes and report from April 26 (CONFIDENTIAL) -- plus other information
Attachments: 2021_04_26_VaST minutes_draft.docx; 2021-04-26 - VaST Report Data Table_draft.docx

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear VaST members and attendees,

Attached are the draft minutes and summary report from the call this week. Please let us know if there are any corrections or comments.

The next VaST call is May 3, 1:30 – 3:00 pm EDT.

Also, below are links to three publications from this week:

- [Safety Monitoring of the Janssen \(Johnson & Johnson\) COVID-19 Vaccine — United States, March–April 2021](#)
- [Anxiety-Related Adverse Event Clusters After Janssen COVID-19 Vaccination — Five U.S. Mass Vaccination Sites, April 2021](#)
- [U.S. case reports of cerebral venous sinus thrombosis with thrombocytopenia after AD26.COV2.S Vaccination—March 2 to April 21, 2021](#)

Lauri Markowitz and Melinda Wharton

Lauri Markowitz, MD
VaST Co-Lead
Division of Viral Diseases
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

Message

From: Markowitz, Lauri (CDC/DDID/NCIRD/DVD) [REDACTED]
Sent: 5/7/2021 5:04:17 PM
To: Anderson, Steven [REDACTED] Beresnev, Tatiana H (NIH) [REDACTED] Broder, Karen R (CDC) [REDACTED] Calvert, Geoffrey M (CDC) [REDACTED] Clark, Matthew (IHS) [REDACTED] Clark, Thomas A (CDC) [REDACTED] Cohn, Amanda C (CDC) [REDACTED] Collins, Limone [REDACTED] Cunningham, Fran [REDACTED] Daley, Matt [REDACTED] DeStefano, Frank (CDC) [REDACTED] Edwards, Kathy [REDACTED] Farizo, Karen [REDACTED] Forshee, [REDACTED] Gee, Julianne M (CDC) [REDACTED] Hause, Anne M (CDC) [REDACTED] Helfand, Rita (CDC) [REDACTED] Hiers, Susan G (CDC) [REDACTED] Hopkins, Bob [REDACTED] Jackson, Lisa [REDACTED] Kelman, Jeffrey A (CMS) [REDACTED] LaPorte, Kathleen (CDC) [REDACTED] Lee, Grace [REDACTED] MacNeil, Jessica R (CDC) [REDACTED] Markowitz, Lauri (CDC) [REDACTED] Marquez, Paige L (CDC) [REDACTED] Mbaeyi, Sarah A (CDC) [REDACTED] Myers, Tanya R (CDC) [REDACTED] Nair, Narayan [REDACTED] Oliver, Sara E (CDC) [REDACTED] Patricia Whitley-Williams [REDACTED] Riley, Laura [REDACTED] Rubin, Mary (HRSA) [REDACTED] Schechter, Robert [REDACTED] Schindelar, Jessica A (CDC) [REDACTED] Shanley, Edwin (CDC) [REDACTED] Shay, David K (CDC) [REDACTED] Shimabukuro, Tom (CDC) [REDACTED] Sotir, Mark J (CDC) [REDACTED] Steinberg, Judith L (OS) [REDACTED] Su, John (CDC) [ezu2@cdc.gov]; Talbot, Keipp [REDACTED] Wasley, Annemarie (CDC) [REDACTED] Weintraub, Eric S (CDC) [REDACTED] Wharton, Melinda (CDC) [REDACTED] Wong, Hui-Lee [REDACTED] Woo, Jared M (CDC) [REDACTED] Young, Mardia A (CDC) [REDACTED]
Subject: [EXTERNAL] VaST - Draft minutes and report from May 3 (CONFIDENTIAL)
Attachments: agenda-2021-05-12-508.pdf; 2021-05-03 - VaST minutes_draft.docx; 2021-05-03 - VaST Report Data Table_draft.docx

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Dear VaST members and attendees,

Attached are the draft minutes and summary report from the call this week. Please let us know if there are any corrections or comments.

The next VaST call is May 10, 1:30 – 3:00 pm EDT.

Of note, there will be an ACIP meeting on May 12 focusing on the Pfizer COVID-19 Vaccine for 12-15 year-olds. The agenda (attached) includes a presentation on TTS and a VaST update.

Lauri Markowitz and Melinda Wharton

*Lauri Markowitz, MD
VaST Co-Lead
CDC COVID-19 Response, Vaccine Task Force
Division of Viral Diseases
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention*

MEETING OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP)
Centers for Disease Control and Prevention
Atlanta, Georgia 30329
May 12, 2021

AGENDA ITEM		PRESIDER/PRESENTER(s)
<u>Wednesday, May 12, 2021</u>		
11:00	Welcome & Introductions	Dr. José Romero (ACIP Chair) Dr. Amanda Cohn (ACIP Executive Secretary, CDC)
11:30	Coronavirus Disease 2019 (COVID-19) Vaccines	
	Introduction	Dr. Beth Bell (ACIP, WG Chair)
	Safety, immunogenicity and efficacy of BNT162b2 in persons aged 12-15 years	Dr. John Perez (Pfizer)
	GRADE: Pfizer-BioNTech COVID-19 vaccine	Dr. Megan Wallace (CDC/NCIRD)
	Evidence to Recommendation Framework: Pfizer-BioNTech COVID-19 vaccine	Dr. Sara Oliver (CDC/NCIRD)
	Clinical considerations and implementation: Adolescent COVID-19 vaccines	Dr. Kate Woodworth (CDC/NCBDDD)
1:30	Break	
2:00	Public Comment	
2:30	Break	
2:45	Discussion	
	<u>VOTE</u>	
	Pfizer COVID-19 Vaccine for 12-15 year olds	Dr. Sara Oliver (CDC/NCIRD)
3:30	Break	
3:45	Update on thrombosis with thrombocytopenia syndrome (TTS) following Janssen COVID-19 vaccine	Dr. Tom Shimabukuro (CDC/NCEZID)
	VaST update	Dr. Grace Lee (ACIP, VaST Chair)
	COVID-19 Vaccine Effectiveness studies	Dr. Katherine Fleming-Dutra (CDC/NCIRD)
	Update on emerging SARS-CoV-2 variants	Dr. Heather Scobie (CDC/CGH)
5:00	Adjourn	
Acronyms		
CDC	Centers for Disease Control and Prevention	
CMS	Centers for Medicare and Medicaid Services	
COVID-19	Coronavirus disease 2019	
EtR	Evidence to Recommendations Framework	
FDA	Food and Drug Administration	
GRADE	Grading of Recommendations Assessment, Development and Evaluation	
HRSA	Health Resources and Services Administration	
IHS	Indian Health Service	
NCHHSTP	National Center for HIV, Hepatitis, STD and TB Prevention [of CDC/OID]	
NCIRD	National Center for Immunization & Respiratory Diseases [of CDC/OID]	
NCEZID	National Center for Emerging and Zoonotic Diseases [of CDC/OID]	
NIAID	National Institute of Allergy and Infectious Diseases	
OIDP	Office of Infectious Disease and HIV/AIDS Policy	
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2	
WG	Work Group	
WHO	World Health Organization	
VE	Vaccine Effectiveness	

Message

From: Markowitz, Lauri (CDC/DDID/NCIRD/DVD) [REDACTED]
Sent: 5/17/2021 4:33:18 PM
To: Anderson, Steven [REDACTED] Beresnev, Tatiana H (NIH) [REDACTED] Broder, Karen R (CDC) [REDACTED] Calvert, Geoffrey M (CDC) [REDACTED] Clark, Matthew (IHS) [REDACTED] Clark, Thomas A (CDC) [REDACTED] Cohn, Amanda C (CDC) [REDACTED] Collins, Limone [REDACTED] Cunningham, Fran [REDACTED] Daley, Matt [REDACTED] DeStefano, Frank (CDC) [REDACTED] Edwards, Kathy [REDACTED] Farizo, Karen [REDACTED] Forshee, Richard [REDACTED] Gee, Julianne M (CDC) [REDACTED] Hause, Anne M (CDC) [REDACTED] Helfand, Rita (CDC) [REDACTED] Hopkins, Bob [REDACTED] Jackson, Lisa [REDACTED] Jennifer Nelson [REDACTED] Kelman, Jeffrey A (CMS) [REDACTED] Lee, Grace [REDACTED] Lu, Yun (CBER) [REDACTED] MacNeil, Jessica R (CDC) [REDACTED] Markowitz, Lauri (CDC) [REDACTED] Marquez, Paige L (CDC) [REDACTED] Mbaeyi, Sarah A (CDC) [REDACTED] Myers, Tanya R (CDC) [REDACTED] Nair, Narayan [REDACTED] Oliver, Sara E (CDC) [REDACTED] Patricia Whitley-Williams [REDACTED] Riley, Laura [REDACTED] Rubin, Mary (HRSA) [REDACTED] Schechter, Robert [REDACTED] Schindelar, Jessica A (CDC) [REDACTED] Shanley, Edwin (CDC) [REDACTED] Shay, David K (CDC) [REDACTED] Shimabukuro, Tom (CDC) [REDACTED] Sotir, Mark J (CDC) [REDACTED] Steinberg, Judith L (OS) [REDACTED] Su, John (CDC) [REDACTED] Talbot, Keipp [REDACTED] Weintraub, Eric S (CDC) [REDACTED] Wharton, Melinda (CDC) [REDACTED] Wong, Hui-Lee [REDACTED] Woo, Jared M (CDC) [REDACTED] Young, Mardia A (CDC) [REDACTED]
CC: Jose [REDACTED] Meaney-Delman, Dana Marie (CDC) [REDACTED]
Subject: [EXTERNAL] VaST - Agenda for May 17 (1:30 - 3 pm ET) and presentations - CONFIDENTIAL
Attachments: 2021-05-17 - VaST Meeting Agenda.docx; Myocarditis following mRNA COVID Vaccines_VaST update_20210517.pdf; VAERS for VaST 17 May 2021.pdf; VSD RCA Covid-19 vax - update VaST - 05-17-2021 - final.pdf; Myocarditis Pericarditis_VA_051721.pdf; Adverse events english ACIP 4_05_21.pdf

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Dear all,

This email includes the VaST agenda well as 4 slide sets for the presentations today. The call will focus on myocarditis.

In addition to the slides for the call today, I attached slides that the Israeli MoH presented to VaST on April 5 (Adverse events english ACIP.pdf). The data on myocarditis are on slides 14, 16-18 and 20. Israeli MoH colleagues will be on the call today but they are not presenting any updated data.

The VaST call information should be on your calendars.
Reminder - all VaST documents and communications are confidential.

Lauri Markowitz and Melinda Wharton

Lauri Markowitz, MD
VaST Co-Lead
CDC COVID-19 Response, Vaccine Task Force
Division of Viral Diseases
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

VaST Agenda – May 17, 2021

Open session

1:30 - 3:00

1:30-1:35 - Announcements

1:35-1:45 - Myocarditis update, DoD (Margaret Ryan, DoD)

1:40-1:50 - discussion

1:50-2:05 - VAERS myopericarditis and TTS/CVST (John Su, CDC)

2:05-2:15 - discussion

2:15-2:25 - VSD RCA (Nicky Klein, KPNC)

2:25-2:35 - discussion

2:35-2:45 - VA RCA (Fran Cunningham, VA)

2:45-2:55 - discussion

2:55-3:00 - MIS-C and discussion (Karen Broder, CDC)



Update: myopericarditis among persons ≤ 18 years of age, and thrombosis with thrombocytopenia syndrome (TTS) following U.S. COVID-19 vaccines

May 17, 2021

**John R. Su, MD, PhD, MPH
CDC COVID-19 Vaccine Task Force
Vaccine Safety Team**

Update – TTS

PSICOVID_0000931

Reporting rates of TTS after Janssen COVID-19 vaccine (as of May 13, 2021)

9.45 million total Janssen COVID-19 vaccine doses administered*
(N=30)

Age group	Females			Males		
	TTS cases	Doses admin	Reporting rate [†] (per million)	TTS cases	Doses admin	Reporting rate [†] (per million)
18-29 yrs old	3	671,584	4.5	2	801,087	2.5
30-39 yrs old	8	669,067	12.0	1	803,939	1.2
40-49 yrs old	7	773,404	9.1	1	845,884	1.2
50-64 yrs old	5	1,518,355	3.3	3	1,616,086	1.8
65+ yrs old	0	854,811	0.0	0	739,294	0.0

* Source of doses administered: <https://covid.cdc.gov/covid-data-tracker/#vaccinations>; † Reporting rate = TTS cases per 1 million Janssen COVID-19 vaccine doses administered

Update on myopericarditis, ages ≤ 18 years

Reported myopericarditis in VAERS (as of May 14, 2021)

- Total reports after COVID-19 vaccines received and processed = **226,917**
 - Myopericarditis **N=309** (0.14%)
- Total doses administered, COVID-19 vaccines* = **267,406,255** (as of May 13, 2021)
- Estimated annual incidence ~ **4.4 per 100,000 person years**[†]
 - Crude estimated rates < estimated annual incidence

* CDC, unpublished data

[†]literature review

** as of May 14, 2021 at 1500

^{††} per million doses administered

5

Age group, years	ID'ed reports**	Doses administered	Crude reporting rate ^{††}
12–15	0	131,010	0.0
16–17	7	2,200,366	3.2
18–24	59	10,512,693	5.6
25–39	87	27,925,682	3.1
40–49	39	20,243,477	1.9
50–64	46	38,861,492	1.2
65+	52	43,041,425	1.2
NR	19	—	—

PSICOVID_00009315

Reported myopericarditis in VAERS (as of May 14, 2021)

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[†]literature review

** as of May 14, 2021 at 1500

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6

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50–64	46	38,861,492	1.2
65+	52	43,041,425	1.2
NR	19	—	—

PSICOVID_00009316

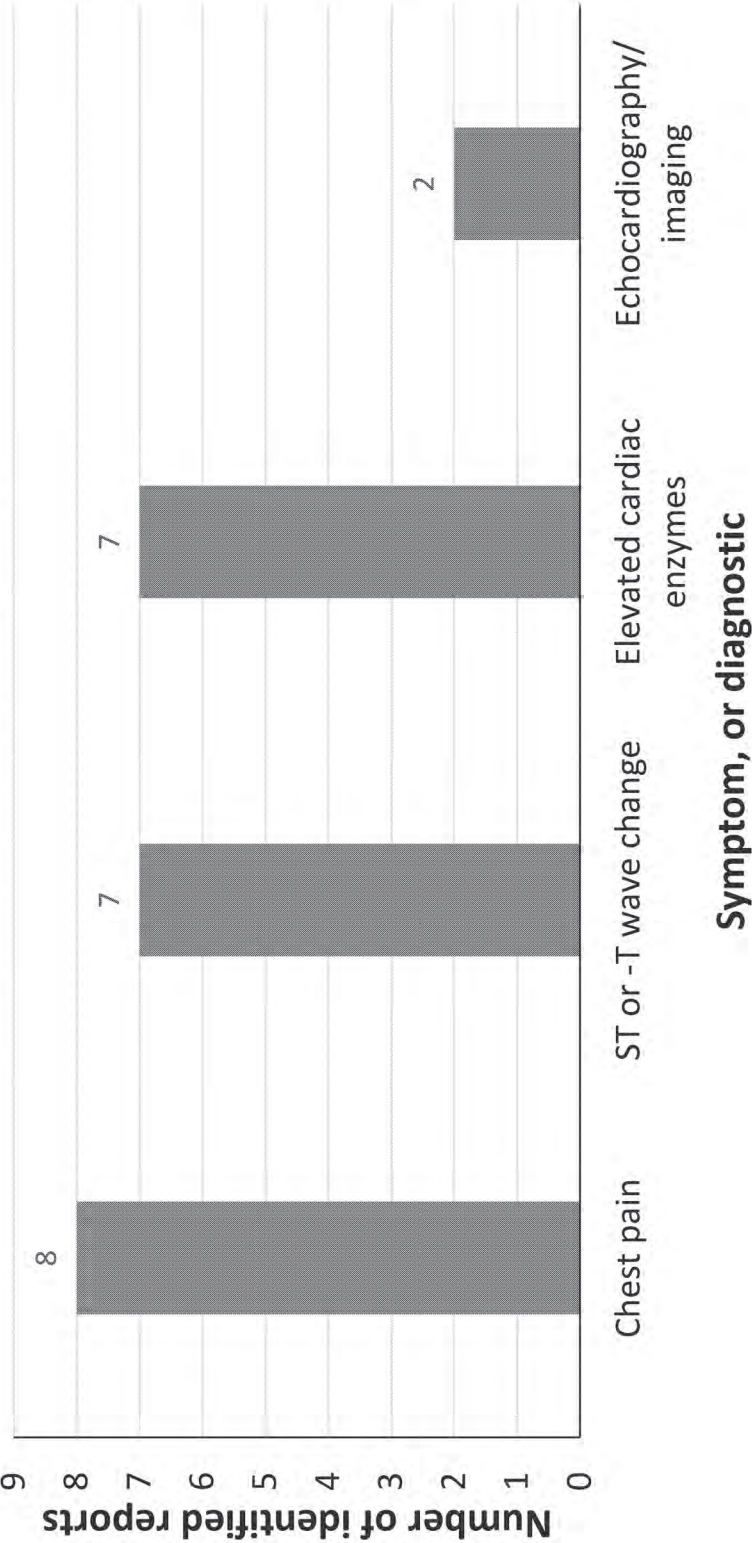
Characteristics of case patients, ≤18 years (as of May 13, 2021)

- Age
 - 4 case patients ≤ 17 years
 - 5 case patients = 18 years
- Sex
 - 9 males
 - 0 females
- Race and ethnicity
 - 4 white (2 non-Hispanic, 2 not reported)
 - 3 Hispanic
 - 2 not reported
- 7 reports after **dose 2** (one after dose 1; one didn't report dose number)

Characteristics of case patients, ≤18 years (cont'd)

- Manufacturer
 - 7 after Pfizer-BioNTech
 - 2 after Moderna (both 18 years)
- Median time, vaccination to symptom onset: **2 days** (range: 1–3)
- Known outcome = 3
 - 2 discharged home
 - 1 recovered at time of report
- All 9 reports preliminarily meet case definition*

**Symptoms and diagnostics, identified reports of
myopericarditis (≤18 years)**



Reports among persons 19–30 years of age

- n = **54** reports
 - Review completed = 15
 - **11** meet case definition
 - Review in progress = 39
 - **17** preliminarily meet case definition
- Sex (n=28)
 - **23** males
 - 5 females
- Median age, years = 23 (range: 19–30)
- Median time, vaccination to symptom onset: **3 days** (range: 0–28)
 - Without outliers, **3 days** (range: 1–11)
- Dose number (n=28)
 - 6 reports after dose 1
 - 19 reports after dose 2
 - 3 reports without dose number reported

Summary

SUMMARY

- Myopericarditis rarely reported to VAERS
 - Background = 4.4 per 100,000 person years
 - Crude reporting rate **3.1–5.6 per 1 million doses administered** (16–39 years of age)
- 9 reports among persons ≤18 years of age
 - All 9 reports preliminarily meet case definition*
 - 9 males, 0 females
 - Median time to symptom onset: **2 days** (range: 1–3)
 - Mostly diagnosed by chest pain, EKG, troponins
 - Of 3 known outcomes, all were **discharged home or recovered**
- Surveillance and efforts to obtain records continue

Extra slides

Case definition for myocarditis*

Suspected case

- Presence of dyspnea, palpitations, or chest pain of probable cardiac origin in a patient with either one of the following:
 - Electrocardiogram (ECG) abnormalities beyond normal variants, not documented previously, including
 - ST-segment or T-wave abnormalities,
 - Paroxysmal or sustained atrial or ventricular arrhythmias,
 - AV nodal conduction delays or intraventricular conduction defects, or
 - Continuous ambulatory electrocardiographic monitoring that detects frequent atrial or ventricular ectopy
 - Evidence of focal or diffuse depressed left-ventricular (LV) function of indeterminate age identified by an imaging study (e.g., echocardiography or radionuclide ventriculography).

Probable case

- Elevated cardiac enzymes, specifically, abnormal levels of cardiac troponin I, troponin T, or creatine kinase myocardial band (a troponin test is preferred);
- Evidence of focal or diffuse depressed LV function identified by an imaging study (e.g., echocardiography or radionuclide ventriculography) that is documented to be of new onset or of increased degree of severity (in the absence of a previous study, findings of depressed LV function are considered of new onset if, on follow-up studies, these findings resolve, improve, or worsen); or
- Abnormal result of cardiac radionuclide imaging (e.g., cardiac MRI with gadolinium or gallium-67 imaging) indicating myocardial inflammation.

Case definition for myocarditis*

Suspected case

- Presence of dyspnea, palpitations, or chest pain of probable cardiac origin in a patient with either one of the following:
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- Abnormal result of cardiac radionuclide imaging (e.g., cardiac MRI with gadolinium or gallium-67 imaging) indicating myocardial inflammation.

Case definition for pericarditis*

Suspected case

- Typical chest pain (i.e., pain made worse by lying down and relieved by sitting up and/or leaning forward) and
- No evidence of any other likely cause of such chest pain.

Probable case

- Pericardial rub, an auscultatory sign with one to three components per beat,
- ECG with diffuse ST-segment elevations or PR depressions without reciprocal ST depressions that are not previously documented, or
- Echocardiogram indicating the presence of an abnormal collection of pericardial fluid (e.g., anterior and posterior pericardial effusion or a large posterior pericardial effusion alone).

Case definition for pericarditis*

Suspected case

- Typical chest pain (i.e., pain made worse by lying down and relieved by sitting up and/or leaning forward) and
- No evidence of any other likely cause of such chest pain.

Probable case

- Pericardial rub, an auscultatory sign with one to three murmurs per beat,
- ECG with diffuse ST-segment elevations or PR depressions without reciprocal ST depressions that are not previously documented, or
- Echocardiogram indicating the presence of an abnormal collection of pericardial fluid (e.g., anterior and posterior pericardial effusion or a large posterior pericardial effusion alone).

- For surveillance, meeting either criteria (myopericarditis or pericarditis) = counted as case of myopericarditis
 - All 9 reports among persons ≤18 years preliminarily meet definition

Line list, myopericarditis ≤18 years

Patient	Age	Race/ ethnicity	Chest pain	-ST or -T wave change	Elevated cardiac enzymes	Echocardiography/ MRI
1	18	Not reported	Y			Y
2	16	Hispanic	Y	Y	Y	
3	18	White, non- Hispanic	Y	Y	Y	
4	17	Hispanic	Y	Y	Y	
5	18	White, non- Hispanic	Y	Y	Y	Y
6	16	Hispanic	Y		Y	
7	18	White	Y	Y	Y	
8	16	Not reported		Y		
9	18	White	Y	Y	Y	

Highlighted =
discharged
home or
recovered

MedDRA terms to search for myopericarditis

Atypical mycobacterium pericarditis	Myocarditis
Autoimmune myocarditis	Myocarditis bacterial
Autoimmune pericarditis	Myocarditis helminthic
Bacterial pericarditis	Myocarditis infectious
Coxsackie myocarditis	Myocarditis meningococcal
Coxsackie pericarditis	Myocarditis mycotic
Cytomegalovirus myocarditis	Myocarditis post infection
Cytomegalovirus pericarditis	Myocarditis septic
Enterovirus myocarditis	Pericarditis
Eosinophilic myocarditis	Pericarditis adhesive
Hypersensitivity myocarditis	Pericarditis constrictive
Immune-mediated myocarditis	Pericarditis helminthic
	Pericarditis infective
	Pericarditis mycoplasmal
	Pleuropericarditis
	Purulent pericarditis
	Viral myocarditis
	Viral pericarditis

**Reported myopericarditis in VAERS among persons ages ≤18 years
(as of May 14, 2021)**

- Total reports after COVID-19 vaccines received and processed =
226,917
 - Total reports of myopericarditis* = **309** (0.14%)
 - Reports among persons ≤18 years* = **9** (3%)
 - 4 reports ≤ 17 years, 5 reports 18 years

* Identified by automated processes; includes reports under review

Rapid Cycle Analysis (RCA) to Monitor the Safety of COVID-19 Vaccines in Near Real-Time within the Vaccine Safety Datalink

Kaiser Permanente Vaccine Study Center
Kaiser Permanente Northern California
Marshfield Clinic Research Institute

Vaccine Safety Datalink – Immunization Safety Office, CDC



Marshfield Clinic®
Research Institute

VSD Rapid Cycle Analysis

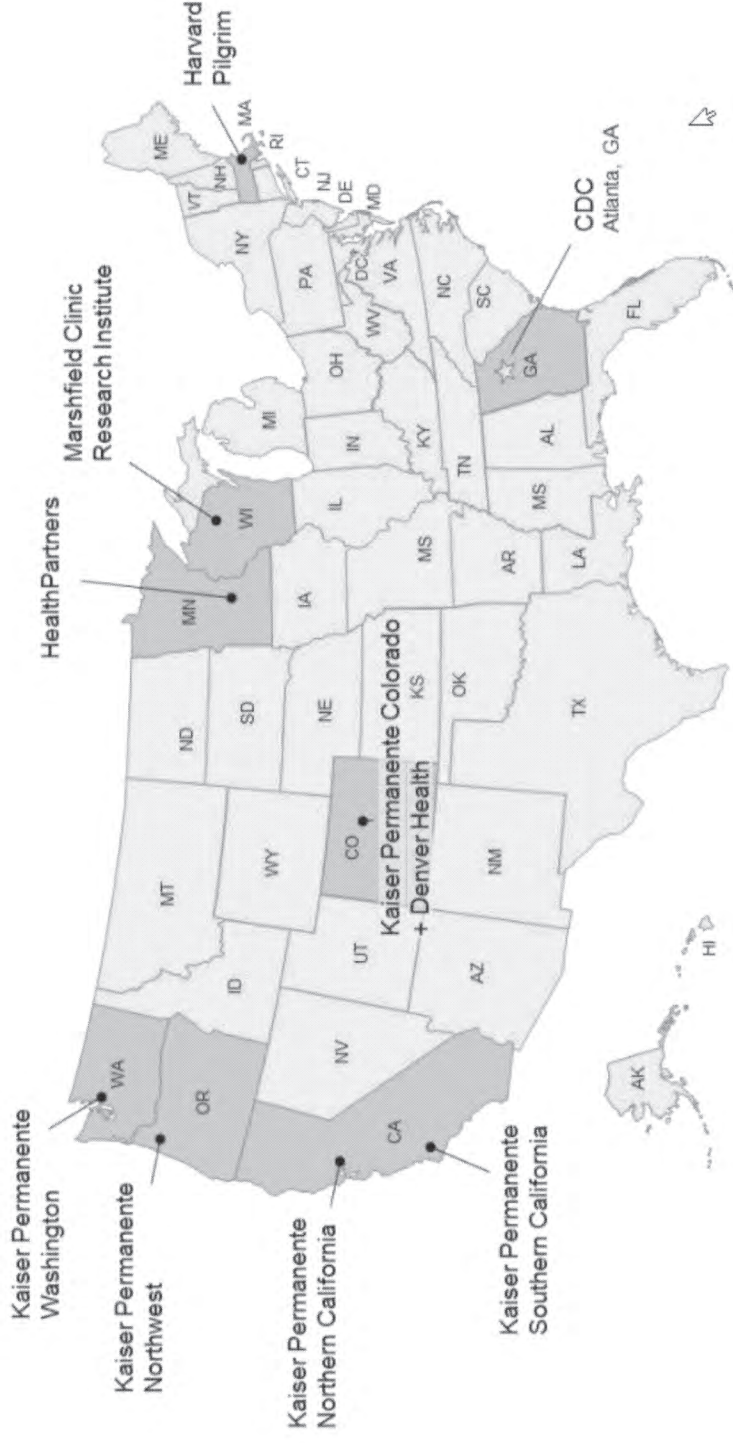
The specific aims:

- To monitor the safety of COVID-19 vaccines weekly using pre-specified outcomes of interest among VSD members.
- To describe the uptake of COVID-19 vaccines over time among eligible VSD members overall and in strata by age, site, and race/ethnicity.

Project Period: Sept 2020 – August 2023 (3 years)

The Vaccine Safety Datalink (VSD)

Participating VSD Healthcare Organizations

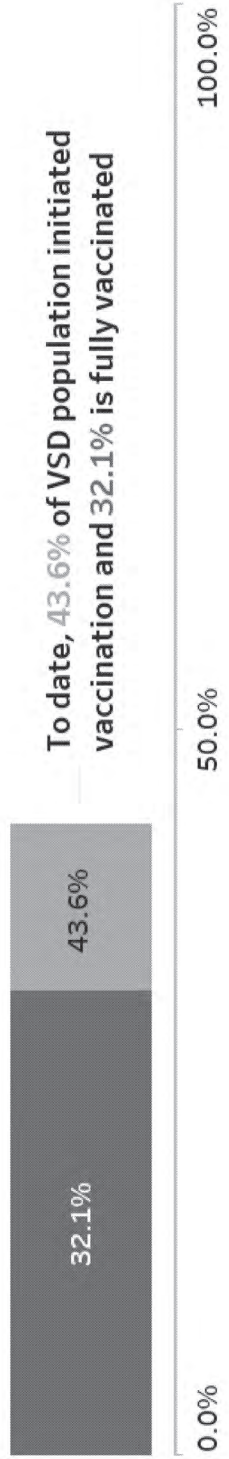


- Established in 1990
- Collaborative project between CDC and Nine Integrated Health Care Organizations

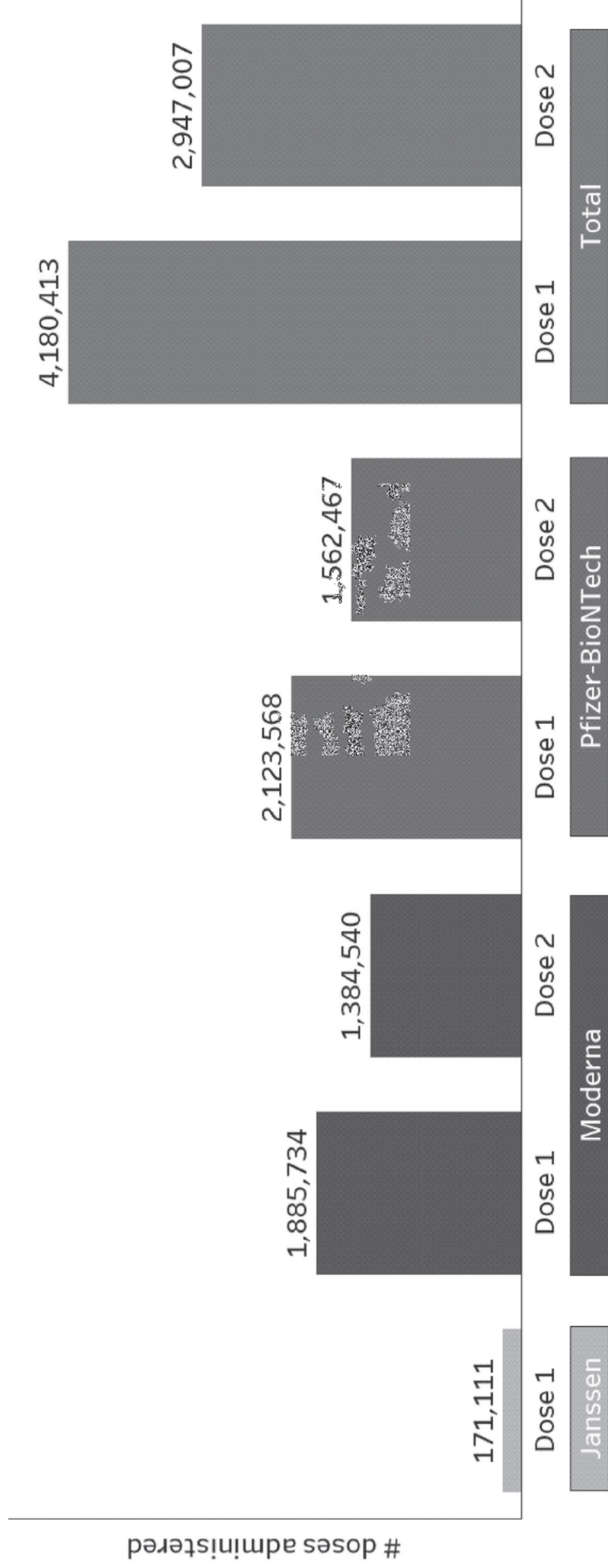
Vaccine Uptake (Data Through 5/8/21)

VSD COVID-19 Vaccine Totals

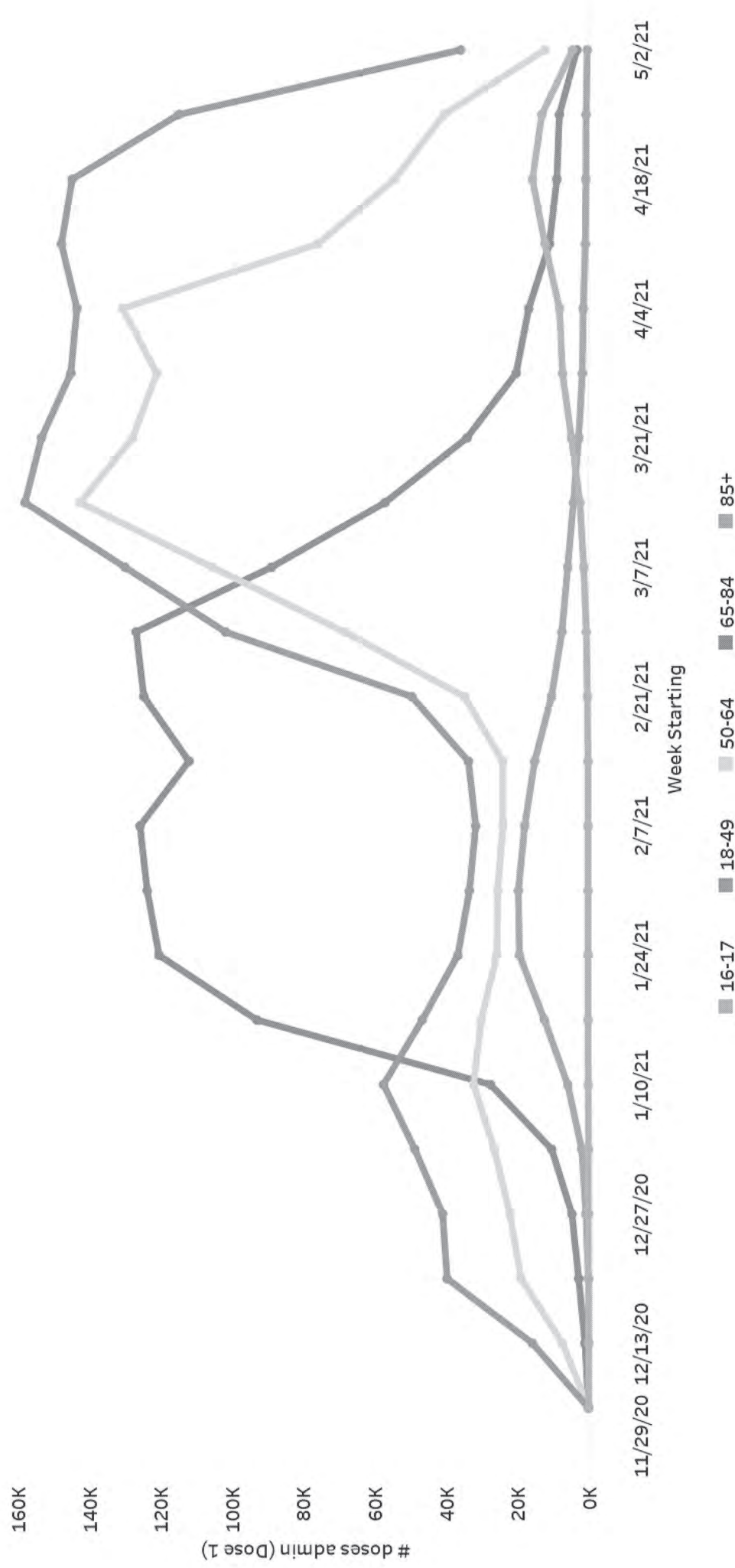
Total Doses Administered	Total Doses Admin per 100K	# People Initiating Vaccination	# People Fully Vaccinated
7,127,420	74,376	4,180,413	3,118,118
+575,312 since last week	+5,971 since last week	+258,484 since last week	+328,054 since last week



VSD COVID-19 Vaccine Totals



Vaccine Totals (Dose 1) by Age Group and Week

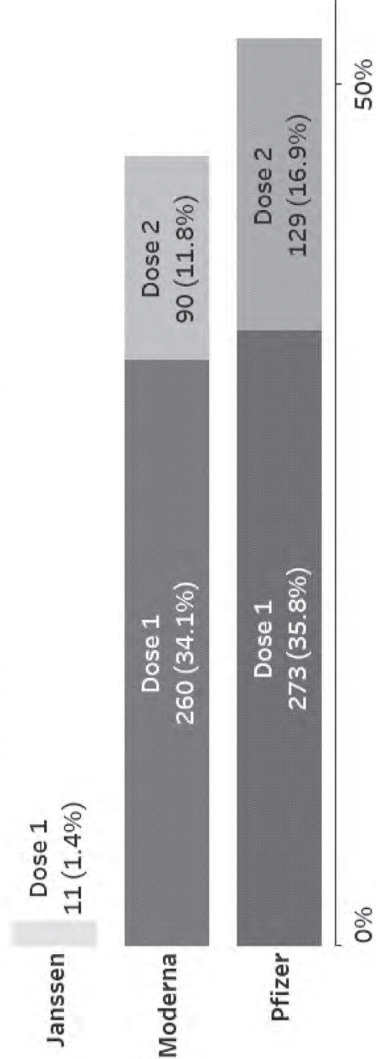


Simultaneous Vaccine Administration with COVID-19 Vaccine

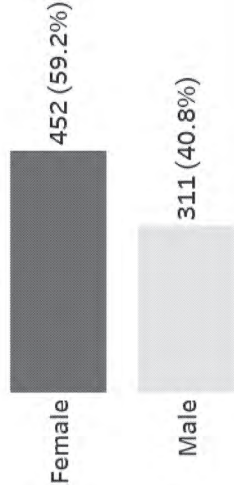
Number of COVID-19 doses admin to date: **7,127,420**

Number of people who received simult vaccs: **763**

By COVID-19 Vaccine Type and Dose

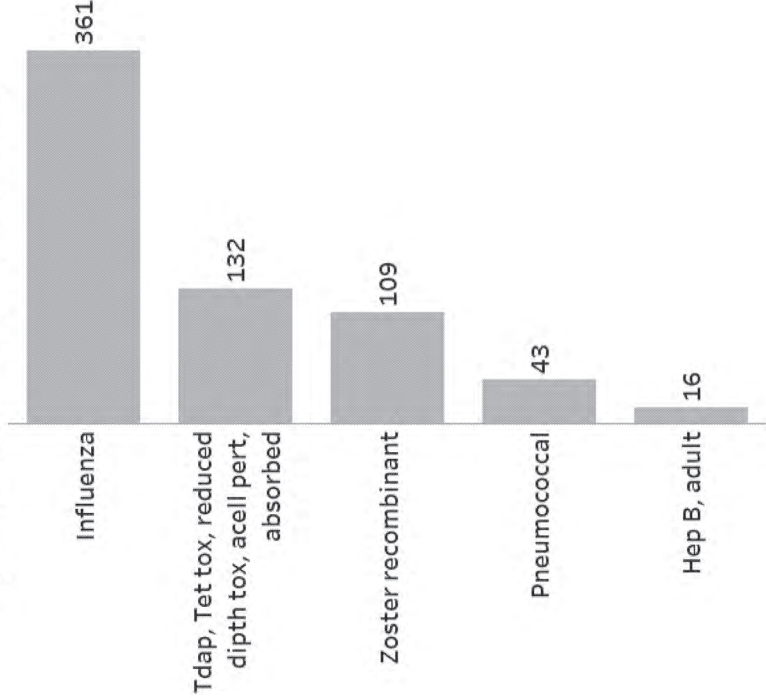


By Sex



Note: Individuals less than 16 years of age are excluded from all visualizations.

Top 5 vaccines administered simultaneously



Analysis (Data Through 5/8/21)

Any signal in the VSD for the 21 day risk interval? Yes or no, by outcome

#	VSD Outcomes	Abbreviation	Signal (Y/N)
1	Acute disseminated encephalomyelitis (settings = E, I)	ADEM	N
2	Acute myocardial infarction (settings = E, I)	AMI	N
3	Acute respiratory distress syndrome (settings = E, I)	ARDS	N/A
4	Anaphylaxis (settings = E, I)	ANAPH	N/A
5	Appendicitis (settings = E, I)	APPND	N
6	Bell's palsy (settings = E, I, O)	BP	N
7	Cerebral Venous Sinus Thrombosis (settings = E, I)	CVST	N
8	Convulsions / seizures (settings = E, I)	SZ	N
9	Disseminated intravascular coagulation (settings = E, I)	DIC	N
10	Encephalitis / myelitis / encephalomyelitis (settings = E, I)	ENCEPH	N
11	Guillain-Barré syndrome (settings = E, I)	GBS	N
12	Thrombotic thrombocytopenic purpura (settings = E, I)	TTP	N
13	Immune thrombocytopenia (settings = E, I, O)	ITP	N
14	Kawasaki disease (settings = E, I)	KD	N
15	Multisystem Inflammatory Syndrome in Children & Adults (MIS-C, MIS-A) (settings = E, I)	MISC	N/A
16	Myocarditis / pericarditis (settings = E, I)	MYOC	N
17	Narcolepsy and cataplexy (settings = E, I, O)	NARC	N/A
18	Stroke, hemorrhagic (settings = E, I)	HSTK	N
19	Stroke, ischemic (settings = E, I)	ISTK	N
20	Transverse myelitis (settings = E, I)	TM	N
21	Venous thromboembolism (settings = E, I, O)	VTE	N
22	Pulmonary embolism (settings = E, I)	PE	N

Abbreviations: E = ED; I = Inpt; O = Outpt

Primary Analyses: Vaccinated Concurrent Comparison “Sequential Analysis”

Outcome events in 21-day risk interval after either dose of any mRNA vaccine

Compared with outcome events in vaccinated comparators on the same calendar days

Outcome Event	Events in Risk Interval	Adjusted Rate Ratio ³	Weekly Analysis ¹		Sequential Test ²	
			95% Confidence Interval	2-Sided P-value	1-sided P-value (Fisher)	'Signal' 1-sided p < 0.0048
Acute disseminated encephalomyelitis	1	.	0.01 - .	0.811	0.811	no
Acute myocardial infarction	455	0.88	0.74 - 1.05	0.160	0.927	no
Appendicitis	415	0.81	0.68 - 0.96	0.018	0.992	no
Bell's palsy	371	1.12	0.91 - 1.39	0.287	0.156	no
CVST	8	0.45	0.15 - 1.36	0.153	0.961	no
Disseminated intravascular coagulation	21	0.50	0.24 - 1.05	0.065	0.980	no
Encephalitis / myelitis / encephalomyelitis	10	0.63	0.21 - 2.15	0.431	0.867	no
Guillain-Barré syndrome	7	0.72	0.17 - 3.64	0.644	0.805	no
Stroke, hemorrhagic	195	0.89	0.68 - 1.18	0.405	0.817	no
Stroke, ischemic	782	0.85	0.75 - 0.97	0.015	0.993	no
Immune thrombocytopenia	34	0.94	0.48 - 1.90	0.841	0.647	no
Myocarditis / pericarditis	46	0.78	0.46 - 1.34	0.350	0.860	no
Seizures	175	0.88	0.66 - 1.19	0.408	0.817	no
Transverse myelitis	1	0.33	0.01 - 12.69	0.491	0.940	no
Thrombotic thrombocytopenic purpura	3	1.47	0.18 - 14.20	0.724	0.537	no
Venous thromboembolism	485	1.13	0.94 - 1.36	0.181	0.098	no
Pulmonary embolism	392	0.95	0.78 - 1.15	0.574	0.730	no

¹**Weekly analyses** include all data to date, but confidence intervals and p-values do not account for the multiple chances for a false positive signal during surveillance.

²**Sequential test** requires 1-sided p < 0.0048 for a signal. This keeps the probability of a false positive signal (due to chance alone) below 0.05 in 2 years of surveillance.

³**Adjusted** for VSD site, 5-year age group, sex, race/ethnicity, and calendar date. ne=not estimable

⁴**Comparison interval** is 22–42 days after either dose.

Outcome events in 21-day risk interval after either dose of any mRNA vaccine

Compared with outcome events in vaccinated comparators on the same calendar days

Outcome Event	Events in Risk Interval	Adjusted Rate Ratio ³	Weekly Analysis ¹		Sequential Test ²	
			95% Confidence Interval	2-Sided P-value	1-sided P-value (Fisher)	'Signal' 1-sided p < 0.0048
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Acute myocardial infarction	455	0.88	0.74 - 1.05	0.160	0.927	no
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Bell's palsy	371	1.12	0.91 - 1.39	0.287	0.156	no
CVST	8	0.45	0.15 - 1.36	0.153	0.961	no
Disseminated intravascular coagulation	21	. 0.50	0.24 - 1.05	0.065	0.980	no
Encephalitis / myelitis / encephalomyelitis	10	0.63	0.21 - 2.15	0.431	0.867	no
Guillain-Barré syndrome	7	0.72	0.17 - 3.64	0.644	0.805	no
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⁴**Comparison interval** is 22–42 days after either dose.

Myocarditis/Pericarditis in 21-day risk interval after either dose of any mRNA vaccine

Compared with outcome events in vaccinated comparators on the same calendar days

Vaccine Type	Dose	Events in Risk Interval	Events in Comparison Interval ⁴	Risk Follow-up Person Days	Comparison Follow-up Person Day	Adjusted Rate Ratio ³	95% Confidence Interval ¹	1-sided P-value (Fisher)	Signal ¹ 1-sided p < 0.0048 ²
Both mRNA	Both Doses	46	23	370,647	181,342	0.78	0.46 - 1.34	0.86	no

¹**Weekly analyses** include all data to date, but confidence intervals and p-values do not account for the multiple chances for a false positive signal during surveillance.

²**Sequential test** requires 1-sided p < 0.0048 for a signal. This keeps the probability of a false positive signal (due to chance alone) below 0.05 in 2 years of surveillance.

³**Adjusted** for VSD site, 5-year age group, sex, race/ethnicity, and calendar date. ne=not estimable

⁴**Comparison interval** is 22–42 days after either dose.

Myocarditis/Pericarditis in 21-day risk interval after either dose of any mRNA vaccine Compared with outcome events in vaccinated comparators on the same calendar days

Vaccine Type	Dose	Events in Risk Interval	Events in Comparison Interval ⁴	Risk Follow-up Person Days	Comparison Follow-up Person Day	Adjusted Rate Ratio ³	95% Confidence Interval ¹	1-sided P-value (Fisher)	Signal ¹ 1-sided p < 0.0048 ²
Both mRNA	Both Doses	46	23	370,647	181,342	0.78	0.46 - 1.34	0.86	no
	Dose 1	22	23	116,038	139,454	0.67	0.34 - 1.31	0.915	no

¹**Weekly analyses** include all data to date, but confidence intervals and p-values do not account for the multiple chances for a false positive signal during surveillance.
²**Sequential test** requires 1-sided p < 0.0048 for a signal. This keeps the probability of a false positive signal (due to chance alone) below 0.05 in 2 years of surveillance.
³**Adjusted** for VSD site, 5-year age group, sex, race/ethnicity, and calendar date. ne=not estimable
⁴**Comparison interval** is 22–42 days after either dose.

Myocarditis/Pericarditis in 21-day risk interval after either dose of any mRNA vaccine

Compared with outcome events in vaccinated comparators on the same calendar days

Vaccine Type	Dose	Events in Risk Interval	Events in Comparison Interval ⁴	Risk Follow-up Person Days	Comparison Follow-up Person Day	Adjusted Rate Ratio ³	95% Confidence Interval ¹	1-sided P-value (Fisher)	Signal ¹ 1-sided $p < 0.0048^2$
Both mRNA	Both Doses	46	23	370,647	181,342	0.78	0.46 - 1.34	0.86	no
	Dose 1	22	23	116,038	139,454	0.67	0.34 - 1.31	0.915	no
	Dose 2	24	16	142,776	129,970	1.19	0.61 - 2.35	0.366	no

¹**Weekly analyses** include all data to date, but confidence intervals and p-values do not account for the multiple chances for a false positive signal during surveillance.

²**Sequential test** requires 1-sided $p < 0.0048$ for a signal. This keeps the probability of a false positive signal (due to chance alone) below 0.05 in 2 years of surveillance.

³**Adjusted** for VSD site, 5-year age group, sex, race/ethnicity, and calendar date. ne=not estimable

⁴**Comparison interval** is 22–42 days after either dose.

Myocarditis/Pericarditis in 21-day risk interval after either dose of any mRNA vaccine Compared with outcome events in vaccinated comparators on the same calendar days

Vaccine Type	Dose	Events in Risk Interval	Events in Comparison Interval ⁴	Risk Follow-up Person Days	Comparison Follow-up Person Day	Adjusted Rate Ratio ³	95% Confidence Interval ¹	1-sided P-value (Fisher)	Signal ¹ 1-sided p < 0.0048 ²
Both mRNA	Both Doses	46	23	370,647	181,342	0.78	0.46 - 1.34	0.86	no
	Dose 1	22	23	116,038	139,454	0.67	0.34 - 1.31	0.915	no
	Dose 2	24	16	142,776	129,970	1.19	0.61 - 2.35	0.366	no
Pfizer	Both Doses	23	9	70,984	25,826	0.82	0.36 - 2	0.757	no

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Myocarditis/Pericarditis in 21-day risk interval after either dose of any mRNA vaccine Compared with outcome events in vaccinated comparators on the same calendar days

Vaccine Type	Dose	Events in Risk Interval	Events in Comparison Interval ⁴	Risk Follow-up Person Days	Comparison Follow-up Person Day	Adjusted Rate Ratio ³	95% Confidence Interval ¹	1-sided P-value (Fisher)	Signal ¹ 1-sided p < 0.0048 ²
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	Dose 2	24	16	142,776	129,970	1.19	0.61 - 2.35	0.366	no
Pfizer	Both Doses	23	9	70,984	25,826	0.82	0.36 - 2	0.757	no
	Dose 1	8	8	15,478	10,021	0.39	0.12 - 1.27	0.973	no

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Myocarditis/Pericarditis in 21-day risk interval after either dose of any mRNA vaccine Compared with outcome events in vaccinated comparators on the same calendar days

Vaccine Type	Dose	Events in Risk Interval	Events in Comparison Interval ⁴	Risk Follow-up Person Days	Comparison Follow-up Person Day	Adjusted Rate Ratio ³	95% Confidence Interval ¹	1-sided P-value (Fisher)	Signal ¹ 1-sided p < 0.0048 ²
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	Dose 2	24	16	142,776	129,970	1.19	0.61 - 2.35	0.366	no
Pfizer	Both Doses	23	9	70,984	25,826	0.82	0.36 - 2	0.757	no
	Dose 1	8	8	15,478	10,021	0.39	0.12 - 1.27	0.973	no
	Dose 2	15	7	25,493	18,199	1.46	0.56 - 4.04	0.298	no

¹**Weekly analyses** include all data to date, but confidence intervals and p-values do not account for the multiple chances for a false positive signal during surveillance.

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Myocarditis/Pericarditis in 21-day risk interval after either dose of any mRNA vaccine Compared with outcome events in vaccinated comparators on the same calendar days

Vaccine Type	Dose	Events in Risk Interval	Events in Comparison Interval ⁴	Risk Follow-up Person Days	Comparison Follow-up Person Day	Adjusted Rate Ratio ³	95% Confidence Interval ¹	1-sided P-value (Fisher)	Signal ¹ 1-sided p < 0.0048 ²
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	Dose 2	24	16	142,776	129,970	1.19	0.61 - 2.35	0.366	no
Pfizer	Both Doses	23	9	70,984	25,826	0.82	0.36 - 2	0.757	no
	Dose 1	8	8	15,478	10,021	0.39	0.12 - 1.27	0.973	no
	Dose 2	15	7	25,493	18,199	1.46	0.56 - 4.04	0.298	no
Moderna	Both Doses	23	15	119,560	71,321	0.68	0.35 - 1.38	0.898	no

¹**Weekly analyses** include all data to date, but confidence intervals and p-values do not account for the multiple chances for a false positive signal during surveillance.

²**Sequential test** requires 1-sided p < 0.0048 for a signal. This keeps the probability of a false positive signal (due to chance alone) below 0.05 in 2 years of surveillance.

³**Adjusted** for VSD site, 5-year age group, sex, race/ethnicity, and calendar date. ne=not estimable

⁴**Comparison interval** is 22–42 days after either dose.

Myocarditis/Pericarditis in 21-day risk interval after either dose of any mRNA vaccine Compared with outcome events in vaccinated comparators on the same calendar days

Vaccine Type	Dose	Events in Risk Interval	Events in Comparison Interval ⁴	Risk Follow-up Person Days	Comparison Follow-up Person Day	Adjusted Rate Ratio ³	95% Confidence Interval ¹	1-sided P-value (Fisher)	Signal ¹ 1-sided p < 0.0048 ²
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	Dose 1	22	23	116,038	139,454	0.67	0.34 - 1.31	0.915	no
	Dose 2	24	16	142,776	129,970	1.19	0.61 - 2.35	0.366	no
Pfizer	Both Doses	23	9	70,984	25,826	0.82	0.36 - 2	0.757	no
	Dose 1	8	8	15,478	10,021	0.39	0.12 - 1.27	0.973	no
	Dose 2	15	7	25,493	18,199	1.46	0.56 - 4.04	0.298	no
Moderna	Both Doses	23	15	119,560	71,321	0.68	0.35 - 1.38	0.898	no
	Dose 1	14	15	42,969	64,489	0.82	0.36 - 1.91	0.751	no

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Myocarditis/Pericarditis in 21-day risk interval after either dose of any mRNA vaccine Compared with outcome events in vaccinated comparators on the same calendar days

Vaccine Type	Dose	Events in Risk Interval	Events in Comparison Interval ⁴	Risk Follow-up Person Days	Comparison Follow-up Person Day	Adjusted Rate Ratio ³	95% Confidence Interval ¹	1-sided P-value (Fisher)	Signal ¹ 1-sided p < 0.0048 ²
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	Dose 2	24	16	142,776	129,970	1.19	0.61 - 2.35	0.366	no
Pfizer	Both Doses	23	9	70,984	25,826	0.82	0.36 - 2	0.757	no
	Dose 1	8	8	15,478	10,021	0.39	0.12 - 1.27	0.973	no
	Dose 2	15	7	25,493	18,199	1.46	0.56 - 4.04	0.298	no
Moderna	Both Doses	23	15	119,560	71,321	0.68	0.35 - 1.38	0.898	no
	Dose 1	14	15	42,969	64,489	0.82	0.36 - 1.91	0.751	no
	Dose 2	9	9	44,381	49,564	0.87	0.32 - 2.36	0.699	no

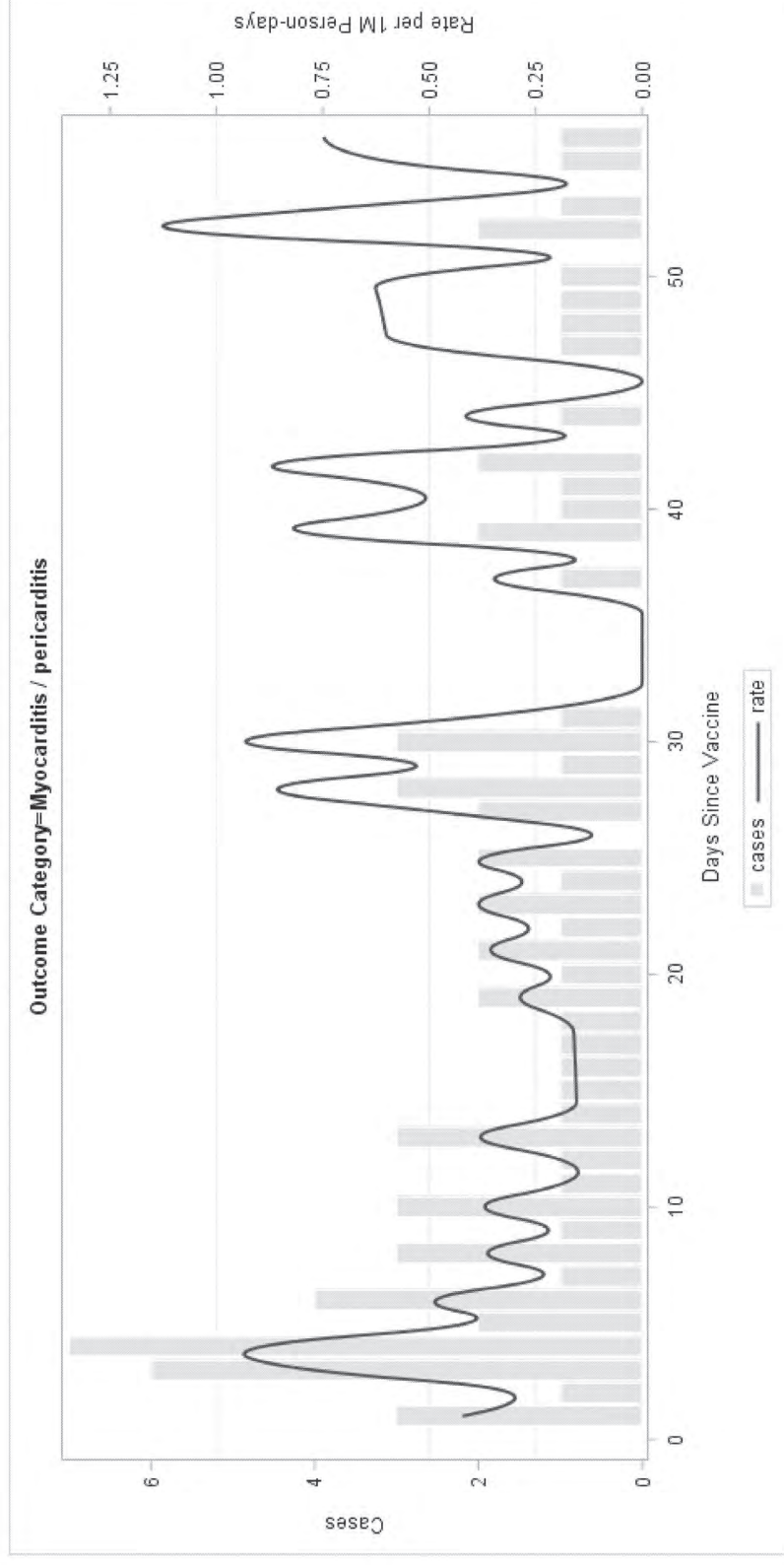
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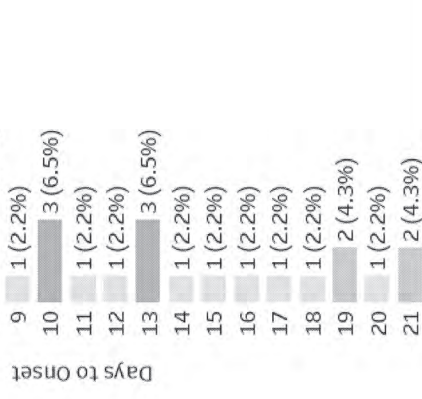
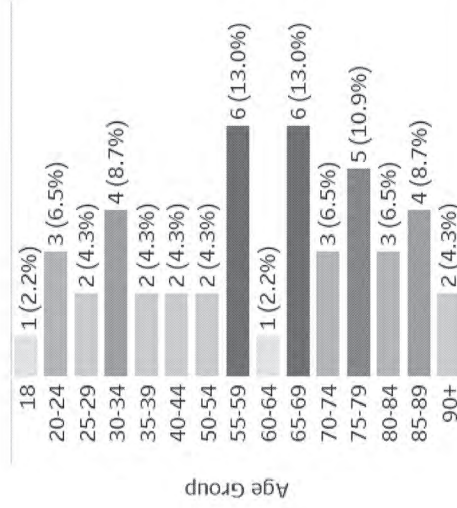
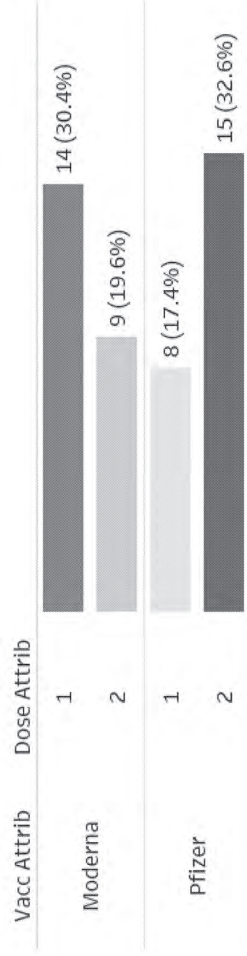
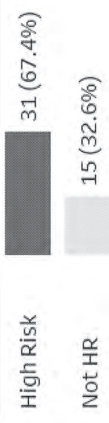
Myocarditis/Pericarditis – Days Since any mRNA Vaccination (all ages) and Rate per Million Person-Days



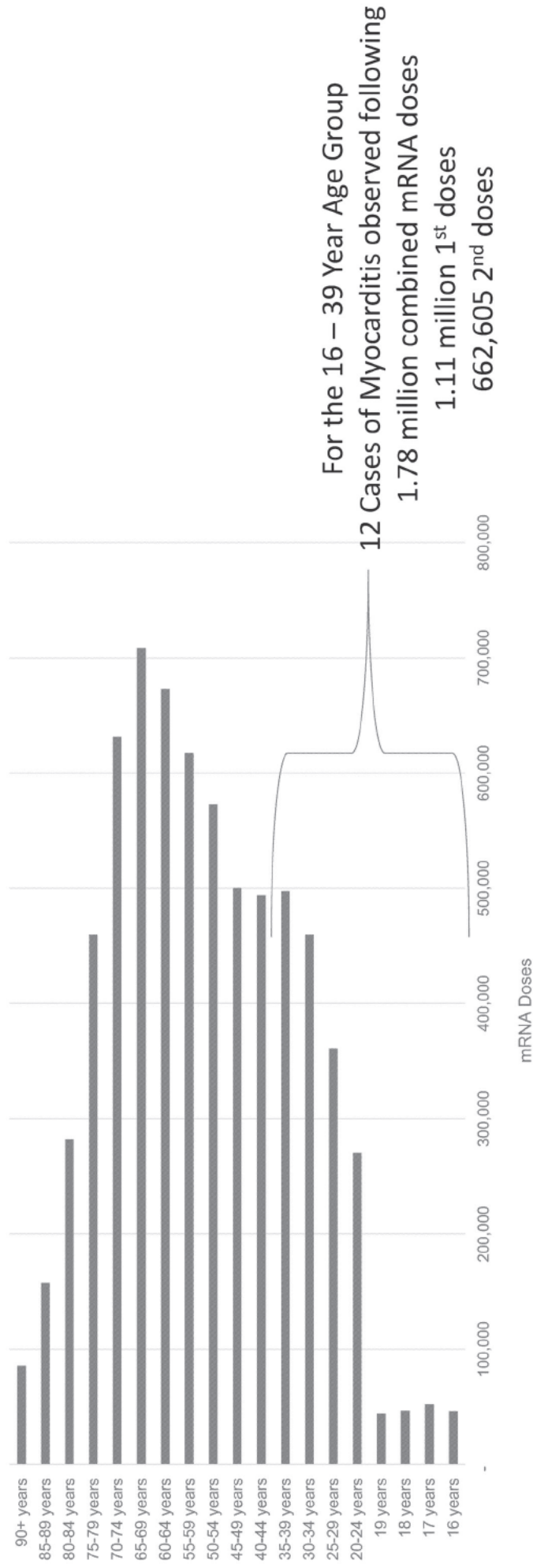
Myocarditis / Pericarditis Automated Summary

46

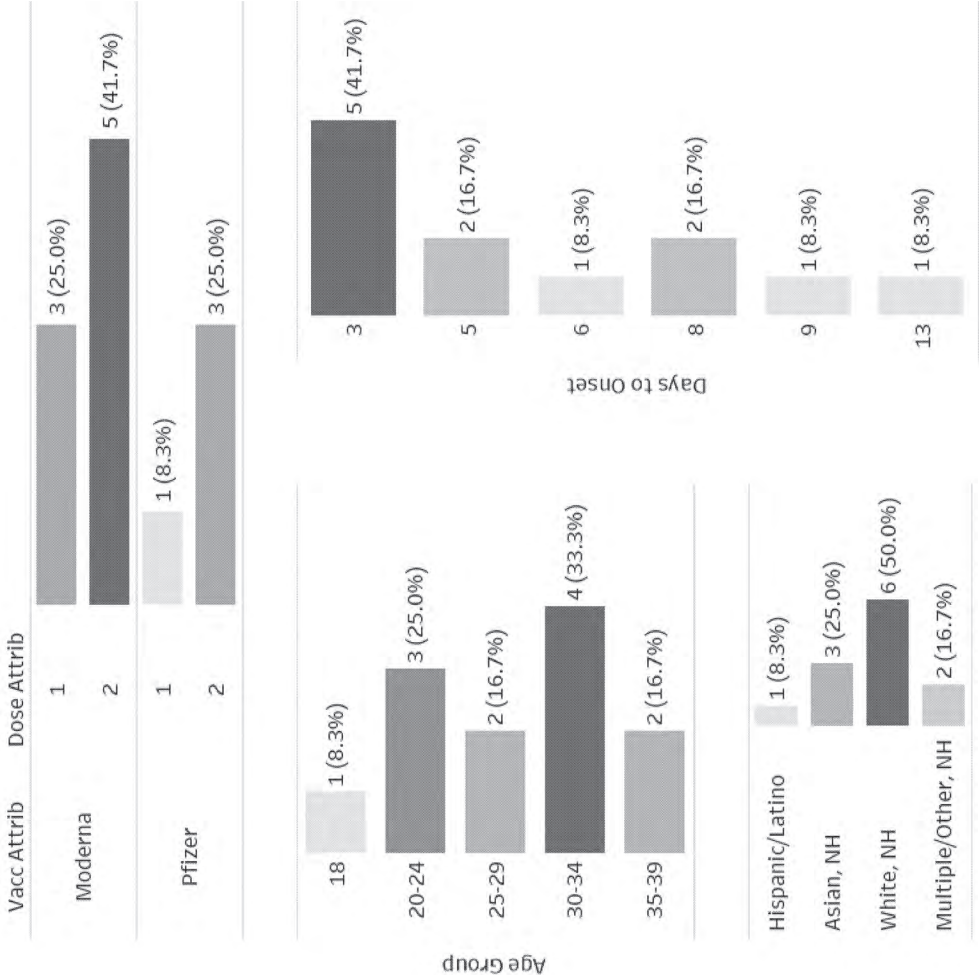
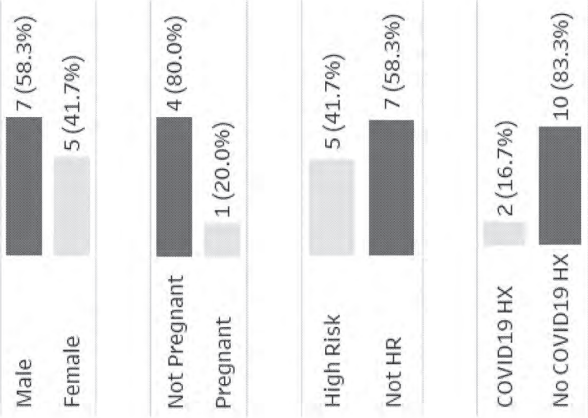
cases identified
in the 1-21 day
risk interval



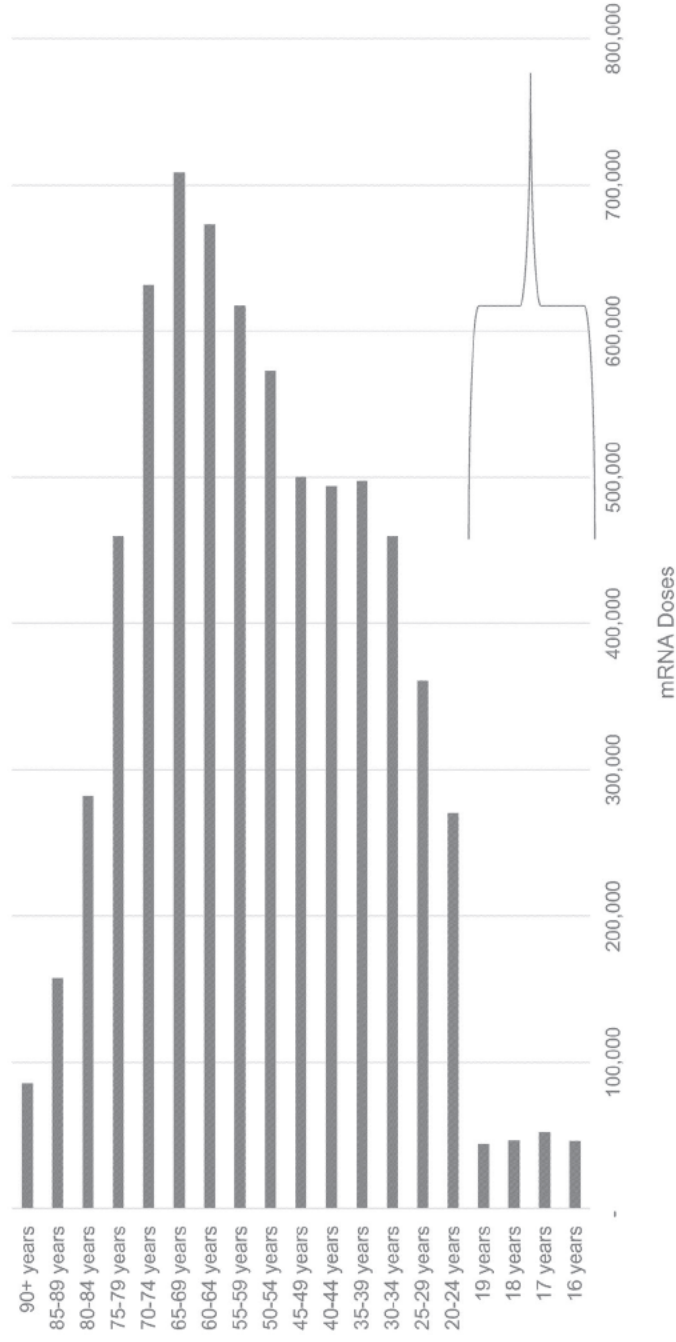
Total mRNA Doses by Age in Years And Myocarditis Cases in 21 Day Risk Interval



Myocarditis/Pericarditis Automated Summary for 16-39 year old age group



Total mRNA Doses by Age in Years And Myocarditis Cases in 21 Day Risk Interval



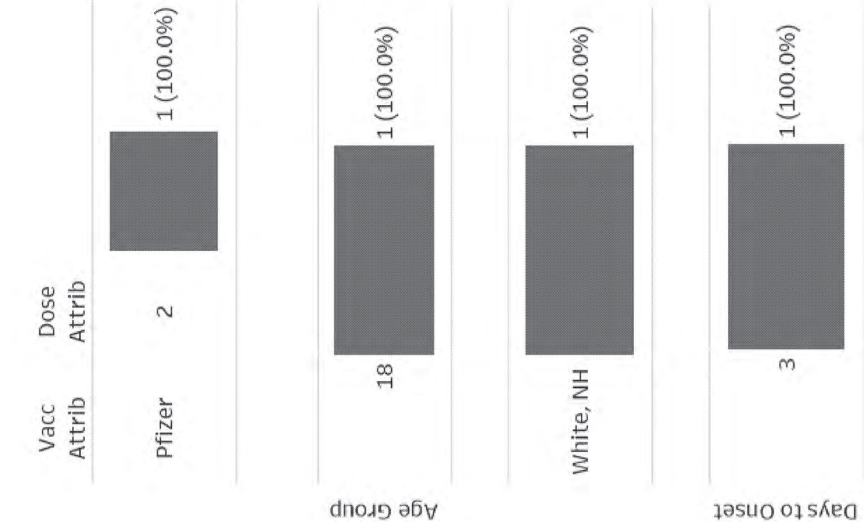
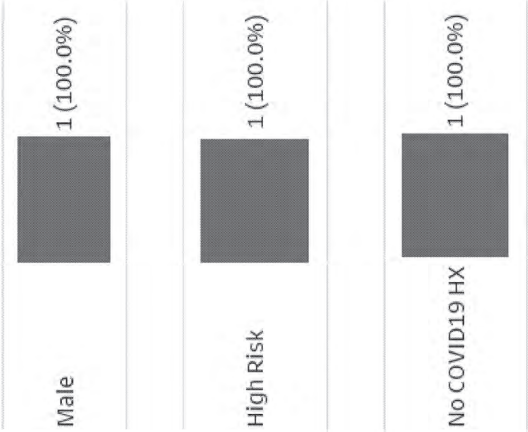
For the 16 – 19 Year Age Group
1 Case of Myocarditis observed
188,465 combined mRNA doses
134,960 1st doses
53,505 2nd doses

~0.45 Cases expected

Myocarditis/Pericarditis Automated Summary for 16-19 year old age group

1

cases identified in the
1-21 day risk interval
among 16-19 year olds



Outcome events in 21-day risk interval after either dose of any mRNA vaccine

Compared with outcome events in vaccinated comparators on the same calendar days

Outcome Event	Events in Risk Interval	Adjusted Rate Ratio ³	Weekly Analysis ¹		Sequential Test ²	
			95% Confidence Interval	2-Sided P-value	1-sided P-value (Fisher)	'Signal' 1-sided p < 0.0048
Acute disseminated encephalomyelitis	1	.	0.01 - .	0.811	0.811	no
Acute myocardial infarction	455	0.88	0.74 - 1.05	0.160	0.927	no
Appendicitis	415	0.81	0.68 - 0.96	0.018	0.992	no
Bell's palsy	371	1.12	0.91 - 1.39	0.287	0.156	no
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Stroke, hemorrhagic	195	0.89	0.68 - 1.18	0.405	0.817	no
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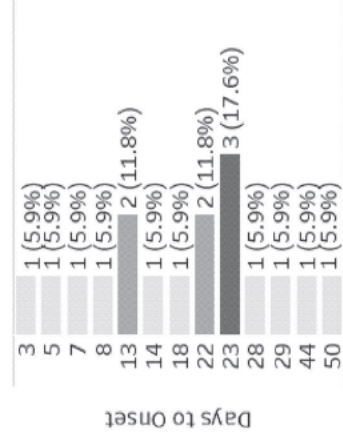
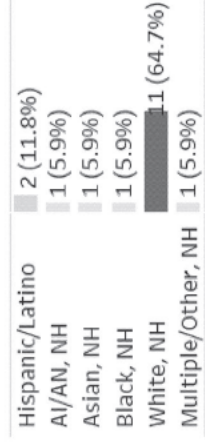
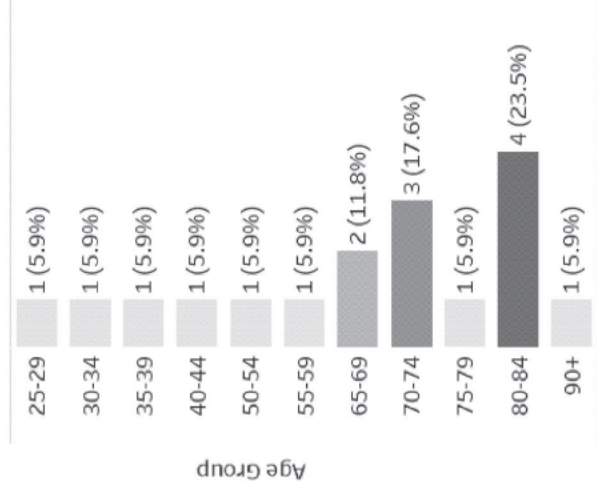
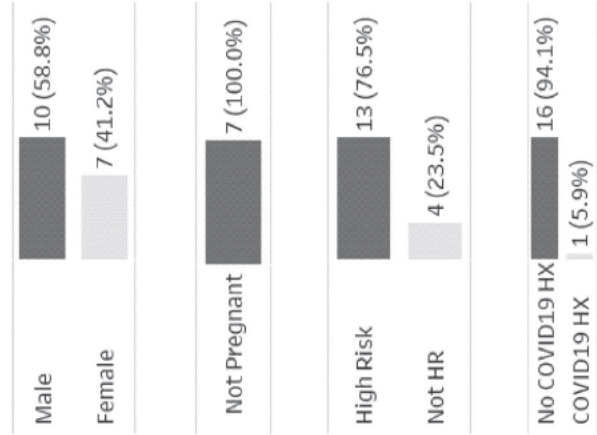
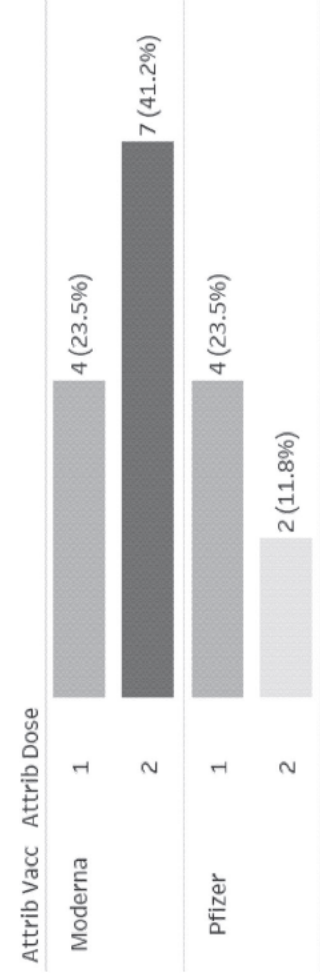
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²**Sequential test** requires 1-sided p < 0.0048 for a signal. This keeps the probability of a false positive signal (due to chance alone) below 0.05 in 2 years of surveillance.
³**Adjusted** for VSD site, 5-year age group, sex, race/ethnicity, and calendar date. ne=not estimable
⁴**Comparison interval** is 22–42 days after either dose.

Cerebral Venous Sinus Thrombosis (CVST): mRNA vaccines

Automated Summary

17

automated cases
identified in the
1-84 day risk interval



Cerebral Venous Sinus Thrombosis (CVST): mRNA vaccines

Quick Chart Review Summary

- 3.7 million doses of Pfizer-BioNTech and 3.3 million doses of Moderna COVID-19 vaccinations administered in VSD as of May 8, 2021
- 17 total ICD-10 coded CVST diagnoses identified following mRNA vaccines (6 after Pfizer-BioNTech and 11 after Moderna vaccination)
 - 14/17 have been reviewed to date, 3 chart reviews are pending.
 - 8/14 were ruled out as incident cases (historical n=2, other known cause=5, chronic cavernous sinus syndrome n=1)
 - This leaves 6 potential CVST incident cases, but all without thrombocytopenia
- No confirmed cases of incident CVST with thrombocytopenia after ~7 million doses of mRNA COVID-19 vaccines administered in VSD

Outcome events in 21-day risk interval after Janssen vaccine

Compared with outcome events in vaccinated comparators on the same calendar days

Outcome Event	Events in Risk Interval	Events in Comparison Interval ⁴	Adjusted Rate Ratio ³	Weekly Analysis ¹			Sequential Test ²	
				95% Confidence Interval	2-Sided P-value	1-sided P-value (Fisher)	'Signal' 1-sided p < 0.0048	
Acute disseminated encephalomyelitis	11	4	2.05	0.57 - 8.37	0.282	0.208	no	
Appendicitis	14	12	1.03	0.44 - 2.43	0.954	0.561	no	
Bell's palsy	18	11	1.35	0.54 - 3.51	0.534	0.342	no	
Disseminated intravascular coagulation	1	0	.	0.07 - .	0.443	0.443	no	
Guillain-Barré syndrome	2	0	.	0.02 - .	0.728	0.728	no	
Disseminated intravascular coagulation	3	2	0.69	0.07 - 6.81	0.732	0.812	no	
Encephalitis / myelitis / encephalomyelitis	18	11	1.77	0.75 - 4.35	0.193	0.132	no	
Immune thrombocytopenia	0	3	0.00	0.00 - 4.05	0.334	0.334	no	
Seizures	5	4	1.04	0.25 - 4.61	0.965	0.619	no	
Thrombotic thrombocytopenic purpura	1	0	.	0.03 - .	0.639	0.639	no	
Venous thromboembolism	17	15	0.78	0.35 - 1.74	0.546	0.792	no	
Pulmonary embolism	6	14	0.27	0.07 - 0.89	0.030	0.994	no	

¹**Weekly analyses** include all data to date, but confidence intervals and p-values do not account for the multiple chances for a false positive signal during surveillance.

²**Sequential test** requires 1-sided p < 0.0048 for a signal. This keeps the probability of a false positive signal (due to chance alone) below 0.05 in 2 years of surveillance.

³**Adjusted** for VSD site, 5-year age group, sex, race/ethnicity, and calendar date. ne=not estimable

⁴**Comparison interval** is 22–42 days after either dose.

CVST events in 21-days risk interval after Janssen Vaccine

Compared with outcome events in unvaccinated comparators on the same calendar days

Weekly Analysis ¹				
Outcome Event	Events in Risk Interval	Events in Unvaccinated	Adjusted Rate Ratio ²	95% Confidence Interval 2-Sided P-value
CVST	0	18	0.0	0.00 – 32.86 0.892

¹**Weekly analyses** include all data to date, but confidence intervals and p-values do not account for the multiple chances for a false positive signal during surveillance.

²**Adjusted** for VSD site, 5-year age group, sex, race/ethnicity, and calendar date. ne=not estimable

Outcome events in 21-day risk interval after Janssen vaccine

Compared with outcome events in vaccinated comparators on the same calendar days

Outcome Event	Events in Risk Interval	Events in Comparison Interval ⁴	Adjusted Rate Ratio ³	Weekly Analysis ¹			Sequential Test ²	
				95% Confidence Interval	2-Sided P-value	1-sided P-value (Fisher)	'Signal' 1-sided p < 0.0048	
Acute disseminated encephalomyelitis	11	4	2.05	0.57 - 8.37	0.282	0.208	no	no
Appendicitis	14	12	1.03	0.44 - 2.43	0.954	0.561	no	no
Bell's palsy	18	11	1.35	0.54 - 3.51	0.534	0.342	no	no
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Guillain-Barré syndrome	2	0	.	0.02 - .	0.728	0.728	no	no
Disseminated intravascular coagulation	3	2	0.69	0.07 - 6.81	0.732	0.812	no	no
Encephalitis / myelitis / encephalomyelitis	18	11	1.77	0.75 - 4.35	0.193	0.132	no	no
Immune thrombocytopenia	0	3	0.00	0.00 - 4.05	0.334	0.334	no	no
Seizures	5	4	1.04	0.25 - 4.61	0.965	0.619	no	no
Thrombotic thrombocytopenic purpura	1	0	.	0.03 - .	0.639	0.639	no	no
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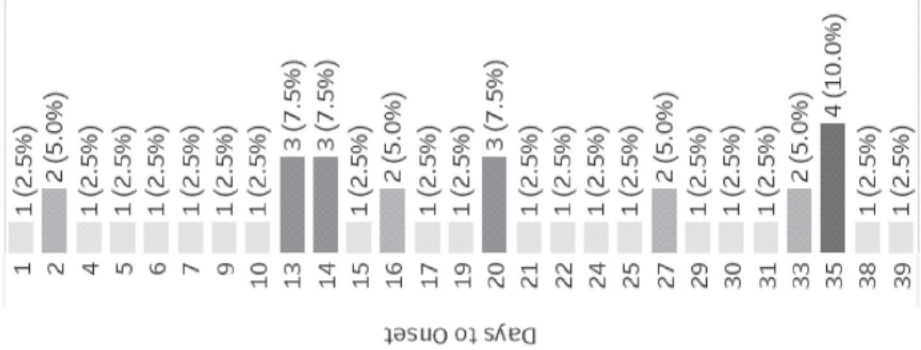
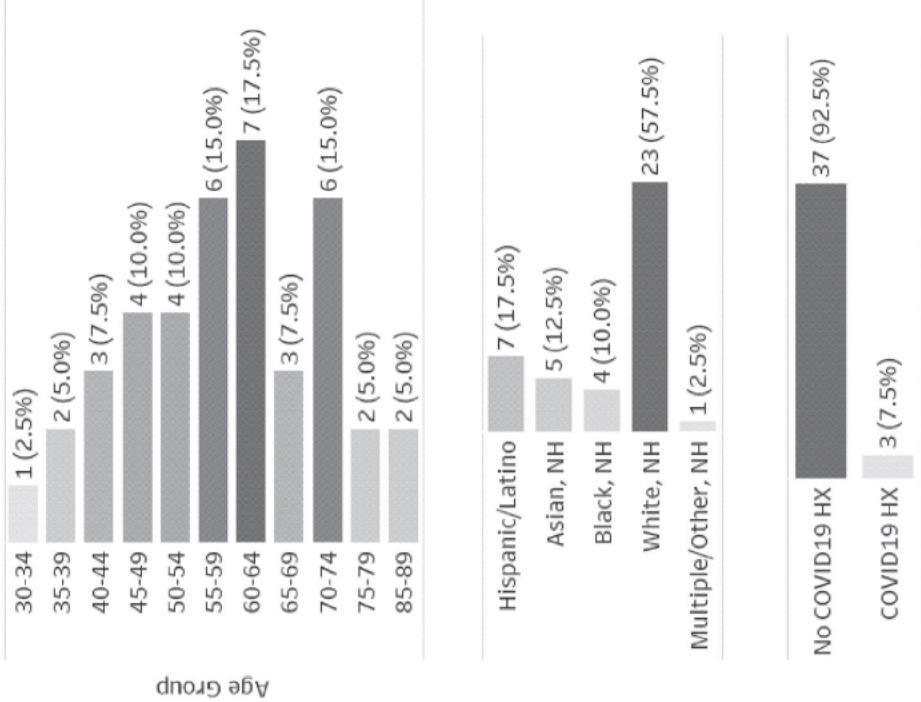
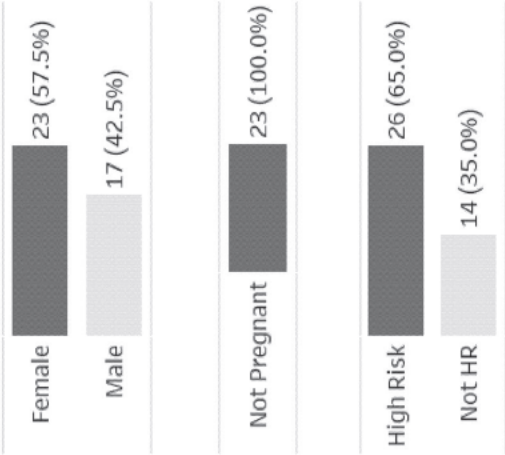
³**Adjusted** for VSD site, 5-year age group, sex, race/ethnicity, and calendar date. ne=not estimable

⁴**Comparison interval** is 22–42 days after either dose.

Venous thromboembolism automated summary: Cases after Janssen vaccine during the 42 days after vaccination

40

automated cases identified
in the 1-42 day risk interval
after Janssen vaccine



Outcome events in 21-day risk interval after Janssen vaccine

Compared with outcome events in vaccinated comparators on the same calendar days

Outcome Event	Events in Risk Interval	Events in Comparison Interval ⁴	Adjusted Rate Ratio ³	Weekly Analysis ¹			Sequential Test ²	
				95% Confidence Interval	2-Sided P-value	1-sided P-value (Fisher)	'Signal' 1-sided p < 0.0048	
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Pulmonary embolism	6	14	0.27	0.07 - 0.89	0.030	0.994	no	

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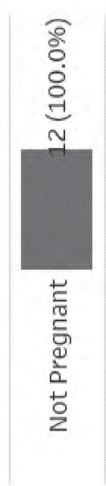
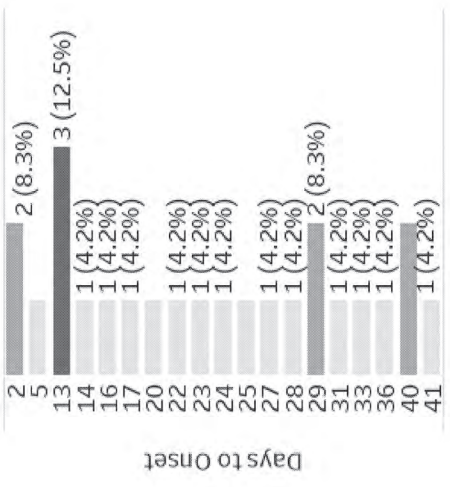
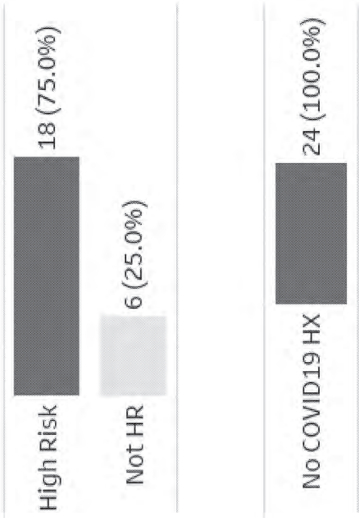
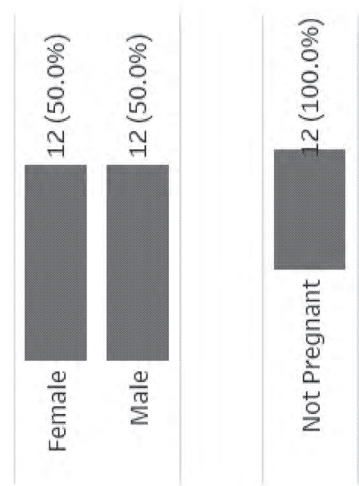
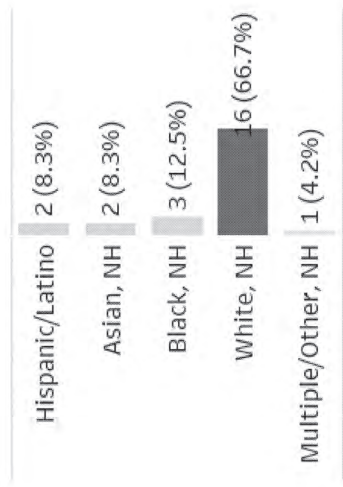
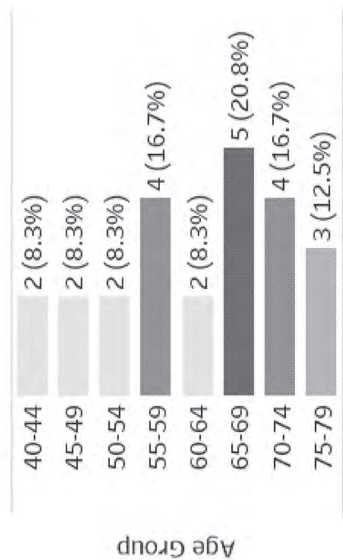
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⁴**Comparison interval** is 22–42 days after either dose.

Pulmonary embolism (PE) automated Summary: Cases after Janssen vaccine during the 42 days after vaccination

24

automated cases identified in the 1-42 day risk interval after Janssen vaccine



VSD: Thrombosis events after Janssen COVID-19 vaccination

- 171,111 Janssen COVID-19 Vaccine doses administered in VSD through May 8, 2021
 - No statistical signals detected for any prespecified Rapid Cycle Analysis outcomes
 - No CVST cases identified

- 57 VTE/PE cases identified in the 1–84 days following vaccination

- 50 of the cases have been quick reviewed to date (7 in progress)

- 50 { • 9 were ruled out as not VTE/PE
• 41 were confirmed VTE/PE cases

VTE = venous thromboembolism
PE = pulmonary embolism

- 41 { ➤ 5 were determined to have symptom onset prior to vaccination
➤ 1 had an indeterminate symptom onset
➤ 35 are potential VTE/PE cases with incidence following vaccination

- 35 { • 21 female (9 PE, 12 VTE), 14 males (8 PE, 6 VTE)
• Ages ranged from 30–89
• 1 with history of COVID-19 infection
• 3 with thrombocytopenia noted at time of VTE/PE
 - All males with PE.
 - Ages ranged from 40-59
 - Full chart review by hematologist pending.

VSD: Thrombosis events with thrombocytopenia after Janssen

COVID-19 vaccination

#	Dx	Sex	Age group	Days post vaccination to automated diagnosis date	Days post vaccination to symptom onset (chart review)	Lowest Platelet Count	History of COVID-19	High risk status	Status at time of chart review
1	PE	M	40-44	31 days	27 days	50,000	No	Yes	Discharged
2	PE	M	55-59	33 days	6 days	63,000	No	Yes	Died
3	PE	M	55-59	52 days	51 days	147,000	No	Yes	Discharged

Anaphylaxis

Anaphylaxis Chart Review Summary

- Chart review completed for 97/103 cases through April 3, 2021*
- 43/97 (44%) cases confirmed as post-vaccination anaphylaxis

*Full review not completed until 30 days after the event

	Pfizer (n=23)	Moderna (n=19)	Janssen (n=1)
Age in years, median (range)	43 (21-74)	45 (30-76)	65
Female sex	23 (100%)	18 (95%)	1 (100%)
Minutes to symptom onset, median (range)	7 (0-300)	12 (2-39)	--
Symptom onset within 15 minutes	13 (57%)	10 (53%)	0 (0%)
Symptom onset within 30 minutes	16 (70%)	13 (68%)	0 (0%)
Prior history of allergies	18 (78%)	13 (68%)	1 (100%)
Prior history of anaphylaxis	11 (48%)	5 (26%)	1 (100%)
Dose 1	19 (83%)	17 (89%)	1 (100%)
Brighton Collaboration case definition level			
1	11 (48%)	6 (32%)	0 (0%)
2	12 (52%)	13 (68%)	1 (100%)
No. confirmed cases (95% CI) per million doses	9.0 (5.7-13.5)	8.3 (5.0-12.9)	8.8 (0.2-49.1)
No. confirmed cases (95% CI) per million female doses	15.4 (9.8-23.1)	13.5 (8.0-21.3)	16.7 (0.4-93.0)
No. confirmed cases (95% CI) per million first doses	12.3 (7.4-19.2)	11.2 (6.5-18.0)	--
No. confirmed cases (95% CI) per million female first doses	21.3 (12.8-33.2)	18.5 (10.6-30.1)	--

GBS Summary

- 24 GBS cases identified following COVID-19 vaccination with mRNA vaccine (Pfizer or Moderna)
 - 20 have been quick reviewed (4 pending)
 - 9 ruled out (4 history, 2 with onset prior to vaccination, 2 GBS ruled out, 1 miscode)
 - 11 proceeded to full review
 - 5 completed full review and adjudication (6 pending)
 - 1 indeterminate case, Brighton Level (BL) 4
 - 4 cases confirmed as GBS with symptom onset following vaccination
 - Female aged 70-74 years with onset 26 days after Pfizer dose 1; BL 2
 - Female aged 70-74 years with onset 5 days after Pfizer dose 2; BL 3
 - Male aged 85-90 years with onset 1 day after Moderna dose 1; BL 2
 - Male aged 40-44 years with onset 4 days after Moderna dose 2; BL 2

GBS Summary

- 9 GBS cases identified following COVID-19 vaccination with Janssen
 - 7 have been quick reviewed (2 pending)
 - 1 ruled out (history)
 - 6 proceeded to full review
 - 2 completed full review and adjudication (4 pending)
 - 2 cases confirmed as GBS with symptom onset following vaccination
 - Female aged 60-64 years with onset 11 days after Janssen vaccine; BL 2
 - Female aged 55-59 years with onset 11 days after Janssen vaccine; BL 2

ADEM & TM Summary

- 2 ADEM cases identified following COVID-19 vaccination
 - 1 confirmed as incident ADEM following vaccination, waiting for 3 months before final Brighton Level classification
 - 1 pending quick review
- 6 TM cases identified following COVID-19 vaccination
 - 3 were ruled out after quick review (2 not incident, 1 with MS)
 - 3 pending full review and adjudication, at least 1 case has a possible alternative etiology

Summary

- No signals observed for all outcomes and all vaccines during the 21 days after vaccination, including PE and myocarditis
- There were 6 potential CVST cases (“quick-reviewed”) after mRNA vaccines, none had thrombocytopenia.
- No CVST cases have been observed during the 42 days after the Janssen vaccine.
- There were 35 potential VTE and/or PE cases after Janssen, 3 had thrombocytopenia noted at the time of their diagnosis.

Next Steps for the VSD

- As more myocarditis cases are accrued following mRNA vaccines, evaluating the feasibility of an age stratified analysis for the 16–39 year olds.
- We are creating a TTS outcome category using diagnostics codes and platelet counts.
 - Focus initially will be on Tier 1 TTS cases
 - Exploring feasibility of capturing Positive (+) heparin-PF4 ELISA HIT antibody results electronically for Tier 2 TTS cases
- In the meantime, we are continuing to chart review all cases of VTE and PE following Janssen vaccine to check for thrombocytopenia.
- Continue quick-reviews of all vaccinated CVST cases to check for thrombocytopenia.
- We will continue monitoring simultaneous vaccines with new recommendation to vaccinate 12-15 year olds.

Acknowledgements

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- Eric Weintraub, Tat'Yana Kenigsberg, Mike McNeil, Jonathan Duffy, Frank Destefano, Tanya Myers, Tom Shimabukuro

- **VSD Sites**

- HealthPartners Institute, Minneapolis, Minnesota
- Kaiser Permanente Colorado, Denver, Colorado
- Kaiser Permanente Northwest, Portland, Oregon
- Kaiser Permanente Southern California, Los Angeles, California
- Kaiser Permanente Washington, Seattle, Washington
- Denver Health, Denver, Colorado

Extra Slides

VSD Weekly Covid-19 Vaccine Coverage Summary

Variable	Moderna		Pfizer		Janssen	Totals		Denominator	Coverage %	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 1	Dose 2	Denominator	Dose 1 Coverage	Series Completion
16	73	27	31,488	9,356	9	31,570	9,383	139,716	22.60	6.72
17	200	117	35,827	13,023	20	36,047	13,140	141,495	25.48	9.30
18	12,793	4,680	19,640	7,690	1,229	33,662	12,370	139,200	24.18	9.77
19	13,153	5,806	16,409	7,035	1,320	30,882	12,841	136,791	22.58	10.35
20-24	78,926	41,717	93,296	48,812	7,274	179,496	90,529	734,519	24.44	13.32
25-29	100,201	59,936	122,229	72,821	9,250	231,680	132,757	796,432	29.09	17.83
30-34	124,524	77,623	154,199	96,572	12,007	290,730	174,195	881,304	32.99	21.13
35-39	133,677	86,131	164,778	106,578	13,245	311,700	192,709	862,698	36.13	23.87
40-44	133,746	87,862	160,789	106,060	13,502	308,037	193,922	799,122	38.55	25.96
45-49	136,744	90,525	159,851	107,065	14,288	310,883	197,590	753,519	41.26	28.12
50-54	160,724	108,049	174,469	124,788	19,926	355,119	232,837	781,201	45.46	32.36
55-59	176,048	119,720	182,144	132,795	22,997	381,189	252,515	785,143	48.55	35.09
60-64	195,534	139,441	190,089	142,872	25,165	410,788	282,313	762,396	53.88	40.33
65-69	190,547	165,665	183,569	162,244	11,722	385,838	327,909	619,937	62.24	54.78
70-74	170,589	150,615	165,557	148,741	8,047	344,193	299,356	517,890	66.46	59.36
75-79	122,023	111,682	119,270	110,164	4,149	245,442	221,846	329,465	74.50	68.59
80-84	74,055	67,588	75,545	69,723	2,694	152,294	137,311	204,999	74.29	68.30
85-89	40,456	36,620	43,987	40,054	1,728	86,171	76,674	119,763	71.95	65.46
90+	21,527	19,150	26,065	22,752	1,206	48,798	41,902	73,511	66.38	58.64
Total	1,885,540	1,372,954	2,119,201	1,529,145	169,778	4,174,519	2,902,099	9,579,101	43.58	32.1

Analyses for Days 1-21 & 1-42 Risk Intervals

Analytic Methods	Moderna			Pfizer			mRNA-Vaccines Combined			Janssen
	Dose 1	Dose 2	Dose 1 & Dose 2 Combined	Dose 1	Dose 2	Dose 1 & Dose 2 Combined	Dose 1	Dose 2	Dose 1 & Dose 2 Combined	Dose 1
Vaccinated Concurrent Comparators	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Unvaccinated Concurrent Comparators	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Historical Background rates	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Historical Well care visits	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

✓ = featured

✓ = available (not featured)

✓ = planned

VTE/PE events 42 days After Janssen:

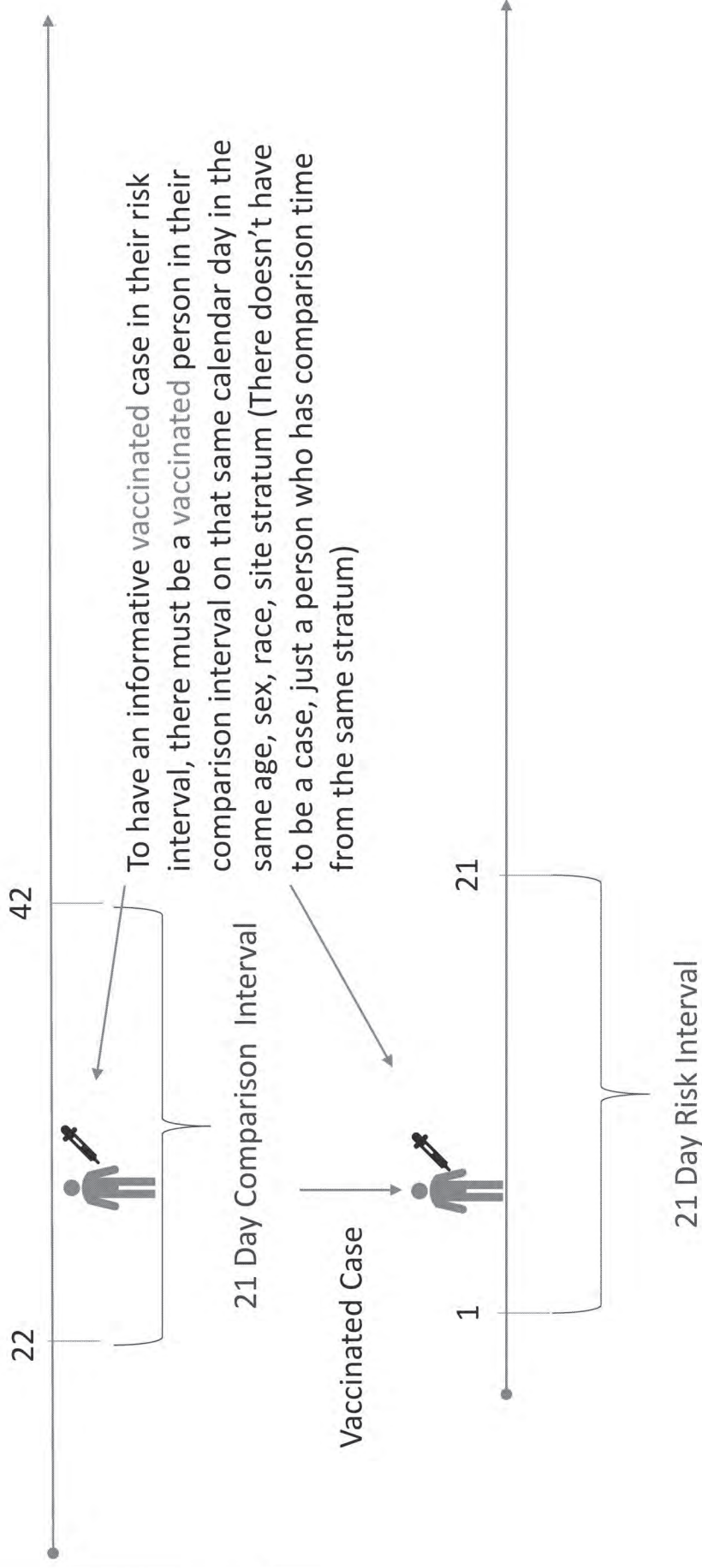
Quick Chart Review Summary

- 32 VTE/PE cases (including 3 cases diagnosed with both VTE and PE) in 1-42 days
- 29 have been quick reviewed to date, 3 are in progress
 - 6/29 were ruled out as not VTE
 - 23/29 were confirmed VTE/PE cases
 - 4/23 were determined to have symptom onset prior to vaccination
 - Including 2 cases with thrombocytopenia documented prior to vaccination
 - 1/23 had an indeterminate symptom onset
 - 18/23 are potential VTE/PE cases with incidence following vaccination
 - 10 female (5 PE, 5 VTE), 8 males (4 PE, 4 VTE)
 - Ages ranged from 30-79
 - None with history of COVID-19 infection or thrombocytopenia noted at time of VTE/PE

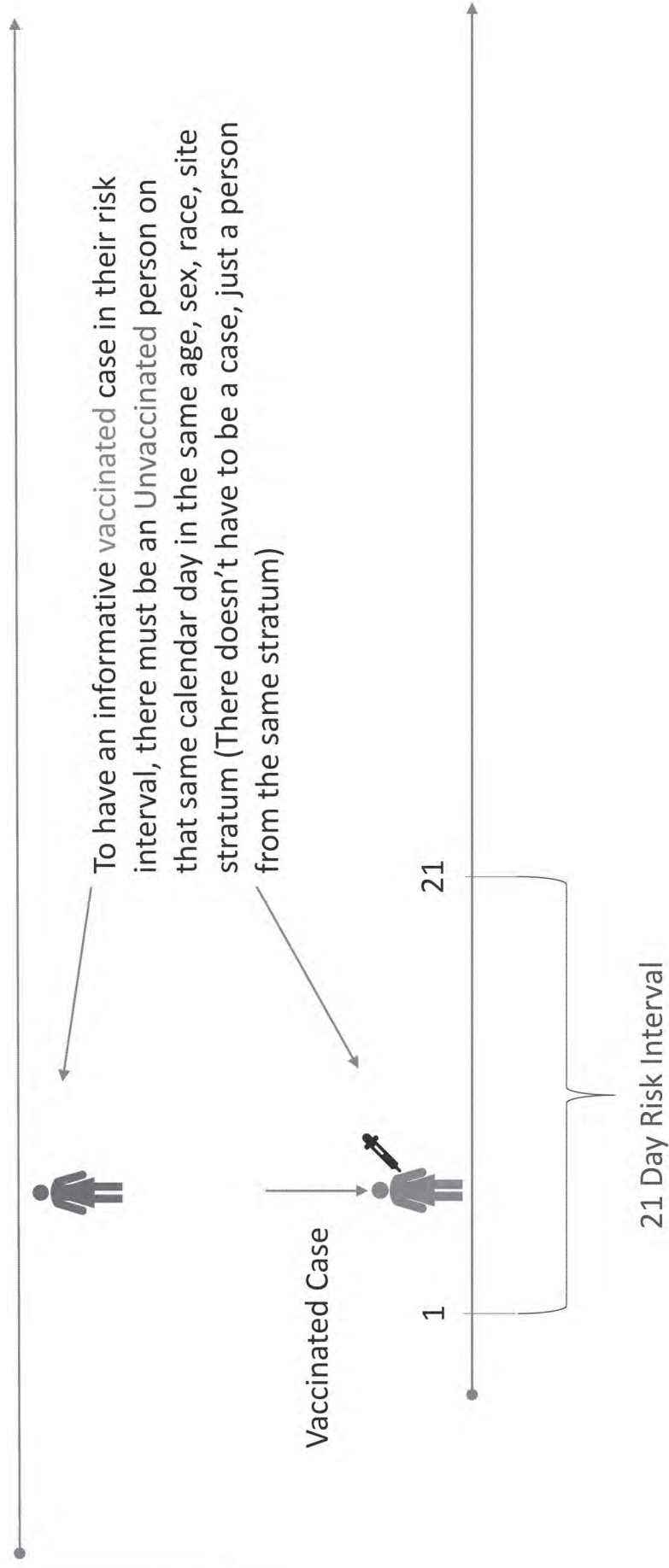
VSD RCA COVID-19 Outcomes

#	VSD Outcomes	Abbreviation	Risk Window (days)	Chart Review	Monitoring Only	Exclude if COVID-19 in the Prior X Days
1	Acute disseminated encephalomyelitis (settings = E, I)	ADEM	1-21, 1-42	Yes		
2	Acute myocardial infarction (settings = E, I) – First Ever	AMI	1-21, 1-42			30 days
3	Acute respiratory distress syndrome (settings = E, I)	ARDS	1-21, 1-42		Yes	42 days
4	Anaphylaxis (settings = E, I) - First in 7 days	ANAPH	0-1	Yes	Yes	
5	Appendicitis (settings = E, I)	APPND	1-21, 1-42			
6	Bell's palsy (settings = E, I, O) - First Ever	BP	1-21, 1-42			30 days
7	Convulsions / seizures (settings = E, I)	SZ	1-21, 1-42 (day 0 included for children)			30 days
8	Disseminated intravascular coagulation (settings = E, I)	DIC	1-21, 1-42			42 days
9	Encephalitis / myelitis / encephalomyelitis (settings = E, I)	ENCEPH	1-21, 1-42			30 days
10	Guillain-Barré syndrome (settings = E, I)	GBS	1-21, 1-42	Yes		
11	Thrombotic thrombocytopenic purpura (settings = E, I)	TTP	1-21, 1-42			30 days
12	Immune thrombocytopenia (settings = E, I, O)	ITP	1-21, 1-42			30 days
13	Kawasaki disease (settings = E, I)	KD	1-21, 1-42			
14	Multisystem Inflammatory Syndrome in Children & Adults (MIS-C, MIS-A) (settings = E, I)	MISC			Yes	
15	Myocarditis / pericarditis (settings = E, I) - First in 60 Days	MYOC	1-21, 1-42			30 days
16	Narcolepsy and cataplexy (settings = E, I, O)	NARC			Yes	
17	Stroke, hemorrhagic (settings = E, I)	HSTK	1-21, 1-42			30 days
18	Stroke, ischemic (settings = E, I)	ISTK	1-21, 1-42			30 days
19	Transverse myelitis (settings = E, I)	TM	1-21, 1-42	Yes		
20	Venous thromboembolism (settings = E, I, O) – First Ever	VTE	1-21, 1-42			30 days
21	Pulmonary embolism (subset of VTE) (settings = E, I) – First Ever	PE	1-21, 1-42			30 days
	Notes: specific settings for code search is noted below (E = ED; I = Inpt; O = Outpt)					

Vaccinated Comparison



Unvaccinated Comparison



Analytic Strategies: Aim 1

The number of events observed in the risk interval will be compared to the number expected, with the expected derived from 3 types of comparators, the first of which will be primary when available:

- vaccinated concurrent comparators in a comparison interval after COVID-19 vaccination.
 - On each day, outcome incidence in the vaccinees who are in their risk interval will be compared to outcome incidence in vaccinees who are concurrently—on the same calendar date—in their comparison interval.
 - Analyses will be stratified in risk sets anchored to the calendar dates of outcome events.
 - Analyses will be stratified by age group, sex, race/ethnicity, and VSD site, as well as by calendar date.
- Unvaccinated concurrent comparators in a comparison interval after COVID-19 vaccination.
 - On each day, outcome incidence in the vaccinees who are in their risk interval will be compared to outcome incidence in Unvaccinated individuals who are concurrently—on the same calendar date—at risk.
 - Analyses will be stratified in risk sets anchored to the calendar dates of outcome events.
 - Analyses will be stratified by age group, sex, race/ethnicity, and VSD site, as well as by calendar date.
- self-controls in a comparison interval after COVID-19 vaccination.
 - Among the vaccinees who had an outcome event in either the risk interval or the comparison interval, we compare outcome incidence in the risk interval with outcome incidence in the comparison interval.

Analytic Strategies: Aim 1

Design	Advantages	Limitations
Primary		
Concurrent Vaccinated	- Not confounded by time-stable co-morbidities, propensities to use health services, or demographics - Follow-up in the comparison interval is on the same calendar dates as follow-up time in the risk interval - Avoids bias that can arise from day-to-day variation in health services - Reduces bias that can arise from data lags	- Transient difficulty finding appropriate comparators soon after a new risk group becomes eligible for vaccine
Unvaccinated concurrent	- Well-adjusted for calendar time	- Bias from comorbidities, demographics, and propensities that may be associated with both the outcome and vaccination status
Supplemental		
Self-Control	- Not confounded by time-stable co-morbidities, propensities to use health services, or demographics as the same vaccinees are contributing person time to both the risk and the comparison intervals	- Bias from differences between risk and comparison intervals in calendar time - Analyses are less timely and can only include vaccinees for whom the control window is complete and for whom the data have settled

- Primary design will be vaccinated concurrent comparators
- If vaccinated concurrent comparators are unavailable, the primary analyses will use Unvaccinated concurrent comparators

Analysis

- Poisson regression will be used to model outcome incidence observed during the risk interval in comparison with incidence expected (under H_0)
- Sequential Analysis is the Vaccinated Comparator
 - Significant Threshold is a 1-Sided P-Value < 0.0048
- Models are adjusted for:
 - Calendar day
 - Age in categories
 - Race
 - Site
 - Sex

Rate Ratio Estimates

Poisson regression will be used to model outcome incidence observed during the risk interval in comparison with incidence expected (under H_0)

- Estimates of the rate ratio (RR) will be reported with nominal 95% confidence intervals rather than confidence intervals that are widened to correspond with the threshold of the sequential tests.
- Trends in outcome incidence over calendar time and time-since-vaccination, and heterogeneity across subgroups will be tracked.
- Supplementary analyses will disaggregate the risk interval (days 1-7, days 8-15, etc.), comparing risk interval weeks with each other and with the incidence expected (under H_0) from our primary comparator. We'll also look at whether incidence varies across the weeks of the comparison interval.

Sequential Tests

- For each outcome, the primary analysis each week will include a sequential test of the one-sided null hypothesis that the vaccine does not increase risk in the risk interval.
- The threshold for a signal is pre-specified by an alpha-spending plan that keeps the overall chance of a Type 1 error below 0.05 for 2 years (104 weekly analyses).
 - With a Pocock style plan, the 2-sided p-value required for a signal at a weekly analysis is 0.0096, amounting to a 1-sided p-value of 0.0048.
- The criteria for signaling are not criteria for “stopping”.
 - After a signal, weekly updates will continue as we add analyses to evaluate the signal.
- The multiplicity of different hypotheses tested will be taken into consideration informally.
 - Our sequential testing adjusts for the multiplicity of weekly looks at each hypothesis, but we will not adjust formally for the multiplicity of hypotheses.

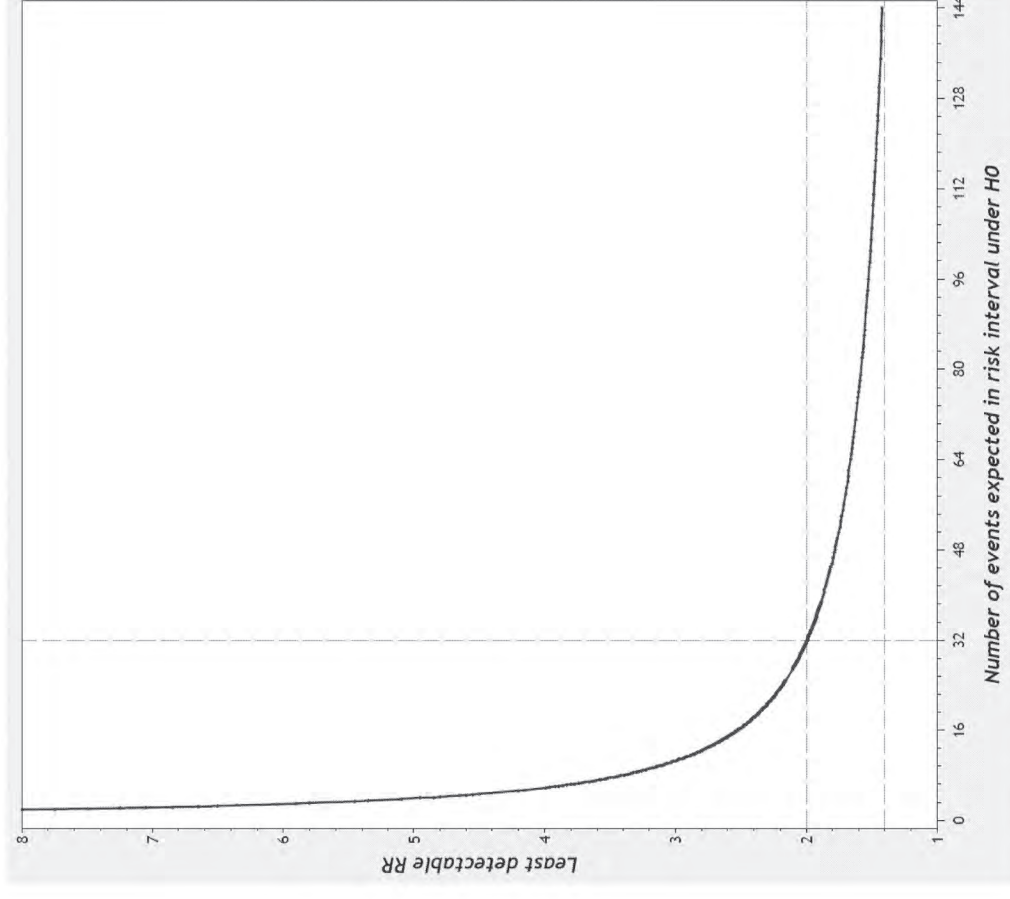
Power (Aim 1)

Power of planned analyses comparing observed outcomes vs expected outcomes in a risk interval—where the expected is based on vaccinees in a comparison interval.

- The magnitude of the rate ratio (RR) detectable with 80% power will decrease as the number of outcomes expected in the risk interval (under H_0) increases.
- If our alpha-spending plan sets the threshold for a signal at 2-sided $p=0.0096$ (amounting to 1-sided $p=0.0048$) then $RR = 2.0$ is detectable when 32 outcomes are expected in the risk interval.
 - RRs of 5, 4, 3, and 1.5 are detectable when 4, 6, 11, and 110 AEs, respectively, are expected in risk interval.
- If E denotes the background rate (outcomes expected per 100,000 person-years under H_0) then an RR of 2.0 is detectable when the number of person-days in the risk interval is:

$$32/E \times 365,000$$

- For example, if the background rate is 32 per 100,000 person years, then an RR of 2 is detectable when 365,000 person days are in the risk interval, which we'd have if 1.74 million vaccinees are each observed 21 days.



Relative risk detectable with 80% power, comparing AEs in risk v. comparison intervals of equal length, By the N of events expected in risk interval under the H_0 that the vaccine is safe.

Time-to-signal by the rate ratio and the N of events expected weekly under H0

- This table reports on the time-to-signal in 5 million simulations of safety surveillance in each of 12 scenarios, defined by:
 - 3 levels of the rate ratio: 1.5, 2, and 3, and
 - 4 levels of outcome incidence expected under H0: 1, 5, 20, or 100 outcome events per week.
- The top row of each panel indicates when the chance of detecting the panel's RR exceeds 50, 80 and 95% for an AE with expected incidence of only 1 per week
 - The top row of the top panel shows time-to-signal if the true RR=1.5 for an outcome so rare that under H0 we expect only 1 AE per week. (An example of such an outcome would be TTP if we have about 500,000 VSD vaccinees per week)
 - For this infrequent outcome (1 AE/week), the chance of detecting RR=1.5 exceeds 50% by the 55th week and exceeds 80% by the 101st week. It won't ever exceed 95%.
 - For this infrequent outcome, the chance of detecting RR=3.0 exceeds 50% by week 7, 80% by week 11, 95% by week 17.
- Similarly, the 2nd row of each panel indicates when the chance of detecting the RR exceeds 50, 80 and 95% for an AE with expected incidence of 5/week (perhaps Bell's Palsy). The chance of detecting RR=2 passes 50% by week 4, 80% by week 7, 95% by week 11.

For simplicity, expected incidence (under H0) was constant in each scenario.

		Week when chance of signal passes:		
		50%	80%	95%
Rate Ratio	AEs/week expected in risk interval			
1.5	1 (TTP)	55	101	
	5 (Bells P.)	12	22	33
	20 (seizure)	4	6	9
	100 (AMI)	1	2	2
2	1 (TTP)	19	32	49
	5 (Bells P.)	4	7	11
	20 (seizure)	2	2	3
	100 (AMI)	1	1	1
3	1 (TTP)	7	11	17
	5 (Bells P.)	2	3	4
	20 (seizure)	1	1	1
	100 (AMI)	1	1	1

Signal Follow-up

- If the criteria for a signal are met, we will already have the supplemental comparators (i.e., Unvaccinated concurrent and self-control) available for context and interpretation of results.
- Further analyses of the potential vaccine-outcome association may be undertaken, such as:
 - Chart review (especially of outcomes during the risk interval)
 - Evaluate for clustering of outcomes if they appear during brief sub-intervals within the risk interval
 - Evaluate for clustering in subgroups defined by:
 - age
 - sex
 - race/ethnicity
 - VSD site
 - prior COVID-19 disease

Chart Review

- We will conduct routine chart review for selected rare outcomes (e.g., GBS, ADEM, TM, anaphylaxis) shortly after a case is detected and prior to analysis.
- If the criteria for a signal are met, further analyses of the potential vaccine-outcome association may be undertaken through chart review.
- In collaboration with MCRI and CDC, with feedback from participating VSD sites, we will design, test, validate, and manage all chart reviews across the participating sites.

Study Design: Aim 2

Aim 2: To describe the uptake of COVID-19 vaccines over time among eligible VSD members overall, and in strata by age, sex, race/ethnicity, and VSD site.

- After a COVID-19 vaccine becomes routinely available in the VSD, we will monitor vaccine coverage overall, and in strata defined by age group, sex, race/ethnicity, and VSD site.
- Surveillance of vaccine coverage will be updated weekly.
 - For each week during the study period, we will tabulate the number of doses delivered, the cumulative number of doses, and vaccine coverage.
 - If different vaccines are in use in the VSD population, we will monitor vaccine coverage separately for each type of vaccine, and for all COVID-19 vaccines combined.

Historical Comparator Analysis

General Analytic Approach

- MFC will use historical comparators
- Most appropriate for infrequent or rare outcomes
- Using historical data accumulated over multiple years provides more stable estimates and greater statistical power, which potentially leads to earlier detection of a safety signal
- Ideally, the historical period starts October 1, 2015 (the start of ICD-10 coding) and ends December 31, 2019 to avoid the influence of the pandemic in the early part of 2020
- Limitation: Secular trends in disease or in diagnostic or coding practices may lead to either false signaling or failure to identify a true signal

Sequential Analysis using MaxSPRT and CMaxSPRT

- Near real-time surveillance based on weekly aggregate data
- Sequential analysis to detect signals, but maintaining a pre-defined type I error rate
- Poisson-based MaxSPRT, developed by VSD researchers (Kulldorff, et al.)
- Compare observed number of events to expected number based on the historical background rates
 - Expected counts based on the incidence rate expected during the risk window multiplied by the number of vaccines administered
 - Reject H_0 of no excess risk if log-likelihood ratio exceeds a critical value → **statistical signal**
- Critical values based on probability of a false positive (e.g. $\alpha=0.05$) and planned length of surveillance, defined in terms of expected counts under the null hypothesis
- Use conditional MaxSPRT (CMaxSPRT) when the number of historical cases is small and background rates are unstable

Historical Comparator Groups

- General VSD population (age comparable)
 - Used to estimate general background person-time rates
 - Rates multiplied by vaccine counts to produce expected (prorated to length of post-vax window)
- Other comparator group(s) defined by care-seeking behavior and/or comparator vaccine visits*
 - Well visits (e.g., ICD10: Z00.00, Z00.01)
 - Non-COVID vaccination (e.g., Td, Tdap, pneumococcal, influenza)
 - Compute number events in post-visit risk windows
- Some combination of well visits and vaccination visits in the historical period?
 - For example, well visit and a flu vaccine in the previous 18 months
- Compare different groups to vaccinated group using baseline covariates

Adverse events following vaccination COVID-19

Data updated March 31st 2021



Division of Epidemiology
Public health services
Ministry of Health Israel

Sources of adverse events reports



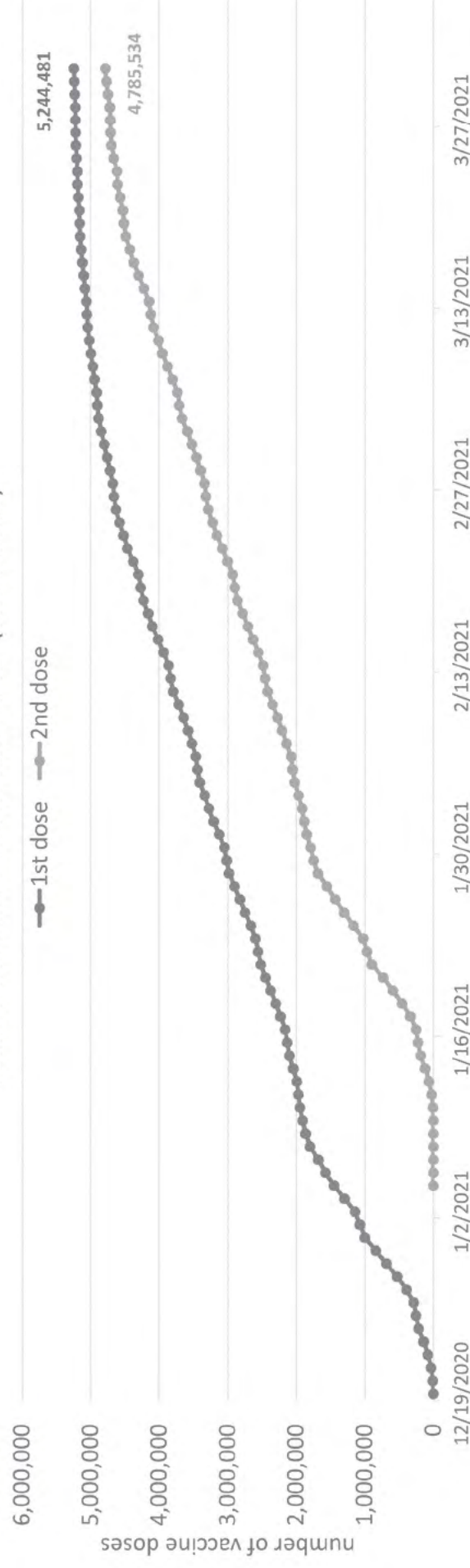
Sources of adverse events reports include:

- Hospitals
- HMOs
- Emergency Medical Services - MDA (for individuals who are vaccinated in nursing homes)
- The Medical Department and the Patient Safety Unit at the MoH
- Israeli Defense Forces (IDF)

Vaccine doses administered in Israel



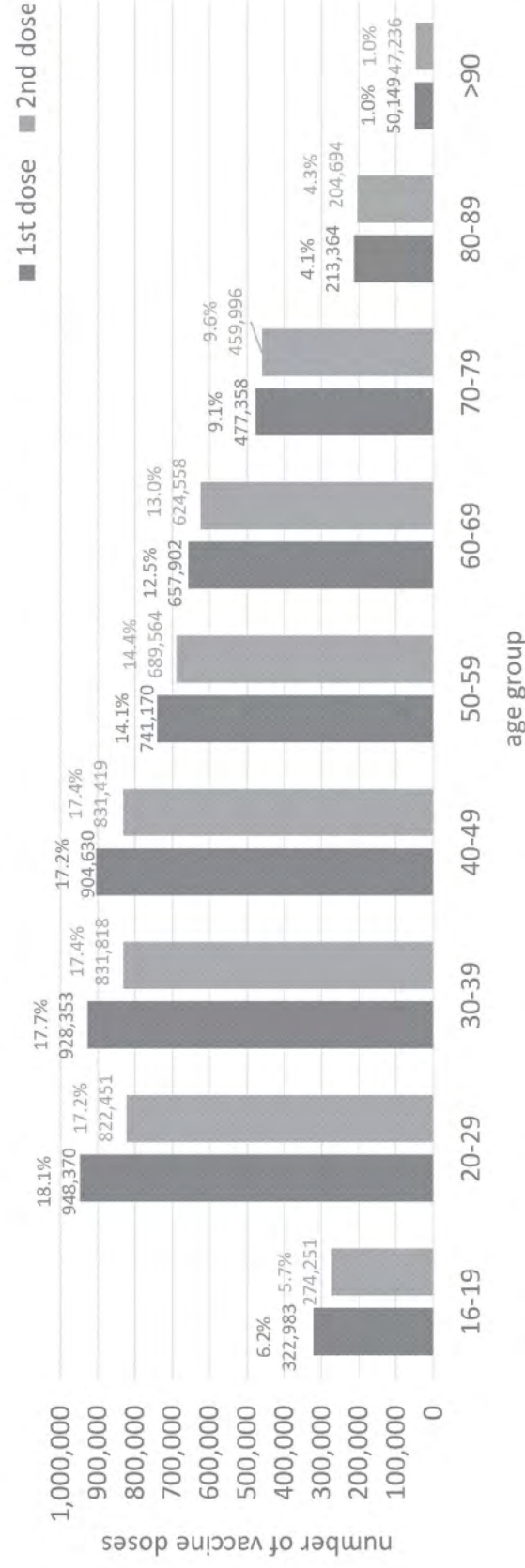
Vaccine doses administered in Israel (cumulative)



Distribution of vaccine recipients according to age



Distribution of vaccine recipients in Israel according to age

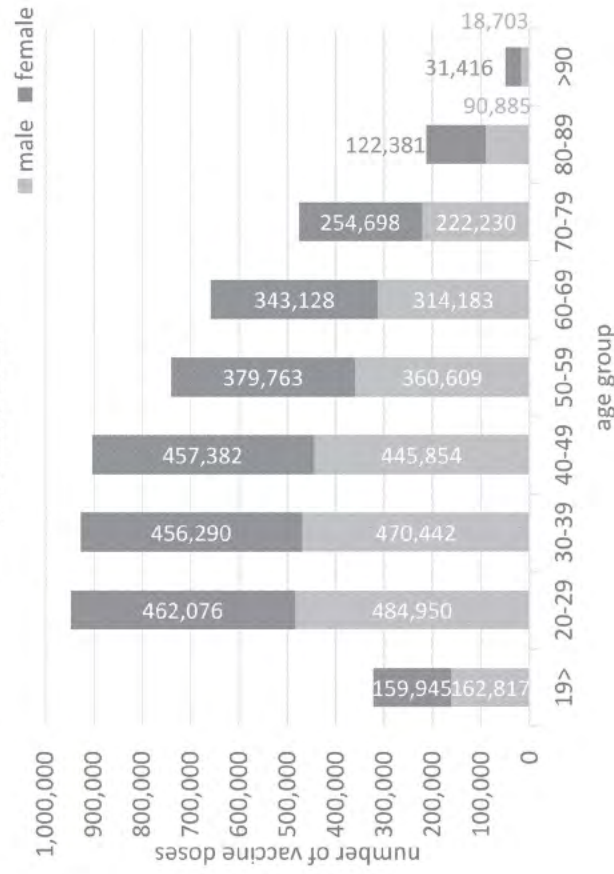


AgeGroup	16-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90<
Vaccine coverage by age group 1 st dose	55.3%	72.9%	77.6%	82.3%	87.2%	88.7%	97.3%	94.6%	97.4%
Vaccine coverage by age group 2 nd dose	47.0%	63.2%	69.5%	75.7%	81.1%	84.2%	93.7%	90.8%	91.7%

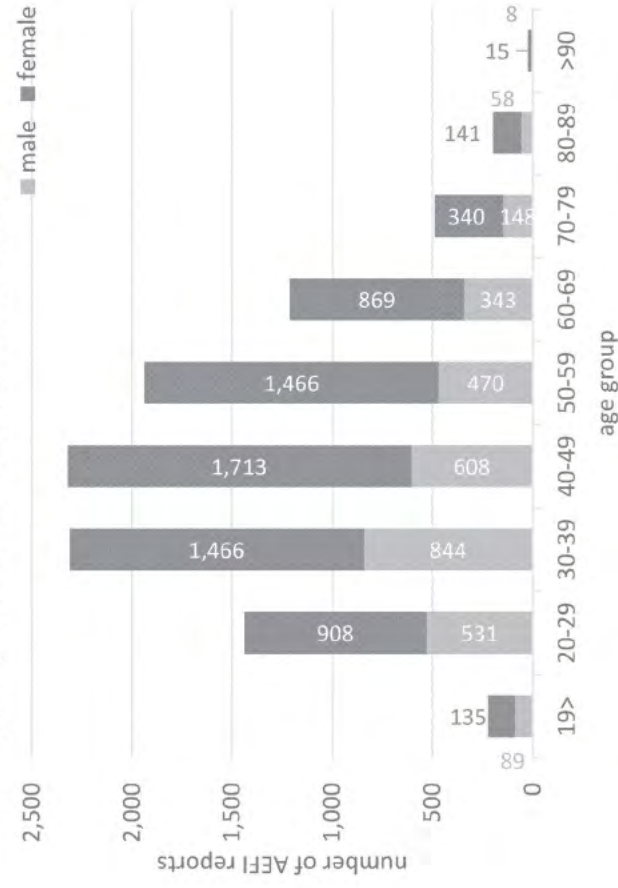
Age and sex distribution among vaccine recipients and those who reported adverse events - FIRST DOSE



Distribution according to age group and sex among recipients of first vaccine dose.

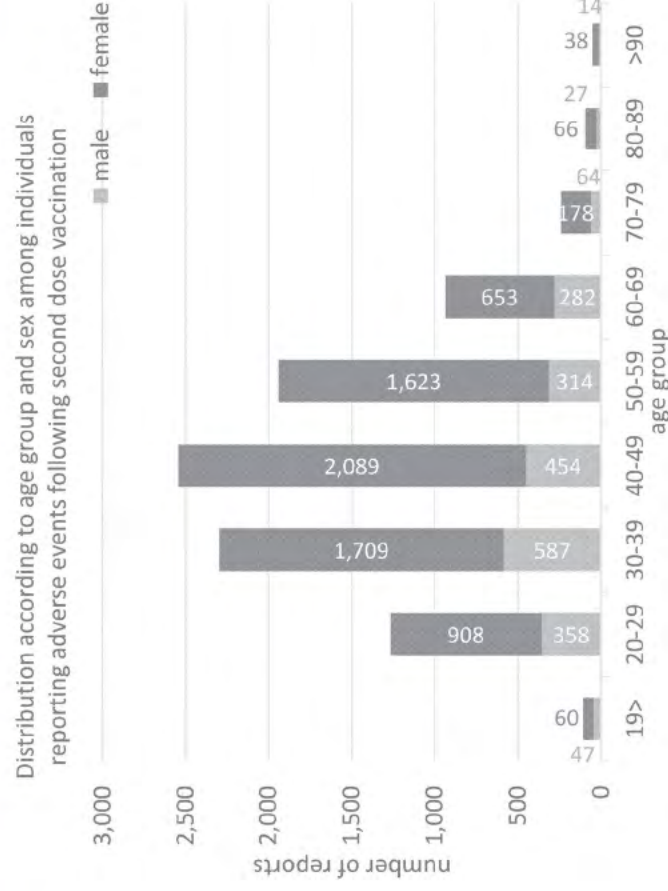
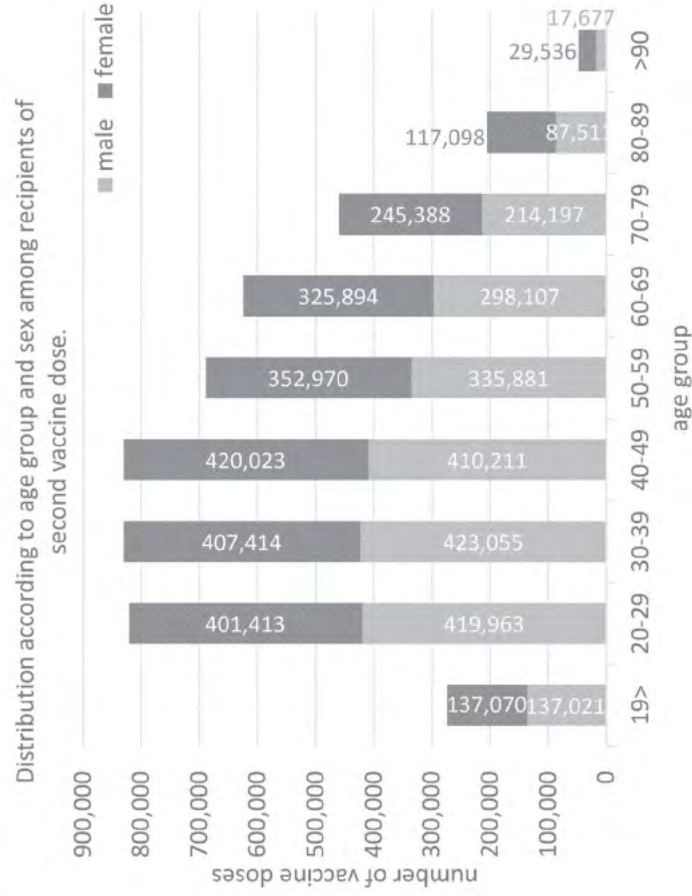


Distribution according to age group and sex among individuals reporting adverse events following first dose vaccination.



Women and younger individuals are more likely to report adverse reactions following vaccination relative to their proportion among the vaccine recipient population

Age and sex distribution among vaccine recipients and those who reported adverse events - SECOND DOSE



Women and younger individuals are more likely to report adverse reactions following vaccination relative to their proportion among the vaccine recipient population

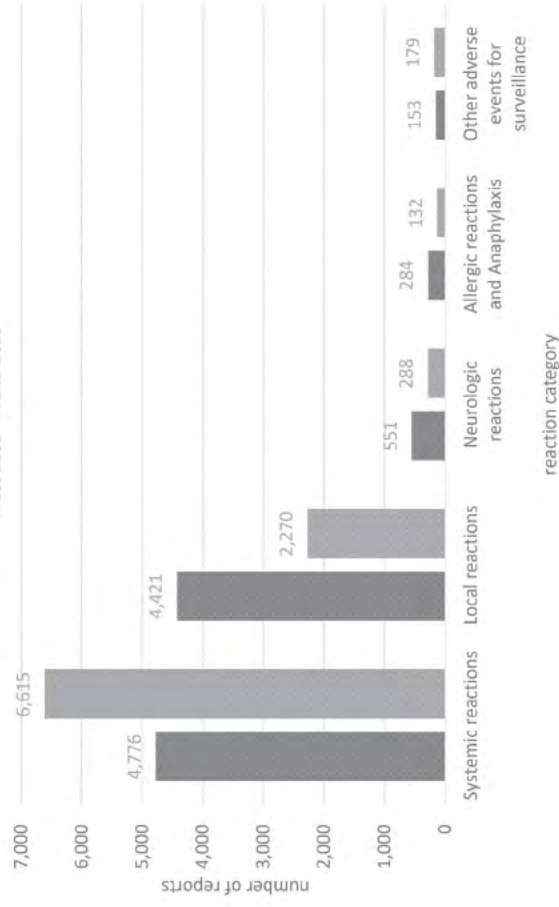
Adverse events following vaccination by category



Adverse event reported following vaccination by category

Number of reports

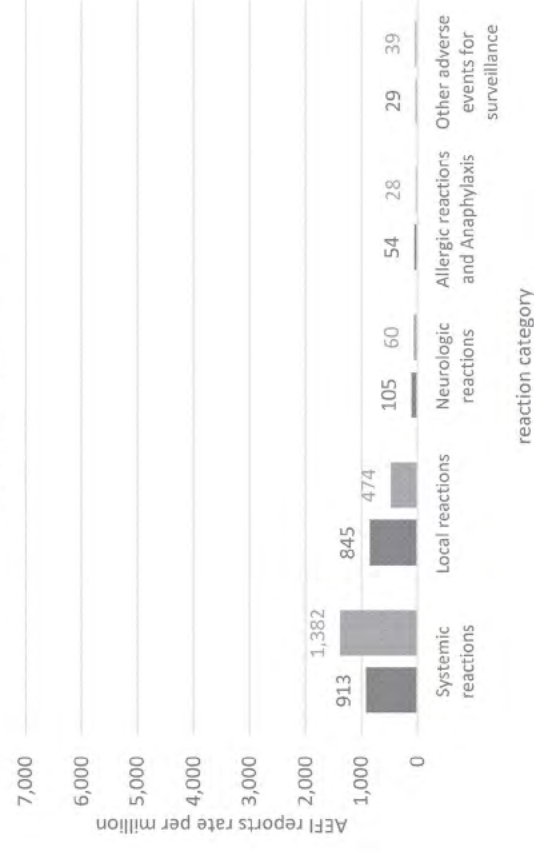
■ 1st dose ■ 2nd dose



Adverse events reported following vaccination by category

rate per million doses

■ 1st dose ■ 2nd dose



Reports among vaccine recipients

1st dose: 5,244,481 2nd dose: 4,785,534

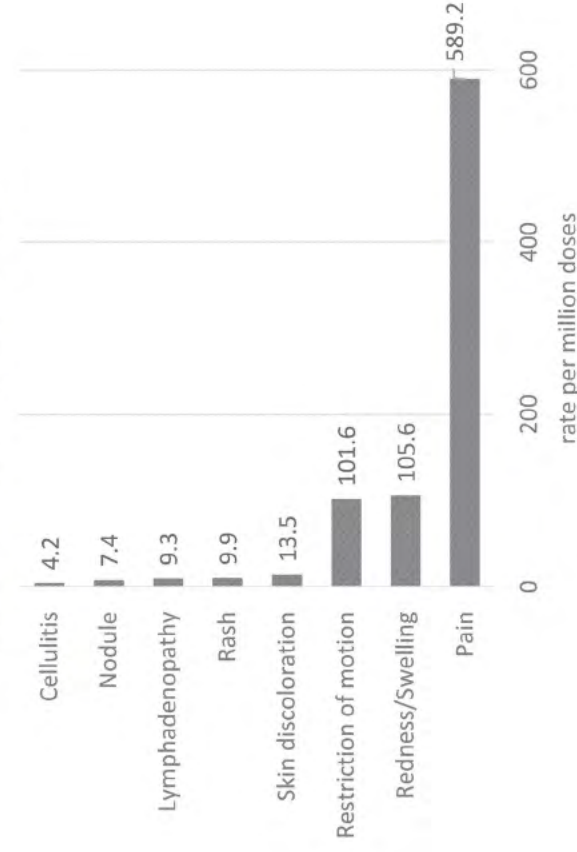
Updated 31/03/2021

Data is based on adverse events reported to the MoH | Some individuals reported more than one adverse event

PSICOID_00009405

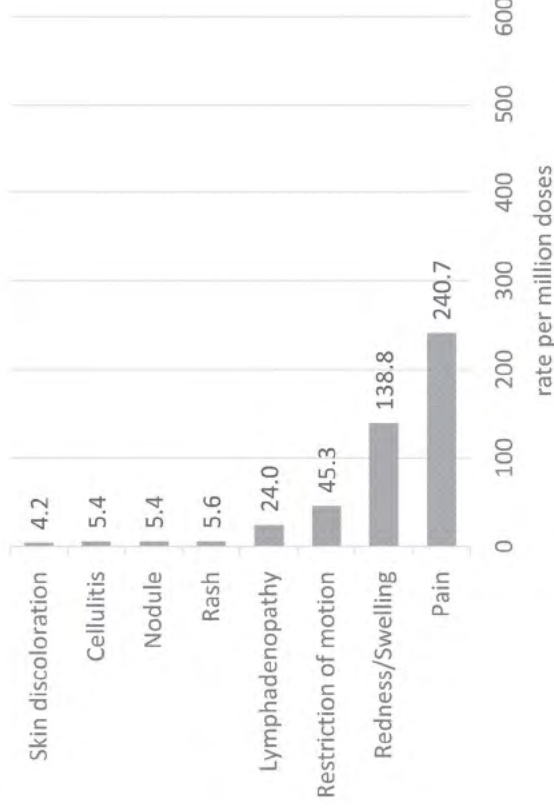
Local reactions

Local reactions (at injection site) reported following vaccination, rate per million doses- first dose



Rate per million vaccine doses out of 5,244,481 vaccine 1st dose recipients

Local reactions (at injection site) reported following vaccination, rate per million doses- second dose



Rate per million vaccine doses out of 4,785,534 vaccine 2nd dose recipients

Updated 31/03/2021

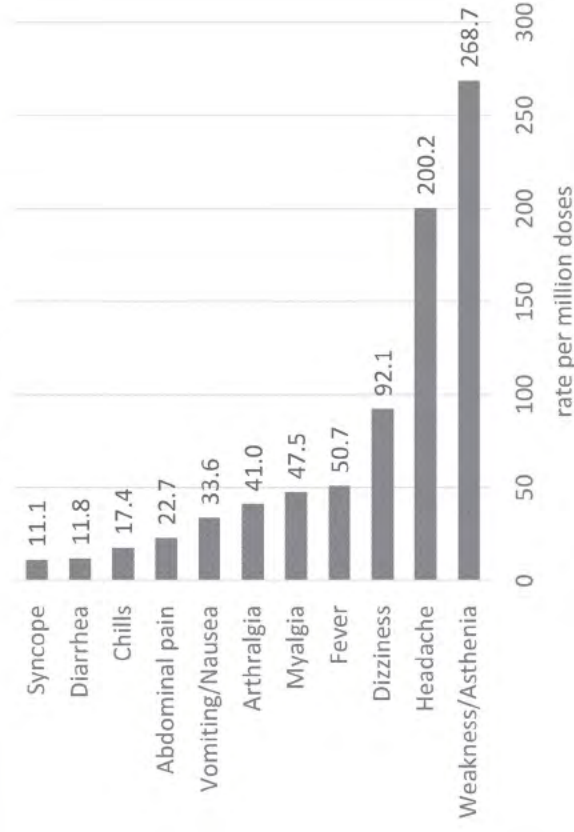
Data is based on adverse events reported to the MoH | Some individuals reported more than one adverse event

PSICOID_00009406

Systemic reactions

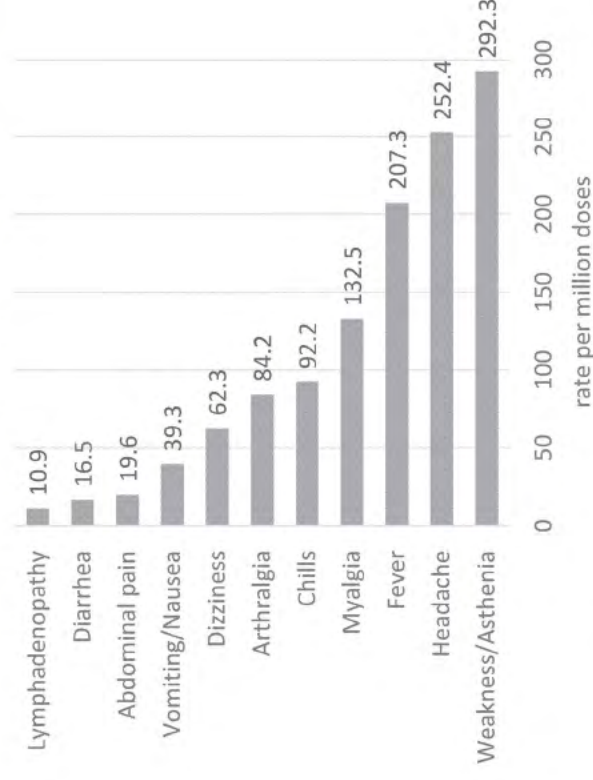


General reactions reported following immunization, rate per million doses- first dose



Rate per million vaccine doses out of 5,244,481 vaccine 1st dose recipients

General reactions reported following immunization, rate per million doses- second dose



Rate per million vaccine doses out of 4,785,534 vaccine 2nd dose recipients

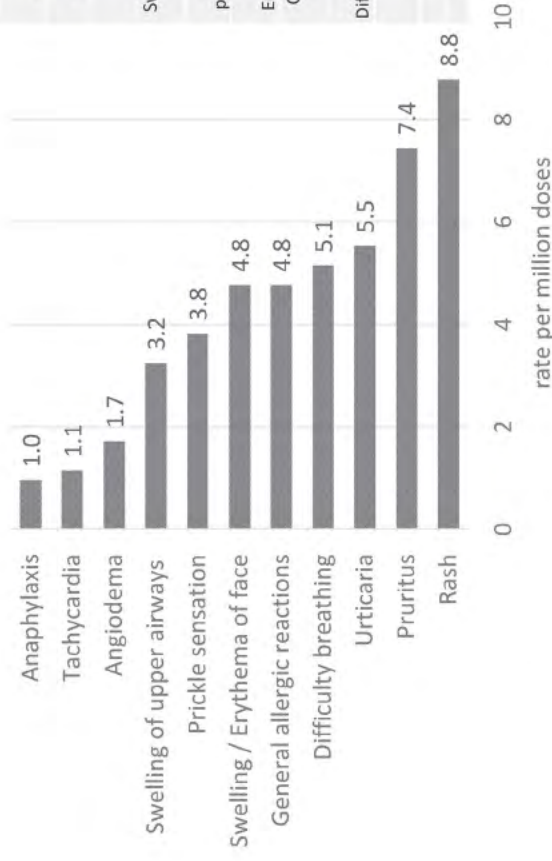
Updated 31/03/2021

Data is based on adverse events reported to the MoH | Some individuals reported more than one adverse event

PSICOVID_00009407

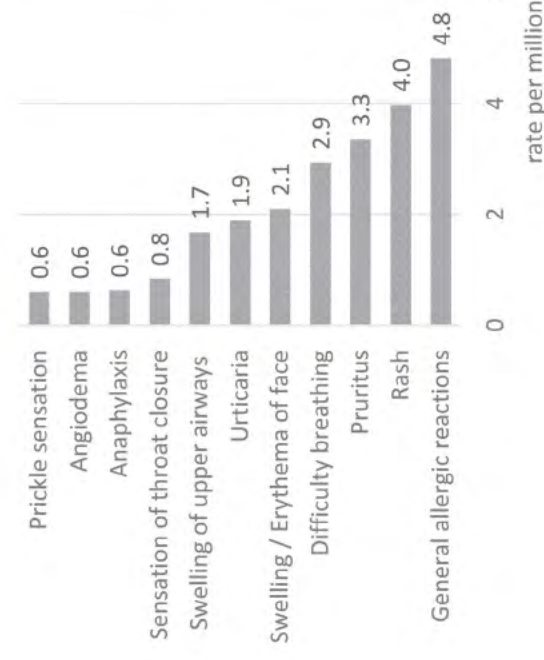
Allergic reactions

Allergic reactions reported following vaccination, rate per million vaccine doses- first dose



Rate per million vaccine doses out of 5,244,481 vaccine 1st dose recipients

Allergic reactions reported following vaccination, rate per million vaccine doses- second dose



Rate per million vaccine doses out of 4,785,534 vaccine 2nd dose recipients

Number of allergic reactions reported 2nd dose	
prickle sensation	3
Angiodema	3
Anaphylaxis	3
Sensation of throat closure	4
Swelling of upper airways	8
Urticaria	9
Swelling / Erythema of face	10
Difficulty breathing	14
Pruritus	16
Rash	19
General allergic reactions	23

Updated 31/03/2021

10

Data is based on adverse events reported to the MoH | Some individuals reported more than one adverse event

PSICOID_00009408

Neurologic reactions

Number of neurologic reactions reported

	Numbness/ Parasthesia	Facial nerve palsy	Other neurologic reactions	Metal or bitter taste in mouth	Seizure (focal or generalized)	Loss of consciousness	Transient ischemic attack
1 st dose	350	64	48	18	18	12	7
2 nd dose	178	26	25	13	8	7	2

Rate of neurological reactions reported following vaccination

Rate per million doses vaccine



Updated 31/03/2021

Data is based on adverse events reported to the MoH | Some individuals reported more than one adverse event

PSICOVID_00009409

Neurologic reactions

	Bell's palsy (1 case pregnant)		Blurred vision		Sudden sensorineural hearing loss		Vertigo		Oculomotor nerve palsy		Trigeminal neuralgia		Seizures		Transient Ischemic Attack		Guillain Barré syndrome (1 case exacerbation)		Multiple sclerosis (1 case exacerbation, 1 new case)		Brachial plexitis	
	1st dose	2nd dose	1st dose	2nd dose	1st dose	2nd dose	1st dose	2nd dose	1st dose	2nd dose	1st dose	2nd dose	1st dose	2nd dose	1st dose	2nd dose	1st dose	2nd dose	1st dose	2nd dose	1st dose	2nd dose
Age group	<20	1	1										2	1							1st dose	2nd dose
	20-29	3	2	1	1						1		2	1	1		1					
	30-39	7	2	3	1	1							2	1								
	40-49	13	5	2	2	2	1						1	5	1				1			
	50-59	11	10	6	1	2	1						2				1					
	60-69	16	4	2	1	1	1	1	1	1			1		1	1	1				1st dose	2nd dose
	70-79	9	2		1	1							4		1	1			1			
	80-89	4			1	2	1						4		3							
	>90														1							
	Total	64	26	13	5	7	7	3	2	3	1	1	18	8	7	2	4	1	2		1	
Follow-up second dose	38	Not relevant	10	Not relevant	5	Not relevant	0	Not relevant	1	Not relevant	1	Not relevant	12	Not relevant	6	Not relevant	1	Not relevant	2	Not relevant	1	Not relevant
Expected number of cases in population age 16 and older, for same time period of vaccination project and same population group	168	128	51	39	180	135	41	30	341	17	12	41	1372	1018	1258	920	139	110	334	260	13	9

The observed numbers are compared to the morbidity data in hospitalized patients from 2017-2019 which includes morbidity data reported among all individuals 16 years and older from the corresponding periods – i.e morbidity cases following the first and second dose is compared to morbidity cases in hospitalized patients from December - March and January - March respectively.
NOTE: In addition to the data presented in the table, the MoH monitors other reactions for which expected numbers cannot be presented.

Updated 31/03/2021

Data is based on adverse events reported to the MoH | Some individuals reported more than one adverse event

PSICOVID_00009410

Other adverse events of interest



Other AEs of interest following vaccination (rate per million vaccine doses) compared to expected rates in the general population according to morbidity data from the corresponding periods of years 2017-2019

Other adverse events of interest	Medical diagnosis	AE rates following first dose (Dec-Mar)	Expected rates (hospitalization data Dec-Mar 2017-2019)	AE rates following second dose (Jan-Mar)	Expected rates (hospitalization data Jan-Mar 2017-2019)
Hematological	Thrombocytopenia	0.6	26.9	0.4	21.0
	Purpura	0.2	21.2	Not reported	15.2
	Sepsis	0.2	71.1	Not reported	53.5
Infections	Herpes zoster	3.4	44.2	3.6	33.4
	Herpes simplex	1.3	15.2	1.3	10.5
	Necrotizing Fasciitis	0.2	6.5	Not reported	4.8
Neurological	Transient Ischemic Attack	1.3	201.8	0.4	147.6
	Encephalitis	0.2	1.4	Not reported	1.1
	Diplopia (double vision)	0.4	9.3	0.6	6.8
	Acute hearing loss	1.3	28.9	1.5	21.6
	Shoulder weakness and severe pain	0.2	2.1	Not reported	1.5
	Facial weakness and severe pain	0.2	6.6	Not reported	5.0
	Blurred vision	2.5	8.2	1.0	6.3
	Vertigo	0.4	59.7	0.6	43.3
	Guillain barre syndrome	0.8	22.3	0.2	17.7

Note: Despite normalization to the number of vaccinees, observed and expected rates cannot be directly compared, because the observed cases are counted differently than the expected ones. The observed cases count morbidity within a time window of a defined event (vaccine administration). The expected cases are calculated by the cumulative incidence over several calendar months. However, the expected cases do give a general order of magnitude for comparison of morbidity following vaccine administration.

The observed rates are compared to the morbidity data in hospitalized patients from 2017-2019 which includes morbidity data reported among all individuals 16 years and older from the corresponding periods – i.e morbidity rates following the first and second dose is compared to morbidity rates in hospitalized patients from December - March and January - March respectively.
NOTE: In addition to the data presented in the table, the MoH monitors other reactions for which expected rates cannot be presented.

Data is based on adverse events reported to the MoH

Other adverse events of interest



Other AEs of interest following vaccination (rate per million vaccine doses) compared to expected rates in the general population according to morbidity data from the corresponding periods of years 2017-2019

Other adverse events of interest	Medical diagnosis	AE rates following first dose (Dec-Mar)	Expected rates (hospitalization data Dec-Mar 2017-2019)	AE rates following second dose (Jan-Mar)	Expected rates (hospitalization data Jan-Mar 2017-2019)
Cardiovascular	Myocardial infarction	0.6	746.1	0.2	554.1
	Heart failure	0.4	859.2	Not reported	648.6
	Subarachnoid hemorrhage	0.2	19.9	Not reported	14.2
	Vasculitis	Not reported	7.3	0.2	4.5
	Pericarditis	1.0	48.7	2.1	36.6
	Myocarditis (including Perimyocarditis)	1.1	21.3	11.7	15.6
	Cardiac tamponade	0.2	3.8	Not reported	2.5
	Venous thrombosis (DVT)	Not reported	65.2	0.6	48.1
	Superficial venous thrombosis	Not reported	3.6	0.2	2.7
	Atrial Fibrillation	0.4	560.4	0.6	414.3
	Stroke	1.0	649.1	0.2	475.6
	Pulmonary embolism	0.2	78.0	0.2	56.4
Ophthalmological Rheumatology	Pericardial effusion	0.4	33.9	0.2	26.8
	Retinopathy	0.2	0.8	Not reported	0.5
	Arthritis	Not reported	252.7	0.2	191.6

Note: Despite normalization to the number of vaccinees, observed and expected rates cannot be directly compared, because the observed cases are counted differently than the expected ones. The observed cases count morbidity within a time window of a defined event (vaccine administration). The expected cases are calculated by the cumulative incidence over several calendar months. However, the expected cases do give a general order of magnitude for comparison of morbidity following vaccine administration.

The observed rates are compared to the morbidity data in hospitalized patients from 2017-2019 which includes morbidity data reported among all individuals 16 years and older from the corresponding periods – i.e morbidity rates following the first and second dose is compared to morbidity rates in hospitalized patients from December - March and January - March respectively.
NOTE: In addition to the data presented in the table, the MoH monitors other reactions for which expected rates cannot be presented.

Data is based on adverse events reported to the MoH

Other adverse events of interest



Other AEs of interest following vaccination (rate per million vaccine doses) compared to expected rates in the general population according to morbidity data from the corresponding periods of years 2017-2019

Other adverse events of interest	Medical diagnosis	AE rates following first dose (Dec-Mar)	Expected rates (hospitalization data Dec-Mar 2017-2019)	AE rates following second dose (Jan-Mar)	Expected rates (hospitalization data Jan-Mar 2017-2019)
Pregnant (rate calculated out of women ages 16-49 whom received the vaccine)	Missed abortion	1.3	1909.4	Not reported	1473.1
	IUFD	1.3	71.6	Not reported	53.8
	CMV	Not reported	3.8	0.7	3.2
Respiratory	Pleuritis	0.2	2.4	Not reported	1.7
	Pulmonary edema	Not reported	259.8	0.2	196.0
	Severe acute respiratory syndrome	Not reported	177.5	0.2	132.9
Organ damage	Acute liver damage	0.2	3.9	Not reported	2.8
	Acute kidney damage	0.2	227.4	Not reported	168.7
	Erythema Multiforme	0.2	3.4	Not reported	2.6
Other	Loss of smell (anosmia)/loss of taste (ageusia)	1.3	1.8	1.0	1.2
	Appendicitis	Not reported	315.9	0.2	235.3
	Acute thyroiditis	Not reported	2.4	0.2	1.9
	Multiple sclerosis (1 relapse and 1 new diagnosis)	0.4	53.6	Not reported	41.8
	Hemorrhagic cystitis	0.2	4.9	Not reported	3.9
	Rhabdomyolysis	Not reported	20.6	0.2	16.0

Note: Despite normalization to the number of vaccinees, observed and expected rates cannot be directly compared, because the observed cases are counted differently than the expected ones. The observed cases count morbidity within a time window of a defined event (vaccine administration). The expected cases are calculated by the cumulative incidence over several calendar months. However, the expected cases do give a general order of magnitude for comparison of morbidity following vaccine administration.

The observed rates are compared to the morbidity data in hospitalized patients from 2017-2019 which includes morbidity data reported among all individuals 16 years and older from the corresponding periods – i.e morbidity rates following the first and second dose is compared to morbidity rates in hospitalized patients from December - March and January - March respectively.
NOTE: In addition to the data presented in the table, the MoH monitors other reactions for which expected rates cannot be presented.

Data is based on adverse events reported to the MoH

Myocarditis following vaccination



To date, 62 cases of myocarditis following vaccination have been reported

Myocarditis after first dose (N=6)

- 4 males, 2 females
- 1 case myocarditis, 5 cases of Perimyocarditis
- 4 events occurred within 10 days of receiving the vaccine, 1 event occurred within 2 weeks and 1 event occurred within 3 weeks following vaccination.
- 3 cases with comorbidities (HTN, dyslipidemia)
- All cases were discharged from the hospital and are under observation in the community
- 2 cases received a second dose with no adverse reactions reported

Myocarditis after second dose (N=56)

- 50 males and 6 females
- 37 cases of Myocarditis, 19 cases of Perimyocarditis
- 23 events occurred within 10 days of receiving the vaccine, 2 events occurred within 2 weeks, 1 events occurred within 3 weeks, 2 events occurred within 4 weeks following vaccination.
- 28 cases with comorbidities (HTN, smoking, asthma, dyslipidemia, DM, hypercholesterolemia)
- 53 cases were discharged from the hospital and are under observation at community level. 1 case is under investigation, 2 cases died (1 case fulminant myocarditis, 1 case is still under investigation)
- None of the cases reported adverse reactions after receipt of the first dose

Pericarditis following vaccination



To date, 15 cases of Pericarditis following vaccination have been reported

Pericarditis after first dose (N=5)

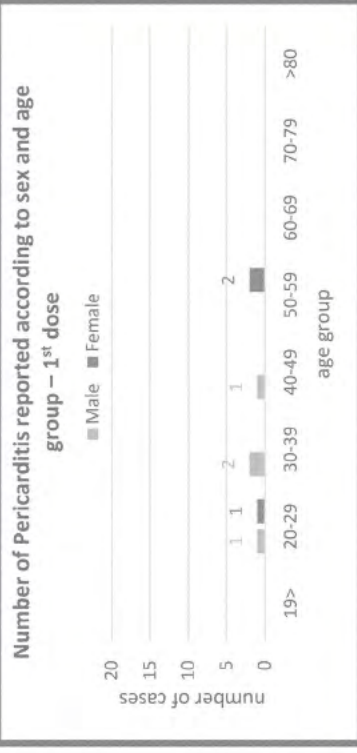
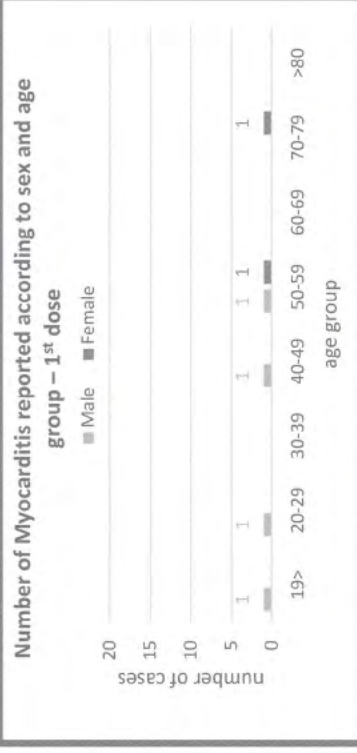
- 3 males, 2 females
- All events occurred within 4 days of receiving the vaccine.
- 2 cases with comorbidities (history of Pericarditis, heart valve)
- All cases were discharged from the hospital and are under observation in the community
- 3 cases received a second dose with no adverse reactions reported

Pericarditis after second dose (N=10)

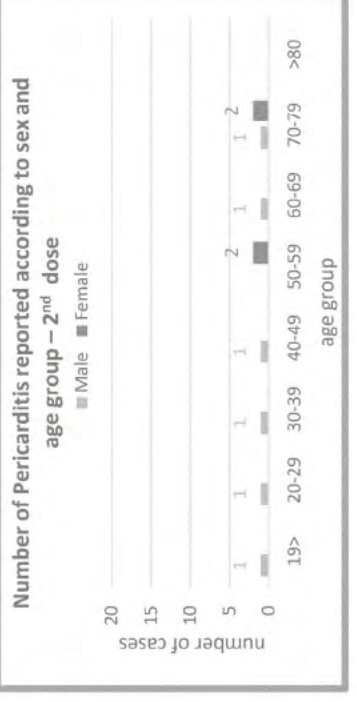
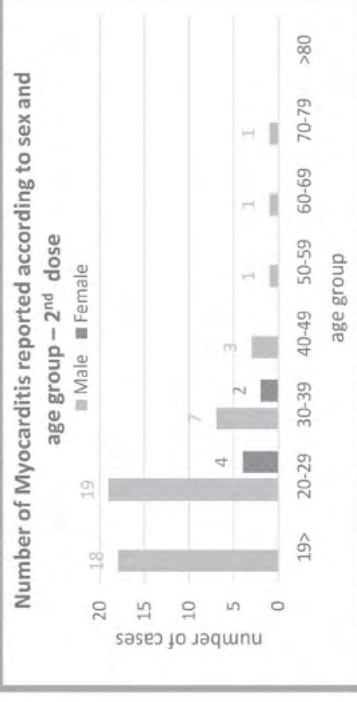
- 6 males and 4 females
- 8 events occurred within 7 days of receiving the vaccine, 1 events occurred within 3 weeks, 1 events occurred within 5 weeks following vaccination.
- 8 cases with comorbidities (HTN, obesity, hypercholesterolemia, dyslipidemia, renal disease)
- 9 cases were discharged from the hospital and are under observation at community level. 1 is under investigation.
- None of the cases reported adverse reactions after receipt of the first dose

Myocarditis / Pericarditis following vaccination

Myocarditis / Perimyocarditis

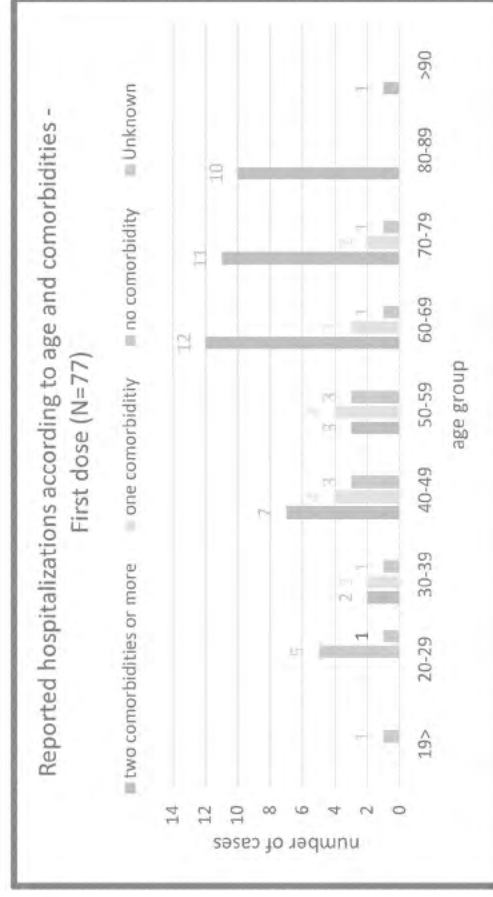


Pericarditis

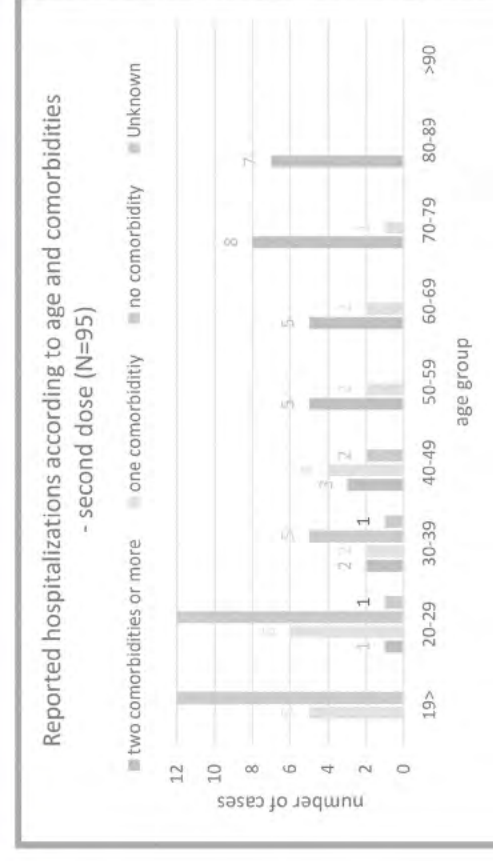


Data is based on adverse events reported to the MoH

Hospitalizations reported following vaccination



Among 77 hospitalizations following receiving the first dose, 34 cases were related to neurological diseases out of which 30 cases had comorbidities, 25 hospitalizations were related to underlying cardiovascular diseases out of which 18 had comorbidities, 6 hospitalizations were related to allergic reactions, 2 infectious and 7 hospitalizations were related to other underlying diseases. 3 hospitalizations were related to pregnancy complications.



Among 95 hospitalization following receiving the second dose, 75 cases were related to cardiovascular diseases and of those 38 were with significant underlying diseases. 10 hospitalizations were related to underlying neurological diseases and of those 8 were with significant underlying diseases and 4 hospitalizations were related to underlying respiratory diseases, and 8 hospitalizations were related to other underlying diseases.

Reports among vaccine recipients
1st dose: 5,244,481 2nd dose: 4,785,534

Data is based on adverse events reported to the MoH

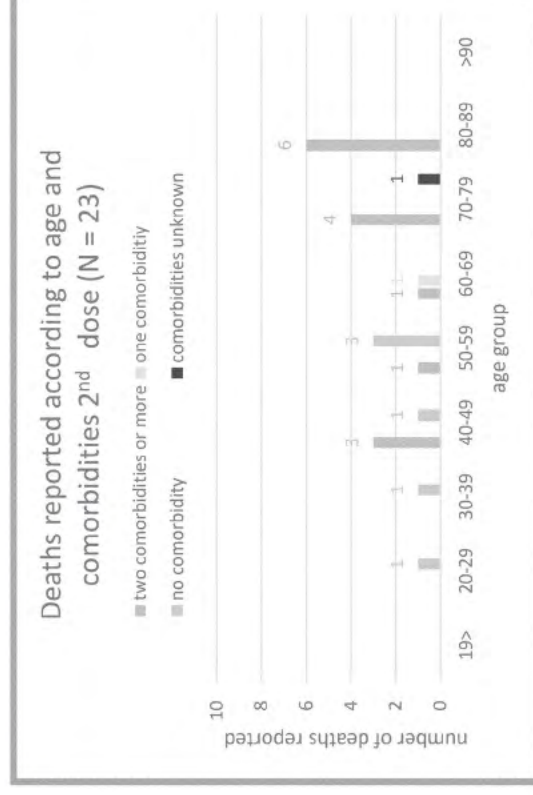
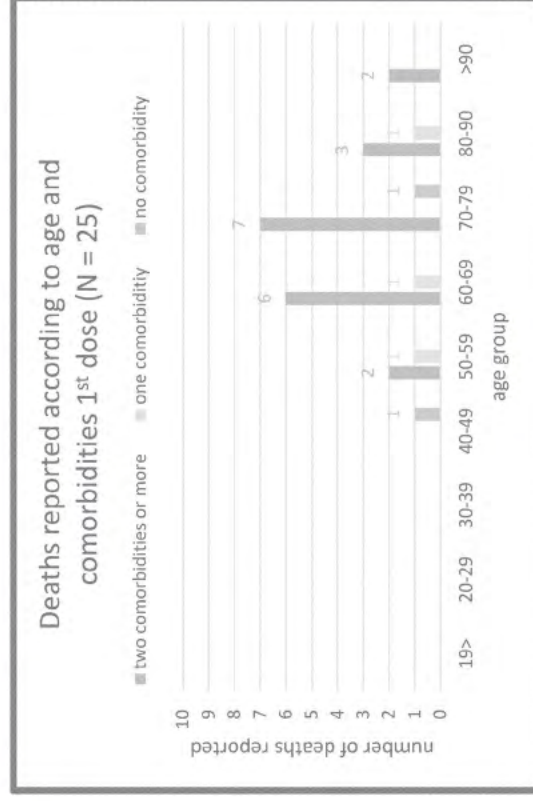
Deaths reported following vaccination

- 48 persons were reported to die in proximity to vaccination (up to 30 days following vaccination).
- 42 deaths occurred within 10 days following vaccination
- Out of 48 reported cases, 14 are <60 y old:
 - 2 were diagnosed in ER with myocarditis (1 case fulminant myocarditis, 1 case still under investigation)
 - 2 PM in cases of sudden death excluded myocarditis in one and showed blocked LAD.
 - 10 cases are under investigation: relatively young persons with sudden death.

Reports among vaccine recipients
1st dose: 5,244,481 2nd dose: 4,785,534

Data is based on adverse events reported to the MoH

Deaths reported following vaccination



Reports among vaccine recipients
1st dose: 5,244,481 2nd dose: 4,785,534

Data is based on adverse events reported to the MoH

Deaths reported following vaccination observed and expected



Age group	Mortality cases reported following 1 st dose	Mortality cases expected all causes (Dec-Mar)	Sudden death reported following 1 st dose	Sudden death expected (Dec-Mar)	Mortality cases reported following 2 nd dose	Mortality cases expected all causes (Jan-Mar)	Sudden death reported following 2 nd dose	Sudden death expected (Jan-Mar)	Total cases reported
Male									
20-29	0	74	0	0	0	48	0	0	0
30-39	0	108	0	0	1	72	1	0	1
40-49	0	235	0	1	4	165	4	1	4
50-59	2	564	2	5	3	392	2	4	5
60-69	4	1220	1	5	2	865	0	3	6
70-79	6	2353	0	6	1	1727	0	3	7
80<	3	4349	0	9	3	3153	0	6	6
Female									
20-29	0	30	0	0	1	20	0	0	1
30-39	0	59	0	0	0	41	0	0	0
40-49	1	139	1	0	0	95	0	0	1
50-59	1	336	1	1	1	235	1	1	2
60-69	3	773	0	1	0	561	0	1	3
70-79	2	1714	1	4	4	1252	0	3	6
80<	3	5398	0	13	3	3889	0	10	6
Total	25	17,352	6	45	23	12,515	8	32	48

The overall mean of expected total deaths in the population of Israel 2015-2018, for December-March for the first dose, and January-March for the second dose, normalized for the number of vaccinated persons.

Data is based on adverse events reported to the MoH

Note: Despite normalization to the number of vaccinees, observed and expected rates cannot be directly compared, because the observed cases are counted differently than the expected ones. The observed cases count deaths within a time window of a defined event (vaccine administration). The expected cases are calculated by the cumulative incidence over several calendar months. However, the expected cases do give a general order of magnitude for comparison of deaths following vaccine administration.

No specific signal associated with all causes of death and specifically sudden death

COVID-19 vaccination Israel "BACK TO LIFE"

Message

From: Markowitz, Lauri (CDC/DDID/NCIRD/DVD) [REDACTED]
Sent: 5/21/2021 5:50:44 PM
To: Anderson, Steven [REDACTED] Beresnev, Tatiana H (NIH) [REDACTED] Broder, Karen R (CDC) [REDACTED] Calvert, Geoffrey M (CDC) [REDACTED] Clark, Matthew (IHS) [REDACTED] Clark, Thomas A (CDC) [REDACTED] Cohn, Amanda C (CDC) [REDACTED] Collins, Limone [REDACTED] Cunningham, Fran [REDACTED] Daley, Matt [REDACTED] DeStefano, Frank (CDC) [REDACTED] Edwards, Kathy [REDACTED] Farizo, Karen [REDACTED] Forshee, Richard [REDACTED] Gee, Julianne M (CDC) [REDACTED] Hause, Anne M (CDC) [REDACTED] Helfand, Rita (CDC) [REDACTED] Hicks, Lauri (CDC) [REDACTED] Hopkins, Bob [REDACTED] Jackson, Lisa [REDACTED] Jennifer Nelson [REDACTED] Kelman, Jeffrey A (CMS) [REDACTED] Lee, Grace [REDACTED] Lu, Yun (CBER) [REDACTED] MacNeil, Jessica R (CDC) [REDACTED] Markowitz, Lauri (CDC) [REDACTED] Marquez, Paige L (CDC) [REDACTED] Mbaeyi, Sarah A (CDC) [REDACTED] McNally, Veronica [REDACTED] Mcneil, Michael M (CDC) [REDACTED] Myers, Tanya R (CDC) [REDACTED] Nair, Narayan [REDACTED] Oliver, Sara E (CDC) [REDACTED] Patricia Whitley-Williams [REDACTED] Riley, Laura [REDACTED] Rubin, Mary (HRSA) [REDACTED] Schechter, Robert [REDACTED] Schindelar, Jessica A (CDC) [REDACTED] Shanley, Edwin (CDC) [REDACTED] Shay, David K (CDC) [REDACTED] Shimabukuro, Tom (CDC) [REDACTED] Sotir, Mark J (CDC) [REDACTED] Steinberg, Judith L (OS) [REDACTED] Su, John (CDC) [REDACTED] Talbot, Keipp [REDACTED] Weintraub, Eric S (CDC) [REDACTED] Wharton, Melinda (CDC) [REDACTED] Wong, Hui-Lee [REDACTED] Woo, Jared M (CDC) [REDACTED] Young, Mardia A (CDC) [REDACTED]
Subject: [EXTERNAL] VaST - Draft minutes and report from May 17 (CONFIDENTIAL)
Attachments: 2021-05-17 - VaST minutes_draft.docx; 2021-05-17 - VaST Report Data Table_draft.docx

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear VaST members and attendees,

- Attached are the draft confidential minutes and summary report from the call this week. Please let us know if there are any corrections or comments.
- A VaST report from Monday, May 17 is posted on the CDC/ACIP website here:
[VaST Technical Reports](#)
[May 17, 2021](#)
- The next VaST call is May 24, 1:30 – 3:00 pm EDT. The first half will be a maternal immunization focused session, and the second half will be on myocarditis.

Lauri Markowitz and Melinda Wharton

*Lauri Markowitz, MD
VaST Co-Lead
CDC COVID-19 Response, Vaccine Task Force
Division of Viral Diseases
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention*

Combined Systems Safety Monitoring Report - DRAFT

May 17, 2021

Confidential

The VaST session on May 17, 2021 included several presentations that focused on myocarditis. Specifically, VaST reviewed case summaries of myocarditis following mRNA vaccines reported to the Department of Defense (DoD), data from the Vaccine Adverse Event Reporting System (VAERS) and Vaccine Safety Datalink (VSD), along with brief updates from the Veteran's Administration (VA) and the Clinical Immunization Safety Assessment (CISA) groups about their plans for future investigation.

VaST concluded that there were similar patterns in the cases presented: they seem to occur predominantly in young persons, males > females, dose 2 > dose 1, and within 4 days post vaccination. Most cases appear to be mild and follow-up of cases is ongoing.

Within CDC safety monitoring systems, rates of myocarditis reports in the window following COVID-19 vaccination have not differed from expected baseline rates; however, VaST members felt that information about reports of myocarditis should be communicated to providers.

VaST comments:

- Further information should be collected through medical record review about potential myocarditis cases that were reported into VAERS.
- Information about this potential adverse event should be provided to clinicians to enhance early recognition and appropriate management of persons who develop myocarditis symptoms following vaccination.
- Collaboration between infectious diseases, cardiology, and rheumatology specialists is needed to provide guidance on diagnosis, treatment, and management of myocarditis.
- VaST would like to continue to monitor myocarditis data from VAERS, VSD, VA and DoD. Age-stratified analyses would be useful, with a focus on those in age groups < 30 years.
- The lack of a signal in some safety systems could be due to the limited number of second vaccine doses administered in the younger age group to date.
- In the context of these reports, some members expressed concern about the updated clinical guidance for simultaneous vaccination of COVID-19 vaccines with other adolescent vaccines.
- Additional information about the risk of myocarditis following COVID-19 infection, as well as background rates of myocarditis, is needed to better understand benefit-risk balance.

Table 1. COVID-19 vaccine monitoring systems reviewed by the VaST – Pfizer BioNTech (recommended for use in persons age ≥ 16 years)

Red indicates updated or new data this week

Vaccine Safety Program	Outcomes Monitored	Population Monitored	Population captured	Analyses	Selected Results	Assessment/action
Passive Surveillance						
Vaccine Adverse Event Reporting System (VAERS) (Data through 5/14/21)	All health events, adverse events of special interest ^a	US population	146.3 million total doses administered	Descriptive and empirical Bayesian data mining	0 confirmed TTS reports to VAERS 3.1–5.6 myopericarditis reports per 1 million (age-stratified) doses administered across all vaccines • Background rate: 4.4 per 100,000 person years • 7 reports of patients aged ≤18	Anaphylaxis associated with vaccination, first detected by reports from UK and early reporting in the US; assessed by follow-up with providers, chart review, CISA consultations; clinical guidance changed (initially in December 2020 and last updated March 5, 2021) Further work being done to define potential myocarditis risk No concerns raised
VA ADERS (Data through 4/11/2021)	All health events	VA employees and Veteran patients	1,071,630 first doses administered; 826,866 second doses administered	Descriptive	No signals in the analysis for combined mRNA vaccines	
DoD VAERS (Population data through 3/19/2021; Results data through 4/3/2021)	All health events, adverse events of special interest	Active duty and beneficiaries	976,479 vaccines administered	Descriptive	22 cases of myocarditis following mRNA vaccines (16 Moderna, 6 Pfizer) • Background rate: 2-23 cases 19 cases of myocarditis following dose 2 of mRNA vaccines • Background rate: 1-9 cases	Ongoing discussion regarding communication of myocarditis risk in younger males
Indian Health Services (IHS) VAERS (Data through 4/26/2021)	All health events, adverse events of special interest ^a	Persons who identify as American Indian/Alaska Native	425k vaccines administered	Descriptive	84 total AE reports • 48 medically attended health impact events • 12 suspected AESIs	No concerns raised

Active Surveillance						
V-safe (Data through 3/13/2021)		Vaccinees who enroll	2,267,127 persons enrolled; 26,091 pregnancies ^c	Descriptive	623 reports overall (all submitted to VAERS) • 57 serious reports • Solicited reactions higher after dose 2 than dose 1 Pregnancy and neonatal outcomes of interest within background rates	No concerns raised
V-safe Pregnancy Registry (Data through 4/26/2021)		Vaccinees who enroll	2,376 enrolled	Descriptive		No concerns raised
Department of Veterans Affairs (VA) Active Surveillance System (Data through 5/13/21)	Pre-specified health outcomes ^a	Veteran Patients	1,153,987 first doses administered; 966,957 second doses administered	Descriptive; historical comparator analysis	Possible early signal for myopericarditis in the historical comparator analysis • Relative risk: 2.0	Only signal for anaphylaxis. Further work being done to investigate myopericarditis
Vaccine Safety Datalink (VSD) (Data through 5/8/21)	Pre-specified health outcomes ^a	Patients enrolled in participating health care organization	3.7 million total doses	Descriptive; Vaccinated and unvaccinated concurrent comparison, sequential analyses	No confirmed cases of incident CVST with thrombocytopenia in the analyses for combined mRNA vaccines No signal for myopericarditis using a 21-day risk interval in vaccinated comparator analysis	No concerns raised
Vaccine Safety Datalink (VSD) Mortality Study (Vaccinated through 2/27 and death data through 3/20/21)	Deaths	VSD sites enrolled in the mortality study; vaccinated before 2/27 and number of deaths before 3/20	219,570 first doses administered; 105,919 second doses administered	Descriptive; Vaccinated and unvaccinated concurrent comparison, sequential analyses	0.8 dose 1 mortality rate per 100 person-years 0.7 dose 2 mortality rate per 100 person-years 1.0 comparator mortality rate per 100 person-years	No concerns raised
Defense Medical Surveillance System (DMSS)^b	Pre-specified health outcomes ^a					

FDA - Centers for Medicare and Medicaid Services (CMS)^b (Data through 4/3/2021)	Pre-specified health outcomes ^a	CMS population 65 and above		Historical comparator analysis	Relative risk of 1.10 for AMI, after seasonality adjustment. The RR was not statistically significant. Relative risk of 1.31 for PE, after seasonality adjustment. The RR was statistically significant. Relative risk of 1.31 for DIC, after seasonality adjustment. The RR was not statistically significant.	Further investigation including signal characterization and evaluation in other databases is needed in order to properly assess the signals.
BEST Initiative^b	Pre-specified health outcomes ^a					
NPTC Vaccine Sentinel Survey (Data through 4/26/21)	Pre-specified health outcomes	Persons who identify as American Indian/Alaska Native	425K vaccines administered	Descriptive	256 total AE reports • 67 medically attended health impact events • 23 suspected AESIs	No concerns raised
Vaccine Trials (Manufacturer)					See GRADE tables https://www.cdc.gov/vaccines/acip/racs/grade/covid-19-pfizer-biontech-vaccine.html	

^aSee Table 4 for the complete list of health outcomes

^bData are currently being processed and will be reported when received

^cAt the time of vaccination

Table 2. COVID-19 vaccine monitoring systems reviewed by the VaST – Moderna (recommended for use in persons age ≥ 18 years)

Red indicates new results this week

Vaccine Safety Program	Outcomes Monitored	Population Monitored	Population captured	Analyses	Selected Results	Assessment/action
Passive Surveillance						
Vaccine Adverse Event Reporting System (VAERS) (Data through 5/14/21)	All health events, adverse events of special interest ^a	US population	116.8 million total doses administered	Descriptive and empirical Bayesian data mining	0 confirmed TTS reports to VAERS 3.1–5.6 myopericarditis reports per 1 million doses administered across all vaccines • Background rate: 4.4 per 100,000 person years • 2 reports of patients aged 18 or under	Anaphylaxis associated with vaccination, first detected by early reporting in the US; assessed by follow-up with providers, chart review, CISA consultations; clinical guidance changed (initially in December 2020 and last updated March 5, 2021) Further work being done to define potential myocarditis risk
VA ADERS (Data through 4/11/2021)	All health events	VA employees and Veteran patients	1,262,482 first doses administered; 977,202 second doses administered	Descriptive	No signals in the analysis for combined mRNA vaccines	No concerns raised
DoD VAERS (Population data through 3/19/2021; Results data through 4/3/2021)	All health events, adverse events of special interest	Active duty and beneficiaries	852,548 vaccines administered	Descriptive	22 cases of myocarditis following mRNA vaccines • Background rate: 2-23 cases 19 cases of myocarditis following dose 2 of mRNA vaccines • Background rate: 1-9 cases	Ongoing discussion regarding communication of myocarditis risk in younger males
Indian Health Services (IHS) VAERS (Data through 4/26/2021)	All health events, adverse events of special interest ^a	Persons who identify as American Indian/Alaska Native	700k vaccines administered	Descriptive	71 total AE reports • 43 medically attended health impact events • 15 suspected AESIs	No concerns raised

Active Surveillance						
V-safe (Data through 3/13/2021)		Vaccinees who enroll	2,627,416 persons enrolled; 23,064 pregnancies ^c	Descriptive	126 reports overall (all submitted to VAERS) • 27 serious reports • Solicited reactions higher after dose 2 than dose 1	No concerns raised
V-safe Pregnancy Registry (Data through 4/26/2021)		Vaccinees who enroll	2,073 enrolled	Descriptive	Pregnancy and neonatal outcomes of interest within background rates	No concerns raised
Department of Veterans Affairs (VA) Active Surveillance System (Data through 5/13/2021)	Pre-specified health outcomes ^a	Veteran Patients	1,344,556 first doses administered; 1,151,578 second doses administered	Descriptive; historical comparator analysis	No signal for myopericarditis in the analysis	Only signal for anaphylaxis, as identified earlier in other post-authorization safety monitoring No concerns raised
Vaccine Safety Datalink (VSD) (Data through 5/8/21)	Pre-specified health outcomes ^a	Patients enrolled in participating health care organization	3.2 million total doses	Descriptive; Vaccinated and unvaccinated concurrent comparison, sequential analyses	No confirmed cases of incident CVST with thrombocytopenia in the analyses for combined mRNA vaccines No signal for myopericarditis using a 21-day risk interval in the vaccinated comparator analysis	No concerns raised
Vaccine Safety Datalink (VSD) Mortality Study (Vaccinated through 2/27 and death data through 3/20/21)	Deaths	VSD sites enrolled in the mortality study; vaccinated before 2/27 and number of deaths before 3/20	220,799 first doses administered; 86,650 second doses administered	Descriptive; Vaccinated and unvaccinated concurrent comparison, sequential analyses	0.6 dose 1 mortality rate per 100 person-years 0.7 dose 2 mortality rate per 100 person-years 1.0 comparator mortality rate per 100 person-years	No concerns raised
Defense Medical Surveillance System (DMSS)^b	Pre-specified health outcomes ^a					

FDA - Centers for Medicare and Medicaid Services (CMS)^b (Data through 4/3/2021) BEST initiative^b	Pre-specified health outcomes ^a	CMS population 65 and above		Historical comparator analysis	No signals in the analysis	No concerns raised
NPTC Vaccine Sentinel Survey (Data through 4/26/21)	Pre-specified health outcomes ^a	Persons who identify as American Indian/Alaska Native	700k vaccines administered	Descriptive	214 total AE reports • 39 medically attended health impact events • 21 suspected AESIs	No concerns raised
Vaccine Trials (Manufacturer)					See GRADE tables https://www.cdc.gov/vaccines/acip/records/grade/covid-19-pfizer-biontech-vaccine.html	

^aSee Table 4 for the complete list of health outcomes

^bData are currently being processed and will be reported when received

^cat the time of vaccination

Table 3. COVID-19 vaccine monitoring systems reviewed by the VaST – Janssen/Johnson & Johnson (recommended for use in persons age ≥ 18 years)

Red indicates new results this week

Vaccine Safety Program	Outcomes Monitored	Population Monitored	Population captured	Analyses	Selected Results	Assessment/action
Passive Surveillance						
Vaccine Adverse Event Reporting System (VAERS) (TTS data through 5/13/21; Myocarditis data through 5/14/21)	All health events, adverse events of special interest ^a	US population	9.6 million total doses administered	Descriptive and empirical Bayesian data mining	30 confirmed TTS reports to VAERS 12.0 reporting rate per million for females aged 30-39 years 9.1 reporting rates per million for females aged 40-49 years 3.1–5.6 myocarditis reports per 1 million doses administered across all vaccines - Background rate: 4.4 per 100,000 person years	Warning and other information provided in updated EUA and MMWR last week, and reflected in clinical guidance
VA ADERS (Data through 4/11/2021)	All health events	VA employees and Veteran patients	109,483 vaccines administered	Descriptive	No signals were detected	No concerns raised
DoD VAERS (Data through 3/19/2021)	All health events, adverse events of special interest	Active duty and beneficiaries	28,640 vaccines administered	Descriptive	4 total AE reports 0 serious AE reports 0 death reports	No concerns raised
Indian Health Services (IHS) VAERS (Data through 4/26/2021)	All health events, adverse events of special interest ^a	Persons who identify as American Indian/Alaska Native	20k vaccines administered	Descriptive	3 total AE reports 2 medically attended health impact events 0 suspected AESIs	No concerns raised
Active Surveillance						
V-safe (Data through 4/26/2021)		Vaccinees who enroll	332,084 persons enrolled	Descriptive	28.3% of participants reported being unable to do normal daily activities	No concerns raised

				3,118 pregnancies		1.4% of participants reported requiring a medical visit	
V-safe Pregnancy Registry (Data through 4/26/2021)		Vaccinees who enroll	262 enrolled	Descriptive	Pregnancy and neonatal outcomes of interest within background rates	No concerns raised	
Department of Veterans Affairs (VA) Active Surveillance System (Data through 4/25/2021)	Pre-specified health outcomes ^a	Veteran Patients	117,162 vaccines administered	Descriptive; historical comparator analysis	No signals detected	No concerns raised	
Vaccine Safety Datalink (VSD) (Data through 5/8/21)	Pre-specified health outcomes ^a	Patients enrolled in participating health care organization	171,111 doses administered	Descriptive; Sequential analysis will be added when available	35 potential cases of VTE/PE following vaccination. • 3 cases with thrombocytopenia at time of VTE/PE (full chart review by hematologist pending)	No concerns raised, but small number of doses administered	
Vaccine Safety Datalink (VSD) Mortality Study (Vaccinated through 2/27 and death data through 3/20/21)	Deaths	VSD sites enrolled in the mortality study; vaccinated before 2/27 and number of deaths before 3/20	Data not yet available	Descriptive; Vaccinated and unvaccinated concurrent comparison, sequential analyses	Data not yet available		
Defense Medical Surveillance System (DMSS)^b	Pre-specified health outcomes ^a						
FDA - Centers for Medicare and Medicaid Services (CMS)^b	Pre-specified health outcomes ^a	CMS population 65 and above		Historical comparator analysis	Data not yet available		
BEST initiative^b	Pre-specified health outcomes ^a						

NPTC Vaccine Sentinel Survey (Data through 4/26/21)		Persons who identify as American Indian/Alaska Native	20k vaccines administered	Descriptive	10 total AE reports • 1 medically attended health impact events • 0 suspected AESIs	No concerns raised
Vaccine Trials (Manufacturer)					See GRADE tables [HYPERLINK "https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/28-03-01/03-COVID-Gargano.pdf"]	

^aSee Table 4. for the complete list of health outcomes

^bData are currently being processed and will be reported when received

^cAt the time of vaccination

Table 4. Health systems and pre-specified health outcomes

	VAERS	VSD	VA*	DMESS*	CMS*	BEST*
Acute disseminated encephalomyelitis (ADEM)	X ^{1,2}	X	X			
Acute myocardial infarction	X	X	X		X	X
Anaphylaxis	X	X	X		X	X
Appendicitis	X	X	X		X	X
Acute respiratory distress syndrome (ARDS)		X	X			
Arthritis and arthralgia (not osteoarthritis or traumatic arthritis)	X ¹	X				
Ataxia	X ^{1,2}					
Autoimmune disease	X ¹					
Bell's palsy	X	X	X		X	X
Chronic inflammatory demyelinating polyneuropathy (CIDP)	X ^{1,2}					
COVID-19	X					
Death	X					
Disseminated intravascular coagulation (DIC)	X	X	X		X	X
Encephalitis	X	X	X			
Encephalomyelitis	X ^{1,2}	X	X		X	X
Encephalopathy	X ^{1,2}	X	X			
Guillain-Barré syndrome (GBS)	X	X	X		X	X
Immune thrombocytopenic purpura (ITP)		X	X		X	X
Kawasaki disease	X	X				X
Meningitis	X ^{1,2}	X	X			
Meningoencephalitis	X ^{1,2}	X	X			
Multiple sclerosis (MS)	X ^{1,2}					
Multisystem Inflammatory Syndrome in Adults (MIS-A)	X	X ³	X		X	X
Multisystem Inflammatory Syndrome in Children (MIS-C)	X	X ³				X
Myelitis	X ^{1,2}	X	X			
Myocarditis / pericarditis	X	X	X		X	X
Narcolepsy / cataplexy	X	X	X		X	X ⁴
Non-anaphylactic allergic reactions	X ¹					

Optic neuritis (ON)	X ^{1,2}					
Seizures / convulsions (convulsion is now an LLT under PT seizure)	X	X				X
Stroke	X	X			X	X
Thrombocytopenia	X					
Transverse myelitis (TM)	X	X			X	X
Vaccination during pregnancy/adverse pregnancy outcomes	X					X
Venous thromboembolism (VTE)	X	X				-
Pulmonary embolism	-	X			X	X
Deep vein thrombosis	-	-			X	X

¹Health outcomes are counted, but adverse event reports are not abstracted

²Diagnoses are grouped and reported as "Other clinically serious neurologic AEs" in VAERS

³Health outcomes are counted, and no sequential analysis is conducted

⁴Only includes narcolepsy

*TBD

Message

From: Markowitz, Lauri (CDC/DDID/NCIRD/DVD) [REDACTED]
Sent: 5/28/2021 5:53:14 PM
To: Anderson, Steven [REDACTED] Beresnev, Tatiana H (NIH) [REDACTED] Broder, Karen R (CDC) [REDACTED] Clark, Matthew (IHS) [REDACTED] Clark, Thomas A (CDC) [REDACTED] Cohn, Amanda C (CDC) [REDACTED] Collins, Limone [REDACTED] Cunningham, Fran [REDACTED] Daley, Matt [REDACTED] DeStefano, Frank (CDC) [REDACTED] Edwards, Kathy [REDACTED] Farizo, Karen [REDACTED] Forshee, Richard [REDACTED] Gee, Julianne M (CDC) [REDACTED] Hause, Anne M (CDC) [REDACTED] Helfand, Rita (CDC) [REDACTED] Hicks, Lauri (CDC) [REDACTED] Hopkins, Bob [REDACTED] Jackson, Lisa [REDACTED] Jennifer Nelson [REDACTED] Kelman, Jeffrey A (CMS) [REDACTED] Lee, Grace [REDACTED] Lu, Yun (CBER) [REDACTED] MacNeil, Jessica R (CDC) [REDACTED] Markowitz, Lauri (CDC) [REDACTED] Marquez, Paige L (CDC) [REDACTED] Mbaeyi, Sarah A (CDC) [REDACTED] McNally, Veronica [REDACTED] Mcneil, Michael M (CDC) [REDACTED] Myers, Tanya R (CDC) [REDACTED] Nair, Narayan [REDACTED] Oliver, Sara E (CDC) [REDACTED] Patricia Whitley-Williams [REDACTED] Riley, Laura [REDACTED] Rubin, Mary (HRSA) [REDACTED] Schechter, Robert [REDACTED] Schindelar, Jessica A (CDC) [REDACTED] Shanley, Edwin (CDC) [REDACTED] Shay, David K (CDC) [REDACTED] Shimabukuro, Tom (CDC) [REDACTED] Sotir, Mark J (CDC) [REDACTED] Steinberg, Judith L (OS) [REDACTED] Su, John (CDC) [REDACTED] Talbot, Keipp [REDACTED] Weintraub, Eric S (CDC) [REDACTED] Wharton, Melinda (CDC) [REDACTED] Wong, Hui-Lee [REDACTED] Woo, Jared M (CDC) [REDACTED] Young, Mardia A (CDC) [REDACTED]
Subject: [EXTERNAL] VaST - Draft minutes and report from May 24 (CONFIDENTIAL)
Attachments: 2021-05-24 - VaST Report Data Table_draft.docx; 2021-05-24 - VaST minutes_draft.docx

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear VaST members and call attendees,

- Attached are the draft confidential minutes and summary report from the call this week. Please let us know if there are any corrections or comments.
- There is no call on Monday, May 31. The next VaST call is June 7, 1:30 – 3:00 pm EDT (unless there is need to have one before). Slides with brief updates from VAERS and VSD will be distributed to all next week.
- As noted yesterday in an email, CDC posted information on the web about myocarditis and pericarditis. Links are here:
[Myocarditis and Pericarditis Following mRNA COVID-19 Vaccination | CDC](#)
[Clinical Considerations: Myocarditis after mRNA COVID-19 Vaccines | CDC](#)

Thanks to all and we hope everyone has a good Memorial Day weekend!

Lauri Markowitz and Melinda Wharton

Lauri Markowitz, MD
VaST Co-Lead
CDC COVID-19 Response, Vaccine Task Force
Division of Viral Diseases
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

Combined Systems Safety Monitoring Report - DRAFT

May 24, 2021

Confidential

The VaST session focused on COVID-19 vaccination during pregnancy and on myocarditis. This was the fourth VaST pregnancy focused session. There were presentations from the v-safe pregnancy registry, the Vaccine Adverse Event Reporting System (VAERS) and the Vaccine Safety Datalink (VSD). After the pregnancy focused session, VaST reviewed data on myocarditis, a continuation of the topic discussed on the May 17. Specifically, members again reviewed data from VAERS and VSD, along with a brief update from the Veteran's Administration (VA).

Vaccination during pregnancy

VaST members felt that:

- The current data are reassuring [no safety signals] for COVID-19 vaccination during pregnancy based on data from the v-safe pregnancy registry, VAERS and VSD, with the caveat that data are still limited for early pregnancy.
- The data from VSD on stillbirths, presented for the first time, contribute to the data from v-safe and VAERS, suggesting no safety concerns to date.
- There is great interest in the data on vaccine safety in pregnancy; these data should be presented publicly at the next ACIP meeting.
- VaST is interested to hear from the manufacturers regarding further clinical data they have as well as planned studies in pregnant women.

Myocarditis

- Data from VAERS show that in the window following dose 2 mRNA COVID-19 vaccination, there was a higher number of observed than expected myopericarditis cases in 16–24 year-olds.
- Data from VSD do not show that rates of myopericarditis reports in the window following COVID-19 vaccination differ from expected at this time; however, analyses suggest that these data need to be carefully followed as more persons in younger age groups are vaccinated. VSD found no concerns among the over 20 other adverse events of special interest being monitored.

VaST members felt that:

- Information should be provided to clinicians to enhance early recognition and appropriate management of persons who develop myopericarditis following vaccination.
- Further information should continue to be collected through medical record review of potential cases reported into VAERS and observed in VSD.
- Data from vaccine safety monitoring systems for potential cases of myopericarditis should continue to be obtained as vaccination rates increase in younger age groups.
- VaST would like to see age- and gender-specific rates (following vaccine vs. background vs. following COVID-19 infection).
- Collaboration between cardiology, infectious diseases, and rheumatology specialists is needed to provide clinical guidance about early recognition, differential diagnosis, diagnostic testing, and appropriate management of persons who develop myocarditis.
- Long-term follow up of myopericarditis cases is needed to understand clinical course and natural history following both COVID-19 infection and COVID-19 vaccination.
- If COVID-19 booster doses are recommended in the future, guidance will be needed regarding vaccination of persons with myopericarditis after vaccination.

Table 1. COVID-19 vaccine monitoring systems reviewed by the VaST – Pfizer BioNTech (recommended for use in persons age ≥ 12 years)

Red indicates updated or new data this week

Vaccine Safety Program	Outcomes Monitored	Population Monitored	Population captured	Analyses	Selected Results	Assessment/action
Passive Surveillance						
Vaccine Adverse Event Reporting System (VAERS) (Myocarditis data through 5/20/21; Pregnancy data through 5/14/21)	All health events, adverse events of special interest ^a	US population	154.1 million total doses administered	Descriptive and empirical Bayesian data mining	0 confirmed TTS reports to VAERS 434 automated myocarditis reports across all vaccines. 138 after dose 1; 232 after dose 2; 64 unk. • Median age: 33 years • Median time to onset: 3 days 255 reports after Pfizer-BioNTech vaccine – 61 after dose 1, 152 after dose 2, and 42 unk 562 pregnancy reports submitted to VAERS • 107 serious reports • Median age: 33 years • Median gestational age at time of vaccination: 14 weeks • 1 maternal death	Anaphylaxis associated with vaccination, first detected by reports from UK and early reporting in the US; assessed by follow-up with providers, chart review, CISA consultations; clinical guidance changed (initially in December 2020 and last updated March 5, 2021) Further work being done to define potential myocarditis risk. Observed number of cases higher than expected in 16-24 yr-olds post dose 2 No disproportional reporting for any pregnancy specific or non-pregnancy specific events. No concerns raised. No concerns raised.

VA ADERS (Data through 4/11/2021)	All health events	VA employees and Veteran patients	1,071,630 first doses administered; 826,866 second doses administered	Descriptive	No signals in the analysis for combined mRNA vaccines	No concerns raised
DoD VAERS (Population data through 3/19/2021; Results data through 4/3/2021)	All health events, adverse events of special interest	Active duty and beneficiaries	976,479 vaccines administered	Descriptive	22 cases of myocarditis following mRNA vaccines (16 Moderna, 6 Pfizer) • Background rate: 2-23 cases 19 cases of myocarditis following dose 2 of mRNA vaccines • Background rate: 1-9 cases	Ongoing discussion regarding communication of myocarditis risk in younger males
Indian Health Services (IHS) VAERS (Data through 4/26/2021)	All health events, adverse events of special interest ^a	Persons who identify as American Indian/Alaska Native	425k vaccines administered	Descriptive	84 total AE reports • 48 medically attended health impact events • 12 suspected AESIs	No concerns raised
Active Surveillance						
V-safe (Data through 3/13/2021)		Vaccinees who enroll	2,267,127 persons enrolled; 26,091 pregnancies ^c	Descriptive	623 reports overall (all submitted to VAERS) • 57 serious reports • Solicited reactions higher after dose 2 than dose 1	No concerns raised
V-safe Pregnancy Registry (Data through 5/20/2021)		Vaccinees who enroll	2,535 enrolled	Descriptive	Pregnancy and neonatal outcomes of interest within background rates	No concerns raised
Department of Veterans Affairs (VA) Active Surveillance System (Data through 5/13/21)	Pre-specified health outcomes ^a	Veteran Patients	1,153,987 first doses administered; 966,957 second doses administered	Descriptive; historical comparator analysis	Possible early signal for myopericarditis in the historical comparator analysis • Relative risk: 2.0	Only signal for anaphylaxis. Further work being done to investigate myopericarditis
Vaccine Safety Datalink (VSD) (Data through 5/15/21)	Pre-specified health outcomes ^a	Patients enrolled in participating	2.4 million first doses administered;	Descriptive; Vaccinated and	No signal for myopericarditis, or any other AESI, using a 21-day risk interval in vaccinated comparator analysis	Further analyses of myopericarditis in younger age groups in VSD

		health care organization	1.9 million second doses administered	unvaccinated concurrent sequential analyses		needed: analyses are neither alarming nor reassuring
Vaccine Safety Datalink (VSD) Mortality Study (Vaccinated through 2/27 and death data through 3/20/21)	Deaths	VSD sites enrolled in the mortality study; vaccinated before 2/27 and number of deaths before 3/20	219,570 first doses administered; 105,919 second doses administered	Descriptive; Vaccinated and unvaccinated concurrent sequential analyses	0.8 dose 1 mortality rate per 100 person-years 0.7 dose 2 mortality rate per 100 person-years 1.0 comparator mortality rate per 100 person-years	No concerns raised
Defense Medical Surveillance System (DMSS)^b	Pre-specified health outcomes ^a					
FDA - Centers for Medicare and Medicaid Services (CMS)^b (Data through 4/3/2021)	Pre-specified health outcomes ^a	CMS population 65 and above		Historical comparator analysis	Relative risk of 1.10 for AMI, after seasonality adjustment. The RR was not statistically significant. Relative risk of 1.31 for PE, after seasonality adjustment. The RR was statistically significant. Relative risk of 1.31 for DIC, after seasonality adjustment. The RR was not statistically significant.	Further investigation including signal characterization and evaluation in other databases is needed in order to properly assess the signals.
BEST initiative^b	Pre-specified health outcomes ^a					
NPTC Vaccine Sentinel Survey (Data through 4/26/21)	Pre-specified health outcomes	Persons who identify as American Indian/Alaska Native	425k vaccines administered	Descriptive	256 total AE reports • 67 medically attended health impact events • 23 suspected AESIs	No concerns raised

Vaccine Trials (Manufacturer)						See GRADE tables https://www.cdc.gov/vaccines/acip/refs/grade/covid-19-pfizer-biontech-vaccine.html	
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^aSee Table 4 for the complete list of health outcomes

^bData are currently being processed and will be reported when received

^cAt the time of vaccination

Table 2. COVID-19 vaccine monitoring systems reviewed by the VaST – Moderna (recommended for use in persons age ≥ 18 years)

Red indicates new results this week

Vaccine Safety Program	Outcomes Monitored	Population Monitored	Population captured	Analyses	Selected Results	Assessment/action
Passive Surveillance						
Vaccine Adverse Event Reporting System (VAERS) (Myopericarditis data through 5/20/21; Pregnancy data through 5/14/21)	All health events, adverse events of special interest ^a	US population	121.1 million total doses administered	Descriptive and empirical Bayesian data mining	0 confirmed TTS reports to VAERS 434 automated myopericarditis reports across all vaccines. 138 after dose 1; 232 after dose 2; and 64 unk. • Median age: 33 years • Median time to onset: 3 days 156 reports after Moderna; 61 after dose 1; 152 after dose 2; 42 unk 503 pregnancy reports submitted to VAERS • 62 serious reports • Median age: 33 years • Median gestational age at time of vaccination: 15 weeks • 1 maternal death	Anaphylaxis associated with vaccination, first detected by early reporting in US; assessed by follow-up with providers; chart review, CISA consultations; clinical guidance changed (initially in December 2020 and last updated March 5, 2021) Further work being done to define potential myocarditis risk. Observed number of cases higher than expected in 16-24 yr-olds post dose 2 No disproportional reporting for any pregnancy specific or non-pregnancy specific events. No concerns raised
VA ADERS (Data through 4/11/2021)	All health events	VA employees and Veteran patients	1,262,482 first doses administered; 977,202 second	Descriptive	No signals in the analysis for combined mRNA vaccines	No concerns raised

			doses administered			
DoD VAERS (Population data through 3/19/2021; Results data through 4/3/2021)	All health events, adverse events of special interest	Active duty and beneficiaries	852,548 vaccines administered	Descriptive	22 cases of myocarditis following mRNA vaccines • Background rate: 2-23 cases 19 cases of myocarditis following dose 2 of mRNA vaccines • Background rate: 1-9 cases 71 total AE reports • 43 medically attended health impact events • 15 suspected AESIs	Ongoing discussion regarding communication of myocarditis risk in younger males
Indian Health Services (IHS) VAERS (Data through 4/26/2021)	All health events, adverse events of special interest ^a	Persons who identify as American Indian/Alaska Native	700k vaccines administered	Descriptive	No concerns raised	No concerns raised
Active Surveillance						
V-safe (Data through 3/13/2021)		Vaccinees who enroll	2,627,416 persons enrolled; 23,064 pregnancies ^c	Descriptive	126 reports overall (all submitted to VAERS) • 27 serious reports • Solicited reactions higher after dose 2 than dose 1	No concerns raised
V-safe Pregnancy Registry (Data through 5/20/2021)		Vaccinees who enroll	2,192 enrolled	Descriptive	Pregnancy and neonatal outcomes of interest within background rates	No concerns raised
Department of Veterans Affairs (VA) Active Surveillance System (Data through 5/13/2021)	Pre-specified health outcomes ^a	Veteran Patients	1,344,556 first doses administered; 1,151,578 second doses administered	Descriptive; historical comparator analysis	No signal for myopericarditis in the analysis	Only signal for anaphylaxis, as identified earlier in other post-authorization safety monitoring No concerns raised
Vaccine Safety Datalink (VSD) (Data through 5/15/21)	Pre-specified health outcomes ^a	Patients enrolled in participating health care organization	2.1 million first doses administered; 1.6 million	Descriptive; Vaccinated and unvaccinated concurrent	No signal for myopericarditis, or any other AESI, using a 21-day risk interval in vaccinated comparator analysis	Further analyses of myopericarditis in younger age groups in VSD needed: analyses are neither alarming nor reassuring

Vaccine Safety Datalink (VSD) Mortality Study (Vaccinated through 2/27 and death data through 3/20/21)	Deaths	VSD sites enrolled in the mortality study; vaccinated before 2/27 and number of deaths before 3/20	second doses administered 220,799 first doses administered; 86,650 second doses administered	comparison, sequential analyses Descriptive; Vaccinated and unvaccinated concurrent comparison, sequential analyses	0.6 dose 1 mortality rate per 100 person-years 0.7 dose 2 mortality rate per 100 person-years 1.0 comparator mortality rate per 100 person-years	No concerns raised
Defense Medical Surveillance System (DMSS)^b	Pre-specified health outcomes ^a					
FDA - Centers for Medicare and Medicaid Services (CMS)^b (Data through 4/3/2021)	Pre-specified health outcomes ^a	CMS population 65 and above		Historical comparator analysis	No signals in the analysis	No concerns raised
BEST initiative^b	Pre-specified health outcomes ^a					
NPTC Vaccine Sentinel Survey (Data through 4/26/21)		Persons who identify as American Indian/Alaska Native	700k vaccines administered	Descriptive	214 total AE reports • 39 medically attended health impact events • 21 suspected AESIs	No concerns raised
Vaccine Trials (Manufacturer)					See GRADE tables https://www.cdc.gov/vaccines/acip/records/grade/covid-19-pfizer-biontech-vaccine.html	

^aSee Table 4 for the complete list of health outcomes.

^bData are currently being processed and will be reported when received at the time of vaccination

Table 3. COVID-19 vaccine monitoring systems reviewed by the VaST – Janssen/Johnson & Johnson (recommended for use in persons age ≥ 18 years)

Red indicates new results this week

Vaccine Safety Program	Outcomes Monitored	Population Monitored	Population captured	Analyses	Selected Results	Assessment/action
Passive Surveillance						
Vaccine Adverse Event Reporting System (VAERS) (TTS data through 5/21/21; Myopericarditis data through 5/20/21; Pregnancy data through 5/14/21)	All health events, adverse events of special interest ^a	US population	10.3 million total doses administered	Descriptive and empirical Bayesian data mining	32 confirmed TTS reports to VAERS 11.3 reporting rate per million for females aged 30-39 years 8.6 reporting rates per million for females aged 40-49 years 434 automated myopericarditis reports across all vaccines. 138 after dose 1; 232 after dose 2; 64 unk. - Median age: 33 years - Median time to onset: 3 days 22 reports had myopericarditis after Janssen/J&J vaccine 155 pregnancy reports submitted to VAERS 14 serious reports - Median age: 32 years - Median gestational age at time of vaccination: 17 weeks 0 maternal death No signals were detected	Warning and other information provided in updated EUA and MMWR last week, and reflected in clinical guidance No concerns raised No disproportional reporting for any pregnancy specific or non-pregnancy specific events. No concerns raised.
VA ADERS (Data through 4/11/2021)	All health events	VA employees and Veteran patients	109,483 vaccines administered	Descriptive	No signals were detected	No concerns raised
DoD VAERS (Data through 3/19/2021)	All health events, adverse events of special interest	Active duty and beneficiaries	28,640 vaccines administered	Descriptive	4 total AE reports 0 serious AE reports 0 death reports	No concerns raised

Indian Health Services (IHS) VAERS (Data through 4/26/2021)	All health events, adverse events of special interest ^a	Persons who identify as American Indian/Alaska Native	20k vaccines administered	Descriptive	3 total AE reports • 2 medically attended health impact events • 0 suspected AESIs	No concerns raised
Active Surveillance						
V-safe (Data through 4/26/2021)		Vaccinees who enroll	332,084 persons enrolled 3,118 pregnancies	Descriptive	28.3% of participants reported being unable to do normal daily activities 1.4% of participants reported requiring a medical visit	No concerns raised
V-safe Pregnancy Registry (Data through 5/20/2021)		Vaccinees who enroll	277 enrolled	Descriptive	Pregnancy and neonatal outcomes of interest within background rates	No concerns raised
Department of Veterans Affairs (VA) Active Surveillance System (Data through 4/25/2021)	Pre-specified health outcomes ^a	Veteran Patients	117,162 vaccines administered	Descriptive; historical comparator analysis	No signals detected	No concerns raised
Vaccine Safety Datalink (VSD) (Data through 5/15/21)	Pre-specified health outcomes ^a	Patients enrolled in participating health care organization	208,027 doses administered	Descriptive; Sequential analysis will be added when available	32 potential cases of VTE/PE following vaccination. • 18 are potential cases with incidence following vaccination	No concerns raised, but small number of doses administered
Vaccine Safety Datalink (VSD) Mortality Study (Vaccinated through 2/27 and death data through 3/20/21)	Deaths	VSD sites enrolled in the mortality study; vaccinated before 2/27 and number of deaths before 3/20	Data not yet available	Descriptive; Vaccinated and unvaccinated concurrent comparison, sequential analyses	Data not yet available	
Defense Medical Surveillance System (DMSS)^b	Pre-specified health outcomes ^a					

FDA - Centers for Medicare and Medicaid Services (CMS) ^b	Pre-specified health outcomes ^a	CMS population 65 and above		Historical comparator analysis	Data not yet available	
BEST initiative^b	Pre-specified health outcomes ^a					
NPTC Vaccine Sentinel Survey (Data through 4/26/21)		Persons who identify as American Indian/Alaska Native	20k vaccines administered	Descriptive	10 total AE reports • 1 medically attended health impact events • 0 suspected AESIs	No concerns raised
Vaccine Trials (Manufacturer)					See GRADE tables [HYPERLINK " https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/28-03-01/03-COVID-Gargano.pdf "]	

^aSee Table 4. for the complete list of health outcomes

^bData are currently being processed and will be reported when received

^cAt the time of vaccination

Table 4. Health systems and pre-specified health outcomes

	VAERS	VSD	VA*	DMESS*	CMS*	BEST*
Acute disseminated encephalomyelitis (ADEM)	X ^{1,2}	X	X			
Acute myocardial infarction	X	X	X		X	X
Anaphylaxis	X	X	X		X	X
Appendicitis	X	X	X		X	X
Acute respiratory distress syndrome (ARDS)		X	X			
Arthritis and arthralgia (not osteoarthritis or traumatic arthritis)	X ¹	X				
Ataxia	X ^{1,2}					
Autoimmune disease	X ¹					
Bell's palsy	X	X	X		X	X
Chronic inflammatory demyelinating polyneuropathy (CIDP)	X ^{1,2}					
COVID-19	X					
Death	X					
Disseminated intravascular coagulation (DIC)	X	X	X		X	X
Encephalitis	X	X	X			
Encephalomyelitis	X ^{1,2}	X	X		X	X
Encephalopathy	X ^{1,2}	X	X			
Guillain-Barré syndrome (GBS)	X	X	X		X	X
Immune thrombocytopenic purpura (ITP)		X	X		X	X
Kawasaki disease	X	X				X
Meningitis	X ^{1,2}	X	X			
Meningoencephalitis	X ^{1,2}	X	X			
Multiple sclerosis (MS)	X ^{1,2}					
Multisystem Inflammatory Syndrome in Adults (MIS-A)	X	X ³	X		X	X
Multisystem Inflammatory Syndrome in Children (MIS-C)	X	X ³				X
Myelitis	X ^{1,2}	X	X			
Myocarditis / pericarditis	X	X	X		X	X
Narcolepsy / cataplexy	X	X	X		X	X ⁴
Non-anaphylactic allergic reactions	X ¹					

VaST meeting notes - DRAFT
May 24, 2021
Confidential

Presentation slides were distributed; presentations are briefly summarized in meeting notes. Chat notes not answered verbally on the call are available and some have been incorporated into the minutes.

Participants

Workgroup members: Matt Daley, Kathy Edwards, Bob Hopkins (NVAC-Chair), Lisa Jackson, Grace Lee (Chair), Veronica McNally, Jennifer Nelson, Laura Riley, Rob Schechter, Keipp Talbot, Pat Whitley-Williams

Ex officio and liaison participants: Tatiana Beresnev (NIH), Matthew Clark (IHS), Karen Farizo (FDA), Mary Rubin (HRSA) Judith Steinberg (OIDP), Hui-Lee Wong (FDA)

Federal partners: Limone Collins (DoD), Fran Cunningham (VA), Kwan Hur (VA), Jeff Kelman (CMS)

CDC: Karen Broder, Tom Clark, Demetre Daskalakis, Frank Destefano, Sascha Ellington, Julianne Gee, Anne Hause, Rita Helfand, Lauri Hicks, Shin Kim, Jessica MacNeil, Lauri Markowitz (CDC Co-lead), Paige Marquez, Michael McNeil, Pedro Moro, Titilope Oduyebo, Sara Oliver, Christine Olson, Jessica Schindelar, David Shay, Tom Shimabukuro, Eddie Shanley, John Su, Eric Weintraub, Melinda Wharton (CDC Co-lead), Jared Woo

Technical SMEs: Steve Anderson (FDA), Laurie Aukes (VSD), Kevin Ault (KUMC), Richard Beigi (UPMC), Ed Belongia (VSD), James Donahue (VSD), Bruce Fireman (VSD), Kristin Goddard (VSD), Victoria Greenberg (Health Partners), Kayla Hanson (VSD), Brenna Hughes (Duke), Denise Jamieson (Emory), Elyse Kharbanda (Health Partners) Nicky Klein (VSD), Ned Lewis (VSD), Heather Lipkind (Yale), Yun Lu (FDA), Narayan Nair (FDA), Gabriela Vazquez (Yale), Ousseny Zerbo (VSD)

Agenda

Pregnancy focused session

- v-safe registry (Sascha Ellington, CDC)
- VAERS (Pedro Moro, CDC)
- VSD (Elyse Kharbanda, Health Partners)

Myocarditis session

- Updates overall and v-safe (Tom Shimabukuro, CDC)
- VAERS - TTS/CVST, myocarditis (John Su, CDC)
- VSD RCA (Nicky Klein, KPNC)
- VA RCA (Fran Cunningham, VA)

Administrative issues and announcements - Co-chairs and Co-leads

- Reminders about COI and confidentiality
- Doses distributed: 357,250,375; Doses administered: 285,720,586 (last updated: May 23)
 - Doses distributed: Pfizer-BioNTech: 188,398,275; Moderna: 148,157,400; Janssen/J&J: 20,694,700
 - Doses administered: Pfizer-BioNTech: 154,119,424; Moderna: 121,125,577;

- Janssen/J&J: 10,265,423; Unknown: 210,162
- First doses: 163,309,414; Fully vaccinated: 130,014,175
- These data are posted on the CDC website and are updated regularly ([HYPERLINK "https://covid.cdc.gov/covid-data-tracker/" \l "vaccinations").%E2%80%AF" \t "_blank"]

v-safe pregnancy registry – Dr. Sascha Ellington, CDC

Dr. Ellington provided updates on the v-safe pregnancy registry data for all COVID-19 vaccines. Overall, there are 5,004 women enrolled. Pregnancy and neonatal outcomes of interest are all within background rates. The number of neonatal outcomes among pregnant women who were vaccinated in their second trimester is increasing. The prevalence of spontaneous abortions (SAB) among participants that received mRNA COVID-19 vaccine was 6.5% (137/2097). A brief report will be submitted for publication.

Questions and discussion

1. What is expected prevalence of SAB compared to 6% of observed?
 - National estimates of SAB are 10-25% among women aged 15-44 years.
 - Source: U.S. Population-Based Background Incidence Rates of Medical Conditions for Use in Safety Assessment of COVID-19 Vaccines [HYPERLINK "https://www.sciencedirect.com/science/article/pii/S0264410X21005788"]
2. Can you confirm that the SAB/stillbirth occurred after vaccination?
 - Yes, inclusion criteria for the registry ensures that vaccination occurs before any observed outcomes.
3. Is there any health disparity by race/ethnicity regarding SAB/still birth?
 - The data are overwhelming from non-Hispanic whites. The team is actively looking into any disparities with the growing number of participants in the registry.
4. Why were there changes in the number of pregnancies over time?
 - The team suspects that change in demographic population enrolled into v-safe (shift from older to younger) has contributed to small changes; over time, there has also been a reduction in the number of mis-clicks indicating pregnancy.
5. What is the target journal for the brief report?
 - The v-safe pregnancy registry team is discussing and will let VaST know once decided.
6. Out of the entire cohort, the number is 2,097 for < 20 weeks. How many of the 2,097 were immunized in the first trimester?
 - The team is looking into this; plans to include this information in the upcoming brief report.

VAERS pregnancy – Dr. Pedro Moro, CDC

Dr. Moro provided an update on the VAERS pregnancy data. There were 1,222 pregnancy reports submitted to VAERS (Pfizer-BioNTech: 562, Moderna: 503, Janssen: 155, Unknown: 2). The most common AEsIs reported were systemic and local reactions, which is consistent with previous updates. There were 413 pregnancy and neonatal specific reports, of which 280 were SAB. Empirical Bayesian data mining did not detect any disproportionality alerts for pregnancy/neonatal outcomes.

Questions and discussion

1. Did the women who reported fever have a recorded temperature?
 - The VAERS form does not have a specific field to capture temperature.
2. In the disproportionality analyses, how big was the comparator group receiving other vaccines? And what other vaccines were included?

- The comparison group is most other vaccines in the VAERS database given during pregnancy.
3. Were there any common clinical elements or patterns among the maternal deaths?
 - The VAERS team has a death certificate from only 1 of the maternal deaths. Based on other information received, Dr. Moro does not see a pattern.

VSD pregnancy – Dr. Elyse Kharbanda, Health Partners

Dr. Kharbanda presented an update on the stillbirth surveillance being conducted in VSD. There was a brief overview of each of the 8 cases of stillbirths in women who received 1 or more COVID-19 vaccines in pregnancy. The clinical reviews have not identified any concerning patterns regarding stillbirths. A case-control study is planned.

Questions and discussion

1. Is there any indication of TTS among the pregnant women?
 - Most of the demise appeared to be due to mechanical causes.

Overall vaccine safety updates – Dr. Tom Shimabukuro, CDC

Dr. Shimabukuro provided a verbal update on v-safe and on myopericarditis. He also discussed the communication and state HANs that have gone out regarding myopericarditis. Currently the VAERS team is reviewing cases and coordinating with SMEs to investigate cases. CDC is developing communications and will notify VaST when they are ready.

VAERS - TTS/CVST, myocarditis – Dr. John Su, CDC

Dr. Su presented updates on TTS and myopericarditis in VAERS. There are 2 new TTS reports since last week's update, resulting in no major changes in reporting rates. There were 434 reports of myopericarditis in VAERS as of May 20. The cases are occurring mostly after mRNA vaccines, are more frequently in male patients in younger age groups, especially after a second dose. The number of observed reports is greater than expected after dose 2 in patients aged 16-24 years. Among the 65 reports that have a known disposition, 57 were discharged and 8 were still hospitalized. Of the 57 patients discharged, 83% had fully recovered.

Questions and discussion

1. What is the timing of the 434 automated reports - how many by month or week?
 - All 434 were reported in 2021 (Jan = 12, Feb = 21, Mar = 19, Apr = 65, and May to date = 65). These data align with anecdotes that cases of myopericarditis among adolescents and young adults began appearing mid-April.
2. Is VAERS signaling for myopericarditis now?
 - For the age groups 16-17 years and 18-24 years, yes.
3. Any sense typically of what percent of the reports end up being dropped after chart reviews? i.e., what percent of the totals reported in automated will likely be myocarditis - since that will affect the expected vs observed?
 - For various reasons, it is difficult to try imputing anticipated counts of reports based upon past proportions. The VAERS team is also updating the operating case definition, which may have an impact on the number of reports.
4. Is there a need for adjustment for seasonality in determining observed/expected?
 - Given the seasonality of viral causes like enteroviruses, yes. However, there isn't such much information in the review of the literature to date for background rates of myopericarditis.

5. What is the prior history of COVID-19 infection for the VAERS reports; are other causes ruled out?
 - As part of record review, ISO does look for past history of COVID-19 disease as well as testing for viral causes (typically coxsackievirus, adenovirus, and enteroviruses). However, frequently providers diagnose myopericarditis without necessarily looking for a cause.
6. The very wide range of possible expected cases suggests that the elevation of the observed over expected could be much higher if the "true" expected is near the lower end of the range.
7. Future risk communications should have an assessment of risk of cardiac disease post-COVID-19 infection, in addition to more information on background rates.

VA RCA – Dr. Fran Cunningham, VA

Dr. Cunningham provided a verbal update on the VA RCA myocarditis analyses and TTS. The VA is continuing to evaluate using a step-wise approach and is currently in the process of analyzing the data in the 1-21 day window for doses 1 and 2; there is currently no signal. The VA has given more than 5 million doses (Pfizer-BioNTech: 2.3 million, Moderna: 2.7 million, Janssen/J&J: 140,000). There were 5 cases of TTS following Janssen/J&J, that are still under review. The VA will have the final updates on Thursday.

Questions and discussion

1. Can you provide any details of the 5 cases, were they women <50 years?
 - 3 in males and 2 in females – none <50 years. The cases are currently being reviewed by hematologists.

VSD RCA – Dr. Nicky Klein, KPNC

Dr. Klein presented the VSD RCA data focusing on myopericarditis. There were no signals for myopericarditis or for any other AESI in the 21 days after vaccination overall after mRNA vaccines. There was also no signal for myopericarditis in the subset of the population aged 16-39 years; more data needs to be accumulated to be informative. The analyses in this age group by dose and manufacturer are neither alarming nor reassuring. A quick chart review of the potential myopericarditis cases suggests that most are probable cases.

Questions and discussion

1. Are the case definitions similar between VSD and VAERS?
 - VAERS uses MedDRA terms whereas VSD using ICD-10 codes.
2. Has the VSD team considered adjusting the time window of investigation?
 - Narrowing the time window to 7 days or less is currently being discussed.
3. How should providers communicate the myopericarditis messaging?
 - CDC is drafting communication materials. VaST will be updated on the status of these.
4. Please clarify what it means by high risk for complication of COVID-19.
 - It means high risk for severe COVID-19 disease based on underlying medical conditions.
5. Can you clarify the risk for adolescents (vs. adults)?
 - The data are rapidly accruing in this age group. VSD will have substantially more power in next 2-3 weeks.
6. The lack of comparator data makes it difficult to analyze, but VSD has seen that the earliest available comparator time has tended to have lower rates that stabilize later. We don't know if that will recur for myocarditis, but that has been the pattern so far in this RCA.
7. The DoD liaison mentioned that the DoD manuscript on 22 myocarditis cases has been accepted for publication in JAMA cardiology.

Message

From: Markowitz, Lauri (CDC/DDID/NCIRD/DVD) [REDACTED]
Sent: 6/21/2021 1:20:22 AM
To: Anderson, Steven [REDACTED] Beresnev, Tatiana H (NIH) [REDACTED] Broder, Karen R (CDC) [REDACTED] Clark, Matthew (IHS) [REDACTED] Clark, Thomas A (CDC) [REDACTED] Cohn, Amanda C (CDC) [REDACTED]; Collins, Limone [REDACTED] Cunningham, Fran [REDACTED] Daley, Matt [REDACTED] Daskalakis, Demetre C (CDC) [REDACTED] DeStefano, Frank (CDC) [REDACTED] Edwards, Kathy [REDACTED] Farizo, Karen [REDACTED]; Forshee, Richard [REDACTED] Gee, Julianne M (CDC) [REDACTED] Hause, Anne M (CDC) [REDACTED] Helfand, Rita (CDC) [REDACTED] Hicks, Lauri (CDC) [REDACTED] Hopkins, Bob [REDACTED] Jackson, Lisa [REDACTED] Jennifer Nelson [REDACTED] Kelman, Jeffrey A (CMS) [REDACTED] Lee, Grace [REDACTED] Lu, Yun (CBER) [REDACTED] MacNeil, Jessica R (CDC) [REDACTED] Markowitz, Lauri (CDC) [REDACTED] Marquez, Paige L (CDC) [REDACTED] Mbaeyi, Sarah A (CDC) [REDACTED] McNally, Veronica [REDACTED] Mcneil, Michael M (CDC) [REDACTED] Myers, Tanya R (CDC) [REDACTED] Nair, Narayan [REDACTED] Oliver, Sara E (CDC) [REDACTED] Patricia Whitley-Williams [REDACTED] Riley, Laura [REDACTED] Rubin, Mary (HRSA) [REDACTED] Schechter, Robert [REDACTED] Schindelar, Jessica A (CDC) [REDACTED] Shanley, Edwin (CDC) [REDACTED] Shay, David K (CDC) [REDACTED] Shimabukuro, Tom (CDC) [REDACTED] Sotir, Mark J (CDC) [REDACTED] Steinberg, Judith L (OS) [REDACTED] Su, John (CDC) [REDACTED] Talbot, Keipp [REDACTED] Weintraub, Eric S (CDC) [REDACTED] Wharton, Melinda (CDC) [REDACTED] Wong, Hui-Lee [REDACTED] Woo, Jared M (CDC) [REDACTED] Young, Mardia A (CDC) [REDACTED]
Subject: [EXTERNAL] VaST - Draft minutes and report from June 14 (CONFIDENTIAL)
Attachments: 2021-06-14 - VaST minutes draftv3.docx; 2021-06-14 - VaST Report Data Table draft.docx

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear VaST members and attendees,

- Attached are the draft minutes and summary report (with VaST comments) from the call on June 14. Please let us know if there are any corrections or edits.
- The next VaST call is Monday, June 21, 1:30 – 3:00 pm EDT. Slides will be send out before the call.

Lauri Markowitz and Melinda Wharton

*Lauri Markowitz, MD
VaST Co-Lead
CDC COVID-19 Response, Vaccine Task Force
Division of Viral Diseases
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention*

VaST meeting notes – DRAFTv3
June 14, 2021
Confidential

Presentation slides were distributed; presentations are briefly summarized in meeting notes. Chat notes not answered verbally on the call are available and some have been incorporated into the minutes.

Participants

Workgroup members: Matt Daley, Bob Hopkins (NVAC-Chair), Lisa Jackson, Grace Lee (Chair), Veronica McNally, Jennifer Nelson, Laura Riley, Keipp Talbot, Pat Whitley-Williams

Ex officio and liaison participants: Tatiana Beresnev (NIH), Matthew Clark (IHS), Karen Farizo (FDA), Mary Rubin (HRSA) Judith Steinberg (OIDP), Hui-Lee Wong (FDA)

Federal partners: Limone Collins (DoD), Fran Cunningham (VA), Kwan Hur (VA), Jeff Kelman (CMS)

CDC: Karen Broder, Tom Clark, Frank Destefano, Julianne Gee, Anne Hause, Rita Helfand, Gayle Langley, Jessica MacNeil, Lauri Markowitz (CDC Co-lead), Paige Marquez, Michael McNeil, Kristen Nordlund, Sara Oliver, Jessica Schindelar, David Shay, Tom Shimabukuro, Eddie Shanley, John Su, Eric Weintraub, Melinda Wharton (CDC Co-lead), Jared Woo

Technical SMEs: Meghna Alimchandani (FDA), Steve Anderson (FDA), Laurie Aukes (VSD), Ed Belongia (VSD), James Donahue (VSD), Bruce Fireman (VSD), Rich Forshee (FDA), Kristin Goddard (VSD), Kayla Hanson (VSD), Nicky Klein (VSD), Ned Lewis (VSD), Patricia Lloyd (FDA), Yun Lu (FDA), Narayan Nair (FDA), Oussen Zerbo (VSD), Cindy Zhou (FDA)

Agenda

- Updates (Tom Shimabukuro, CDC)
- FDA CMS signals
 - FDA CMS (Cindy Zhou, FDA)
 - VSD RCA (Nicky Klein, KPNC)
 - VA RCA (Fran Cunningham, VA)
 - Communication plans and discussion
- Guillain-Barre Syndrome (GBS) following Janssen J&J vaccine
 - VAERS (Narayan Nair, FDA)
 - VSD RCA (Nicky Klein, KPNC)
- Preparation for ACIP meeting on June 18

Administrative issues and announcements – Co-chairs and Co-leads

- Reminders about COI and confidentiality
- Doses distributed: 374,398,105; Doses administered: 309,322,545 (last updated: June 13)
 - Doses distributed: Pfizer-BioNTech: 198,595,605; Moderna: 154,405,600; Janssen/J&J: 21,396,900
 - Doses administered: Pfizer-BioNTech: 168,784,549; Moderna: 128,785,935; Janssen/J&J: 11,517,956; Unknown: 234,105
 - First doses: 173,840,483; Fully vaccinated: 143,921,222

- These data are posted on the CDC website and are updated regularly ([HYPERLINK "https://covid.cdc.gov/covid-data-tracker/" \l "vaccinations).%E2%80%AF" \t "_blank"]

FDA CMS – Dr. Cindy Zhou, CDC

Dr. Zhou presented the FDA CMS rapid cycle analysis results for acute myocardial infarction (AMI), pulmonary embolism (PE), disseminated intravascular coagulation (DIC), and immune thrombocytopenia (ITP). There were statistical signals for these four events following Pfizer-BioNTech vaccination; results were sensitive to the choice of background rates. Results from quality assurance and signal characterization efforts were presented.

Questions and discussion

1. There was discussion about use of type 2 or type 1 AMI for the claims data analysis and that it might be better to restrict to type I.
2. What are examples of type 2 AMI?
 - Coronary artery spasm, coronary embolism, anemia, arrhythmias, hypertension or hypotension.
 - Type 2 MI is defined as "myocardial infarction secondary to ischaemia due to either increased oxygen demand or decreased supply, e.g. coronary artery spasm, coronary embolism, anemia, arrhythmias, hypertension or hypotension."
 - FDA-CMS can restrict to type 1 but has not done this.
 - FDA supported a VSD study to look at type 1 for a different vaccine study; 80% of type 1 represented real AMI.
3. There was substantial discussion about limitations of claims data.
 - Some VaST members said statistical signals should be accompanied by medical record review. The FDA presenters believe that sometimes action can be taken before medical record review is complete – since chart retrieval can take several weeks.
 - Date of onset of a condition is not collected in claims data; the only variables available are admission date and discharge date. CMS Medicare used admission date for the inpatient setting.
4. Were any COVID-19 positive?
 - 7% of Pfizer-BioNTech reports had record of prior COVID-19 diagnoses (medically attended). Other patients may have had COVID-19 without any healthcare claim.
5. Would there be value comparing the data with data during H1N1 pandemic?
 - This was discussed internally; since the data are from more than a decade ago, it was felt that would not be helpful.
6. Since we know that PE/thromboembolic events occur with COVID, is it possible that background rates are underestimated for 2020/21?
 - FDA estimated both pre-COVID and peri-COVID-19 background rates (<https://www.bestinitiative.org/vaccines-and-allergenics>). The peri-COVID-19 rates dipped but returned to historical rates by November 2020. Sensitivity analysis using Nov-Dec 2020 (peri-COVID-19 time) background rates for PE resulted in a non-statistically significant association for PE with relative risk of 1.22.
7. Was the secondary comparison group involving flu vaccine recipients a subset of the original historical cohort?
 - Yes, it was a subset of the original historical cohort.
8. Is there an inclusion date that ensures the patient has not had a history of AMI or PE or other similar types of conditions?

- There is a 1 year of 'clean window' prior to vaccination to define incident outcomes. The clean window is applied both to the historical cohort and COVID-19 vaccinees to define incident events.
9. Which AESIs do and do not include outpatient diagnoses?
 - See slide 7: only inpatient for AMI; PE and ITP include outpatient; DIC includes ED
 10. What number (and proportion) of cases have been reviewed for AMI and PE?
 - For the claims profile review, there were 100 cases each for AMI and PE. This was not a medical chart review; charts are being requested now for that review.
 11. Were only cases, not historical controls reviewed?
 - Only cases were reviewed.
 12. Does the CMS RCA also have results for myocarditis?
 - Not myocarditis separately. Only myocarditis and pericarditis combined. There was no statistical signal observed in CMS Medicare and Optum Pre-Adjudicated claims as of June 14, 2021

VSD RCA – Dr. Nicky Klein, KPNC

Dr. Klein provided a verbal update on AMI, PE, DIC, and ITP based on data presented previously to VaST. There were no statistical signals the last time analyses were run. VSD has completed sub-group analyses looking at restricted age groups and will re-run these now that they have seen the updated FDA CMS results. The data will be available at the end of the week.

Questions and discussion

1. When will the results for 65+ be available?
 - VSD will be discussing internally when they can make that available
 - VSD has previously ran a 65+ analysis on AMI, VTE and PE (focused mostly on PE when presenting to VaST).

VA RCA – Dr. Fran Cunningham, VA

Dr. Cunningham presented an updated analysis on myopericarditis (overall and in the 18-39 year age group) and also provided a verbal update on all ages for AMI, DIC, PE, and ITP. There was a non-significant elevated RR for myopericarditis among 18-39 year-olds (~4 with 21-day window). There are no statistical signals to date for myopericarditis or for any of the outcomes observed in the FDA CMS analyses. The VA is in the process of updating analyses for AMI, DIC, PE and ITP for persons 65+ years and the analyses will be available within the next week.

Communication plan

1. Is there a standard practice for FDA for communication of signals from claims data?
 - There are no established guidelines for communicating these data.
2. FDA next steps
 - General high-level posting hopefully within the next week. Sponsors will also be notified.
3. There was discussion on the challenges of communicating FDA RCA findings to the public before completing further investigations. There are major limitations to the current analysis due to lack of chart confirmation, unknown onset dates, and potential for confounding.
4. The data seems to be driven by the nursing home population
 - FDA has stratified analyses by nursing homes. RRs for the nursing home population compared to the non-nursing home population for PE (RR=1.66 to 1.47), AMI (RR=1.53 to 1.34), and DIC (RR=2.72 to 1.28).

GBS in VAERS – Dr. Narayan Nair, FDA

Dr. Nair presented on GBS following Janssen vaccine in the VAERS data. There are 80 GBS reports following Janssen vaccine; median age is 57 years and median time to onset is 32 days. The reporting rate for GBS is higher for Janssen than for mRNA vaccines. More data are needed to make any conclusions and the immediate next step is to obtain medical records and to apply the GBS Brighton case definition.

Questions and discussion

1. There was interest in hearing any data available for other adenovirus vectored vaccines.
2. Are there any data about AZ vaccine from other countries?
 - EMA is analyzing GBS cases after AZ vaccine and the FDA has requested an update. There is no timeline for when the assessment will be concluded.
3. Is FDA planning to make a public statement on the GBS VAERS analysis?
 - More data are needed to evaluate the relationship between GBS and vaccination.
4. Can the age groups be broken down slightly more finely (e.g. currently 18-64)?
 - Yes, the O/E analysis with more age stratification can be run for future iterations.
5. Why 5 deaths in backup slides?
 - The 5 deaths in the back up slides refers to Pfizer-BioNTech data.
6. Are there any geographical clusters?
 - FDA has not evaluated the data for geographical clustering yet.

VSD RCA on GBS – Dr. Nicky Klein, KPNC

Dr. Klein presented the VSD RCA data focusing on GBS. There were no signals for GBS, or for any other outcome, in the 21 days after vaccination in the overall VSD population. There were 8 confirmed GBS cases identified within 1-98 days of an mRNA vaccine (4 between 1-21 days and 4 between 22-42 days) and 5 confirmed GBS cases between 1-21 days after Janssen vaccine. The chart confirmed incidence is much higher following Janssen vaccine versus mRNA vaccine; monitoring is ongoing.

Preparation for June 18 ACIP meeting – all

Sara Oliver, CDC lead for ACIP CVWG, gave a brief overview of plans for the meeting. The meeting session that focuses on myocarditis will include a presentation by a pediatric cardiologist reviewing myocarditis, a presentation by CDC on data from safety monitoring, a presentation on VaST impressions, and ACIP CVWG considerations. No vote is planned.

Questions and discussion

The CDC/ISO presentation will be basically the same presentation made to VRBPAC last week but will include more detailed and updated data. That presentation, and the VaST presentation, will be shared with VaST members before Friday.

There was general discussion about myocarditis among VaST members. More data are needed on outcomes. The DoD has a myocarditis registry and is following cases; most are post smallpox vaccine. The majority of patients have recovered and were able to fulfill service training requirements. More information is needed regarding the long-term clinical course of post-vaccination myocarditis.

Combined Systems Safety Monitoring Report - DRAFT

June 14, 2021

Confidential

The VaST session on June 14, 2021 was focused on: 1) the Food and Drug Administration (FDA) Centers for Medicare & Medicaid Services (CMS) rapid cycle analysis (RCA) signals, some of which had been presented to VaST previously on April 19 and May 3; 2) new data presented on Guillain-Barré syndrome (GBS) following Janssen vaccine from the Vaccine Adverse Event Reporting System (VAERS) and the Vaccine Safety Datalink (VSD) RCA; and 3) plans for the June 18 ACIP meeting to review myocarditis following mRNA vaccines.

CMS RCA

- The CMS RCA found statistical signals for pulmonary embolism (PE), acute myocardial infarction (AMI), disseminated intravascular coagulation (DIC), and immune thrombocytopenic purpura (ITP) for Pfizer-BioNTech mRNA vaccine, based on claims data only, using historical comparators.
 - Background rates from 2017-2020 were standardized for nursing home, age, sex, and race.
 - After seasonality adjustment only PE remained statistically significant.
 - Several analyses for signal characterization were performed using claims-only data; these raised concerns about misclassification and confounding.
 - Type 2 AMI codes were more common during the study period than historical period, suggesting secular trends in coding practices.
 - For AMI and PE, a higher proportion of inpatient claims-based codes occurred in a non-primary diagnosis position in the study period.
 - Nursing home residents were more likely to be vaccinated with Pfizer vaccine than the general elderly population; this was not observed for Moderna or Janssen vaccines.
 - Temporal scan statistics were not concerning.
 - 10-24% of cases after Pfizer-BioNTech vaccination had a history of prior COVID-19 diagnosis
 - Evaluation of claims profiles indicated that up to the following percentages were unlikely to be true cases: 25-40% for AMI; 40-50% for PE, 57% for ITP. Only 15% of DIC had profiles that indicated likely true cases.
- There were no signals for AMI, PE, ITP or DIC overall or among those aged 65 years and older in the VSD or Department of Veterans Affairs (VA) RCAs to date. VSD uses concurrent vaccinated comparators; the VA RCA uses historical comparators.

VaST members discussed the following key points:

- There are many limitations of the CMS RCA including:
 - Use of claims-only data without chart validation to confirm cases. Review of at least a sample of medical records is important as a routine part of any signal evaluation.
 - Use of a historical comparison cohort that does not account for secular trends in health services utilization or coding practices.
 - Use of both primary and secondary diagnosis codes for identification, resulting in previously diagnosed problems being included.
 - Use of both type 2 and type 1 AMI codes in the analyses.
 - Lack of stratified analyses for nursing home and non-nursing home populations and lack of adjustment for other medical co-morbidities associated with outcomes of interest.
- There very likely is substantial confounding or misclassification in the CMS data analyses.
- VaST encourages review of findings with subject matter experts.

- VaST questions whether type 2 and type 1 AMI should both be included in the same analysis.
- VaST would like to see updated data from all RCAs for these four outcomes and an analysis of the FDA CMS data stratified by nursing home residency.

GBS following Janssen vaccine

- In VAERS, there were 80 reports of GBS after Janssen vaccine.
 - Observed reports were greater than expected across age groups; reporting rate for GBS was higher for Janssen than for mRNA vaccines.
- In VSD, the chart confirmed incidence of GBS during the 21 days after the Janssen vaccine, unadjusted for age-race-sex-site, was much higher than during the 21 days after mRNA vaccines.
 - VSD currently has not identified a statistical signal in the primary analyses; continued monitoring is warranted.

VaST members discussed the following key points:

- These new data regarding GBS are concerning and need to be investigated further.
- Members agreed with FDA that next steps are to obtain additional follow-up/medical records for Janssen reports and determine whether they meet the Brighton Collaboration GBS case definition.
- VaST members are interested to know the EMA assessment of GBS after Astra Zeneca vaccine.
- VaST members are interested to know any data from industry for other adenovirus vectored products.
- Follow-up is needed with further analyses from BEST/CMS and VSD active surveillance, including medical record review.

Preparation for the ACIP meeting

- The safety portion of the ACIP meeting on June 18 will focus on myocarditis following mRNA vaccines.
- VaST will prepare comments to follow the CDC Immunization Safety Office presentation.
- Further evaluation of other safety signals will continue, with consideration of presentation to ACIP in the future.

Table 1. COVID-19 vaccine monitoring systems reviewed by the VaST – Pfizer BioNTech (recommended for use in persons age ≥ 12 years)

Red indicates updated or new data this week

Vaccine Safety Program	Outcomes Monitored	Population Monitored	Population captured	Analyses	Selected Results	Assessment/action
Passive Surveillance						
Vaccine Adverse Event Reporting System (VAERS) (Myocarditis/pericarditis data through 6/4/21; GBS data through 6/1/21)	All health events, adverse events of special interest ^a	US population	161 million total doses administered	Descriptive and empirical Bayesian data mining	0 confirmed TTS reports to VAERS 1,029 automated myocarditis and pericarditis reports across all vaccines. 259 after dose 1; 626 after dose 2; 144 unk 537 reports after Pfizer-BioNTech vaccine – 125 after dose 1, 412 after dose 2 144 GBS reports to VAERS; crude reporting rate .9/million doses administered	Anaphylaxis associated with vaccination, first detected by reports from UK and early reporting in the US; assessed by follow-up with providers, chart review, CISA consultations; clinical guidance changed (initially in December 2020 and last updated March 5, 2021) Further work being done to define potential myocarditis risk. Observed number of cases higher than expected in 16-24 yr-olds post dose 2. No concerns raised
VA ADERS (Data through 4/11/2021)	All health events	VA employees and Veteran patients	1,071,630 first doses administered; 826,866 second doses administered	Descriptive	No signals in the analysis for combined mRNA vaccines	No concerns raised

DoD VAERS (Population data through 3/19/2021; Results data through 4/3/2021)	All health events, adverse events of special interest	Active duty and beneficiaries	976,479 vaccines administered	Descriptive	22 cases of myocarditis following mRNA vaccines (16 Moderna, 6 Pfizer) • Background rate: 2-23 cases 19 cases of myocarditis following dose 2 of mRNA vaccines • Background rate: 1-9 case 84 total AE reports • 48 medically attended health impact events • 12 suspected AESIs	Ongoing discussion regarding communication of myocarditis risk in younger males
Indian Health Services (IHS) VAERS (Data through 4/26/2021)	All health events, adverse events of special interest ^a	Persons who identify as American Indian/Alaska Native	425k vaccines administered	Descriptive		No concerns raised
Active Surveillance						
V-safe (Data through 5/31/2021)		Vaccinees who enroll	46,533 adolescent persons (12-15 years) enrolled;	Descriptive	Injection site pain, fatigue, and headache were the top 3 solicited reactions reported 0-7 days after vaccine Persons aged 12-15 years reported solicited reactions slightly less frequently than those aged 16-25 years Pregnancy and neonatal outcomes of interest within background rates	No concerns raised
V-safe Pregnancy Registry (Data through 5/20/2021)		Vaccinees who enroll	2,535 enrolled	Descriptive		No concerns raised
Department of Veterans Affairs (VA) Active Surveillance System (Data through 6/6/21)	Pre-specified health outcomes ^a	Veteran Patients	1,303,967 first doses administered; 1,184,335 second doses administered	Descriptive; historical comparator analysis	No signal for myopericarditis in the 21- or 42-day window historical comparator analysis	Only signal for anaphylaxis. Further work being done to investigate myopericarditis and age stratifications
Vaccine Safety Datalink (VSD) (Data through 6/5/21)	Pre-specified health outcomes ^a	Patients enrolled in participating health care organization	2.9 million first doses administered; 2.4 million	Descriptive; Vaccinated and unvaccinated concurrent	No signal for myopericarditis, or any other AESI, using a 21-day risk interval in vaccinated comparator analysis	Further analyses of myopericarditis in younger age groups in VSD needed: analyses are neither alarming nor reassuring

Vaccine Safety Datalink (VSD) Mortality Study (Vaccinated through 2/27 and death data through 3/20/21)	Deaths	VSD sites enrolled in the mortality study; vaccinated before 2/27 and number of deaths before 3/20	second doses administered 219,570 first doses administered; 105,919 second doses administered	comparison, sequential analyses Descriptive; Vaccinated and unvaccinated concurrent comparison, sequential analyses	0.8 dose 1 mortality rate per 100 person-years 0.7 dose 2 mortality rate per 100 person-years 1.0 comparator mortality rate per 100 person-years	No concerns raised
Defense Medical Surveillance System (DMSS)^b FDA - Centers for Medicare and Medicaid Services (CMS)^b (Data through 6/14/2021)	Pre-specified health outcomes ^a Pre-specified health outcomes ^a	CMS population 65 and above		Historical comparator analysis	Relative risk of 1.24 for AMI, after seasonality adjustment. The RR was not statistically significant. Relative risk of 1.35 for PE, after seasonality adjustment. The RR was statistically significant. Relative risk of 1.59 for DIC, after seasonality adjustment. The RR was not statistically significant. Relative risk of 1.35 for ITP, after seasonality adjustment. The RR was not statistically significant.	Further investigation including signal characterization and evaluation in other databases is needed in order to properly assess the signals
BEST initiative^b	Pre-specified health outcomes ^a					
NPTC Vaccine Sentinel Survey (Data through 4/26/21)	Pre-specified health outcomes	Persons who identify as AI/AN	425k vaccines administered	Descriptive	256 total AE reports • 67 medically attended health impact events • 23 suspected AEsIs	No concerns raised

Vaccine Trials (Manufacturer)						See GRADE tables https://www.cdc.gov/vaccines/acip/refs/grade/covid-19-pfizer-biontech-vaccine.html	
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^aSee Table 4 for the complete list of health outcomes

^bData are currently being processed and will be reported when received

^cAt the time of vaccination

Table 2. COVID-19 vaccine monitoring systems reviewed by the VaST – Moderna (recommended for use in persons age ≥ 18 years)

Red indicates new results this week

Vaccine Safety Program	Outcomes Monitored	Population Monitored	Population captured	Analyses	Selected Results	Assessment/action
Passive Surveillance						
Vaccine Adverse Event Reporting System (VAERS) (Myocarditis/pericarditis data through 6/4/21; GBS data through 6/1/21)	All health events, adverse events of special interest ^a	US population	125 million total doses administered	Descriptive and empirical Bayesian data mining	0 confirmed TTS reports to VAERS 1,029 automated myocarditis and pericarditis reports across all vaccines. 259 after dose 1; 626 after dose 2; 144 unk. 319 reports after Moderna – 107 after dose 1; 212 after dose 2 117 GBS reports to VAERS; crude reporting rate .93/million doses administered No signals in the analysis for combined mRNA vaccines	Anaphylaxis associated with vaccination, first detected by early reporting in US; assessed by follow-up with providers, chart review, CISA consultations; clinical guidance changed (initially in December 2020 and last updated March 5, 2021) Further work being done to define potential myocarditis risk. Observed number of cases higher than expected in 16-24 yr-olds post dose 2. No concerns raised No concerns raised
VA ADERS (Data through 4/11/2021)	All health events	VA employees and Veteran patients	1,262,482 first doses administered; 977,202 second doses administered	Descriptive		

DoD VAERS (Population data through 3/19/2021; Results data through 4/3/2021)	All health events, adverse events of special interest	Active duty and beneficiaries	852,548 vaccines administered	Descriptive	22 cases of myocarditis following mRNA vaccines • Background rate: 2-23 cases 19 cases of myocarditis following dose 2 of mRNA vaccines • Background rate: 1-9 cases	Ongoing discussion regarding communication of myocarditis risk in younger males
Indian Health Services (IHS) VAERS (Data through 4/26/2021)	All health events, adverse events of special interest ^a	Persons who identify as AI/AN	700k vaccines administered	Descriptive	71 total AE reports • 43 medically attended health impact events • 15 suspected AESIs	No concerns raised
Active Surveillance						
V-safe (Data through 5/24/2021)		Vaccinees who enroll	2,627,416 persons enrolled; 23,064 pregnancies ^c	Descriptive	126 reports overall (all submitted to VAERS) • 27 serious reports • Solicited reactions higher after dose 2 than dose 1	No concerns raised
V-safe Pregnancy Registry (Data through 5/20/2021)		Vaccinees who enroll	2,192 enrolled	Descriptive	Pregnancy and neonatal outcomes of interest within background rates	No concerns raised
Department of Veterans Affairs (VA) Active Surveillance System (Data through 6/6/2021)	Pre-specified health outcomes ^a	Veteran Patients	1,502,339 first doses administered; 1,413,653 second doses administered	Descriptive; historical comparator analysis	No signal for myopericarditis in the 21- or 42-day window historical comparator analysis	Only signal for anaphylaxis, as identified earlier in other post-authorization safety monitoring No concerns raised
Vaccine Safety Datalink (VSD) (Data through 6/5/21)	Pre-specified health outcomes ^a	Patients enrolled in participating health care organization	2.3 million first doses administered; 2.0 million second doses administered	Descriptive; Vaccinated and unvaccinated concurrent comparison, sequential analyses	No signal for myopericarditis, or any other AESI, using a 21-day risk interval in vaccinated comparator analysis Imbalance of case split after dose 2 driving the observed elevated rate ratios	Further analyses of myopericarditis in younger age groups in VSD needed: analyses are neither alarming nor reassuring

Vaccine Safety Datalink (VSD) Mortality Study (Vaccinated through 2/27 and death data through 3/20/21)	Deaths	VSD sites enrolled in the mortality study; vaccinated before 2/27 and number of deaths before 3/20	220,799 first doses administered; 86,650 second doses administered	Descriptive; Vaccinated and unvaccinated concurrent comparison, sequential analyses	0.6 dose 1 mortality rate per 100 person-years 0.7 dose 2 mortality rate per 100 person-years 1.0 comparator mortality rate per 100 person-years	No concerns raised
Defense Medical Surveillance System (DMSS)^b	Pre-specified health outcomes ^a					
FDA - Centers for Medicare and Medicaid Services (CMS)^b (Data through 4/3/2021)	Pre-specified health outcomes ^a	CMS population 65 and above		Historical comparator analysis	No signals in the analysis	No concerns raised
BEST initiative^b	Pre-specified health outcomes ^a					
NPTC Vaccine Sentinel Survey (Data through 4/26/21)		Persons who identify as American Indian/Alaska Native	700k vaccines administered	Descriptive	214 total AE reports • 39 medically attended health impact events • 21 suspected AESIs	No concerns raised
Vaccine Trials (Manufacturer)					See GRADE tables https://www.cdc.gov/vaccines/acip/racs/grade/covid-19-pfizer-biontech-vaccine.html	

^aSee Table 4 for the complete list of health outcomes

^bData are currently being processed and will be reported when received

^cat the time of vaccination

Table 3. COVID-19 vaccine monitoring systems reviewed by the VaST – Janssen/Johnson & Johnson (recommended for use in persons age ≥ 18 years)

Red indicates new results this week

Vaccine Safety Program	Outcomes Monitored	Population Monitored	Population captured	Analyses	Selected Results	Assessment/action
Passive Surveillance						
Vaccine Adverse Event Reporting System (VAERS) (TTS and Myocarditis/pericarditis data through 6/4/21; GBS data through 6/1/21)	All health events, adverse events of special interest ^a	US population	11 million total doses administered	Descriptive and empirical Bayesian data mining	35 confirmed TTS reports to VAERS 12.3 reporting rate per million for females aged 30-39 years 9.6 reporting rates per million for females aged 40-49 years 1,029 automated myocarditis and pericarditis reports across all vaccines. 259 after dose 1; 626 after dose 2; 144 unk. 27 reports after Janssen/J&J vaccine 80 GBS reports to VAERS; crude reporting rate 7.37 million doses administered	Warning and other information provided in updated EUA and MMWR last week, and reflected in clinical guidance No concerns raised Further investigation needed in VAERS and by different systems
VA ADERS (Data through 4/11/2021)	All health events	VA employees and Veteran patients	109,483 vaccines administered	Descriptive	No signals were detected	No concerns raised
DoD VAERS (Data through 3/19/2021)	All health events, adverse events of special interest	Active duty and beneficiaries	28,640 vaccines administered	Descriptive	4 total AE reports 0 serious AE reports 0 death reports	No concerns raised
Indian Health Services (IHS) VAERS (Data through 4/26/2021)	All health events, adverse events of special interest ^a	Persons who identify as AI/AN	20k vaccines administered	Descriptive	3 total AE reports 2 medically attended health impact events 0 suspected AESIs	No concerns raised
Active Surveillance						

V-safe (Data through 5/24/2021)		Vaccinees who enroll	332,084 persons enrolled 3,118 pregnancies	Descriptive	28.3% of participants reported being unable to do normal daily activities 1.4% of participants reported requiring a medical visit Pregnancy and neonatal outcomes of interest within background rates	No concerns raised
V-safe Pregnancy Registry (Data through 5/20/2021)		Vaccinees who enroll	277 enrolled	Descriptive		No concerns raised
Department of Veterans Affairs (VA) Active Surveillance System (Data through 6/6/2021)	Pre-specified health outcomes ^a	Veteran Patients	169,294 doses administered	Descriptive; historical comparator analysis	No signals for CVST or myopericarditis in the 42-day window historical comparator analysis	No concerns raised
Vaccine Safety Datalink (VSD) (Data through 6/5/21)	Pre-specified health outcomes ^a	Patients enrolled in participating health care organization	261,150 doses administered	Descriptive; Sequential analysis will be added when available	5 confirmed cases of GBS following vaccination. • All cases had a time to symptom onset between 1-21 days following vaccination	Further analysis of GBS following vaccine is needed.
Vaccine Safety Datalink (VSD) Mortality Study (Vaccinated through 2/27 and death data through 3/20/21)	Deaths	VSD sites enrolled in the mortality study; vaccinated before 2/27 and number of deaths before 3/20	Data not yet available	Descriptive; Vaccinated and unvaccinated concurrent comparison, sequential analyses	Data not yet available	
Defense Medical Surveillance System (DMSS)^b	Pre-specified health outcomes ^a					
FDA - Centers for Medicare and Medicaid Services (CMS)^b	Pre-specified health outcomes ^a	CMS population 65 and above		Historical comparator analysis	Data not yet available	

BEST initiative ^b	Pre-specified health outcomes ^a	Persons who identify as American Indian/Alaska Native	20k vaccines administered	Descriptive	10 total AE reports 1 medically attended health impact events 0 suspected AESIs	No concerns raised
NPTC Vaccine Sentinel Survey (Data through 4/26/21)					See GRADE tables [HYPERLINK " https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/28-03-01/03-COVID-Gargano.pdf "]	
Vaccine Trials (Manufacturer)						

^aSee Table 4. for the complete list of health outcomes

^bData are currently being processed and will be reported when received

^cAt the time of vaccination

Table 4. Health systems and pre-specified health outcomes

	VAERS	VSD	VA*	DMS*	CMS*	BEST*
Acute disseminated encephalomyelitis (ADEM)	X ^{1,2}	X	X			
Acute myocardial infarction	X	X	X		X	X
Anaphylaxis	X	X	X		X	X
Appendicitis	X	X	X		X	X
Acute respiratory distress syndrome (ARDS)		X	X			
Arthritis and arthralgia (not osteoarthritis or traumatic arthritis)	X ¹	X				
Ataxia	X ^{1,2}					
Autoimmune disease	X ¹					
Bell's palsy	X	X	X		X	X
Chronic inflammatory demyelinating polyneuropathy (CIDP)	X ^{1,2}					
COVID-19	X					
Death	X					
Disseminated intravascular coagulation (DIC)	X	X	X		X	X
Encephalitis	X	X	X			
Encephalomyelitis	X ^{1,2}	X	X		X	X
Encephalopathy	X ^{1,2}	X	X			
Guillain-Barré syndrome (GBS)	X	X	X		X	X
Immune thrombocytopenic purpura (ITP)		X	X		X	X
Kawasaki disease	X	X				X
Meningitis	X ^{1,2}	X	X			
Meningoencephalitis	X ^{1,2}	X	X			
Multiple sclerosis (MS)	X ^{1,2}					
Multisystem Inflammatory Syndrome in Adults (MIS-A)	X	X ³	X		X	X
Multisystem Inflammatory Syndrome in Children (MIS-C)	X	X ³				X
Myelitis	X ^{1,2}	X	X			
Myocarditis / pericarditis	X	X	X		X	X
Narcolepsy / cataplexy	X	X	X		X	X ⁴
Non-anaphylactic allergic reactions	X ¹					

Optic neuritis (ON)	X ^{1,2}					
Seizures / convulsions (convulsion is now an LLT under PT seizure)	X	X				X
Stroke	X	X			X	X
Thrombocytopenia	X					
Transverse myelitis (TM)	X	X			X	X
Vaccination during pregnancy/adverse pregnancy outcomes	X					X
Venous thromboembolism (VTE)	X	X				-
Pulmonary embolism	-	X			X	X
Deep vein thrombosis	-	-			X	X

¹Health outcomes are counted, but adverse event reports are not abstracted

²Diagnoses are grouped and reported as "Other clinically serious neurologic AEs" in VAERS

³Health outcomes are counted, and no sequential analysis is conducted

⁴Only includes narcolepsy

*TBD

Message

From: Markowitz, Lauri (CDC/DDID/NCIRD/DVD) [REDACTED]
Sent: 6/25/2021 8:18:26 PM
To: Anderson, Steven [REDACTED] Beresnev, Tatiana H (NIH) [REDACTED] Broder, Karen R (CDC) [REDACTED] Clark, Matthew (IHS) [REDACTED] Clark, Thomas A (CDC) [REDACTED] Cohn, Amanda C (CDC) [REDACTED] Collins, Limone [REDACTED] Cunningham, Fran [REDACTED] Daley, Matt [REDACTED] Daskalakis, Demetre C (CDC) [REDACTED] DeStefano, Frank (CDC) [REDACTED] Edwards, Kathy [REDACTED] Farizo, Karen [REDACTED] Forshee, Richard [REDACTED] Gee, Julianne M (CDC) [REDACTED] Hause, Anne M (CDC) [REDACTED] Helfand, Rita (CDC) [REDACTED] Hicks, Lauri (CDC) [REDACTED] Hopkins, Bob [REDACTED] Jackson, Lisa [REDACTED] Jennifer Nelson [REDACTED] Kelman, Jeffrey A (CMS) [REDACTED] Lee, Grace [REDACTED] Lu, Yun (CBER) [REDACTED] MacNeil, Jessica R (CDC) [REDACTED] Markowitz, Lauri (CDC) [REDACTED] Marquez, Paige L (CDC) [REDACTED] Mbaeyi, Sarah A (CDC) [REDACTED] McNally, Veronica [REDACTED] Mcneil, Michael M (CDC) [REDACTED] Myers, Tanya R (CDC) [REDACTED] Nair, Narayan [REDACTED] Oliver, Sara E (CDC) [REDACTED] Patricia Whitley-Williams [REDACTED] Riley, Laura [REDACTED] Rubin, Mary (HRSA) [REDACTED] Schechter, Robert [REDACTED] Schindelar, Jessica A (CDC) [REDACTED] Shanley, Edwin (CDC) [REDACTED] Shay, David K (CDC) [REDACTED] Shimabukuro, Tom (CDC) [REDACTED] Sotir, Mark J (CDC) [REDACTED] Steinberg, Judith L (OS) [REDACTED] Su, John (CDC) [REDACTED] Talbot, Keipp [REDACTED] Weintraub, Eric S (CDC) [REDACTED] Wharton, Melinda (CDC) [REDACTED] Wong, Hui-Lee [REDACTED] Woo, Jared M (CDC) [REDACTED] Young, Mardia A (CDC) [REDACTED]
Subject: [EXTERNAL] VaST - Draft minutes and report from June 21 (CONFIDENTIAL)
Attachments: 2021-06-21 - VaST minutes draft clean.docx; 2021-06-21 - VaST Report Data Table draft.docx

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear VaST members and attendees,

Attached are the draft minutes and summary report (with VaST comments) from the June 21 call. Please let us know if there are any corrections or edits.

The next VaST call is Monday, June 28 @ 1:30 – 3:00 pm EDT. The first half of the call will be a pregnancy-focused session, and the second half will cover other issues VaST is reviewing. Slides will be sent before the call.

Lauri Markowitz and Melinda Wharton

Lauri Markowitz, MD
VaST Co-Lead
CDC COVID-19 Response, Vaccine Task Force
Division of Viral Diseases
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

VaST meeting notes – DRAFT
June 21, 2021
Confidential

Presentation slides were distributed; presentations are briefly summarized in meeting notes. Chat notes not answered verbally on the call are available and some have been incorporated into the minutes.

Participants

Workgroup members: Bob Hopkins (NVAC-Chair), Lisa Jackson, Grace Lee (Chair), Veronica McNally, Laura Riley, Rob Schechter, Keipp Talbot, Pat Whitley-Williams

Ex officio and liaison participants: Tatiana Beresnev (NIH), Matthew Clark (IHS), Karen Farizo (FDA), Mary Rubin (HRSA) Judith Steinberg (OIDP), Hui-Lee Wong (FDA)

Federal partners: Fran Cunningham (VA), Kwan Hur (VA), Jeff Kelman (CMS)

CDC: Karen Broder, Tom Clark, Frank Destefano, Kathleen Dooling, Julianne Gee, Anne Hause, Rita Helfand, Lauri Hicks, Gayle Langley, Jessica MacNeil, Lauri Markowitz (CDC Co-lead), Paige Marquez, Michael McNeil, Tanya Myers, Sara Oliver, Jessica Schindelar, David Shay, Tom Shimabukuro, John Su, Melinda Wharton (CDC Co-lead), Jared Woo

Technical SMEs: Steve Anderson (FDA), Laurie Aukes (VSD), Ed Belongia (VSD), James Donahue (VSD), Rich Forshee (FDA), Kristin Goddard (VSD), Kayla Hanson (VSD), Ned Lewis (VSD), Yun Lu (FDA), Narayan Nair (FDA), Ousseney Zerbo (VSD)

Agenda

- v-safe - adolescents (Tanya Myers, CDC)
- VAERS TTS/CVST (John Su, CDC)
- VAERS GBS (Narayan Nair, FDA)
- RCA
 - FDA CMS - verbal update only (Richard Forshee, FDA)
 - VSD RCA - slides only
 - VA RCA (Fran Cunningham, VA)
- ACIP presentation dry runs
 - ISO – Tom Shimabukuro
 - VaST – Grace Lee

Administrative issues and announcements – Co-chairs and Co-leads

- Reminders about COI and confidentiality
- Doses distributed: 379,003,410; Doses administered: 317,966,408 (last updated: June 20)
 - Doses distributed: Pfizer-BioNTech: 200,685,030; Moderna: 156,884,080; Janssen/J&J: 21,434,300
 - Doses administered: Pfizer-BioNTech: 174,521,867; Moderna: 131,213,452; Janssen/J&J: 11,986,595; Unknown: 244,494
 - First doses: 177,088,290; Fully vaccinated: 149,667,646
 - These data are posted on the CDC website and are updated regularly ([HYPERLINK "https://covid.cdc.gov/covid-data-tracker/" \l "vaccinations").%E2%80%AF" \t "_blank"]

Session orientation

The VaST session included updated information on several signals and potential signals that VaST has been following: thrombosis with thrombocytopenia syndrome (TTS) after Janssen vaccine, Guillain-Barré syndrome (GBS) following Janssen vaccine, statistical signals for pulmonary embolism (PE), acute myocardial infarction (AMI), disseminated intravascular coagulation (DIC), and immune thrombocytopenic purpura (ITP) following Pfizer-BioNTech vaccine, and myocarditis following mRNA vaccines. After the v-safe and the VAERS presentations, the RCA updates addressed several different outcomes evaluated.

v-safe adolescents – Dr. Tanya Myers, CDC

Dr. Tanya Myers presented an update on the v-safe data among participants aged 12–15 years. The comparison of top solicited reactions between participants aged 12–15 years and 16–25 years showed that 12–15 year participants report less frequently across both doses of Pfizer-BioNTech vaccine. Reporting rates were also lower than from that age group in the clinical trials.

VAERS CVST/TTS – Dr. John Su, CDC

Dr. John Su presented a brief verbal update on CVST/TTS. There were no additional confirmed TTS reports since last week. The total remained at 36 cases post Janssen vaccination.

VAERS GBS – Dr. Narayan Nair, FDA

Dr. Narayan Nair presented an update and addressed questions from last week on GBS following Janssen vaccine in VAERS data. There are more observed than expected reports across all age groups and there is no obvious evidence of geographic clustering. FDA is working to obtain follow-up and/or medical records to confirm GBS cases.

Questions and discussion

1. There have been reports of GBS after AZ vaccine in India and the UK, which have reported bilateral facial weakness. Have we also seen this with Janssen vaccine?
 - FDA is waiting for medical records for a more thorough review. From the VAERS records, FDA has not seen bilateral facial paralysis; cases have had ascending symmetrical paralysis, as seen in typical GBS cases.
 - FDA has not seen Miller-Fisher GBS variant.
2. There was a comment about seasonality of GBS, such as GBS related to campylobacter gastrointestinal infections; what impact that could have on the observed post-vaccination data?
3. What is the timeline of availability of updates on GBS from EMA and BEST/CMS?
 - There is no timeline for EMA for the completion of their GBS evaluation following AZ vaccine.
 - GBS has been included in both CMS and BEST and has not signaled.

CMS RCA update – Dr. Rich Forshee, FDA

Dr. Forshee gave a brief verbal update on the CMS RCA statistical signals discussed at VaST last week. There were no new data to present, but work is ongoing and sensitivity analyses for PE and AMI will begin soon. There were no signals for GBS or myocarditis.

Questions and discussion

1. In CMS RCA as of May 1, 2021, the crude relative risk in males was larger compared to females for ITP (1.68 vs. 1.28) but no formal testing for the difference. No difference by sex was observed for AMI, PE and DIC.
2. FDA did not analyses data separately by AMI type 1 or 2.

VSD RCA (slides only)

Slides were circulated to update last analyses from June 14. The new analyses included more chart reviewed data and analyses among 12–39 years-olds as opposed to the previous analyses in 16–39 year-olds. These data also are included in Tom Shimabukuro's presentation.

- There were no signals for myocarditis/pericarditis in the 21 days after vaccination in the overall VSD population. However, for the 12–39 year-old sub-analysis for myocarditis/pericarditis, the Moderna dose 2 analysis has 16 cases in the risk compared to 0 in the comparison interval. The imbalance in the case split after Moderna dose 2 is driving observed elevated rate ratios. For the 1-7 day risk window, Pfizer dose 2, the RR was 6.0.
- The chart confirmed incidence of GBS during the 21 days after the Janssen vaccine, unadjusted for age-race-sex-site, is much higher than during the 21 days after mRNA vaccines. VSD has not identified a signal for GBS in primary analyses; continued monitoring is warranted.
- There were no signals for the four outcomes being investigated in the CMS RCA.

VA RCA – Dr. Fran Cunningham, VA

Dr. Fran Cunningham presented an update on the VA RCA. There were no signals for TTS, GBS or other outcomes following Janssen vaccine using a 42 day window. For Pfizer-BioNTech or Moderna vaccines, using 21 and 42 day windows, outcomes identified in the CMS RCA (PE, AMI, ITP and DIC) as well as GBS and myocarditis/pericarditis were investigated. There were no signals.

The analyses for PE, AMI, ITP and DIC were also conducted restricted to persons aged 65 years and older; there were no signals. The VA currently is conducting more chart reviews to confirm myocarditis/pericarditis cases.

Questions and discussion

1. What definition for AMI is used in the VA system?
 - The VA is using both type 1 and type 2 together. They can separate them upon request.
 - VSD also is including both type 1 and 2 AMI.

ACIP presentation – Dr. Tom Shimabukuro, CDC

Dr. Shimabukuro gave his draft presentation for the June 23 ACIP meeting. The presentation includes VSD and VAERS data and focuses on myocarditis/pericarditis.

Questions and discussion

1. Does abnormal echo and imaging include cMRI?
 - Yes, it does include cMRI.
2. Of 218 hospitalized, what was the average LOS
 - The VAERS data don't consistently capture LOS among hospitalized persons. Many appear to be between 2-4 days.

3. For the 2 of 29 with ICU stays is there any indication of the severity of clinical illness?
 - Both had ~4-5 hospital stays, mostly for monitoring. VSD will investigate further.
 - Regarding severity of cases overall, the qualitative impression is that cases were milder than generally seen in usual myocarditis.
4. VSD numbers for chart confirmed are 26 on some slides and 29 on others.
 - That's because there are 3 cases with symptom onset on day 0 (day of vaccination; the analyses use a 1–21 or 1–7 day risk interval.
 - There were 26 cases for days 1–21 and 29 cases include 3 cases that had chart confirmed symptom onset on day 0.

ACIP presentation – Dr. Grace Lee, VaST

Dr. Lee presented an overview of VaST discussion and interpretation of COVID-19 vaccine safety data regarding on myocarditis/pericarditis; the risk of myocarditis following mRNA vaccination in adolescents and young adults is notably higher after dose 2 and in males.

Questions and discussion

1. The group felt that the wording should be changed from “potential association” to “likely association”. Some additional suggestions for wording changes were also made.

Combined Systems Safety Monitoring Report - DRAFT

June 21, 2021

Confidential

The VaST session on June 21, 2021 included updated information on several signals and potential signals that VaST has been following: thrombosis with thrombocytopenia syndrome (TTS) after Janssen vaccine, Guillain-Barré syndrome (GBS) following Janssen vaccine, statistical signals for pulmonary embolism (PE), acute myocardial infarction (AMI), disseminated intravascular coagulation (DIC), and immune thrombocytopenic purpura (ITP) following Pfizer-BioNTech vaccine, and myocarditis following mRNA vaccines.

There were presentations or updated data from v-safe, the Vaccine Adverse Event Reporting System (VAERS), the Vaccine Safety Datalink (VSD) and Department of Veterans Affairs (VA) rapid cycle analyses (RCAs), and a brief update from the Food and Drug Administration (FDA) Centers for Medicare & Medicaid Services (CMS) RCA. VaST also heard dry runs for the ACIP meeting this week, which will focus on myocarditis.

- Adolescent v-safe data: The v-safe presentation showed that persons aged 12-15 years reported solicited reactions slightly less frequently than those aged 16-26 years. Reporting rates in v-safe were also lower than from that age group in the clinical trials.
- GBS: Additional analyses in VAERS showed elevated observed/expected reports after the Janssen vaccine in all age groups, and no evidence of geographic clustering. GBS did not signal in any of the RCAs.
- FDA CMS RCA statistical signals: There were no new data from the FDA CMS RCA analyses. The VSD and VA RCAs continue to show no statistical signals for PE, AMI, DIC or ITP, including in an updated VA RCA analysis restricted to persons age 65 years and older.
- Myocarditis: Compared with the last VaST review of myocarditis from VAERS and VSD on June 7, substantially more data are now available and suggest a likely association with mRNA vaccination.

VaST members felt that:

- Full presentation of the myocarditis data to ACIP this week is important, as well as the planned presentation on risks and benefits.
- The myocarditis cases need to be put into context of the risk and morbidity of COVID-19 infection. With schools opening and other in-person activities resuming, the risk associated with COVID-19 disease to unvaccinated persons will likely increase.
- It is important to obtain a more complete picture of the clinical course of myocarditis cases. While cases appear mild, more data are needed to fully describe any morbidity.
- Long-term follow up of myocarditis cases is needed to understand clinical course and natural history following COVID-19 vaccination.
- VaST members discussed a variety of issues, including possible under ascertainment of morbidity due to 'silent' myocarditis, persons not seeking care due to lack of access, and lack of clinical advice for restricted physical activity post disease.
- VaST members discussed potential sources of data, including asking clinical trials to consider adding an earlier blood draw to look for elevated troponin levels in children and adults.
- Data from vaccine safety monitoring systems for potential cases of myocarditis should continue to be obtained as vaccination rates increase in younger age groups.
- Further data are needed on the additional potential signals being reviewed by VaST.

Table 1. COVID-19 vaccine monitoring systems reviewed by the VaST – Pfizer BioNTech (recommended for use in persons age ≥ 12 years)

Red indicates updated or new data this week

Vaccine Safety Program	Outcomes Monitored	Population Monitored	Population captured	Analyses	Selected Results	Assessment/action
Passive Surveillance						
Vaccine Adverse Event Reporting System (VAERS) (Myocarditis/pericarditis data through 6/11/21; GBS data through 6/1/21)	All health events, adverse events of special interest ^a	US population	161 million total doses administered	Descriptive and empirical Bayesian data mining	0 confirmed TTS reports to VAERS 791 myocarditis/pericarditis reports after Pfizer-BioNTech vaccine – 150 after dose 1, 563 after dose 2, 78 unknown 144 GBS reports to VAERS; crude reporting rate .9/million doses administered	Anaphylaxis associated with vaccination, first detected by reports from UK and early reporting in the US; assessed by follow-up with providers, chart review, CISA consultations; clinical guidance changed (initially in December 2020 and last updated March 5, 2021) Further work being done to define myocarditis risk. For any mRNA vaccine, observed cases higher than expected in 7-day window post dose 2 in 12-49 yr-old males and 12-29 yr-old females No concerns raised
VA ADERS (Data through 4/11/2021)	All health events	VA employees and Veteran patients	1,071,630 first doses administered; 826,866 second doses administered	Descriptive	No signals in the analysis for combined mRNA vaccines	No concerns raised

DoD VAERS (Population data through 3/19/2021; Results data through 4/3/2021)	All health events, adverse events of special interest	Active duty and beneficiaries	976,479 vaccines administered	Descriptive	22 cases of myocarditis following mRNA vaccines (16 Moderna, 6 Pfizer) • Background rate: 2-23 cases 19 cases of myocarditis following dose 2 of mRNA vaccines • Background rate: 1-9 case 84 total AE reports • 48 medically attended health impact events • 12 suspected AESIs	Ongoing discussion regarding communication of myocarditis risk in younger males
Indian Health Services (IHS) VAERS (Data through 4/26/2021)	All health events, adverse events of special interest ^a	Persons who identify as American Indian/Alaska Native	425k vaccines administered	Descriptive		No concerns raised
Active Surveillance						
V-safe (Data through 6/13/2021)		Vaccinees who enroll	57,126 adolescent persons (12-15 years) enrolled	Descriptive	Injection site pain, fatigue, and headache were the top 3 solicited reactions 0-7 days after vaccine Solicited reactions among 12-15 year-olds reported less frequently than 16-25 year-olds Pregnancy and neonatal outcomes of interest within background rates	No concerns raised
V-safe Pregnancy Registry (Data through 5/20/2021)		Vaccinees who enroll	2,535 enrolled	Descriptive		No concerns raised
Department of Veterans Affairs (VA) Active Surveillance System (Data through 6/6/21)	Pre-specified health outcomes ^a	Veteran Patients	1,303,967 first doses administered; 1,184,335 second doses administered	Descriptive; historical comparator analysis	No signal for myocarditis/pericarditis in the 21- or 42-day window for veterans 18-39 years or 65+ years.	Only signal for anaphylaxis. Continued monitoring and chart reviews are being done to investigate myocarditis/pericarditis and age stratifications
Vaccine Safety Datalink (VSD) (Data through 6/12/21)	Pre-specified health outcomes ^a	Patients enrolled in participating health care organization	3.1 million first doses administered; 2.7 million second doses administered	Descriptive; Vaccinated and unvaccinated concurrent comparison,	No signal for myocarditis/pericarditis, GBS, or any other AESI, using a 21-day risk interval in vaccinated comparator analysis. Elevated RR now observed after dose 2 for 12-39 year-olds	Further monitoring and analyses of myocarditis/pericarditis in younger age groups needed

Vaccine Safety Datalink (VSD) Mortality Study (Vaccinated through 2/27 and death data through 3/20/21)	Deaths	VSD sites enrolled in the mortality study; vaccinated before 2/27 and number of deaths before 3/20	219,570 first doses administered; 105,919 second doses administered	Descriptive; Vaccinated and unvaccinated concurrent comparison, sequential analyses	0.8 dose 1 mortality rate per 100 person-years 0.7 dose 2 mortality rate per 100 person-years 1.0 comparator mortality rate per 100 person-years	No concerns raised
Defense Medical Surveillance System (DMSS)^b	Pre-specified health outcomes ^a					
FDA - Centers for Medicare and Medicaid Services (CMS)^b (Data through 6/14/2021)	Pre-specified health outcomes ^a	CMS population 65 and above		Historical comparator analysis	Relative risk of 1.24 for AMI, after seasonality adjustment. The RR was not statistically significant. Relative risk of 1.35 for PE, after seasonality adjustment. The RR was statistically significant. Relative risk of 1.59 for DIC, after seasonality adjustment. The RR was not statistically significant. Relative risk of 1.35 for ITP, after seasonality adjustment. The RR was not statistically significant.	Further investigation including signal characterization and evaluation in other databases is needed in order to properly assess the signals
BEST initiative^b	Pre-specified health outcomes ^a					
NPTC Vaccine Sentinel Survey (Data through 4/26/21)	Pre-specified health outcomes	Persons who identify as AI/AN	425k vaccines administered	Descriptive	256 total AE reports • 67 medically attended health impact events • 23 suspected AESIs	No concerns raised

Vaccine Trials (Manufacturer)						See GRADE tables https://www.cdc.gov/vaccines/acip/refs/grade/covid-19-pfizer-biontech-vaccine.html	
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^aSee Table 4 for the complete list of health outcomes

^bData are currently being processed and will be reported when received

^cAt the time of vaccination

Table 2. COVID-19 vaccine monitoring systems reviewed by the VaST – Moderna (recommended for use in persons age ≥ 18 years)

Red indicates new results this week

Vaccine Safety Program	Outcomes Monitored	Population Monitored	Population captured	Analyses	Selected Results	Assessment/action
Passive Surveillance						
Vaccine Adverse Event Reporting System (VAERS) (Myocarditis/pericarditis data through 6/11/21; GBS data through 6/1/21)	All health events, adverse events of special interest ^a	US population	125 million total doses administered	Descriptive and empirical Bayesian data mining	0 confirmed TTS reports to VAERS 117 myocarditis/pericarditis reports after Moderna – 117 after dose 1; 264 after dose 2; 54 unknown	Anaphylaxis associated with vaccination, first detected by early reporting in US; assessed by follow-up with providers, chart review, CISA consultations; clinical guidance changed (initially in December 2020 and last updated March 5, 2021) Further work being done to define myocarditis risk. For any mRNA vaccine, observed cases higher than expected in 7-day window post dose 2 in 12-49 yr-old males and 12-29 yr-old females No concerns raised
VA ADERS (Data through 4/11/2021)	All health events	VA employees and Veteran patients	1,262,482 first doses administered; 977,202 second doses administered	Descriptive	117 GBS reports to VAERS; crude reporting rate .93/million doses administered No signals in the analysis for combined mRNA vaccines	No concerns raised
DoD VAERS (Population data through 3/19/2021; Results data through 4/3/2021)	All health events, adverse	Active duty and beneficiaries	852,548 vaccines administered	Descriptive	22 cases of myocarditis following mRNA vaccines • Background rate: 2-23 cases	Ongoing discussion regarding communication of myocarditis risk in younger males

	events of special interest						19 cases of myocarditis following dose 2 of mRNA vaccines Background rate: 1-9 cases	
Indian Health Services (IHS) VAERS (Data through 4/26/2021)	All health events, adverse events of special interest ^a	Persons who identify as AI/AN	700k vaccines administered	Descriptive	71 total AE reports 43 medically attended health impact events 15 suspected AESIs	No concerns raised		
Active Surveillance								
V-safe (Data through 5/24/2021)		Vaccinees who enroll	2,627,416 persons enrolled; 23,064 pregnancies ^c	Descriptive	126 reports overall (all submitted to VAERS) 27 serious reports - Solicited reactions higher after dose 2 than dose 1	No concerns raised		
V-safe Pregnancy Registry (Data through 5/20/2021)		Vaccinees who enroll	2,192 enrolled	Descriptive	Pregnancy and neonatal outcomes of interest within background rates	No concerns raised		
Department of Veterans Affairs (VA) Active Surveillance System (Data through 6/6/2021)	Pre-specified health outcomes ^a	Veteran Patients	1,502,339 first doses administered; 1,413,653 second doses administered	Descriptive; historical comparator analysis	No signal for myocarditis or pericarditis in the 42-day window for veterans 18-39 years or 65+ years	Only signal for anaphylaxis, as identified earlier in other post-authorization safety monitoring	No concerns raised	
Vaccine Safety Datalink (VSD) (Data through 6/12/21)	Pre-specified health outcomes ^a	Patients enrolled in participating health care organization	2.4 million first doses administered; 2.2 million second doses administered	Descriptive; Vaccinated and unvaccinated concurrent comparison, sequential analyses	No signal for myocarditis/pericarditis, GBS, or any other AESI, using a 21-day risk interval in vaccinated comparator analysis	Further monitoring and analyses of myocarditis/pericarditis in younger age groups in VSD needed		
Vaccine Safety Datalink (VSD) Mortality Study	Deaths	VSD sites enrolled in the mortality study; vaccinated	220,799 first doses administered; 86,650 second	Descriptive; Vaccinated and unvaccinated	Imbalance of case split after dose 2 driving the observed elevated rate ratios for patients 12-39 years	0.6 dose 1 mortality rate per 100 person-years	No concerns raised	

(Vaccinated through 2/27 and death data through 3/20/21)		before 2/27 and number of deaths before 3/20	doses administered	concurrent comparison, sequential analyses	0.7 dose 2 mortality rate per 100 person-years 1.0 comparator mortality rate per 100 person-years	
Defense Medical Surveillance System (DMSS)^b	Pre-specified health outcomes ^a					
FDA - Centers for Medicare and Medicaid Services (CMS)^b (Data through 4/3/2021)	Pre-specified health outcomes ^a	CMS population 65 and above		Historical comparator analysis	No signals in the analysis	No concerns raised
BEST initiative^b	Pre-specified health outcomes ^a					
NPTC Vaccine Sentinel Survey (Data through 4/26/21)		Persons who identify as American Indian/Alaska Native	700k vaccines administered	Descriptive	214 total AE reports • 39 medically attended health impact events • 21 suspected AESIs	No concerns raised
Vaccine Trials (Manufacturer)					See GRADE tables https://www.cdc.gov/vaccines/acip/records/grade/covid-19-pfizer-biontech-vaccine.html	

^aSee Table 4 for the complete list of health outcomes

^bData are currently being processed and will be reported when received

^cat the time of vaccination

Table 3. COVID-19 vaccine monitoring systems reviewed by the VaST – Janssen/Johnson & Johnson (recommended for use in persons age ≥ 18 years)

Red indicates new results this week

Vaccine Safety Program	Outcomes Monitored	Population Monitored	Population captured	Analyses	Selected Results	Assessment/action
Passive Surveillance						
Vaccine Adverse Event Reporting System (VAERS) (TTS and Myocarditis/pericarditis data through 6/4/21; GBS data through 6/1/21)	All health events, adverse events of special interest ^a	US population	11 million total doses administered	Descriptive and empirical Bayesian data mining	35 confirmed TTS reports to VAERS 12.3 reporting rate per million for females aged 30-39 years 9.6 reporting rates per million for females aged 40-49 years 27 reports after Janssen/J&J vaccine Elevated observed/expected in all age groups; no geographic clustering. 80 GBS reports; crude reporting rate 1.51 per 100,000 person years No signals were detected	Warning and other information provided in updated EUA and MMWR last week, and reflected in clinical guidance No concerns raised Further investigation needed in VAERS and by different systems
VA ADERS (Data through 4/11/2021)	All health events	VA employees and Veteran patients	109,483 vaccines administered	Descriptive	No signals were detected	No concerns raised
DoD VAERS (Data through 3/19/2021)	All health events, adverse events of special interest	Active duty and beneficiaries	28,640 vaccines administered	Descriptive	4 total AE reports 0 serious AE reports 0 death reports	No concerns raised
Indian Health Services (IHS) VAERS (Data through 4/26/2021)	All health events, adverse events of special interest ^a	Persons who identify as AI/AN	20k vaccines administered	Descriptive	3 total AE reports 2 medically attended health impact events 0 suspected AESIs	No concerns raised
Active Surveillance						
V-safe (Data through 5/24/2021)		Vaccinees who enroll	332,084 persons enrolled	Descriptive	28.3% of participants reported being unable to do normal daily activities	No concerns raised

				3,118 pregnancies		1.4% of participants reported requiring a medical visit	
V-safe Pregnancy Registry (Data through 5/20/2021)		Vaccinees who enroll	277 enrolled	Descriptive	Pregnancy and neonatal outcomes of interest within background rates	No concerns raised	
Department of Veterans Affairs (VA) Active Surveillance System (Data through 6/6/2021)	Pre-specified health outcomes ^a	Veteran Patients	169,294 doses administered	Descriptive; historical comparator analysis	No signals for CVST, myocarditis/pericarditis, GBS or other AESI in the 42-day window historical comparator analysis	No concerns raised	
Vaccine Safety Datalink (VSD) (Data through 6/12/21)	Pre-specified health outcomes ^a	Patients enrolled in participating health care organization	294,848 doses administered	Descriptive; Sequential analysis will be added when available	6 confirmed cases of GBS following vaccination.	Further analysis of GBS following vaccine is needed.	
Vaccine Safety Datalink (VSD) Mortality Study (Vaccinated through 2/27 and death data through 3/20/21)	Deaths	VSD sites enrolled in the mortality study; vaccinated before 2/27 and number of deaths before 3/20	Data not yet available	Descriptive; Vaccinated and unvaccinated concurrent comparison, sequential analyses	Data not yet available		
Defense Medical Surveillance System (DMSS)^b	Pre-specified health outcomes ^a						
FDA - Centers for Medicare and Medicaid Services (CMS)^b	Pre-specified health outcomes ^a	CMS population 65 and above		Historical comparator analysis	Data not yet available		
BEST initiative^b	Pre-specified health outcomes ^a						

NPTC Vaccine Sentinel Survey (Data through 4/26/21)		Persons who identify as American Indian/Alaska Native	20k vaccines administered	Descriptive	10 total AE reports • 1 medically attended health impact events • 0 suspected AESIs	No concerns raised
Vaccine Trials (Manufacturer)					See GRADE tables [HYPERLINK "https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/28-03-01/03-COVID-Gargano.pdf"]	

^aSee Table 4. for the complete list of health outcomes

^bData are currently being processed and will be reported when received

^cAt the time of vaccination

Table 4. Health systems and pre-specified health outcomes

	VAERS	VSD	VA*	DMESS*	CMS*	BEST*
Acute disseminated encephalomyelitis (ADEM)	X ^{1,2}	X	X			
Acute myocardial infarction	X	X	X		X	X
Anaphylaxis	X	X	X		X	X
Appendicitis	X	X	X		X	X
Acute respiratory distress syndrome (ARDS)		X	X			
Arthritis and arthralgia (not osteoarthritis or traumatic arthritis)	X ¹	X				
Ataxia	X ^{1,2}					
Autoimmune disease	X ¹					
Bell's palsy	X	X	X		X	X
Chronic inflammatory demyelinating polyneuropathy (CIDP)	X ^{1,2}					
COVID-19	X					
Death	X					
Disseminated intravascular coagulation (DIC)	X	X	X		X	X
Encephalitis	X	X	X			
Encephalomyelitis	X ^{1,2}	X	X		X	X
Encephalopathy	X ^{1,2}	X	X			
Guillain-Barré syndrome (GBS)	X	X	X		X	X
Immune thrombocytopenic purpura (ITP)		X	X		X	X
Kawasaki disease	X	X				X
Meningitis	X ^{1,2}	X	X			
Meningoencephalitis	X ^{1,2}	X	X			
Multiple sclerosis (MS)	X ^{1,2}					
Multisystem Inflammatory Syndrome in Adults (MIS-A)	X	X ³	X		X	X
Multisystem Inflammatory Syndrome in Children (MIS-C)	X	X ³				X
Myelitis	X ^{1,2}	X	X			
Myocarditis / pericarditis	X	X	X		X	X
Narcolepsy / cataplexy	X	X	X		X	X ⁴
Non-anaphylactic allergic reactions	X ¹					

Optic neuritis (ON)	X ^{1,2}					
Seizures / convulsions (convulsion is now an LLT under PT seizure)	X	X				X
Stroke	X	X			X	X
Thrombocytopenia	X					
Transverse myelitis (TM)	X	X			X	X
Vaccination during pregnancy/adverse pregnancy outcomes	X					X
Venous thromboembolism (VTE)	X	X				-
Pulmonary embolism	-	X			X	X
Deep vein thrombosis	-	-			X	X

¹Health outcomes are counted, but adverse event reports are not abstracted

²Diagnoses are grouped and reported as "Other clinically serious neurologic AEs" in VAERS

³Health outcomes are counted, and no sequential analysis is conducted

⁴Only includes narcolepsy

*TBD