

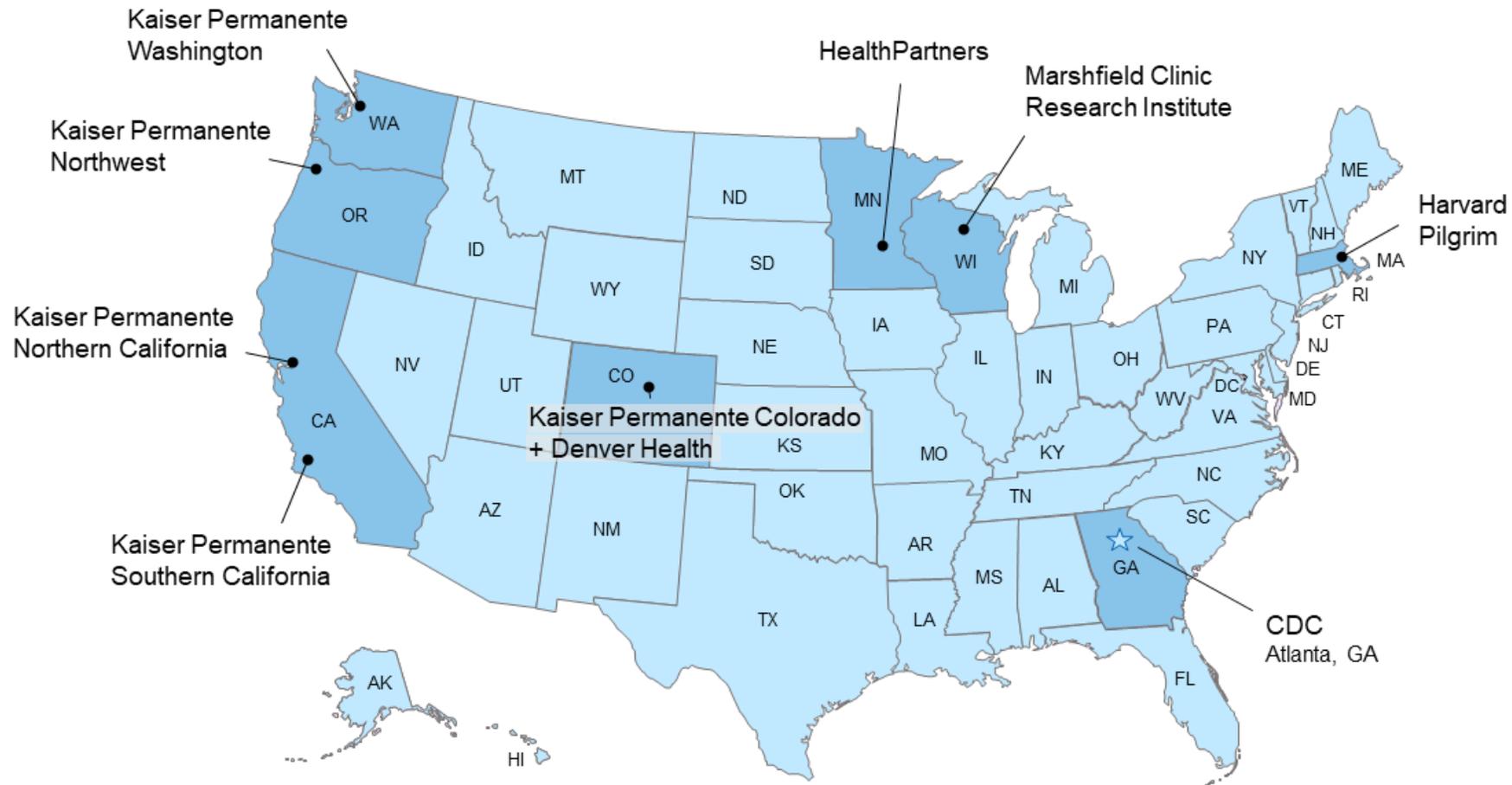
Vaccine Safety Datalink Rapid Cycle Analyses: Uptake and Safety of COVID-19 Vaccines in 5–11 and 12–17-Year-Olds

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The Vaccine Safety Datalink (VSD)



- Established in 1990
- Collaborative project between CDC and 9 integrated healthcare organizations

VSD Rapid Cycle Analysis (RCA)

Aims:

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

Surveillance began in December 2020.

VSD COVID-19 Vaccine RCA Outcomes

#	Outcomes	Settings	Risk Interval (days)	Chart Review	Monitoring Only	Exclude if COVID-19 in the Prior X Days
1	Acute disseminated encephalomyelitis	E, I	1-21, 1-42	Yes		
2	Acute myocardial infarction – First Ever	E, I	1-21, 1-42			30 days
3	Acute respiratory distress syndrome	E, I	0-84		Yes	42 days
4	Anaphylaxis – First in 7 days	E, I	0-1	Yes	Yes	
5	Appendicitis	E, I	1-21, 1-42			
6	Bell's palsy – First Ever	E, I, O	1-21, 1-42			30 days
7	Cerebral venous sinus thrombosis	E, I	1-21, 1-42	Yes		30 days
8	Disseminated intravascular coagulation	E, I	1-21, 1-42			42 days
9	Encephalitis / myelitis / encephalomyelitis	E, I	1-21, 1-42			30 days
10	Guillain-Barré syndrome	E, I	1-21, 1-42	Yes		
11	Immune thrombocytopenia	E, I, O	1-21, 1-42			30 days
12	Kawasaki disease	E, I	1-21, 1-42			
13	Multisystem inflammatory syndrome in children/adults (MIS-C/MIS-A)	E, I	0-84		Yes	
14	Myocarditis / pericarditis – First in 60 Days	E, I	1-21, 1-42	Yes (40 years of age and younger)		30 days
15	Narcolepsy / cataplexy	E, I, O	0-84		Yes	
16	Pulmonary embolism – First Ever	E, I	1-21, 1-42			30 days
17	Seizures	E, I	1-21, 1-42			30 days
18	Stroke, hemorrhagic	E, I	1-21, 1-42			30 days
19	Stroke, ischemic	E, I	1-21, 1-42			30 days
20	Thrombosis with thrombocytopenia syndrome – First Ever	E, I	1-21, 1-42	Yes		30 days
21	Thrombotic thrombocytopenic purpura	E, I	1-21, 1-42			30 days
22	Transverse myelitis	E, I	1-21, 1-42	Yes		
23	Venous thromboembolism – First Ever	E, I, O	1-21, 1-42			30 days

Abbreviations: E=ED, I=Inpatient, O=Outpatient

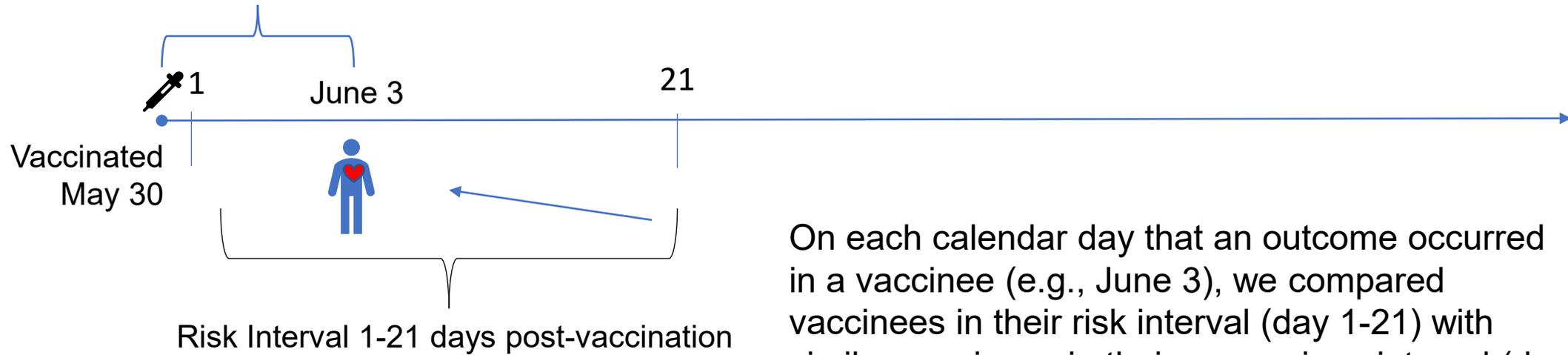
Myocarditis/Pericarditis: Electronic Case Identification using ICD-10 Codes

Initial Code List (based on consultation with cardiologist)	Revised Code List (based on VSD feedback)
<ul style="list-style-type: none">• B33.22 Viral myocarditis• B33.23 Viral pericarditis• I30.* Acute pericarditis• I40.* Acute myocarditis	<ul style="list-style-type: none">• B33.22 Viral myocarditis• B33.23 Viral pericarditis• I30.* Acute pericarditis• I40.* Acute myocarditis• I51.4 Myocarditis, unspecified• I31.9 Disease of the pericardium, unspecified

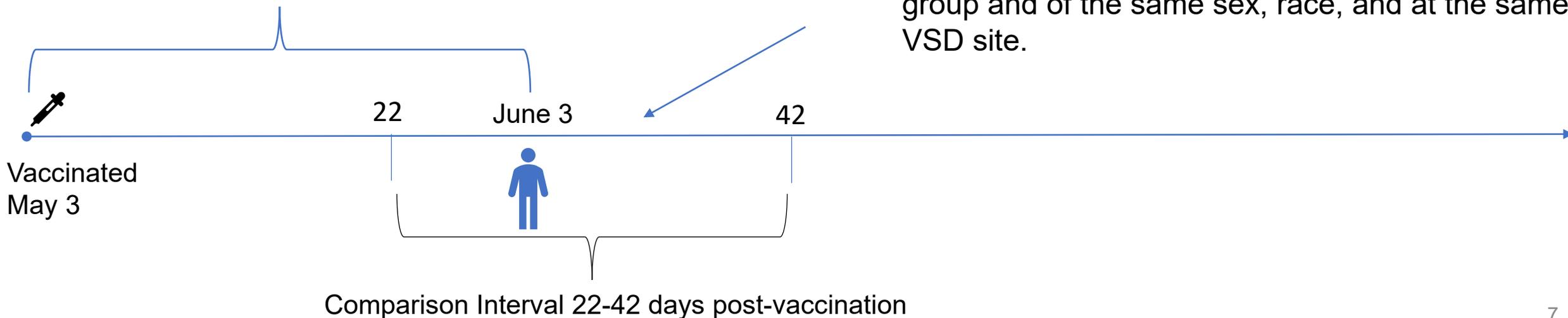
Analytic Strategy

- For the primary analysis, the number of outcomes observed in the risk interval (1-21 days) after COVID-19 vaccination were compared to the number expected.
- The expected was derived from “vaccinated concurrent comparators” who were in a comparison interval (days 22-42) after COVID-19 vaccination.
- On each day that an outcome occurred, vaccinees who were in their risk interval were compared with similar vaccinees who were concurrently in their comparison interval.
 - Comparisons were adjusted for age group, sex, race/ethnicity, VSD site, as well as calendar date.

Vaccinees with Myocarditis in Risk Interval and a Concurrent Comparator



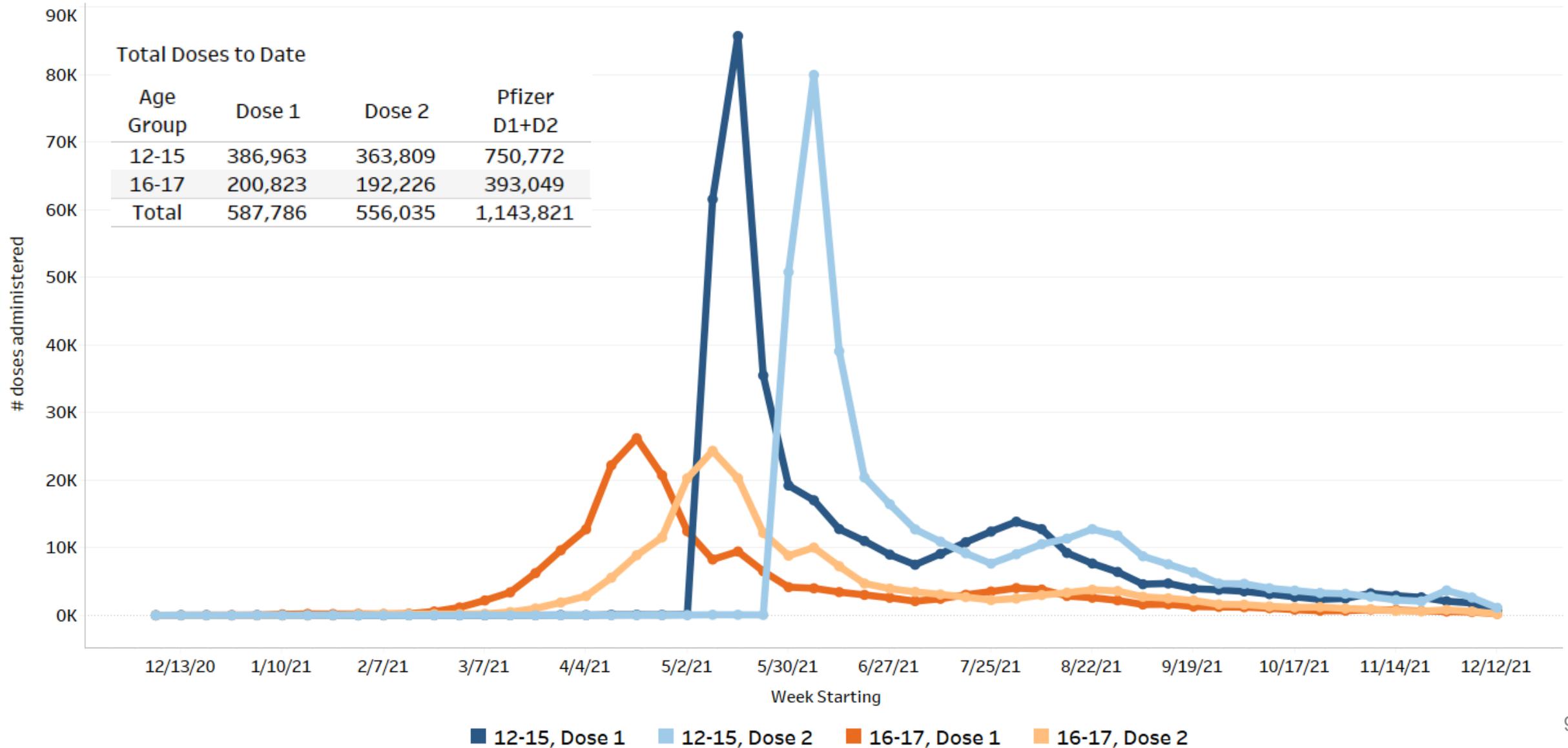
On each calendar day that an outcome occurred in a vaccinee (e.g., June 3), we compared vaccinees in their risk interval (day 1-21) with similar vaccinees in their comparison interval (day 22-42).



By similar, we mean they were in the same age group and of the same sex, race, and at the same VSD site.

**COVID-19 Vaccine Uptake &
Myocarditis/Pericarditis Analyses
among 12–17-Year-Olds
(Data Through 12/25/2021)**

Pfizer Vaccine Totals by Week and Adolescent Age Group



Myocarditis/Pericarditis Chart Review Summary

- Chart review completed through **December 30, 2021** for 53/75 cases aged 12-17 years (22 pending)
 - ✓ Cases identified any time after dose 1 or 2 of Pfizer COVID-19 vaccine
- Initial chart review followed with adjudication by an infectious disease clinician and/or a cardiologist
 - ✓ Confirm incident following vaccination
 - ✓ Meet CDC case definition (myocarditis, pericarditis, or myopericarditis)
 - ✓ Evaluate level of certainty for myocarditis
- **Adjudication confirmed 47/53 (89%) myocarditis/pericarditis cases**
 - ✓ 43 validated cases among 12–17-year-olds, with onset 0-21 days after vaccination
 - ✓ 39 validated cases among 12–17-year-olds, with onset 0-7 days after vaccination

Characteristics of Validated Myocarditis/Pericarditis Cases Aged 12-17 Years in the 0-21 Days after Pfizer COVID-19 Vaccine (N=43)

Descriptive Characteristics	No. (%)
12-15 years of age	29 (67%)
16-17 years of age	14 (33%)
Male sex	37 (86%)
Race/ethnicity	
White	17 (40%)
Black	3 (7%)
Asian	1 (2%)
Hispanic	16 (37%)
Native American/Pacific Islander	1 (2%)
Multiple/other	1 (2%)
Unknown	4 (9%)
History of COVID-19 infection	2 (5%)
History of myocarditis/pericarditis	2 (5%)
Symptom onset post-vaccination, median (range)	2 days (0-20 days)
Adjudication diagnosis	
Acute myocarditis	23 (53%)
Myopericarditis	18 (42%)
Acute pericarditis	2 (5%)

Characteristics of Validated Myocarditis/Pericarditis Cases Aged 12-17 Years in the 0-21 Days after Pfizer COVID-19 Vaccine (N=43)

Level of Care and Status	No. (%)
Highest level of care	
Emergency department	4 (9%)
Admitted to hospital (not ICU)	28 (65%)
Admitted to ICU	11 (26%)
Length of hospital stay, median days (range)	2 (0-7)
0 days (same day discharge)	3 (7%)
1 day	12 (28%)
2 days	8 (19%)
3 days	8 (19%)
4 days	5 (12%)
5 days*	4 (9%)
≥6 days*	3 (7%)
Discharged to home	43 (100%)
Follow-up visit noted at the time of chart review	31 (72%)

*All cases with a length of stay ≥5 days were admitted to the ICU

Characteristics of Validated Myocarditis/Pericarditis Cases Aged 12-17 Years that were **Admitted to the ICU** (N=11)

- Age range: 13-17 years
- Sex: All male
- Race/ethnicity: 5 Hispanic, 4 White, 1 Black, 1 unknown
- Adjudicated Diagnosis: 4 acute myocarditis, 7 myopericarditis
- Among those admitted to ICU during hospitalization, median LOS (range): 5 days (2-7 days)
- Chart notes for 2 cases indicated ICU admission was preventative; one additional chart noted that ICU admission was unrelated to myocarditis.

**Analyses of Validated
Myocarditis/Pericarditis after Pfizer COVID-19
Vaccine among 12–17-Year-Olds
(Data Through 12/25/2021)**

Validated Myocarditis/Pericarditis, among **12–17-Year-Olds** in the 0-7 and 0-21 Day Risk Interval after Pfizer Vaccine by Dose Compared with Outcome Events in Vaccinated Comparators on the Same Calendar Days

				Analysis			
Risk Interval	Dose	Events in Risk Interval	Events in Comparison Interval ¹	Adjusted Rate Ratio ²	95% Confidence Interval	2-Sided P-value	Excess Cases in Risk Period per 1 Million Doses
Days 0-21	Both Doses	45	3	10.16	3.41 – 42.39	<0.001	36.2
	Dose 1	3	3	1.16	0.17 – 8.05	0.873	0.7
	Dose 2	39	3	15.21	5.07 – 63.70	<0.001	70.8
Days 0-7	Both Doses	41	3	29.63	9.76 – 125.24	<0.001	34.6
	Dose 1	1	3	1.25	0.04 – 13.93	0.836	0.3
	Dose 2	37	3	46.18	15.07 – 196.40	<0.001	70.2

¹Comparison interval is 22–42 days after either dose.

²Adjusted for VSD site, 5-year age group, sex, race/ethnicity, and calendar date.

Validated Myocarditis/Pericarditis: Follow-up Chart Review

- Follow-up chart review conducted 3 months after initial diagnosis to obtain information on:
 - ✓ Symptoms and diagnostic evaluation at most recent follow-up visit
 - ✓ Recovery status at most recent follow-up visit including:
 - Ongoing symptoms
 - Medications
 - Exercise restrictions
- As of December 30, 2021, follow-up reviews have been completed for 32 validated cases among 12–17-year-olds that were time-eligible for follow-up review
- Of these 32 cases, **24** had at least 1 follow-up visit at least 1 month since the initial encounter

Follow-Up Information on Validated Myocarditis/Pericarditis Cases Aged 12-17 Years (N=24)*

Follow-Up Visit Timing, Symptoms, and Diagnostic Testing	No. (%)
Time from discharge to follow-up visit, median (range)	88.5 days (28-153 days)
Follow-up visit at least 3 months since initial encounter	13 (54%)
No new or worsening symptoms noted	13 (54%)
Any new or worsening symptom (not mutually exclusive)	11 (46%)
Chest pain/pressure/discomfort	9 (38%)
Shortness of breath/pain with breathing	3 (13%)
Palpitations	3 (13%)
Fatigue	1 (4%)
Other (orthostatic hypotension, dizziness, etc.)	3 (13%)
Troponin level obtained	18 (75%)
Abnormal troponin level	4/18 (22%)
Electrocardiogram completed	18 (75%)
Abnormal findings	9/18 (50%)
Echocardiogram completed	17 (71%)
Abnormal findings	2/17 (12%)
Cardiac MRI completed	1 (4%)
Abnormal findings	0 (0%)

*Only included cases with at least 1 follow-up visit at least 1 month since initial episode.
6 of these cases were admitted to the ICU during their initial encounter.

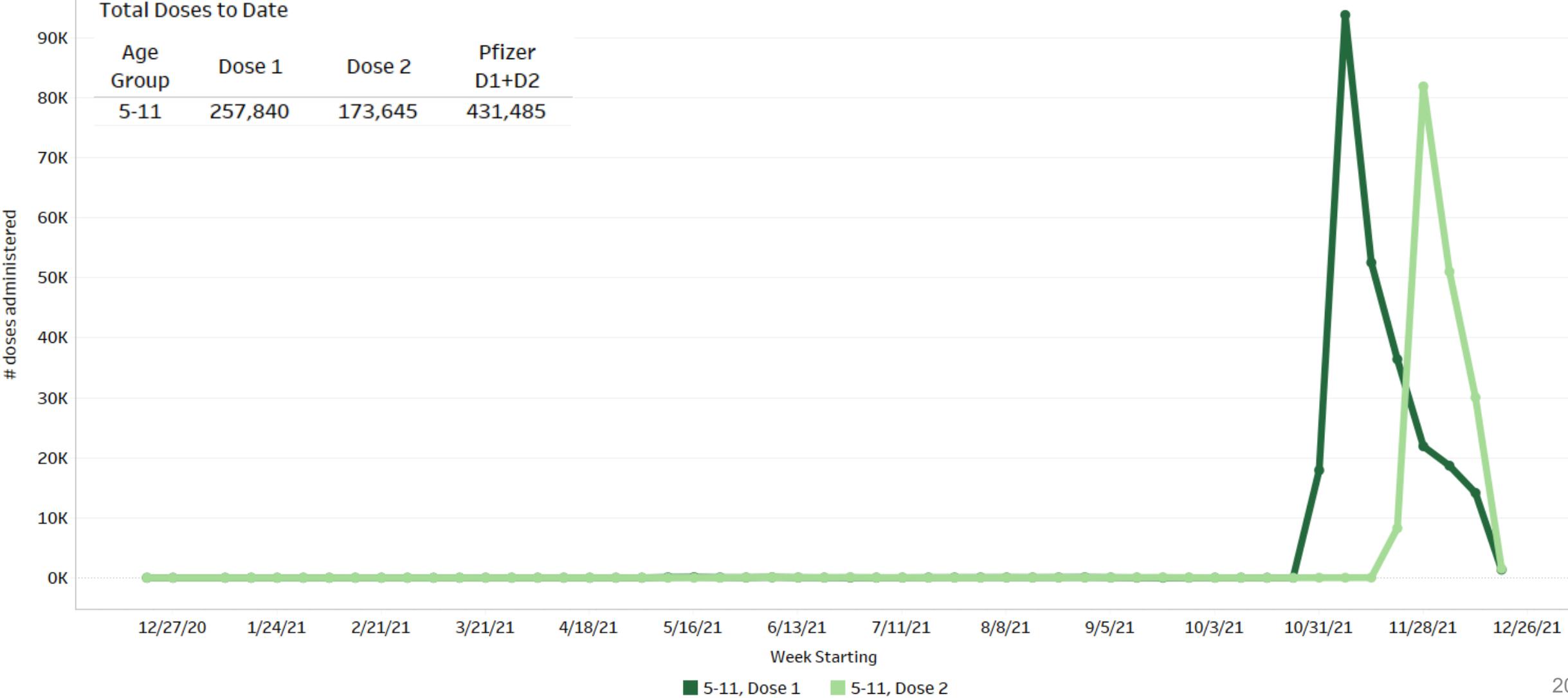
Follow-Up Information on Validated Myocarditis/Pericarditis Cases Aged 12-17 Years (N=24)*

Status at Time of Most Recent Follow-Up Visit	No. (%)
Current Status (not mutually exclusive)	
Recovered: no symptoms, medication, or exercise restrictions	11 (46%)
Still symptomatic	7 (29%)
Still on medication (e.g., NSAIDs, colchicine)	2 (8%)
Still on exercise/physical activity restrictions	6 (25%)

*Only included cases with at least 1 follow-up visit at least 1 month since initial episode.
6 of these cases were admitted to the ICU during their initial encounter.

**COVID-19 Vaccine Uptake
& Primary Analyses
among 5–11-Year-Olds
(Data Through 12/11/2021)**

Pfizer Vaccine Totals by Week for Children Aged 5-11 Years



RCA Analyses for 5–11-Year-Olds

- Same methods used for children aged 5-11 years, as for adults and adolescents
- In the VSD, there are ~848,300 children aged 5-11 years
- As of Dec 25, 2021, 431,485 doses of Pfizer COVID-19 vaccine have been administered in this age group
 - Dose 1: 257,840
 - Dose 2: 173,645
- In the 1–21-day risk window, we have electronically identified small numbers of cases for:
 - Appendicitis (n=9)
 - Seizures (n=2)
 - Myocarditis/pericarditis (n=2)
- So far 2 potential cases of myocarditis/pericarditis have been chart reviewed
 - Of the 2, chart review verified one 11-year-old as acute pericarditis 19 days after dose 2; chart review did not verify the other.
- No statistical signals have been identified to date

Summary of the Analyses of COVID-19 Vaccine Safety Among 12–17 and 5–11-Year-Olds

- Among 12–17-year-olds, the rate ratio for myocarditis/pericarditis was elevated during days 0-7 after Dose 2.
 - The excess risk was 0.3 cases per million 1st doses.
 - The excess risk was 70 cases per million 2nd doses.
- The VSD has administered 431,485 Pfizer doses to children aged 5-11 years.
- In the VSD, there have been no safety signals among 5–11-year-olds.

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