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

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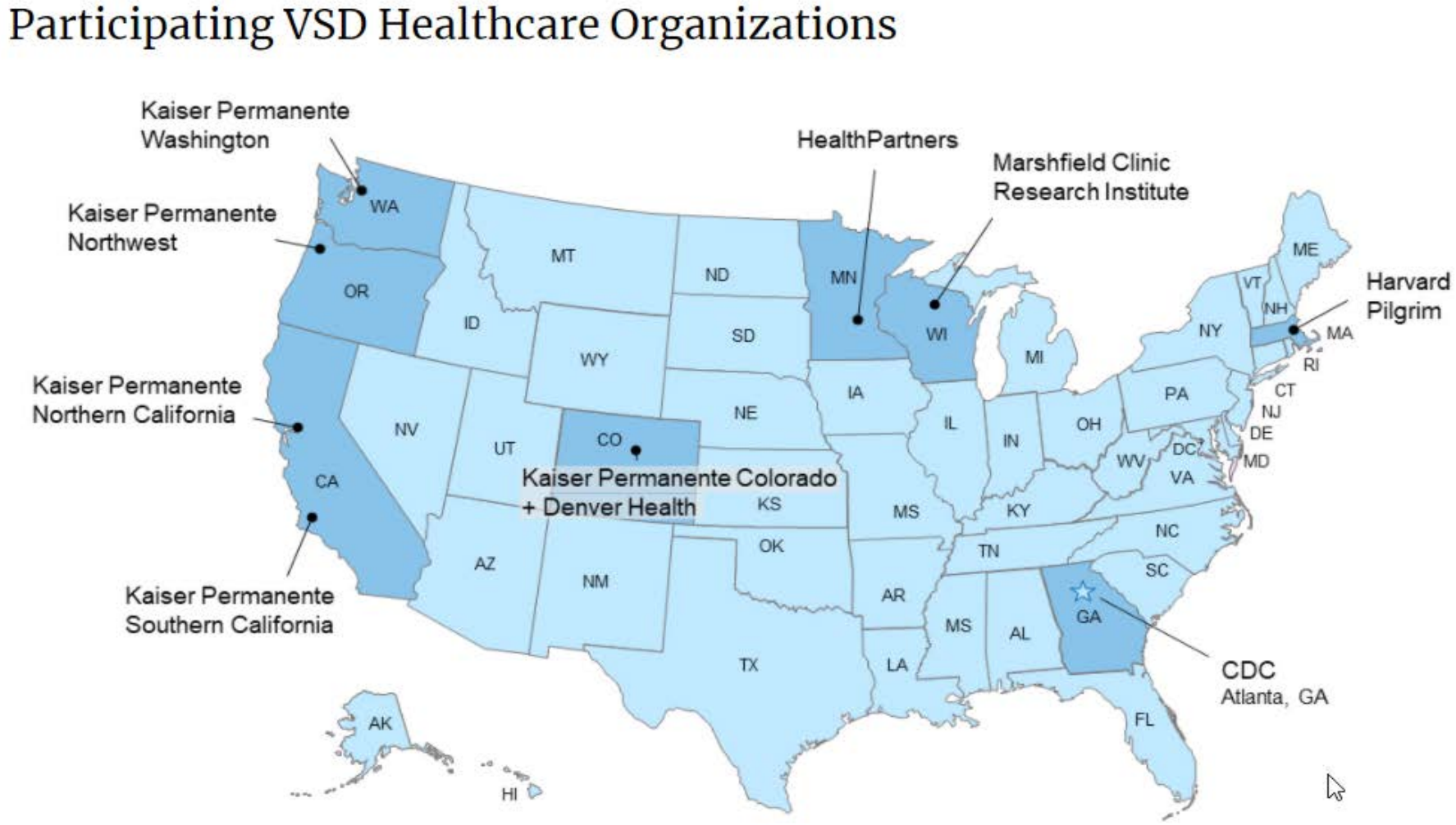
The Vaccine Safety Datalink (VSD)



- Established in 1990
- Collaborative project between CDC and 9 Integrated Health Care Organizations

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.

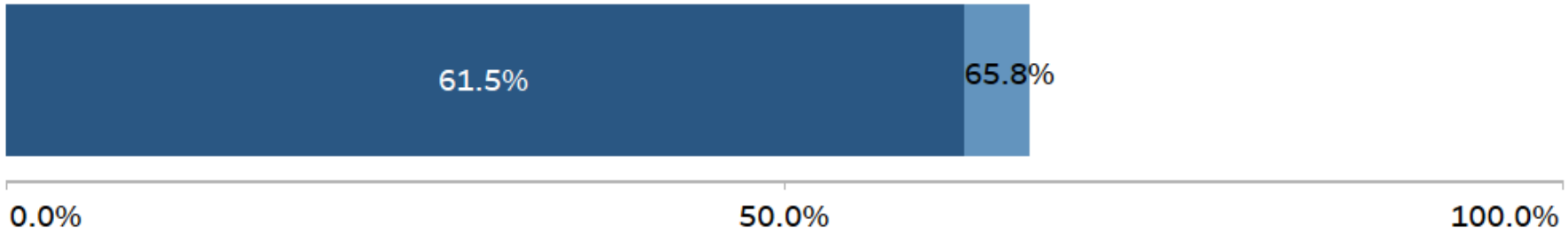
Project Period: Sept 2020 – August 2023 (3 years)

COVID-19 Vaccine Uptake (Through 7/10/21)

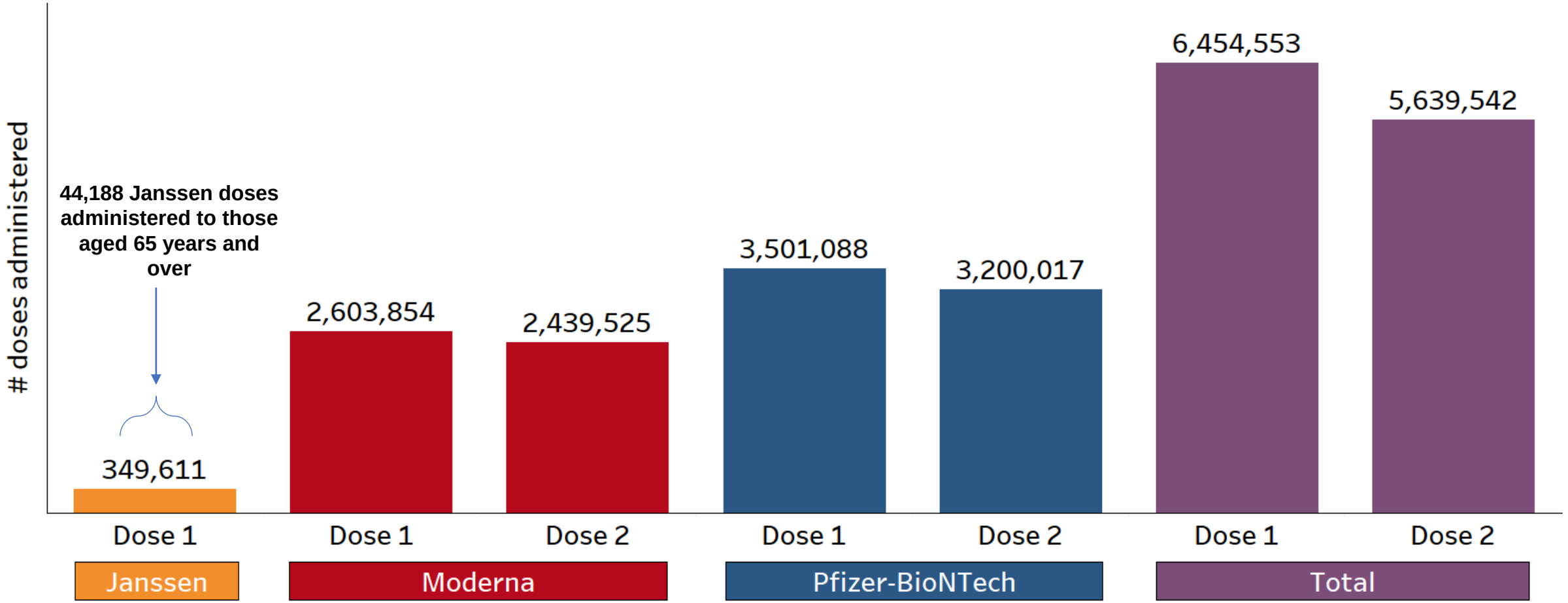
VSD COVID-19 Vaccine Totals

Total Doses Administered	Total Doses Admin per 100K	# People Received At Least One Dose	# People Fully Vaccinated
12,470,120	129,637	6,615,646	6,219,867

To date, 65.8% of the age eligible VSD population received 1st dose and 61.5% is fully vaccinated



VSD COVID-19 Vaccine Totals



Primary Analyses: Vaccinated Concurrent Comparisons with Sequential Tests (Data through July 10, 2021)

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

			Sequential Test[1]	
Outcome Event	**Events in Risk Interval**	**Adjusted Rate Ratio[2]**	**1-sided P-value (Fisher)**	**'Signal' 1-sided p < 0.0048**
Acute disseminated encephalomyelitis[3]	2	NE	0.660	No
Acute myocardial infarction	626	1.02	0.405	No
Appendicitis	821	0.83	0.999	No
Bell's palsy	562	1.02	0.423	No
Cerebral venous sinus thrombosis[3]	8	1.61	0.386	No
Disseminated intravascular coagulation	31	0.59	0.979	No
Encephalitis / myelitis / encephalomyelitis	18	1.50	0.312	No
Guillain-Barré syndrome[3]	10	0.69	0.828	No
Stroke, hemorrhagic	254	0.96	0.653	No
Stroke, ischemic	1098	0.99	0.609	No
Immune thrombocytopenia	48	0.95	0.627	No
Kawasaki disease	0	0.00	0.163	No
Myocarditis / pericarditis	92	1.16	0.269	No
Seizures	298	1.01	0.472	No
Transverse myelitis[3]	4	3.02	0.302	No
Thrombotic thrombocytopenic purpura	6	1.67	0.379	No
Thrombosis with thrombocytopenia syndrome	76	0.88	0.780	No
Venous thromboembolism	646	1.17	0.016	No
Pulmonary embolism	519	0.99	0.555	No

NE= not estimable

[1]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.

[2]Adjusted for VSD site, 5-year age group, sex, race/ethnicity, and calendar date. Comparison interval is 22–42 days after either dose.

[3]Analyses include only confirmed cases. Cases initially confirmed via "quick review" are subsequently removed if not confirmed after full chart review and adjudication.

Outcome events in 21-day risk interval after Janssen vaccine

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

			Sequential Test[1]	
Outcome Event	Events in Risk Interval	Adjusted Rate Ratio[2]	1-sided P-value (Fisher)	'Signal' 1-sided p < 0.0048
Acute myocardial infarction	20	1.32	0.308	No
Appendicitis	29	1.08	0.456	No
Bell's palsy	27	1.70	0.107	No
Disseminated intravascular coagulation	2	1.14	0.692	No
Guillain-Barré syndrome[3]	8	1.19	0.682	No
Stroke, hemorrhagic	7	0.79	0.762	No
Stroke, ischemic	36	1.25	0.243	No
Immune thrombocytopenia	4	2.32	0.295	No
Myocarditis / pericarditis	1	3.86	0.313	No
Seizures	9	0.73	0.811	No
Thrombotic thrombocytopenic purpura	2	2.67	0.496	No
Thrombosis with thrombocytopenia syndrome[3]	2	NE	0.622	No
Venous thromboembolism	22	1.00	0.574	No
Pulmonary embolism	11	0.43	0.989	No

NE= not estimable

[1]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.

[2]Adjusted for VSD site, 5-year age group, sex, race/ethnicity, and calendar date. Comparison interval is 22–42 days after either dose.

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GBS Chart Review Summary
(Data through July 3, 2021)

Guillain-Barré Syndrome following any mRNA COVID-19 Vaccine: Chart Review Summary (as of July 3, 2021)

- 40 GBS cases identified within 1-98 days following any mRNA vaccine
  - After quick review ruled out 16/39 (1 pending), 23/39 proceeded to full review.
  - 21/23 with completed full review and adjudication (2 pending).

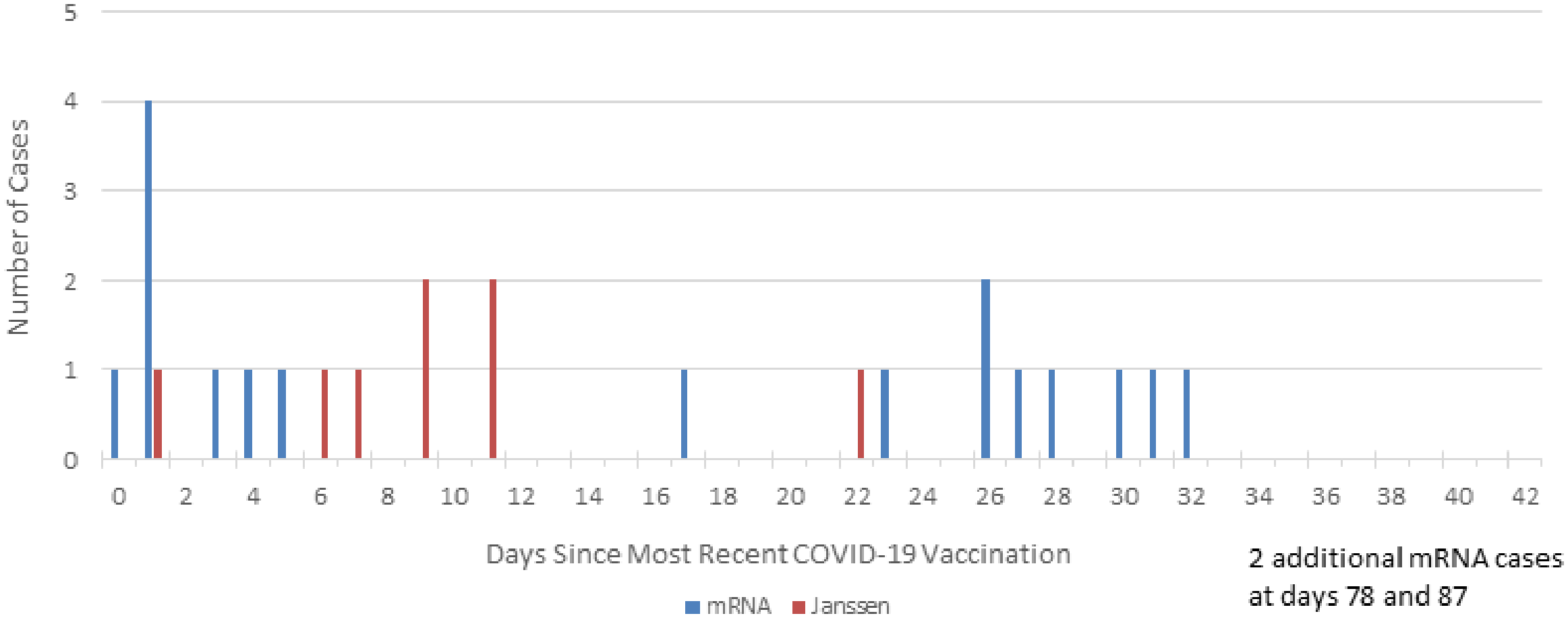
- **Adjudication confirmed 19/21 as GBS following any mRNA vaccine**
  - 1 case post-vaccination day 0
  - **8 cases post-vaccination days 1-21**
  - 8 cases post-vaccination days 22-42
  - 2 case post-vaccination days 43-98

Guillain-Barré Syndrome following Janssen COVID-19 Vaccine: Chart Review Summary (as of July 3, 2021)

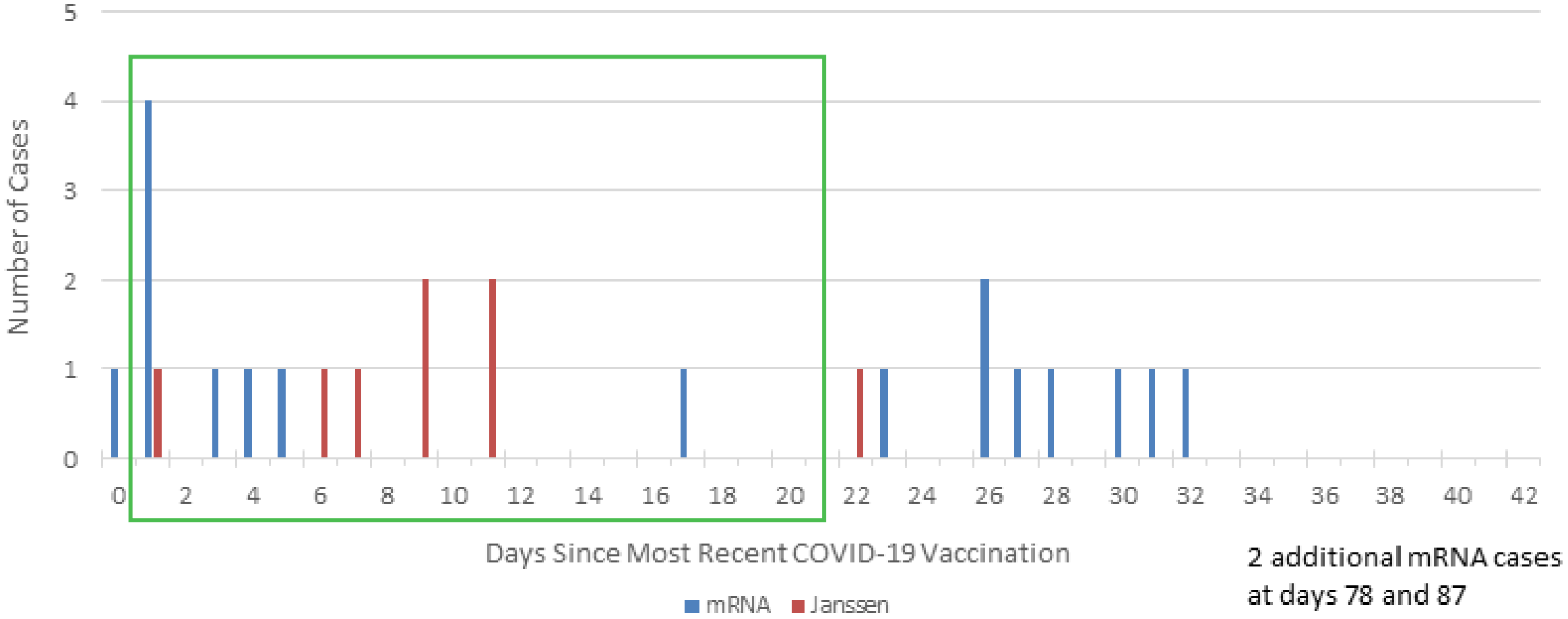
- 14 GBS cases identified within 1-98 days following Janssen vaccine
  - All 14 cases were quick reviewed (2 ruled out) and 12/14 proceeded to full review.
  - 10/12 with completed review and adjudication (2 pending).

- **Adjudication confirmed 8/10 as GBS following Janssen vaccination**
  - **7 cases post-vaccination days 1-21**
  - 1 case post-vaccination days 22-42

Timing of Confirmed Guillain-Barré Syndrome 0-98 days after COVID-19 Vaccines



Timing of Confirmed Guillain-Barré Syndrome 0-98 days after COVID-19 Vaccines



Characteristics of Confirmed GBS Cases: 1-21 Days

	mRNA (n=8)	Janssen (n=7)
Age in years, median (range)	70 (44-92)	60 (53-63)
Age group		
18-64 years	2 (25%)	7 (100%)
≥65 years	6 (75%)	0 (0%)
Male sex	4 (50%)	5 (71%)
Days to symptom onset from most recent dose, median (range)	2 (1-17)	8 (1-11)
Symptom onset within 21 days of most recent dose	8 (100%)	7 (100%)
Dose 1	5 (63%)	7 (100%)
Brighton Collaboration case definition level		
1	0 (0%)	1 (14%)
2	4 (50%)	3 (43%)
3	1 (13%)	1 (14%)
4	3 (38%)	2 (29%)
History of COVID-19	0 (0%)	0 (0%)
Outcome at the time of chart review		
Recovered without neurologic sequelae	0 (0%)	0 (0%)
Recovered with neurologic sequelae	3 (38%)	3 (43%)
Illness on-going	3 (38%)	4 (57%)
Died	2 (25%)	0 (0%)

Unadjusted Incidence Rate of Chart-Confirmed Guillain-Barré Syndrome 1-21 Days after Vaccination

Vaccine	Chart Confirmed Cases in 1-21 Day Risk Interval	Number of Doses	Person-Years	Unadjusted Rate per Million Doses[1] (95% CI)	Unadjusted Rate per 100,000 Person-Year[1] (95% CI)
mRNA – Either Dose	8	11,715,092	673,558	0.7 (0.3 - 1.3)	1.2 (0.5 – 2.3)
Janssen	7	345,700	19,876	20.2 (8.1- 41.7)	35.2 (14.2 - 72.5)

[1]Incidence rates are not adjusted for age, race, sex or VSD site.

Guillain-Barré Syndrome in the VSD after COVID-19 Vaccination: Summary

- The VSD has not identified a signal for any outcome in the primary analyses, including GBS, after the mRNA or Janssen vaccines
  - Analyses do not include head-to-head comparisons of Janssen with mRNA vaccines

- The chart confirmed unadjusted incidence rate of GBS during the 21 days after the Janssen vaccine is much higher than during the 21 days after mRNA vaccines.

- Weekly uptake of Janssen in the VSD has been minimal – ~2,500 to 11,400 doses a week.

- Continued VSD monitoring of GBS is warranted.
  - The VSD will continue to chart review every case of GBS within 1-98 days following any COVID-19 vaccination.

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