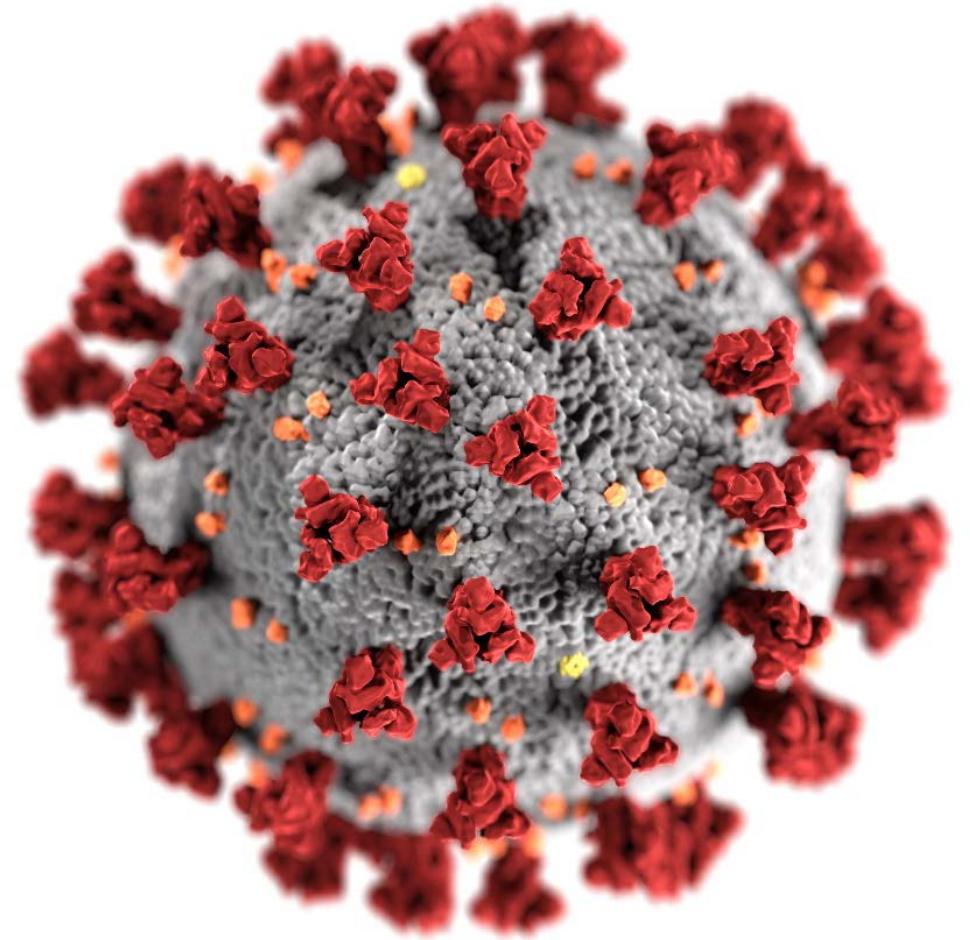


COVID-19 Vaccine Booster Dose Safety

Advisory Committee on Immunization Practices
(ACIP)

November 19, 2021

Tom Shimabukuro, MD, MPH, MBA
Vaccine Safety Team
CDC COVID-19 Vaccine Task Force



cdc.gov/coronavirus

Topics

- COVID-19 vaccine booster dose* safety
 - V-safe surveillance findings
 - Vaccine Adverse Event Reporting System (VAERS) monitoring

* For this surveillance review, Pfizer-BioNTech vaccination doses administered beginning September 22, 2021, and Moderna and Janssen vaccination doses administered beginning October 20, 2021, are assumed to be booster doses. Some doses might be additional doses administered to immunocompromised individuals and therefore misclassified as booster doses.



CDC vaccine safety monitoring

- COVID-19 vaccines are being administered under **the most intensive vaccine safety monitoring effort in U.S. history**
- Strong, complementary systems are in place—both new and established

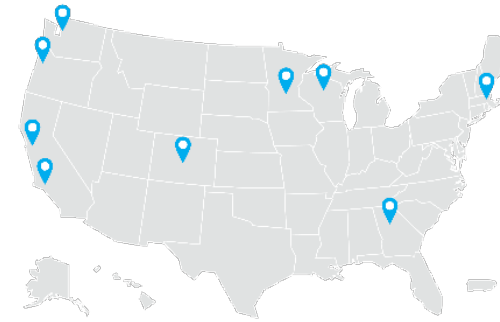
v-safe



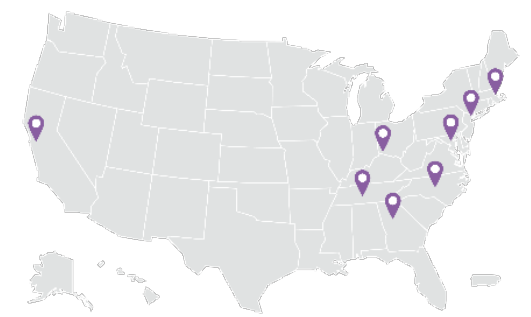
VAERS



VSD



CISA Project



Full list of U.S. COVID-19 vaccine safety monitoring systems

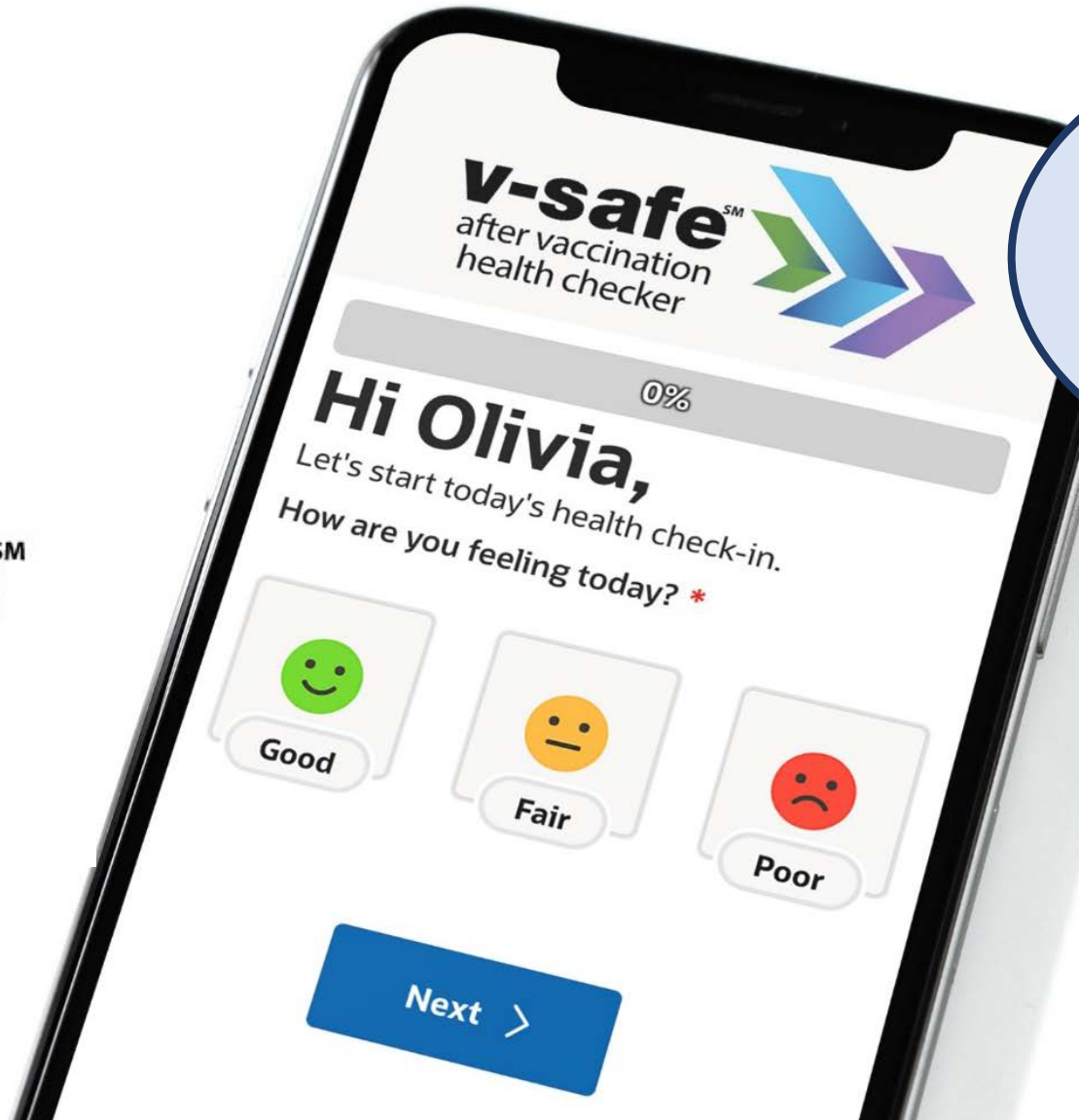
<https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety.html>



Smartphone-based active safety monitoring



<http://cdc.gov/vsafe>



Now available!

- Enrolling **children**
- **3rd** dose reporting

Active safety monitoring for COVID-19 vaccines

V-safe is a CDC smart phone-based monitoring program for COVID-19 vaccine safety in the United States

- Uses text messaging and web surveys to check in with vaccine recipients after vaccination
- Participants can register at any time: after first, second, or third dose
- Parents and guardians can register on behalf of children*
- **V-safe** solicits participants' reports on how they feel after COVID-19 vaccination
 - Local injection site reactions (i.e., pain, redness, swelling)
 - Systemic reactions (i.e., fatigue, headache, muscle aches)
 - Health impacts (unable to perform normal daily activities, missed school or work, or received care)

* Children ≤ 15 years of age must be enrolled under a parent or guardian's account



Patterns of vaccination for 725,917 v-safe participants who reported a booster dose*

Primary series

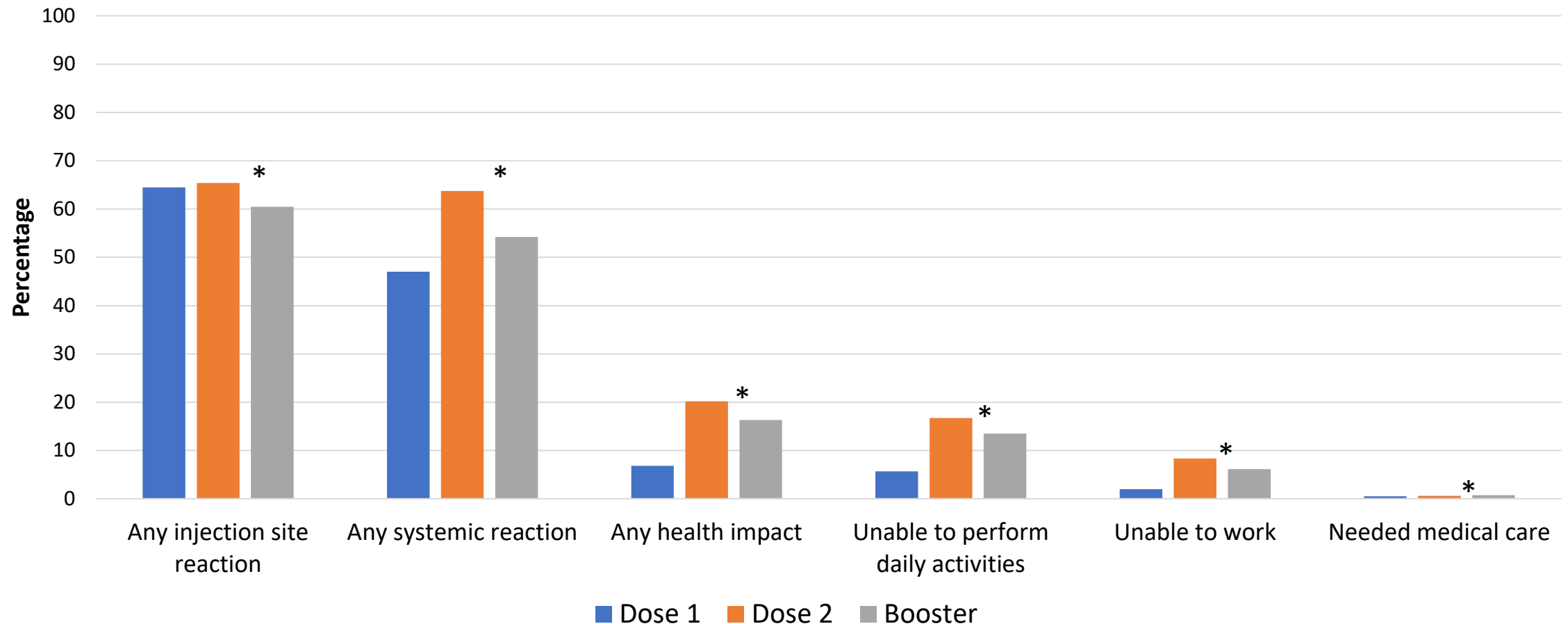
Booster dose

	Moderna (%)	Pfizer-BioNTech (%)	Janssen (%)	Total
Moderna	290,630 (95)	5,315	21,419	317,364
Pfizer-BioNTech	14,304	375,608 (99)	11,987	401,899
Janssen	170	144	6,340 (16)	6,654
Total	305,104	381,067	39,746	725,917

* Data as of November 14, 2021. Includes participants who completed at least one survey in the first week after booster dose (administered beginning Sep 22, 2021, for Pfizer-BioNTech and Oct 20, 2021, for Moderna and Janssen)



Reactions and health impact events reported at least once in days 0-7 after Pfizer-BioNTech vaccination, by dose

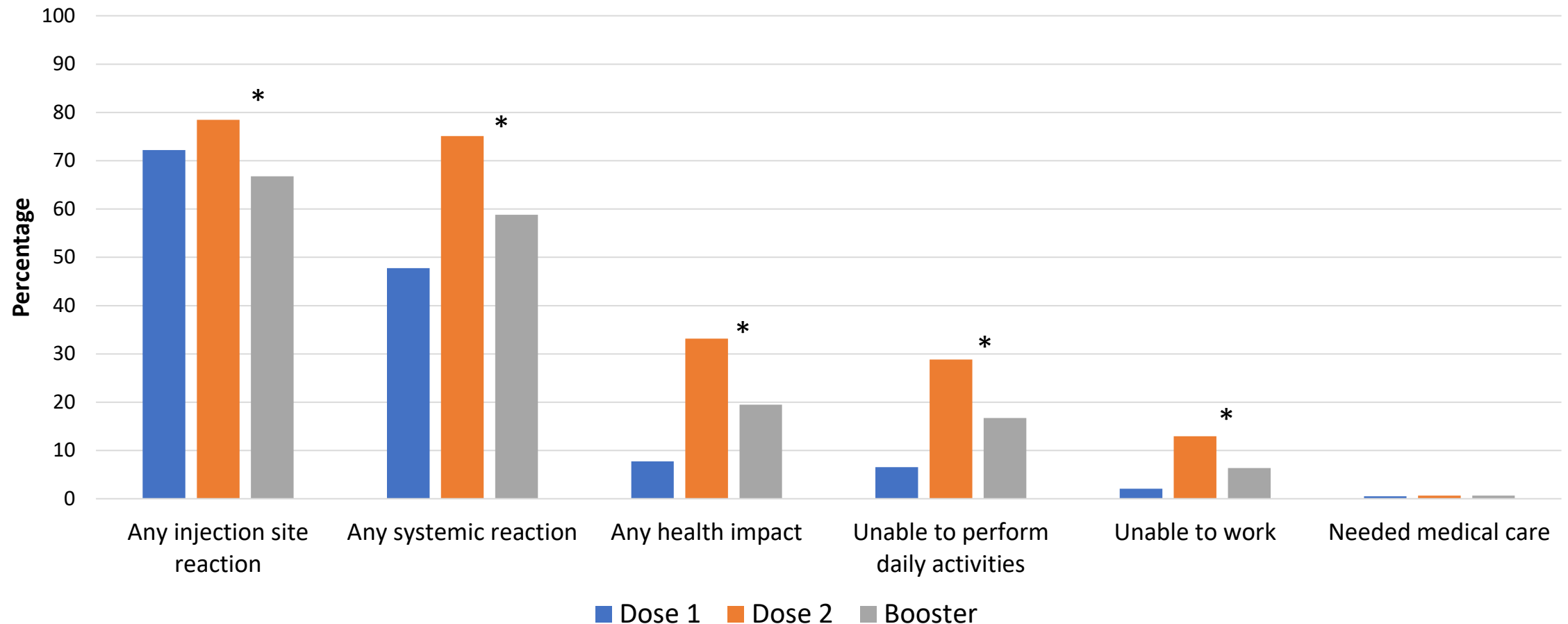


Includes 268,805 participants who completed at least one survey in the first week after each dose, data collected during Sep 22–Nov 14, 2021

* Dose 2 compared to booster: statistically significant difference (p-value <0.05) using multivariable generalized estimating equations model that accounted for the correlation between registrants and adjusted for demographic variables.



Reactions and health impact events reported at least once in days 0-7 after Moderna vaccination, by dose

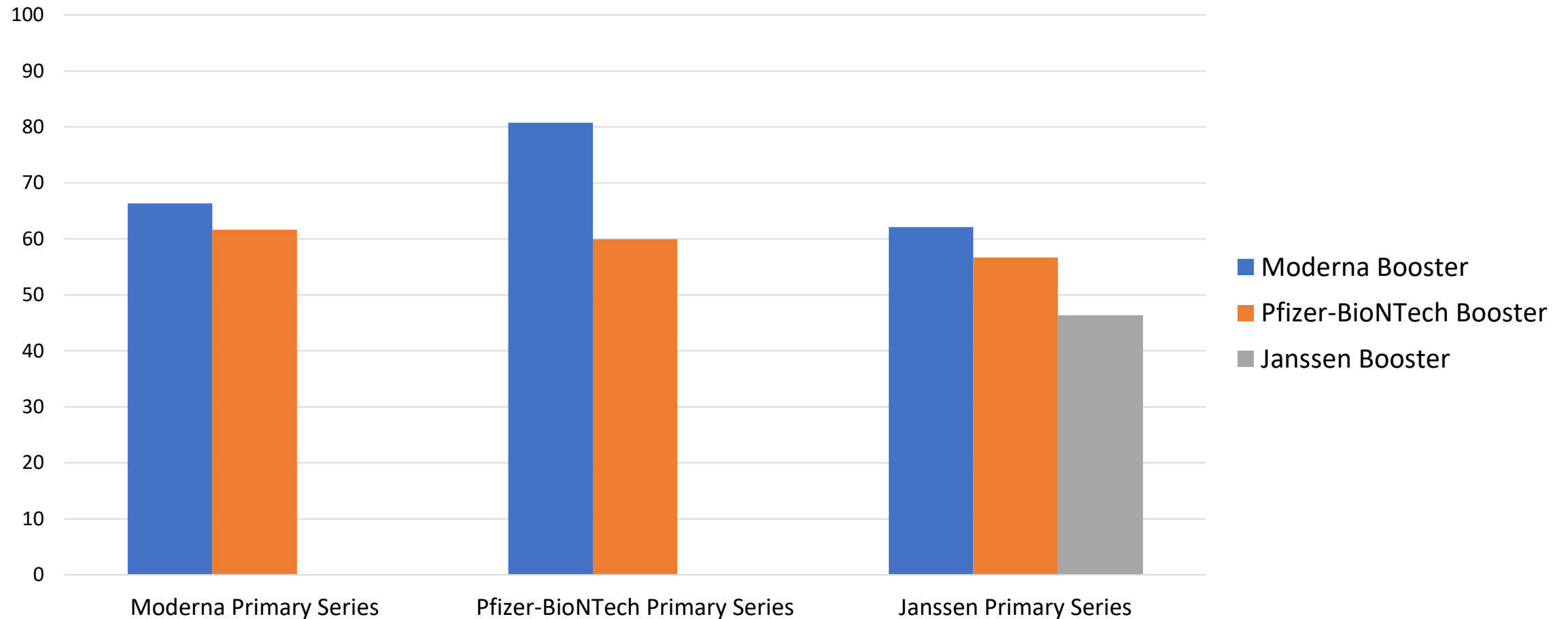


Includes 223,062 participants who completed at least one survey in the first week after each dose, data collected during Oct 20–Nov 14, 2021

* Dose 2 compared to booster: statistically significant difference (p-value <0.05) using multivariable generalized estimating equations model that accounted for the correlation between registrants and adjusted for demographic variables.



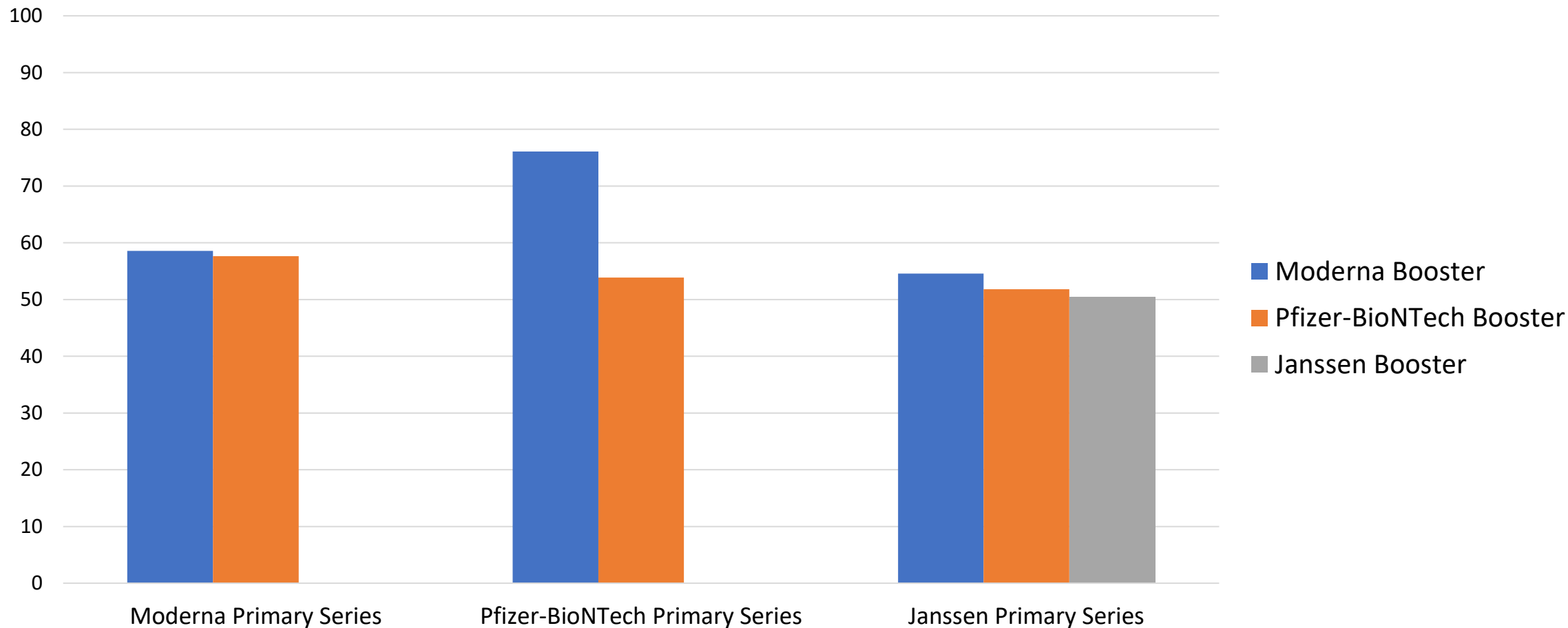
Any local reactions reported at least once 0-7 days after booster dose by pattern of vaccination (heterologous vs. homologous prime-boost)



Includes 725,603 participants who completed at least one survey in the first week after booster dose (administered beginning Sep 22, 2021, for Pfizer-BioNTech and Oct 20, 2021, for Moderna and Janssen). Participants who received an mRNA primary series followed by a Janssen booster were excluded due to insufficient data.

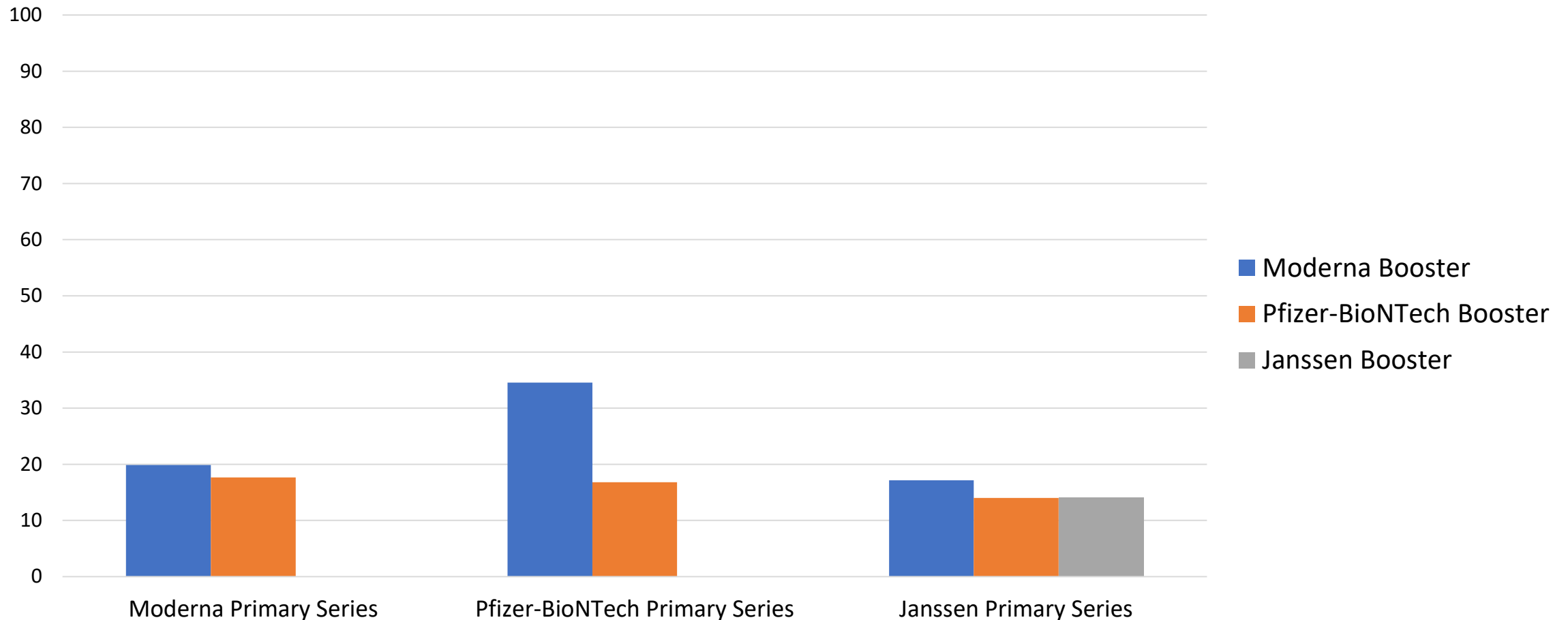


Any systemic reactions reported at least once 0-7 days after booster dose by pattern of vaccination (heterologous vs. homologous prime-boost)



Includes 725,603 participants who completed at least one survey in the first week after booster dose (administered beginning Sep 22, 2021, for Pfizer-BioNTech and Oct 20, 2021, for Moderna and Janssen). Participants who received an mRNA primary series followed by a Janssen booster were excluded due to insufficient data.

Any health impact event reported at least once 0-7 days after booster dose by pattern of vaccination (heterologous vs. homologous prime-boost)



Includes 725,603 participants who completed at least one survey in the first week after booster dose (administered beginning Sep 22, 2021, for Pfizer-BioNTech and Oct 20, 2021 for Moderna and Janssen). Participants who received an mRNA primary series followed by a Janssen booster were excluded due to insufficient data. Health impact event = unable to perform normal daily activities, missed school or work, or received care.



Summary of v-safe findings

- 725,917 v-safe registrants reported a booster dose
 - Most reported a primary mRNA vaccine series followed by a booster dose from the same manufacturer
- Consistent with findings on reactogenicity following a primary series:
 - Generally, Moderna booster appears to be more reactogenic than Pfizer-BioNTech booster, regardless of the primary series manufacturer
- For Pfizer-BioNTech and Moderna, local and systemic reactions and health impacts were reported less frequently following a booster dose than dose 2 of the primary series



VAERS is the nation's early warning system for vaccine safety



VAERS

Vaccine Adverse Event Reporting System

<http://vaers.hhs.gov>



VAERS accepts reports from everyone

Regardless of the plausibility of the vaccine causing the event or the clinical seriousness of the event

Key strengths

- Rapidly detects potential safety problems
- Can detect rare adverse events

Key limitations

- Passive surveillance system
- Inconsistent quality and completeness of information
- Reporting biases
- Generally, cannot determine cause and effect ←



Reports to VAERS following COVID-19 booster dose vaccination*

(as of Nov 15, 2021)

Manufacturer	Non-serious	Serious [†]	Total
Pfizer-BioNTech (16.3 million doses admin)	7,017 (94%)	473 (6%)	7,490
Moderna (9.7 million doses admin)	4,159 (97%)	133 (3%)	4,292
Janssen (334 thousand doses admin)	114 (93%)	8 (7%)	122
Total	11,290 (95%)	614 (5%)	11,904

- Regardless of manufacturer, ≥93% of reports non-serious

* Among reports of persons known to be ≥18 years of age, who received a Pfizer-BioNTech booster vaccination during Sep 22–Nov 15, 2021, or a Moderna booster vaccination during Oct 20–Nov 15, 2021, or a Janssen booster vaccination during Oct 20–Nov 15, 2021; received as of Nov 15, 2021

[†] Per federal law, includes reports of hospitalization, prolongation of existing hospitalization, life threatening condition, permanent disability, congenital deformity or birth defect, or death



Crude reporting rates to VAERS for COVID-19 booster dose vaccination* (per million doses administered as of Nov 15, 2021)

Manufacturer	Doses administered	All reports (per million doses admin)	Serious reports[†] (per million doses admin)
Pfizer-BioNTech	16,252,879	461	29
Moderna	9,666,388	444	14
Janssen	334,240	365	24

* Among reports of persons known to be ≥18 years of age, who received a Pfizer-BioNTech booster vaccination during Sep 22–Nov 15, 2021, or a Moderna booster vaccination during Oct 20–Nov 15, 2021, or a Janssen booster vaccination during Oct 20–Nov 15, 2021; received as of Nov 15, 2021

[†] Per federal law, includes reports of hospitalization, prolongation of existing hospitalization, life threatening condition, permanent disability, congenital deformity or birth defect, or death



Reports of adverse events to VAERS following COVID-19 booster dose vaccination*

- Median age: 62 years (IQR[†]: 45–71 years)
- Most reports (67%) in females

Patient characteristics	n (%)
Age group, years	
18–49	3,619 (30)
50–64	2,979 (25)
65+	5,306 (46)
Sex	
male	3,856 (32)
female	7,938 (67)
unknown	110 (1)



* Among reports of persons known to be ≥18 years of age, who received a Pfizer-BioNTech booster vaccination during Sep 22–Nov 15, 2021, or a Moderna booster vaccination during Oct 20–Nov 15, 2021, or a Janssen booster vaccination during Oct 20–Nov 15, 2021; received as of Nov 15, 2021

[†] IQR = interquartile range

Reports to VAERS following COVID-19 booster dose vaccination, by race and ethnicity*

- Most reports were in persons of white, non-Hispanic race and ethnicity, or unknown race or ethnicity

* Among reports of persons known to be ≥18 years of age, who received a Pfizer-BioNTech booster vaccination during Sep 22–Nov 15, 2021, or a Moderna booster vaccination during Oct 20–Nov 15, 2021, or a Janssen booster vaccination during Oct 20–Nov 15, 2021; received as of Nov 15, 2021

† Includes persons identified of Hispanic ethnicity of unknown race



Race and ethnicity	mRNA booster (%)	Janssen booster (%)
Non-Hispanic White	5,350 (45)	69 (57)
Unknown	5,095 (43)	29 (24)
Hispanic [†]	514 (4)	6 (5)
Non-Hispanic Black	349 (3)	13 (11)
Non-Hispanic Asian	265 (2)	0 (0)
Non-Hispanic multiracial	86 (1)	4 (3)
Non-Hispanic American Indian/Alaskan Native	72 (1)	0 (0)
Non-Hispanic other	43 (<1)	1 (1)
Non-Hispanic Native Hawaiian or other Pacific Islander	8 (<1)	0 (0)
Total	11,782	122

Most frequently reported adverse events to VAERS following COVID-19 booster dose vaccination*

Non-serious (n= 11,290)

Rank	Adverse event [†]	n
1	Headache	1,729
2	Fever	1,712
3	Fatigue	1,567
4	Pain	1,484
5	Chills	1,471

Serious (n = 614)

Rank	Adverse event [†]	n
1	Dyspnoea	90
2	Death	82
3	Fever	68
4	Chest pain	59
5	Asthenia	58

* Among reports of persons known to be ≥18 years of age, who received a Pfizer-BioNTech booster vaccination during Sep 22–Nov 15, 2021, or a Moderna booster vaccination during Oct 20–Nov 15, 2021, or a Janssen booster vaccination during Oct 20–Nov 15, 2021; received as of Nov 15, 2021; received as of Nov 15, 2021. Per federal law, serious adverse events include reports of hospitalization, prolongation of existing hospitalization, life threatening condition, permanent disability, congenital deformity or birth defect, or death. Excludes 5 duplicate reports.

[†] Not mutually exclusive



Reports to VAERS of death following COVID-19 booster dose vaccination*

Serious (n = 614)

Rank	Adverse event [†]	n
1	Dyspnoea	90
2	Death	82
3	Fever	68
4	Chest pain	59
5	Asthenia	58

26.3 million booster doses administered in the United States

- 82 initial reports of death submitted to VAERS
 - Pfizer-BioNTech (60), Moderna (22), Janssen (0)
 - Median age: 79 years (IQR: 69–90 years)

- Preliminary impression of cause of death when sufficient information available*

- Myocardial infarction
- COVID-19 disease
- Stroke
- Pulmonary embolism
- Pneumonia and sepsis
- Cardiomyopathy
- Congestive heart failure
- Acute leukemia
- Glioblastoma
- Renal failure, end stage renal disease
- General decompensation, end stage disease
- Respiratory and/or cardiac arrest

Abra et al. Expected Rates of Select Adverse Events following Immunization for COVID-19 Vaccine Safety Monitoring. medRxiv. doi: <https://doi.org/10.1101/2021.08.31.21262919>.

“We estimated that we would expect 236.5 coincident all-cause deaths in 10,000,000 vaccinated people within 1 day of vaccination; 1,655.5 coincident all-cause deaths in 10,000,000 vaccinated people within 7 days of vaccination; and 9,932.8 coincident all-cause deaths in 10,000,000 vaccinated people within 42 days of vaccination.”

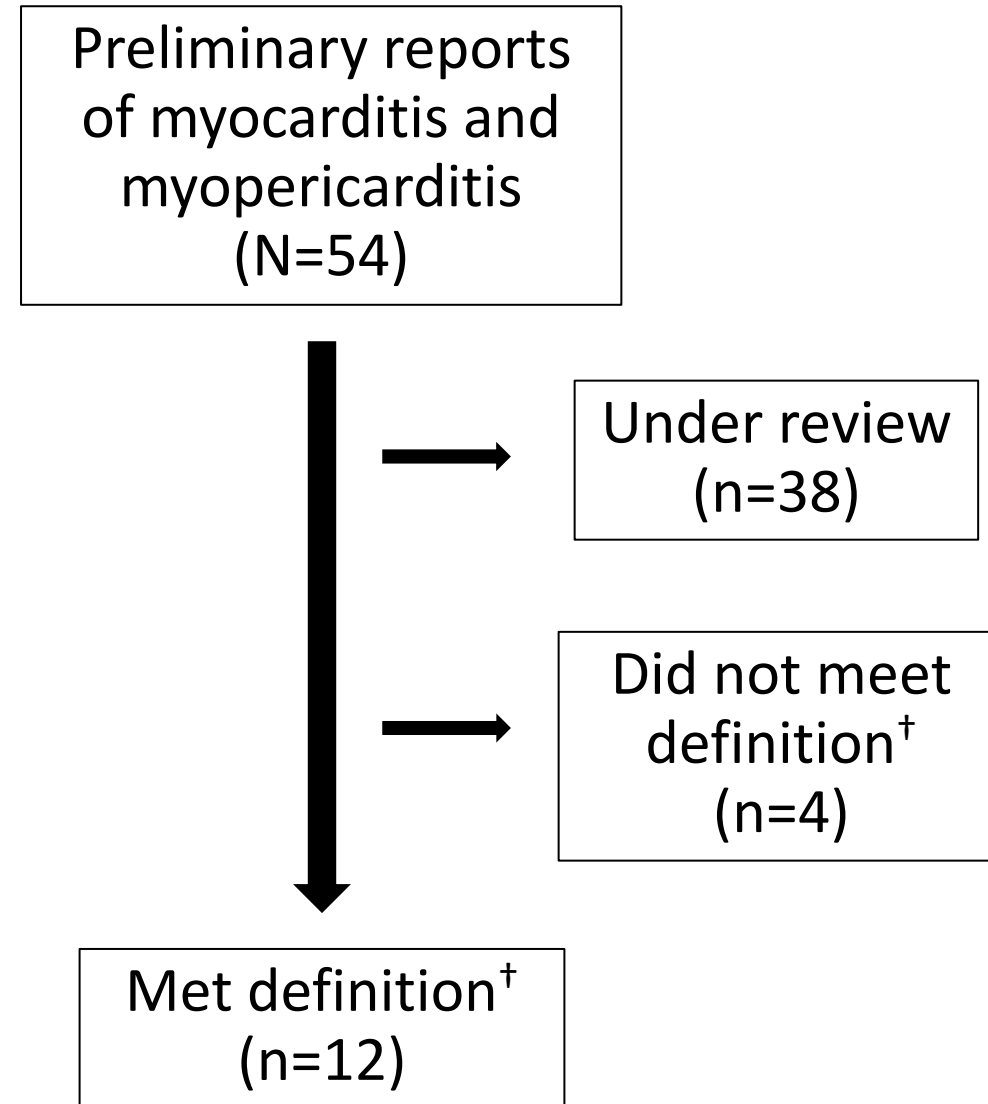


* Based on CDC physician review of initial VAERS report and available documentation, including death certificates

Myocarditis and myopericarditis cases following COVID-19 booster dose vaccination

(25.9 million mRNA and 334K Janssen COVID-19 vaccine doses admin)

- 54 preliminary reports of myocarditis and myopericarditis*
 - All after Pfizer-BioNTech or Moderna vaccination
 - Median age: 51 years (IQR: 38–67 years)
 - Median time to onset: 3 days (IQR: 1–7 days)
 - 29 males, 24 females, 1 sex not reported
 - Crude unadjudicated reporting rate of 2.1 cases per million mRNA COVID-19 vaccine doses admin
- Characteristics of reports appear to reflect the population for booster dose recommendations (i.e., older adults)



* Among reports of persons known to be ≥18 years of age, who received a Pfizer-BioNTech booster vaccination during Sep 22–Nov 15, 2021, or a Moderna booster vaccination during Oct 20–Nov 15, 2021, or a Janssen booster vaccination during Oct 20–Nov 15, 2021; received as of Nov 15, 2021

[†] Adjudicated after healthcare provider interview and/or medical record review

Reports of myocarditis and myopericarditis following COVID-19 booster dose vaccination that have met CDC case definition (N=12)*

- Median age = 46 years (IQR = 36–62y)
- Median onset = 4 days (IQR = 1–6d)
- Sex
 - Male = 9
 - Female = 3
- Race and ethnicity
 - Hispanic = 1
 - Non-Hispanic white = 7
 - Non-Hispanic black = 1
 - Non-Hispanic Asian = 1
 - Not reported = 2
- Manufacturer
 - Pfizer-BioNTech = 8
 - Moderna = 4
- Outcomes
 - Known to be hospitalized = 10
 - Discharged home = 10
 - Recovery status known = 8
 - **6 (75%)** known to have recovered from symptoms at time of report



* Among reports of persons known to be ≥18 years of age, who received a Pfizer-BioNTech booster vaccination during Sep 22–Nov 15, 2021, or a Moderna booster vaccination during Oct 20–Nov 15, 2021, or a Janssen booster vaccination during Oct 20–Nov 15, 2021; received as of Nov 15, 2021; received as of Nov 15, 2021; adjudicated after healthcare provider interview and/or medical record review

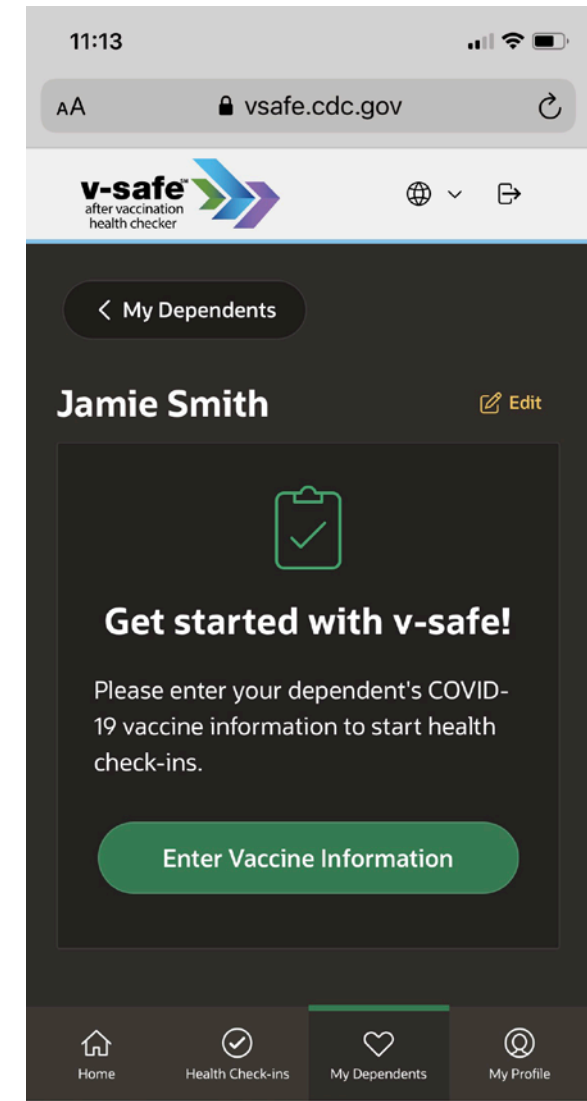
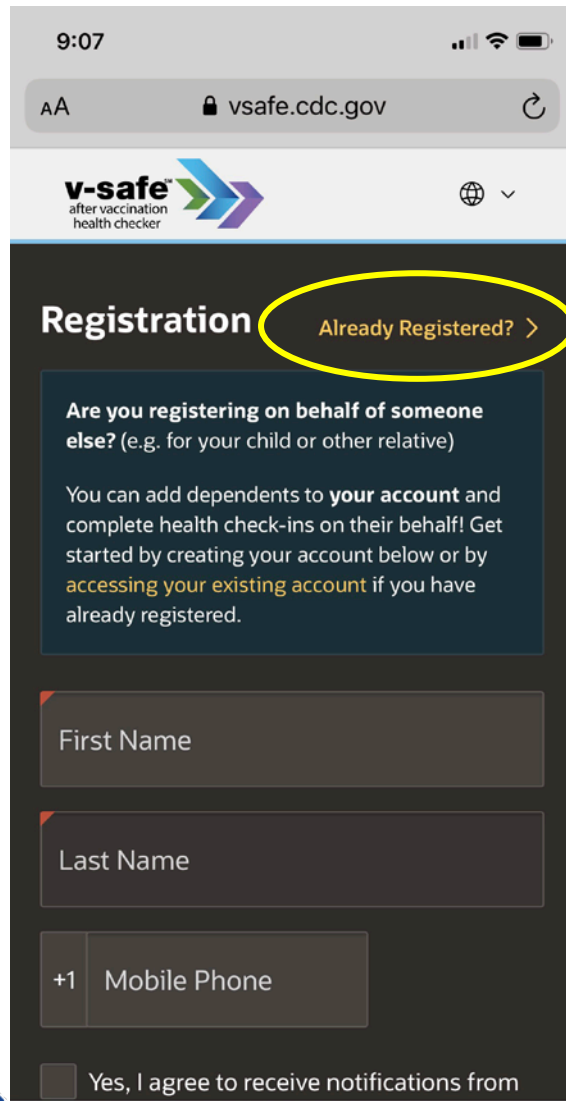
Summary of VAERS findings

- During Sep 22–Nov 5, 2021, 25.9 million mRNA and 334 thousand Janssen vaccine booster doses administered
 - Most reports ($\geq 93\%$) were non-serious (similar to primary series)
 - Almost half of reports among persons ≥ 65 years of age; two thirds in females
 - Most frequently reported non-serious AEs were known and well characterized AEs associated with COVID-19 vaccination
 - No unusual or unexpected patterns observed with respect to reports of deaths following COVID-19 booster vaccination
 - 54 preliminary reports of myocarditis and myopericarditis
 - 12 reports met CDC case definition, 38 reports under review, 4 ruled out
 - Characteristics of reports appear to reflect population for booster dose recommendations (i.e., older adults)*

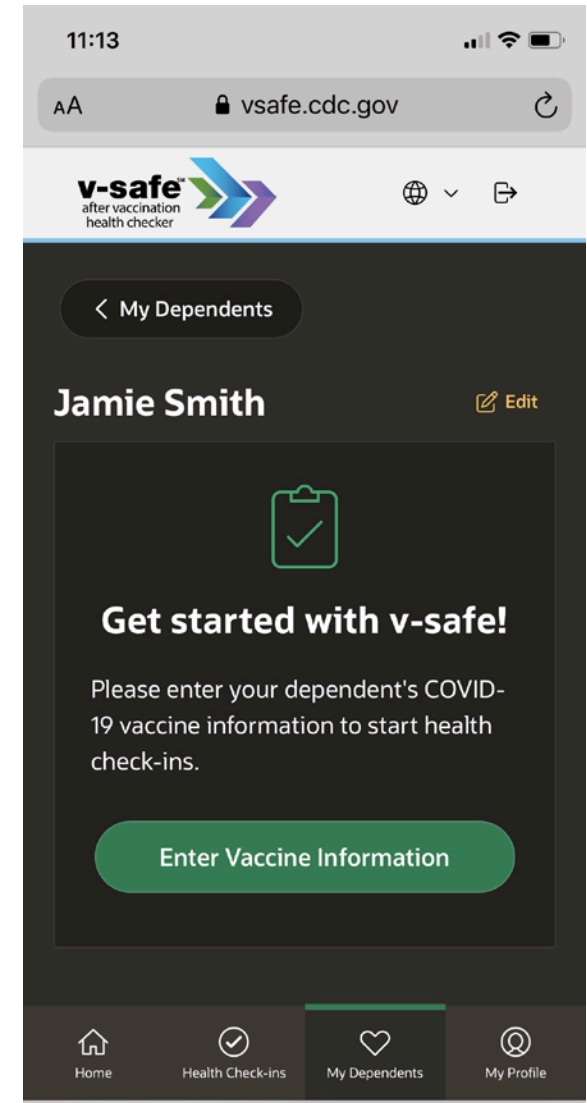
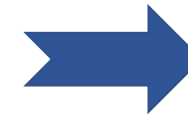
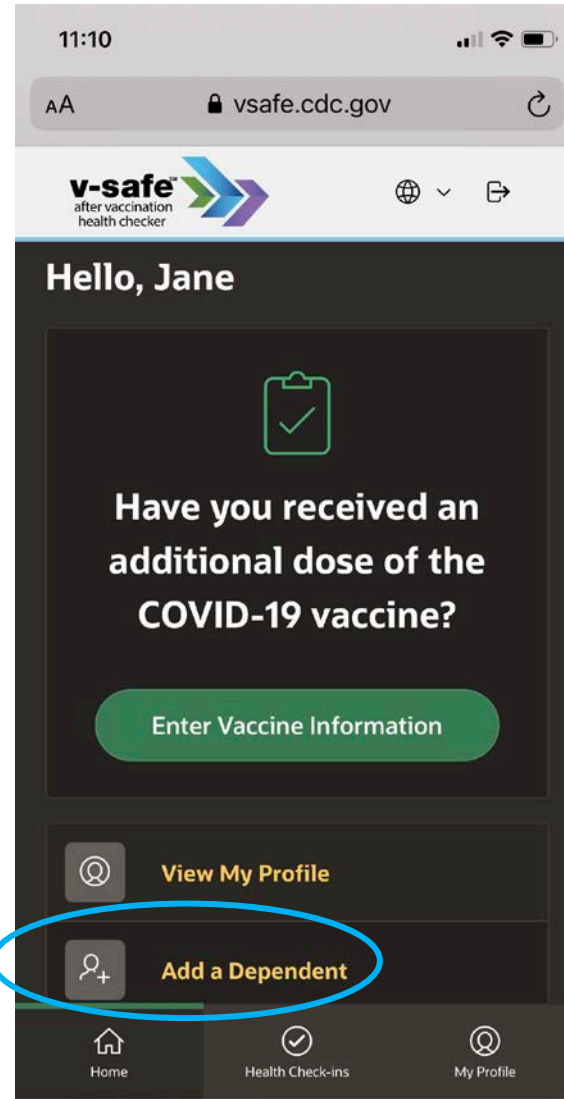
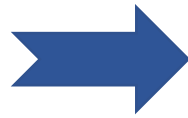
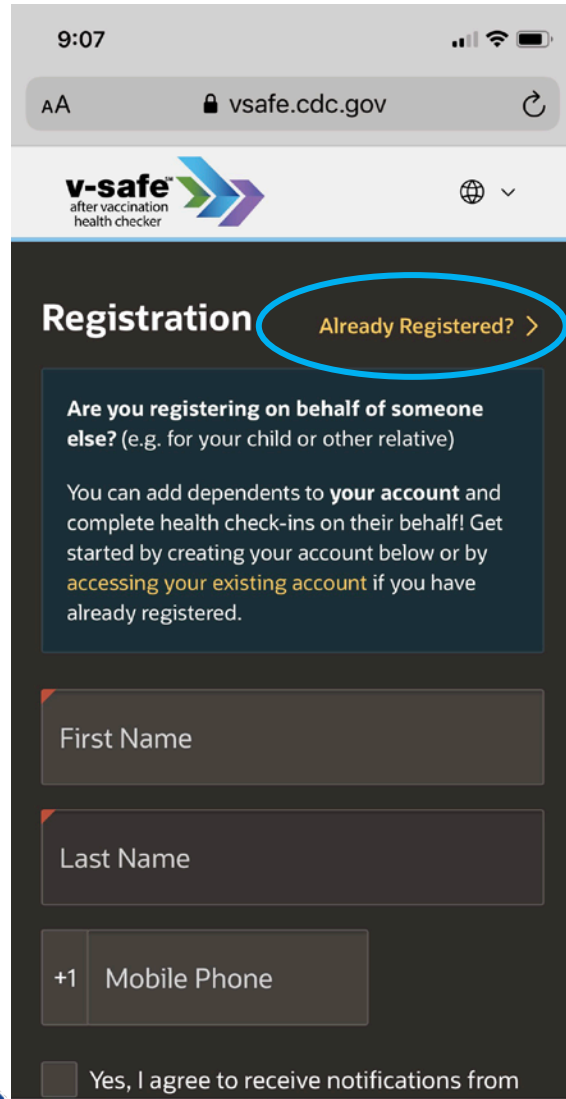
* Background incidence of myocarditis is 1–10 cases per 100,000 persons per year (Gubernot et al. Population-Based background incidence rates of medical conditions for use in safety assessment of COVID-19 vaccines. *Vaccine*. 2021;39:3666-3677).



Adding booster dose to v-safe



Adding dependents to v-safe



Acknowledgments

Thanks to the many people who made analysis of these data possible:

- **V-safe Team**
- **VAERS Team**
 - VAERS TTS abstraction team
 - VAERS Myopericarditis abstraction team
 - VAERS Data team
- **Clinical Immunization Safety Assessment (CISA) Project**
- **COVID-19 Vaccine Task Force Data Monitoring and Reporting Group**
- **FDA/Center for Biologics Evaluation and Research**

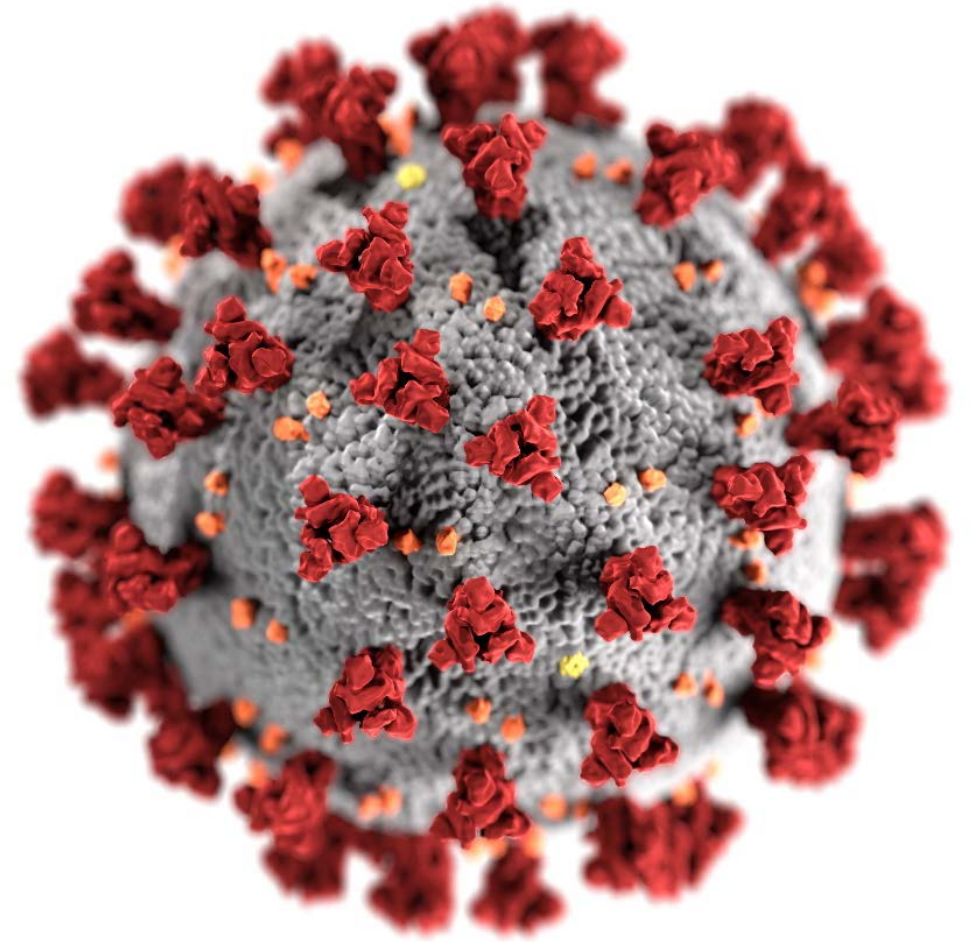


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- The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC)
- Mention of a product or company name is for identification purposes only and does not constitute endorsement by CDC



Thank you!



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