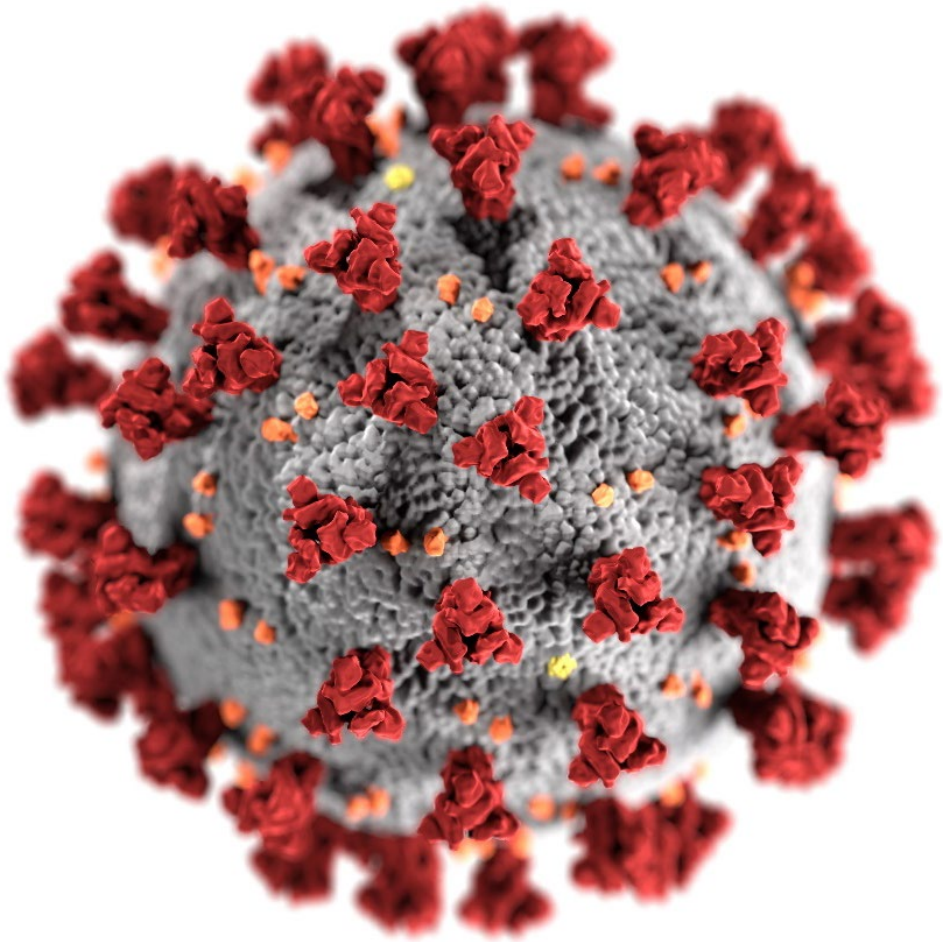
COVID-19 vaccine safety updates: Bivalent mRNA COVID-19 Vaccines and Coadministration of mRNA COVID-19 and Inactivated Influenza Vaccines

National Adult and Influenza Immunization Summit

December 8, 2022

John R. Su, MD, PhD, MPH
Immunization Safety Office



cdc.gov/coronavirus

Overview

- Data on Bivalent mRNA COVID-19 Vaccines
- Data on Coadministration of mRNA COVID-19 and Inactivated Influenza Vaccines
  - Data from the Vaccine Adverse Event Reporting System (VAERS)
  - Data from V-safe
  - Brief mention from the Vaccine Safety Datalink (VSD)

Bivalent mRNA COVID-19 Vaccines

(Originally presented to the Global Advisory Committee on Vaccine Safety November 29, 2022)

National Passive safety monitoring in VAERS

VAERS accepts reports from everyone (healthcare professionals, patients, parents, caregivers, manufacturers, etc.) 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

CDC + FDA

VAERS

Demographic summary of 5,542 VAERS reports among persons aged ≥12 years following a bivalent booster dose

Characteristic	% of reports
Sex	
Female	64.2
Male	35.0
Unknown	0.8
Median age, y (range)	60 (12-101)

Characteristic	% of reports
Hispanic or Latino	4.7
Not Hispanic or Latino	
AI/AN	0.4
Asian	2.6
Black or AA	3.1
NHPI	0.04
White	45.6
Multiracial	0.6
Other	0.3
Unknown	42.7

Data as of October 23, 2022. Abbreviations: AI/AN = American Indian/Alaska Native; NHPI = Native Hawaiian or other Pacific Islander; AA=African American.

Vaccine errors (N = 1,913) reported to VAERS for persons aged ≥12 years following a bivalent booster dose

Vaccination errors	N (%) of vaccine error reports
Error without adverse health event	1,688 (88.2)
Error with adverse health event	225 (11.8)
Error with nonserious health event*	218 (11.4)
Error with serious health event	7 (0.4)

1,913 (34.5%) reports of vaccine error
Most (88.2%) without an adverse health event

Vaccination error MedDRA PTs	N (%) of vaccine error reports
Incorrect product formulation administered	425 (22.2)
Incorrect dose administered	422 (22.1)
Underdose	356 (18.6)
Wrong product administered	208 (10.9)
Extra dose administered	147 (7.7)
Inappropriate schedule of product administration	94 (4.9)
Product storage error	89 (4.7)
Interchange of vaccine products	51 (2.7)
Syringe issue	45 (2.4)
Off label use	41 (2.1)

CDC + FDA
VAERS

Data as of October 23, 2022.
* Adverse health events coded for reports with nonserious vaccination errors included arthralgia, headache, injection site erythema, injection site swelling, fever, pain, and pain in extremity.

Nonserious reports (N = 5,291) to VAERS for persons aged ≥12 years following a bivalent booster dose

MedDRA PTs*	N (%) of reports
Headache	628 (11.9)
Fatigue	575 (10.9)
Fever	561 (10.6)
Pain	524 (9.9)
Chills	459 (8.7)
Pain in extremity	376 (7.1)
Nausea	357 (6.8)
Dizziness	347 (6.6)
Injection site pain	259 (4.9)
COVID-19	258 (4.9)

Data as of October 23, 2022.

* Includes the top 10 most frequently coded MedDRA PTs among nonserious reports (excluding vaccination error MedDRA PTs). Signs and symptoms in VAERS reports are assigned MedDRA PTs by VAERS staff members. Each VAERS report might be assigned more than one MedDRA PT, which can include normal diagnostic findings. A MedDRA PT does not indicate a medically confirmed diagnosis.

Serious* reports (N = 251) to VAERS for persons aged ≥12 years following a bivalent booster dose

Clinical impressions	N of reports
Allergic reaction/Anaphylaxis	8
Appendicitis	5
Arrythmia	13
Atrial fibrillation	9
COVID-19	20
Death†	36
Dyspnea	5
Fall	7
Guillain-Barré syndrome	2

Clinical impressions	N of reports
Hypertension, acute	10
Pericarditis§	4
Pneumonia	7
Seizure	6
Thrombotic event	31
Chest pain, not otherwise specified	12
Myocardial infarction	8
Myocarditis¶	5

Data as of October 23, 2022.

* VAERS reports are classified as serious if any of the following are reported: hospitalization, prolongation of hospitalization, life-threatening illness, permanent disability, congenital anomaly or birth defect, or death. Serious reports to VAERS were reviewed by CDC physicians to form preliminary clinical impressions.

† For reports of death, cause of death was available for four reports: cardiac arrest, dementia, metastatic prostate cancer, and myocardial infarction.

§ All four reports of pericarditis have been verified by medical record review.

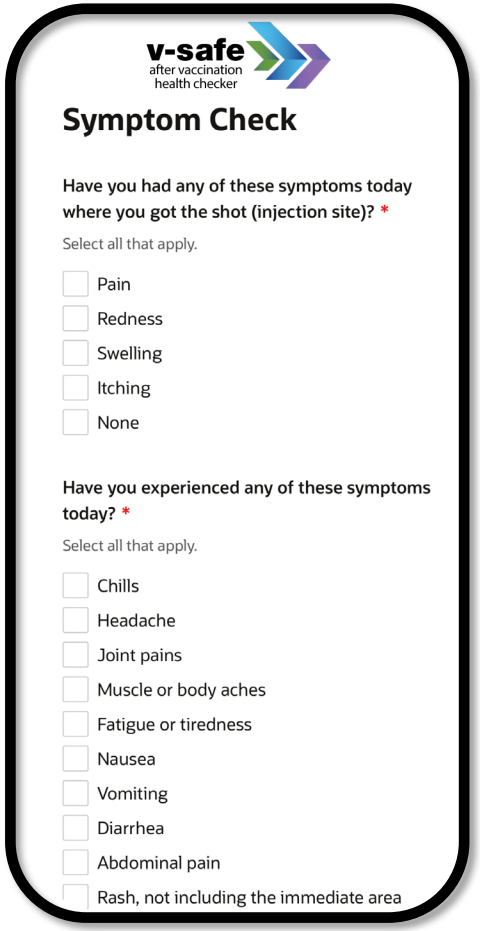
¶ Three of the five reports of myocarditis have been verified by medical record review.

CDC + FDA

VAERS

Health surveys ask questions about local and systemic reactions and health events

- V-safe sends surveys daily during the week following each dose of vaccine
  - Then weekly through 6 weeks and at 3, 6, and 12 months
- Questions solicit adverse events and health impacts after COVID-19 vaccination
  - Local (e.g. pain, redness, swelling)
  - Systemic reactions (e.g. fatigue, headache, muscle pain)
  - Health impacts (e.g., unable to perform normal daily activities, missed school or work, or received medical care)
- Children aged <16 years can be added to a registered parent's account



v-safe
after vaccination
health checker

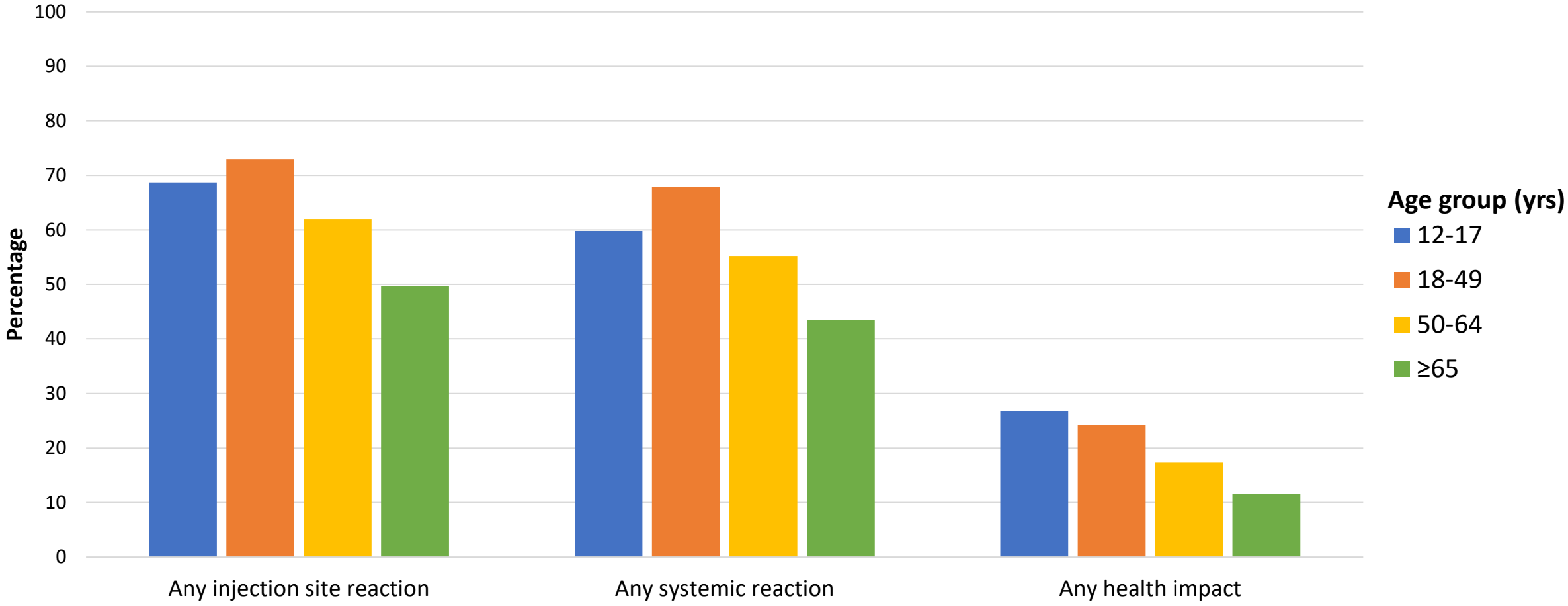
Vaccination characteristics of 211,959 v-safe participants aged ≥12 years who reported a bivalent booster dose

Characteristic	% of participants
Manufacturer	
Pfizer-BioNTech	58.0
Moderna	42.0
Total COVID-19 doses received*	
2	0.1
3	3.8
4	45.4
5	50.2
6	0.5

Characteristic	% of participants
Co-administration	
Yes	39.8
Influenza vaccine	39.2
Other vaccine	0.7
No	60.2

Data as of October 23, 2022. Includes participants who completed at least one survey in the first week after booster dose.
* Including bivalent booster

Reactions and health impacts reported by v-safe participants aged ≥12 years at least once 0-7 days after bivalent booster dose, by age group



Data as of October 23, 2022. Includes 211,959 participants who completed at least one survey in the first week after booster dose.

Bivalent Booster Dose Summary

- Most (96%) VAERS reports were nonserious
  - Vaccine errors were the most (35%) common events reported
  - 5 reports of myocarditis and 4 of pericarditis following administration of 22.6 million doses

- Over 211,959 v-safe registrants reported a bivalent booster dose
  - Reporting frequencies of reactions and health impacts were similar to those described after 1st and 2nd booster vaccination

- MMWR published November 4: https://www.cdc.gov/mmwr/volumes/71/wr/mm7144a3.htm

Coadministration of mRNA COVID-19 and Inactivated Influenza Vaccines – Vaccine Adverse Event Reporting System (VAERS)

U.S. reports to VAERS of coadministration of mRNA COVID-19 and inactivated influenza vaccines* (as of June 30, 2022)

Total reports	Median age	Male† n (%)	Female† n (%)	Non-serious n (%)	Serious‡ n (%)
2,449	48 years	909 (37)	1,532 (63)	2,062 (84)	387 (16)

- Quadrivalent inactivated influenza (IIV4) most commonly coadministered (1,587 (65%))
- Coadministered mRNA COVID-19 vaccines
  - Pfizer-BioNTech/BNT162b2 = 1,663 (68%)
  - Moderna/mRNA-1273 = 786 (33%)

* Among people vaccinated during July 1, 2021 – June 30, 2022.

† For 8 reports, sex was not reported

‡ Based on the Code of Federal Regulations if one of the following is reported: death, life-threatening illness, hospitalization or prolongation of hospitalization, permanent disability, congenital anomaly or birth defect

Most frequent MedDRA Preferred Terms* reported to VAERS coadministration of mRNA COVID-19 and inactivated influenza vaccines† (as of June 30, 2022)

Non-serious reports (N=1,332)

Rank	MedDRA PT (not mutually exclusive)	n (%)
1	Injection Site Reactions	193 (14.5)
2	Headache	181 (13.6)
3	Pain	171 (12.8)
4	Pyrexia/Fever	169 (12.7)
5	Fatigue	167 (12.5)
6	Chills	124 (9.3)
7	Dizziness	121 (9.1)
8	Nausea	102 (7.7)
9	Pain In Extremity	88 (6.6)
10	COVID-19	87 (6.5)

Serious reports (N=253)

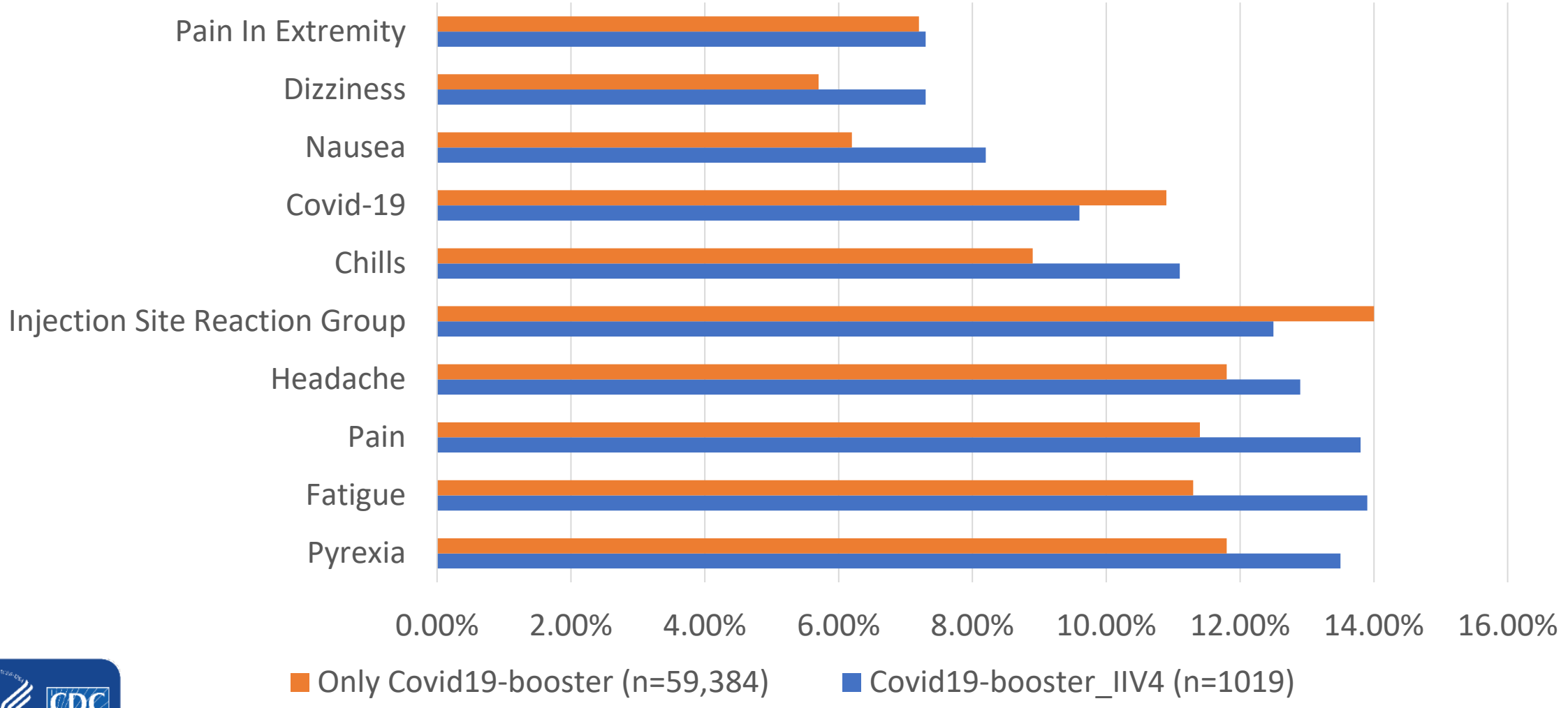
Rank	MedDRA PT (not mutually exclusive)	n (%)
1	Dyspnoea	38 (14.9)
2	COVID-19	32 (12.6)
3	Chest Pain	27 (10.6)
4	Condition Aggravated	26 (10.2)
5	Fatigue	22 (8.7)
6	Pain	21 (8.3)
7	Death	19 (7.5)
8	Asthenia	16 (6.3)
9	Headache	16 (6.3)
10	Nausea	16 (6.3)

* Medical Dictionary for Regulatory Activities Preferred Terms (https://www.meddra.org/how-to-use/basics/hierarchy)

† Among people vaccinated during July 1, 2021 – June 30, 2022.

‡ Determined by subject matter expert consensus

Reported symptoms generally similar after mRNA COVID-19 coadministered with inactivated influenza vaccines or administered alone (as of June 30, 2022)



Preliminary reports of Adverse Events of Special Interest reported to VAERS after coadministration of mRNA COVID-19 and inactivated influenza vaccines

(as of June 30, 2022)

- Bell's palsy (19)
- Myocarditis/pericarditis (16)
  - 3 reports of myocarditis, 1 report of pericarditis met CDC case definition
- Anaphylaxis (6)
  - 1 report = Brighton Level 3 diagnostic certainty
- Multisystem Inflammatory Syndrome in Children (2)
- Guillain Barre Syndrome (1) = Brighton Level 2 diagnostic certainty

Preliminary reports of Adverse Events of Special Interest reported to VAERS after coadministration of mRNA COVID-19 and inactivated influenza vaccines (continued) (as of June 30, 2022)

- Death (47)
  - 24 males, 23 females
  - Median age 73 years (IQR: 62–84 years)
  - Causes of death consistent with all-cause mortality for age groups
    - Cardiovascular (heart failure, atherosclerotic coronary and vascular disease, myocardial infarction, etc.) (43%)
    - Unevaluable (30%)
    - Infectious (COVID-19, sepsis) (17%)
    - Respiratory (respiratory failure, neoplasm) (9%)

V-safe data

(Originally presented to the National Vaccine Advisory Committee September 23, 2022)

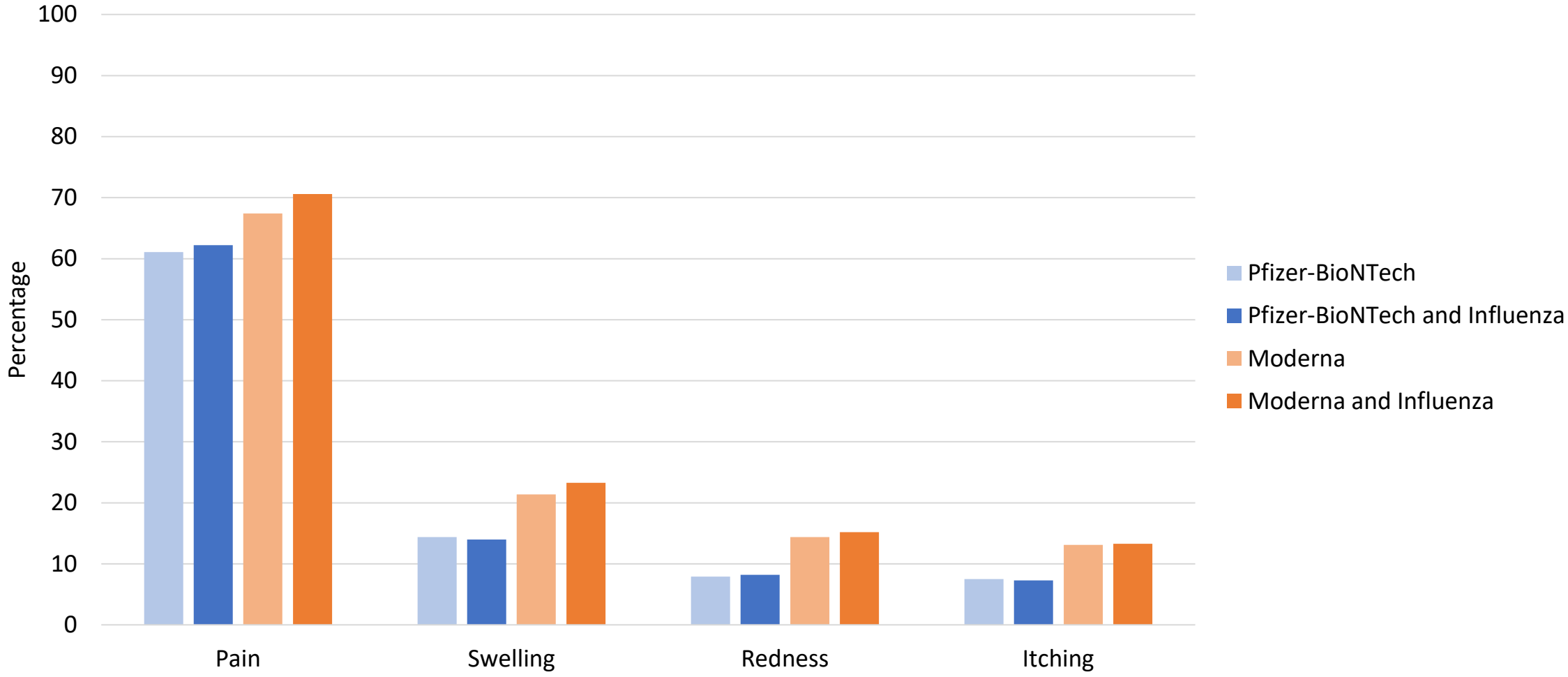
Study design[1]

- Compared reactions and health impacts reported to v-safe in the week following simultaneous seasonal influenza vaccine and an mRNA COVID-19 booster vs. an mRNA COVID-19 booster alone
- Data collected from September 22, 2021, through May 1, 2022
- Excluded from the analysis were persons who reported
  - Simultaneous administration of mRNA COVID-19 booster dose, influenza vaccine, and **additional vaccine(s)** (n=2,647)
  - Booster dose **prior to** authorization (n=26,960)
  - Moderna vaccination in persons **<18 years** or Pfizer-BioNTech vaccination in persons aged **<12 years** (n=18)

Vaccine	Simultaneous influenza and mRNA booster	mRNA booster alone	Total
Pfizer-BioNTech	60,390	466,439	526,829
Moderna	30,633	422,637	453,270
Total	92,023	889,076	981,099

1. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2794318

Injection site reactions* reported at least once in days 0-7 following mRNA COVID-19 booster vaccination

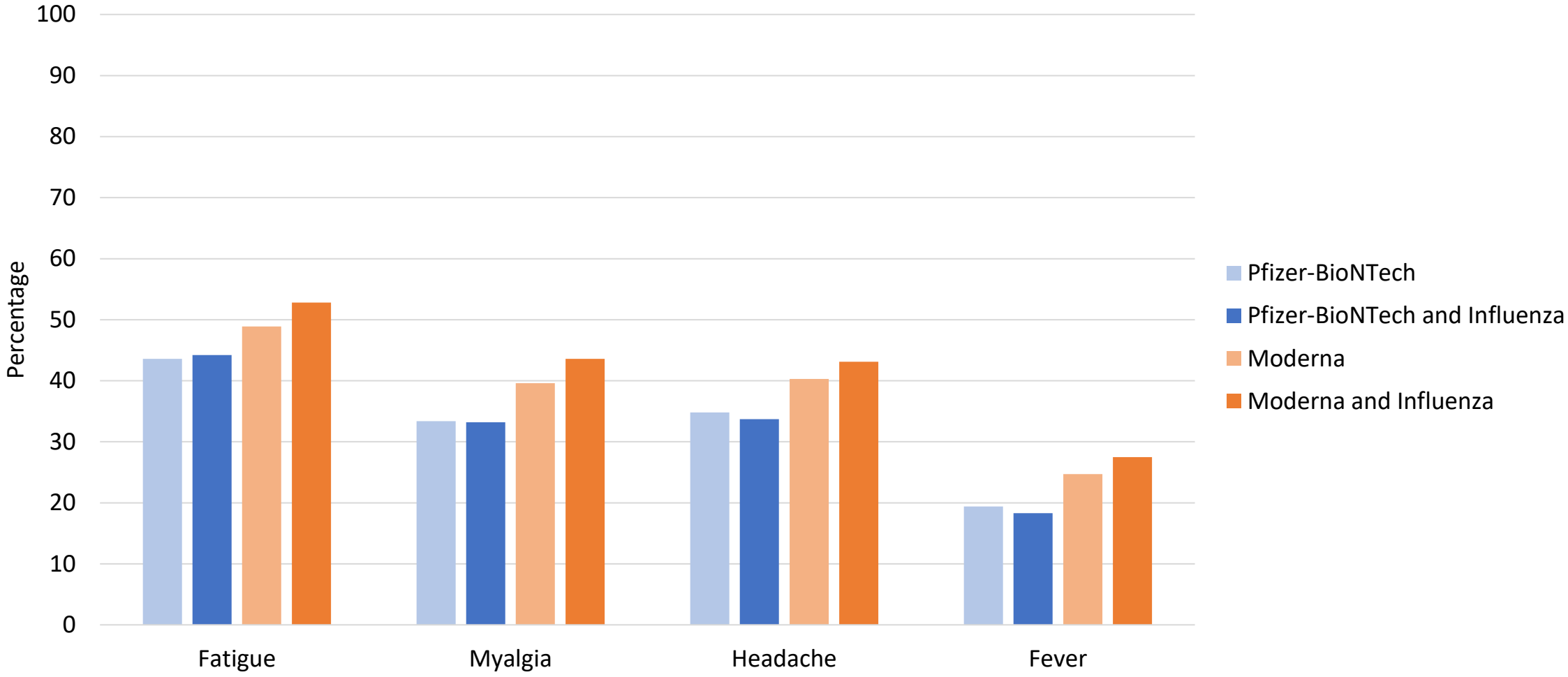


Data collected during September 22, 2021 through May 1, 2022

* If multiple vaccines were administered, local injection site reactions include reactions at all vaccination sites

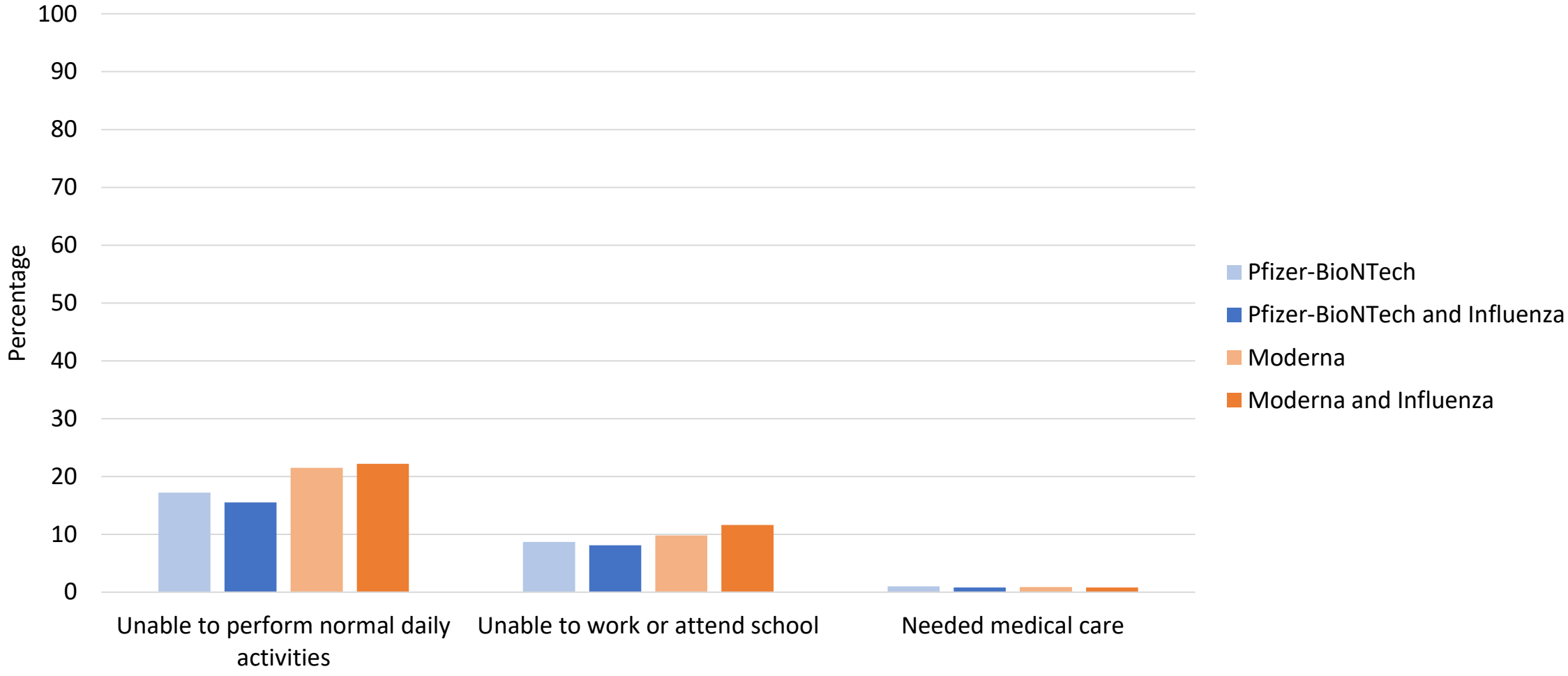
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2794318

Systemic reactions reported at least once in days 0-7 following mRNA COVID-19 booster vaccination



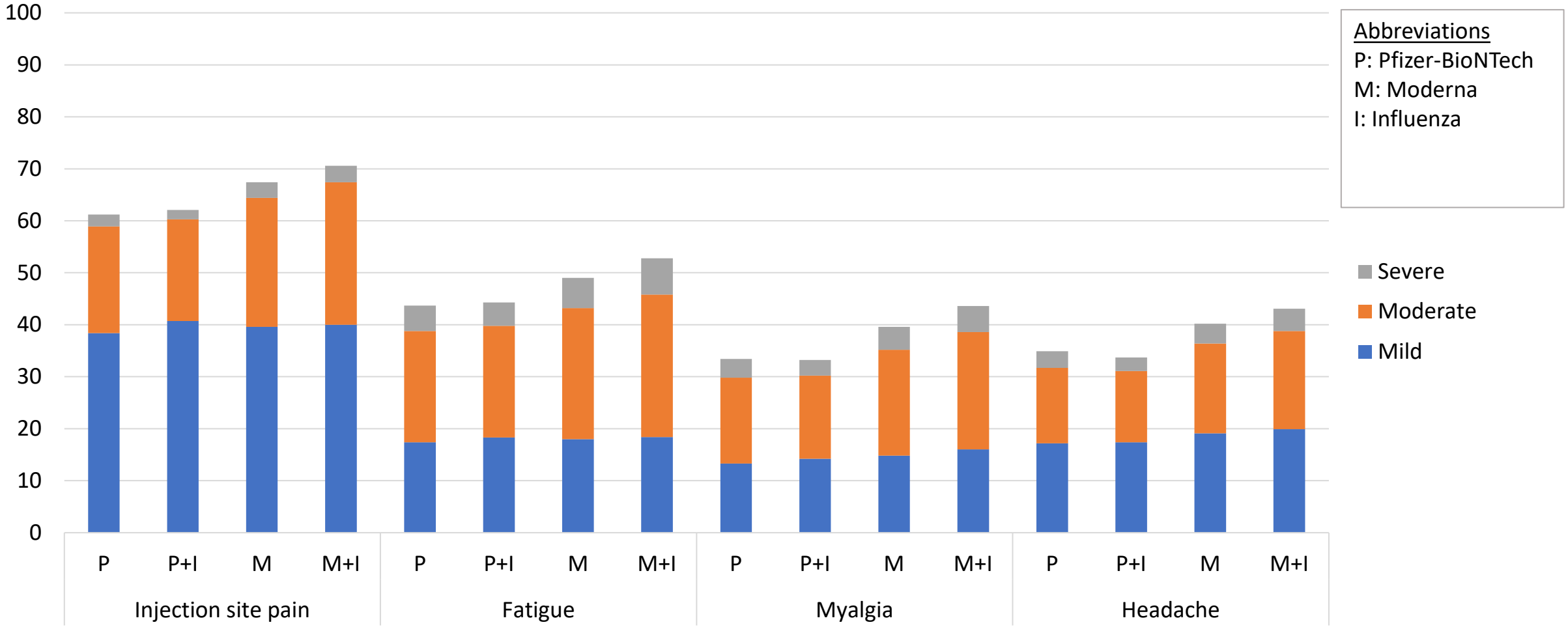
Data collected during September 22, 2021 through May 1, 2022
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2794318

Health impacts reported at least once in days 0-7 following mRNA COVID-19 booster vaccination



Data collected during September 22, 2021 through May 1, 2022
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2794318

Most common reactions reported at least once in days 0-7 following vaccination, by severity*



Data collected during September 22, 2021 through May 1, 2022

* Severity self-reported as mild (symptoms noticeable, but not a problem), moderate (symptoms limit normal daily activities), or severe (symptoms make daily activities difficult or impossible).

† If multiple vaccines were administered, local injection site reactions include reactions at all vaccination sites

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2794318

VSD data

VSD – most common simultaneous vaccinations with booster dose bivalent mRNA COVID-19 vaccines (as of October 8, 2022)

Rank #	Vaccine Combination	Frequency Count	% of Total Bivalent Doses - 610,611
1	Influenza IIV4 - preservative free	134,579	22.0
2	Influenza HD-IIV4	94,923	15.5
3	Influenza ccIIV4	9,602	1.6
4	Influenza aIIV4	8,381	1.4
5	Zoster Recombinant	3,269	0.5
6	Influenza IIV4	2,537	0.4
7	Influenza IIV4 pf + Zoster Recombinant	1,350	0.2
8	Influenza HD-IIV4 + Zoster Recombinant	1,337	0.2
9	Tdap	973	0.2
10	Influenza IIV4 pf + Tdap	969	0.2

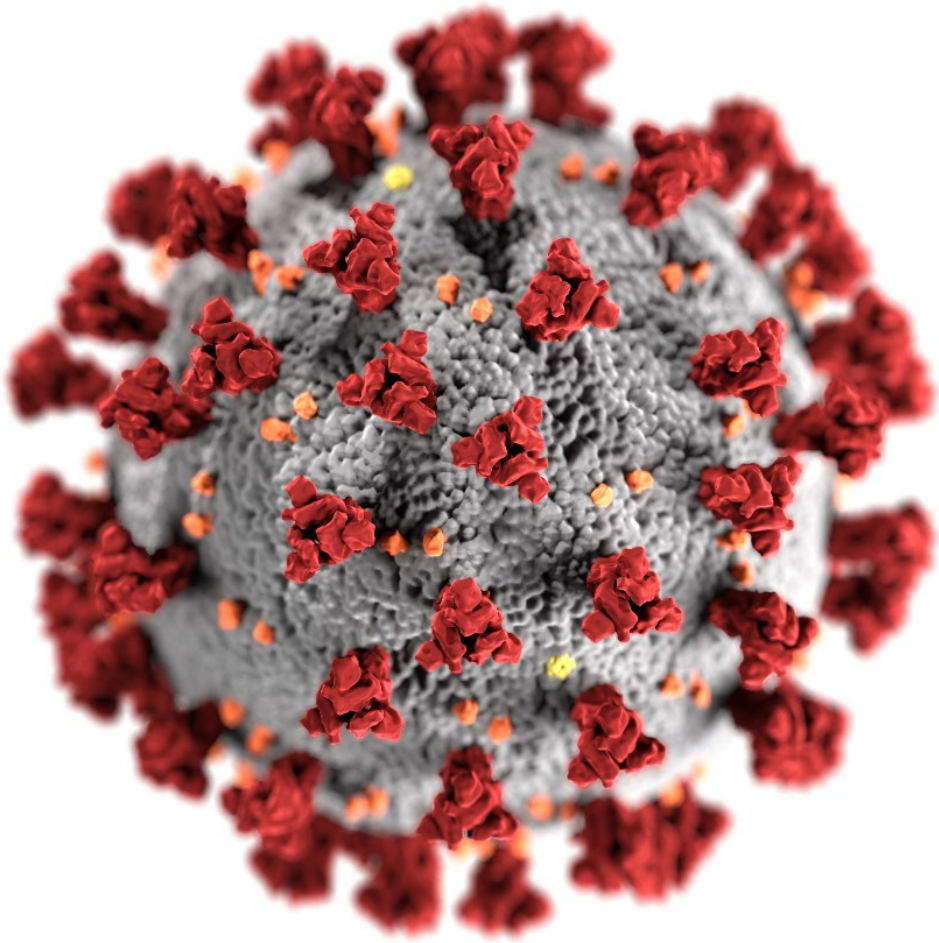
- ~230,000 doses of bivalent mRNA COVID-19 vaccine coadministered with influenza vaccine

VSD vaccine safety datalink

Summary — Coadministration of mRNA COVID-19 booster dose and influenza vaccines

- VAERS (N = 2,449 reports) (as of June 30, 2022)
  - Most (84%) non-serious; reported symptoms comparable to mRNA COVID-19 vaccine administered alone
  - Reported deaths (n=47) reflect age-appropriate causes
- V-safe (N = 92,023 coadministered doses) (as of May 1, 2022)
  - Frequency and severity of local and systemic reactions comparable to mRNA COVID-19 vaccine administered alone
  - ~10% or less unable to work or attend school; ≤3% sought medical care
- VSD (as of Oct 8, 2022)
  - ~230,000 doses of bivalent mRNA COVID-19 vaccine coadministered with influenza vaccine

Thank you!



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

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.

Vaccination summary of 5,542 VAERS reports among persons aged ≥12 years following a bivalent booster dose

Characteristic	% of reports
Manufacturer	
Pfizer-BioNTech	50.0
Moderna	50.0
Co-administration	
Yes	16.9
Influenza vaccine	15.4
Other vaccine	1.6
No	83.1

Data as of October 23, 2022.

VSD – Simultaneous Vaccinations with COVID-19 Bivalent Boosters - Data Through Oct 8, 2022

- Of ~2,000,000 influenza vaccinations this influenza season, **14.0%** have been simultaneously administered with booster dose bivalent mRNA COVID-19 vaccine
  - Booster dose bivalent mRNA COVID-19 vaccines are not available at influenza vaccination clinics.

- Of ~610,000 booster dose bivalent mRNA COVID-19 vaccinations, **42.6%** of have been simultaneously administered with an influenza vaccine
  - For ages 12-17 years, coadministration is as high as 48.6%
  - Appointments are necessary for Bivalent COVID-19 boosters, and if the member has not received an influenza vaccination, they are offered one.

VSD
vaccine safety datalink