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Effectiveness of COVID-19 (2023-2024 Formula) vaccines

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June 2024

Agenda: effectiveness of COVID-19 (2023-2024 Formula) vaccines

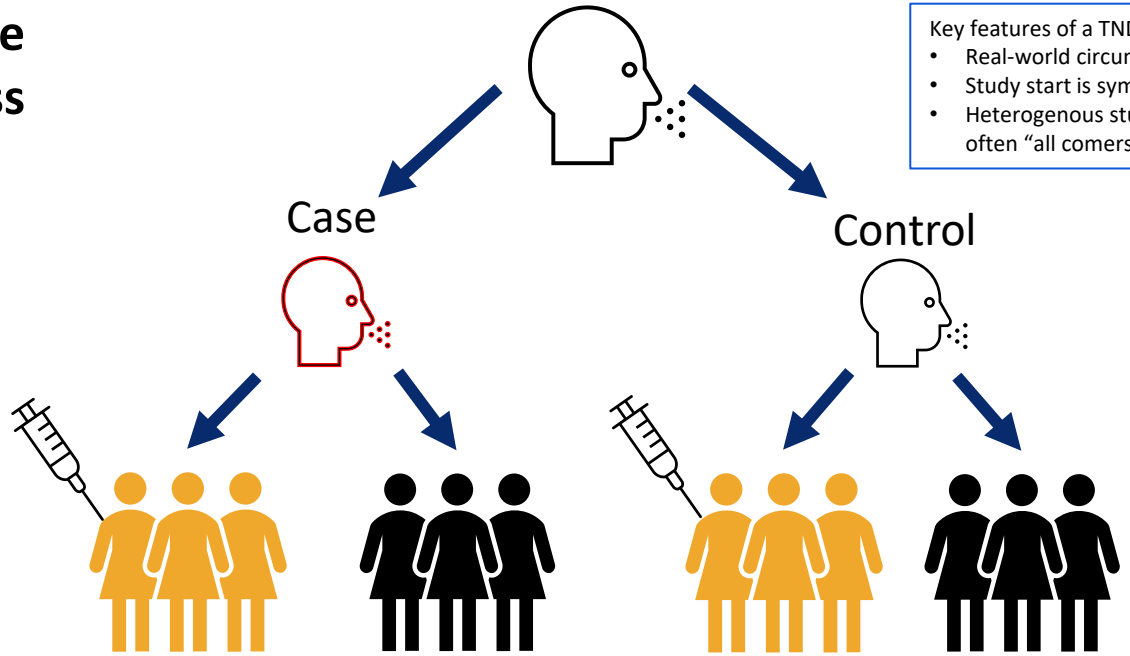
- **Vaccine effectiveness (VE) methods refresher**
- **Context for interpretation of COVID-19 VE**
- **COVID-19 VE in adults, by outcome and variant:**
  - Symptomatic SARS-CoV-2
  - COVID-19-associated emergency department/urgent care (ED/UC) encounters
  - COVID-19-associated hospitalizations, by immunocompromise status
  - COVID-19-associated critical outcomes
- **COVID-19 VE in young children and by age group**

Observational effectiveness measured in a test-negative design (TND) study

Person with acute respiratory illness

Pathogen test
(e.g., SARS-CoV-2, RSV, etc.)

Immunization status



Key features of a TND
- Real-world circumstances
- Study start is symptomatic medical encounter
- Heterogenous study population, often “all comers”

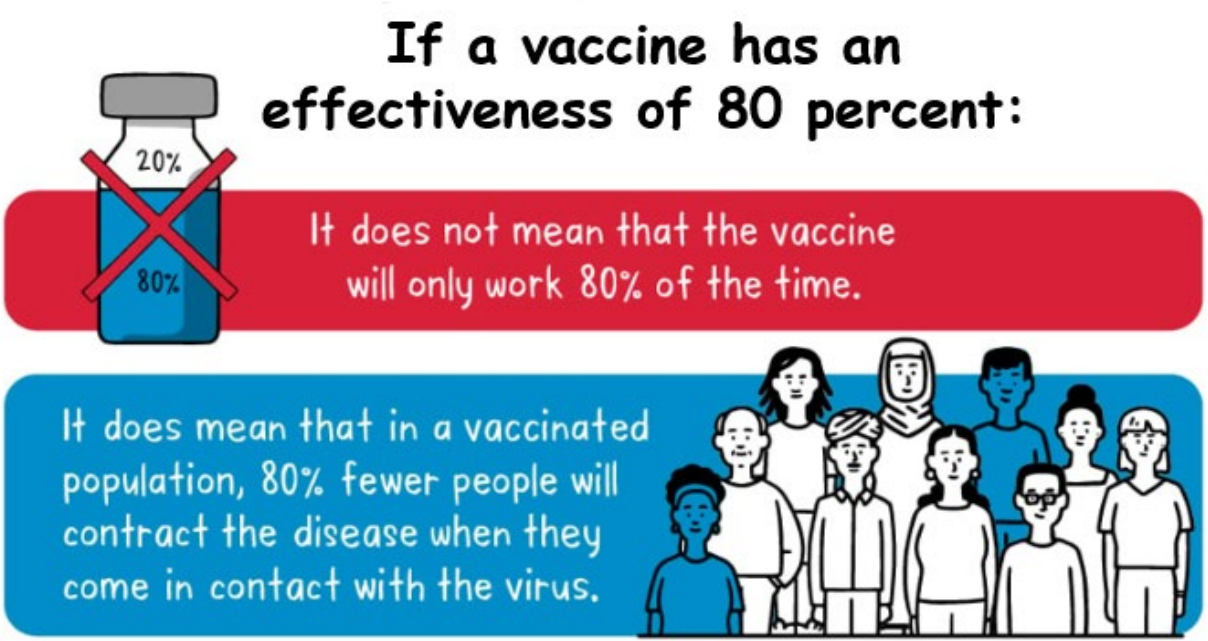
Effectiveness = 1 – (odds ratio) x 100% Odds ratio = $\frac{Odds\ of\ immunization_{cases}}{Odds\ of\ immunization_{controls}}$

Test-negative design methods

- **Benefits**
  - Reduces bias from health-care seeking behavior by including cases and controls who presented to care and received testing (usually at the same facility).
  - Efficient use of resources → allows controls to be selected from same healthcare system or testing location as cases.

- **Considerations**
  - Dependent on sensitivity and specificity of diagnostic testing.
  - Controls positive for another vaccine preventable disease can bias results. Sensitivity analyses excluding influenza positive controls can be helpful in assessing COVID-19 VE.

Vaccine effectiveness is a population level estimate.



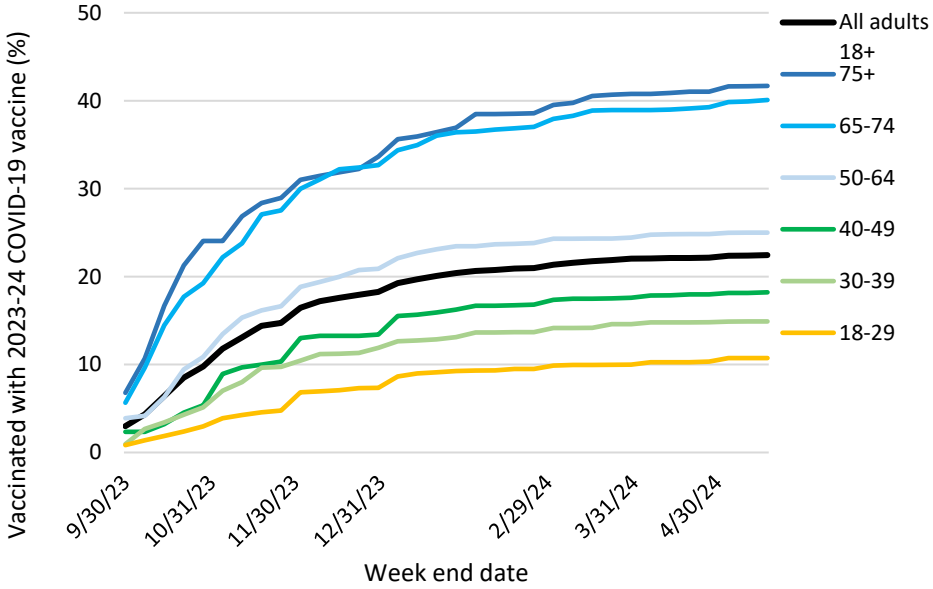
Adapted from: https://www.who.int/news-room/feature-stories/detail/vaccine-efficacy-effectiveness-and-protection

Percent of adults and children who received 2023-24 COVID-19 vaccine

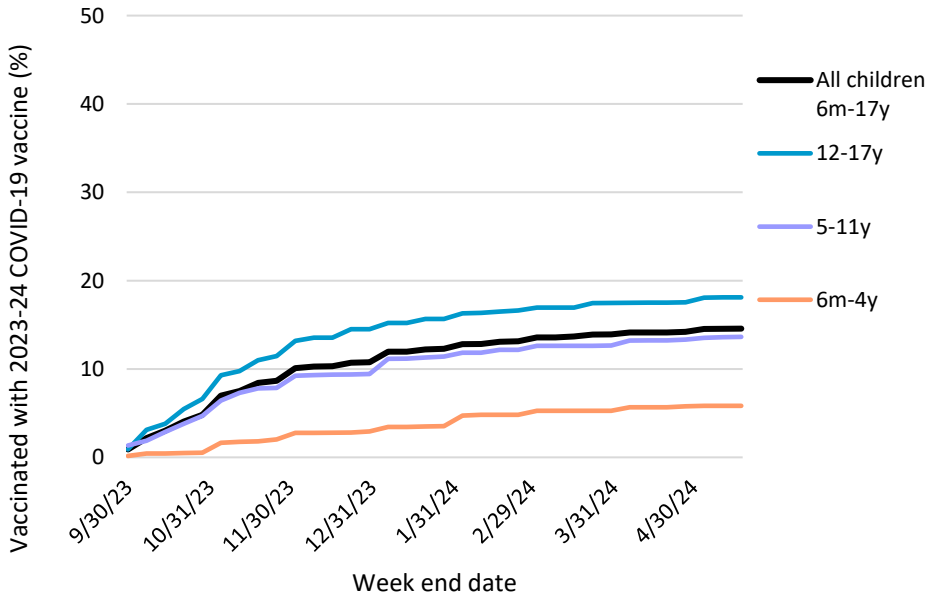
National Immunization Survey-Adult COVID Module (NIS-ACM) and -Child COVID Module (NIS-CCM)

September 2023-April 2024

COVID-19 Vaccination Coverage with 2023-24 Vaccine Among Adults ≥18 Years, NIS-ACM



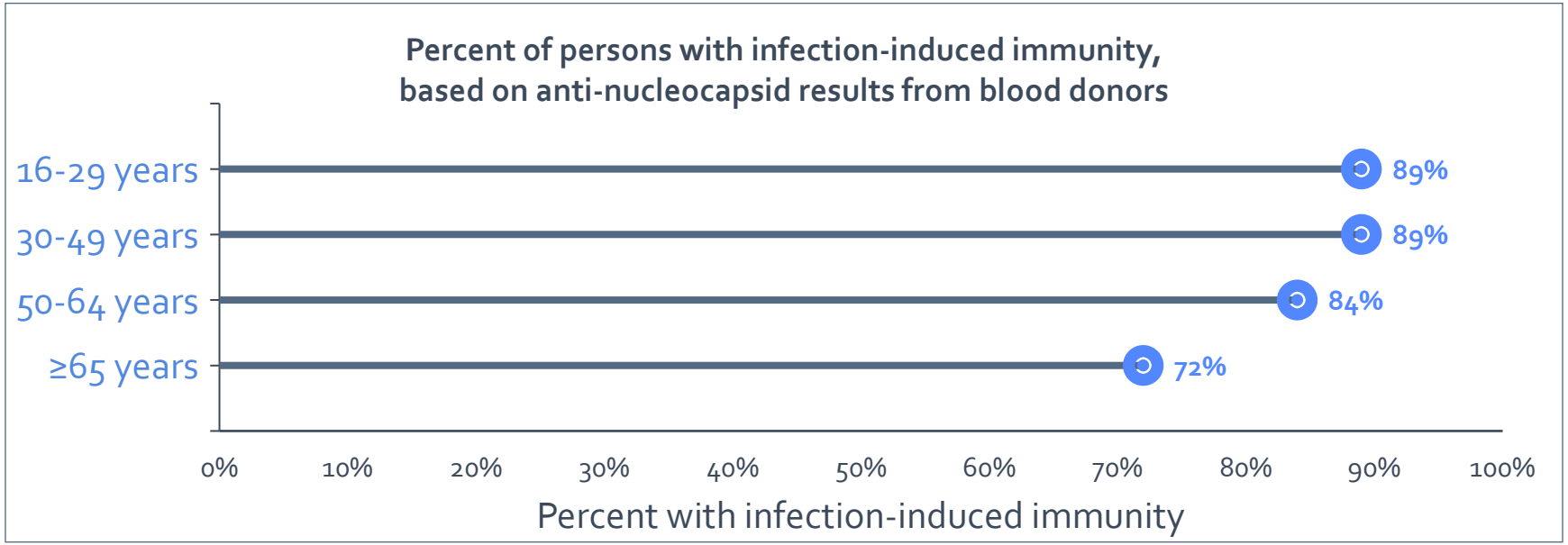
COVID-19 Vaccination Coverage with 2023-24 Vaccine Among Children 6 Months-17 Years, NIS-CCM



https://www.cdc.gov/vaccines/imz-managers/coverage/covidvaxview/index.html

Context for interpreting COVID-19 VE across age groups

- High rates of SARS-CoV-2 infection-induced immunity by July – August 2023.*



VE findings should be interpreted as the incremental benefit provided by COVID-19 vaccination in a population with a high prevalence of vaccine- and infection-induced immunity.

* Internal CDC data. Data on persons aged ≥16 years is from a longitudinal, national cohort of >35,000 blood donors.
Methods and prior data available at: https://covid.cdc.gov/covid-data-tracker/#nationwide-blood-donor-seroprevalence-2022

Measuring 2023-2024 COVID-19 VE

Measure	Definition	Vaccinated group	Comparison group
Absolute VE	Compares frequency of health outcomes in vaccinated and unvaccinated people	Received updated (2023-24) dose	Received no COVID-19 vaccines ever
Relative VE	Compares frequency of health outcomes in people who received one type of vaccine to people who received a different vaccine	Received updated (2023-24) dose	Eligible for, but did not receive, an updated (2023 -24) dose, but received previous doses of COVID-19 vaccine
VE presented today	Compares people who received 2023-2024 COVID-19 vaccine to people who did not, regardless of past vaccination	Received updated (2023-24) dose	Eligible for, but did not receive, an updated (2023 -24) dose, regardless of past vaccination history

Updates to COVID-19 VE against symptomatic infection

Increasing Community Access to Testing (ICATT) program

Data updated from MMWR published February 1, 2024:

Link-Gelles R, Ciesla AA, Mak J, et al. Early Estimates of Updated 2023–2024 (Monovalent XBB.1.5) COVID-19 Vaccine Effectiveness Against Symptomatic SARS-CoV-2 Infection Attributable to Co-Circulating Omicron Variants Among Immunocompetent Adults — Increasing Community Access to Testing Program, United States, September 2023–January 2024. MMWR Morb Mortal Wkly Rep 2024;73:77–83. DOI: http://dx.doi.org/10.15585/mmwr.mm7304a2

Increasing Community Access to Testing (ICATT): COVID-19 VE from national pharmacy testing data

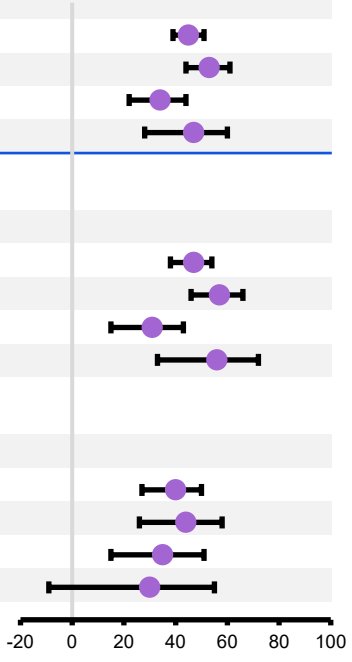
- Nationwide community-based pharmacy SARS-CoV-2 testing
- Self-reported COVID-19 vaccination history at time of registration for SARS-CoV-2 testing*
- **Design:** Test-negative analysis**
- **Population:** Adults ≥18 years with ≥1 COVID-like symptom and nucleic acid amplification testing (NAAT) for SARS-CoV-2
- **Exclusion criteria:** Individuals with self-reported immunocompromising conditions, reported a positive SARS-CoV-2 test in preceding 90 days***
- **Periods for analysis:**
  - Full analysis included tests from September 21, 2023 – May 22, 2024
  - Sub-analysis using S-gene target failure**** included tests from October 27, 2023 – April 3, 2024

*At 5% of testing encounters, COVID-19 vaccination status is collected by clinician interview. Receipt of 2023-2024 COVID-19 vaccine formulation determined by date of most recent dose (i.e., after Sept 12, 2023).
**Odds ratios were calculated using multivariable logistic regression, adjusting for single year of age, gender, race/ethnicity, SVI of the testing location (<0.5 versus ≥0.5), pharmacy contractor, underlying conditions (presence versus absence), U.S. Department of Health and Human Services region of testing location, and date of testing
***Additional exclusion criteria: 1) reported receiving Novavax as their most recent dose and reported receiving <2 total COVID-19 vaccine doses; 2) reported receiving a Janssen (Johnson & Johnson) COVID-19 vaccine dose after May 12, 2023; 3) received most recent COVID-19 dose <7 days prior to the date of testing or during September 1-12, 2023; or 4) registered for testing with a version of the questionnaire that only reported month and year of the most recent vaccine dose rather than calendar date.
**** Results of spike gene (S-gene) amplification in real-time reverse transcription–polymerase chain reaction (RT-PCR) can be used to distinguish certain SARS-CoV-2 lineages over time (2). S-gene target presence (SGTP) was detected in most lineages that circulated in 2023, including XBB lineages, whereas S-gene target failure (SGTF) is detected in JN.1 and other BA.2.86 lineages
Link-Gelles, et al. MMWR 2024: http://dx.doi.org/10.15585/mmwr.mm7304a2 (Results updated with additional data since publication.)

ICATT: VE of *2023-2024 COVID-19 vaccine* against *symptomatic infection* among adults aged ≥18 years, by age group and time since dose

September 2023 – May 2024

Age group/2023 -2024 COVID-19 vaccination status/days since dose	Total tests	SARSCoV-2-test-positive, N (%)	Median interval since last dose among those vaccinated, days (IQR)	Adjusted VE (95% CI)
≥18 years				
No 2023-2024 COVID-19 dose (ref)	12,965	4,661 (36)	687 (436 to 879)	**Ref**
2023-2024 COVID-19 dose, ≥7 days	1,895	483 (25)	70 (38 to 102)	**45 (39 to 51)**
2023-2024 COVID-19 dose, 7-59 days earlier	772	181 (23)	32 (20 to 46)	**53 (44 to 61)**
2023-2024 COVID-19 dose, 60-119 days earlier	809	237 (29)	84 (71 to 97)	**34 (22 to 44)**
2023-2024 COVID-19 dose, 120-179 days earlier	262	60 (23)	140 (128 to 152)	**47 (28 to 60)**
18-49 years				
No 2023-2024 COVID-19 dose (ref)	10,395	3,609 (35)	702 (451 to 887)	**Ref**
2023-2024 COVID-19 dose, ≥7 days	1,167	272 (23)	69 (39 to 101)	**47 (38 to 54)**
2023-2024 COVID-19 dose, 7-59 days earlier	474	96 (20)	32 (19 to 46)	**57 (46 to 66)**
2023-2024 COVID-19 dose, 60-119 days earlier	507	144 (28)	82 (71 to 95)	**31 (15 to 43)**
2023-2024 COVID-19 dose, 120-179 days earlier	147	27 (18)	139 (128 to 154)	**56 (33 to 72)**
≥50 years				
No 2023-2024 COVID-19 dose (ref)	2,570	1,052 (41)	610 (407 to 821)	**Ref**
2023-2024 COVID-19 dose, ≥7 days	728	211 (29)	71 (36 to 103)	**40 (27 to 50)**
2023-2024 COVID-19 dose, 7-59 days earlier	298	85 (29)	32 (21 to 44)	**44 (26 to 58)**
2023-2024 COVID-19 dose, 60-119 days earlier	302	93 (31)	85 (73 to 98)	**35 (15 to 51)**
2023-2024 COVID-19 dose, 120-179 days earlier	115	33 (29)	142 (128 to 152)	**30 (-9 to 55)***

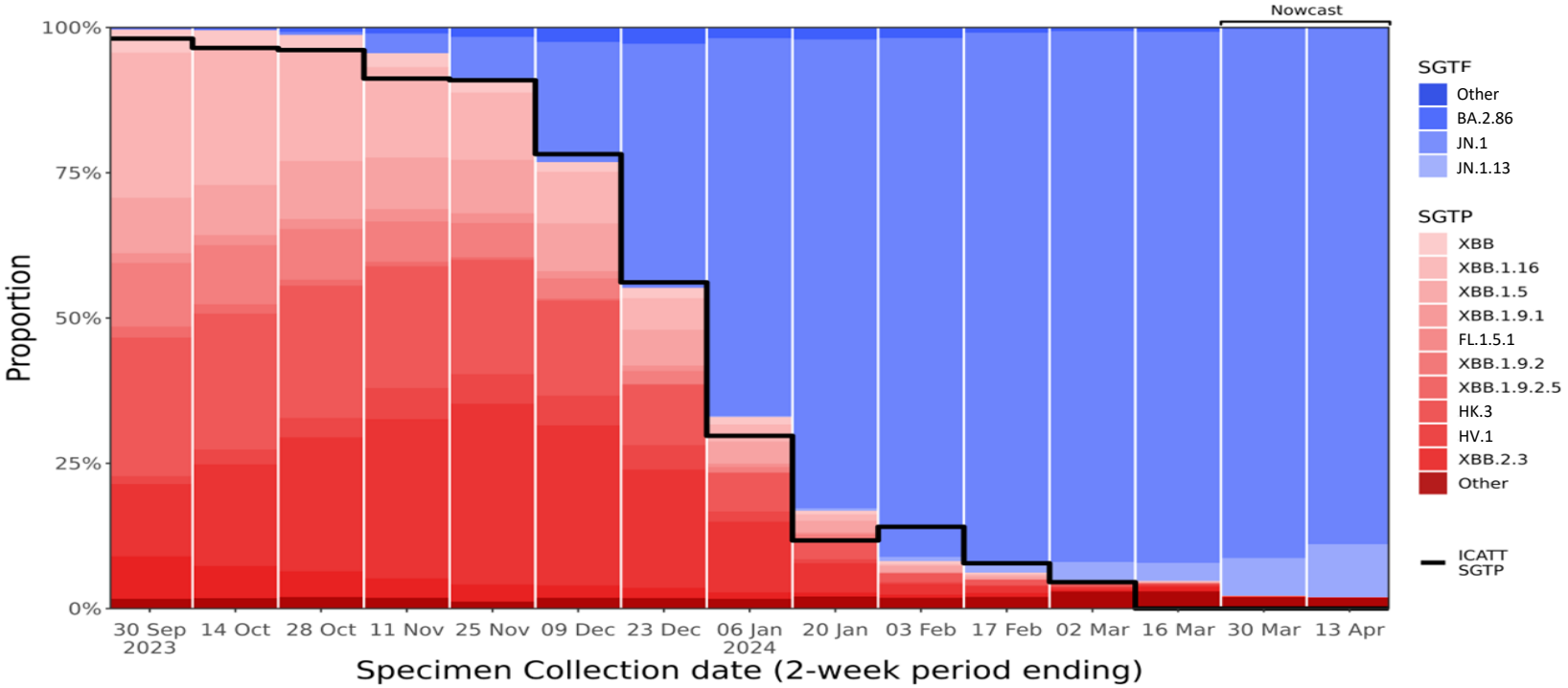


Link-Gelles, et al. MMWR 2024: http://dx.doi.org/10.15585/mmwr.mm7304a2 (Results updated with additional data since publication.)

*Some estimates are imprecise, which might be due to a relatively small number of persons in each level of vaccination or case status. This imprecision indicates that the actual VE could be substantially different from the point estimate shown, and estimates should therefore be interpreted with caution. Additional data accrual could increase precision and allow more precise interpretation. Ref=referent group; IQR=interquartile range; CI=confidence interval

Trends in estimated proportions of SARS-CoV-2 S-gene target presence and variant proportions in ICATT and Nowcast projections from national genomic surveillance

September 2023-April 2024



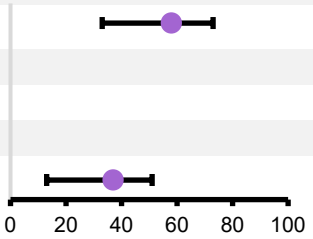
S-gene = spike gene; SGTF = S-gene target failure; SGTP = S-gene target presence

https://covid.cdc.gov/covid-data-tracker/#variant-proportions

ICATT: VE of *2023-2024 COVID-19 vaccine* against *symptomatic infection* among adults aged ≥18 years, by S-gene target (SGT) presence or failure and time since dose

October 2023 – April 2024

SGT status/2023-2024 COVID-19 vaccination status/days since dose	Total tests	SARS-CoV-2 negative		SARS-CoV-2 positive		Adjusted VE (95% CI)
		N (row %)	Median interval since last dose among vaccinated, days (IQR)	N (row %)	Median interval since last dose among vaccinated, days (IQR)	
SGT presence (likely non-JN.1)						
No 2023-2024 COVID-19 dose (ref)	2,357	1,934 (69)	668 (410 to 827)	423 (15)	670 (405 to 800)	**Ref**
2023-2024 COVID-19 dose, 60-119 days earlier	307	282 (77)	85 (72 to 101)	25 (7)	73 (69 to 83)	**58 (33 to 73)**
SGT failure (likely JN.1)						
No 2023-2024 COVID-19 dose (ref)	2,366	1,934 (69)	668 (410 to 827)	432 (15)	686 (426 to 829)	**Ref**
2023-2024 COVID-19 dose, 60-119 days earlier	343	282 (77)	85 (72 to 101)	61 (17)	89 (75 to 101)	**37 (13 to 51)**



Link-Gelles, et al. MMWR 2024: http://dx.doi.org/10.15585/mmwr.mm7304a2 (Results updated with additional data since publication.)

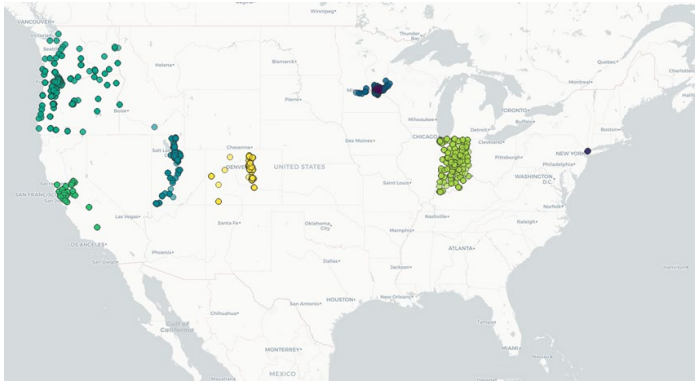
Updates to COVID-19 VE against COVID-19-associated ED/UC encounters

Data updated from MMWR published February 29, 2024:

DeCuir J, Payne AB, Self WH, et al. Interim Effectiveness of Updated 2023–2024 (Monovalent XBB.1.5) COVID-19 Vaccines Against COVID-19–Associated Emergency Department and Urgent Care Encounters and Hospitalization Among Immunocompetent Adults Aged ≥18 Years — VISION and IVY Networks, September 2023–January 2024. MMWR Morb Mortal Wkly Rep 2024;73:180–188. DOI: http://dx.doi.org/10.15585/mmwr.mm7308a5

VISION Multi-Site Network of Electronic Health Records

369 emergency rooms and urgent cares/229 hospitals

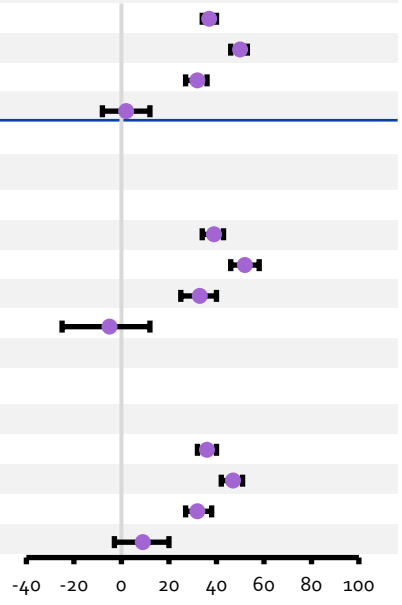


- **Design:** Test-negative analysis
- **Population:** Adults visiting a participating emergency department or urgent care (ED/UC) or hospitalized with COVID-19-like illness (CLI) with a SARS-CoV-2 NAAT test result within 10 days before or 72 hours after encounter
  - **Cases**: CLI with *positive* NAAT for SARS-CoV-2 and no positive NAAT for RSV or influenza
  - **Controls**: CLI with *negative* NAAT for SARS-CoV-2 and no positive NAAT for influenza
- **Vaccination data:** Documented by electronic health records and state and city registries

VISION: VE of *2023-2024 COVID-19 vaccine* against *ED/UC encounters* among immunocompetent adults aged ≥18 years, by age group

September 2023 – April 2024

Age group/2023 -2024 COVID-19 vaccination status/days since dose	Total encounters	SARSCoV-2-test-positive, N (%)	Median interval since last dose among vaccinated among those vaccinated, days (IQR)	Adjusted VE (95% CI)
≥18 years				
No 2023-2024 COVID-19 dose (ref)	194,095	22,114 (11)	712 (467-852)	**Ref**
2023-2024 COVID-19 dose, ≥7 days	35,243	2,613 (7)	78 (44-118)	**37 (34-40)**
2023-2024 COVID-19 dose, 7-59 days earlier	12,898	973 (8)	34 (21-47)	**50 (46-53)**
2023-2024 COVID-19 dose, 60-119 days earlier	13,918	1,150 (8)	87 (73-103)	**32 (27-36)**
2023-2024 COVID-19 dose, 120-179 days earlier	8,427	490 (6)	143 (131-157)	**2 (-8-12)**
18-64 years				
No 2023-2024 COVID-19 dose (ref)	138,644	14,839 (11)	743 (560-879)	**Ref**
2023-2024 COVID-19 dose, ≥7 days	12,727	795 (6)	74 (41-113)	**39 (34-43)**
2023-2024 COVID-19 dose, 7-59 days earlier	5,025	312 (6)	33 (20-46)	**52 (46-58)**
2023-2024 COVID-19 dose, 60-119 days earlier	4,962	339 (7)	87 (73-103)	**33 (25-40)**
2023-2024 COVID-19 dose, 120-179 days earlier	2,740	144 (5)	141 (130-156)	**-5 (-25-12)**
≥65 years				
No 2023-2024 COVID-19 dose (ref)	55,451	7,275 (13)	589 (390-788)	**Ref**
2023-2024 COVID-19 dose, ≥7 days	22,516	1,818 (8)	80 (46-120)	**36 (32-40)**
2023-2024 COVID-19 dose, 7-59 days earlier	7,873	661 (8)	35 (21-47)	**47 (42-51)**
2023-2024 COVID-19 dose, 60-119 days earlier	8,956	811 (9)	87 (73-102)	**32 (27-38)**
2023-2024 COVID-19 dose, 120-179 days earlier	5,687	346 (6)	144 (131-158)	**9 (-3-20)**



*Some estimates are imprecise, which might be due to a relatively small number of persons in each level of vaccination or case status. This imprecision indicates that the actual VE could be substantially different from the point estimate shown, and estimates should therefore be interpreted with caution. Additional data accrual could increase precision and allow more precise interpretation.

https://www.cdc.gov/mmwr/volumes/73/wr/mm7308a5.htm (Results updated with additional data since publication.) VE was calculated as (1 – odds ratio) x 100%, estimated using a test-negative case-control design, adjusted for age, sex, race and ethnicity, geographic region, and calendar time.

Updates to COVID-19 VE against COVID-19-associated hospitalization and critical illness

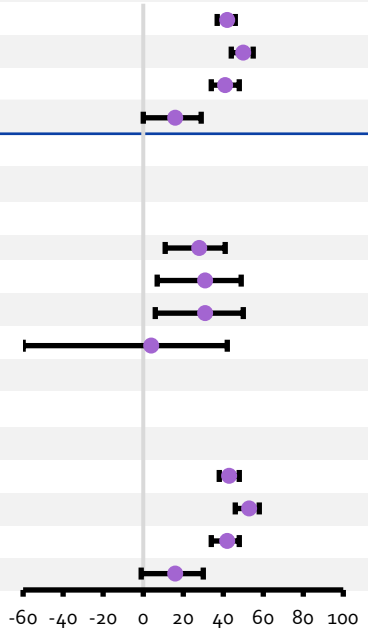
Data updated from MMWR published February 29, 2024:

DeCuir J, Payne AB, Self WH, et al. Interim Effectiveness of Updated 2023–2024 (Monovalent XBB.1.5) COVID-19 Vaccines Against COVID-19–Associated Emergency Department and Urgent Care Encounters and Hospitalization Among Immunocompetent Adults Aged ≥18 Years — VISION and IVY Networks, September 2023–January 2024. MMWR Morb Mortal Wkly Rep 2024;73:180–188. DOI: http://dx.doi.org/10.15585/mmwr.mm7308a5

VISION: VE of *2023-2024 COVID-19 vaccine* against *hospitalization* among immunocompetent adults aged ≥18 years, by age group

September 2023 – April 2024

Age group/2023 -2024 COVID-19 vaccination status/days since dose	Total encounters	SARSCoV-2-test-positive, N (%)	Median interval since last dose among those vaccinated, days (IQR)	Adjusted VE (95% CI)
≥18 years				
No 2023-2024 COVID-19 dose (ref)	58,682	6,295 (11)	682 (434-835)	Ref
2023-2024 COVID-19 dose, ⩾7 days	12,148	881 (7)	79 (44-119)	42 (37-46)
2023-2024 COVID-19 dose, 7-59 days earlier	4,365	340 (8)	34 (20-47)	50 (44-55)
2023-2024 COVID-19 dose, 60-119 days earlier	4,758	367 (8)	88 (73-103)	41 (34-48)
2023-2024 COVID-19 dose, 120-179 days earlier	3,025	174 (6)	143 (131-157)	16 (0-29)
18-64 years				
No 2023-2024 COVID-19 dose (ref)	23,123	1,593 (7)	733 (526-876)	Ref
2023-2024 COVID-19 dose, ≥7 days	2,119	112 (5)	75 (39-112)	28 (11-41)
2023-2024 COVID-19 dose, 7-59 days earlier	838	50 (6)	33 (20-45)	31 (7-49)
2023-2024 COVID-19 dose, 60-119 days earlier	833	45 (5)	88 (74-103)	31 (6-50)
2023-2024 COVID-19 dose, 120-179 days earlier	448	17 (4)	143 (131-157)	4 (-60-42)*
≥65 years				
No 2023-2024 COVID-19 dose (ref)	35,559	4,702 (13)	634 (407-809)	Ref
2023-2024 COVID-19 dose, ≥7 days	10,029	769 (8)	80 (45-121)	43 (38-48)
2023-2024 COVID-19 dose, 7-59 days earlier	3,527	290 (8)	34 (20-47)	53 (46-58)
2023-2024 COVID-19 dose, 60-119 days earlier	3,925	322 (8)	88 (73-103)	42 (34-48)
2023-2024 COVID-19 dose, 120-179 days earlier	2,577	157 (6)	143 (131-158)	16 (-1-30)



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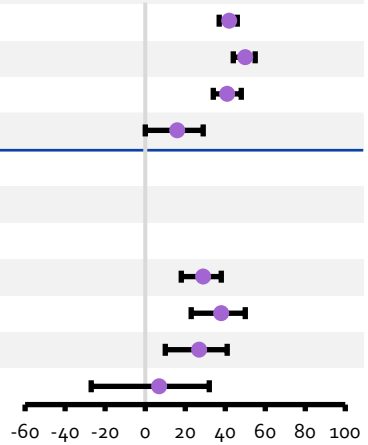
https://www.cdc.gov/mmwr/volumes/73/wr/mm7308a5.htm (Results updated with additional data since publication.) VE was calculated as (1 − odds ratio) x 100%, estimated using a test-negative case-control design, adjusted for age, sex, race and ethnicity, geographic region, and calendar time.

VISION: VE of *2023-2024 COVID-19 vaccine* against *hospitalization* among adults aged ≥18 years, by immunocompromise status

September 2023 – April 2024

Immunocompromise status/2023 -2024 COVID-19 vaccination status/days since dose	Total encounters	SARSCoV-2-test-positive N (%)	Median interval since last dose among those vaccinated, days (IQR)	Adjusted VE (95% CI)
≥18 years, non-immunocompromised				
No 2023-2024 COVID-19 dose (ref)	58,682	6,295 (11)	682 (434-835)	Ref
2023-2024 COVID-19 dose, ⩾7 days	12,148	881 (7)	79 (44-119)	42 (37-46)
2023-2024 COVID-19 dose, 7-59 days earlier	4,365	340 (8)	34 (20-47)	50 (44-55)
2023-2024 COVID-19 dose, 60-119 days earlier	4,758	367 (8)	88 (73-103)	41 (34-48)
2023-2024 COVID-19 dose, 120-179 days earlier	3,025	174 (6)	143 (131-157)	16 (0-29)
≥18 years, immunocompromised				
No 2023-2024 COVID-19 dose (ref)	16,172	1,417 (9)	629 (402-807)	Ref
2023-2024 COVID-19 dose, ≥7 days	4,272	279 (7)	80 (44-120)	29 (18-38)
2023-2024 COVID-19 dose, 7-59 days earlier	1,515	105 (7)	34 (21-46)	38 (23-50)
2023-2024 COVID-19 dose, 60-119 days earlier	1,677	121 (7)	88 (74-105)	27 (10-41)
2023-2024 COVID-19 dose, 120-179 days earlier	1,080	53 (5)	143 (132-158)	7 (-27-32)*



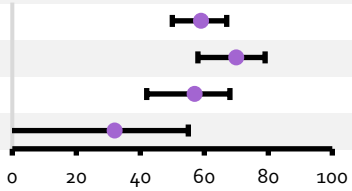
Additional methods, including definition of immunocompromised available: https://www.cdc.gov/mmwr/volumes/73/wr/mm7308a5.htm (Results updated with additional data since publication.) VE was calculated as (1 – odds ratio) x 100%, estimated using a test-negative case-control design, adjusted for age, sex, race and ethnicity, geographic region, and calendar time.

* Some estimates are imprecise, which might be due to a relatively small number of persons in each level of vaccination or case status. This imprecision indicates that the actual VE could be substantially different from the point estimate shown, and estimates should therefore be interpreted with caution. Additional data accrual could increase precision and allow more precise interpretation.

VISION: VE of *2023-2024 COVID-19 vaccine* against *critical illness* among immunocompetent adults aged ≥18 years, by age group

September 2023 – April 2024

Age group/2023 -2024 COVID-19 vaccination status/days since dose	Total encounters	SARSCoV-2-test-positive N (%)	Median interval since last dose among those vaccinated, days (IQR)	Adjusted VE (95% CI)
≥18 years				
No 2023-2024 COVID-19 dose (ref)	53,492	1,105 (2)	683 (436-837)	**Ref**
2023-2024 COVID-19 dose, ≥7 days	11,380	113 (1)	80 (44-120)	**59 (50-67)**
2023-2024 COVID-19 dose, 7-59 days earlier	4,062	37 (1)	34 (20-46)	**70 (58-79)**
2023-2024 COVID-19 dose, 60-119 days earlier	4,441	50 (1)	88 (74-104)	**57 (42-68)**
2023-2024 COVID-19 dose, 120-179 days earlier	2,877	26 (1)	143 (131-158)	**32 (-4-55)***



CDC unpublished data. Critical illness defined as admission to an intensive care unit (ICU) or death while hospitalized or ≤28 days after hospital admission. VE was calculated as (1 − odds ratio) x 100%, estimated using a test-negative case-control design, adjusted for age, sex, race and ethnicity, geographic region, and calendar time.

*Some estimates are imprecise, which might be due to a relatively small number of persons in each level of vaccination or case status. This imprecision indicates that the actual VE could be substantially different from the point estimate shown, and estimates should therefore be interpreted with caution. Additional data accrual could increase precision and allow more precise interpretation.

IVY Network — 26 hospitals, 20 U.S. States

- **Design**: Test-negative, case-control design
- **Population**: Adults aged ≥18 years hospitalized with COVID-like illness (CLI)* and SARS-CoV-2 test results within 10 days of illness onset and 3 days of admission
  - **Cases:** CLI and test *positive* for SARS-CoV-2 by NAAT or antigen
    - Co-infections with influenza and RSV are excluded
  - **Controls**: CLI and test *negative* for SARS-CoV-2 and influenza by RT-PCR
- **Vaccination data:** Electronic medical records (EMR), state and city registries, and plausible self-report
- **Specimens:** Nasal swabs obtained on all patients for central RT-PCR testing and whole genome sequencing

IVY

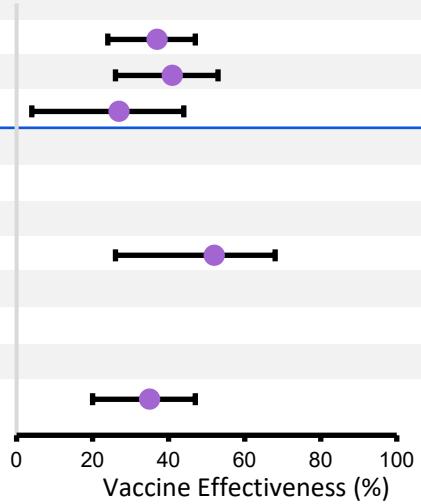
INVESTIGATING RESPIRATORY VIRUSES IN THE ACUTELY ILL

*CLI is defined as presence of any one of the following: fever, cough, shortness of breath, chest imaging consistent with pneumonia, or hypoxemia

IVY: VE of *2023–2024 vaccine* against *hospitalization* among immuno*competent* adults aged ≥18 years, by age group and time since dose

September 21, 2023 – April 30, 2024

COVID-19 dosage pattern/age group	COVID-19 case-patients N (Col %)	COVID-19 control - patients N (Col %)	Median interval since last dose among those vaccinated, days (IQR)	VE* % (95% CI)
≥18 years				
No 2023-2024 COVID-19 dose (ref)	1538 (89)	4149 (84)	681 (430–840)	**Ref**
2023-2024 COVID-19 dose, ≥7 days	191 (11)	786 (16)	81 (43–121)	**37 (24–47)**
2023-2024 COVID-19 dose, 7–89 days earlier	110 (6)	441 (9)	48 (26-69)	**41 (26–53)**
2023-2024 COVID-19 dose, 90–179 days earlier	81 (5)	345 (7)	127 (107–148)	**27 (4–44)**
18–64 years				
No 2023-2024 COVID-19 dose (ref)	530 (95)	2084 (90)	733 (485–879)	**Ref**
2023-2024 COVID-19 dose, ≥7 days	27 (5)	236 (10)	73 (34–112)	**52 (26–68)**
≥65 years				
No 2023-2024 COVID-19 dose (ref)	1008 (86)	2065 (79)	643 (406–802)	**Ref**
2023-2024 COVID-19 dose, ≥7 days	164 (14)	550 (21)	82 (45–123)	**35 (20–47)**



*Logistic regression models were adjusted for age, sex, race and ethnicity, geographic region, and calendar time.

IVY*: VE of *2023–2024 vaccine* against *hospitalization* among adults aged ≥18 years *by SARS-CoV-2 lineage* using viral whole-genome sequencing

- **Population**
  - **Cases:** COVID-like illness (CLI) and test *positive* for SARS-CoV-2[†]; **restricted to patients with sequence-confirmed[§] JN lineage (BA.2.86 and its descendants) infection or XBB lineage (all other co-circulating lineages) infections**
  - **Controls:** CLI and test *negative* for SARS-CoV-2 and influenza viruses by RT-PCR

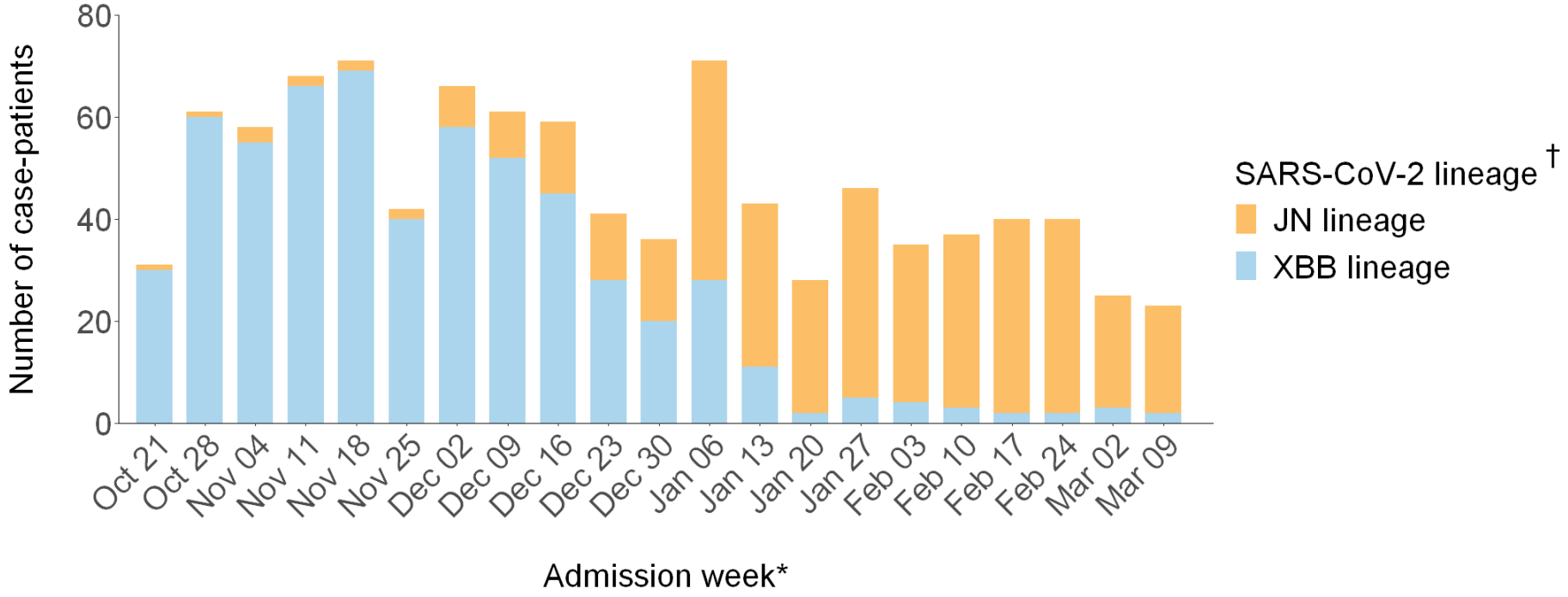
- **Analytic Period:** October 18, 2023–March 9, 2024
  - First date on which a patient was admitted with sequence-confirmed JN lineage infection
  - Last week during which a patient was admitted with sequence-confirmed XBB lineage infection

- VE[¶] against hospitalization was calculated separately using case-patients with sequence-confirmed SARS-CoV-2 JN and XBB lineage infections

* Investigating Respiratory Viruses in the Acutely Ill (IVY) Network. https://www.cdc.gov/flu/vaccines-work/ivy.htm
† Case patients who tested positive for influenza viruses or RSV were excluded.
§ Identification of a SARS-CoV-2 lineage through viral whole-genome sequencing was successful for 63% of case-patients during the analysis period.
¶ Odds ratios were adjusted for age, sex, race and ethnicity, geographic region, calendar time, and Charlson comorbidity index.

IVY: Number of COVID-19 case-patients by hospital admission week and SARS-CoV-2 lineage

October 18, 2023 – March 9, 2024



* Dates are for the end of the admission week.

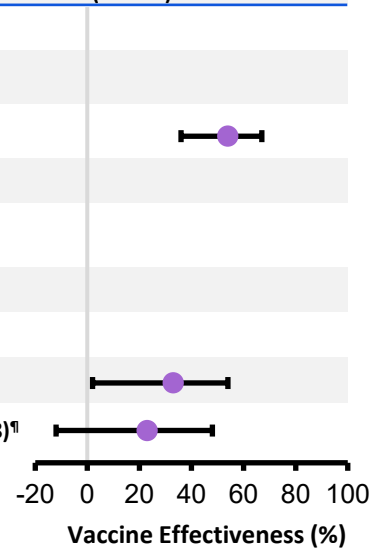
† JN lineages comprised BA.2.86 and its descendants. XBB lineages comprised all other co-circulating lineages.

Identification of a SARS-CoV-2 lineage through viral whole-genome sequencing was successful for 63% of case-patients during the analysis period.

IVY: VE of *2023–2024 COVID-19 vaccine* against *hospitalization* among adults aged ≥18 years*, by SARS-CoV-2 lineage and time since dose

October 18, 2023 – March 9, 2024

COVID-19 dosage pattern	COVID-19 case-patients		COVID-19 control-patients		VE** (95% CI)
	N (Col %)	Median interval since last dose among vaccinated, days (IQR)	N (Col %)	Median interval since last dose among vaccinated, days (IQR)	
XBB lineages†					
No 2023-2024 COVID-19 dose (ref)	532 (91)	557 (385–751)	3736 (82)	688 (429–834)	**Ref**
2023-2024 COVID-19 dose, 7–89 days earlier	47 (8)	44 (22–67)	568 (12)	47 (26–68)	**54 (36–67)**
2023-2024 COVID-19 dose, 90–179 days earlier	6 (1)	92 (91–105)	276 (6)	118 (106–131)	**§**
JN lineages†					
No 2023-2024 COVID-19 dose (ref)	319 (80)	746 (479–855)	3736 (82)	688 (429–834)	**Ref**
2023-2024 COVID-19 dose, 7–89 days earlier	38 (10)	56 (31–74)	568 (12)	47 (26–68)	**33 (2–54)¶**
2023-2024 COVID-19 dose, 90–179 days earlier	40 (10)	118 (107–130)	276 (6)	118 (106–131)	**23 (-12 to 48)¶**



* These results include both immunocompetent and immunocompromised persons.

† JN lineages comprised BA.2.86 and its descendants. XBB lineages comprised all other co-circulating lineages.

§ Based on timing of recommendations to receive 2023–2024 COVID-19 vaccines and JN lineage emergence, limited numbers of individuals with XBB infection were 90–179 days from their updated dose, precluding estimation of VE within this stratum.

¶ Some estimates are imprecise, which might be due to a relatively small number of persons in each level of vaccination or case status. This imprecision indicates that the actual VE could be substantially different from the point estimate shown, and estimates should therefore be interpreted with caution.

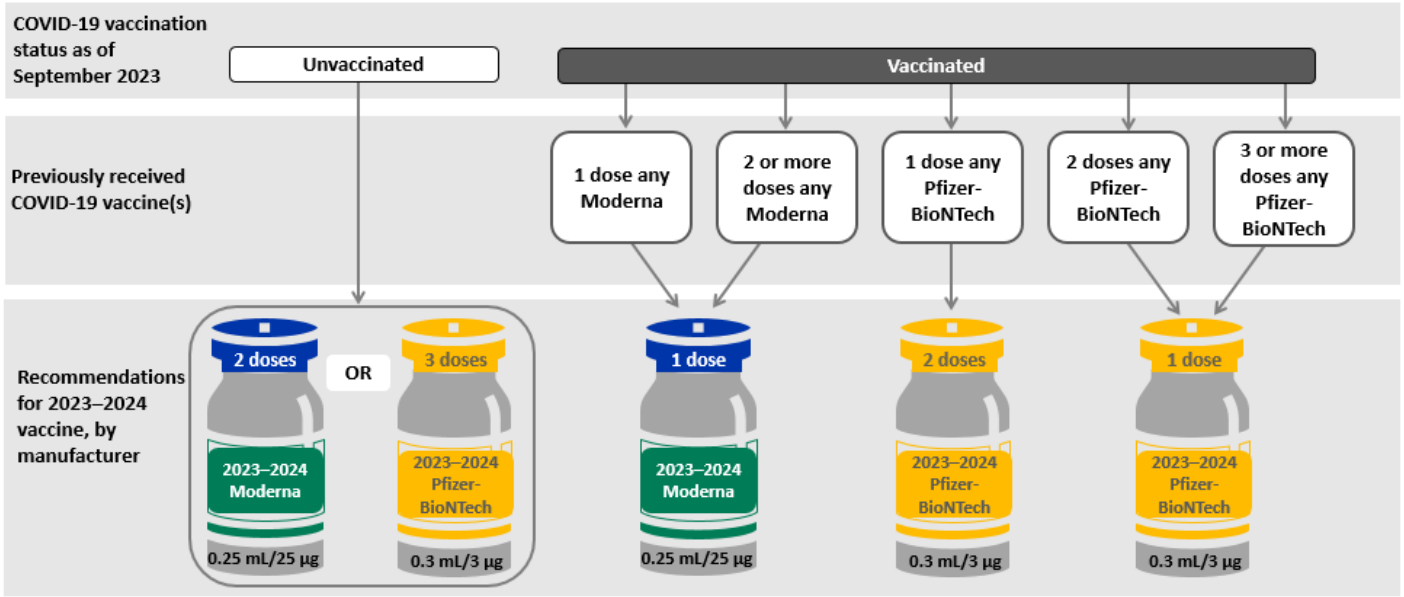
** VE estimates adjusted for age, sex, race and ethnicity, geographic region, calendar time, and Charlson comorbidity index.

CDC unpublished data.

COVID-19 VE in young children and by age group

Reminder: children aged 6 months-4 years continue to be recommended for a complete initial series

Recommended 2023–2024 COVID-19 mRNA vaccines for people who are NOT immunocompromised, aged 6 months–4 years*

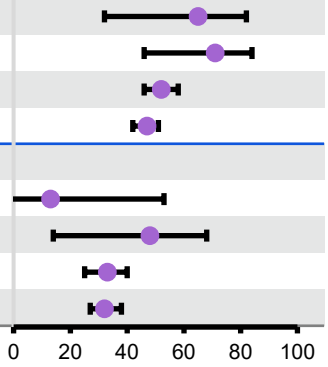


*For information about administration intervals and people who transition from age 4 years to age 5 years during an mRNA vaccination series, see Table 1 in the Interim Clinical Considerations for Use of COVID-19 vaccines.

VISION: VE of *2023–2024 COVID-19 vaccine doses* against *ED/UC encounters* was similar across age groups

September 2023 – May 2024

Age group | COVID-19 vaccination status	Total encounters	SARSCoV-2-test-positive, N (%)	Median interval since last dose among those vaccinated, days (IQR)	Adjusted VE (95% CI)
No updated 2023-2024 COVID-19 vaccine dose*				
9 months-4 years	28,026	1,155 (4)	345 (229437)	**Ref**
5-17 years	34,517	1,421 (4)	642 (438757)	**Ref**
18-64 years	138,644	14,839 (11)	743 (560879)	**Ref**
⩾65 years	55,451	7,275 (13)	589 (390-788)	**Ref**
2023-2024 COVID-19 dose received 7-59 days earlier				
9 months-4 years	524	9 (2)	33 (20-46)	**65 (32-82)**
5-17 years	766	11 (1)	33 (19-47)	**71 (46-84)**
18-64 years	5,025	312 (6)	33 (20-46)	**52 (46-58)**
≥65 years	7,873	661 (8)	35 (21-47)	**47 (42-51)**
2023-2024 COVID-19 dose received 60-119 days earlier				
9 months-4 years	355	11 (3)	88 (74-103)	**13 (-61-53)****
5-17 years	735	17 (2)	91 (75-105)	**48 (14-68)**
18-64 years	4,962	339 (7)	87 (73-103)	**33 (25-40)**
≥65 years	8,956	811 (9)	87 (73-102)	**32 (27-38)**



* Includes all individuals who did not receive a 2023-2024 COVID-19 vaccine. For those aged ≥5 years, this includes unvaccinated persons and persons who were vaccinated with ≥1 original monovalent or bivalent COVID-19 doses. For those aged <5 years, both those in the referent group and those in the vaccinated group were required to have completed an initial series. The 2023-2024 dose could have been part of the initial series or in addition to the initial series.

** Some estimates are imprecise, which might be due to a relatively small number of persons in each level of vaccination or case status. This imprecision indicates that the actual VE could be substantially different from the point estimate shown, and estimates should therefore be interpreted with caution. Additional data accrual could increase precision and allow more precise interpretation.

Conclusions

- 2023-2024 COVID-19 vaccination provided increased protection against symptomatic SARS-CoV-2 infection and COVID-19-associated ED/UC visits and hospitalizations compared to no 2023-2024 vaccine dose.

- Waning patterns appeared similar to previous COVID-19 vaccine formulations; most durable protection appeared to be for critical illness, though statistical power was lacking in the longest time period since vaccination

- As with previous COVID-19 vaccine formulations, effectiveness was similar across age groups

- Receipt of 2023-2024 COVID-19 vaccine provided protection against JN.1 and other circulating variants, though may be lower than protection provided against XBB sublineage variants

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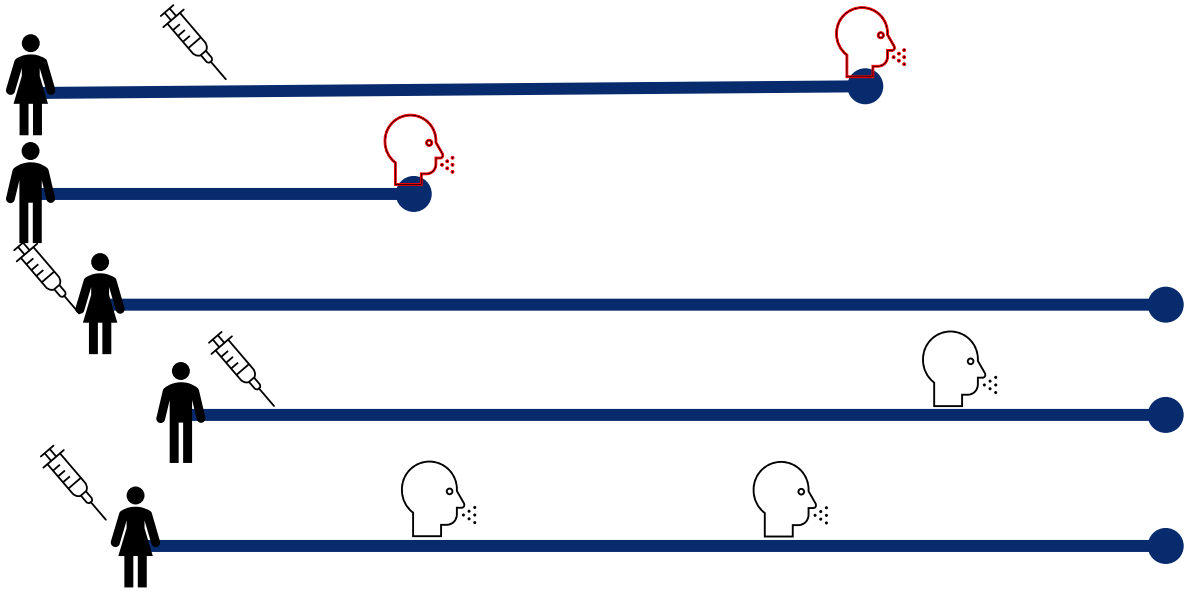
Back-up

Observational effectiveness measured in a cohort study

Key features of an observational cohort
- Real-world circumstances
- People vaccinated before or after enrollment and followed for outcome
- Generally, more heterogenous population vs. randomized controlled trial (RCT)



Symptomatic, tests positive for pathogen of interest

Symptomatic, tests negative for pathogen of interest

Immunization dose received

End of follow-up

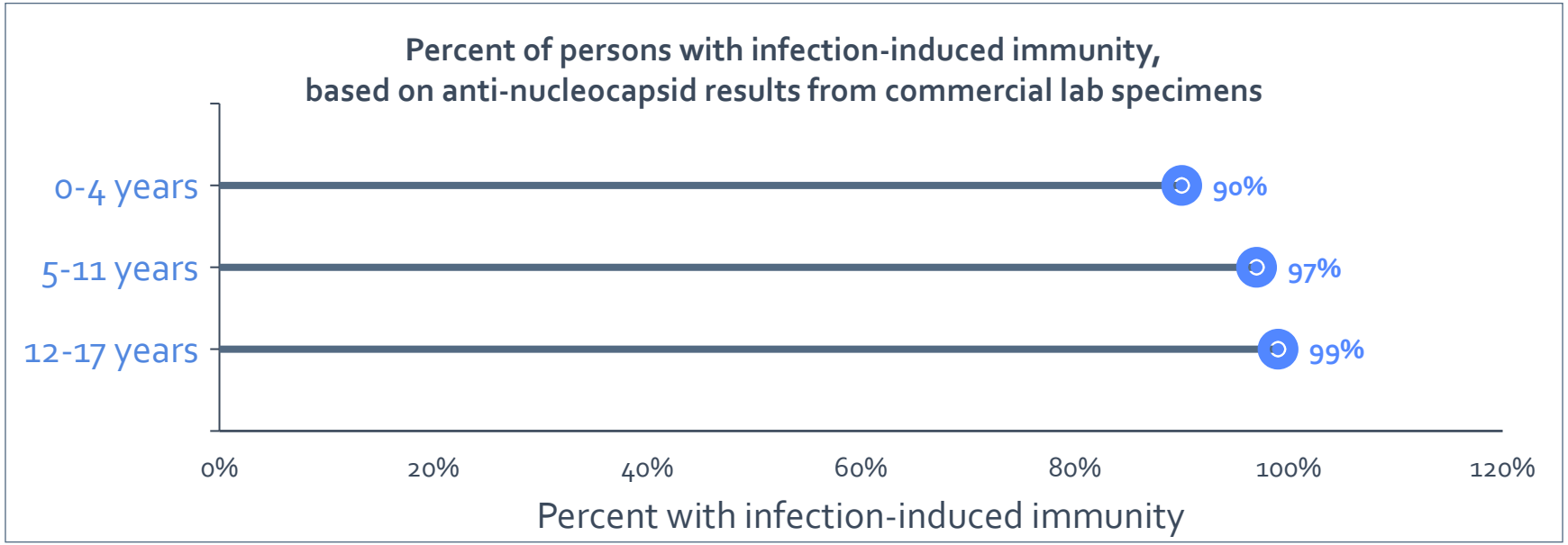
Effectiveness = 1 – (rate ratio*) x 100%

$$\text{Rate ratio}^* = \frac{\text{Disease rate}_{\textbf{vaccinated}}}{\text{Disease rate}_{\textbf{unvaccinated}}}$$

* or risk ratio or hazard ratio

Context for interpreting COVID-19 VE among children

- High rates of SARS-CoV-2 infection-induced immunity by October – December 2022.*



VE findings should be interpreted as the incremental benefit provided by COVID-19 vaccination in a population with a high prevalence of vaccine- and infection-induced immunity.

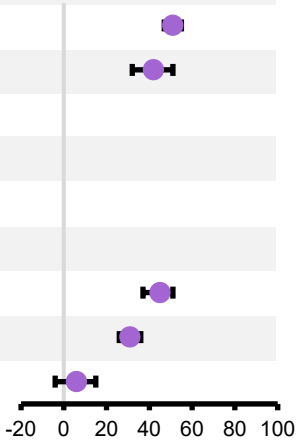
* https://covid.cdc.gov/covid-data-tracker/#pediatric-seroprevalence.

Data on persons <18 years nationwide commercial laboratories and was collected between October 17, 2022 – December 11, 2022.

VISION: VE of *2023-2024 COVID-19 vaccine* against *ED/UC encounters* among adults aged ≥18 years, sub-lineage predominant period and time since dose

September 2023 – April 2024

Sublineage predominant period/2023–2024 COVID-19 vaccination status/days since dose	Total tests	SARS-CoV-2 negative		SARS-CoV-2 positive		Adjusted VE (95% CI)
		N (row %)	Median interval since last dose among vaccinated, days (IQR)	N (row %)	Median interval since last dose among vaccinated, days (IQR)	
XBB sublineage predominant period						
No 2023–2024 COVID-19 dose (ref)	94,084	81,228 (86)	655 (387–775)	12,856 (14)	664 (397–783)	Ref
2023–2024 COVID-19 dose, 7–59 days earlier	8,601	7,930 (92)	31 (19–44)	671 (8)	32 (18–47)	51 (47–55)
2023–2024 COVID-19 dose, 60–119 days earlier	1,773	1,587 (90)	68 (63–75)	186 (10)	68 (64–74)	42 (32–51)
2023–2024 COVID-19 dose, 120–179 days earlier	*	*	*	*	*	*
JN.1 sublineage predominant period						
No 2023–2024 COVID-19 dose (ref)	100,011	90,753 (91)	776 (548–905)	9,258 (9)	762 (530–893)	
2023–2024 COVID-19 dose, 7–59 days earlier	4,297	3,995 (93)	41 (26–51)	302 (7)	42 (26–51)	45 (37–51)
2023–2024 COVID-19 dose, 60–119 days earlier	12,145	11,181 (92)	91 (77–105)	964 (8)	91 (77–103)	31 (26–36)
2023–2024 COVID-19 dose, 120–179 days earlier	8,427	7,937 (94)	135 (131–158)	490 (6)	140 (131–155)	6 (-4–15)



XBB sublineage predominant period: September 21 – December 23, 2023

JN.1 sublineage predominant period: December 24, 2023 – April 13, 2024

CDC unpublished data.

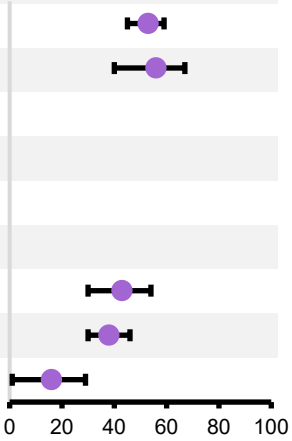
* Based on timing of recommendations to received 23-24 COVID-19 vaccine and JN.1 emergence, no individuals were ≥120 days from their updated dose during the XBB sublineage predominant period.

VE was calculated as (1 – odds ratio) x 100%, estimated using a test-negative case-control design, adjusted for age, sex, race and ethnicity, geographic region, and calendar time.

VISION: VE of *2023-2024 COVID-19 vaccine* against *hospitalization* among adults aged ≥18 years, sub-lineage predominant period and time since dose

September 2023 – April 2024

Sublineage predominant period/2023–2024 COVID-19 vaccination status/days since dose	Total tests	SARS-CoV-2 negative N (row %)	SARS-CoV-2 negative Median interval since last dose among vaccinated, days (IQR)	SARS-CoV-2 positive N (row %)	SARS-CoV-2 positive Median interval since last dose among vaccinated, days (IQR)	Adjusted VE (95% CI)
XBB sublineage predominant period						
No 2023–2024 COVID-19 dose (ref)	29,421	25,810 (88)	621 (374–754)	3,611 (12)	590 (381–752)	Ref
2023–2024 COVID-19 dose, 7–59 days earlier	2,932	2,701 (92)	30 (18–43)	231 (8)	30 (18–46)	**53 (45–59)**
2023–2024 COVID-19 dose, 60–119 days earlier	539	491 (91)	69 (63–74)	48 (9)	66 (63–73)	**56 (40–67)**
2023–2024 COVID-19 dose, 120–179 days earlier	*	*	*	*	*	*
JN.1 sublineage predominant period						
No 2023–2024 COVID-19 dose (ref)	29,261	26,577 (91)	764 (509–887)	2,684 (9)	748 (489–863)	Ref
2023–2024 COVID-19 dose, 7–59 days earlier	1,433	1,324 (92)	41 (26–51)	109 (8)	42 (26–51)	**43 (30–54)**
2023–2024 COVID-19 dose, 60–119 days earlier	4,219	3,900 (92)	91 (77–105)	319 (8)	91 (77–103)	**38 (30–46)**
2023–2024 COVID-19 dose, 120–179 days earlier	3,025	2,851 (94)	143 (131–158)	174 (6)	140 (129–155)	**16 (1–29)**



XBB sublineage predominant period: September 21 – December 23, 2023

JN.1 sublineage predominant period: December 24, 2023 – April 13, 2024

CDC unpublished data.

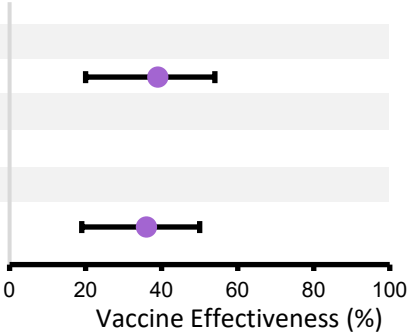
* Based on timing of recommendations to received 23-24 COVID-19 vaccine and JN.1 emergence, no individuals were ≥120 days from their updated dose during the XBB sublineage predominant period.

VE was calculated as (1 – odds ratio) x 100%, estimated using a test-negative case-control design, adjusted for age, sex, race and ethnicity, geographic region, and calendar time.

IVY: VE of *2023–2024 vaccine* against *hospitalization* among immuno*competent* adults aged ≥18 years, by Charlson Comorbidity Index* (CCI) score

September 21, 2023 – April 30, 2024

COVID-19 dosage pattern/CCI score	COVID-19 case-patients N (Col %)	COVID-19 control - patients N (Col %)	Median interval since last dose among those vaccinated, days (IQR)	VE** % (95% CI)
CCI <5				
No 2023-2024 COVID-19 dose (ref)	788 (91)	2517 (87)	710 (452–866)	**Ref**
2023-2024 COVID-19 dose, ≥7 days	77 (9)	379 (13)	79 (44–122)	**39 (20–54)**
CCI ≥5				
No 2023-2024 COVID-19 dose (ref)	750 (87)	1632 (80)	649 (412–807)	**Ref**
2023-2024 COVID-19 dose, ≥7 days	114 (13)	407 (20)	81 (42–120)	**36 (19–50)**



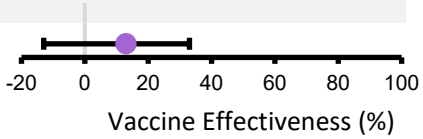
*The Charlson Comorbidity Index is a predictor of 10-year survival calculated using the following patient-level characteristics: age, history of myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular accident or temporary ischemic attack, dementia, chronic obstructive pulmonary disease, connective tissue disease, peptic ulcer disease, liver disease, diabetes, hemiplegia, chronic kidney disease, solid tumor, leukemia, lymphoma, AIDS. Charlson, et al. J Chronic Dis 1987: https://doi.org/10.1016/0021-9681(87)90171-8

**Logistic regression models were adjusted for age, sex, race and ethnicity, geographic region, and calendar time.

IVY: VE of *2023–2024 vaccine* against *hospitalization* among immuno*compromised* adults aged ≥18 years

September 21, 2023 – April 30, 2024

COVID-19 dosage pattern/age group	COVID-19 case-patients N (Col %)	COVID-19 control - patients N (Col %)	Median interval since last dose among those vaccinated, days (IQR)	VE* % (95% CI)
≥18 years				
No 2023-2024 COVID-19 dose (ref)	450 (81)	1260 (78)	611 (399–812)	**Ref**
2023-2024 COVID-19 dose, ≥7 days	107 (19)	350 (22)	81 (44–121)	**13 (-13 to 33)**

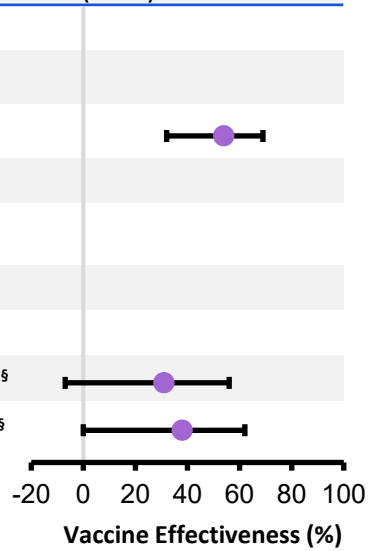


*Logistic regression models were adjusted for age, sex, race and ethnicity, geographic region, and calendar time.

IVY: VE of *2023–2024 COVID-19 vaccine* against *hospitalization* among *immunocompetent adults* aged ≥18 years, by SARS-CoV-2 lineage and time since dose

October 18, 2023 – March 9, 2024

COVID-19 dosage pattern	COVID-19 case-patients		COVID-19 control-patients		VE¶ (95% CI)
	N (Col %)	Median interval since last dose among vaccinated, days (IQR)	N (Col %)	Median interval since last dose among vaccinated, days (IQR)	
XBB lineages*					
No 2023-2024 COVID-19 dose (ref)	404 (92)	558 (389–749)	2871 (83)	707 (442–844)	**Ref**
2023-2024 COVID-19 dose, 7–89 days earlier	32 (7)	45 (23–67)	387 (11)	47 (26–68)	**54 (32–69)**
2023-2024 COVID-19 dose, 90–179 days earlier	4 (1)	91 (91–96)	190 (6)	116 (103–131)	†
JN lineages*					
No 2023-2024 COVID-19 dose (ref)	250 (83)	743 (477–852)	2871 (83)	707 (442–844)	**Ref**
2023-2024 COVID-19 dose, 7–89 days earlier	29 (10)	57 (33–76)	387 (11)	47 (26–68)	**31 (-7 to 56)§**
2023-2024 COVID-19 dose, 90–179 days earlier	23 (8)	120 (109–130)	190 (6)	116 (103–131)	**38 (0 to 62)§**



* JN lineages comprised BA.2.86 and its descendants. XBB lineages comprised all other co-circulating lineages.

† Based on timing of recommendations to receive 2023–2024 COVID-19 vaccines and JN lineage emergence, limited numbers of individuals with XBB infection were 90–179 days from their updated dose, precluding estimation of VE within this stratum.

§ Some estimates are imprecise, which might be due to a relatively small number of persons in each level of vaccination or case status. This imprecision indicates that the actual VE could be substantially different from the point estimate shown, and estimates should therefore be interpreted with caution.

¶ VE estimates adjusted for age, sex, race and ethnicity, geographic region, calendar time, and Charlson comorbidity index.

CDC unpublished data.

IVY: Sensitivity analyses for estimating VE of 2023–2024 COVID-19 vaccine by SARS-CoV-2 lineage using different adjustments for calendar time

- Point estimates and confidence intervals were similar when adjusting for calendar time using different methods:
  - Restriction of analysis period to weeks when vaccination coverage was approximately stable
  - Matching on categorical week or biweek and estimating using conditional logistic regression
  - Inclusion of either categorical week or biweek of admission date as a covariate in multivariable logistic regression
  - Inclusion of either linear calendar time or cubic spline of calendar time as a covariate in multivariable logistic regression