Updates to COVID-19 Vaccine Effectiveness

Advisory Committee on Immunization Practices

September 19, 2025

Agenda – COVID-19 vaccine effectiveness (VE)

- **Vaccine effectiveness methods**
- **Estimates of COVID-19 Vaccine Effectiveness in *Children***
- **Estimates of *Maternal* COVID-19 Vaccine Effectiveness**
- **Estimates of COVID-19 Vaccine Effectiveness in *Adults***
- **Conclusions**

Vaccine effectiveness methods

Randomized clinical trials vs. real-world evidence

- **Randomized clinical trials needed to demonstrate vaccine efficacy for licensure of new vaccines**: does vaccination prevent disease under ideal and controlled conditions (i.e., **placebo or vaccine comparator**)?

- **Observational studies provide real-world evidence of vaccine effectiveness**: does vaccination protect against disease in the population?

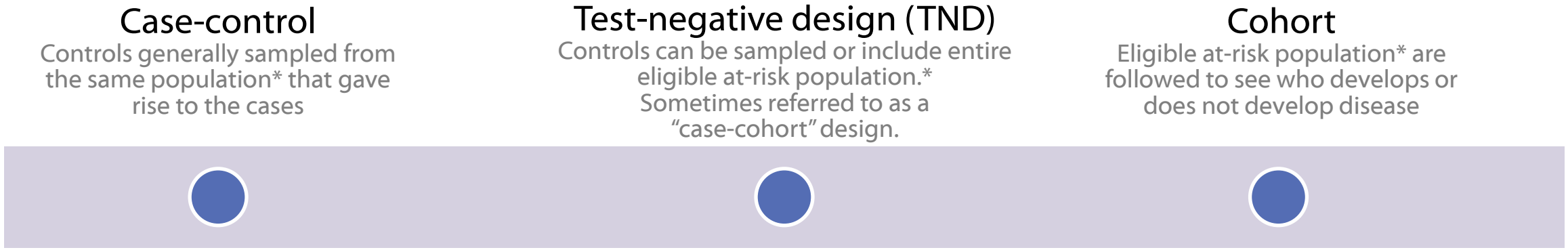
- **Vaccine effectiveness** measures *benefit of current* vaccination* in a population with existing levels of protection due to prior infection, vaccination, or both.

* Varies by pathogen. “Current” for COVID-19 or influenza would indicate this season’s vaccine.

Efficacy and effectiveness are *population level* estimates.

- **If a vaccine has an effectiveness of 80%:**
  - It does not mean that the vaccine will only work 80% of the time.
  - It does mean that in a vaccinated population, 80% fewer people will have the outcome of interest when they are exposed to the virus compared to an unvaccinated population.

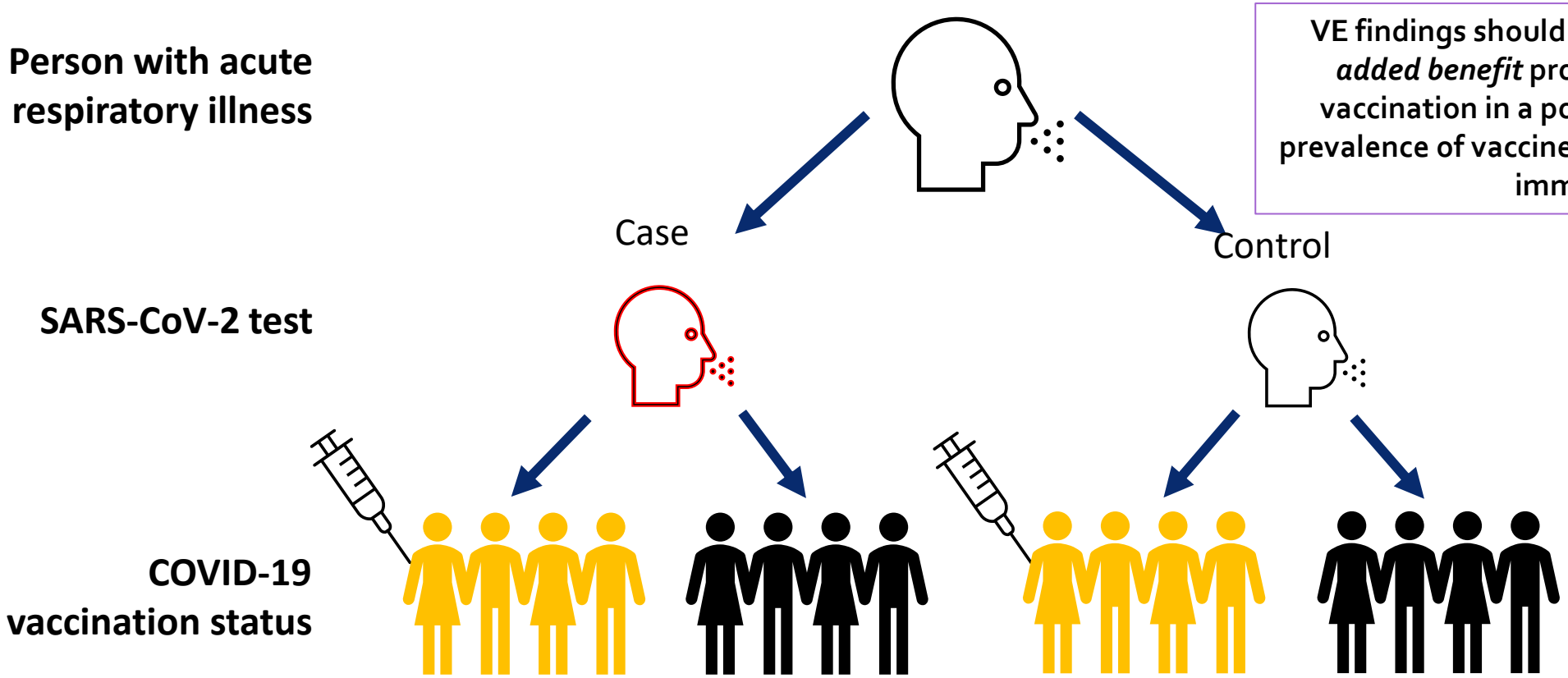
Vaccine effectiveness can be measured using study designs across a spectrum



- A vaccine effectiveness (VE) study measures the extent to which a vaccine reduces the incidence of a specific disease or its severe outcomes in a vaccinated population compared to an unvaccinated population, often expressed as a percentage reduction in disease occurrence.
- VE can be measured using risk ratio, rate ratio, hazard ratio, or odds ratio, usually after adjustment for confounding.

* Population is generally chosen from geographic or hospital-based enrollment.

For respiratory viruses, CDC primarily uses the test-negative design (TND), to measure vaccine effectiveness (VE)



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

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

Vaccine effectiveness can be measured using study designs across a spectrum

Case-control

Controls generally sampled from the same population* that gave rise to the cases

Strengths

- More cost effective than cohorts
- Useful for rare outcomes

Limitations

- Retrospective nature can introduce recall bias (specific to studies that collect information ONLY through interview)
- If controls are sampled from community, misclassification bias can be introduced (no test to confirm negative status)
- Potential for confounding due to health-seeking behaviors
- Residual confounding is possible
- Difficult to establish causality

Test-negative design (TND)

Controls can be sampled or include entire eligible at-risk population.* Sometimes referred to as a "case-cohort" design.

Strengths

- Useful for rare outcomes
- Controls for health-seeking behavior and exposure risk
- Efficient for assessing VE in real-world settings, including against new variants
- Efficient use of resources, especially when electronic health data are used

Limitations

- Requires accurate testing and classification (as with all studies)
- Residual confounding is possible
- Difficult to establish causality

Cohort

Eligible at-risk population* are followed to see who develops or does not develop disease

Strengths

- Allows for assessment of multiple outcomes

Limitations

- Time-consuming and expensive
- If identification of outcomes requires seeking medical care, misclassification bias can be introduced
- Potential for confounding due to health-seeking behaviors
- Residual confounding is possible
- Difficult to establish causality

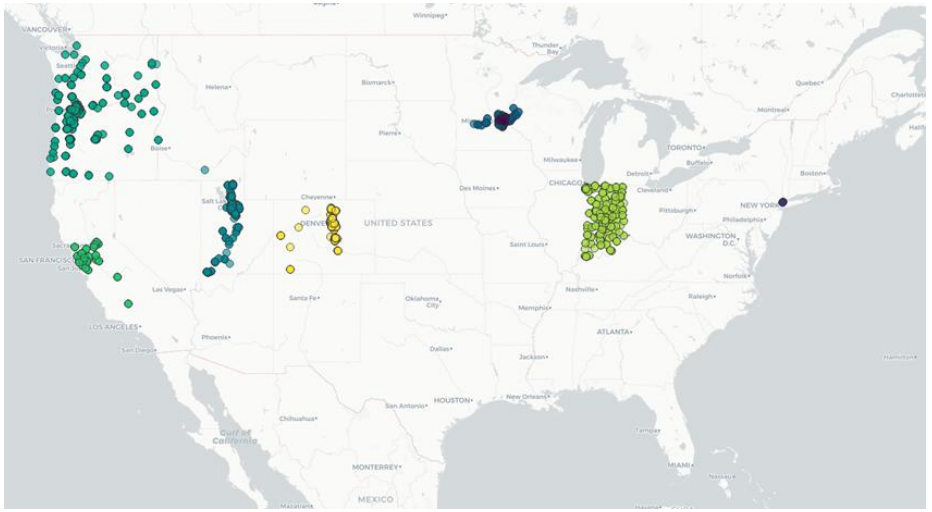
* Population is generally chosen from geographic or hospital-based enrollment.

VISION Multi-Site Network of Electronic Health Records

>300 emergency departments and urgent cares clinics and >200 hospitals

- **Design:** Test-negative design

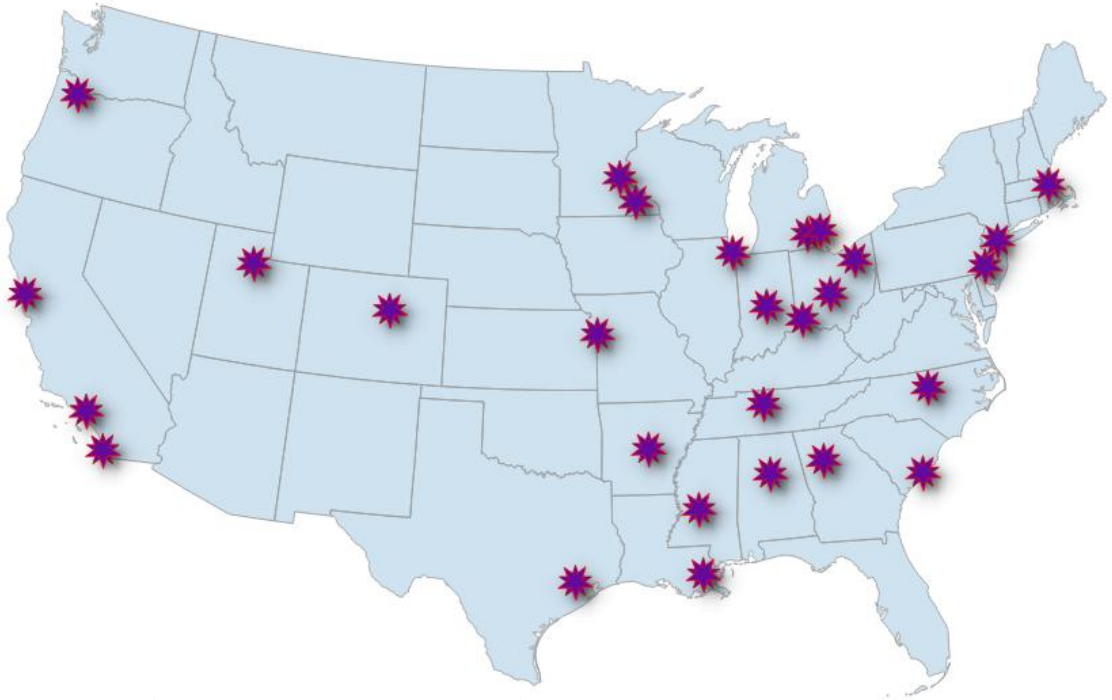
- **Population:** Persons visiting a participating emergency department or urgent care or hospitalized with COVID-19-like illness with a SARS-CoV-2 test result within 10 days before or 72 hours after encounter
  - **Cases**: CLI with *positive* NAAT or antigen for SARS-CoV-2 and no positive NAAT for RSV or influenza
  - **Controls**: CLI with *negative* NAAT for SARS-CoV-2 and no positive NAAT for influenza or RSV (≥60 years)



- **Vaccination data:** Documented by electronic health records and state and city registries

CLI = COVID-19-like illness; ED/UC = emergency department/urgent care; RSV = respiratory syncytial virus; NAAT = nucleic acid amplification test
CLI is defined based on the presence of specific discharge diagnosis codes. Additional methods available: Link-Gelles, et al. MMWR. https://www.cdc.gov/mmwr/volumes/74/wr/mm7406a1.htm

Overcoming COVID-19 Network



- **Case infants:** hospitalized for COVID-19 as the primary reason for admission and with a positive SARS-CoV-2 NAAT or antigen test result
- **Control infants:** hospitalized for COVID-19-like illness and negative SARS-CoV-2 NAAT result, matched to case infants by site; hospitalized within 4 weeks of case infant admission

- **Design:** Case-control study to assess effectiveness of maternal vaccination against COVID-19-related hospitalizations in infants <6 months of age
- **Population:** 26 pediatric hospitals in 20 states
- **Data collection:** Baseline demographic and clinical characteristics obtained via chart abstraction and parent interview
- **Vaccination status:** Maternal vaccination status verified using state vaccination registries, electronic medical records, or other sources

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

- **Design**: Test-negative, case-control design
- **Population**: Adults ages ≥18 years hospitalized with COVID-19-like illness* 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
  - **Controls**: CLI and test *negative* for SARS-CoV-2, influenza (≥18 years) and RSV (≥60 years) by RT-PCR
- **Vaccination data:** Electronic medical records, 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

*COVID-19-like illness = CLI; CLI is defined as presence of any one of the following: fever, cough, shortness of breath, chest imaging consistent with pneumonia, or hypoxemia
NAAT = nucleic acid amplification test

Measuring COVID-19 Vaccine Effectiveness (VE)

Measure	Definition*	Example vaccinated group	Example comparison group
Absolute VE	Compares frequency of health outcomes in vaccinated and unvaccinated people	Received **original monovalent 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 **bivalent dose**	Eligible for, but did not receive, bivalent COVID-19 vaccine, but received **original monovalent dose**
VE "seasonal" COVID-19 vaccines	Compares people who received **this "season's"** COVID-19 vaccine to people who did not, regardless of past COVID-19 vaccination	Received **this "season's"**	Eligible for, but did not receive, **this "season's"**, regardless of past COVID-19 vaccination history

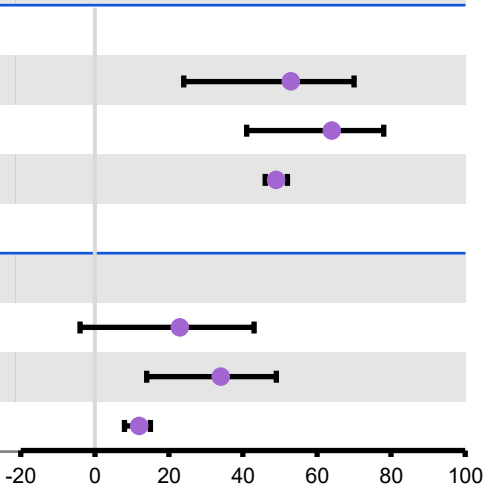
* Prior SARS-CoV-2 infection is not generally considered, as it is documented inconsistently in medical records.

Estimates of COVID-19 Vaccine Effectiveness in Children

VE of 2023–2024 COVID-19 vaccine doses against *emergency department/urgent care encounters* — VISION

September 2023 – August 2024

Age group | COVID-19 vaccination status	Total encounters	SARS-CoV-2-test-positive, N (%)	Median interval since last dose among those vaccinated, days (IQR)	Adjusted vaccine effectiveness % (95% CI)
No updated 2023-2024 COVID-19 vaccine dose*				
9 months-4 years	43,246	1,886 (4)	367 (250 to 461)	**Ref**
5-17 years	54,310	2,071 (4)	679 (491 to 810)	**Ref**
≥18 years	279,733	31,167 (11)	756 (61-189)	**Ref**
2023-2024 COVID-19 dose received 7-59 days earlier				
9 months-4 years	725	18 (2)	32 (20 to 46)	**53 (24 to 70)**
5-17 years	951	16 (2)	34 (19 to 47)	**64 (41 to 78)**
≥18 years	16,082	1,228 (8)	34 (21-47)	**49 (46 to 52)**
2023-2024 COVID-19 dose received 60-299 days earlier				
9 months-4 years	1,345	48 (4)	129 (91 to 178)	**23 (-4 to 43)**
5-17 years	2,510	63 (3)	138 (100 to 185)	**34 (14 to 49)**
≥18 years	49,824	4,701 (9)	149 (100-211)	**12 (8 to 15)**



CDC, unpublished data

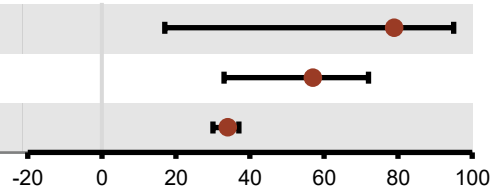
* Includes all individuals who did not receive a 2023-2024 COVID-19 vaccine. For those aged ≥5 years, this includes unvaccinated persons and persons who were vaccinated with ≥1 original monovalent or bivalent COVID-19 doses. For those aged <5 years, children with a partial initial series were excluded.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

Vaccine effectiveness was calculated by comparing the odds of COVID-19 vaccination in case-patients and control-patients using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multivariable logistic regression. The odds ratio was adjusted for age, sex, race and ethnicity, calendar day, and geographic region.

VE of 2024-2025 COVID-19 vaccine doses against *emergency department/urgent care encounters* — VISION

September 2024 – May 2025

Age group | COVID-19 vaccination status	Total encounters	SARS-CoV-2-test-positive, N (%)	Median interval since last dose among those vaccinated, days (IQR)	Adjusted vaccine effectiveness % (95% CI)
No updated 2024-2025 COVID-19 vaccine dose*				
9 months-4 years	31,060	809 (3)	392 (282-662)	**Ref**
5-17 years	38,870	926 (2)	972 (710-1,116)	**Ref**
≥18 years	200,933	12,927 (6)	1,068 (742-1,224)	**Ref**
2024-2025 COVID-19 dose received 7-179 days earlier				
9 months-4 years	393	2 (1)	64 (30-98)	**79 (17 to 95)**
5-17 years	2,208	22 (1)	81 (44-122)	**57 (33 to 72)**
≥18 years	40,043	1,694 (4)	89 (50-129)	**34 (30 to 37)**



CDC, unpublished data

* Includes all individuals who did not receive a 2024-2025 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, children with a partial initial series were excluded. The 2024-2025 dose could have been part of the initial series or in addition to the initial series.

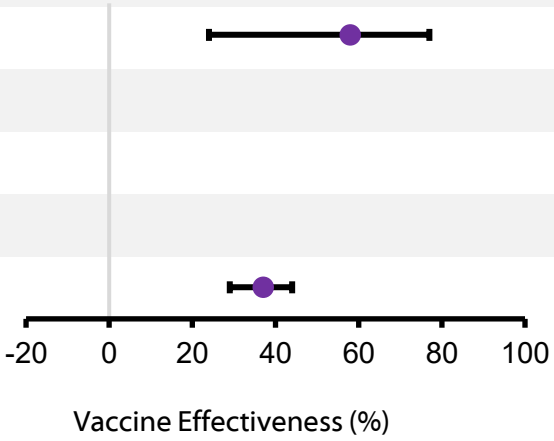
Vaccine effectiveness was calculated by comparing the odds of COVID-19 vaccination in case-patients and control-patients using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multivariable logistic regression. The odds ratio was adjusted for age, sex, race and ethnicity, calendar day, and geographic region.

Estimates of Maternal COVID-19 Vaccine Effectiveness

VISION: VE of *2023-2024* COVID-19 vaccination against COVID-19–associated *emergency department/urgent care encounters* among immuno*competent* women aged 18-45 years, by pregnancy status — VISION

September 2023 – August 2024

Vaccine Dosage Pattern	Total tests	SARS-CoV-2-test-positive, N (%)	Median interval since last dose, days (IQR)	Adjusted VE (95% CI)
Pregnant at CLI encounter				
No 2023-2024 dose (ref)	5058	709 (14)	797 (648, 931)	**Ref**
Most recent 2023-2024 dose received 7-179 days	229	13 (6)	77 (44, 120)	**58 (24-77)**
Not pregnant at CLI encounter				
No 2023-2024 dose (ref)	76,636	8,052 (11)	794 (641, 931)	**Ref**
Most recent 2023-2024 dose received 7-179 days	5,079	313 (6)	83 (45, 126)	**37 (29-44)**



VE=vaccine effectiveness; CLI = COVID-19-like illness

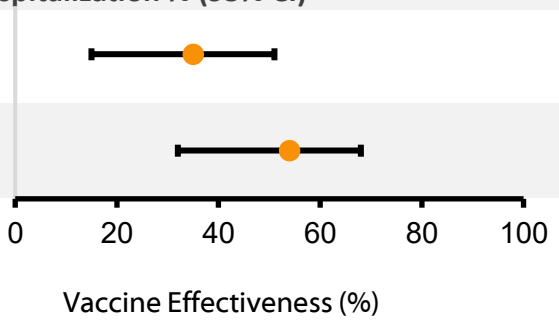
Vaccine effectiveness was calculated by comparing the odds of COVID-19 vaccination in case-patients and control-patients using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multivariable logistic regression. The odds ratio was adjusted for: age, ethnicity, race, underlying medical conditions, gestational age at encounter, site, Medicaid status, day of encounter, site facility urbanicity

CDC unpublished data

Overcoming COVID-19: Effectiveness* of maternal vaccination† in prevention of COVID-19–associated *hospitalization* among infants§

March 9, 2022 – May 31, 2023

Age group of infant	No. vaccinated/Total no. (%) Case-patients	Control patients	Interval between last vaccine dose and infant hospitalization, days (IQR)	Effectiveness of Maternal Vaccination against Infant Covid-19 Hospitalization % (95% CI)
0-5 months	82/377 (22)	94/339 (28)	236 (185–300)	**35 (15–51)**
0-2 months	43/227 (19)	63/214 (29)	219 (152–264)	**54 (32–68)**



Simeone & Zambrano et al., MMWR, 2023: https://www.cdc.gov/mmwr/volumes/72/wr/mm7239a3.htm.

* VE estimates were based on odds of maternal vaccination during pregnancy in case-patients versus control patients, adjusted for U.S. Census Bureau region, admission date (monthly), age (in months), sex, and race and ethnicity (non-Hispanic Black or African American, non-Hispanic White, non-Hispanic other, Hispanic or Latino of any race, or unknown). Study site was included as a repeated effect. VE was calculated as (1 – adjusted odds ratio) x 100%.

† Maternal vaccination status was based on the last date of a COVID-19 mRNA vaccine dose: unvaccinated was defined as mothers who had not received any vaccine dose before or during pregnancy, and vaccinated was defined as mothers who received their last dose of a COVID-19 mRNA vaccine between the first day of pregnancy and 14 days before delivery. Among those vaccinated during pregnancy, mothers could have received ≥1 dose during pregnancy. Mothers could receive 1 dose of Ad.26.CoV2.S (Janssen [Johnson & Johnson]) vaccine before or during pregnancy and 1 dose of an mRNA vaccine during pregnancy. Mothers who received only 1 dose of an mRNA vaccine were considered partially vaccinated and were excluded from the analysis. Mothers whose last vaccine dose occurred before pregnancy were excluded from the analysis.

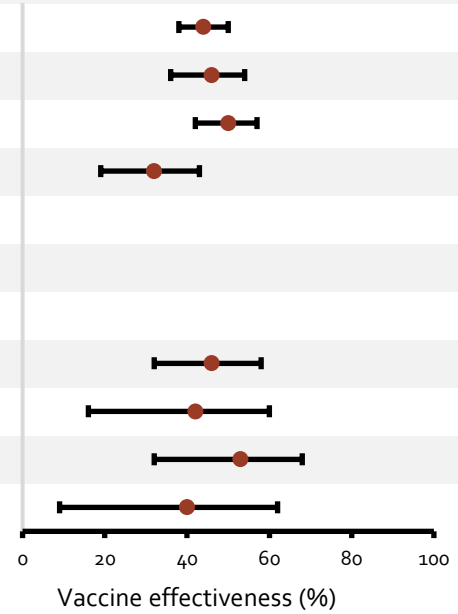
§ Infants were excluded from analysis if they were born to mothers who had received their most recent dose before pregnancy, received only 1 dose of an mRNA vaccine, received their most recent vaccine dose within 14 days of delivery, received only 1 dose of a viral vector vaccine, or whose vaccination status could not be verified or whose timing of vaccination was unknown.

Estimates of COVID-19 Vaccine Effectiveness in Adults

Effectiveness of *2024–2025 COVID-19 vaccination* against COVID-19–associated *hospitalization* among *immunocompetent* adults aged ≥65 years — VISION and IVY Networks

September 2024 – May 2025

Network/2024-2025 COVID-19 vaccination status/days since dose	COVID-19 case-patients N (Col %)	COVID-19 control-patients N (Col %)	Median interval since last dose among vaccinated*, days (IQR)	Adjusted vaccine effectiveness % (95% CI)
VISION				
No **2024-2025 COVID-19 dose** (Ref)	2,943 (85)	34,900 (74)	958 (508-1,187)	**Ref**
Received **2024-2025 COVID-19 dose** 7–179 days earlier	515 (15)	12,043 (26)	92 (51-132)	**44 (38-50)**
2024-2025 COVID-19 dose, 7–59 days earlier	155 (4)	3,604 (8)	34 (20-47)	**46 (36-54)**
2024-2025 COVID-19 dose, 60–119 days earlier	207 (6)	4,509 (10)	90 (75-104)	**50 (42-57)**
2024-2025 COVID-19 dose, 120–179 days earlier	153 (4)	3,930 (8)	147 (133-162)	**32 (19-43)**
IVY				
No **2024-2025 COVID-19 dose** (Ref)	822 (88)	1,824 (79)	Not available	**Ref**
Received **2024-2025 COVID-19 dose** 7–179 days earlier	110 (12)	499 (21)	92 (55–130)	**46 (32-58)**
2024-2025 COVID-19 dose, 7–59 days earlier	43 (5)	124 (5)	32 (20–46)	**42 (16-60)**
2024-2025 COVID-19 dose, 60–119 days earlier	37 (4)	205 (9)	89 (73–103)	**53 (32-68)**
2024-2025 COVID-19 dose, 120–179 days earlier	30 (3)	170 (7)	146 (130–161)	**40 (9-62)**



Updated from: Link-Gelles, et al. MMWR: https://www.cdc.gov/mmwr/volumes/74/wr/mm7406a1.htm

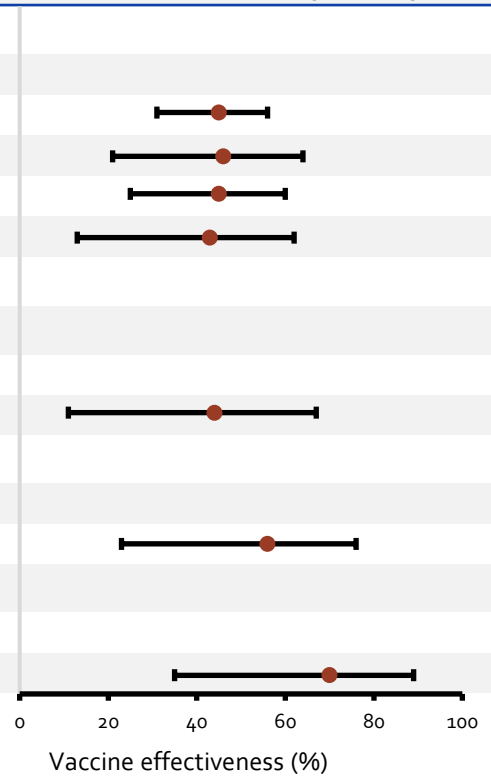
Vaccine effectiveness was calculated by comparing the odds of 2024–2025 COVID-19 vaccination in case-patients and control-patients using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multivariable logistic regression. For VISION, the odds ratio was adjusted for age, sex, race and ethnicity, calendar day, and geographic region. For IVY, the odds ratio was adjusted for age, sex, race and ethnicity, geographic region (U.S. Department of Health and Human Services Region) and calendar time (biweekly intervals). The "no 2024–2025 dose" group included all eligible persons who did not receive a 2024–2025 COVID-19 vaccine dose, regardless of number of previous COVID-19 vaccine doses. VISION data go through May 2025; IVY data go through April 2025.

*Time since vaccination is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, or 2024-2025 COVID-19 vaccine.

Effectiveness of *2024–2025 COVID-19 vaccination* against COVID-19–associated *critical illness* among *immunocompetent* adults aged ≥65 years — VISION and IVY Networks

September 2024 – May 2025

2024-2025 COVID-19 vaccination status/days since dose	COVID-19 case-patients N (Col %)	COVID-19 control-patients N (Col %)	Median interval since last dose among vaccinated*, days (IQR)	Adjusted vaccine effectiveness % (95% CI)
VISION				
No **2024-2025 COVID-19 dose** (Ref)	558 (85)	34,900 (74)	961 (510-1,189)	**Ref**
Received **2024-2025 COVID-19 dose** 7–179 days earlier	97 (15)	12,043 (26)	92 (51-132)	**45 (31-56)**
2024-2025 COVID-19 dose, 7–59 days earlier	28 (4)	3,604 (8)	34 (20-47)	**46 (21-64)**
2024-2025 COVID-19 dose, 60–119 days earlier	44 (7)	4,509 (10)	90 (75-104)	**45 (25-60)**
2024-2025 COVID-19 dose, 120–179 days earlier	25 (4)	3,930 (8)	147 (133-162)	**43 (13-62)**
IVY				
Acute respiratory failure				
No **2024-2025 COVID-19 dose** (Ref)	158 (88)	1,817 (78)	Not available	**Ref**
Received **2024-2025 COVID-19 dose** 7–179 days earlier	21 (12)	498 (22)	96 (59-131)	**44 (11-67)**
ICU admission or death				
No **2024-2025 COVID-19 dose** (Ref)	141 (91)	1,824 (79)	Not available	**Ref**
Received **2024-2025 COVID-19 dose** 7–179 days earlier	14 (9)	499 (21)	96 (60-133)	**56 (23-76)**
Invasive mechanical ventilation or death				
No **2024-2025 COVID-19 dose** (Ref)	74 (94)	1,824 (79)	Not available	**Ref**
Received **2024-2025 COVID-19 dose** 7–179 days earlier	5 (6)	499 (21)	97 (60-133)	**70 (35-89)**



Based on methods in: Link-Gelles, et al. MMWR: https://www.cdc.gov/mmwr/volumes/74/wr/mm7406a1.htm

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For VISION, critical illness is defined as admission to the intensive care unit or in-hospital death. For IVY, acute respiratory failure was defined as new receipt of high-flow nasal canula, noninvasive ventilation, or invasive mechanical ventilation.

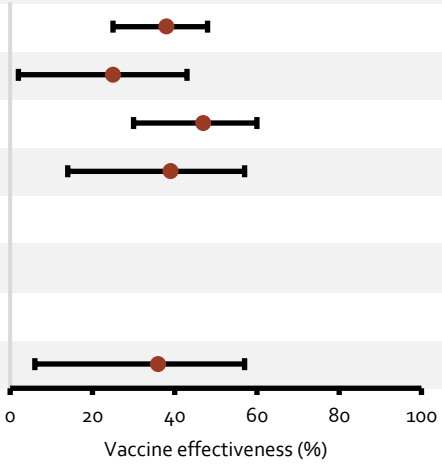
*Time since vaccination is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, or 2024-2025 COVID-19 vaccine.

ICU = intensive care unit

Effectiveness of *2024–2025 COVID-19 vaccination* against COVID-19–associated *hospitalization* among *immunocompromised* adults aged ≥65 years — VISION and IVY Networks

September 2024 – May 2025

Network/2024-2025 COVID-19 vaccination status/days since dose	COVID-19 case-patients N (Col %)	COVID-19 control-patients N (Col %)	Median interval since last dose among vaccinated*, days (IQR)	Adjusted vaccine effectiveness % (95% CI)
VISION				
No **2024-2025 COVID-19 dose** (Ref)	719 (81)	10,035 (69)	882 (451-1,166)	**Ref**
Received **2024-2025 COVID-19 dose** 7–179 days earlier	164 (19)	4,432 (31)	93 (53-133)	**38 (25-48)**
2024-2025 COVID-19 dose, 7–59 days earlier	62 (7)	1,247 (9)	35 (20-47)	**25 (2-43)**
2024-2025 COVID-19 dose, 60–119 days earlier	61 (7)	1,689 (12)	89 (75-104)	**47 (30-60)**
2024-2025 COVID-19 dose, 120–179 days earlier	41 (5)	1,496 (10)	147 (133-163)	**39 (14-57)**
IVY				
No **2024-2025 COVID-19 dose** (Ref)	214 (83)	670 (76)	Not available	**Ref**
Received **2024-2025 COVID-19 dose** 7–179 days earlier	44 (17)	209 (24)	82 (48-133)	**36 (6-57)**



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* Time since vaccination is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, or 2024-2025 COVID-19 vaccine.

Conclusions: effectiveness of COVID-19 vaccines

- **For the respective year, compared to no in-season dose, COVID-19 vaccination provided additional protection against:**
  - COVID-19-associated **emergency department and urgent care* visits among children**; protection was similar across age groups.
  - COVID-19-associated **emergency department and urgent care visits among adults** (data included in back-up).
  - COVID-19-associated **hospitalizations among adults aged ≥65 years with and without immunocompromising conditions**.
  - COVID-19-associated **critical illness among adults aged ≥65 years**; protection appeared to be higher and more durable against critical illness compared to less severe outcomes.

- **VE should be interpreted as the added benefit of 2023–2024 or 2024–2025 COVID-19 vaccination in a population with high levels of infection-induced immunity, vaccine-induced immunity, or both.**
  - Prior SARS-CoV-2 infection contributes protection against future disease, though protection wanes over time.
  - An increase in SARS-CoV-2 circulation in the United States during late summer 2024, just before the 2024–2025 COVID-19 vaccines were approved and authorized, may have resulted in higher population-level immunity against JN.1-lineage strains, which could have resulted in lower measured VE than in a population with less recent infection.

* Due to lower baseline rates of severe disease and lower COVID-19 vaccine coverage, VE against hospitalization and critical illness in children could not be estimated.

Data and analysis were provided by CDC and the following CDC-funded network partners:

VISION Collaborators

IVY Collaborators

Overcoming Collaborators

Back-up

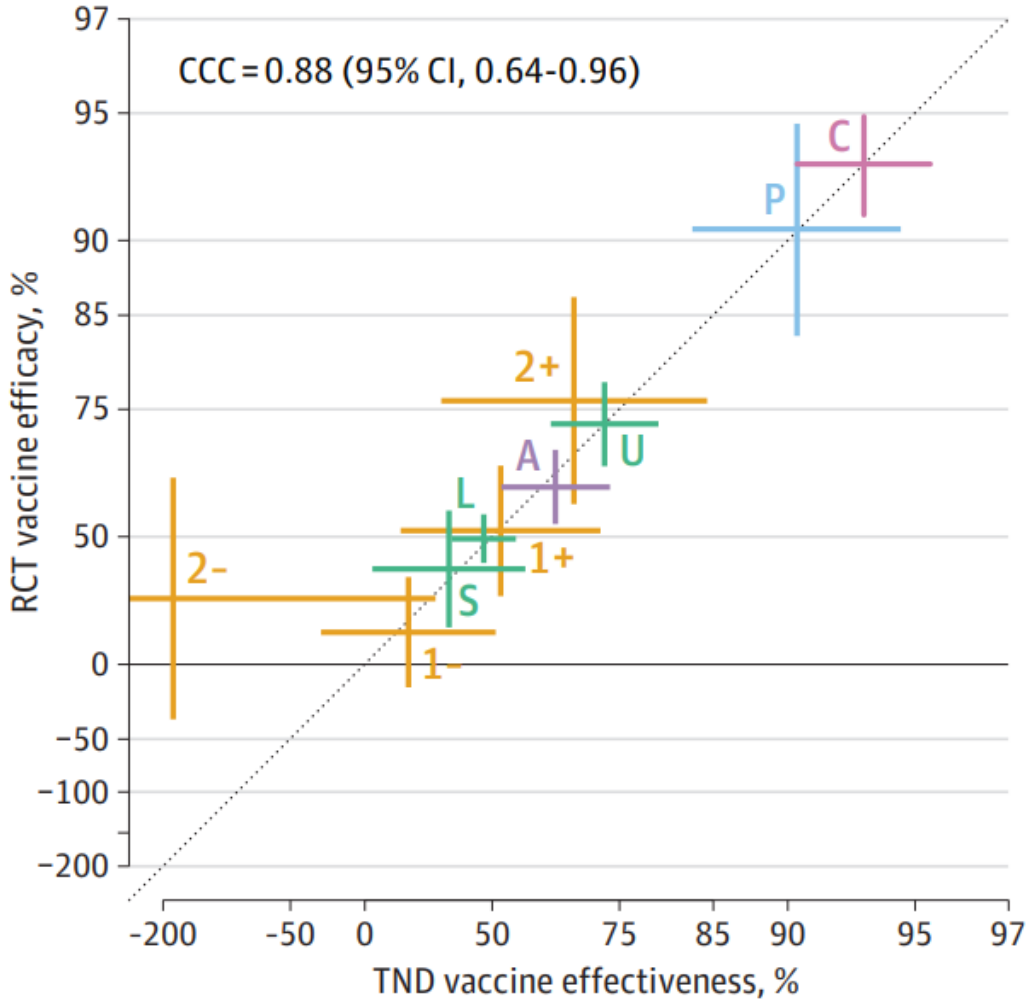
Original Investigation | Statistics and Research Methods

Evaluating the Test-Negative Design for COVID-19 Vaccine Effectiveness Using Randomized Trial Data

A Secondary Cross-Protocol Analysis of 5 Randomized Clinical Trials

Conclusions: “TND provided reliable inferences on COVID-19 vaccine effectiveness in health care–seeking populations for multiple vaccines and symptom definitions”

Estimates based on RCT vs TND analysis

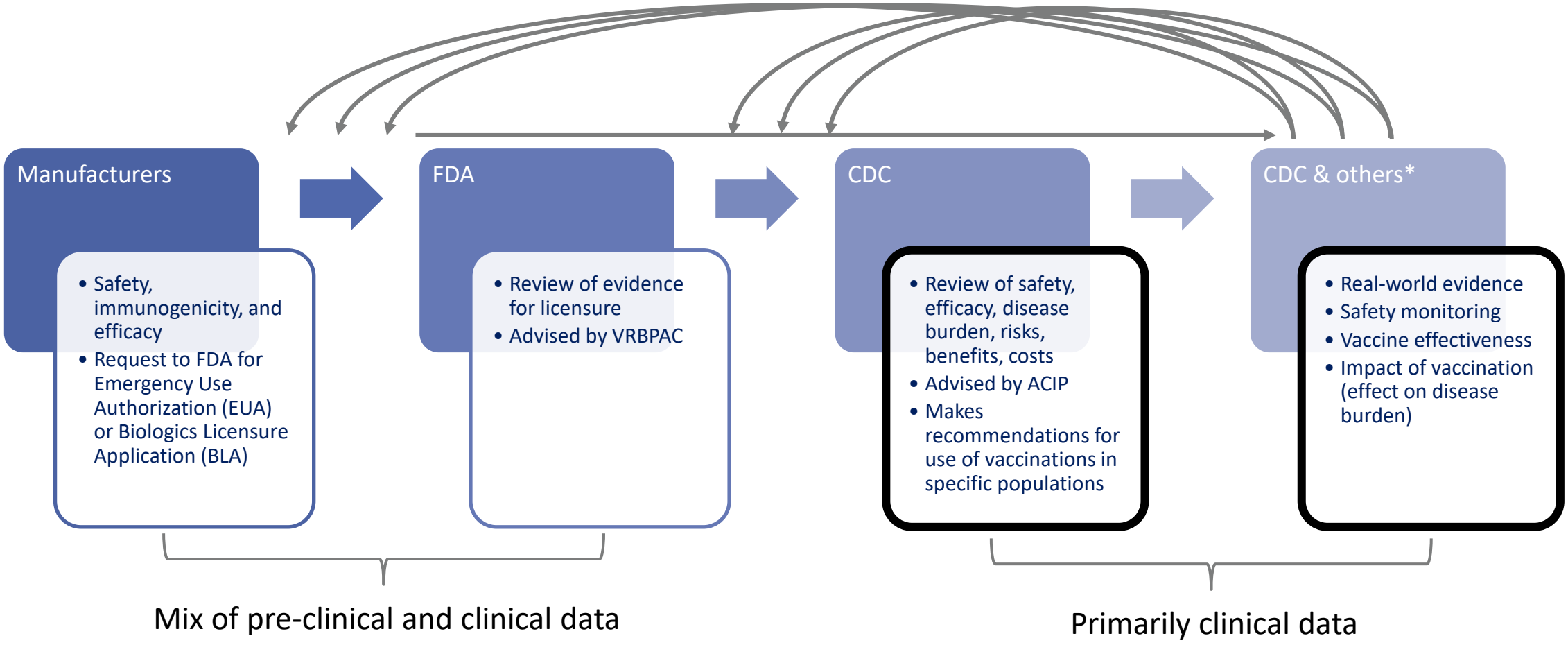


CCC = concordance correlation coefficient

Source: Andrews L et al, JAMA Network Open 2025

[Evaluating the Test-Negative Design for COVID-19 Vaccine Effectiveness Using Randomized Trial Data: A Secondary Cross-Protocol Analysis of 5 Randomized Clinical Trials - PubMed]

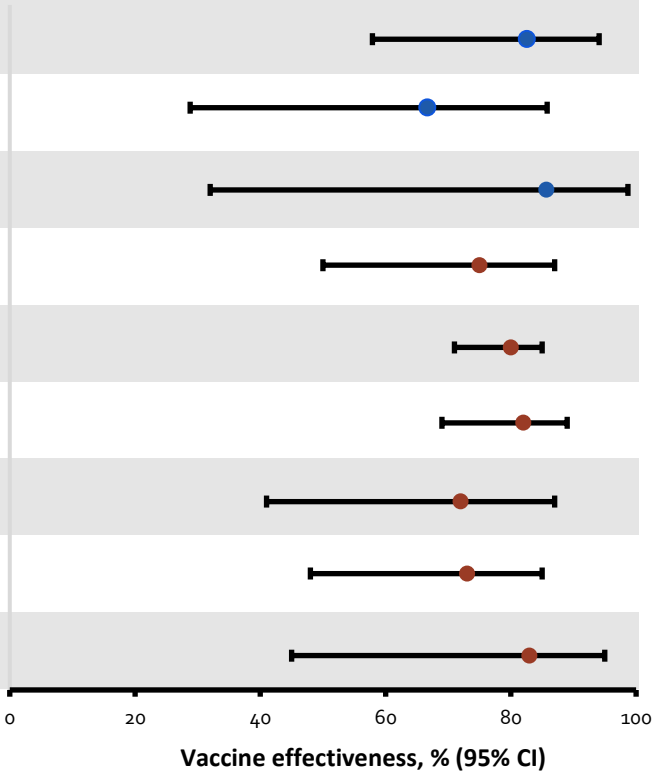
Steps from vaccine licensure to recommendations and post-licensure monitoring and evaluation



* Academic, private and public healthcare, non-profit partners

Observational VE studies show RSV vaccines protect against severe RSV disease, similar to results from trials, although endpoints differ

Outcome	Analysis	Design	Vaccine efficacy/effectiveness, % (95% CI)
Symptomatic, RSV-associated lower respiratory tract disease (LRTD)	GSK trial (≥2 or 3 sx LRTD, primary endpoint)†	RCT	83 (58–94)
	Pfizer trial (≥2 sx LRTI, co-primary endpoint)*	RCT	67 (29–86)
	Pfizer trial (≥3 sx LRTI, co-primary endpoint)*	RCT	86 (32–99)
RSV-associated hospitalization	IVY Network, adults ≥60 years§	TND	75 (50–87)
	VISION, adults ≥60 years, immunocompetent	TND	80 (71–85)
	VHA, adults ≥60 years§	Cohort	82 (69–89)
	Medicare ESRD, otherwise immunocompetent, ≥65y	Cohort	72 (41-87)
	VISION, immunocompromised	TND	73 (48–85)
	Medicare ESRD, additional immunocompromise, ≥65y	Cohort	83 (45-95)



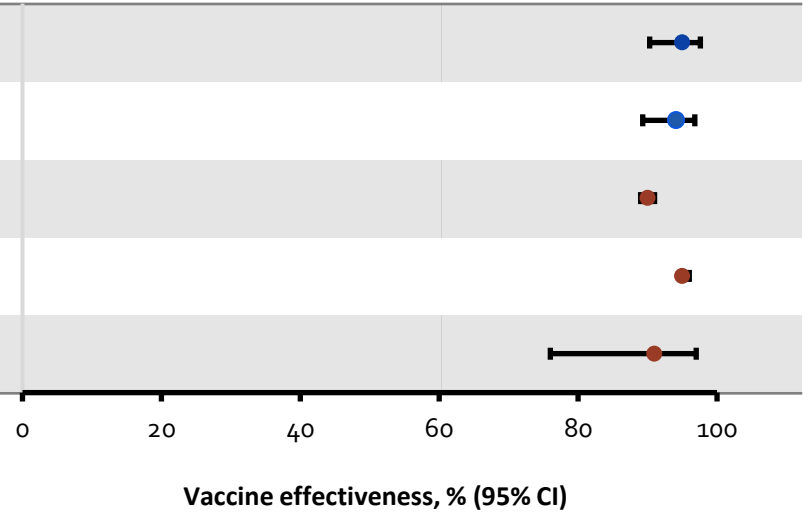
Abbreviations: ESRD = End stage renal disease; LRTI = lower respiratory tract infection; LRTD = lower respiratory tract disease; sx = symptoms or signs; y = years; RCT = randomized controlled trial; TND = test-negative design

† Papi A, et. al. Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults. *N Engl J Med*. 2023;388:595–608. See slide 43 for detailed definitions.
* Walsh E, et. al. Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults. *N Engl J Med*. 2023;388:1465–77. See slide 43 for detailed definitions.
§ Includes patients with immunocompromising conditions in the displayed VE estimate.

Data originally presented at June 2024 ACIP meeting.

Observational COVID-19 VE studies conducted pre-Delta (March-April/May 2021) showed COVID-19 vaccines provided similar protection to estimates from trials for symptomatic SARS-CoV-2 infection

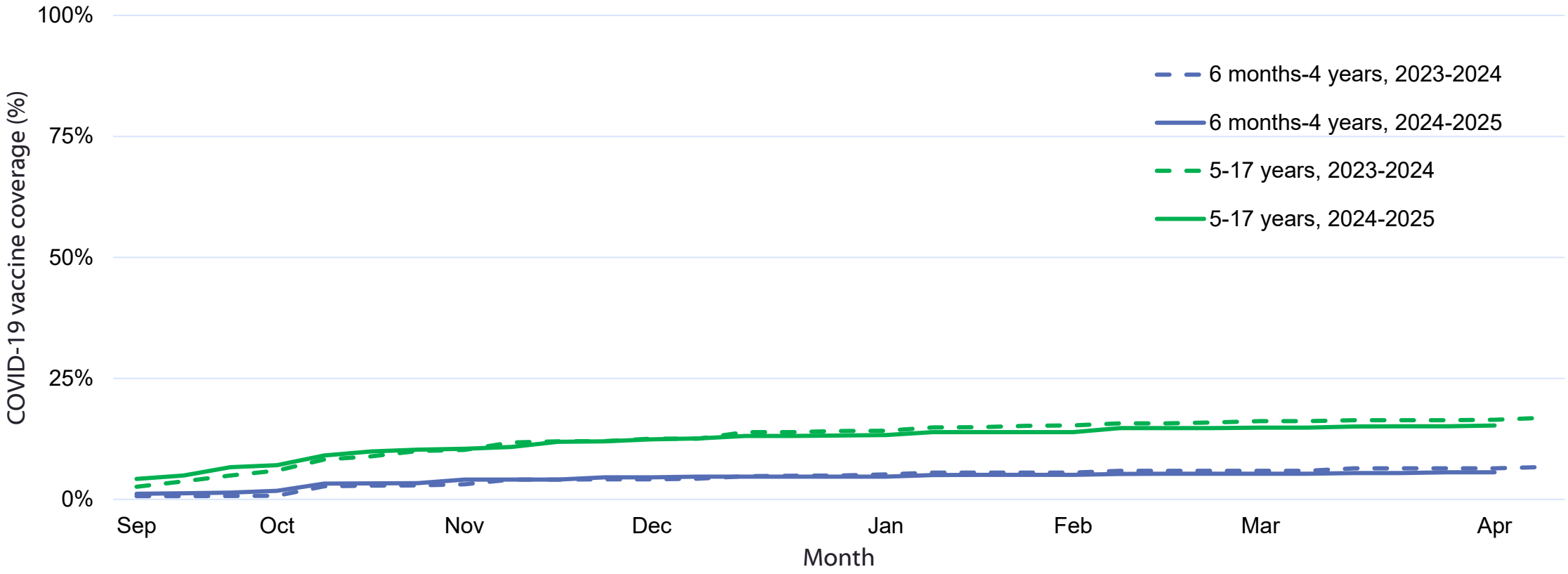
Analysis	Design	Vaccine efficacy/effectiveness, % (95% CI)
Pfizer, median 2 months after 2nd dose	RCT	95.0 (90.3-97.6)
Moderna, median 63 days after 2nd dose	RCT	94.1 (89.3-96.8)
ICATT Pfizer, 14-60 days after 2nd dose	TND	90 (89-91)
ICATT Moderna, 14-60 days after 2nd dose	TND	95 (95-96)
HEROES-RECOVER, median 69 days after 2nd dose	Cohort	91 (76-97)



ICATT = Increasing Community Access to Testing, which is a CDC-funded program to provide SARS-CoV-2 testing in retail pharmacies. ICATT uses a test-negative design.

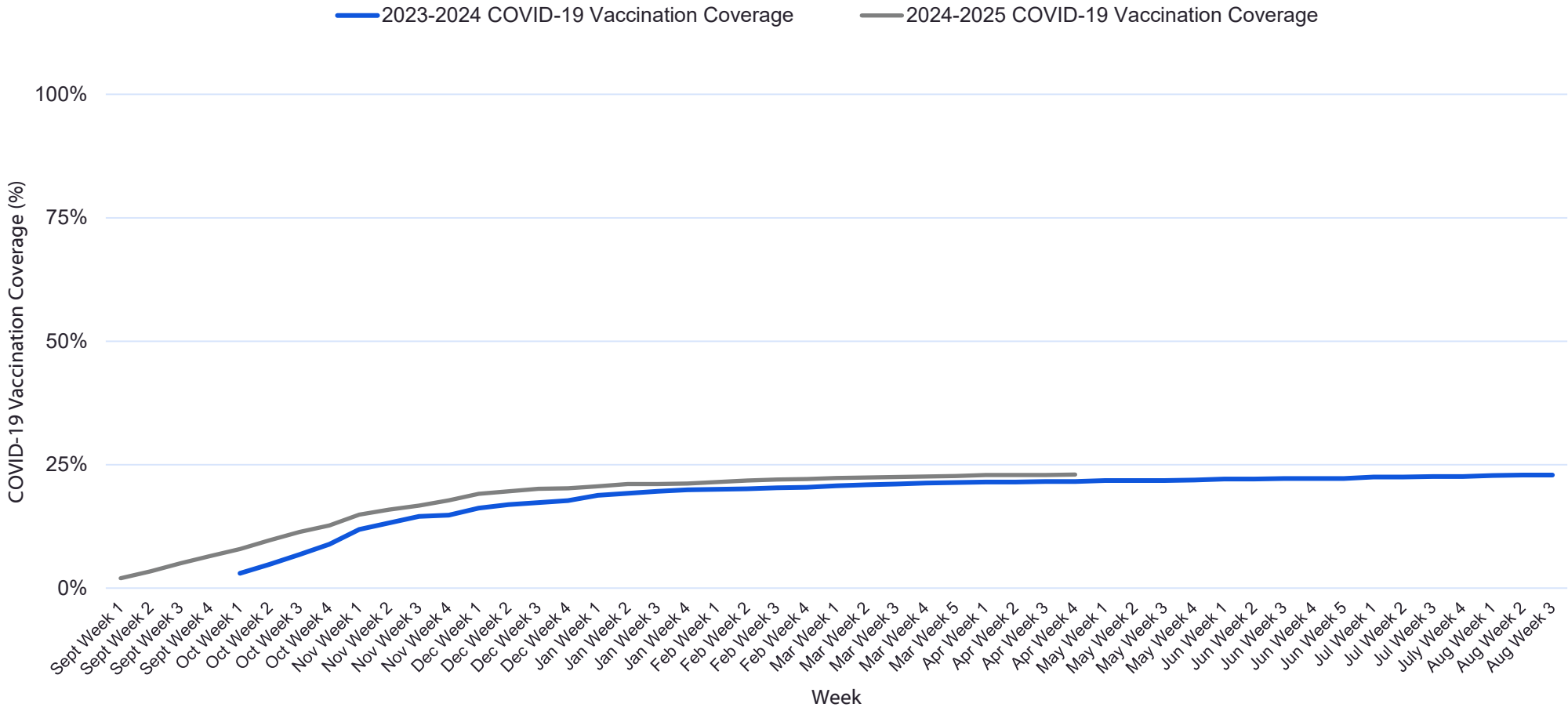
Polack et al., NEJM, 2020: https://www.nejm.org/doi/full/10.1056/NEJMoa2034577
Baden et al., NEJM, 2020: https://www.nejm.org/doi/full/10.1056/NEJMoa2035389
Britton et al., JAMA, 2022: https://jamanetwork.com/journals/jama/fullarticle/2789294
Thompson et al., NEJM, 2021: https://www.nejm.org/doi/full/10.1056/NEJMoa2107058

COVID-19 Vaccination Coverage Among Children and Adolescents 6 Months-17 Years, by Season and Age Group, National Immunization Survey, 2023-2025



Weekly estimates of COVID-19 vaccination coverage for vaccination among children through December 31, 2023, were calculated using data from the National Immunization Survey–Child COVID Module (NIS–CCM). The NIS–CCM was discontinued at the end of 2023 and questions regarding COVID-19 vaccination status and intent were added to the National Immunization Survey–Flu (NIS–Flu).
NIS–CCM and NIS–Flu are national random-digit dial cellular telephone surveys of households with children ages 6 months through 17 years; NIS–Flu is conducted during October-June. The respondent to a NIS–Flu survey is a parent or guardian who said they were knowledgeable about the child's vaccination history. All estimates are based upon parental report of receipt of vaccination and month of that vaccination. More information: https://www.cdc.gov/covidvaxview/weekly-dashboard/child-coverage-vaccination.html

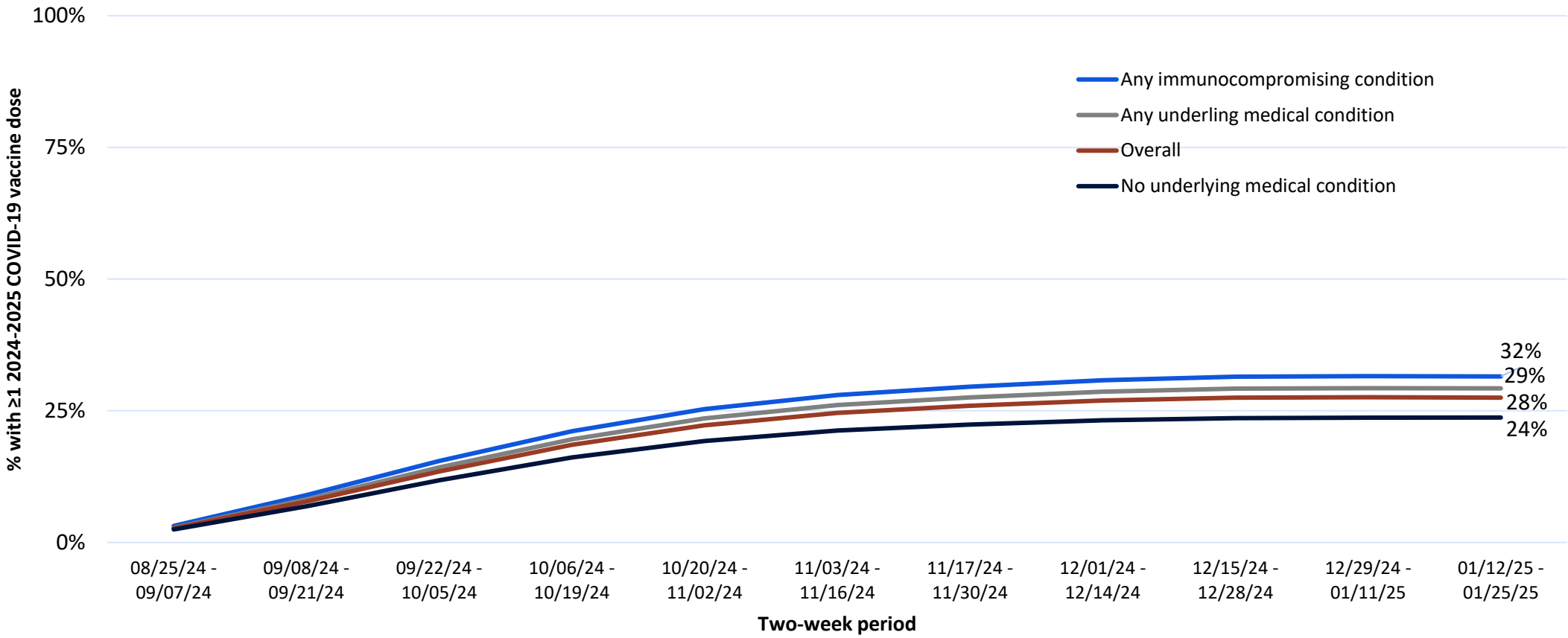
COVID-19 Vaccination Coverage Among Adults ≥18 Years, 2023-2024 and 2024-2025, NIS-ACM



National Immunization Survey-Adult COVID Module: Data from adults age ≥18 years are collected by telephone interview using a random-digit-dialed sample of cell telephone numbers stratified by state, the District of Columbia, five local jurisdictions (Bexar County TX, Chicago IL, Houston TX, New York City NY, and Philadelphia County PA), and Puerto Rico and the U.S. Virgin Islands. Data are weighted to represent the non-institutionalized U.S. population and mitigate possible bias that can result from an incomplete sample frame (exclusion of households with no phone service or only landline telephones) or non-response. All responses are self-reported. For more information about the survey, see https://www.cdc.gov/nis/about/index.html.

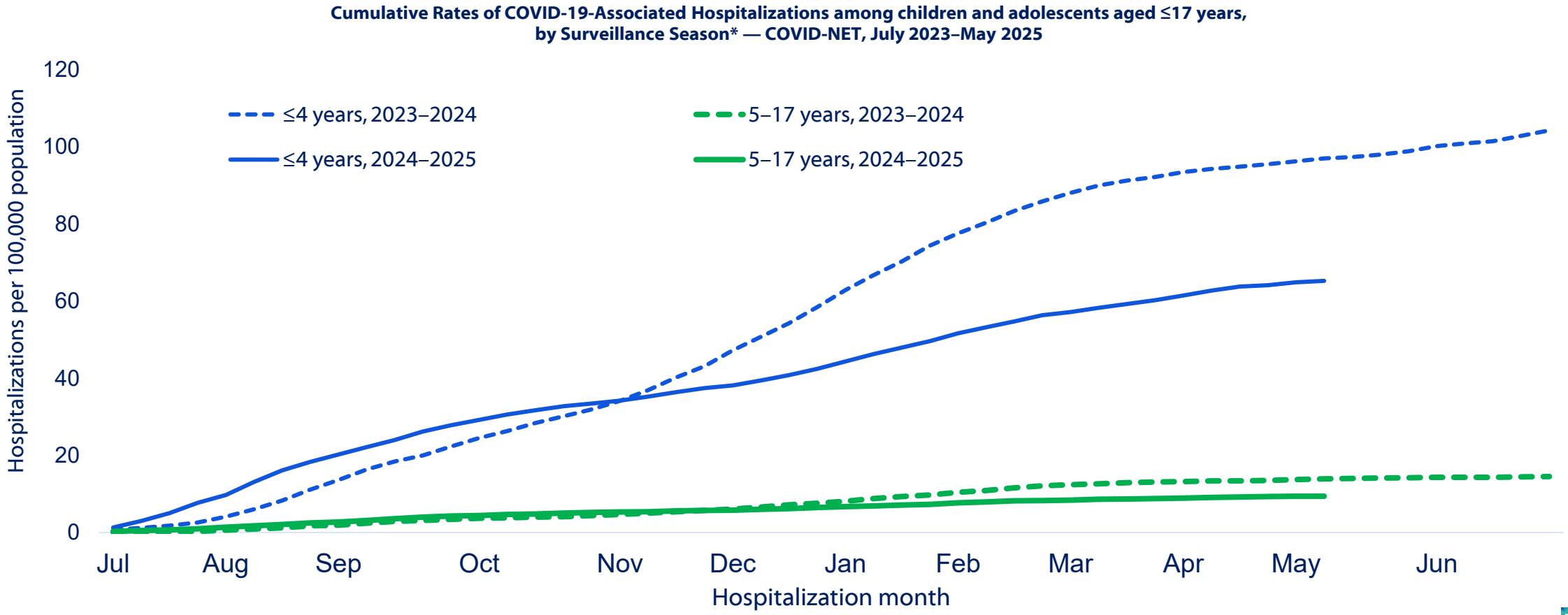
Medicare fee-for-service beneficiaries aged ≥65 years were more likely to receive a 2024-2025 COVID-19 vaccine dose if they had an underlying medical condition

Weekly cumulative COVID-19 vaccination coverage, by underlying medical condition status, Medicare fee-for-service beneficiaries aged ≥65 years, August 2024-January 2025



Fee-for-Service: enrolled in Medicare Parts A/B (and not Part C) for 365 days prior to reporting period. Estimates are based on data released by Medicare claims data through January 2025; data may be incomplete after December 7, 2024, due to 6-week reporting lag. Data on uptake by season, race, and ethnicity can be accessed at: https://www.cdc.gov/covidvaxview/weekly-dashboard/adults-65yrs-older-vaccination.html. Data on uptake by underlying medical condition from internal, unpublished analyses.

Cumulative rates of COVID-19–associated hospitalizations for the 2024–2025 season are lower compared to 2023-2024 season.



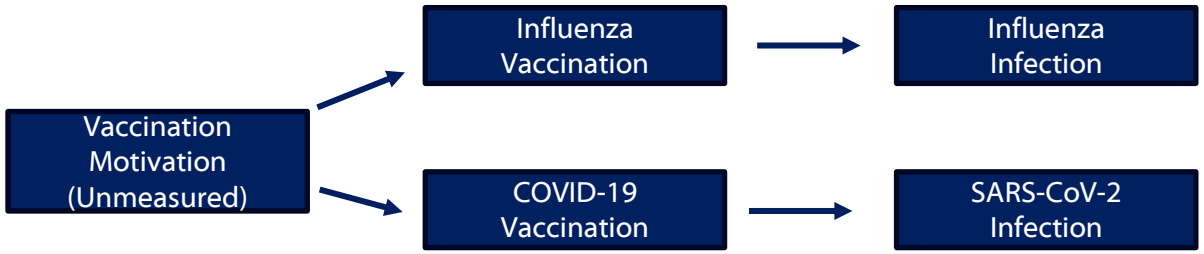
* Seasons are defined as July through June. The 2024–2025 season shows data from July 2024–April 2025 and is ongoing.

Data source: https://www.cdc.gov/resp-net/dashboard/

Note that rates are not adjusted for testing or limited to admissions where the respiratory infection is the likely primary reason for admission.

Accounting for correlated vaccination behaviors

- **Pivotal assumption (when estimating VE against ARI causing pathogens):** risk of alternative causes of ARI (e.g., influenza infection) is *independent* of exposure status (i.e., COVID-19 vaccination)
  - If violated, VE estimates may be biased
- **Three key considerations**
  - **When is this assumption violated?**
    - When controls are positive for other vaccine preventable illness (e.g., influenza) → due to the correlation between vaccination behaviors, influenza infection is not independent of exposure (COVID-19 vaccination)



  - **How might it impact VE estimates?**
    - Over representation of unvaccinated controls and underestimation of COVID-19 VE
    - Magnitude of bias depends on
      - Proportion of controls positive for alternative vaccine preventable ARI
      - Vaccination coverage
      - True VE

	SARS-CoV-2 +	SARS-CoV-2 -
Vaccinated	a	b
Unvaccinated	c	d

OR = a ÷ c / b ÷ d

VE = (1- OR) x 100%

  - **What can be done to mitigate?**
    - **Design:** Exclude influenza positive controls
    - **Analysis:** Adjust for influenza vaccination

Doll MK et al. 2022 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9129127/

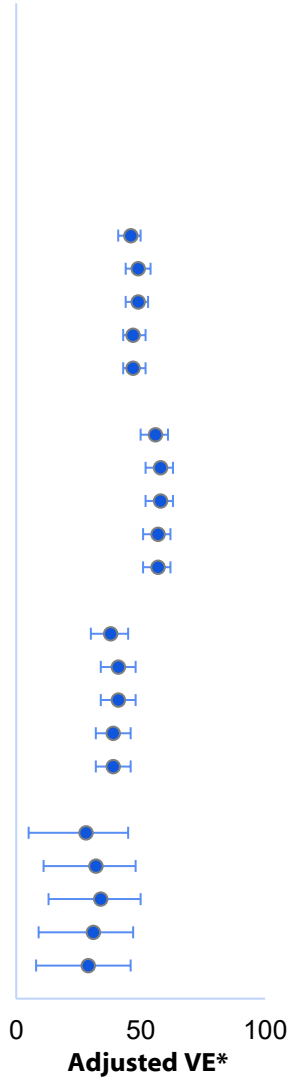
VE = vaccine effectiveness | ARI = acute respiratory infection

Accounting for correlated vaccination behaviors

- **COVID-19 VE estimates are robust**
  - Little variation in VE estimates, regardless of accounting for correlated vaccination behaviors

Model	Description
A	**Ignore potential correlation**
B	**Control for influenza and RSV vaccination status in model**
C	**Limit to controls confirmed influenza- and RSV-negative**
D	**Limit controls to tested for SARS-CoV-2, influenza, and RSV**
E	**Limit to controls presumed influenza- and RSV-negative**

Vaccination Status	Model	Total	Adjusted VE*, % (95% CI)
No 2023-2024 dose			
	A	33,935	Ref
	B	33,935	Ref
	C	20,355	Ref
	D	22,989	Ref
	E	30,810	Ref
2023-2024 dose, 7-179 days			
	A	9,182	46 (41-50)
	B	9,182	49 (44-54)
	C	6,179	49 (44-53)
	D	6,963	47 (43-52)
	E	8,314	47 (43-52)
2023-2024 dose, 7-59 days			
	A	3,848	56 (50-61)
	B	3,848	58 (52-63)
	C	2,498	58 (52-63)
	D	2,785	57 (51-62)
	E	3,535	57 (51-62)
2023-2024 dose, 60-119 days			
	A	4,375	38 (30-45)
	B	4,375	41 (34-48)
	C	3,007	41 (34-48)
	D	3,442	39 (32-46)
	E	3,897	39 (32-46)
2023-2024 dose, 120-179 days			
	A	959	28 (5-45)
	B	959	32 (11-48)
	C	674	34 (13-50)
	D	736	31 (9-47)
	E	882	29 (8-46)



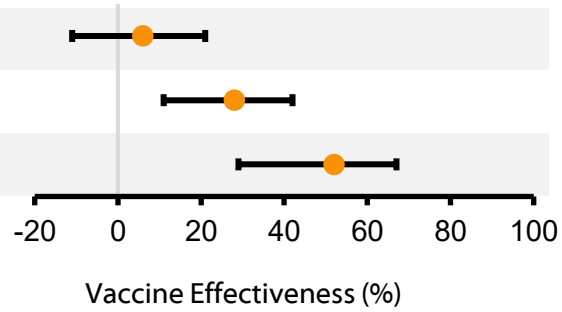
VE = Vaccine Effectiveness

*VE against COVID-19-associated hospitalization among adults aged ≥60 years was calculated as (1-odds ratio) x 100%, estimated using a test-negative case-control design, adjusting for age, sex, race and ethnicity, VISION site ID, and calendar time (days since July 1, 2023). The reference group for all models was no 23/24 vaccine recipe regardless of prior vaccination history.

CDC Unpublished Data; Payne AB et al. 2023 https://pmc.ncbi.nlm.nih.gov/articles/PMC11823735/

Absolute VE of COVID-19 *original monovalent and bivalent* doses received *prior to* or *during* pregnancy against COVID-19–associated *emergency department/urgent care encounters* among immuno*competent* pregnant women aged 18-45 years — VISION
June 2022 – August 2023

Vaccine Dosage Pattern	Total tests	SARS-CoV-2-test-positive, N (%)	Median interval since last dose, days (IQR)	Adjusted VE (95% CI)
Absolute VE				
Unvaccinated (ref)	2991	403 (13)	--	*Ref*
Most recent monovalent or bivalent dose received:				
≥6 months before pregnancy	3014	365 (12)	483 (393,579)	**6 (-11, 21)**
<6 months before pregnancy	1203	143 (12)	267 (204, 325)	**28 (11, 42)**
During pregnancy	469	35 (7)	91 (45, 158)	**52 (29, 67)**

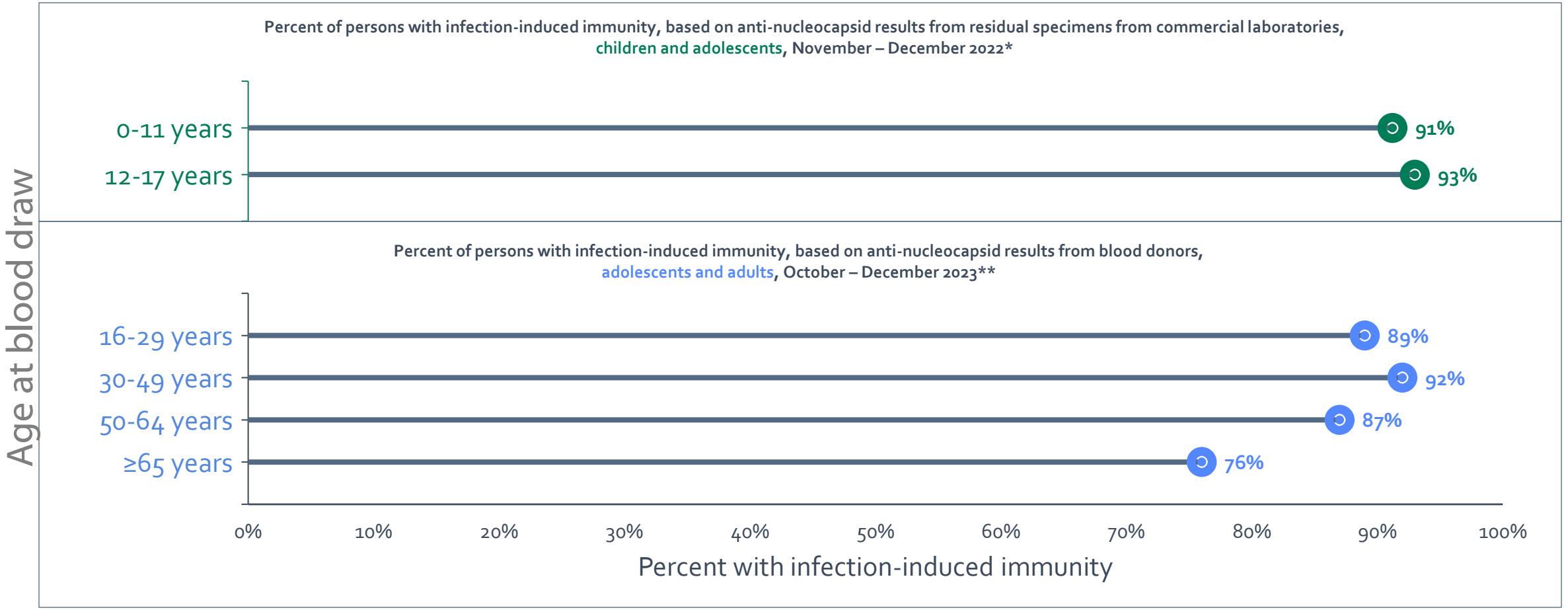


Vaccine effectiveness was calculated by comparing the odds of COVID-19 vaccination in case-patients and control-patients using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multivariable logistic regression. The odds ratio was adjusted for age, ethnicity, race, underlying medical conditions, gestational age at encounter, site, Medicaid status, day of encounter, site facility urbanicity.

Pregnant women were classified as (1) unvaccinated (no COVID-19 vaccine doses) or (2) vaccinated with the last COVID-19 vaccine dose ≥7 days before the index date (including the original monovalent and/or bivalent vaccines). The index date was defined as (1) the collection date of a respiratory specimen associated with the most recent positive or negative SARS-CoV-2 test result before the ED/UC encounter or (2) the encounter date, if testing occurred only after the encounter. COVID-19 vaccination dates and vaccine types were identified by electronic medical records. Original monovalent COVID-19 vaccines (11 December 2020–31 August 2022) include Moderna, Pfizer-BioNTech, and Janssen (Johnson & Johnson), and bivalent COVID-19 vaccines include Moderna and Pfizer-BioNTech. Bivalent vaccines (1 September 2022–10 September 2023) contain components from the SARS-CoV-2 ancestral and Omicron BA.4/BA.5 strains.

Ciesla et al., OFID 2024, https://academic.oup.com/ofid/article/11/9/ofae481/7743292

Context for interpreting COVID-19 VE across age groups: high infection-induced seroprevalence in children and adults



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

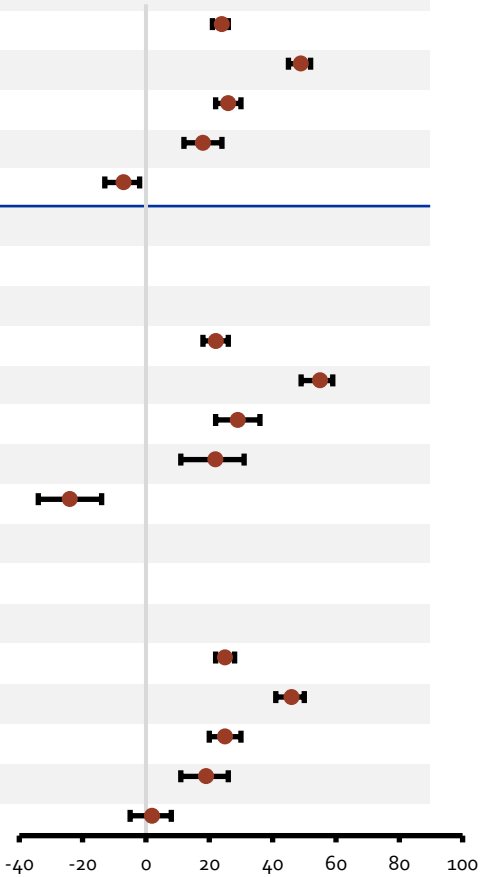
* Data on persons aged 0-17 years from nationwide commercial laboratory testing of residual serum specimens from ~27,000 children and adolescents originally submitted for routine screening or clinical management, https://covid.cdc.gov/covid-data-tracker/#pediatric-seroprevalence

** Data on persons aged ≥16 years from a longitudinal, national cohort of ~35,000 blood donors, https://covid.cdc.gov/covid-data-tracker/#nationwide-blood-donor-seroprevalence-2022

VISION: VE of *2023-2024 COVID-19 vaccine* against COVID-19-associated *emergency department/urgent care encounters* among immunocompetent adults aged ≥18 years, by age group

September 2023 – August 2024

Age group/2023-2024 COVID-19 vaccination status/days since dose	Total encounters	SARS-CoV-2-test-positive, N (%)	Median interval since last dose among vaccinated, days (IQR)	Adjusted VE (95% CI)
≥18 years				
No 2023-2024 COVID-19 dose (ref)	279,733	31,167 (11)	756 (543-920)	**ref**
2023-2024 COVID-19 dose, 7-299 days earlier	65,906	5,929 (9)	117 (61-189)	**24 (21 to 26)**
2023-2024 COVID-19 dose, 7-59 days earlier	16,082	1,228 (8)	34 (21-47)	**49 (45 to 52)**
2023-2024 COVID-19 dose, 60-119 days earlier	17,653	1,521 (9)	88 (73-103)	**26 (22 to 30)**
2023-2024 COVID-19 dose, 120-179 days earlier	13,815	875 (6)	147 (133-163)	**18 (12 to 24)**
2023-2024 COVID-19 dose, 180-299 days earlier	18,356	2,305 (13)	231 (204-261)	**-7 (-13 to -2)**
18-64 years				
No 2023-2024 COVID-19 dose (ref)	200,443	21,053 (10)	789 (624-934)	**ref**
2023-2024 COVID-19 dose, 7-299 days earlier	23,655	1,893 (8)	116 (59-187)	**22 (18 to 26)**
2023-2024 COVID-19 dose, 7-59 days earlier	5,952	360 (6)	34 (20-47)	**55 (49 to 59)**
2023-2024 COVID-19 dose, 60-119 days earlier	6,285	436 (7)	88 (74-104)	**29 (22 to 36)**
2023-2024 COVID-19 dose, 120-179 days earlier	4,971	256 (5)	147 (133-163)	**22 (11 to 31)**
2023-2024 COVID-19 dose, 180-299 days earlier	6,447	841 (13)	230 (203-260)	**-24 (-34 to -14)**
≥65 years				
No 2023-2024 COVID-19 dose (ref)	79,290	10,114 (13)	669 (436-868)	**ref**
2023-2024 COVID-19 dose, 7-299 days earlier	42,251	4,036 (10)	117 (62-190)	**25 (22 to 28)**
2023-2024 COVID-19 dose, 7-59 days earlier	10,130	868 (9)	34 (21-47)	**46 (41 to 50)**
2023-2024 COVID-19 dose, 60-119 days earlier	11,368	1,085 (10)	88 (73-103)	**25 (20 to 30)**
2023-2024 COVID-19 dose, 120-179 days earlier	8,844	619 (7)	148 (133-163)	**19 (11 to 26)**
2023-2024 COVID-19 dose, 180-299 days earlier	11,909	1,464 (12)	232 (204-262)	**2 (-5 to 8)**

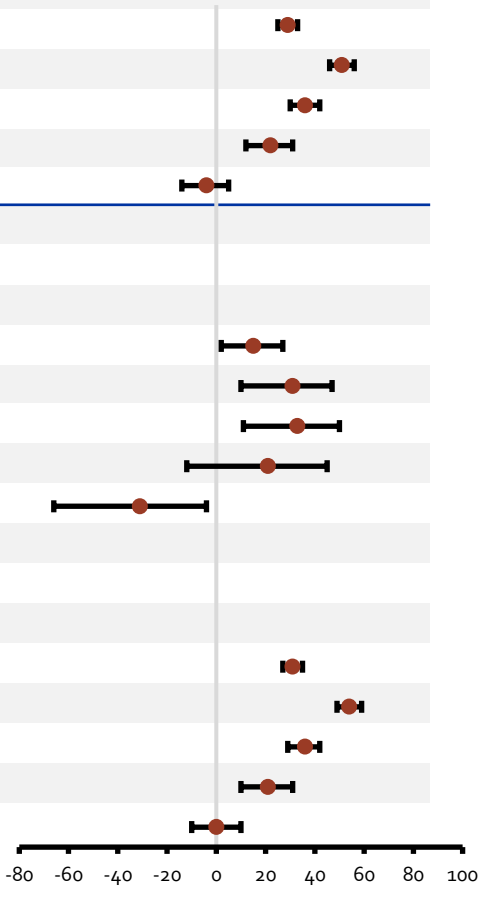


Link-Gelles et al., JAMA Network Open. VE was calculated as (1 – odds ratio) x 100%, estimated using a test-negative case-control design, with the odds ratio adjusted for age, sex, race and ethnicity, geographic region, and calendar time. A VE estimate less than zero is possible due to the waning protection from COVID-19 vaccines coupled with the existing infection-induced immunity in unvaccinated participants. As protection from vaccination wanes, and unvaccinated people accumulate protection from repeated infections, this may yield negative VE.

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

September 2023 – August 2024

Age group/2023-2024 COVID-19 vaccination status/days since dose	Total encounters	SARS-CoV-2-test-positive, N (%)	Median interval since last dose among vaccinated, days (IQR)	Adjusted VE (95% CI)
≥18 years				
No 2023-2024 COVID-19 dose (ref)	87,718	8,480 (10)	733 (507-918)	**ref**
2023-2024 COVID-19 dose, 7-299 days earlier	24,213	1,900 (8)	123 (63-193)	**29 (25 to 33)**
2023-2024 COVID-19 dose, 7-59 days earlier	5,618	417 (7)	34 (21-47)	**51 (46 to 56)**
2023-2024 COVID-19 dose, 60-119 days earlier	6,231	486 (8)	88 (74-104)	**36 (30 to 42)**
2023-2024 COVID-19 dose, 120-179 days earlier	5,275	306 (6)	149 (134-164)	**22 (12 to 31)**
2023-2024 COVID-19 dose, 180-299 days earlier	7,089	691 (10)	230 (203-260)	**-4 (-14 to 5)**
18-64 years				
No 2023-2024 COVID-19 dose (ref)	35,303	2,229 (6)	788 (606-940)	**ref**
2023-2024 COVID-19 dose, 7-299 days earlier	4,249	234 (6)	120 (62-188)	**15 (2 to 27)**
2023-2024 COVID-19 dose, 7-59 days earlier	1,005	60 (6)	33 (21-46)	**31 (10 to 47)**
2023-2024 COVID-19 dose, 60-119 days earlier	1,113	52 (5)	89 (75-104)	**33 (11 to 50)**
2023-2024 COVID-19 dose, 120-179 days earlier	936	33 (4)	148 (135-164)	**21 (-12 to 45)**
2023-2024 COVID-19 dose, 180-299 days earlier	1,195	89 (7)	229 (201-259)	**-31 (-66 to -4)**
≥65 years				
No 2023-2024 COVID-19 dose (ref)	52,415	6,251 (12)	698 (467-899)	**ref**
2023-2024 COVID-19 dose, 7-299 days earlier	19,964	1,666 (8)	123 (63-194)	**31 (27 to 35)**
2023-2024 COVID-19 dose, 7-59 days earlier	4,613	357 (8)	34 (21-47)	**54 (49 to 59)**
2023-2024 COVID-19 dose, 60-119 days earlier	5,118	434 (8)	88 (73-104)	**36 (29 to 42)**
2023-2024 COVID-19 dose, 120-179 days earlier	4,339	273 (6)	149 (134-164)	**21 (10 to 31)**
2023-2024 COVID-19 dose, 180-299 days earlier	5,894	602 (10)	230 (204-261)	**0 (-10 to 10)**



Link-Gelles et al., JAMA Network Open. VE was calculated as (1 – odds ratio) x 100%, estimated using a test-negative case-control design, with the odds ratio adjusted for age, sex, race and ethnicity, geographic region, and calendar time. A VE estimate less than zero is possible due to the waning protection from COVID-19 vaccines coupled with the existing infection-induced immunity in unvaccinated participants. As protection from vaccination wanes, and unvaccinated people accumulate protection from repeated infections, this may yield negative VE.

Characteristics of emergency department and urgent care encounters and hospitalizations among adults aged ≥18 years with COVID-19-like illness, by COVID-19 case status and CDC vaccine effectiveness network — VISION and IVY Networks

September 2024–May 2025

Characteristic	Vaccine effectiveness network and setting, no. (column %)								
	VISION ED/UC encounters, all adults aged ≥18 years			VISION hospitalizations, all adults aged ≥65 years			IVY hospitalizations, all adults aged ≥65 years		
	Total	COVID-19 case-patients	COVID-19 control-patients	Total	COVID-19 case-patients	COVID-19 control-patients	Total	COVID-19 case-patients	COVID-19 control-patients
Total	**240,976**	**14,621**	**226,355**	**65,751**	**4,341**	**61,410**	**4,392**	**1,190**	**3,202**
Median age	52 [34, 71]	57 [36, 74]	52 [34, 71]	78 [71, 84]	79 [73, 86]	78 [71, 84]	75 [70, 82]	77 [71, 84]	75 [69, 81]
Age group									
18-64 years	158,028 (66)	8,688 (59)	149,340 (66)	--	--	--	--	--	--
≥65 years	82,948 (34)	5,933 (41)	77,015 (34)	65,751 (100)	4,341 (100)	61,410 (100)	4,392 (100)	1,190 (100)	3,202 (100)
Immunocompromised*	--	--	--	15,350 (23)	883 (20)	14,467 (24)	1,137 (26)	258 (22)	879 (28)

Updated from Link-Gelles, et al. MMWR: https://www.cdc.gov/mmwr/volumes/74/wr/mm7406a1.htm

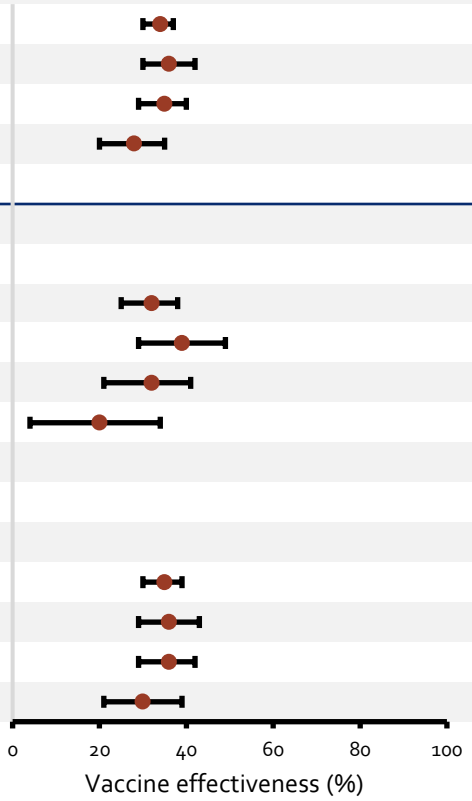
ED/UC = emergency department/urgent care; VISION data go through May 2025; IVY data go through April 2025

* Immunocompromised status is not evaluated for ED/UC encounters due to a higher likelihood of incomplete discharge diagnosis codes in this setting.

Effectiveness of *2024–2025 COVID-19* vaccination against COVID-19–associated *emergency department/urgent care* encounters by age group — VISION

September 2024 – May 2025

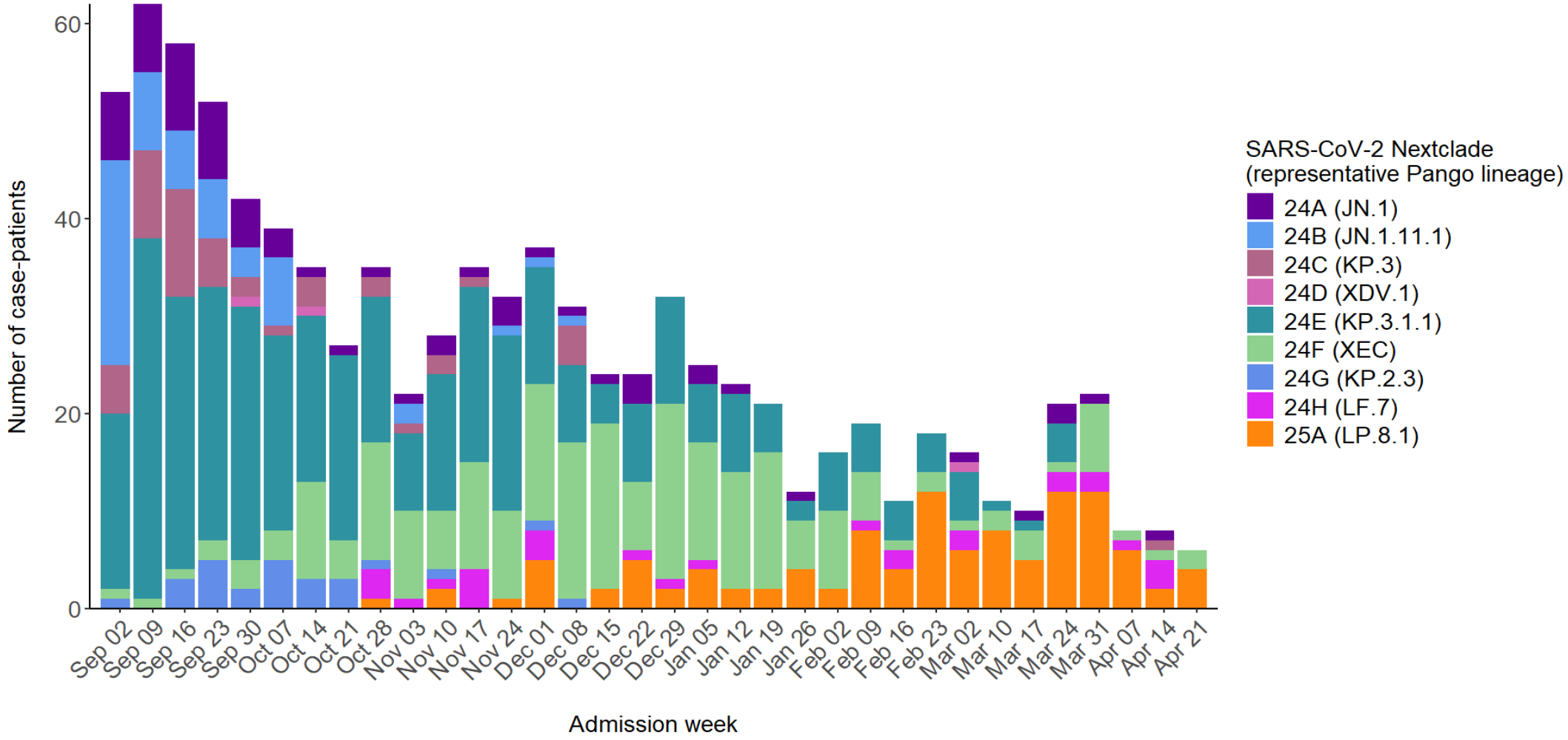
Age group/2024-2025 COVID-19 vaccination status/days since dose	COVID-19 case-patients N (Col %)	COVID-19 control-patients N (Col %)	Median interval since last dose among vaccinated*, days (IQR)	Adjusted vaccine effectiveness % (95% CI)
≥18 years				
No **2024-2025 COVID-19 dose** (Ref)	12,927 (88)	188,006 (83)	1,068 (742-1,224)	**Ref**
Received **2024-2025 COVID-19 dose** 7–179 days earlier	1,694 (12)	38,349 (17)	89 (50-129)	**34 (30-37)**
2024-2025 COVID-19 dose, 7–59 days earlier	572 (4)	11,763 (5)	34 (21-47)	**36 (30-42)**
2024-2025 COVID-19 dose, 60–119 days earlier	695 (5)	14,685 (6)	89 (74-104)	**35 (29-40)**
2024-2025 COVID-19 dose, 120–179 days earlier	427 (3)	11,901 (5)	147 (133-162)	**28 (20-35)**
18-64 years				
No **2024-2025 COVID-19 dose** (Ref)	8,212 (95)	136,067 (91)	1,105 (866-1,245)	**Ref**
Received **2024-2025 COVID-19 dose** 7–179 days earlier	476 (5)	13,273 (9)	86 (48-127)	**32 (25-38)**
2024-2025 COVID-19 dose, 7–59 days earlier	156 (2)	4,244 (3)	33 (20-46)	**39 (29-49)**
2024-2025 COVID-19 dose, 60–119 days earlier	199 (2)	5,155 (3)	89 (74-104)	**32 (21-41)**
2024-2025 COVID-19 dose, 120–179 days earlier	121 (1)	3,874 (3)	147 (132-163)	**20 (4-34)**
≥65 years				
No **2024-2025 COVID-19 dose** (Ref)	4,715 (79)	51,939 (67)	907 (448-1,166)	**Ref**
Received **2024-2025 COVID-19 dose** 7–179 days earlier	1,218 (21)	25,076 (33)	91 (51-131)	**35 (30-39)**
2024-2025 COVID-19 dose, 7–59 days earlier	416 (7)	7,519 (10)	34 (21-47)	**36 (29-43)**
2024-2025 COVID-19 dose, 60–119 days earlier	496 (8)	9,530 (12)	90 (75-105)	**36 (29-42)**
2024-2025 COVID-19 dose, 120–179 days earlier	306 (5)	8,027 (10)	147 (133-162)	**30 (21-39)**



Updated from: Link-Gelles, et al. MMWR: https://www.cdc.gov/mmwr/volumes/74/wr/mm7406a1.htm. Vaccine effectiveness was calculated by comparing the odds of 2024–2025 COVID-19 vaccination in case-patients and control-patients using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multivariable logistic regression. The odds ratio was adjusted for age, sex, race and ethnicity, calendar day, and geographic region. The "no 2024–2025 dose" group included all eligible persons who did not receive a 2024–2025 COVID-19 vaccine dose, regardless of number of previous COVID-19 vaccine doses (if any) received. * Time since vaccination is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, or 2024-2025 COVID-19 vaccine.

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

September 1, 2024–April 27, 2025



Dates are for the start of the admission week.

IVY: Effectiveness of *2024–2025 COVID-19 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† KP.3.1.1 lineage (Nextstrain clade 24E) or XEC lineage (Nextstrain clade 24F)**
  - **Controls:** CLI and test *negative* for SARS-CoV-2, influenza viruses, and RSV (≥60 years) by RT-PCR

- **Analytic Period:** September 1, 2024–April 27, 2025

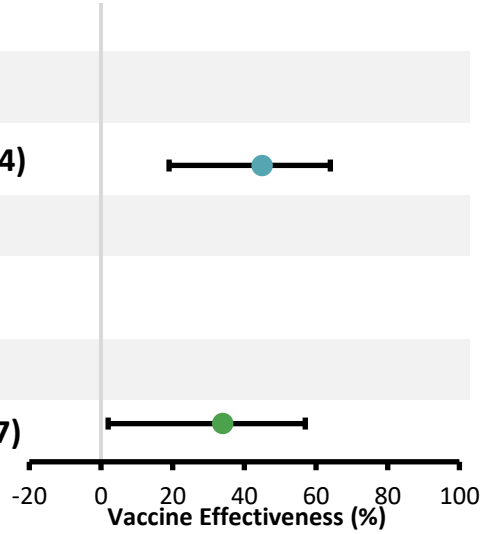
- VE§ against hospitalization was calculated separately using case-patients with sequence-confirmed SARS-CoV-2 KP.3.1.1 and XEC lineage infections

* Case patients who were co-infected with influenza viruses or RSV were excluded.
† Identification of a SARS-CoV-2 lineage through viral whole-genome sequencing was successful for 49% of case-patients during the analysis period.
§ Vaccine effectiveness was calculated by comparing the odds of 2024–2025 COVID-19 vaccination in case-patients and control-patients using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multivariable logistic regression. The odds ratio was adjusted for age, sex, race and ethnicity, geographic region (U.S. Department of Health and Human Services Region) and calendar time (biweekly intervals).

IVY: Effectiveness of *2024–2025 COVID-19 vaccine* against *hospitalization* among adults aged ≥18 years* *by SARS-CoV-2 lineage†*

September 1, 2024 – April 27, 2025

Lineage and 2024-2025 COVID-19 vaccination status	COVID-19 case-patients		COVID-19 control-patients		Vaccine Effectiveness§ % (95% CI)
	N (Col %)	Median interval since last dose among vaccinated, days (IQR)	N (Col %)	Median interval since last dose among vaccinated, days (IQR)	
KP.3.1.1					
No **2024-2025 COVID-19 dose** (Ref)	309 (91)	Not available	5,202 (84)	Not available	**Ref**
Received **2024-2025 COVID-19 dose** 7–179 days earlier	29 (9)	56 (33–75)	1,027 (16)	94 (57–133)	**45 (19–64)**
XEC					
No **2024-2025 COVID-19 dose** (Ref)	173 (84)	Not available	5,202 (84)	Not available	**Ref**
Received **2024-2025 COVID-19 dose** 7–179 days earlier	32 (16)	87 (52–112)	1,027 (16)	94 (57–133)	**34 (2–57)**



* These results include both immunocompetent and immunocompromised persons.

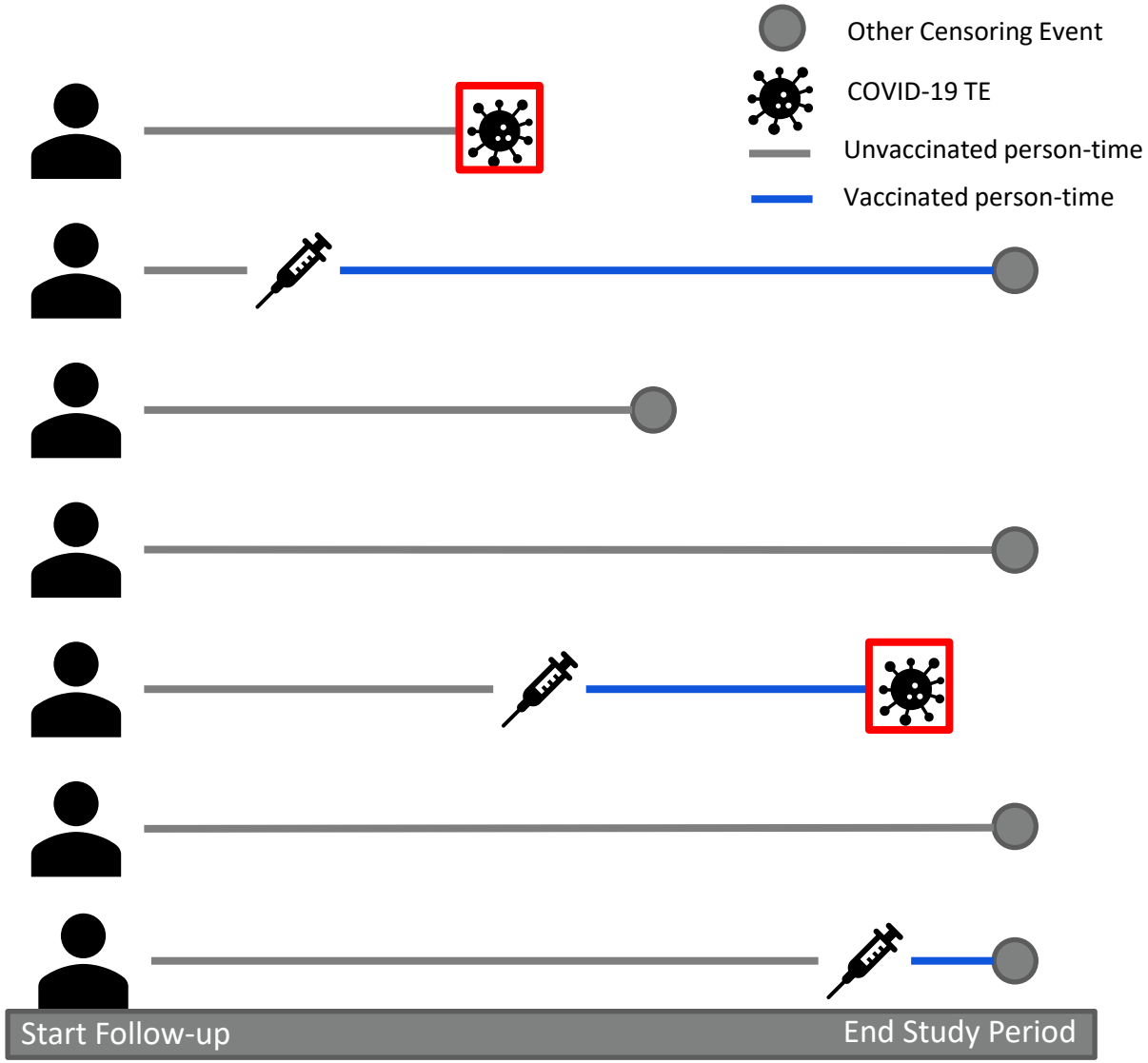
† KP.3.1.1 lineage was defined by Nextstrain clade 24E and XEC lineage was defined by Nextstrain clade 24F.

§ Vaccine effectiveness was calculated by comparing the odds of 2024–2025 COVID-19 vaccination in case-patients and control-patients using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multivariable logistic regression. The odds ratio was adjusted for age, sex, race and ethnicity, geographic region (U.S. Department of Health and Human Services Region) and calendar time (biweekly intervals).

Medicare data

- **Design:** Retrospective cohort
- **Data source:** Medicare fee-for-service claims data*
- **Population:** Persons aged ≥65, recent nursing home stay
- **Censoring events:**
  - COVID-19-associated thromboembolic event (TE)
  - Death
  - Disenrollment in Medicare Parts A/B
  - Enrollment in Medicare Part C
  - Admission to hospice facility
  - Dialysis encounter
  - Receipt of a 2023-2024 COVID-19 vaccine dose <60 days from bivalent COVID-19 vaccine dose
  - Receipt of a second 2023-2024 COVID-19 vaccine dose <120 days from first 2023-2024 COVID-19 vaccine dose
  - Receipt of a third 2023-2024 COVID-19 vaccine dose
  - End of study period
- **VE = (1 - adjusted hazard ratio**) x 100%**

where adjusted hazard ratio = $\frac{rate\ of\ COVID\text{-}19\text{-}associated\ TE_{vaccinated}}{rate\ of\ COVID\text{-}19\text{-}associated\ TE_{unvaccinated}}$



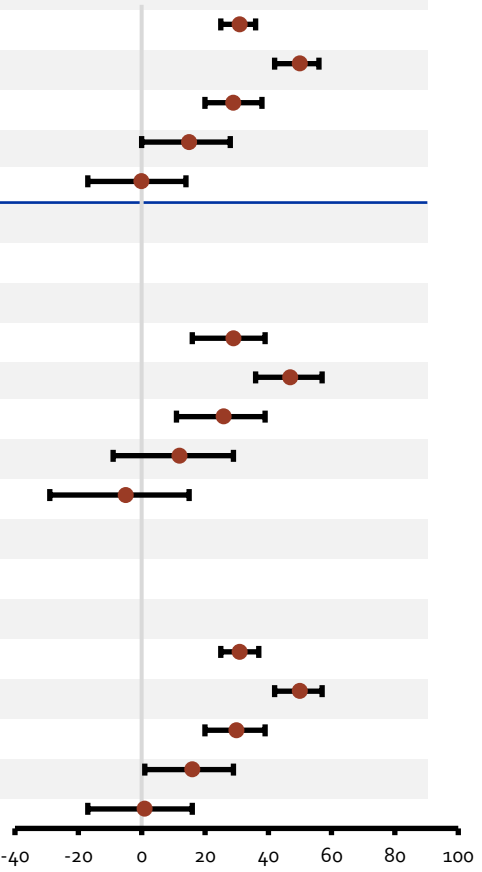
*Data sources included Medicare Enrollment Database (EDB) and Common Medicare Environment (CME), Common Working File (CWF) and Shared System Data (SSD) Medicare Parts A/B claims data, Minimum Data Set (MDS), and CDC/ATSDR Social Vulnerability Index (SVI)

**Hazard ratios adjusted for age group, sex, race, long/short nursing home stay status, social vulnerability index, state, rural/urban classification, number of underlying medical conditions, 2022-2023 influenza vaccination status, and bivalent COVID-19 vaccination status.

VE of *2023-2024 COVID-19 vaccine* against COVID-19 related thromboembolic events among immunocompetent Medicare fee-for-service beneficiaries residing in a nursing home, by age group and time since vaccination

September 2023 – July 2024

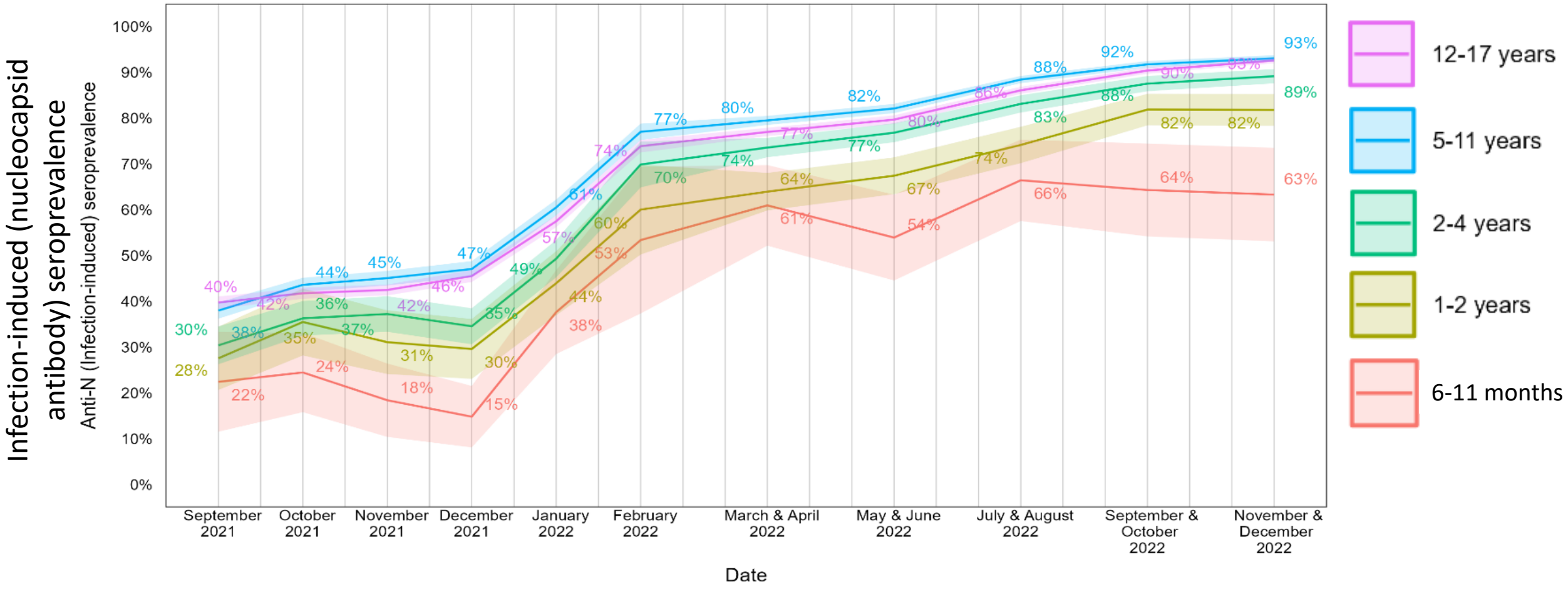
Age group/2023-2024 COVID-19 vaccination status/days since dose	Number of Beneficiaries	Number of Outcomes	Median Follow-up Time Contributed to Category (Days)	Adjusted VE (95% CI)
≥65+ years				
No 2023-2024 COVID-19 dose (ref)	516,176	4,335	142	*Ref*
2023-2024 COVID-19 dose, ≥ 7 days earlier	209,228	726	161	31% (25%, 36%)
2023-2024 COVID-19 dose, 7-59 days earlier	26,646	198	53	50% (42%, 56%)
2023-2024 COVID-19 dose, 60-119 days earlier	37,426	238	60	29% (20%, 38%)
2023-2024 COVID-19 dose, 120-179 days earlier	23,558	138	60	15% (0%, 28%)
2023-2024 COVID-19 dose, ≥ 180 days earlier	121,598	152	65	0% (-17%, 14%)
65-74 years				
No 2023-2024 COVID-19 dose (ref)	116,278	1,025	176	*Ref*
2023-2024 COVID-19 dose, ≥ 7 days earlier	40,719	132	178	29% (16%, 39%)
2023-2024 COVID-19 dose, 7-59 days earlier	5,029	34	53	47% (36%, 57%)
2023-2024 COVID-19 dose, 60-119 days earlier	6,646	55	60	26% (11%, 39%)
2023-2024 COVID-19 dose, 120-179 days earlier	4,984	22	60	12% (-9%, 29%)
2023-2024 COVID-19 dose, ≥ 180 days earlier	24,060	21	64	-5% (-29%, 15%)
≥75+ years				
No 2023-2024 COVID-19 dose (ref)	399,898	3,310	135	*Ref*
2023-2024 COVID-19 dose, ≥ 7 days earlier	168,509	594	157	31% (25%, 37%)
2023-2024 COVID-19 dose, 7-59 days earlier	21,617	164	53	50% (42%, 57%)
2023-2024 COVID-19 dose, 60-119 days earlier	30,780	183	60	30% (20%, 39%)
2023-2024 COVID-19 dose, 120-179 days earlier	18,574	116	60	16% (1%, 29%)
2023-2024 COVID-19 dose, ≥ 180 days earlier	97,538	131	65	1% (-17%, 16%)



CDC, unpublished data

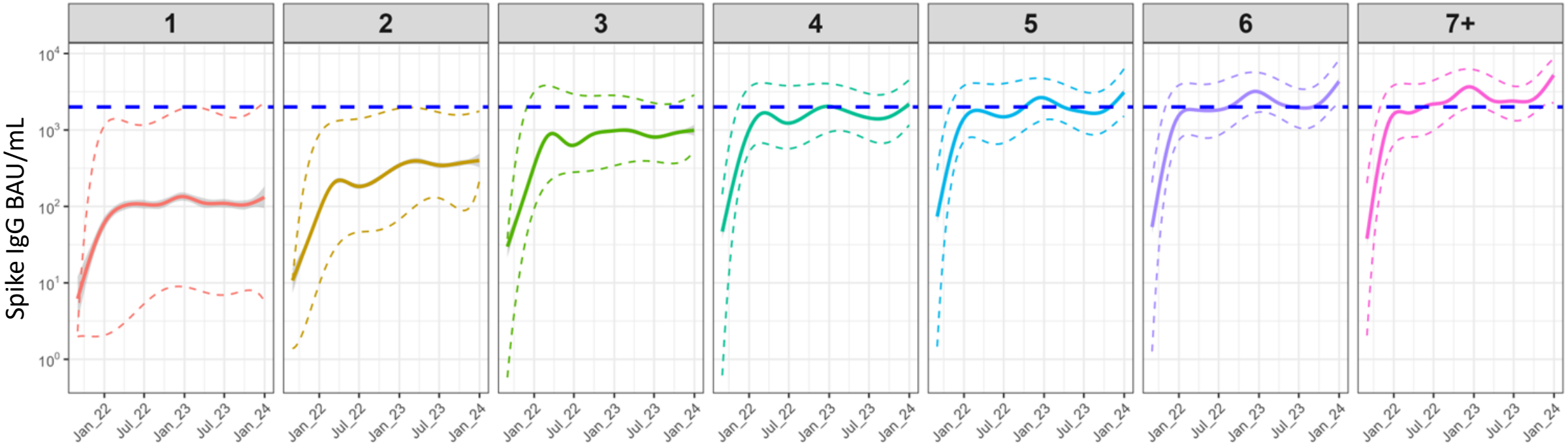
Models are adjusted for *age group, sex, race, long/short NH stay status, social vulnerability index (SVI), state, rural/urban classification, number of UMC categories, 2022-2023 influenza vaccination status, and bivalent COVID-19 vaccination status.*

Infection-induced SARS-CoV-2 seroprevalence among U.S. children — September 2021 – December 2022



Shaded ranges depict 95% confidence intervals for the estimated seroprevalence shown by the dark line in the corresponding color.
Source: https://covid.cdc.gov/covid-data-tracker/#pediatric-seroprevalence
Accessed: March 20, 2025

Population SARS-CoV-2 spike antibody over time by the cumulative number of combined infections and vaccinations - U.S. blood donors ages ≥16 years, September 2021-December 2023



Solid lines represent mean anti-spike IgG levels; dotted lines represent model based 25th-75th% percentiles

Higher number of cumulative SARS-CoV-2 infections and COVID-19 vaccinations leads to higher antibody levels, but with smaller incremental increases in antibodies with each exposure

Source: https://covid.cdc.gov/covid-data-tracker/#nationwide-blood-donor-seroprevalence-2022, CDC unpublished data

COVID-19 mRNA vaccination associated with reduced occurrence of Long COVID following COVID-19: June 2021-September 2022

Among children aged 5 – 17 years:

Completion of the primary vaccine series prior to infection associated with **reduced likelihood** of Long COVID symptoms[1]

- **57% for 1 or more symptoms**
- **73% for 2 or more symptoms**
- **72% for respiratory symptoms**

Among adults:

3 doses of original monovalent vaccine prior to infection associated with **reduced likelihood** of Long COVID symptoms[2]

- **63% for gastrointestinal symptoms**
- **44% for neurological symptoms**
- **52% for other non-specific symptoms**

1. Yousaf AR, Mak J, Gwynn L, et al. COVID-19 Vaccination and Odds of Post–COVID-19 Condition Symptoms in Children Aged 5 to 17 Years. *JAMA Netw Open.* 2025;8(2):e2459672.
2. Mak J, Khan S, Britton A et al. Association of Messenger RNA Coronavirus Disease 2019 (COVID-19) Vaccination and Reductions in Post COVID Conditions Following Severe Acute Respiratory Syndrome Coronavirus 2 Infection in a US Prospective Cohort of Essential Workers, The Journal of Infectious Diseases, Volume 231, Issue 3, 15 March 2025, Pages 665–676

COVID-19 vaccine impact on transmission

- **Data that explicitly quantifies vaccine effectiveness against transmission is ideal, but it is often not feasible.**
- **Other data can help us understand the impact of COVID-19 vaccination on transmission, vaccine effectiveness against infection and infectiousness**
  - COVID-19 vaccines provide moderate protection against infection in older children and adults.[1,2,3]
  - COVID-19 vaccines may provide less protection against infection in young, infection-naïve children.[4]
  - COVID-19 vaccines moderately reduce infectiousness in individuals after they are infected with SARS-CoV-2 (see next slides).[5]
- **Preventing infections further reduces transmission by stopping future transmission chains.**

1 Feldstein L, et al. Effectiveness of mRNA COVID-19 Vaccines and Hybrid Immunity in Preventing SARS-CoV-2 Infection and Symptomatic COVID-19 Among Adults in the United States. https://academic.oup.com/jid/article/231/4/e743/7945315

2 Feldstein L, et al. Effectiveness of Bivalent mRNA COVID-19 Vaccines in Preventing SARS-CoV-2 Infection in Children and Adolescents Aged 5 to 17 Years. https://jamanetwork.com/journals/jama/fullarticle/2814536

3 Kirwan PD, et al. Protection of vaccine boosters and prior infection against mild/asymptomatic and moderate COVID-19 infection in the UK SIREN healthcare worker cohort: October 2023 to March 2024. https://www.sciencedirect.com/science/article/pii/S0163445324002275?via%3Dihub

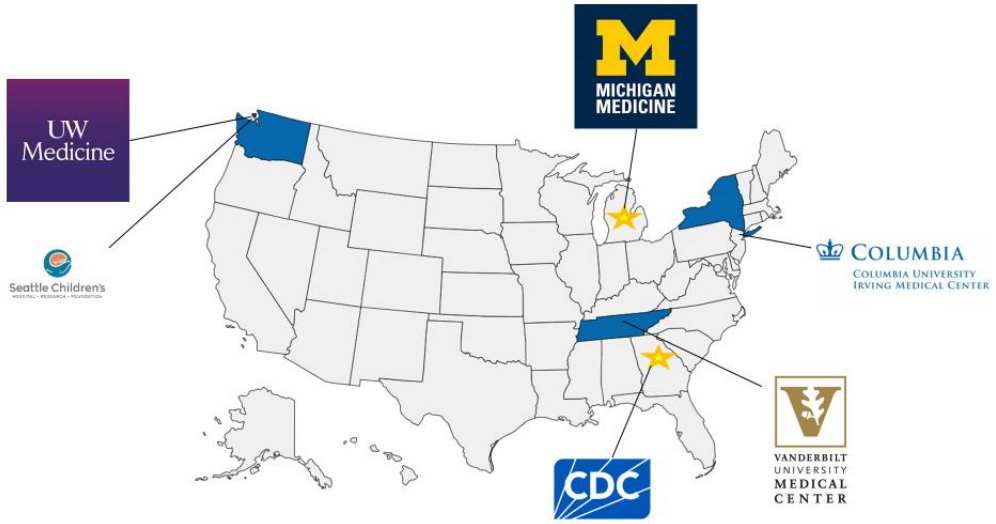
4 Feldstein L, et al. Protection From COVID-19 Vaccination and Prior SARS-CoV-2 Infection Among Children Aged 6 Months–4 Years, United States, September 2022–April 2023 https://academic.oup.com/jpids/article/14/1/piae121/7917119

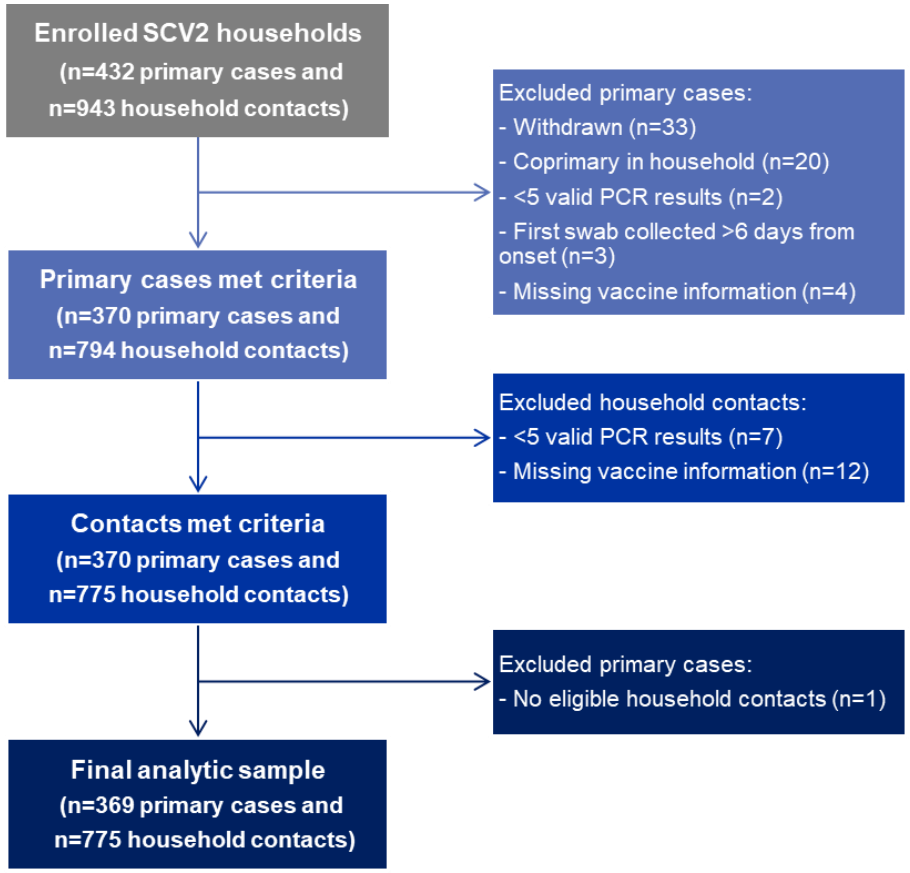
5 CDC. Respiratory Illness: Gauge of Household Transmission (RIGHT) Study, unpublished with manuscript in progress.

COVID-19 Vaccine Effectiveness against SARS-CoV-2 (SCV2) Infectiousness

Respiratory Illness: Gauge of Household Transmission (RIGHT) Study

Prospective household transmission study of SARS-CoV-2, *January 2024–January 2025*



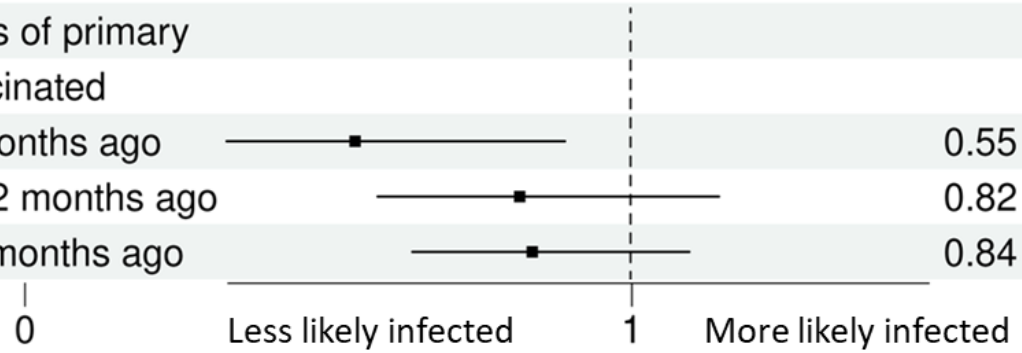


Preliminary analysis (unpublished, manuscript in progress) from RIGHT Study shared by research teams at CDC, Vanderbilt University Medical Center, University of Washington, and Columbia University Irvin Medical Center.

Individuals with SARS-CoV-2 infection who had received a COVID-19 vaccination within prior 6 months had lower risk of transmitting to other household contacts. Vaccine effectiveness at reducing transmission to others was 45%.

Adjusted* Risk of SARS-CoV-2 Infection in Household Contact by Primary Case Vaccination Status

Exposure	Adjusted RR	Vaccine Effectiveness†
Vaccination status of primary		
Ref: Never vaccinated		
Last dose ≤6 months ago	0.55 (0.33, 0.89)	45% (11%, 67%)
Last dose >6-12 months ago	0.82 (0.58, 1.15)	18% (-15%, 42%)
Last dose >12 months ago	0.84 (0.64, 1.10)	16% (-10%, 36%)



*Adjusted for age of contact, COVID-19 vaccination status of contact, age of primary case, enrollment state, number of people in the home, enrollment timing, and clustering by household

† Vaccine effectiveness against infection

Preliminary analysis (unpublished, manuscript is progress) from RIGHT Study Jan 2024-Jan 2025 shared by research teams at CDC, Vanderbilt University Medical Center, University of Washington, and Columbia University Irvin Medical Center.