

Updates to COVID-19 Vaccine Effectiveness

COVID-19 Session

Coronavirus and Other Respiratory Viruses Division

June 25, 2025

Agenda – COVID-19 vaccine effectiveness (VE)

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

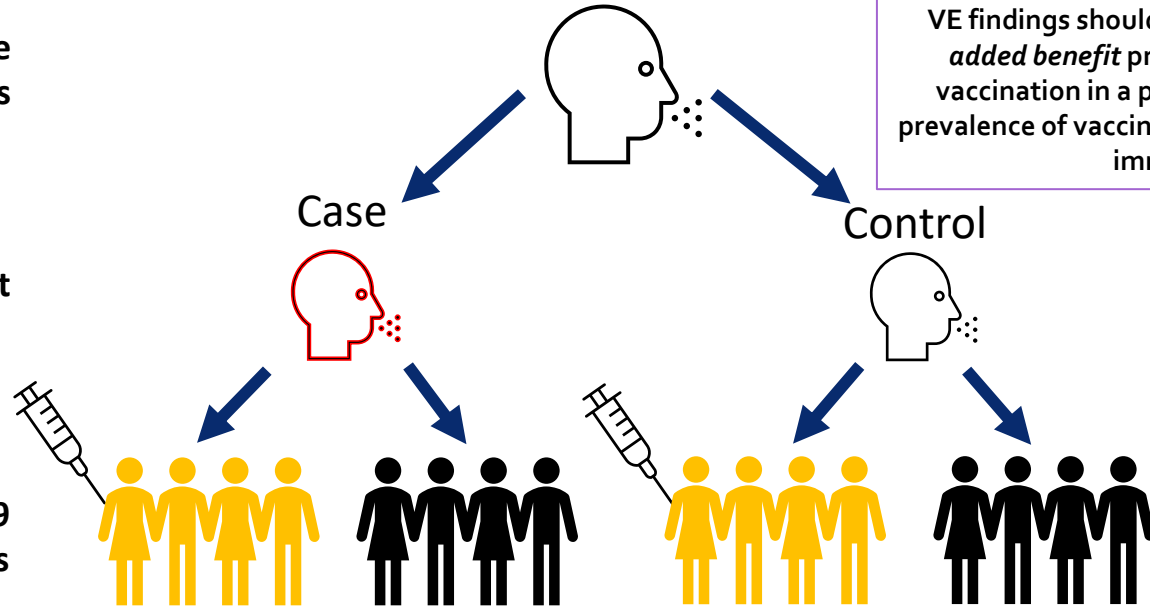
Methods & Context

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

Person with acute respiratory illness

SARS-CoV-2 test

COVID-19 vaccination status



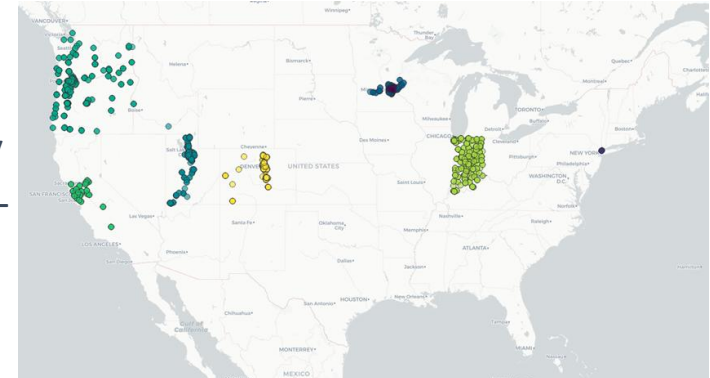
VE findings should be interpreted as the *added benefit* provided by COVID-19 vaccination in a population with a high prevalence of vaccine- and infection-induced immunity.

$$\text{Effectiveness} = 1 - (\text{odds ratio}) \times 100\% \quad \text{Odds ratio} = \frac{\text{Odds of immunization}_{\text{cases}}}{\text{Odds of immunization}_{\text{controls}}}$$

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 NAAT 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 (≥ 18 years) or RSV (≥ 60 years)
- **Vaccination data:** Documented by electronic health records and state and city registries

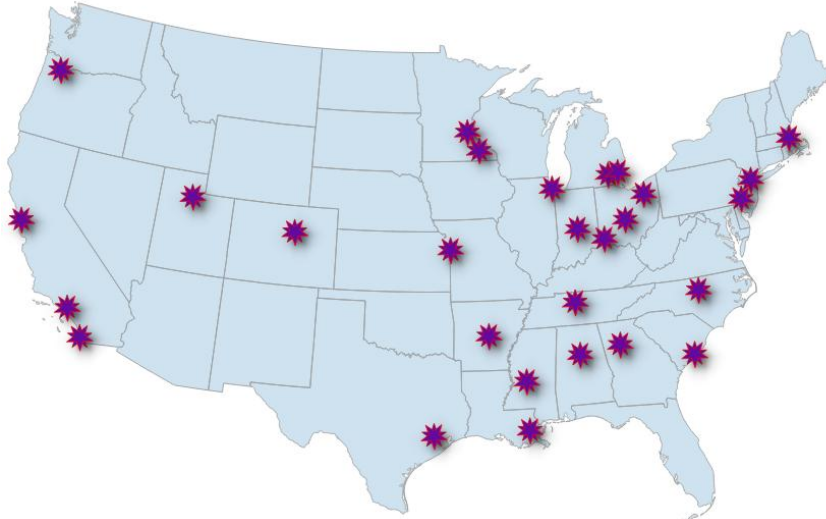


CLI = COVID-19-like illness; ED/UC = emergency department/urgent care; RSV = respiratory syncytial virus; NAAT = nucleic acid amplification test

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

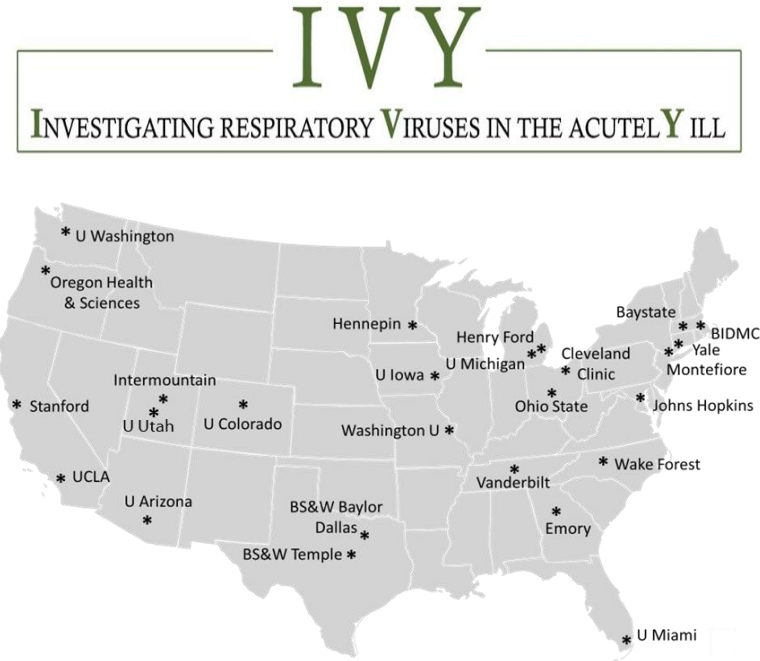


- **Case infants:** hospitalized for COVID-19 as the primary reason for admission and with a positive SARS-CoV-2 NAAT or antigen test result
- **Control infants:** hospitalized for COVID-19-like illness and negative SARS-CoV-2 NAAT result, matched to case infants by site; hospitalized within 4 weeks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



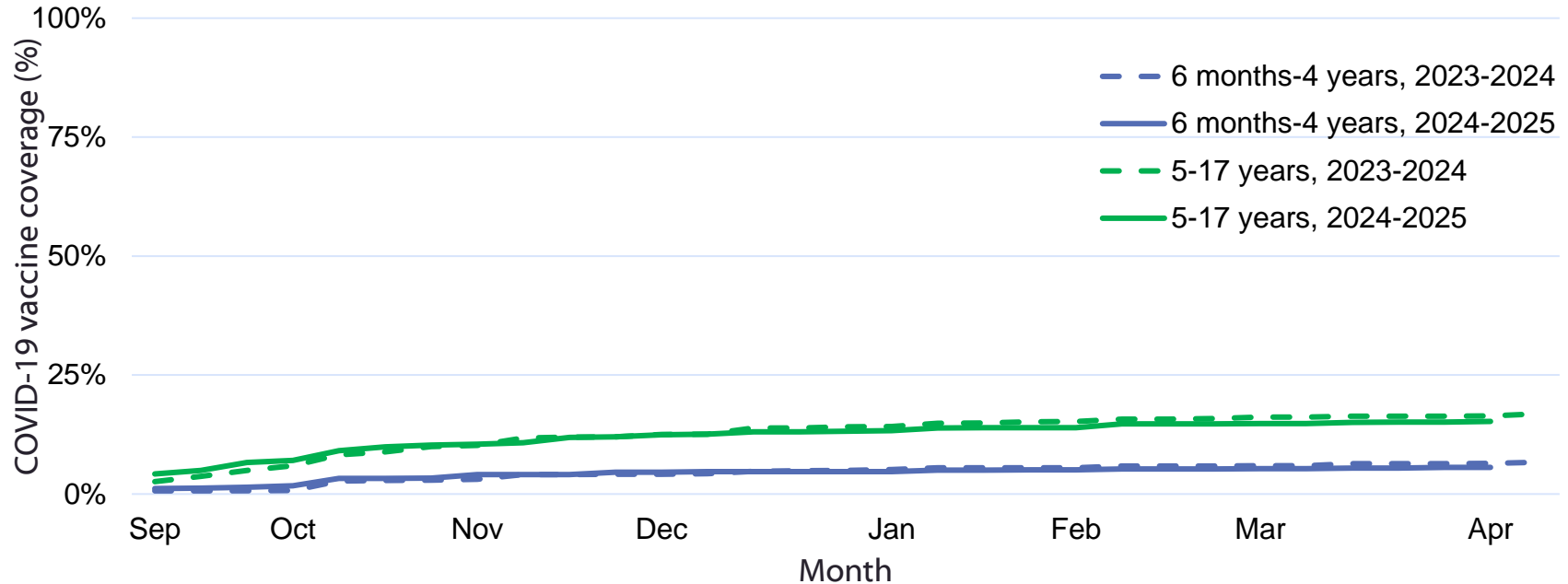
*COVID-19-like illness = CLI; CLI is defined as presence of any one of the following: fever, cough, shortness of breath, chest imaging consistent with pneumonia, or hypoxemia
NAAT = nucleic acid amplification test

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 of 2023-2024 COVID-19 vaccines	Compares people who received 2023-2024 COVID-19 vaccine to people who did not, regardless of past COVID-19 vaccination	Received 2023-2024 dose	Eligible for, but did not receive, a 2023-2024 dose , regardless of past COVID-19 vaccination history
VE of 2024-2025 COVID-19 vaccines	Compares people who received 2024-2025 COVID-19 vaccine to people who did not, regardless of past COVID-19 vaccination	Received 2024-2025 dose	Eligible for, but did not receive, a 2024-2025 dose , regardless of past COVID-19 vaccination history

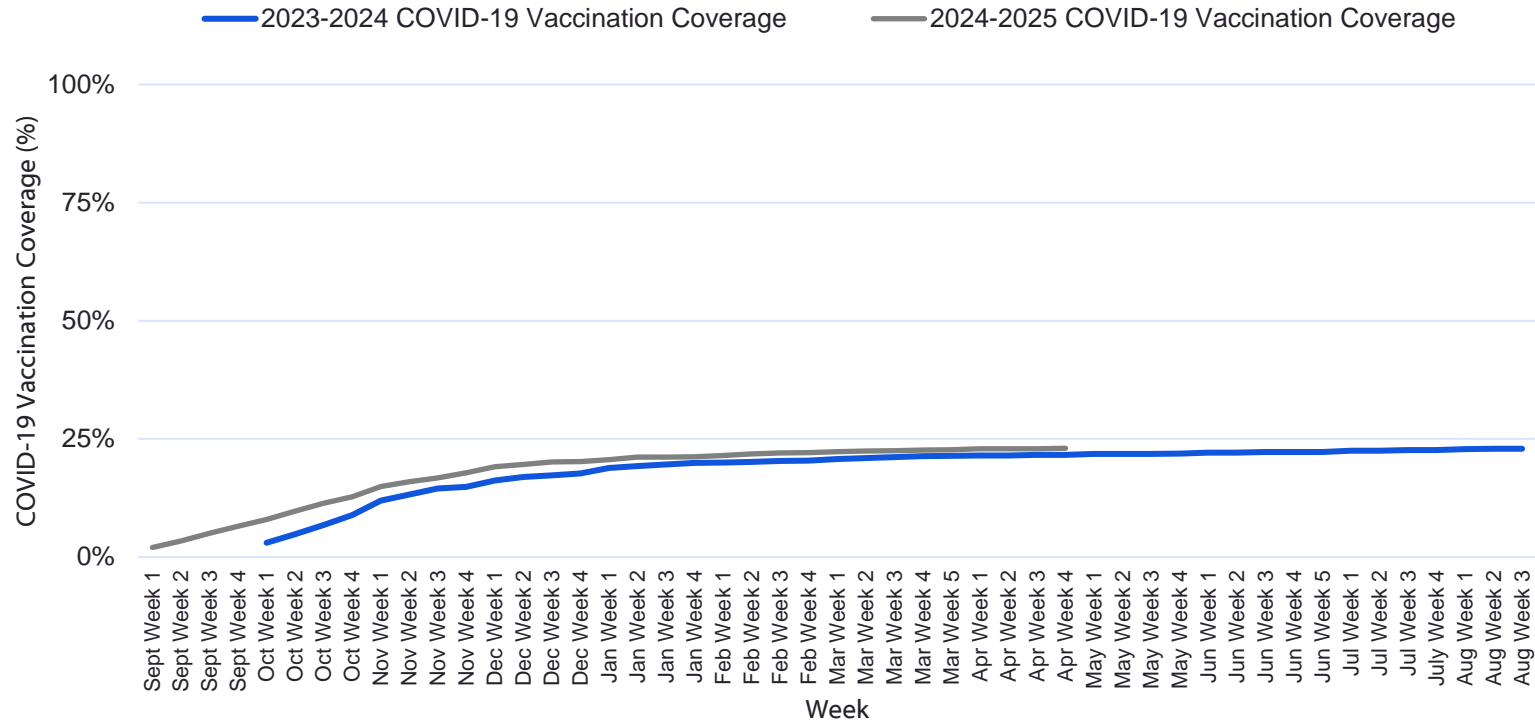
* Prior SARS-CoV-2 infection is not generally considered, as it is documented inconsistently in medical records.

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>

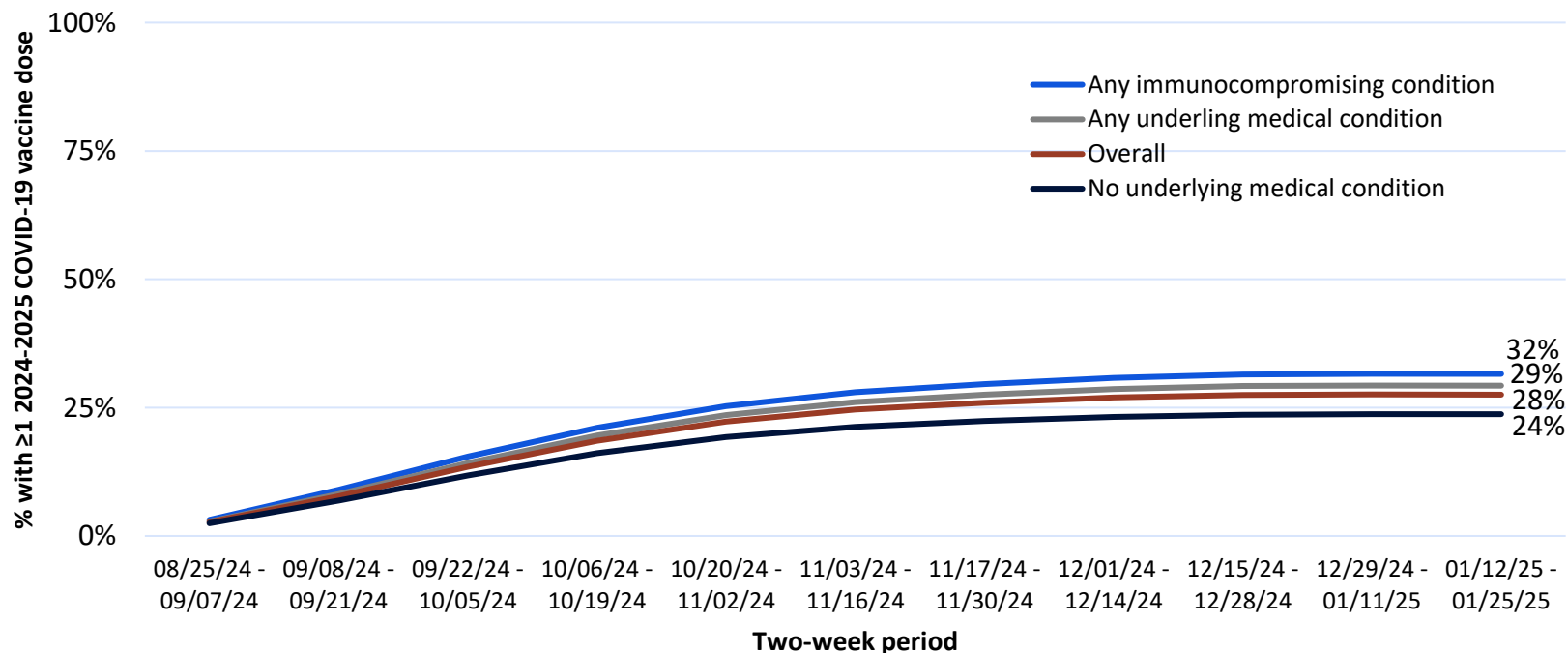
COVID-19 Vaccination Coverage Among Adults ≥ 18 Years, 2023-2024 and 2024-2025, NIS-ACM



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

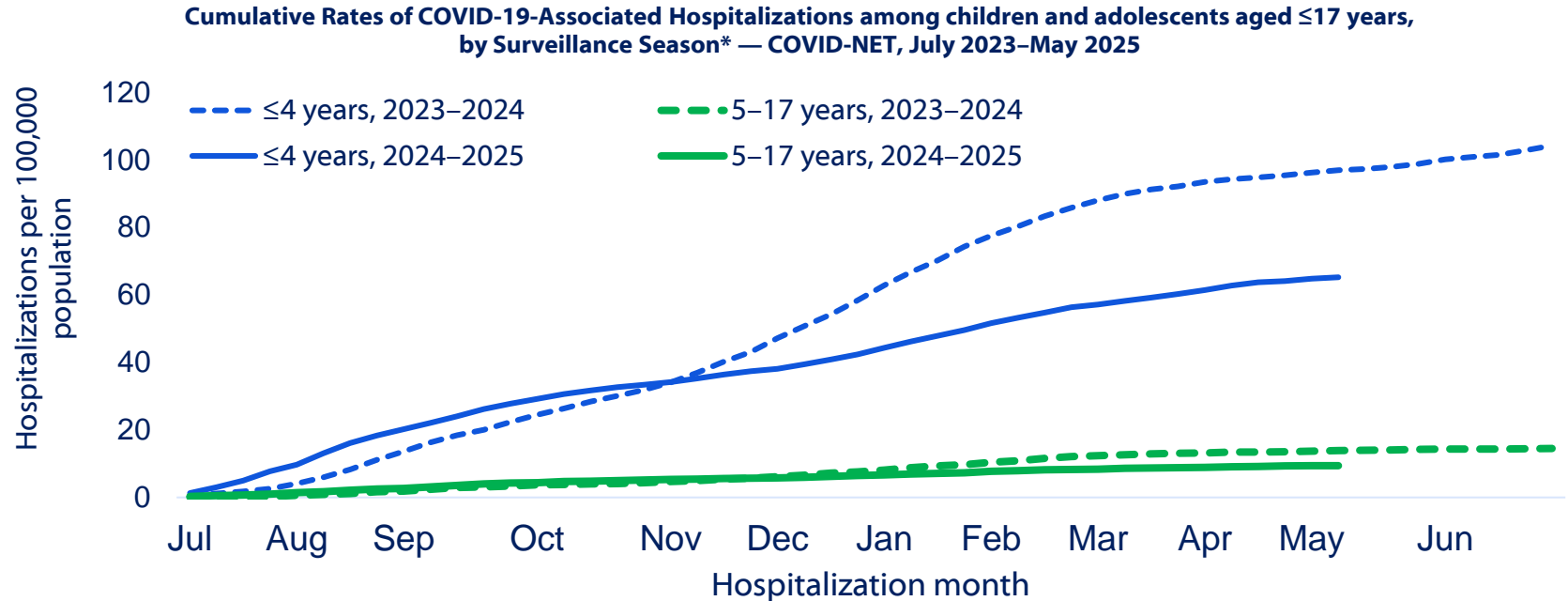
Weekly cumulative COVID-19 vaccination coverage, by underlying medical condition status,
Medicare fee-for-service beneficiaries aged ≥ 65 years, August 2024-January 2025



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.

Estimates of COVID-19 Vaccine Effectiveness in Children

Cumulative rates of COVID-19 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.

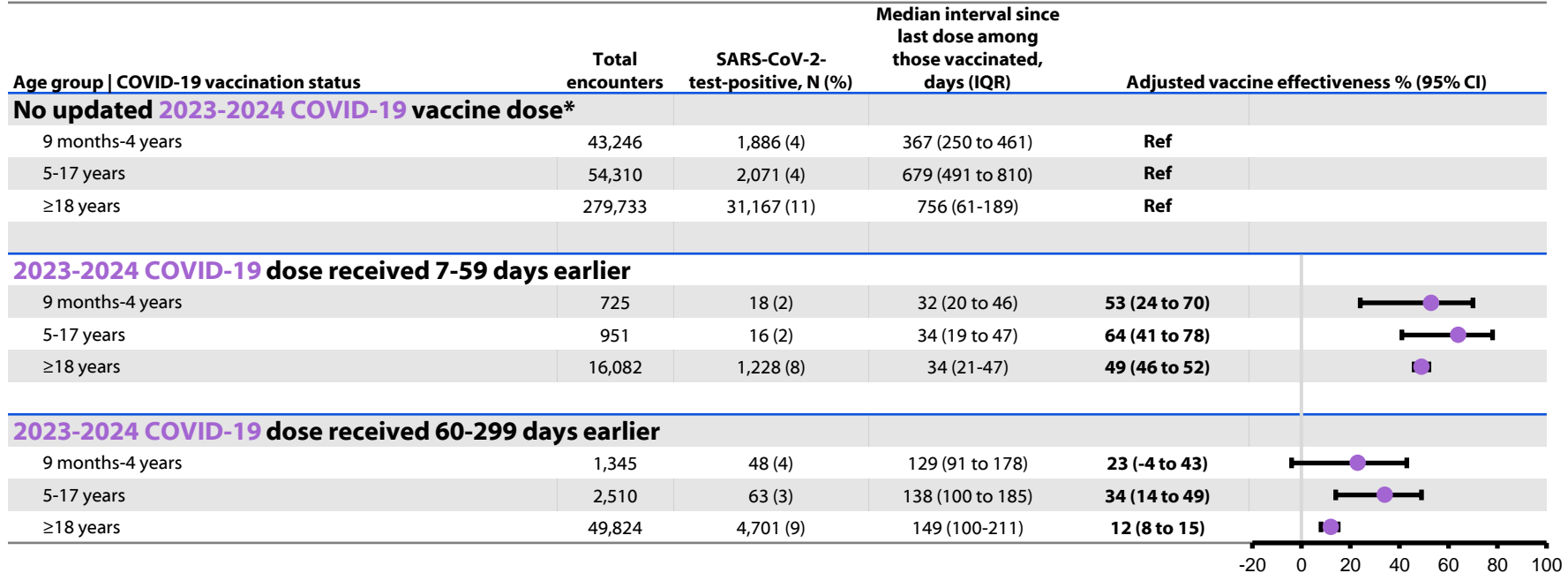
Data source: <https://www.cdc.gov/resp-net/dashboard/>

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



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

September 2023 – August 2024



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, 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.

Vaccine effectiveness was calculated by comparing the odds of COVID-19 vaccination in case-patients and control-patients using the equation: $(1 - \text{adjusted odds ratio}) \times 100\%$. 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)

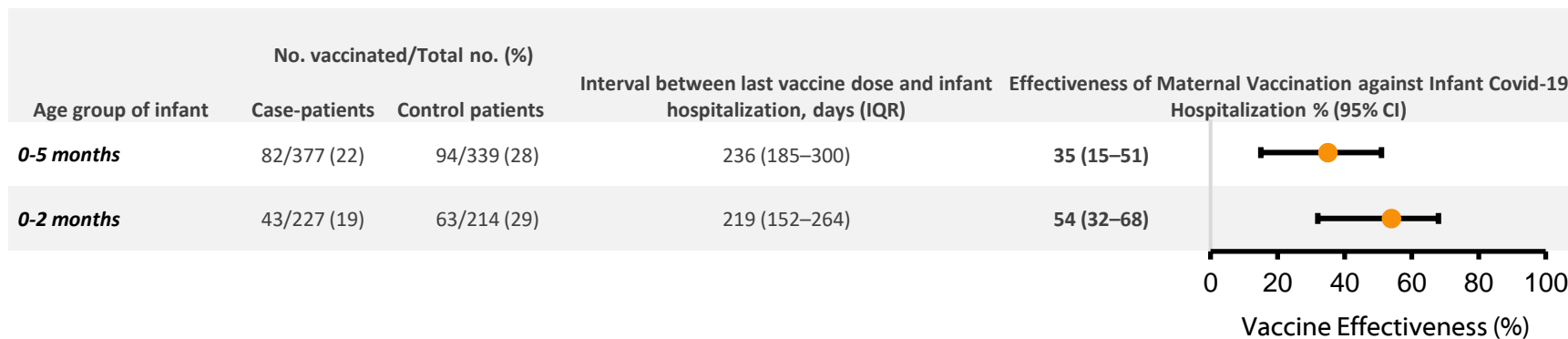
CDC, unpublished data

* 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, both those in the referent group and those in the vaccinated group were required to have completed an initial series. 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.

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

March 9, 2022 – May 31, 2023



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 $(1 - \text{adjusted odds ratio}) \times 100\%$.

[†] 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

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 immunocompetent pregnant women aged 18-45 years — VISION
June 2022 – August 2023

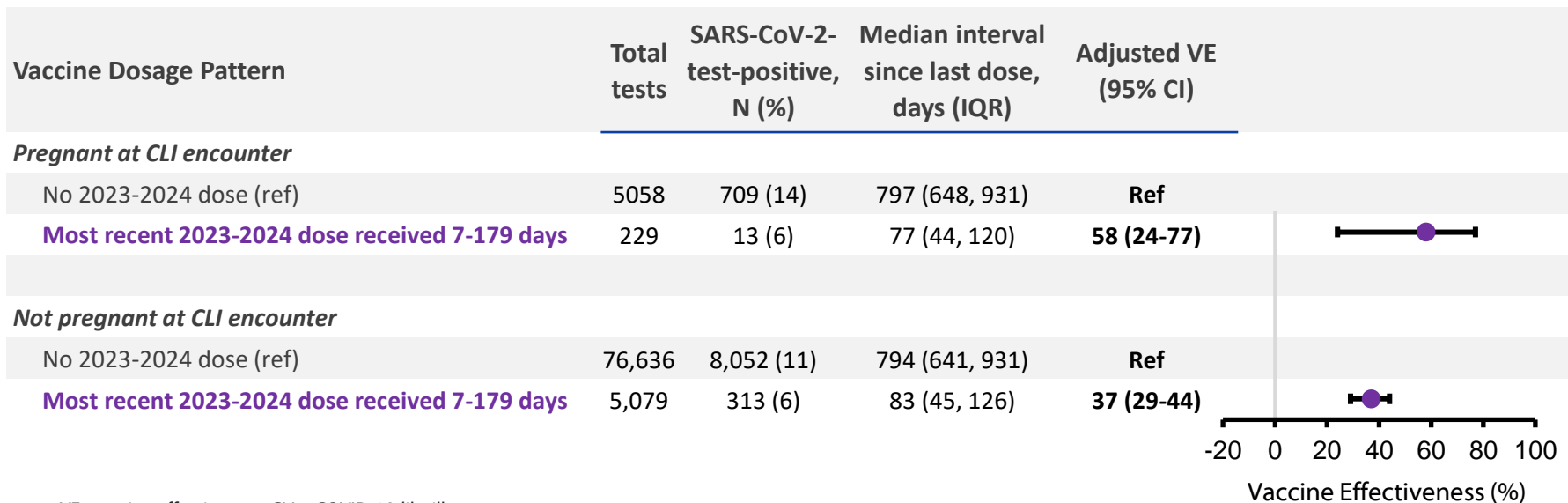
Vaccine Dosage Pattern	Total tests	SARS-CoV-2- test-positive, N (%)	Median interval since last dose, days (IQR)	Adjusted VE (95% CI)
Absolute VE				
Unvaccinated (ref)	2991	403 (13)	--	Ref
Most recent monovalent or bivalent dose received:				
≥6 months before pregnancy	3014	365 (12)	483 (393,579)	6 (-11, 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: $(1 - \text{adjusted odds ratio}) \times 100\%$. 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.

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

September 2023 – August 2024



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: $(1 - \text{adjusted odds ratio}) \times 100\%$. 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

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)

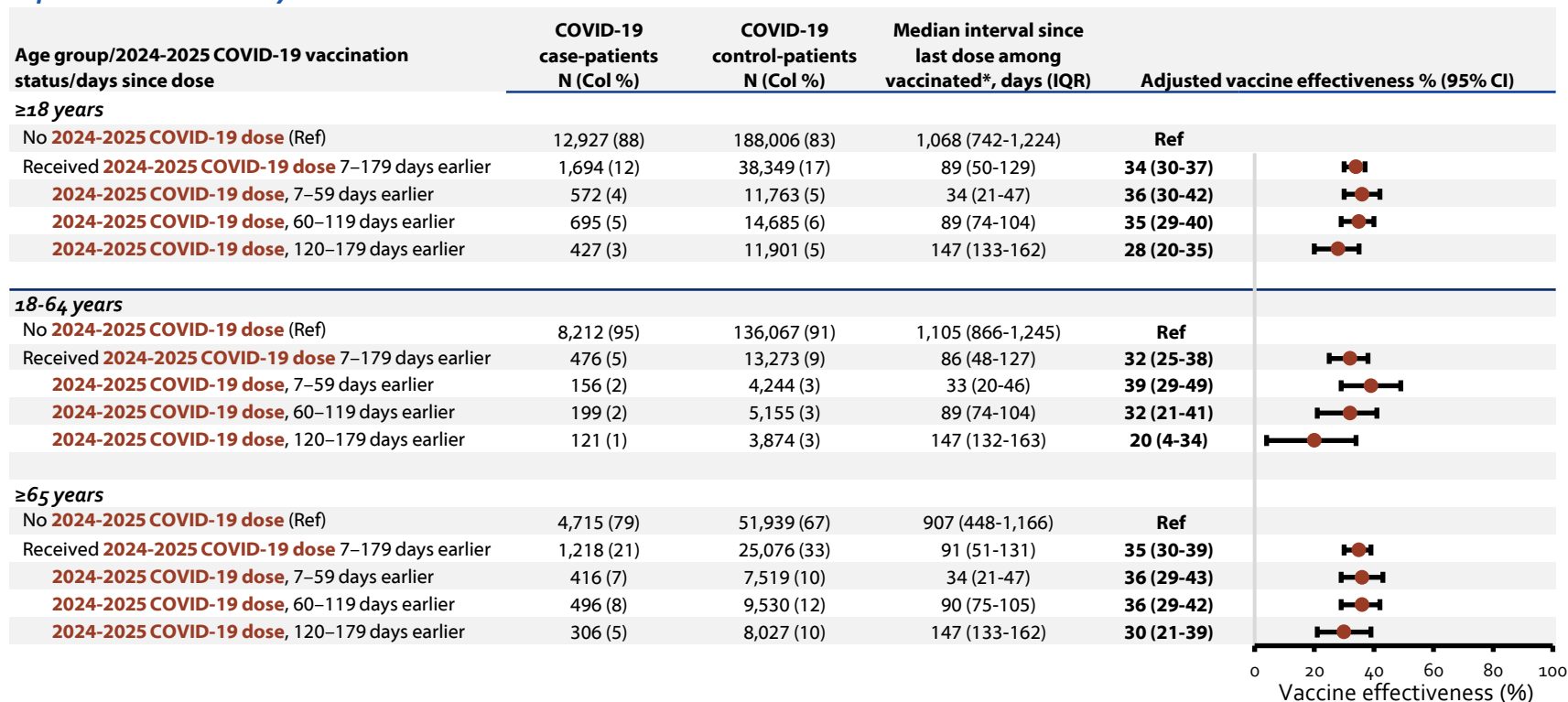
Updated from Link-Gelles, et al. MMWR: <https://www.cdc.gov/mmwr/volumes/74/wr/mm7406a1.htm>

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

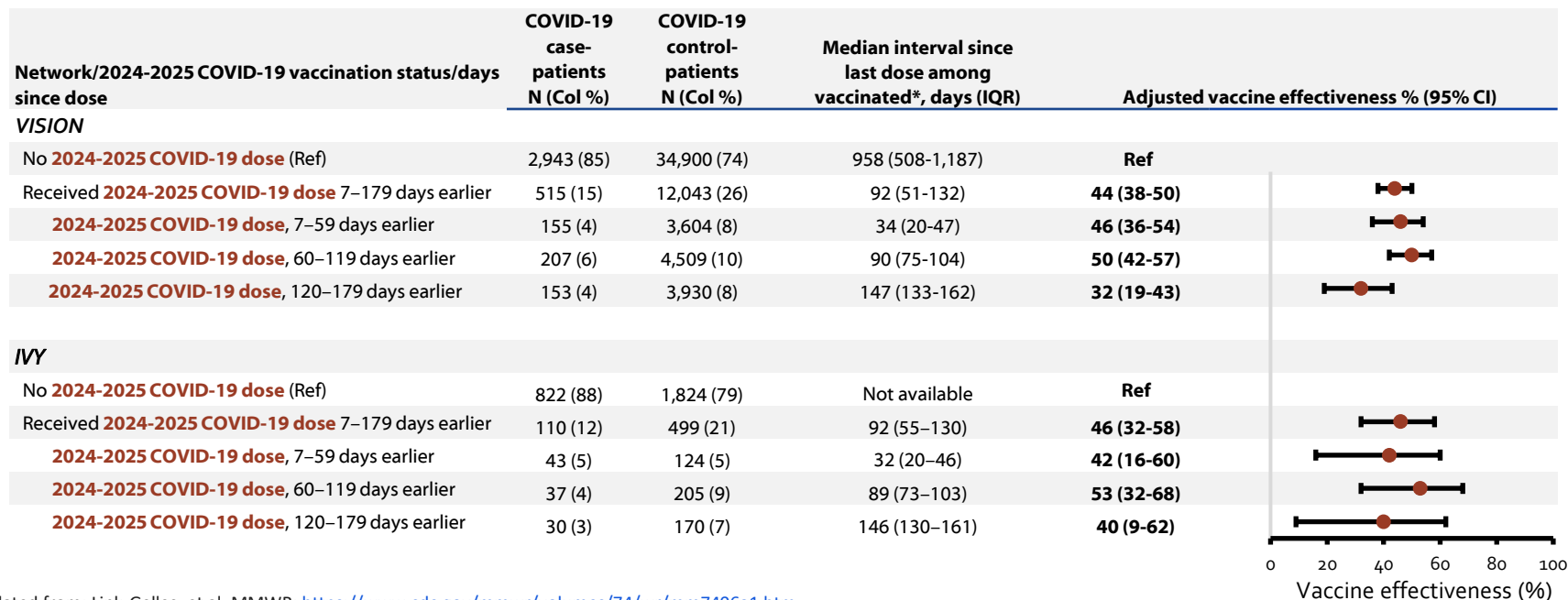
September 2024 – May 2025



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: $(1 - \text{adjusted odds ratio}) \times 100\%$. 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.

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



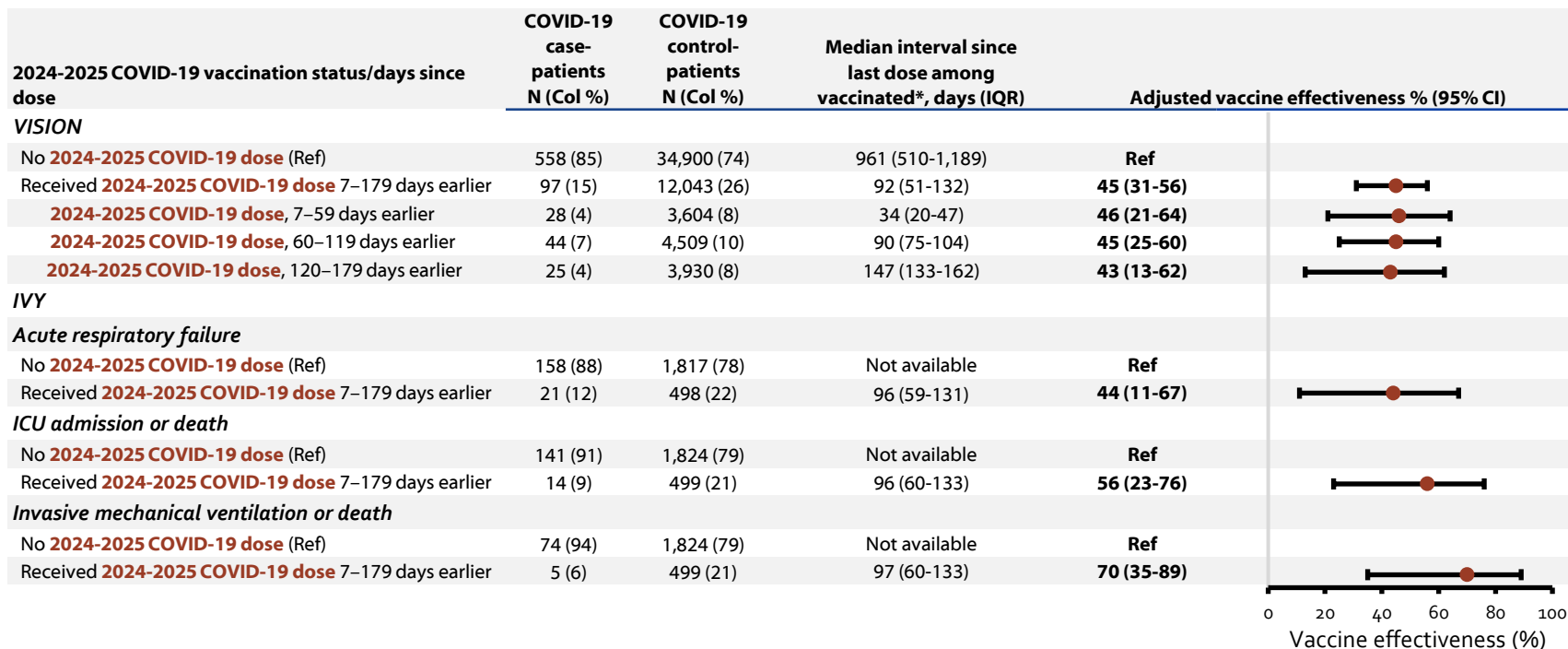
Updated from: Link-Gelles, et al. MMWR: <https://www.cdc.gov/mmwr/volumes/74/wr/mm7406a1.htm>

Vaccine effectiveness was calculated by comparing the odds of 2024–2025 COVID-19 vaccination in case-patients and control-patients using the equation: $(1 - \text{adjusted odds ratio}) \times 100\%$. 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



Based on methods in: 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: $(1 - \text{adjusted odds ratio}) \times 100\%$. 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.

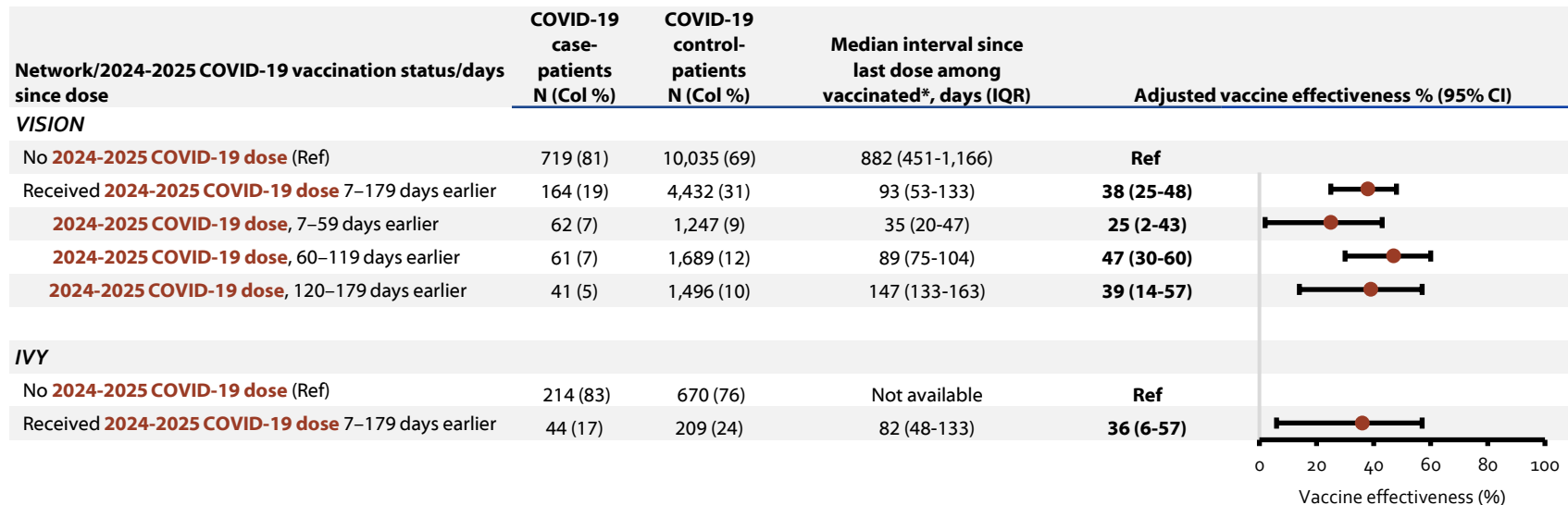
For VISION, critical illness is defined as admission to the intensive care unit or in-hospital death. For IVY, acute respiratory failure was defined as new receipt of high-flow nasal cannula, noninvasive ventilation, or invasive mechanical ventilation.

*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



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: $(1 - \text{adjusted odds ratio}) \times 100\%$. 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 (if any) received. 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.

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

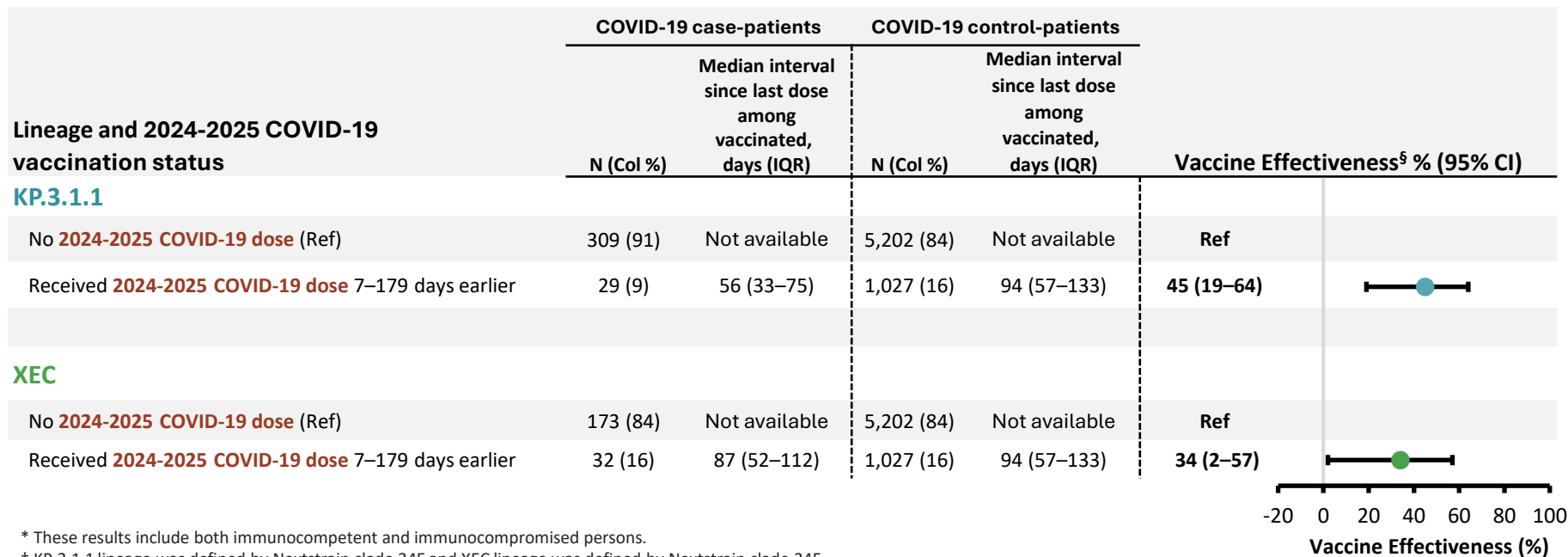
* Case patients who were co-infected with influenza viruses or RSV were excluded.

[†] 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: $(1 - \text{adjusted odds ratio}) \times 100\%$. 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



* 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: $(1 - \text{adjusted odds ratio}) \times 100\%$. 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).

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 generally similar across age groups.
 - COVID-19-associated **emergency department and urgent care visits among adults.**
 - 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:

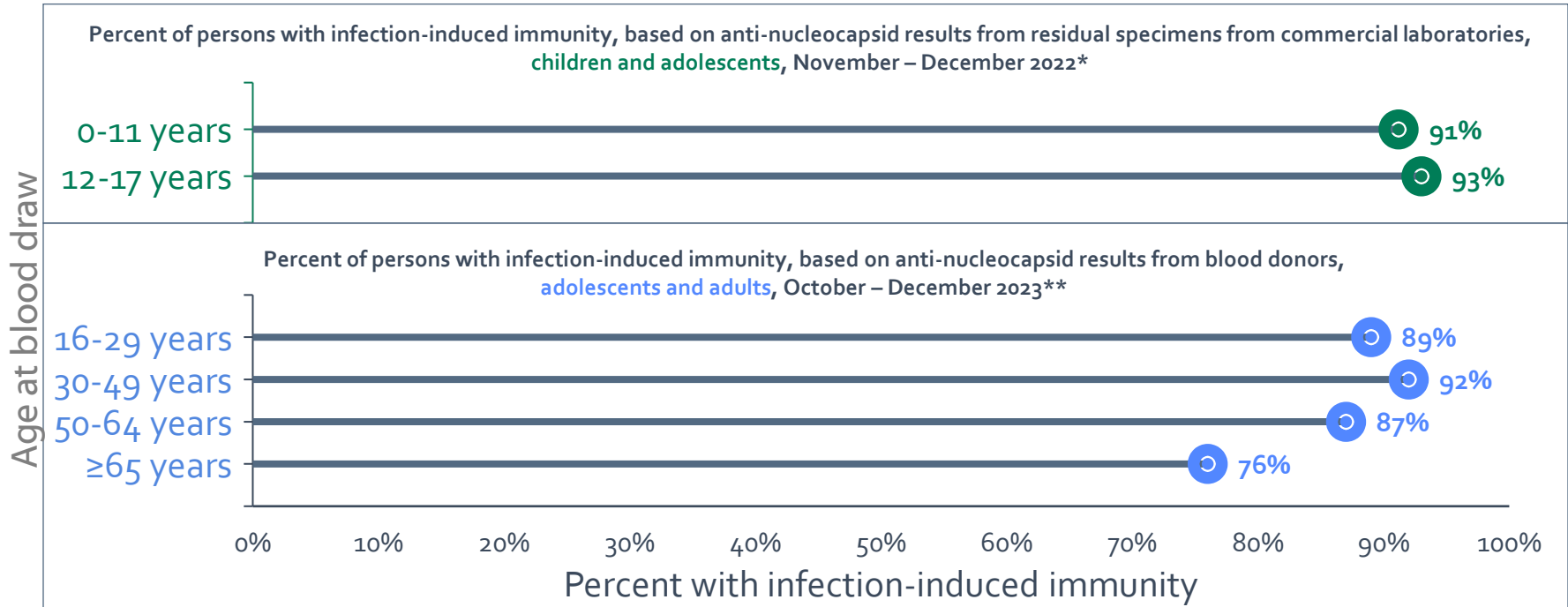
VISION Collaborators

IVY Collaborators

Overcoming Collaborators

Back-up

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

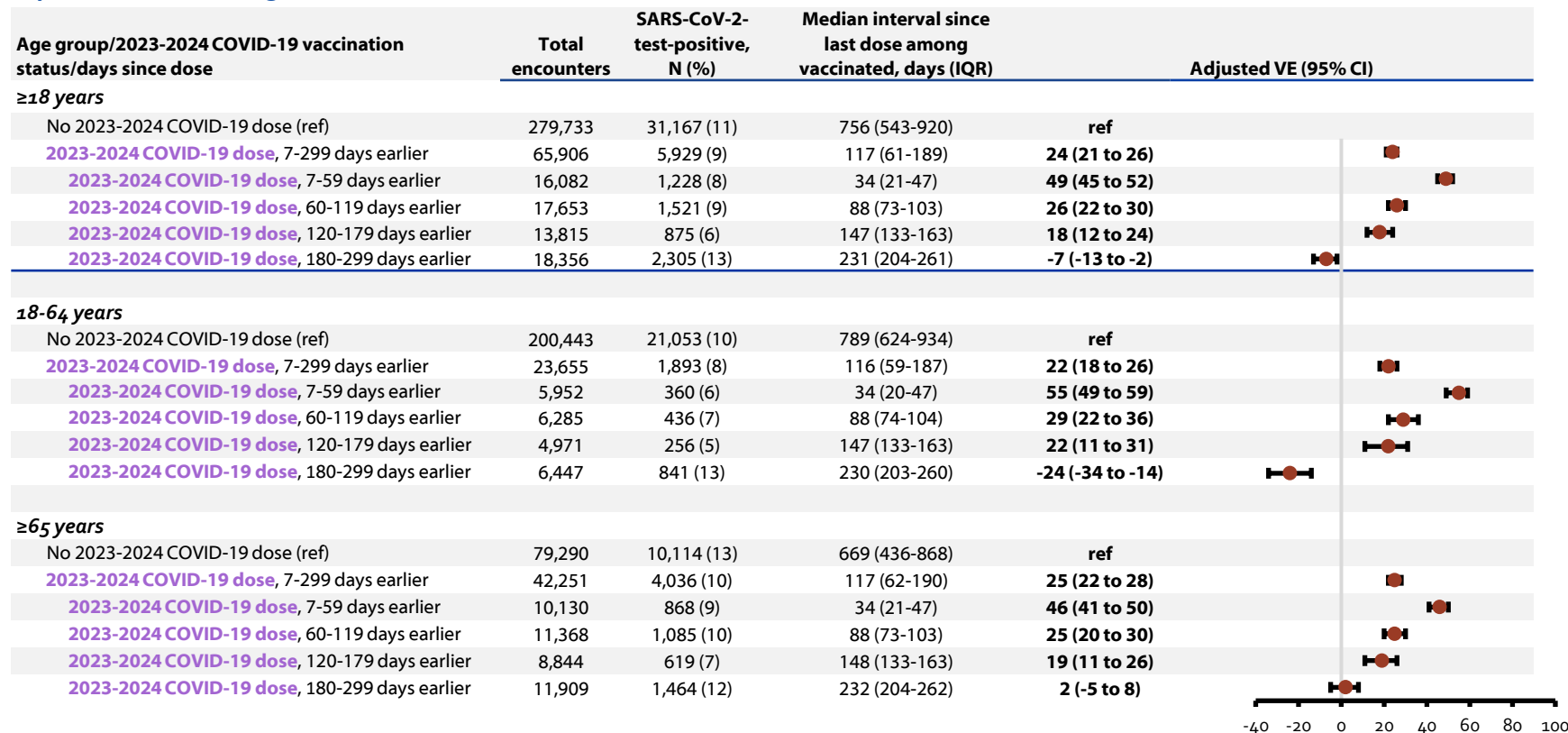


VE findings should be interpreted as the *added benefit* provided by COVID-19 vaccination in a population with a high prevalence infection-induced immunity.

* 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>

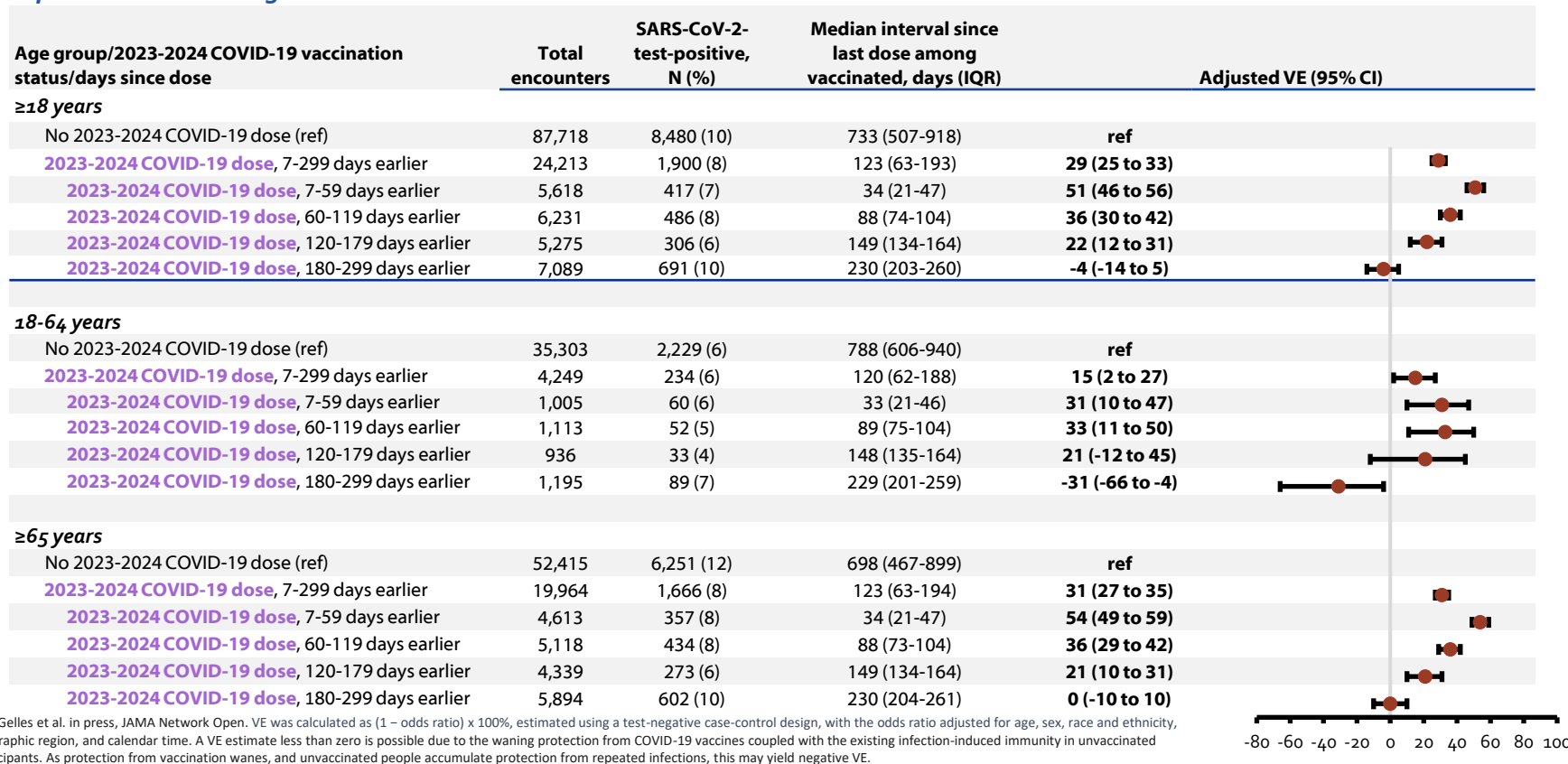
VISION: VE of 2023-2024 COVID-19 vaccine against COVID-19-associated *emergency department/urgent care encounters* among immunocompetent adults aged ≥18 years, by age group September 2023 – August 2024



Link-Gelles et al. in press, JAMA Network Open. VE was calculated as $(1 - \text{odds ratio}) \times 100\%$, 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.

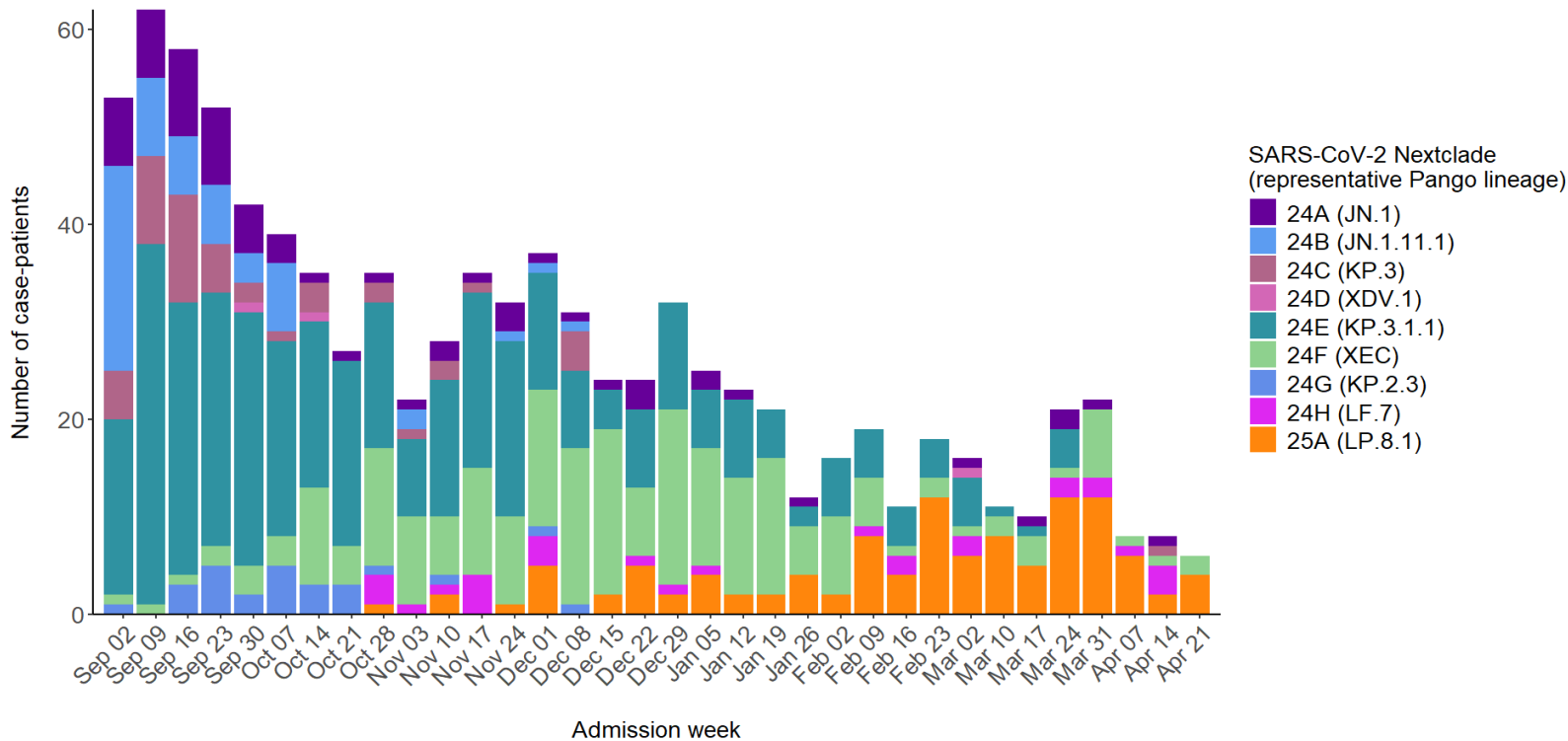
VISION: VE of 2023-2024 COVID-19 vaccine against COVID-19-associated hospitalization among immunocompetent adults aged ≥18 years, by age group

September 2023 – August 2024



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.

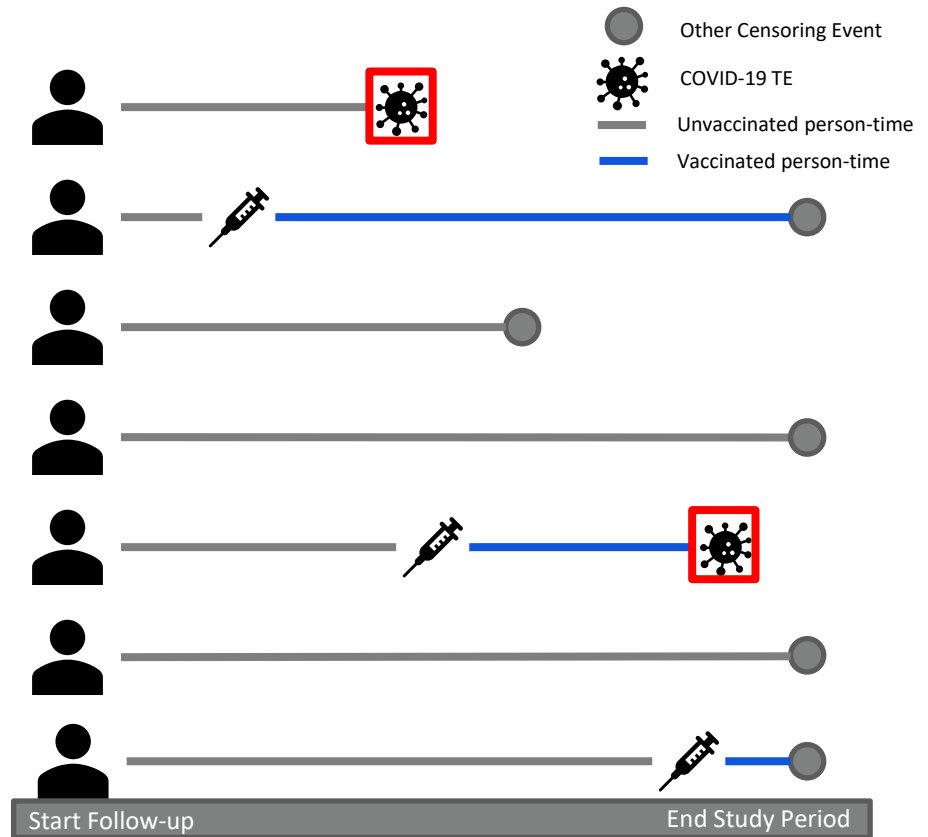
Medicare data

- **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 = $(1 - \text{adjusted hazard ratio}^{**}) \times 100\%$**

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

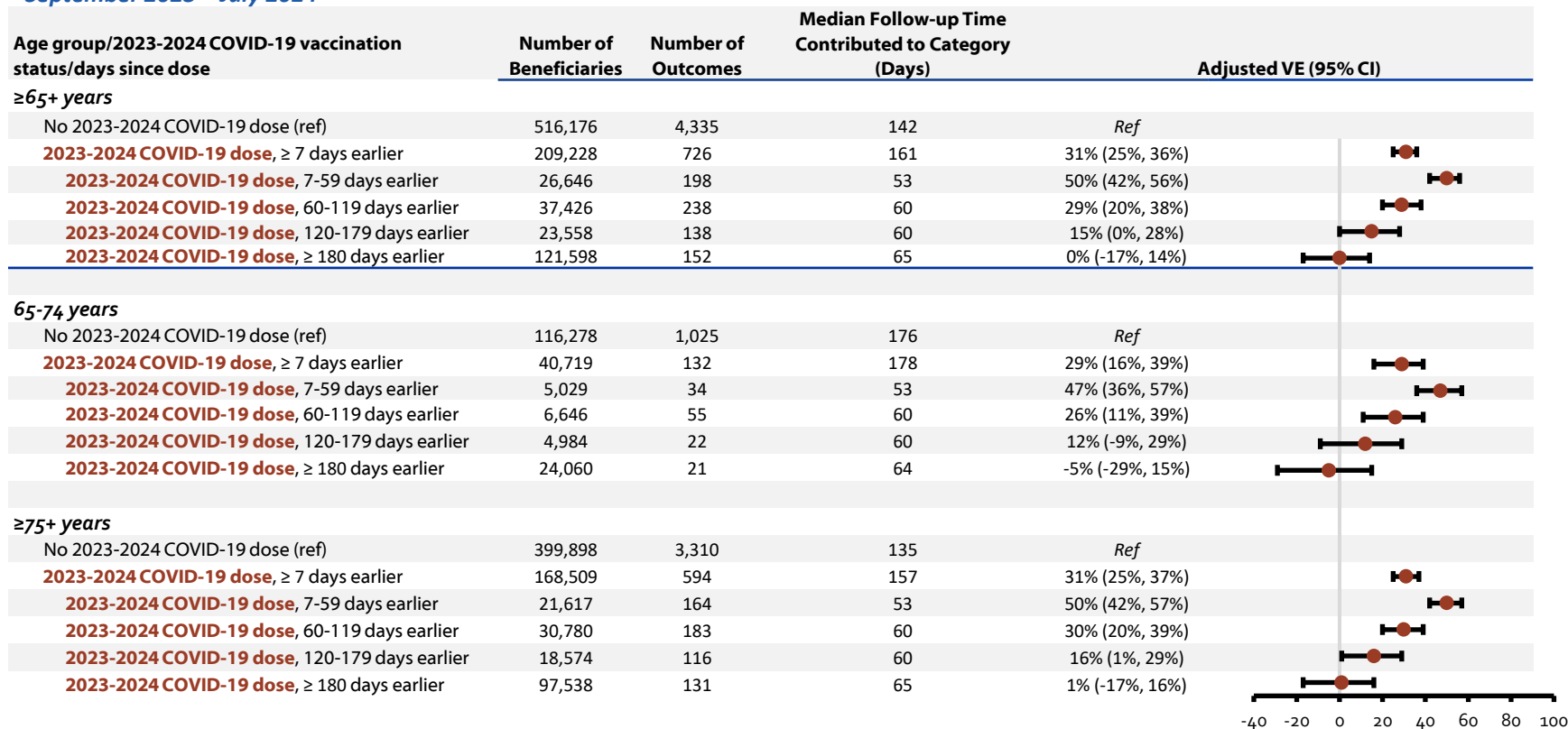
*Data sources included Medicare Enrollment Database (EDB) and Common Medicare Environment (CME), Common Working File (CWF) and Shared System Data (SSD) Medicare Parts A/B claims data, Minimum Data Set (MDS), and CDC/ATSDR Social Vulnerability Index (SVI)

**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



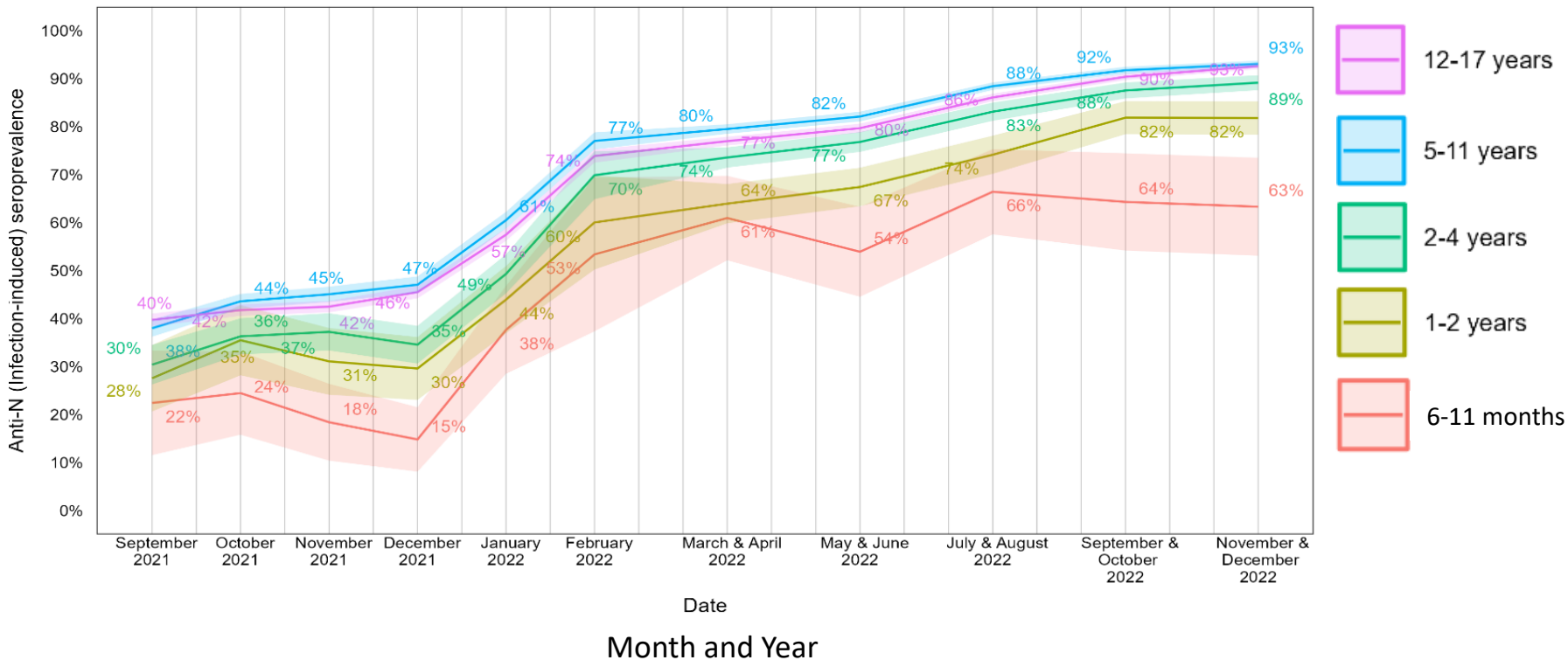
CDC, unpublished data

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

Infection-induced (nucleocapsid antibody) seroprevalence

Anti-N (Infection-induced) seroprevalence

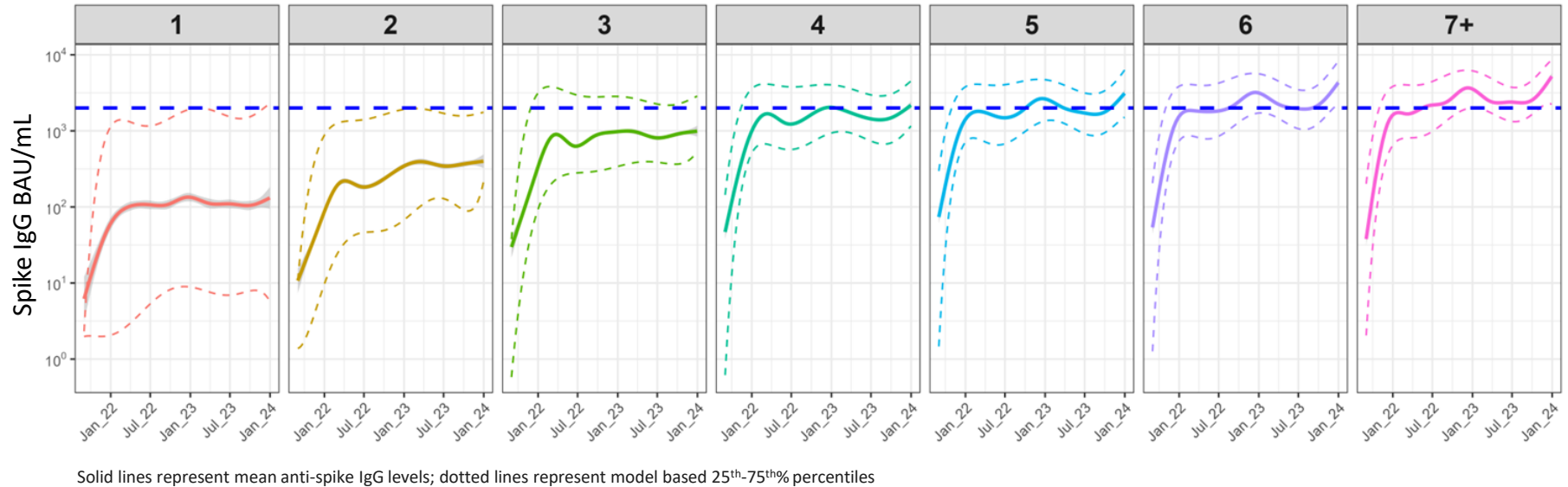


Shaded ranges depict 95% confidence intervals for the estimated seroprevalence shown by the dark line in the corresponding color.

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




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

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 symptoms¹

- 
- **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 symptoms²

- 
- **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

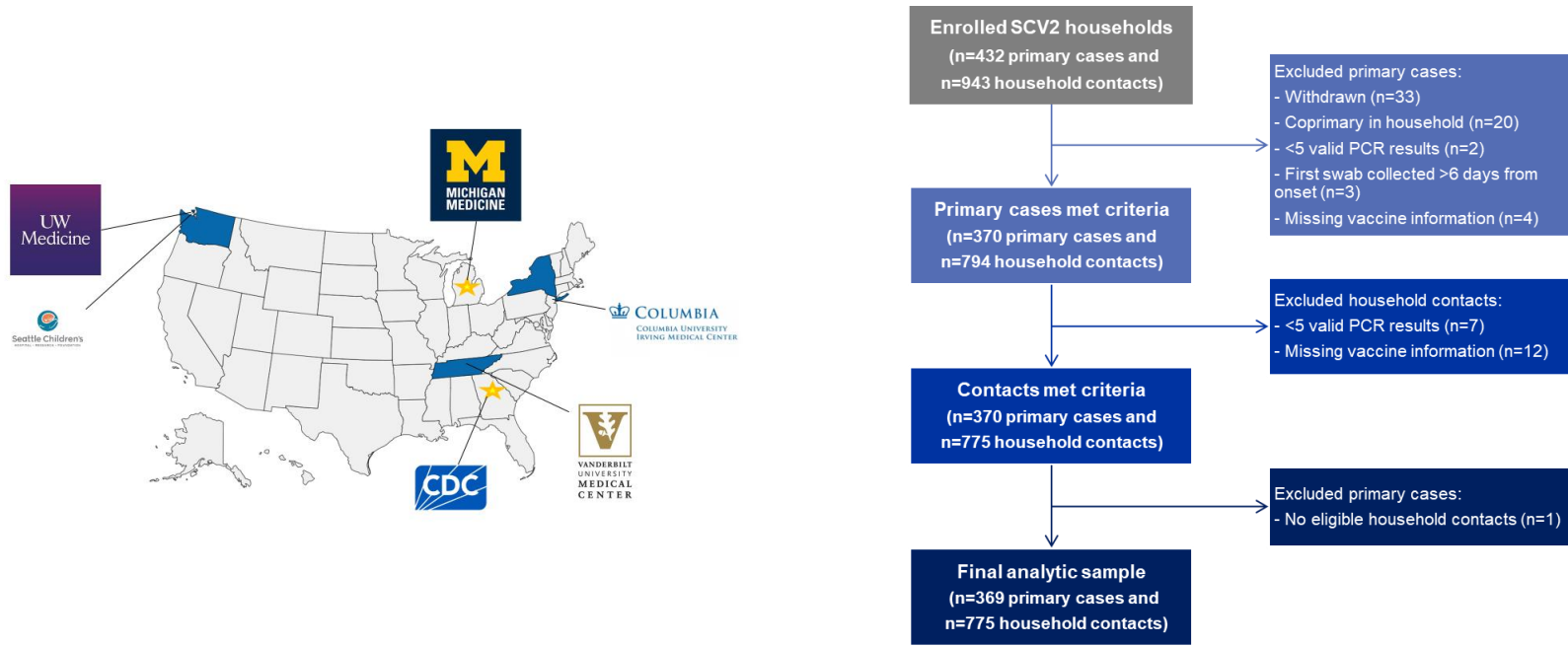
<https://academic.oup.com/jpids/article/14/1/piae121/7917119>

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

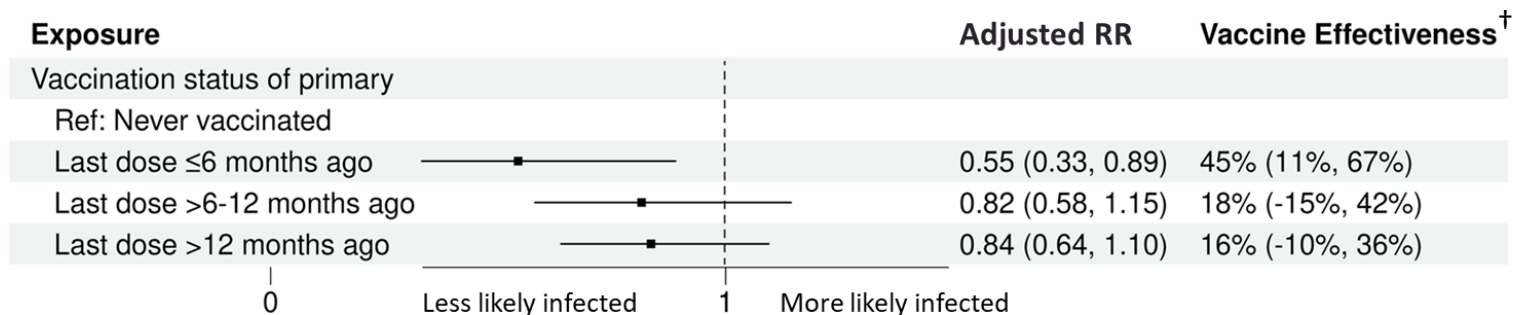
Respiratory Illness: Gauge of Household Transmission (RIGHT) Study

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



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



*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