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Updates on COVID-19 Vaccine Effectiveness

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Centers for Disease Control and Prevention

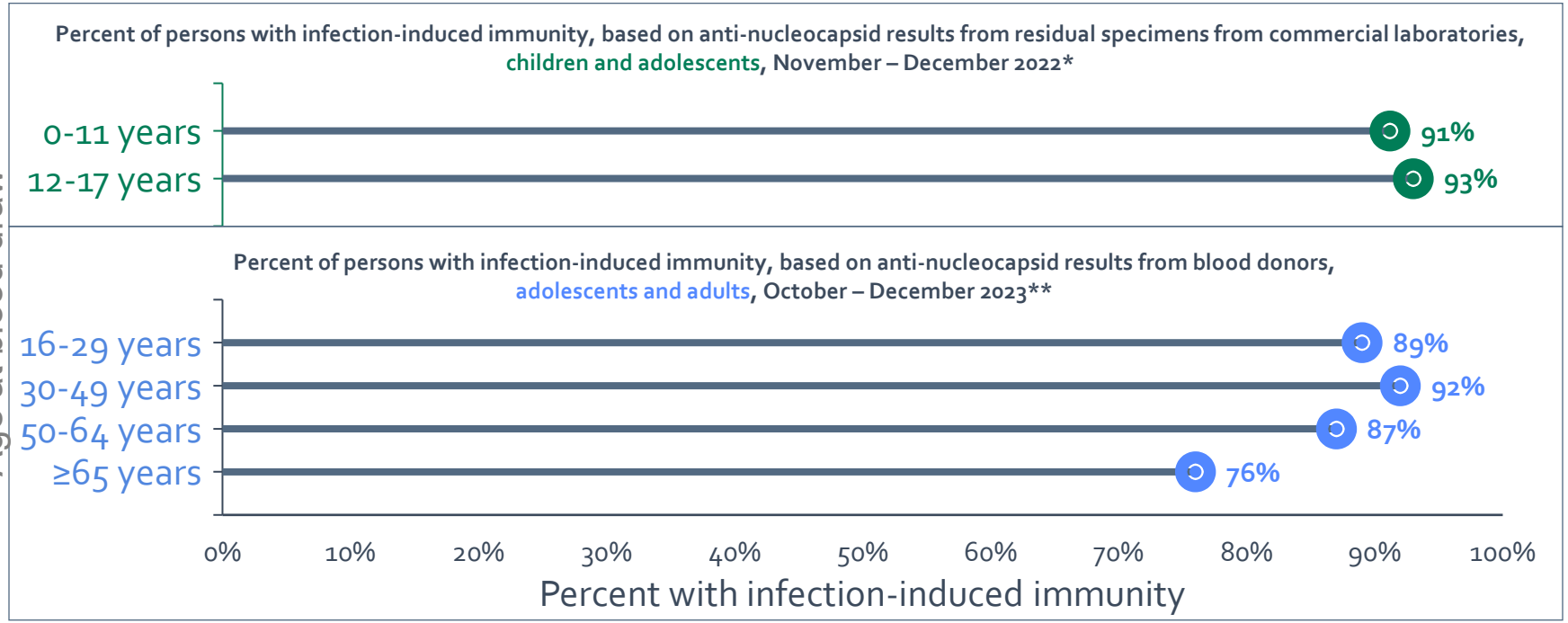
May 28, 2026

Agenda – COVID-19 vaccine effectiveness (VE)

- Context and VE methods
- Estimates of 2024-2025 COVID-19 VE
- Interim Estimates of 2025-2026 COVID-19 VE
- Estimates of COVID-19 VE by genetic differences between variant and vaccine composition

Context & methods

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



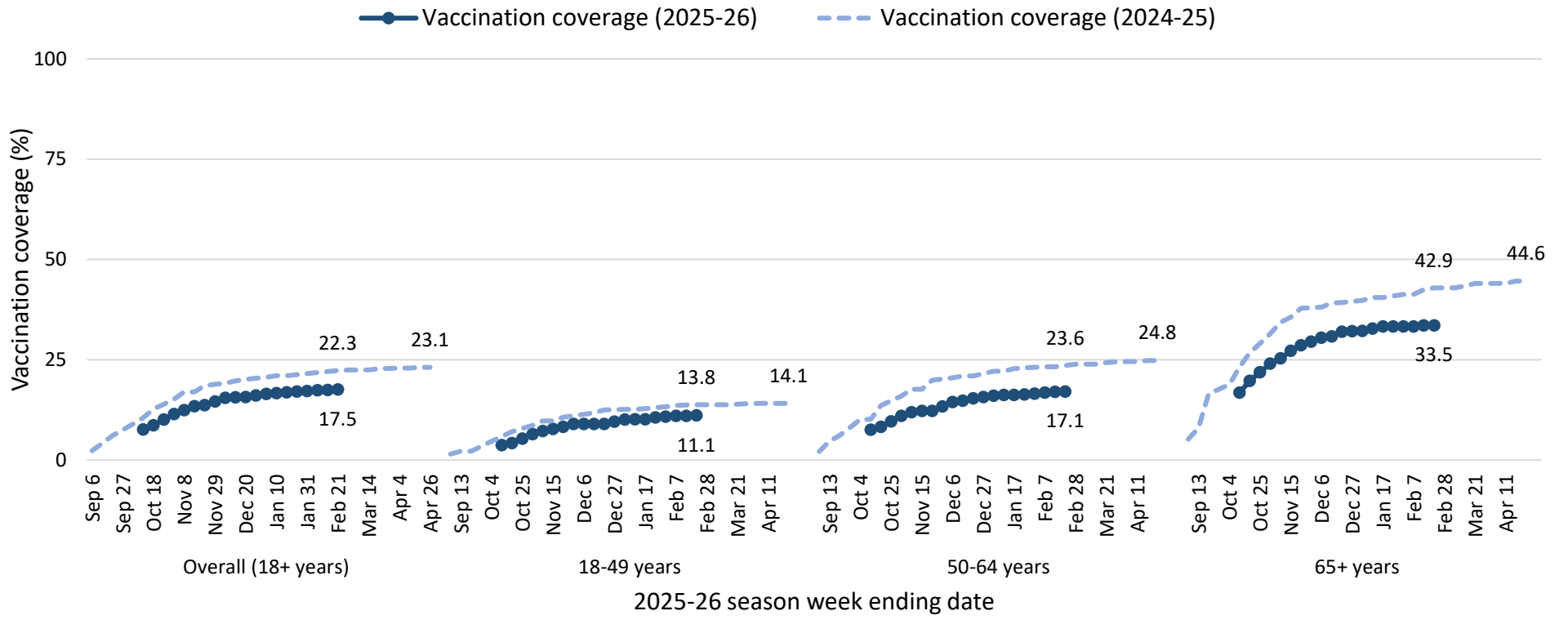
VE findings should be interpreted as the added benefit provided by COVID-19 vaccination in a population with a high prevalence of vaccine- and infection-induced immunity.

* Data on persons 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

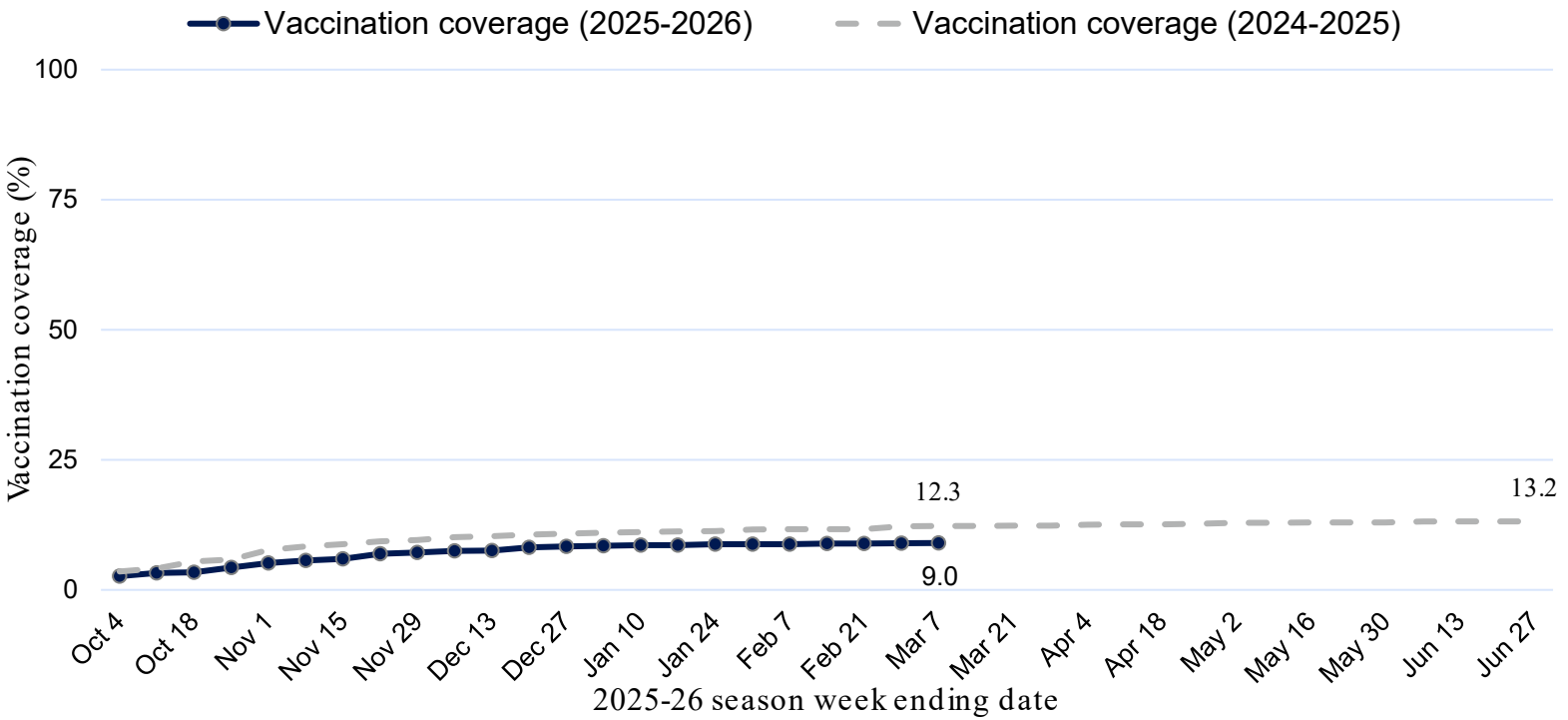
COVID-19 vaccination coverage (≥1 dose) among adults aged ≥18 years, 18-49 years, 50-64 years and ≥65 years, 2024-25 and 2025-26

National Immunization Survey-Fall Respiratory Virus Module



COVID-19 vaccination coverage* among children aged 6 months–17 years, 2024-25 and 2025-26

National Immunization Survey-Flu

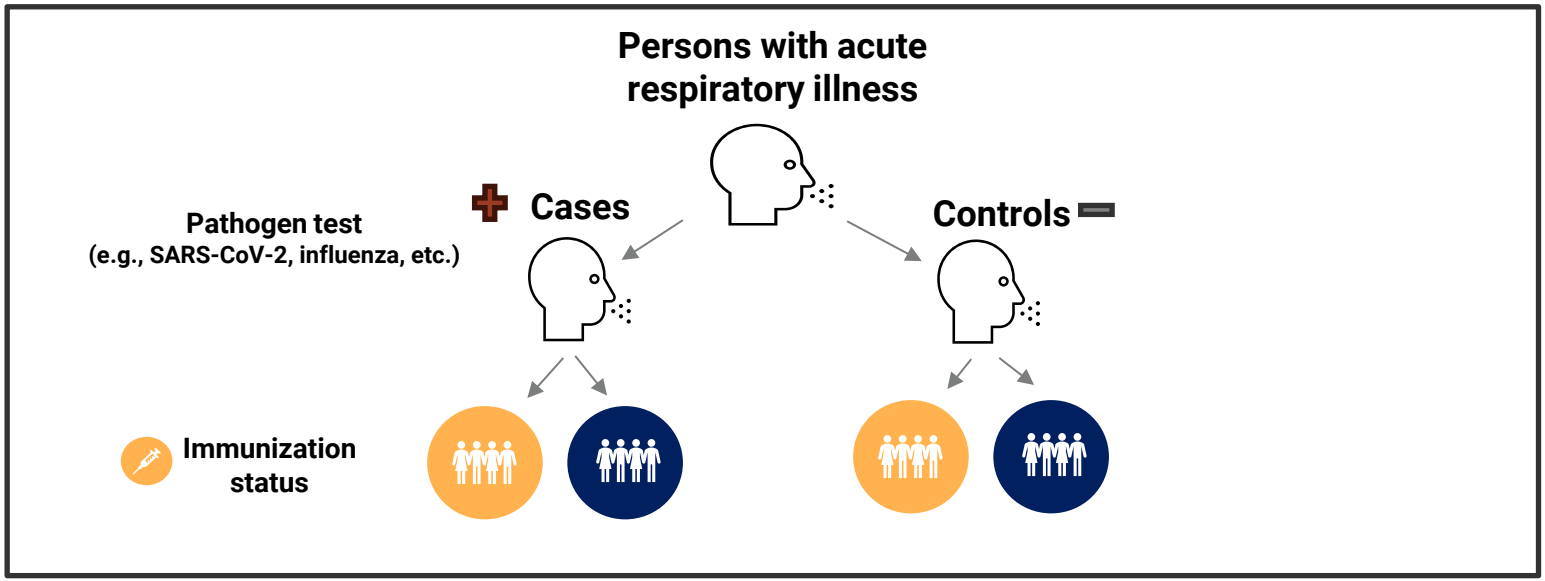


2025-2026 season coverage as of March 7, 2026:

6 months-4 years: **8.5%**
5-11 years: **9.2%**
12-17 years: **9.0%**

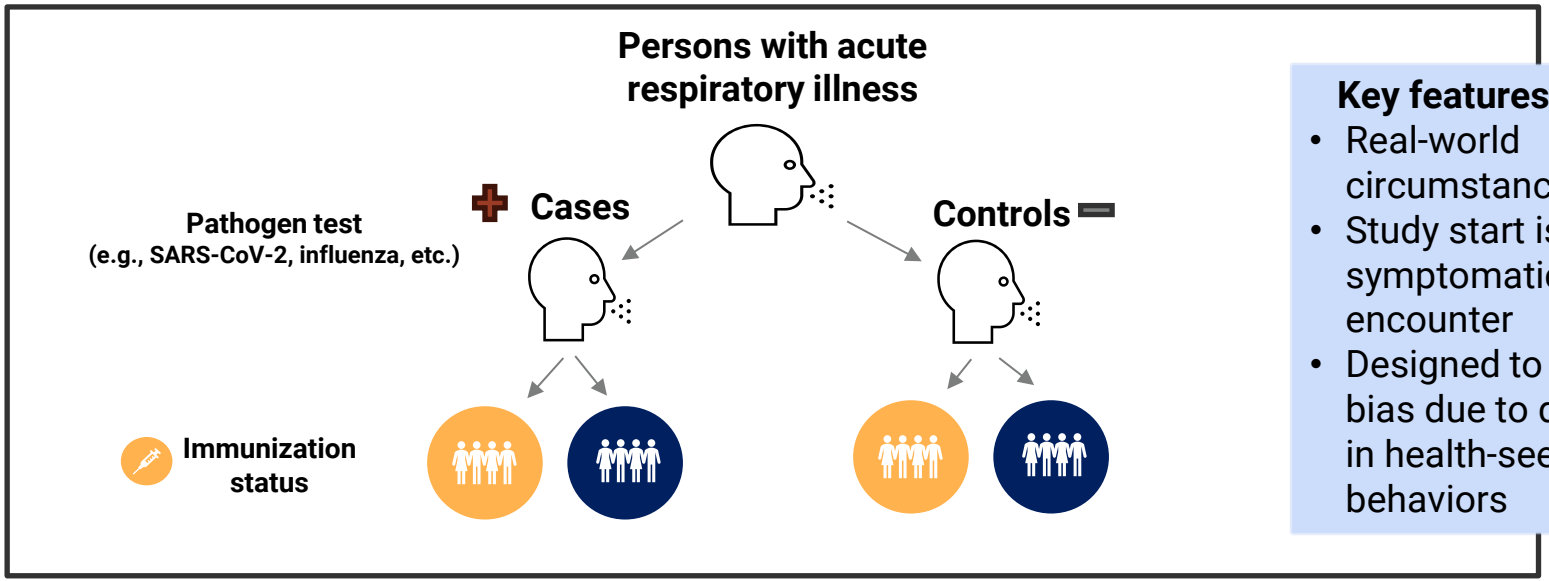
* Up-to-date with the updated 2024–25 COVID-19 vaccine is defined as receipt of at least one vaccination since August 22, 2024, for children ≥5 years; for children <5 years, up-to-date status was defined based on the current recommendations that also take into account number of doses and brand of vaccine. Up-to-date status was determined by survey questions on month and year of most recent COVID-19 vaccine, and for children <5 years, total number of COVID-19 vaccinations received and brand of most recent COVID-19 vaccine.

Test-negative design (TND) study for respiratory viruses



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

TND study for respiratory viruses



Key features of a TND

- Real-world circumstances
- Study start is symptomatic medical encounter
- Designed to minimize bias due to differences in health-seeking behaviors

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

VISION multi-site network of electronic health records

>300 emergency departments and urgent care sites and >200 hospitals

- **Design:** Test-negative design

- **Population:** Children aged 9 month – 17 years and adults aged ≥18 years visiting a participating emergency department or urgent care (ED/UC) or hospitalized with COVID-19-like illness (CLI)* and a SARS-CoV-2 test result within 10 days before or 72 hours after encounter
  - **Cases**: CLI with *positive* NAAT or antigen test 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/city immunization registries

*CLI is defined based on the presence of specific discharge diagnosis codes.

RSV = respiratory syncytial virus; NAAT = nucleic acid amplification test

IVY network — 26 hospitals, 20 U.S. states

- **Design**: Test-negative design
- **Population**: Adults aged ≥18 years hospitalized with COVID-like illness (CLI)* and SARS-CoV-2 test results within 10 days of illness onset and 3 days of admission
  - **Cases:** CLI and test *positive* for SARS-CoV-2 by NAAT or antigen
  - **Controls**: CLI and test *negative* for SARS-CoV-2, influenza and RSV (≥60 years) by NAAT
- **Vaccination data:** Electronic medical records, state/city immunization registries, and plausible self-report
- **Specimens:** Nasal swabs obtained on all patients for central RT-PCR testing and whole genome sequencing

IVY

INVESTIGATING RESPIRATORY VIRUSES IN THE ACUTELY ILL

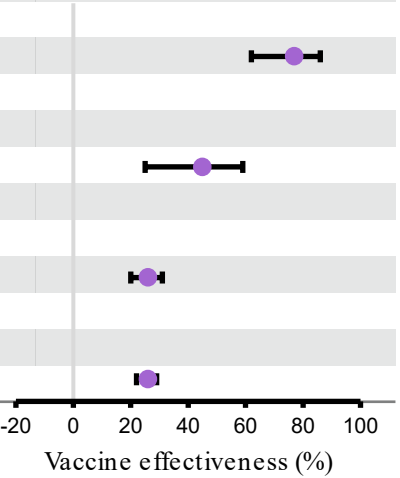
*CLI is defined as presence of any one of the following: fever, cough, shortness of breath, chest imaging consistent with pneumonia, or hypoxemia
NAAT = nucleic acid amplification test

Estimates of 2024-2025 COVID-19 vaccine effectiveness

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

September 2024 – September 2025

Age group | COVID-19 vaccination status	COVID-19 case-patients N (Col %)	COVID-19 control - patients N (Col %)	Median interval since last dose among those vaccinated, days (IQR)	Adjusted vaccine effectiveness (95% CI)
9 months-4 years				
No 2024-2025 COVID-19 dose* (Ref)	1,280 (99)	41.402 (95)	407 (290- 675)	**Ref**
Received 2024-2025 COVID-19 dose 7–299 days earlier	15 (1)	2,192 (5)	91 (49- 147)	**77 (62 to 86)**
5-17 years				
No 2024-2025 COVID-19 dose* (Ref)	1,299 (97)	49,680 (94)	986 (722- 1,135)	**Ref**
Received 2024-2025 COVID-19 dose 7–299 days earlier	44 (3)	3,108 (6)	105 (55- 167)	**45 (25 to 59)**
18-64 years				
No 2024-2025 COVID-19 dose* (Ref)	11,641 (93)	177,201 (89)	1,135 (911- 1,289)	**Ref**
Received 2024-2025 COVID-19 dose 7–299 days earlier	886 (3)	20,871 (11)	119 (65- 186)	**26 (20 to 31)**
≥65 years				
No 2024-2025 COVID-19 dose* (Ref)	6,371 (74)	71,515 (63)	985 (532 - 1,226)	**Ref**
Received 2024-2025 COVID-19 dose 7–299 days earlier	2,274 (26)	42,503 (37)	121 (66 - 188)	**26 (22 to 30)**



IQR = interquartile range | VE = vaccine effectiveness | CI = confidence interval

* 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.

†Encounters occurring during August 29, 2024 – September 2, 2025 included in analysis.

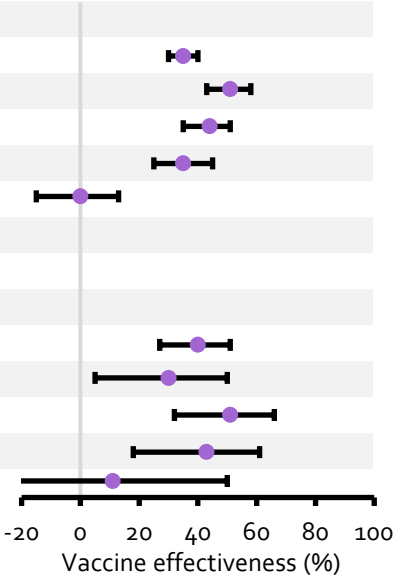
Pediatric results: Irving et al. (2025). *MMWR Morb Mortal Wkly Rep.* http://dx.doi.org/10.15585/mmwr.mm7440a1.

Adult results: Wiegand et al. (2026). *JAMA Intern Med*, in press

Effectiveness of 2024–2025 COVID-19 vaccination against COVID-19–associated hospitalization among immunocompetent adults aged ≥18 years — VISION and IVY Networks

September 2024 – September 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)	4,307 (83)	69,879 (76)	1,063 (706–1,267)	**Ref**
Received 2024-2025 COVID-19 dose 7–299 days earlier	911 (17)	22,566 (24)	126 (68–194)	**35 (30 to 40)**
2024-2025 COVID-19 dose, 7–59 days earlier	186 (4)	4,849 (5)	34 (20–47)	**51 (43 to 58)**
2024-2025 COVID-19 dose, 60–119 days earlier	244 (5)	5,858 (6)	90 (75–105)	**44 (35 to 51)**
2024-2025 COVID-19 dose, 120–179 days earlier	197 (4)	5,167 (6)	148 (133–163)	**35 (25 to 45)**
2024-2025 COVID-19 dose, 180–299 days earlier	284 (5)	6,692 (7)	229 (202–260)	**0 (-15 to 13)**
IVY				
No 2024-2025 COVID-19 dose (Ref)	1,282 (89)	3,846 (82)	Not available	**Ref**
Received 2024-2025 COVID-19 dose 7–254 days earlier	153 (11)	850 (18)	106 (61–150)	**40 (27 to 51)**
2024-2025 COVID-19 dose, 7–59 days earlier	56 (4)	183 (4)	31 (20–46)	**30 (5 to 50)**
2024-2025 COVID-19 dose, 60–119 days earlier	43 (3)	300 (6)	89 (74–105)	**51 (32 to 66)**
2024-2025 COVID-19 dose, 120–179 days earlier	36 (3)	273 (6)	145 (131–161)	**43 (18 to 61)**
2024-2025 COVID-19 dose, 180–254 days earlier	18 (1)	94 (2)	196 (188–207)	**11 (-49 to 50)**



IQR = interquartile range | VE = vaccine effectiveness | CI = confidence interval

VISION results from: Wiegand, et al. (2026). *JAMA Intern Med*, in press. IVY results from: Ma, et al. (2026). *JAMA Network Open.*

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, Charlson Comorbidity Index, geographic region (U.S. Department of Health and Human Services Region) and calendar time (biweekly intervals). The "no 2024–2025 COVID-19 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.

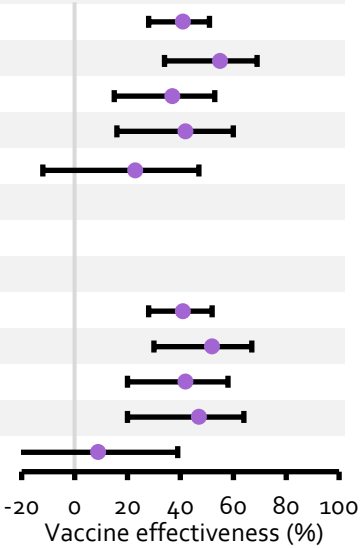
* IVY Network data are from September 2024 to April 2025.

†Interval since last dose is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, or 2024-2025 COVID-19 vaccine for the VISION Network.

Effectiveness of 2024–2025 COVID-19 vaccination against COVID-19–associated critical illness among immunocompetent adults aged ≥18 years — VISION

September 2024 – September 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)
≥18 years				
No 2024-2025 COVID-19 dose (Ref)	816 (84)	69,879 (76)	1,066 (712-1,269)	**Ref**
Received 2024-2025 COVID-19 dose 7–299 days earlier	151 (16)	22,566 (24)	125 (68-193)	**41 (28 to 51)**
2024-2025 COVID-19 dose, 7–59 days earlier	31 (3)	4,849 (5)	34 (20-47)	**55 (34 to 69)**
2024-2025 COVID-19 dose, 60–119 days earlier	52 (5)	5,858 (6)	90 (75-105)	**37 (15 to 53)**
2024-2025 COVID-19 dose, 120–179 days earlier	34 (4)	5,167 (6)	148 (133-163)	**42 (16 to 60)**
2024-2025 COVID-19 dose, 180–299 days earlier	34 (4)	6,692 (7)	228 (202-259)	**23 (-12 to 47)**
≥65 years				
No 2024-2025 COVID-19 dose (Ref)	587 (82)	41,005 (68)	1,015 (602-1,247)	**Ref**
Received 2024-2025 COVID-19 dose 7–299 days earlier	133 (18)	18,914 (32)	125 (68-193)	**41 (28 to 52)**
2024-2025 COVID-19 dose, 7–59 days earlier	30 (4)	4,071 (7)	34 (20-47)	**52 (30 to 67)**
2024-2025 COVID-19 dose, 60–119 days earlier	44 (6)	4,918 (8)	90 (75-104)	**42 (20 to 58)**
2024-2025 COVID-19 dose, 120–179 days earlier	28 (4)	4,359 (7)	148 (133-163)	**47 (20 to 64)**
2024-2025 COVID-19 dose, 180–299 days earlier	31 (4)	5,566 (9)	228 (202-259)	**9 (-37 to 39)**



IQR = interquartile range | VE = vaccine effectiveness | CI = confidence interval

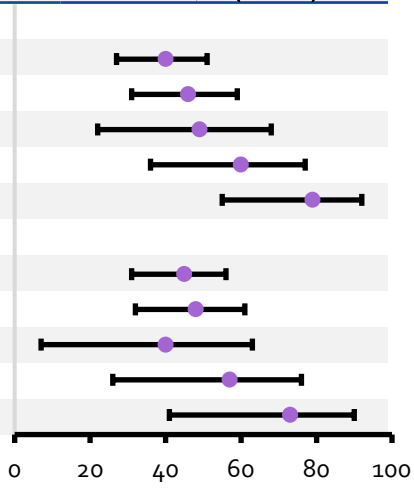
Vaccine effectiveness was calculated by comparing the odds of 2024–2025 COVID-19 vaccination in case-patients and control-patients using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multivariable logistic regression. The odds ratio was adjusted for age, sex, race and 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.

Critical illness is defined as admission to the intensive care unit or in-hospital death. *Interval since last dose is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, or 2024-2025 COVID-19 vaccine. Results from: Wiegand, et al. (2026). *JAMA Intern Med*, in press.

Effectiveness of 2024–2025 COVID-19 vaccination against COVID-19–associated severe in-hospital outcomes among immunocompetent adults aged ≥18 years — IVY Network

September 2024 – April 2025

Outcome	No. of vaccinated cases/Total cases, n (%)	No. of vaccinated controls/Total controls, n (%)	Median interval since last dose among vaccinated cases, days (IQR)	Median interval since last dose among vaccinated controls, days (IQR)	Adjusted vaccine effectiveness, % (95% CI)
≥18, years					
Hospitalization	153/1,435 (11)	850/4,696 (18)	80 (43–137)	108 (66–151)	**40 (27–51)**
Supplemental oxygen therapy	84/850 (10)	846/4,665 (18)	81 (39–135)	109 (66–151)	**46 (31–59)**
Acute respiratory failure	25/288 (9)	846/4,665 (18)	87 (58–123)	109 (66–151)	**49 (22–68)**
ICU admission	18/254 (7)	850/4,696 (18)	89 (59–122)	108 (66–151)	**60 (36–77)**
IMV or death	6/128 (5)	850/4,696 (18)	90 (54–133)	108 (66–151)	**79 (55–92)**
≥65, years					
Hospitalization	127/962 (13)	608/2,488 (24)	82 (49–137)	109 (67–155)	**45 (31–56)**
Supplemental oxygen therapy	73/587 (12)	607/2,479 (24)	82 (41–130)	109 (67–155)	**48 (32–61)**
Acute respiratory failure	25/188 (13)	607/2,479 (24)	87 (58–123)	109 (67–155)	**40 (7–63)**
ICU admission	15/154 (10)	608/2,488 (24)	90 (65–130)	109 (67–155)	**57 (26–76)**
IMV or death	6/83 (7)	608/2,488 (24)	90 (54–133)	109 (67–155)	**73 (41–90)**

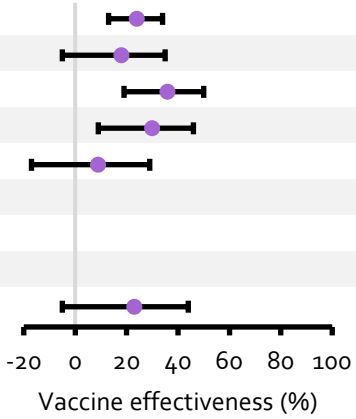


IQR = interquartile range | VE = vaccine effectiveness | CI = confidence interval | IMV = invasive mechanical ventilation | ICU = intensive care unit.
Supplemental oxygen therapy was defined as supplemental oxygen at any flow rate and by any device for those not on chronic oxygen therapy or with escalation of oxygen therapy for patients receiving chronic oxygen therapy. Acute respiratory failure was defined as new receipt of high-flow nasal canula, noninvasive ventilation, or IMV.
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, Charlson Comorbidity Index, geographic region (U.S. Department of Health and Human Services Region) and calendar time (biweekly intervals). Results from: Ma, et al. (2026). *JAMA Network Open.*

Effectiveness of 2024–2025 COVID-19 vaccination against COVID-19–associated hospitalization among immunocompromised adults aged ≥18 years — VISION and IVY Networks

September 2024 – September 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)	1,148 (78)	21,979 (71)	1,024 (620-1,256)	**Ref**
Received 2024-2025 COVID-19 dose 7–299 days earlier	325 (22)	9,177 (29)	129 (70-195)	**24 (13 to 34)**
2024-2025 COVID-19 dose, 7–59 days earlier	91 (6)	1,851 (6)	35 (20-47)	**18 (-3 to 35)**
2024-2025 COVID-19 dose, 60–119 days earlier	83 (6)	2,355 (8)	89 (74-104)	**36 (19 to 50)**
2024-2025 COVID-19 dose, 120–179 days earlier	68 (5)	2,142 (7)	147 (133-163)	**30 (9 to 46)**
2024-2025 COVID-19 dose, 180–299 days earlier	83 (6)	2,829 (9)	229 (201-259)	**9 (-17 to 29)**
IVY				
No 2024-2025 COVID-19 dose (Ref)	390 (86)	1535 (80)	Not available	**Ref**
Received 2024-2025 COVID-19 dose 7–257 days earlier	63 (14)	374 (20)	101 (58-146)	**23 (-5 to 44)**



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VISION results from: Wiegand, et al. (2026). *JAMA Intern Med*, in press. IVY results from: Ma, et al. (2026). *JAMA Network Open.*

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. 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.

* IVY Network data span September 2024 to April 2025.

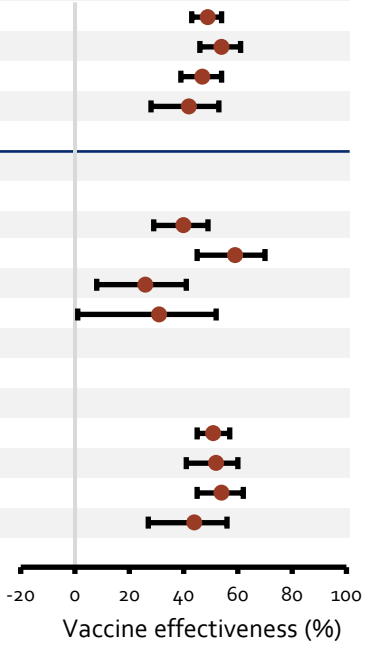
† Interval since last dose is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, or 2024-2025 COVID-19 vaccine for VISION.

Interim estimates of 2025-2026 COVID-19 vaccine effectiveness in adults

Effectiveness of 2025–2026 COVID-19 vaccination against COVID-19–associated emergency department/urgent care encounters among adults by age group — VISION

September 2025 – April 2026

Age group/2025 -2026 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 2025-2026 COVID-19 dose (Ref)	5,739 (92)	123,027 (85)	1,326 (532–1,529)	**Ref**
Received 2025-2026 COVID-19 dose 7–179 days earlier	466 (8)	22,001 (15)	80 (45–117)	**49 (43 to 54)**
2025-2026 COVID-19 dose, 7–59 days earlier	147 (2)	7,738 (5)	34 (21–47)	**54 (46 to 61)**
2025-2026 COVID-19 dose, 60–119 days earlier	221 (4)	9,138 (6)	88 (74–103)	**47 (39 to 54)**
2025-2026 COVID-19 dose, 120–179 days earlier	98 (2)	5,125 (4)	142 (130–156)	**42 (28 to 53)**
18-64 years				
No 2025-2026 COVID-19 dose (Ref)	3,667 (96)	81,540 (93)	1,416 (1,001–1,569)	**Ref**
Received 2025-2026 COVID-19 dose 7–179 days earlier	157 (4)	6,373 (7)	76 (42–113)	**40 (29 to 49)**
2025-2026 COVID-19 dose, 7–59 days earlier	41 (1)	2,437 (3)	33 (20–47)	**59 (45 to 70)**
2025-2026 COVID-19 dose, 60–119 days earlier	85 (2)	2,565 (3)	87 (74–102)	**26 (8 to 41)**
2025-2026 COVID-19 dose, 120–179 days earlier	31 (1)	1,371 (2)	141 (129–154)	**31 (1 to 52)**
≥65 years				
No 2025-2026 COVID-19 dose (Ref)	2,072 (87)	41,487 (73)	885 (392–1,451)	**Ref**
Received 2025-2026 COVID-19 dose 7–179 days earlier	309 (13)	15,628 (27)	82 (47–118)	**51 (45 to 57)**
2025-2026 COVID-19 dose, 7–59 days earlier	106 (4)	5,301 (9)	34 (21–47)	**52 (41 to 60)**
2025-2026 COVID-19 dose, 60–119 days earlier	136 (6)	6,573 (12)	89 (74–103)	**54 (45 to 62)**
2025-2026 COVID-19 dose, 120–179 days earlier	67 (3)	3,754 (7)	142 (130–157)	**44 (27 to 56)**



IQR = interquartile range | VE = vaccine effectiveness | CI = confidence interval

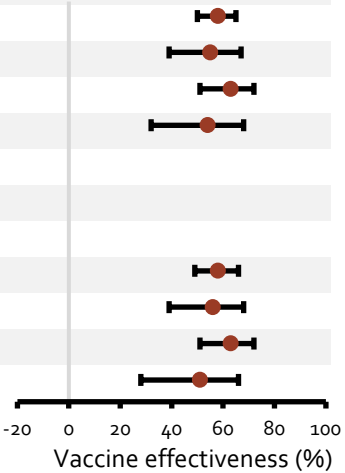
VISION unpublished results.

Vaccine effectiveness was calculated by comparing the odds of 2025–2026 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 2025–2026 dose" group included all eligible persons who did not receive a 2025–2026 COVID-19 vaccine dose, regardless of number of previous COVID-19 vaccine doses (if any) received. * Interval since last dose is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, 2024-2025, or 2025-2026 COVID-19 vaccine.

Effectiveness of 2025–2026 COVID-19 vaccination against COVID-19–associated hospitalization among immunocompetent adults by age group — VISION

September 2025 – April 2026

Age group/2025 -2026 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 2025-2026 COVID-19 dose (Ref)	1,578 (92)	36,166 (83)	1,183 (455-1,501)	**Ref**
Received 2025-2026 COVID-19 dose 7–179 days earlier	129 (8)	7,367 (17)	81 (45-116)	**58 (50 to 65)**
2025-2026 COVID-19 dose, 7–59 days earlier	44 (3)	2,546 (6)	33 (20-46)	**55 (39 to 67)**
2025-2026 COVID-19 dose, 60–119 days earlier	56 (3)	3,120 (7)	89 (74-104)	**63 (51 to 72)**
2025-2026 COVID-19 dose, 120–179 days earlier	29 (2)	1,701 (4)	141 (129-155)	**54 (32 to 68)**
≥65 years				
No 2025-2026 COVID-19 dose (Ref)	1,204 (91)	22,832 (78)	1,064 (416-1,469)	**Ref**
Received 2025-2026 COVID-19 dose 7–179 days earlier	118 (9)	6,350 (22)	82 (45-117)	**58 (49 to 66)**
2025-2026 COVID-19 dose, 7–59 days earlier	39 (3)	2,163 (7)	33 (20-46)	**56 (39 to 68)**
2025-2026 COVID-19 dose, 60–119 days earlier	50 (4)	2,701 (9)	89 (74-104)	**63 (51 to 72)**
2025-2026 COVID-19 dose, 120–179 days earlier	29 (2)	1,486 (5)	141 (129-156)	**51 (28 to 66)**



IQR = interquartile range | VE = vaccine effectiveness | CI = confidence interval

VISION unpublished results.

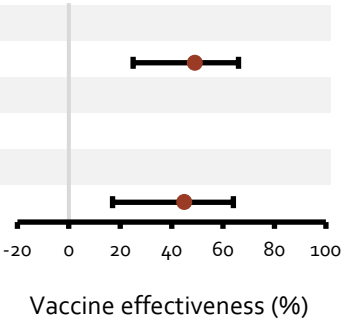
Vaccine effectiveness was calculated by comparing the odds of 2025–2026 COVID-19 vaccination in case-patients and control-patients using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multivariable logistic regression. The odds ratio was adjusted for age, sex, race and ethnicity, calendar day, and geographic region. The "no 2025–2026 dose" group included all eligible persons who did not receive a 2025–2026 COVID-19 vaccine dose, regardless of number of previous COVID-19 vaccine doses.

*Interval since last dose is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, 2024-2025, or 2025-2026 COVID-19 vaccine.

Effectiveness of 2025–2026 COVID-19 vaccination against COVID-19–associated critical illness among immunocompetent adults by age group — VISION

September 2025 – April 2026

2025-2026 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 2025-2026 COVID-19 dose (Ref)	299 (91)	36,166 (83)	1,186 (456–1,502)	**Ref**
Received 2025-2026 COVID-19 dose 7–179 days earlier	28 (9)	7,367 (17)	81 (45–116)	**49 (25 to 66)**
≥65 years				
No 2025-2026 COVID-19 dose (Ref)	221 (89)	22,832 (78)	1,066 (417–1,470)	**Ref**
Received 2025-2026 COVID-19 dose 7–179 days earlier	26 (11)	6,350 (22)	82 (45–117)	**45 (17 to 64)**



IQR = interquartile range | VE = vaccine effectiveness | CI = confidence interval

VISION unpublished results.

Vaccine effectiveness was calculated by comparing the odds of 2025–2026 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 2025–2026 COVID-19 dose" group included all eligible persons who did not receive a 2025–2026 COVID-19 vaccine dose, regardless of number of previous COVID-19 vaccine doses.

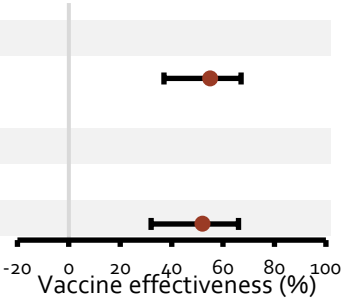
Critical illness is defined as admission to the intensive care unit or in-hospital death.

* Interval since last dose is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, 2024-2025, or 2025-2026 COVID-19 vaccine.

Effectiveness of 2025–2026 COVID-19 vaccination against COVID-19–associated hospitalization among immunocompromised adults by age group — VISION

September 2025 – April 2026

2025-2026 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 2025-2026 COVID-19 dose (Ref)	393 (91)	11,572 (79)	1,084 (421-1,470)	**Ref**
Received 2025-2026 COVID-19 dose 7–179 days earlier	41 (9)	3,028 (21)	79 (45-116)	**55 (37 to 67)**
≥65 years				
No 2025-2026 COVID-19 dose (Ref)	284 (88)	7,354 (74)	817 (390-1,433)	**Ref**
Received 2025-2026 COVID-19 dose 7–179 days earlier	38 (12)	2,548 (26)	80 (46-116)	**52 (32 to 66)**



IQR = interquartile range | VE = vaccine effectiveness | CI = confidence interval

VISION unpublished results.

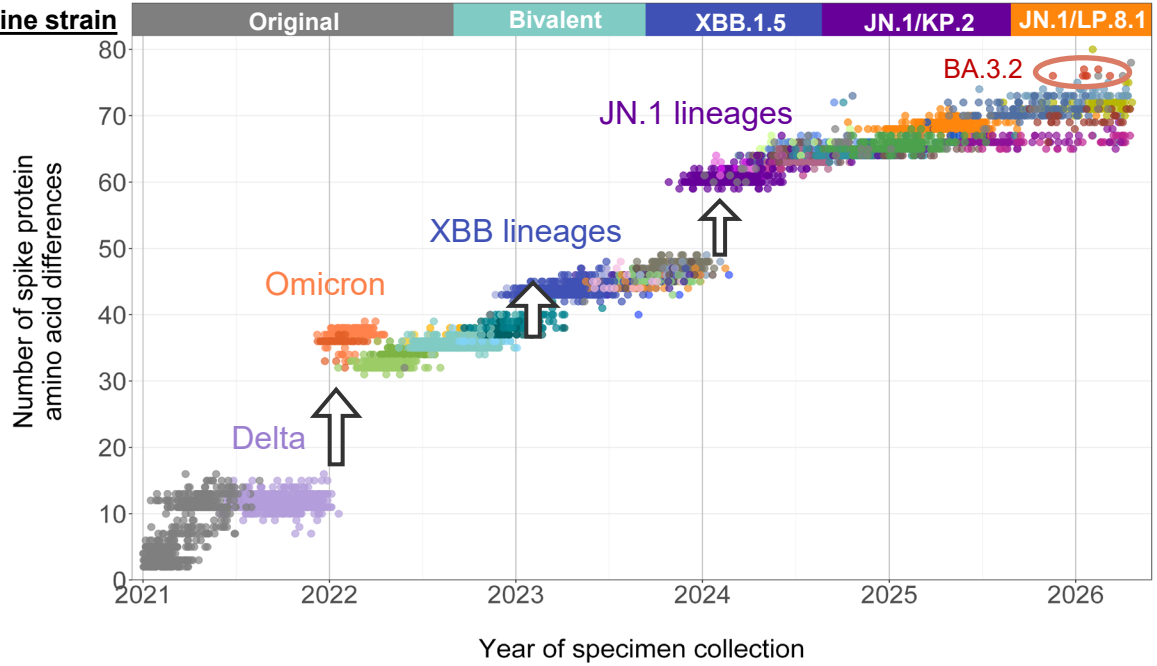
Vaccine effectiveness was calculated by comparing the odds of 2025–2026 COVID-19 vaccination in case-patients and control-patients using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multivariable logistic regression. The odds ratio was adjusted for age, sex, race and ethnicity, calendar day, and geographic region. The "no 2025–2026 dose" group included all eligible persons who did not receive a 2025–2026 COVID-19 vaccine dose, regardless of number of previous COVID-19 vaccine doses (if any) received).

* Interval since last dose is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, 2024-2025, or 2025-2026 COVID-19 vaccine.

Estimates of COVID-19 VE by genetic differences between variant and vaccine composition

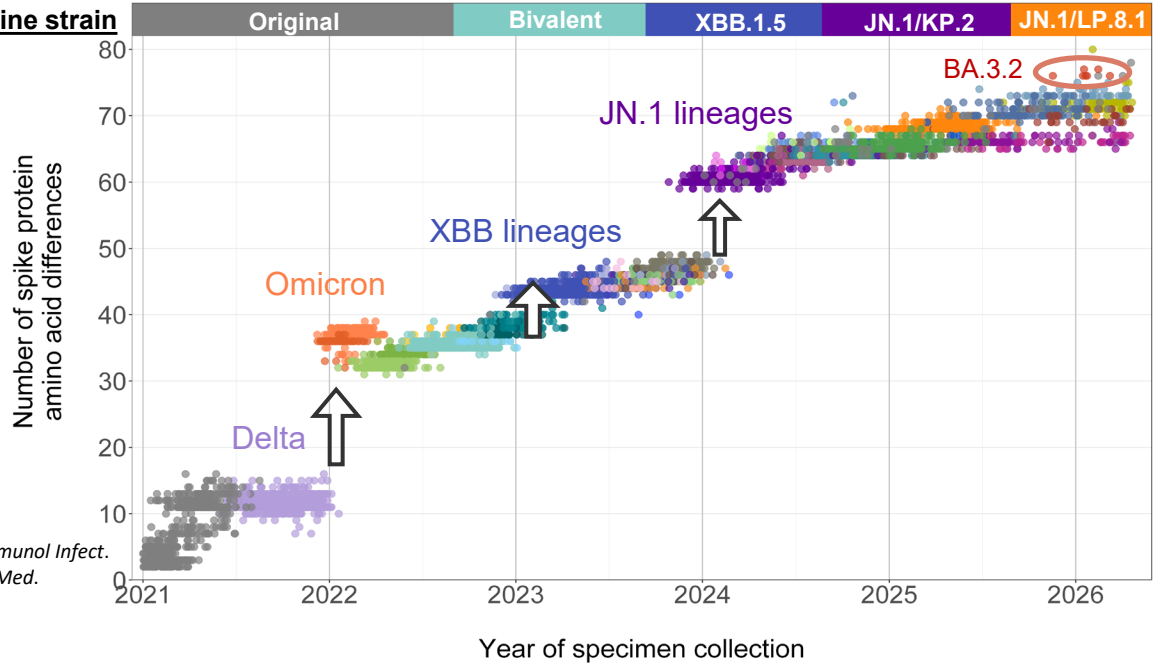
Background

- COVID-19 vaccines have been updated annually since 2023 to keep pace with SARS-CoV-2 evolution, which has occurred through a combination of 1) gradual accumulation of spike protein mutations and 2) infrequent evolutionary jumps (e.g., Delta to Omicron)



Background

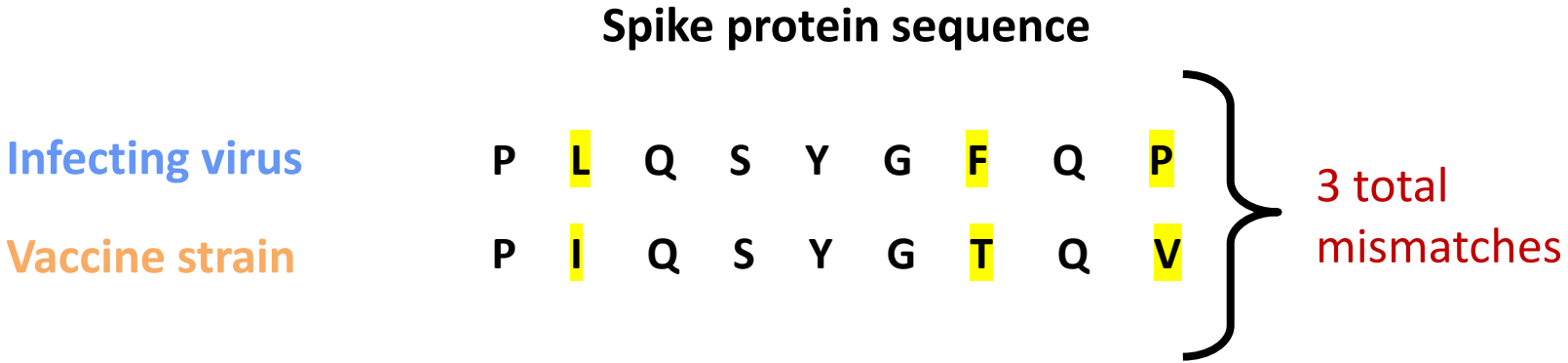
- Evolutionary jumps have been associated with decreases in COVID-19 vaccine effectiveness (VE)[1-6]
- However, the impact of gradual spike evolution on VE is largely unknown: **do small to moderate genetic mismatches with the vaccine strain also impact protection?**



[1]Ma, et al. (2025). *J Microbiol Immunol Infect*.
[2]Andrews, et al. (2022). *N Engl J Med*.
[3]Kirsebom, et al. (2024). *J Infect*.
[4]Lauring, et al. (2022). *BMJ*.
[5]Ma, et al. (2024). *Clin Infect Dis*.
[6]Link-Gelle, et al. (2025). *JAMA Netw Open*.

Spike genetic divergence

- The S1 domain is the primary immunogenic portion of the spike protein
- To calculate genetic divergence, we totaled the number of nonsynonymous mutations in the S1 domain relative to a given season's COVID-19 vaccine strain for each sequenced case-patient
- Genetic divergence is correlated with laboratory measurements of antigenic distance in multiple studies (e.g., Islas et al 2025, Zhu et al 2026)



Characteristics of hospitalized adults by COVID-19 case and vaccination status

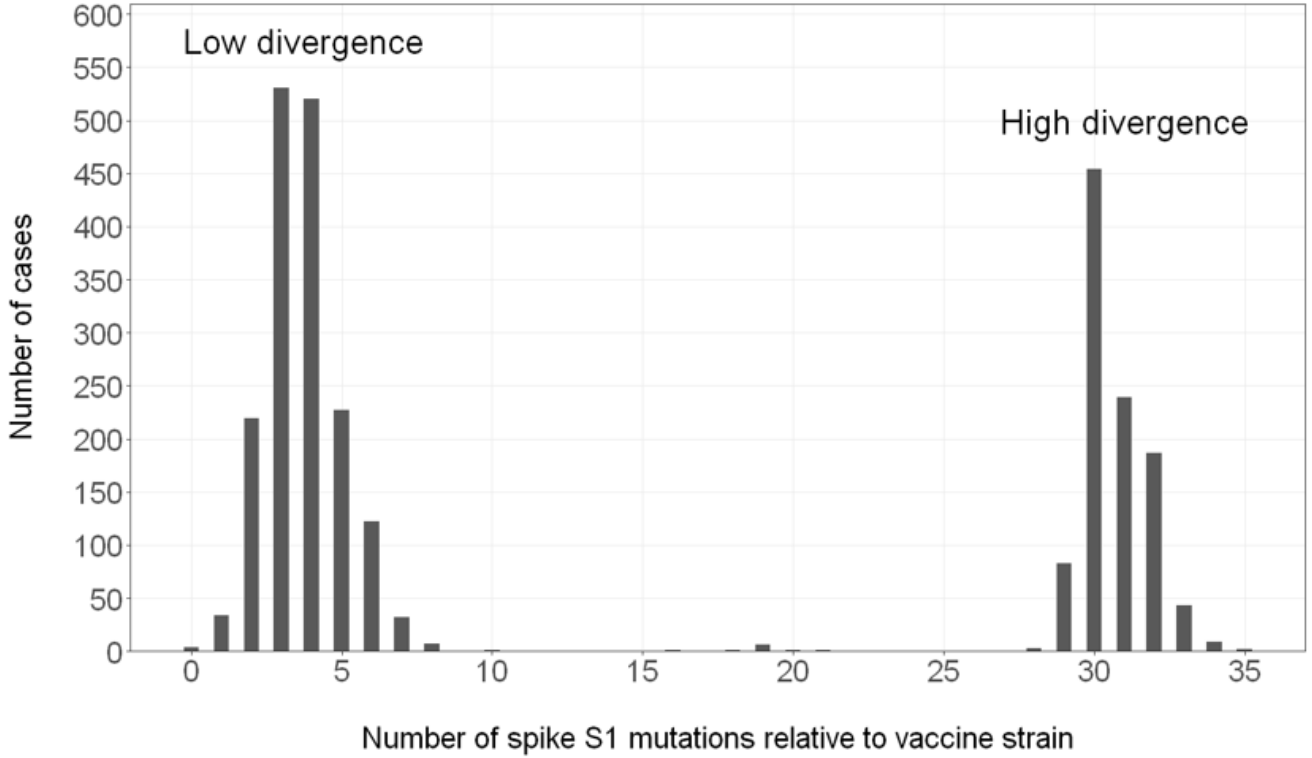
September 2023–April 2025, IVY Network

Characteristic	Overall (N=17,597)	COVID-19 case-control status		COVID-19 vaccination status during season of hospitalization	
		COVID-19 cases with sequenced specimens (n = 2,727)	Test-negative controls (n = 14,870)	Did not receive vaccine (n = 14,586)	Received vaccine (n = 3,011)
Age, median (IQR)	66 (54, 76)	72 (61, 81)	65 (52, 75)	64 (52, 75)	72 (63, 80)
Received COVID-19 vaccine during season of hospitalization					
Yes	3,011 (17%)	388 (14%)	2,623 (18%)	--	--
No	14,586 (83%)	2,339 (86%)	12,247 (82%)	--	--
COVID-19 vaccine formulation					
XBB.1.5-based	1,932 (11%)	305 (11%)	1,627 (11%)	--	1,932 (64%)
KP.2-based	1,079 (6%)	83 (3%)	996 (7%)	--	1,079 (36%)
Season of COVID-19–like illness hospitalization					
2023–2024	10,365 (59%)	1,797 (66%)	8,568 (58%)	8,433 (58%)	1,932 (64%)
2024–2025	7,232 (41%)	930 (34%)	6,302 (42%)	6,153 (42%)	1,079 (36%)

Ma et al., (2026) SSRN (preprint)

Numbers of COVID-19 cases by count of spike protein S1 domain mutations

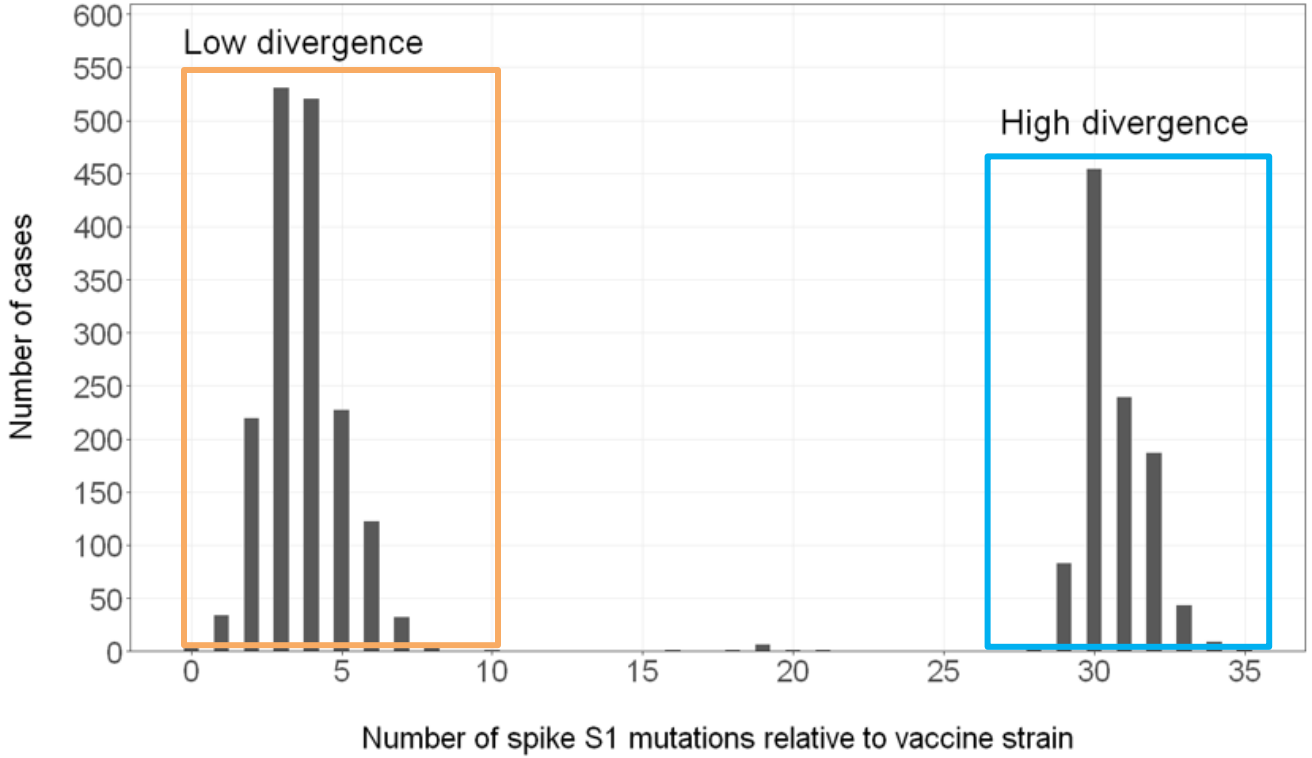
September 2023–April 2025, IVY Network



Ma et al., (2026) SSRN (preprint)

Numbers of COVID-19 cases by count of spike protein S1 domain mutations

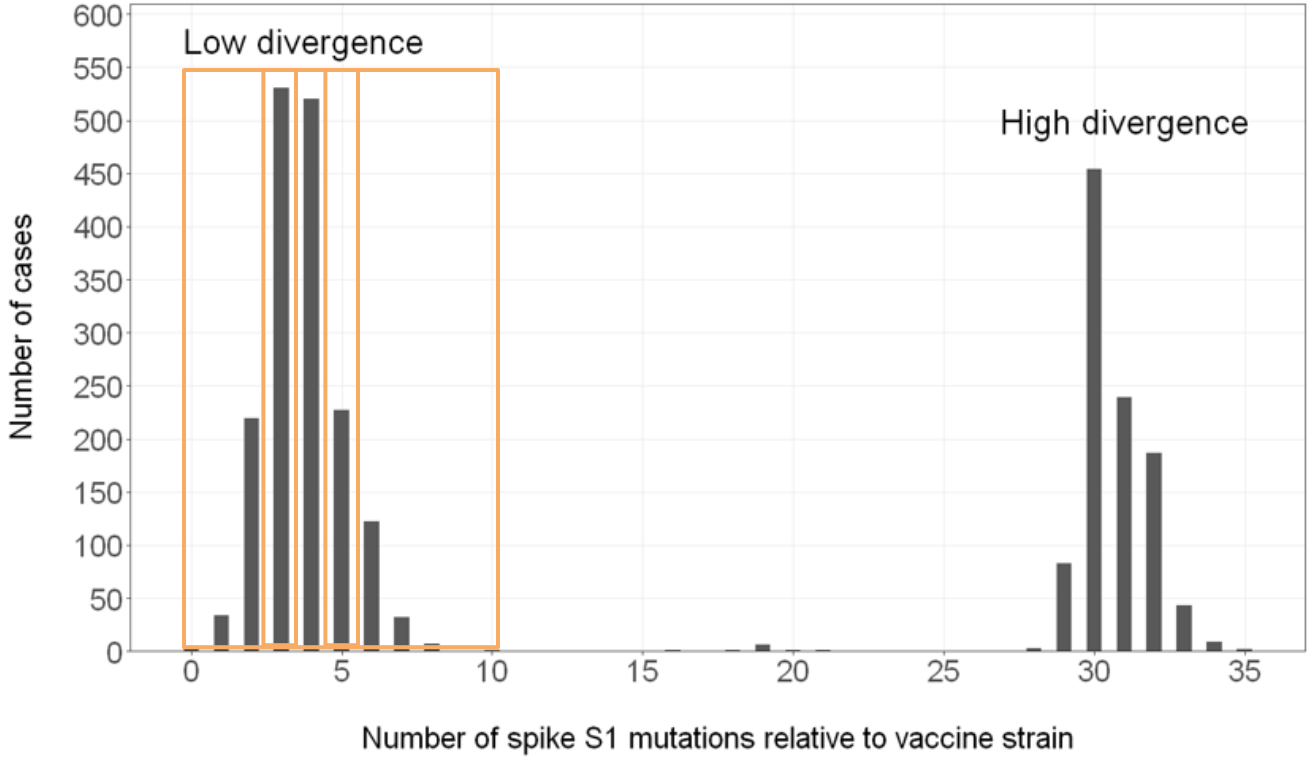
September 2023–April 2025, IVY Network



Ma et al., (2026) SSRN (preprint)

Numbers of COVID-19 cases by count of spike protein S1 domain mutations

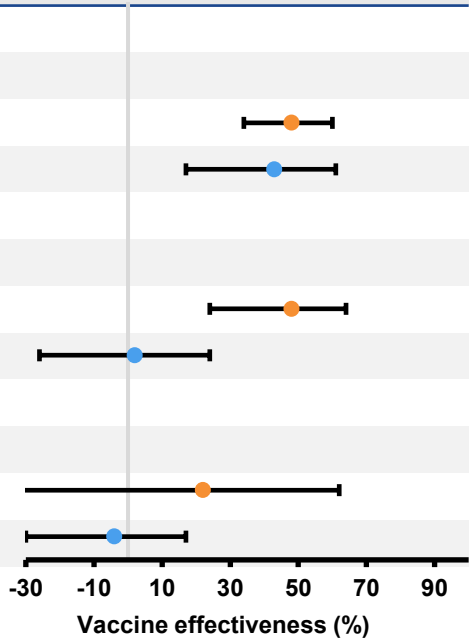
September 2023–April 2025, IVY Network



Ma et al., (2026) SSRN (preprint)

Effectiveness of COVID-19 mRNA vaccines against hospitalization by number of SARS-CoV-2 spike protein S1 domain mutations relative to vaccine strain (≤10 vs 28-35)

Time since COVID-19 dose receipt, case-control status, and number of spike S1 mutations relative to vaccine strain	No. of vaccinated patients/Total patients, n (%)	Median interval since dose among vaccinated patients, days (IQR)	Adjusted vaccine effectiveness, % (95% CI)	Standard error
Received COVID-19 dose **7–89 days earlier**				
Test-negative control	969/13,216 (7%)	51 (28–72)	Reference	--
Case, ≤10 mutations	80/1,654 (5%)	51 (29–68)	48% (34–60)	0.13
Case, 28–35 mutations	33/789 (4%)	55 (33–71)	43% (17–61)	0.19
Received COVID-19 dose **90–179 days earlier**				
Test-negative control	1,064/13,311 (8%)	131 (112–152)	Reference	--
Case, ≤10 mutations	34/1,608 (2%)	131 (123–151)	48% (24–64)	0.19
Case, 28–35 mutations	87/843 (10%)	140 (117–158)	2% (-26 to 24)	0.13
Received COVID-19 dose **≥180 days earlier**				
Test-negative control	590/12,837 (5%)	226 (198–265)	Reference	--
Case, ≤10 mutations	9/1,583 (1%)	197 (192–213)	22% (-59 to 62)	0.37
Case, 28–35 mutations	144/900 (16%)	252 (219–279)	-4% (-30 to 17)	0.11

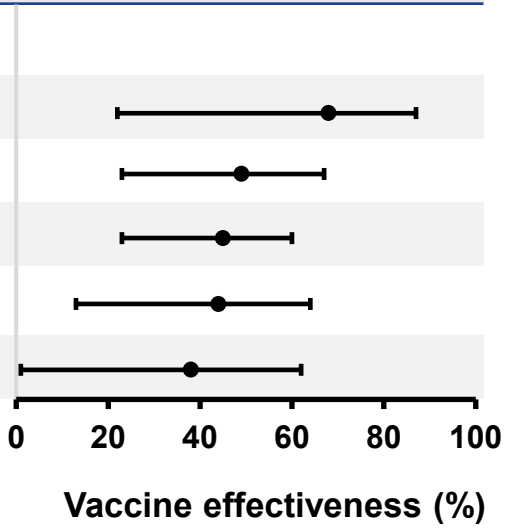


Vaccine effectiveness was calculated by comparing the odds of COVID-19 mRNA vaccination among cases and controls using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multinomial logistic regression adjusted for age, sex, race and ethnicity, geographic region (U.S. Department of Health and Human Services Region), cubic spline of admission date, season of hospitalization, and Charlson comorbidity index using an outcome variable indicating test-negative control or case status stratified by spike S1 mutation category. These results include both immunocompetent and immunocompromised persons.

Ma et al., (2026) SSRN (preprint)

Effectiveness of COVID-19 mRNA vaccines against hospitalization by number of SARS-CoV-2 spike protein S1 domain mutations relative to vaccine strain (between 0 and 10)

Case-control status and number of spike S1 mutations relative to vaccine strain	No. of vaccinated patients/Total patients, n (%)	Median interval since dose among vaccinated patients, days (IQR)	Adjusted vaccine effectiveness, % (95% CI)	Standard error
Test-negative control	2623/14,870 (18%)	117 (66–171)	Reference	--
Case, 0–2 mutations[a]	5/257 (2%)	27 (21–54)	68% (22–87)	0.46
Case, 3 mutations	25/531 (5%)	46 (27–67)	49% (23–67)	0.22
Case, 4 mutations	46/520 (9%)	63 (38–84)	45% (23–60)	0.17
Case, 5 mutations	25/227 (11%)	100 (52–136)	44% (13–64)	0.22
Case, 6–10 mutations[b]	22/162 (14%)	144 (125–172)	38% (1–62)	0.24



[a] Within this category, 4 cases had 0 mutations, 34 had 1 mutation, and the majority (n = 219) had 2 mutations.

[b] Within this category, the majority (n = 122) had 6 mutations, 32 had 7 mutations, 7 had 8 mutations, and 1 case had 10 mutations.

Vaccine effectiveness was calculated by comparing the odds of COVID-19 mRNA vaccination among cases and controls using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multinomial logistic regression adjusted for age, sex, race and ethnicity, geographic region (U.S. Department of Health and Human Services Region), cubic spline of admission date, season of hospitalization, and Charlson comorbidity index using an outcome variable indicating test-negative control or case status stratified by spike S1 mutation category. These results include both immunocompetent and immunocompromised persons.

Ma et al., (2026) SSRN (preprint)

Effectiveness of COVID-19 mRNA vaccines against hospitalization by number of SARS-CoV-2 spike protein S1 domain mutations relative to vaccine strain (between 0 and 10)

Case-control status and number of spike S1 mutations relative to vaccine strain	No. of vaccinated patients/Total patients, n (%)	Median interval since dose among vaccinated patients, days (IQR)	Adjusted vaccine effectiveness, % (95% CI)	Standard error
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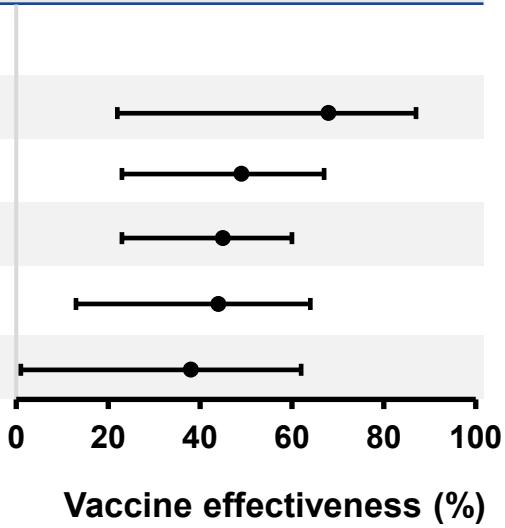
Case, 5 mutations	25/227 (11%)	100 (52–136)	44% (13–64)	0.22
Case, 6–10 mutations[b]	22/162 (14%)	144 (125–172)	38% (1–62)	0.24



[a] Within this category, 4 cases had 0 mutations, 34 had 1 mutation, and the majority (n = 219) had 2 mutations.

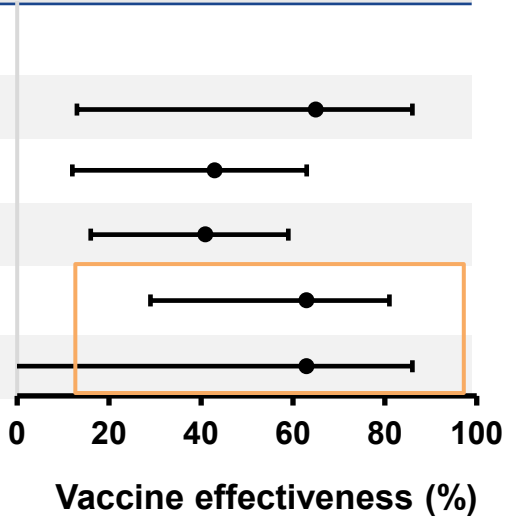
[b] Within this category, the majority (n = 122) had 6 mutations, 32 had 7 mutations, 7 had 8 mutations, and 1 case had 10 mutations.

Vaccine effectiveness was calculated by comparing the odds of COVID-19 mRNA vaccination among cases and controls using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multinomial logistic regression adjusted for age, sex, race and ethnicity, geographic region (U.S. Department of Health and Human Services Region), cubic spline of admission date, season of hospitalization, and Charlson comorbidity index using an outcome variable indicating test-negative control or case status stratified by spike S1 mutation category. These results include both immunocompetent and immunocompromised persons.

Ma et al., (2026) SSRN (preprint)

Effectiveness of COVID-19 mRNA vaccines against hospitalization 7–89 days after vaccination by number of SARS-CoV-2 spike protein S1 domain mutations relative to vaccine strain

Case-control status and number of spike S1 mutations relative to vaccine strain	No. of vaccinated patients/Total patients, n (%)	Median interval since dose among vaccinated patients, days (IQR)	Adjusted vaccine effectiveness, % (95% CI)	Standard error
Test-negative control	969/13,216 (7%)	117 (66–171)	Reference	--
Case, 0–2 mutations[a]	5/257 (2%)	27 (21–54)	65% (13-86)	0.46
Case, 3 mutations	24/530 (5%)	45 (24–60)	43% (12–63)	0.22
Case, 4 mutations	37/511 (7%)	54 (33–68)	41% (16–59)	0.18
Case, 5 mutations	10/212 (5%)	44 (36–64)	63% (29–81)	0.33
Case, 6–10 mutations[b]	4/144 (3%)	80 (75–81)	63% (-3 to 86)	0.52



[a] Within this category, 4 cases had 0 mutations, 34 had 1 mutation, and the majority (n = 219) had 2 mutations.

[b] Within this category, the majority (n = 110) had 6 mutations, 27 had 7 mutations, 6 had 8 mutations, and 1 case had 10 mutations.

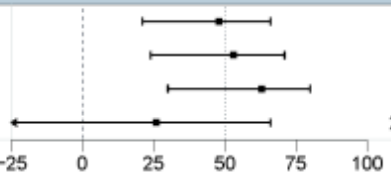
Vaccine effectiveness was calculated by comparing the odds of COVID-19 mRNA vaccination among cases and controls using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multinomial logistic regression adjusted for age, sex, race and ethnicity, geographic region (U.S. Department of Health and Human Services Region), cubic spline of admission date, season of hospitalization, and Charlson comorbidity index using an outcome variable indicating test-negative control or case status stratified by spike S1 mutation category. These results include both immunocompetent and immunocompromised persons.

Ma et al., (2026) SSRN (preprint)

Effectiveness of 2025–2026 COVID-19 vaccination against COVID-19–associated medically attended illness among participants aged ≥12 years — Canadian Sentinel Practitioner Surveillance Network (SPSN)

October 2025 – March 2026

	Cases, n		Controls, n			Cases, TSV (weeks)		Controls, TSV (weeks)	
	Vac (%)	Total	Vac (%)	Total	VE (95% CI)	Median (IQR)	Range	Median (IQR)	Range
All case viruses	**29 (9%)**	**310**	**577 (17%)**	**3492**	**48 (21, 66)**	**7 (4–13)**	**2–19**	**9 (5–13)**	**2–21**
Case viruses successfully characterized by WGS	21 (9%)	235	577 (17%)	3492	53 (24, 71)	7 (5–14)	2–19	9 (5–13)	2–21
XFG−lineage case viruses	12 (7%)	164	577 (17%)	3492	63 (30, 80)	8 (5–13)	2–16	9 (5–13)	2–21
Case viruses not successfully characterized by WGS	8 (11%)	74	577 (17%)	3492	26 (−63, 66)	6.5 (3.5–7.5)	3–13	9 (5–13)	2–21



Skowronski, et al. (2026). *Euro Surveill*

CI = confidence interval | IQR = interquartile range | TSV = time since vaccination | Vac = vaccinated | VE = vaccine effectiveness | WGS = whole genome sequencing

Primary VE analyses among participants >12 years of age are shown in bold. Primary analyses include all contributing COVID-19 case viruses. Displayed subset analyses explore VE with restriction based upon WGS, namely: restriction to case viruses that were (n=235) or were not (n=74) successfully characterized by WGS, excluding 1 case virus for which WGS remains pending. Among case viruses successfully sequenced by WGS, VE analyses were further limited to the subset identified as XFG-lineage case viruses (Pango nomenclature) [2]. Case viruses not successfully characterized by WGS include those failed sequencing (n = 29) as well as those not sequenced due to cycle threshold >30 (n=45, all from Ontario).

Current vaccination status based upon provincial immunization registry documentation of 2025/26 LP.8.1 COVID-19 vaccine receipt. Analyses restricted to participants >12 years from the provinces of British Columbia (BC), Ontario or Quebec. VE assessed at >2 weeks post-vaccination; participants vaccinated <2 weeks before illness onset excluded. VE analyses are without regard to prior COVID-19 vaccination history and exclude influenza infections from COVID-19 controls (retaining influenza co-infections among COVID-19 cases). All estimates are adjusted for age group (12-49, 50-64, >65 years), province (BC, Ontario, Quebec), and calendar time (based upon specimen collection date, bi-weekly except weeks 07 to 09). TSV refers to interval between 2025/26 COVID-19 vaccination and acute respiratory illness onset among vaccinated participants, except those for whom onset date is unknown, assigned instead based on specimen collection date (n=9)

Conclusions: effectiveness of COVID-19 vaccines

- In a population with high levels of infection- and/or vaccine-induced immunity, compared to no 2024-2025 vaccine dose, **2024-2025 COVID-19 vaccination**
  - provided additional **protection against medically attended COVID-19-associated illness** among children and adults, including adults with immunocompromise
  - provided additional **protection against COVID-19-associated critical illness** among adults; protection appeared to be higher and more robust against the most severe outcomes compared to less severe outcomes

- Interim VE estimates indicate **2025-2026 COVID-19 vaccination** provided additional protection against **COVID-19-associated emergency department and urgent care visits and hospitalizations** compared to no 2025-2026 vaccine dose among adults with and without immunocompromise.

Conclusions: effectiveness of COVID-19 vaccines

- **During 2023-2024 and 2024-2025, mRNA COVID-19 vaccines protected against severe COVID-19, including during periods of increased genetic divergence from vaccine strains**
  - Protection was stable against SARS-CoV-2 viruses with low to moderate genetic divergence but durability was diminished against highly divergent lineages

- **Early data suggest the 2025-2026 COVID-19 vaccines provide protection against non-LP.8.1 lineage SARS-CoV-2 viruses.**

Acknowledgements

CDC staff

VISION collaborators

IVY collaborators

Backup Slides

Measuring COVID-19 vaccine effectiveness

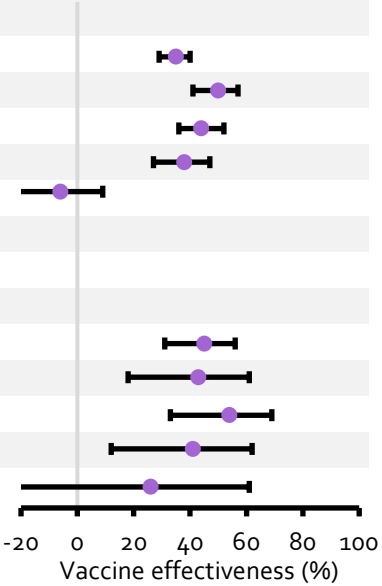
Measure	Definition*	Example vaccinated group	Example comparison group
Absolute VE	Compares frequency of health outcomes in vaccinated and unvaccinated people	Received original monovalent dose	Received no COVID-19 vaccines ever
Relative VE	Compares frequency of health outcomes in people who received one 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 vaccination	Received 2023-2024 dose	Eligible for, but did not receive, an 2023-2024 dose, regardless of past 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 vaccination	Received 2024-25 dose	Eligible for, but did not receive, an 2024-25 dose, regardless of past vaccination history

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

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

September 2024 – September 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)	3,210 (79)	41,005 (68)	1,012 (597-1,244)	**Ref**
Received 2024-2025 COVID-19 dose 7–299 days earlier	829 (21)	18,914 (32)	125 (68-193)	**35 (29-40)**
2024-2025 COVID-19 dose, 7–59 days earlier	175 (4)	4,071 (7)	34 (20-47)	**50 (41-57)**
2024-2025 COVID-19 dose, 60–119 days earlier	221 (5)	4,918 (8)	90 (75-104)	**44 (36-52)**
2024-2025 COVID-19 dose, 120–179 days earlier	173 (4)	4,359 (7)	148 (133-163)	**38 (27-47)**
2024-2025 COVID-19 dose, 180–299 days earlier	260 (6)	5,566 (9)	228 (202-259)	**-6 (-22-9)**
IVY				
No 2024-2025 COVID-19 dose (Ref)	835 (87)	1,880 (76)	Not available	**Ref**
Received 2024-2025 COVID-19 dose 7–254 days earlier	127 (13)	608 (24)	107 (63–153)	**45 (31-56)**
2024-2025 COVID-19 dose, 7–59 days earlier	43 (4)	126 (5)	32 (20–46)	**43 (18-61)**
2024-2025 COVID-19 dose, 60–119 days earlier	37 (4)	212 (9)	89 (74–104)	**54 (33-69)**
2024-2025 COVID-19 dose, 120–179 days earlier	32 (3)	193 (8)	148 (132–163)	**41 (12-62)**
2024-2025 COVID-19 dose, 180–254 days earlier	15 (2)	77 (3)	197 (190–209)	**26 (-31 to 61)**



IQR = interquartile range | VE = vaccine effectiveness | CI = confidence interval

VISION results from: Wiegand, et al. (2026). *JAMA Intern Med*, in press. IVY results from: Ma, et al. (2026). *JAMA Network Open.*

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, Charlson Comorbidity Index, 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.

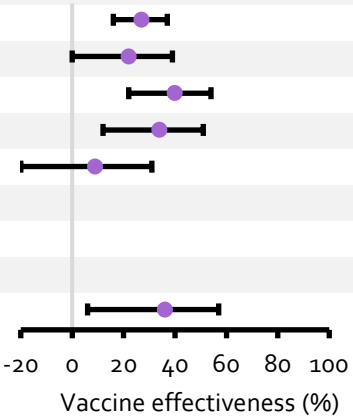
* IVY Network data span September 2024 to April 2025.

† Interval since last dose is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, or 2024-2025 COVID-19 vaccine for the VISION Network.

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

September 2024 – September 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)	835 (75)	13,074 (64)	965 (531-1,232)	**Ref**
Received 2024-2025 COVID-19 dose 7–299 days earlier	279 (25)	7,478 (36)	129 (71-194)	**27 (16 to 37)**
2024-2025 COVID-19 dose, 7–59 days earlier	78 (7)	1,474 (7)	35 (20-47)	**22 (0 to 39)**
2024-2025 COVID-19 dose, 60–119 days earlier	72 (6)	1,944 (9)	89 (75-104)	**40 (22 to 54)**
2024-2025 COVID-19 dose, 120–179 days earlier	57 (5)	1,756 (9)	148 (133-163)	**34 (12 to 51)**
2024-2025 COVID-19 dose, 180–299 days earlier	72 (6)	2,304 (11)	229 (202-259)	**9 (-20 to 31)**
IVY				
No 2024-2025 COVID-19 dose (Ref)	213 (82)	691 (74)	Not available	**Ref**
Received 2024-2025 COVID-19 dose 7–257 days earlier	47 (18)	248 (26)	101 (54-147)	**36 (6 to 57)**



IQR = interquartile range | VE = vaccine effectiveness | CI = confidence interval

VISION results from: Wiegand, et al. (2026). *JAMA Intern Med*, in press. IVY results from: Ma, et al. (2026). *JAMA Network Open.*

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. 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.

* IVY Network data span September 2024 to April 2025.

† Interval since last dose is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, or 2024-2025 COVID-19 vaccine for the VISION Network.

Characteristics of emergency department and urgent care encounters and hospitalizations among immunocompetent adults aged ≥18 years with COVID-19-like illness, by COVID-19 case status — VISION

September 2025–March 2026

Characteristic	Vaccine effectiveness network and setting, no. (column %)					
	VISION ED/UC encounters, all adults aged ⩾18 years			VISION hospitalizations, all adults aged ⩾18 years		
	Total	COVID-19 case-patients	COVID-19 control-patients	Total	COVID-19 case-patients	COVID-19 control-patients
Total	**151,233**	**6,205**	**145,028**	**45,240**	**1,707**	**43,533**
Median age [IQR]	56 [36–74]	56 [35–73]	56 [36–74]	72 [60–82]	77 [66–85]	72 [60–82]
Age group						
18-64 years	91,737 (61)	3,824 (62)	87,913 (61)	14,736 (33)	385 (23)	14,351 (33)
≥65 years	59,496 (39)	2,381 (38)	57,115 (39)	30,504 (67)	1,322 (77)	29,182 (67)
Median UMC categories [IQR]*	1 [0–3]	1 [0–3]	1 [0–3]	4 [2–7]	4 [1–6]	4 [2–7]

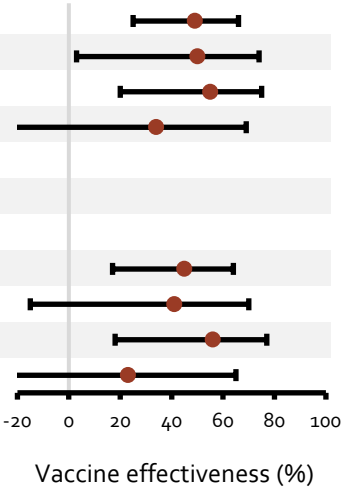
ED/UC = emergency department/urgent care | UMC=underlying medical condition

*Defined as the presence of a relevant ICD-10 code in the encounter discharge diagnosis. UMC categories considered: cardiovascular; cerebrovascular; endocrine; gastrointestinal; hematologic; musculoskeletal/neurologic; pulmonary; and renal.

Effectiveness of 2025–2026 COVID-19 vaccination against COVID-19–associated critical illness among immunocompetent adults by age group — VISION

September 2025 – March 2026

2025-2026 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 2025-2026 COVID-19 dose (Ref)	299 (91)	36,166 (83)	1,186 (456-1,502)	**Ref**
Received 2025-2026 COVID-19 dose 7–179 days earlier	28 (9)	7,367 (17)	81 (45-116)	**49 (25 to 66)**
2025-2026 COVID-19 dose, 7–59 days earlier	9 (3)	2,546 (6)	33 (20-47)	**50 (3 to 74)**
2025-2026 COVID-19 dose, 60–119 days earlier	12 (4)	3,120 (7)	89 (74-104)	**55 (20 to 75)**
2025-2026 COVID-19 dose, 120–179 days earlier	7 (2)	1,701 (4)	141 (129-155)	**34 (-43 to 69)**
≥65 years				
No 2025-2026 COVID-19 dose (Ref)	221 (89)	22,832 (78)	1,066 (417-1,470)	**Ref**
Received 2025-2026 COVID-19 dose 7–179 days earlier	26 (11)	6,350 (22)	82 (45-117)	**45 (17 to 64)**
2025-2026 COVID-19 dose, 7–59 days earlier	9 (4)	2,163 (7)	33 (20-46)	**41 (-15 to 70)**
2025-2026 COVID-19 dose, 60–119 days earlier	10 (4)	2,701 (9)	89 (74-104)	**56 (18 to 77)**
2025-2026 COVID-19 dose, 120–179 days earlier	7 (3)	1,486 (5)	141 (129-156)	**23 (-68 to 65)**



IQR = interquartile range | VE = vaccine effectiveness | CI = confidence interval

Vaccine effectiveness was calculated by comparing the odds of 2025–2026 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 2025–2026 dose" group included all eligible persons who did not receive a 2025–2026 COVID-19 vaccine dose, regardless of number of previous COVID-19 vaccine doses.

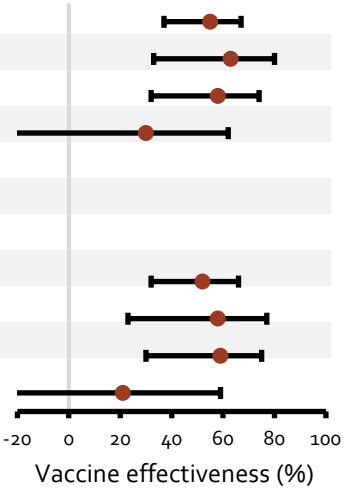
Critical illness is defined as admission to the intensive care unit or in-hospital death.

* Interval since last dose is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, 2024-2025, or 2025-2026 COVID-19 vaccine.

Effectiveness of 2025–2026 COVID-19 vaccination against COVID-19–associated hospitalization among immunocompromised adults by age group — VISION

September 2025 – April 2026

2025-2026 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 2025-2026 COVID-19 dose (Ref)	393 (91)	11,572 (79)	1,084 (421-1,470)	**Ref**
Received 2025-2026 COVID-19 dose 7–179 days earlier	41 (9)	3,028 (21)	79 (45-116)	**55 (37 to 67)**
2025-2026 COVID-19 dose, 7–59 days earlier	11 (3)	1,078 (7)	34 (22-47)	**63 (33 to 80)**
2025-2026 COVID-19 dose, 60–119 days earlier	18 (4)	1,258 (9)	88 (73-104)	**58 (32 to 74)**
2025-2026 COVID-19 dose, 120–179 days earlier	12 (3)	692 (5)	142 (131-157)	**30 (-29 to 62)**
≥65 years				
No 2025-2026 COVID-19 dose (Ref)	284 (17)	7,354 (17)	817 (390-1,433)	**Ref**
Received 2025-2026 COVID-19 dose 7–179 days earlier	38 (2)	2,548 (6)	80 (46-116)	**52 (32 to 66)**
2025-2026 COVID-19 dose, 7–59 days earlier	11 (1)	875 (2)	34 (22-47)	**58 (23 to 77)**
2025-2026 COVID-19 dose, 60–119 days earlier	16 (1)	1,083 (2)	89 (73-104)	**59 (30 to 75)**
2025-2026 COVID-19 dose, 120–179 days earlier	11 (1)	590 (1)	141 (131-157)	**21 (-52 to 59)**



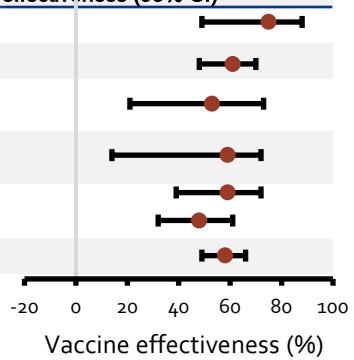
IQR = interquartile range | VE = vaccine effectiveness | CI = confidence interval

Vaccine effectiveness was calculated by comparing the odds of 2025–2026 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 2025–2026 dose" group included all eligible persons who did not receive a 2025–2026 COVID-19 vaccine dose, regardless of number of previous COVID-19 vaccine doses (if any) received).

* Interval since last dose is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, 2024-2025, or 2025-2026 COVID-19 vaccine.

Summary of estimates of effectiveness of 2025–2026 COVID-19 vaccination against COVID-19–associated outcomes among adults aged ≥65 years

Study	Study design	Location	Outcome	Median interval since last dose among vaccinated, days (IQR)	Adjusted vaccine effectiveness (95% CI)
Appaneal, et al. (2026)*Nat Commun.*	TND	United States	hospitalization	30 (22-43)	**75 (49 to 88)**
Holm-Hansen, et al. (2026). *Lancet Infect Dis*	Cohort	Denmark	hospitalization	84*	**61 (48 to 70)**
Skowronski, et al. (2026). *Euro Surveill*	TND	Canada	medically attended	cases: 52.5 (35-94.5) controls: 63 (35-91)	**53 (21 to 73)**
Delaunay, et al. (2026). *SSRN*	TND	Europe	medically attended	cases: 36 (34-50) controls: 36 (23-54)	**59 (14 to 83)**
Vicic, et al. (2026). *medRxiv.*	Cohort	United States	hospitalization	mRNA-1283: 69 (42–95) BNT162b2: 70 (44–94)	**mRNA-1283: 59 (39 to 73)** **BNT162b2: 48 (32 to 61)**
VISION†	TND	United States	hospitalization	82 (45-117)	**58 (49 to 66)**



TND = test-negative design | VE = vaccine effectiveness | CI = confidence interval

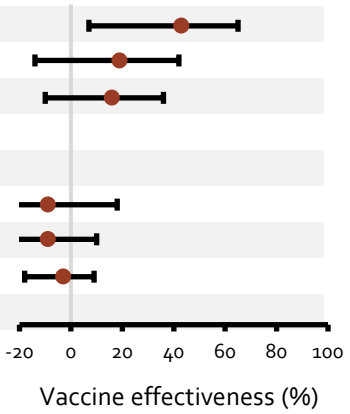
*Average follow-up days

†Vaccine effectiveness was calculated by comparing the odds of 2025–2026 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 2025–2026 dose" group included all eligible persons who did not receive a 2025–2026 COVID-19 vaccine dose, regardless of number of previous COVID-19 vaccine doses.

COVID-19 vaccine effectiveness against SARS-CoV-2 infection, by household contact vaccination status – RIGHT

January 2024 - January 2025

Time since COVID-19 vaccination	Adjusted vaccine effectiveness (95% CI)
Primary case participant	
⩽6 mo	43 (7 to 65)
7-12 mo	19 (-14 to 42)
>12 mo	16 (-10 to 36)
Unvaccinated	0 [Reference]
Household contact	
≤6 mo	-9 (-44 to 18)
7-12 mo	-9 (-33 to 10)
>12 mo	-3 (-18 to 9)
Unvaccinated	0 [Reference]



VE = vaccine effectiveness | CI = confidence interval

Benist, et al. (2026). *JNO*.

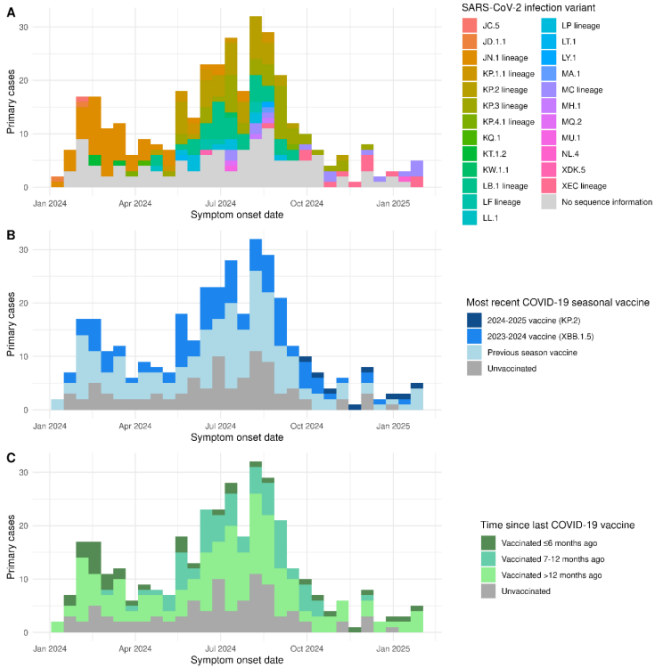
Vaccine effectiveness was calculated as 1 minus the adjusted relative risk. The adjusted relative risk was estimated using a modified Poisson regression model accounting for clustering at the household level and adjusting for the primary case participant COVID-19 vaccination status, household contact COVID-19 vaccination status, primary case participant age, household contact age, enrollment state, total number of people in the household, and enrollment period.

*Only SARS-CoV-2 sequences that passed quality control rules were included in analyses. To display all lineages, direct sub lineages were grouped.

†Vaccine season refers to the most recent COVID-19 vaccine received by the participant categorized as receiving a 2024-2025 COVID-19 vaccine, a 2023-2024 COVID-19 vaccine, or during a previous season prior to release of 2023-2024 COVID-19 vaccines.

§COVID-19 vaccination timing was defined according to months from the most recent dose to primary case participant onset.

(A)Frequency of SARS-CoV-2 PANGO Lineage* | (B)Most Recent COVID-19 Season Vaccine Received† | (C) Time Since the Most Recent COVID-19 Vaccine§ by Symptom Onset Date Among Primary Case Participants (n = 362)



IVY Network study design for COVID-19 vaccine effectiveness by genetic differences between variant and vaccine composition

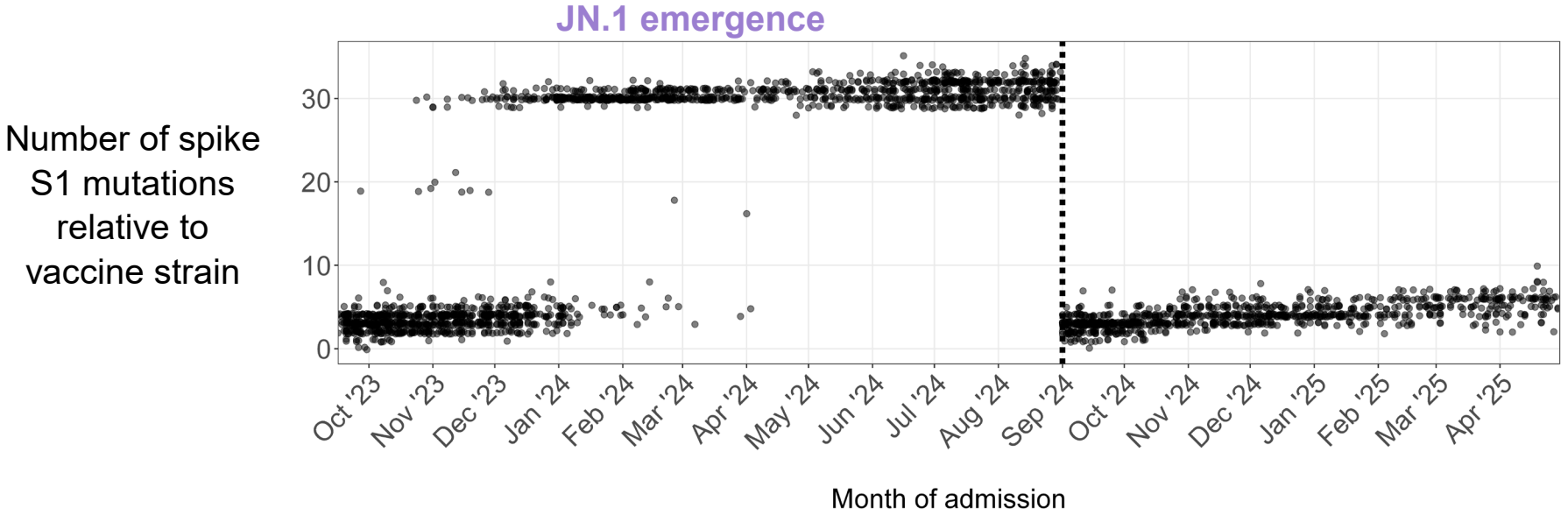
- **Design**: Test-negative, case-control
- **Study period:** September 13, 2023 to April 30, 2025
- **Population**: Adults hospitalized with COVID-19-like illness who received SARS-CoV-2 testing within 10 days of illness onset and 3 days of admission
  - **Cases:** COVID-19-like illness, test *positive* for SARS-CoV-2 by NAAT or antigen, SARS-CoV-2 successfully sequenced from a clinical specimen
  - **Controls**: COVID-19-like illness and test *negative* for SARS-CoV-2
- **Exposure:** receipt of the current COVID-19 mRNA vaccine, as determined by electronic medical records, state and city registries, or plausible self-report
  - XBB.1.5-adapted vaccines were used during 2023–2024, and KP.2-adapted vaccines were used during 2024–2025
  - Novavax vaccine was excluded due to low counts

Statistical analysis for COVID-19 vaccine effectiveness by genetic differences between variant and vaccine composition

- Multinomial regression was used to estimate the odds of COVID-19 vaccination between cases with varying S1 spike mutation count categories and test-negative controls
- Odds ratios were adjusted for continuous age, sex (male, female), race/ethnicity (Hispanic or Latino, non-Hispanic Black, non-Hispanic White, non-Hispanic other race, unknown), HHS region, cubic spline of admission date, season of hospitalization, and Charlson comorbidity index category (0, 1–2, 3–4, 5–6, ≥7)
- VE against COVID-19–associated hospitalization for each spike mutation category was calculated as (1 − adjusted odds ratio) × 100%
- VE can wane naturally due to antibody decay, so VE was further stratified by time since dose receipt in 90-day windows

Number of SARS-CoV-2 spike protein S1 domain mutations relative to the COVID-19 mRNA vaccine strain by date of hospitalization

September 2023–April 2025, IVY Network



Number of SARS-CoV-2 spike protein S1 domain mutations relative to the COVID-19 mRNA vaccine strain by days since COVID-19 vaccine first available

September 2023–April 2025, IVY Network