Centers for Disease Control and Prevention
National Center for Immunization and Respiratory Diseases

Vaccine effectiveness of updated (2023-2024) COVID-19 vaccines

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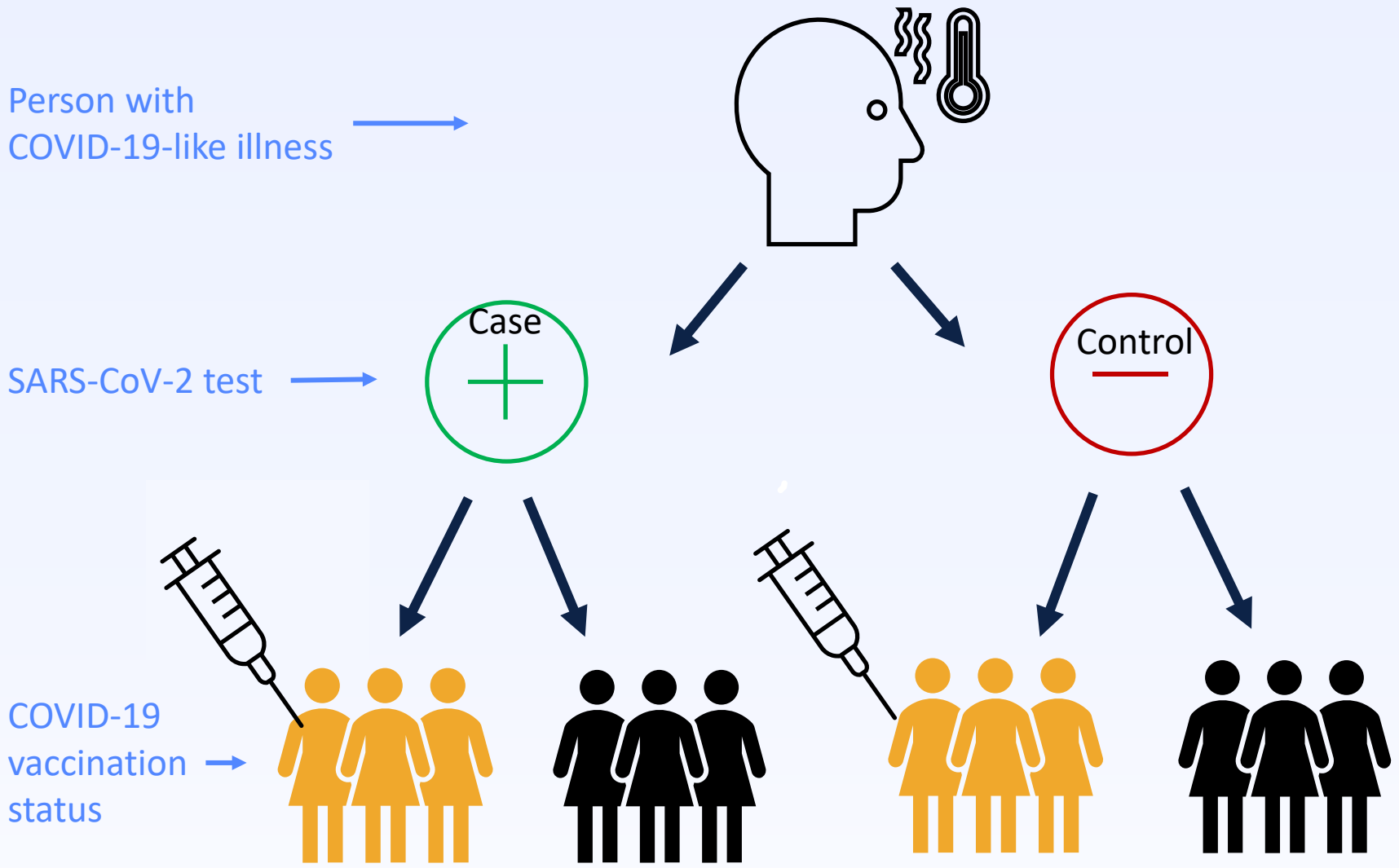
Agenda: vaccine effectiveness (VE) of updated 2023-24 COVID-19 vaccines

- VE refresher
- Context for interpretation of VE
- VE against:
  - Symptomatic SARS-CoV-2, Increasing Community Access to Testing (ICATT) program
  - COVID-19-associated emergency department/urgent care encounters, VISION Network
  - COVID-19-associated hospitalizations, VISION and IVY Networks

Test negative design



Vaccine effectiveness = (1 – adjusted odds ratio)*100%

$$\text{where odds ratio} = \frac{\text{Odds of vaccination in cases}}{\text{Odds of vaccination in controls}}$$

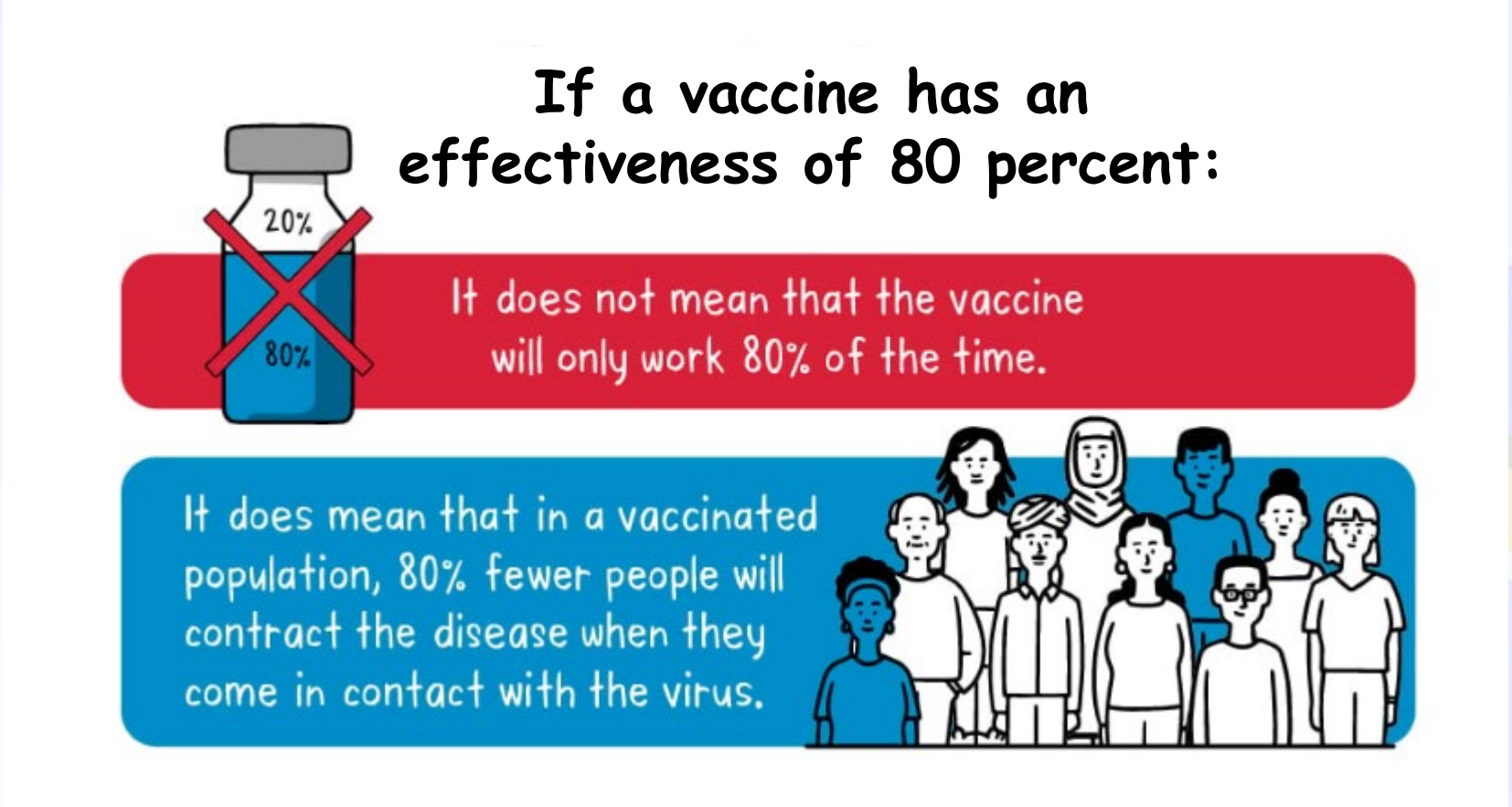
Slide adapted from Amadea Britton.

Test negative design

- Benefits
  - Reduces bias from health-care seeking behavior by including cases and controls who presented to care and received testing (usually at the same facility)
  - Efficient use of an existing surveillance system
- Considerations
  - Dependent on sensitivity and specificity of diagnostic testing
  - Controls + for another vaccine preventable disease can bias results. Sensitivity analyses dropping RSV+ and flu+ positive controls can be helpful.

Slide adapted from Amadea Britton.

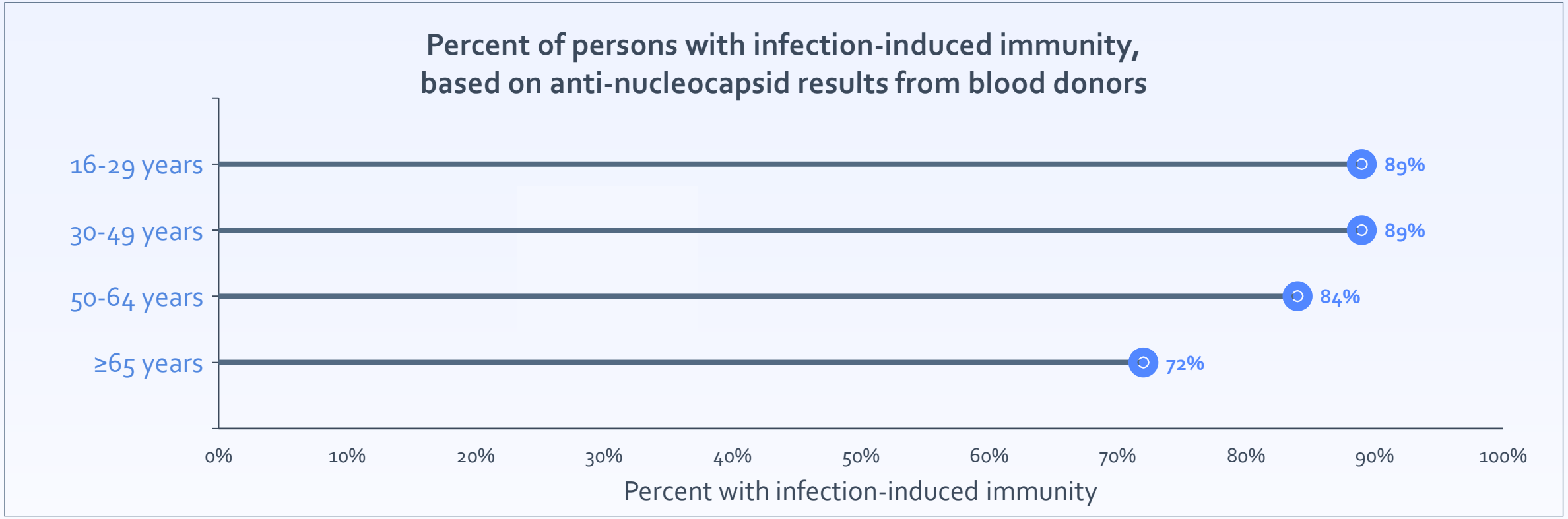
Efficacy and effectiveness are population level estimates.



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

Context for interpreting VE across age groups

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



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

* Internal CDC data. Data on persons aged ≥16 years is from a longitudinal, national cohort of >35,000 blood donors.

Measuring updated (2023-2024) COVID-19 VE

- **Previously for COVID-19 VE**:
  - **Absolute VE**: comparing the frequency of health outcomes in vaccinated and unvaccinated people
    - Example: comparing outcomes in people vaccinated with an updated (2023-24) dose versus no COVID-19 vaccine received ever
  - **Relative VE**: comparing the frequency of health outcomes in people who received one type of vaccine to people who received a different vaccine or by comparing people who received more vaccine doses to those who received fewer doses
    - Example: comparing outcomes in people vaccinated with an updated (2023-24) dose versus no updated (2023-24) dose
- **Analyses presented today:**
  - Vaccinated group: received updated (2023-24) dose
  - Comparison group: eligible for, but did not receive, an updated (2023-24) dose, regardless of past vaccination history

Updates to vaccine effectiveness against symptomatic infection

Increasing Community Access to Testing (ICATT) program

Data updated from MMWR published February 1, 2024:

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

Increasing Community Access to Testing: VE from national pharmacy testing data

- Nationwide community-based drive-through SARS-CoV-2 testing via pharmacies
- Self-reported vaccine history at time of registration for SARS-CoV-2 testing*
- **Design**: Test-negative analysis**
- **Population**: Adults ≥18 years with ≥1 COVID-like symptom and nucleic acid amplification testing (NAAT)
- **Major exclusion criteria:** Individuals with immunocompromising conditions, reported a positive SARS-CoV-2 test in preceding 90 days***
- **Periods for analysis:**
  - Full analysis included tests from September 21, 2023 – February 18, 2024
  - Sub-analysis using SGTF**** included tests from October 27, 2023 – February 15, 2024

*At 5% of testing encounters, COVID-19 vaccination status is collected by clinician interview

**Odds ratios were calculated using multivariable logistic regression, adjusting for single year of age, gender, race/ethnicity, SVI of the testing location (<0.5 versus ≥0.5), pharmacy contractor, underlying conditions (presence versus absence), U.S. Department of Health and Human Services region of testing location, and date of testing

***Additional exclusion criteria: 1) reported receiving Novavax as their most recent dose and reported receiving <2 total COVID-19 vaccine doses; 2) reported receiving a Janssen (Johnson & Johnson) COVID-19 vaccine dose after May 12, 2023; 3) received most recent dose <7 days prior to the date of testing or during September 1-12, 2023; or 4) registered for testing with a version of the questionnaire that only reported month and year of the most recent vaccine dose rather than calendar date.

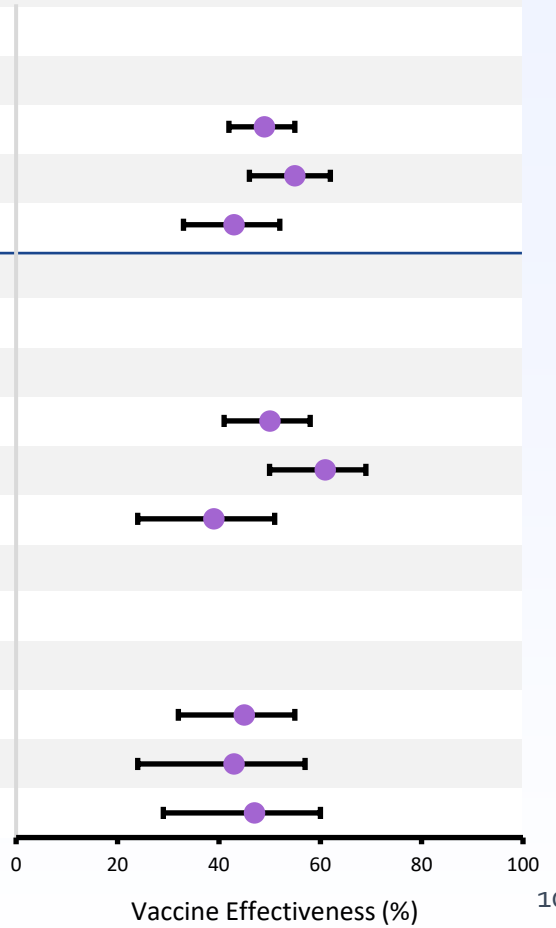
**** Results of spike gene (S-gene) amplification in real-time reverse transcription–polymerase chain reaction (RT-PCR) can be used to distinguish certain SARS-CoV-2 lineages over time (2). S-gene target presence (SGTP) was detected in most lineages that circulated in 2023, including XBB lineages, whereas S-gene target failure (SGTF) is detected in JN.1 and other BA.2.86 lineages

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

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

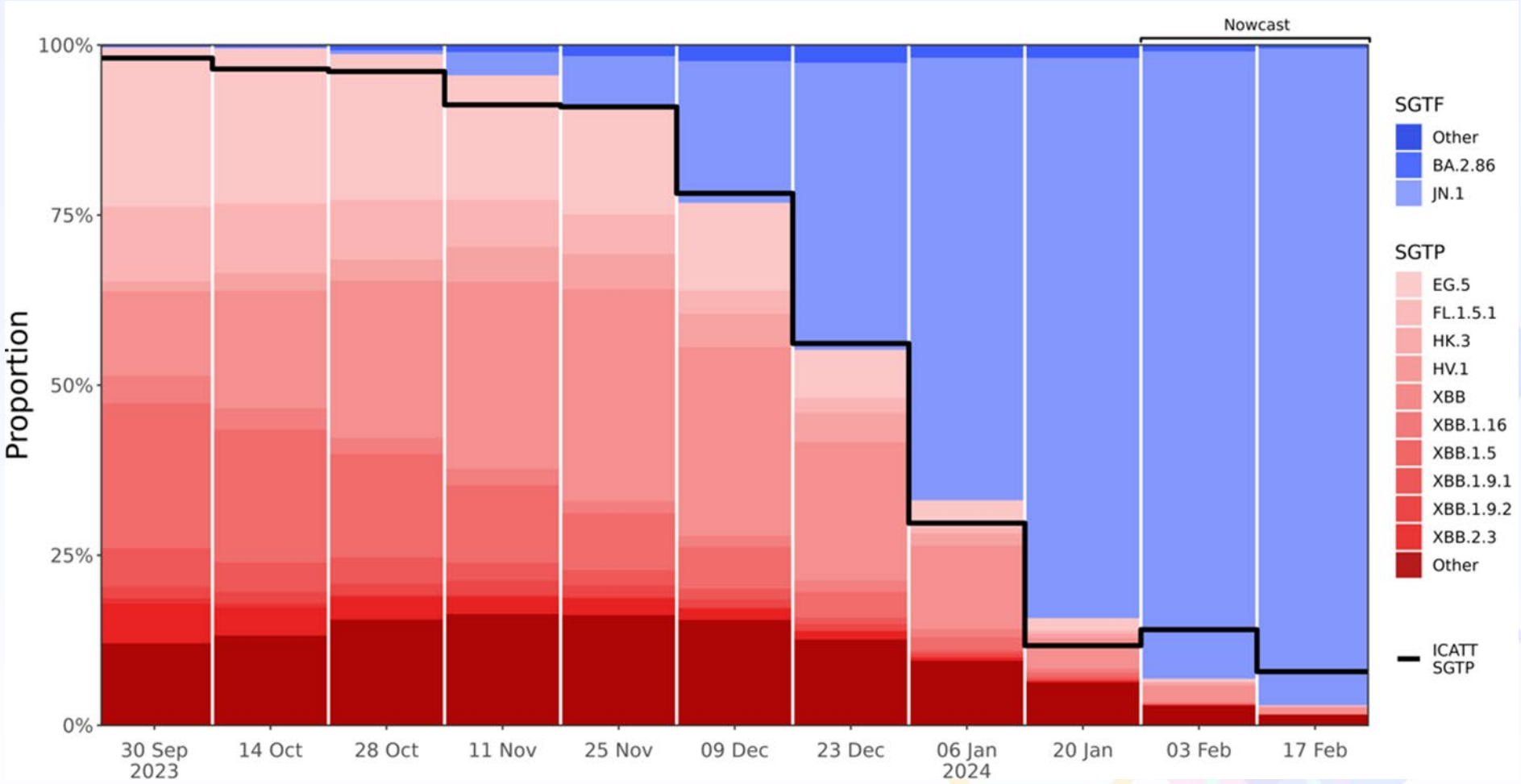
September 2023 – February 2024

COVID-19 dosage pattern/age group	Total tests	SARS-CoV-2-test-positive, N (%)	Median interval since last dose among vaccinated among those vaccinated, days (IQR)	Adjusted VE (95% CI)
≥18 years				
No updated (2023-2024) monovalent dose (ref)	10,829	4,080 (38)	676 (427 to 859)	**Ref**
Updated (2023-2024) monovalent dose, ≥7 days	1,537	408 (27)	61 (33 to 86)	**49 (42 – 55)**
Updated (2023-2024) monovalent dose, 7-59 days earlier	735	170 (23)	32 (20 to 46)	**55 (46 – 62)**
Updated (2023-2024) monovalent dose, 60-119 days earlier	720	214 (30)	82 (71 to 95)	**43 (33 – 52)**
18-49 years				
No updated (2023-2024) monovalent dose (ref)	8,676	3,152 (36)	691 (439 to 877)	**Ref**
Updated (2023-2024) monovalent dose, ≥7 days	943	229 (24)	61 (34 to 85)	**50 (41 – 58)**
Updated (2023-2024) monovalent dose, 7-59 days earlier	452	87 (19)	32 (19 to 46)	**61 (50 – 69)**
Updated (2023-2024) monovalent dose, 60-119 days earlier	445	130 (29)	81 (70 to 94)	**39 (24 – 51)**
≥50 years				
No updated (2023-2024) monovalent dose (ref)	2,153	928 (43)	593 (400 to 800)	**Ref**
Updated (2023-2024) monovalent dose, ≥7 days	594	179 (30)	62 (32 to 89)	**45 (32 – 55)**
Updated (2023-2024) monovalent dose, 7-59 days earlier	283	83 (29)	32 (21 to 44)	**43 (24 – 57)**
Updated (2023-2024) monovalent dose, 60-119 days earlier	275	84 (31)	84 (72 to 98)	**47 (29 – 60)**



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

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



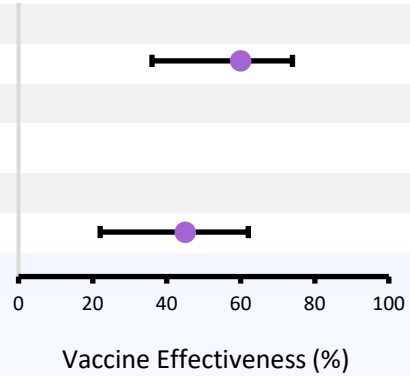
Specimen collection date (2-week period ending)

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

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

October 2023 – February 2024

COVID-19 dosage pattern/age group	Total tests	SARS-CoV-2 negative: No. (row %)	SARS-CoV-2 negative: Median interval since last dose among vaccinated, days (IQR)	SARS-CoV-2 positive: N (row %)	SARS-CoV-2 positive: Median interval since last dose among vaccinated, days (IQR)	Adjusted VE (95% CI)
SGT presence (likely non-JN.1)						
No updated (2023-2024) monovalent dose (ref)	2,497	1,705 (68)	659 (403 to 820)	422 (17)	671 (405 to 801)	**Ref**
Updated (2023-2024) monovalent dose, 60-119 days earlier	329	252 (77)	84 (72 to 98)	25 (8)	73 (69 to 83)	**60 (36 to 74)**
SGT failure (likely JN.1)						
No updated (2023-2024) monovalent dose (ref)	2,497	1,705 (68)	659 (403 to 820)	370 (15)	682 (426 to 822)	**Ref**
Updated (2023-2024) monovalent dose, 60-119 days earlier	329	252 (77)	84 (72 to 98)	52 (16)	86 (72 to 95)	**45 (22 to 62)**



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

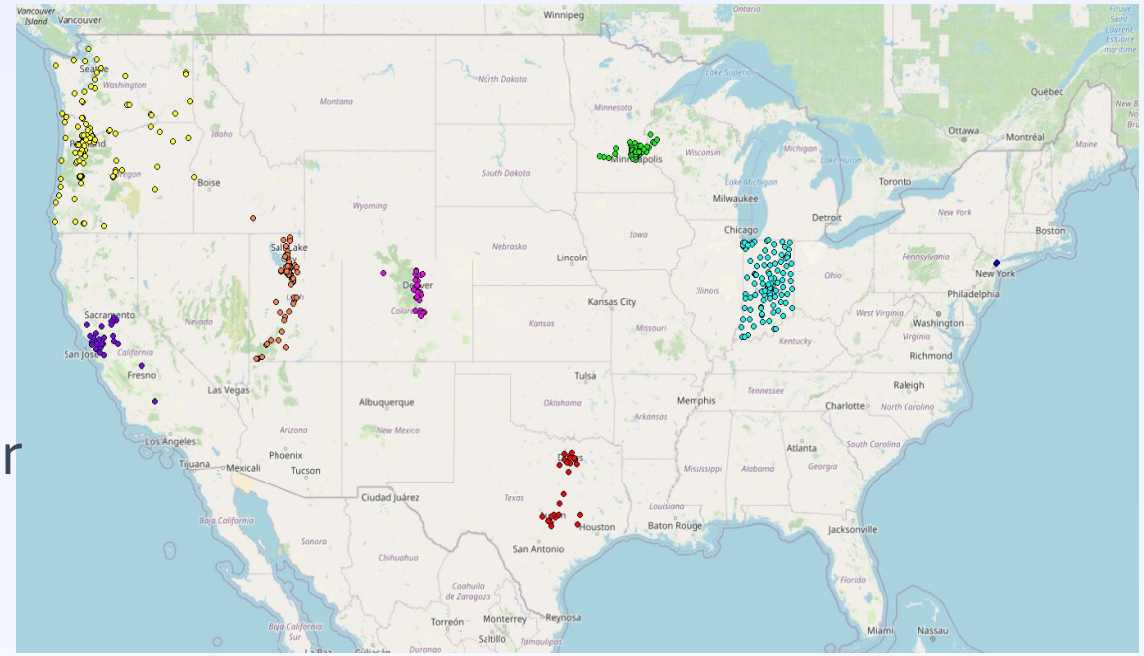
VISION ED/UC

Joint VISION/IVY MMWR to be published February 29, 2024

VISION Multi-Site Network of Electronic Health Records

369 emergency rooms and urgent cares/229 hospitals

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

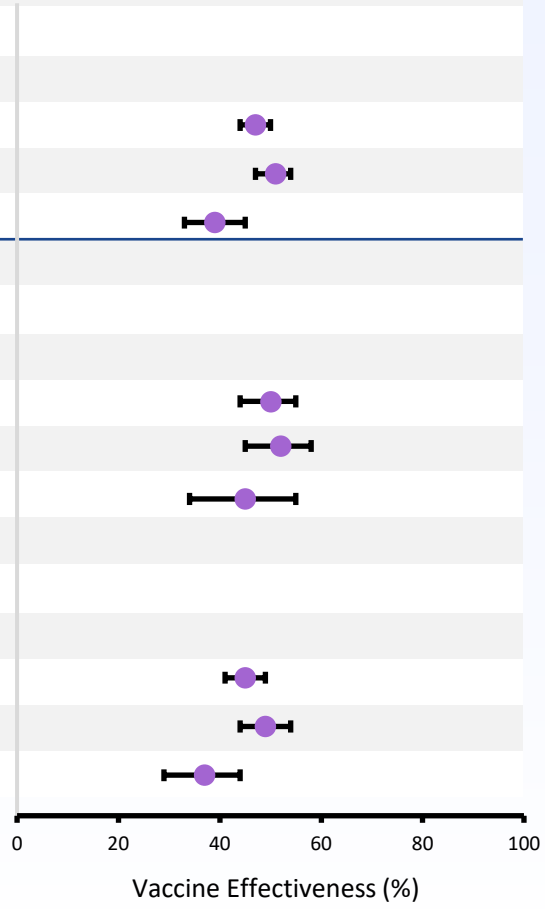


- **Vaccination data:** Documented by electronic health records and state and city registries

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

September 2023 – January 2024

COVID-19 dosage pattern/age group	COVID-19 case-patients N (Col %)	COVID-19 control-patients N (Col %)	Median interval since last dose among vaccinated among those vaccinated, days (IQR)	Adjusted VE (95% CI)
≥18 years				
No updated (2023-2024) monovalent dose (ref)	15,932 (92)	98,218 (88)	669 (403-792)	**Ref**
Updated (2023-2024) monovalent dose, ≥7 days	1,297 (8)	13,378 (12)	44 (26-64)	**47 (44-50)**
Updated (2023-2024) monovalent dose, 7-59 days earlier	825 (5)	9,372 (8)	33 (20-46)	**51 (47-54)**
Updated (2023-2024) monovalent dose, 60-119 days earlier	472 (3)	4,006 (4)	74 (66-83)	**39 (33-45)**
18-64 years				
No updated (2023-2024) monovalent dose (ref)	10,582 (97)	69,423 (94)	697 (480-832)	**Ref**
Updated (2023-2024) monovalent dose, ≥7 days	377 (3)	4,739 (6)	42 (24-62)	**50 (44-55)**
Updated (2023-2024) monovalent dose, 7-59 days earlier	259 (2)	3,457 (5)	31 (19-45)	**52 (45-58)**
Updated (2023-2024) monovalent dose, 60-119 days earlier	118 (1)	1,282 (2)	73 (66-83)	**45 (34-55)**
≥65 years				
No updated (2023-2024) monovalent dose (ref)	5,350 (85)	28,795 (77)	509 (362-733)	**Ref**
Updated (2023-2024) monovalent dose, ≥7 days	920 (15)	8,639 (23)	46 (27-66)	**45 (41-49)**
Updated (2023-2024) monovalent dose, 7-59 days earlier	566 (9)	5,915 (16)	33 (21-46)	**49 (44-54)**
Updated (2023-2024) monovalent dose, 60-119 days earlier	354 (6)	2,724 (7)	74 (66-83)	**37 (29-44)**



VE estimates adjusted for age, sex, race and ethnicity, geographic region, and calendar time. MMWR to be published February 29, 2024

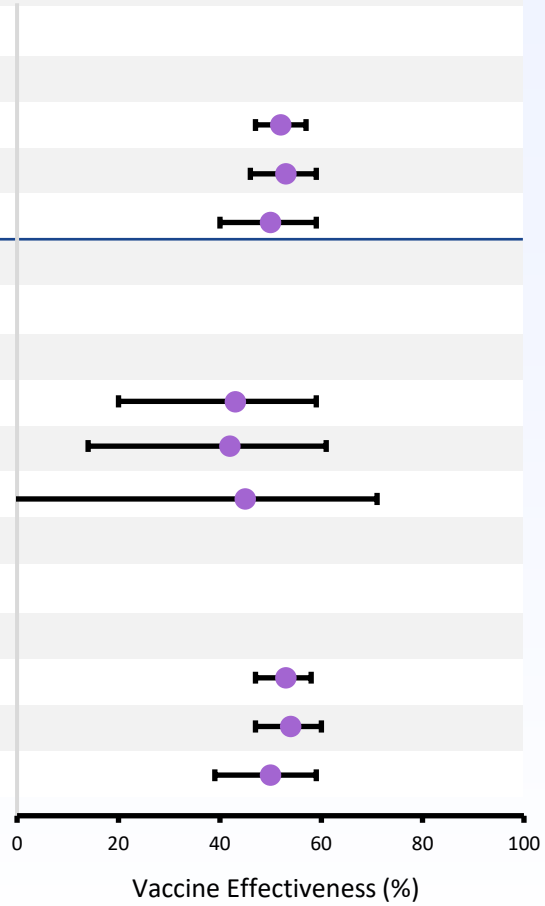
VISION/IVY Hospitalization

Joint VISION/IVY MMWR to be published February 29

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

September 2023 – January 2024

COVID-19 dosage pattern/age group	COVID-19 case-patients N (Col %)	COVID-19 control-patients N (Col %)	Median interval since last dose among vaccinated among those vaccinated, days (IQR)	Adjusted VE (95% CI)
≥18 years				
No updated (2023-2024) monovalent dose (ref)	4,194 (91)	28,715 (87)	627 (383-765)	**Ref**
Updated (2023-2024) monovalent dose, ≥7 days	395 (9)	4,199 (13)	42 (24-62)	**52 (47-57)**
Updated (2023-2024) monovalent dose, 7-59 days earlier	270 (6)	3,056 (9)	32 (19-45)	**53 (46-59)**
Updated (2023-2024) monovalent dose, 60-119 days earlier	125 (3)	1,143 (3)	73 (66-81)	**50 (40-59)**
18-64 years				
No updated (2023-2024) monovalent dose (ref)	938 (96)	11,342 (95)	685 (447-829)	**Ref**
Updated (2023-2024) monovalent dose, ≥7 days	38 (4)	657 (5)	38 (22-58)	**43 (20-59)**
Updated (2023-2024) monovalent dose, 7-59 days earlier	28 (3)	503 (4)	30 (19-44)	**42 (14-61)**
Updated (2023-2024) monovalent dose, 60-119 days earlier	10 (1)	154 (1)	74 (67-81)	**45 (-6-71)***
≥65 years				
No updated (2023-2024) monovalent dose (ref)	3,256 (90)	17,373 (83)	549 (370-745)	**Ref**
Updated (2023-2024) monovalent dose, ≥7 days	357 (10)	3,542 (17)	43 (25-62)	**53 (47-58)**
Updated (2023-2024) monovalent dose, 7-59 days earlier	242 (7)	2,553 (12)	32 (19-46)	**54 (47-60)**
Updated (2023-2024) monovalent dose, 60-119 days earlier	115 (3)	989 (5)	73 (66-81)	**50 (39-59)**



VE estimates adjusted for age, sex, race and ethnicity, geographic region, and calendar time. MMWR to be published February 29, 2024

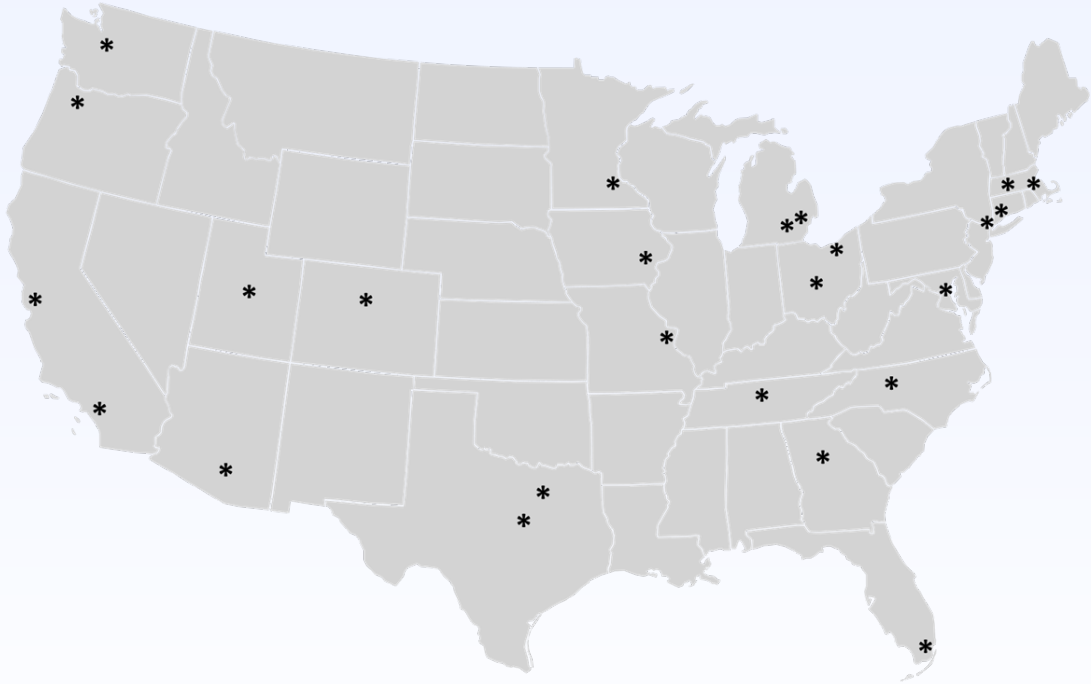
*Some estimates are imprecise, which might be due to a relatively small number of persons in each level of vaccination or case status. This imprecision indicates that the actual VE could be substantially different from the point estimate shown, and estimates should therefore be interpreted with caution.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

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

- **Design**: Case-control, prospective enrollment
- **Population**: Adults aged ≥18 years hospitalized with Acute respiratory illness (ARI)*
  - **Cases:** ARI and test *positive* for SARS-CoV-2 by NAAT or antigen test within 10 days of illness and not positive for influenza or RSV
  - **Controls**: ARI and test *negative* for SARS-CoV-2 and influenza by NAAT within 10 days of illness
- **Vaccination data:** Electronic medical records (EMR), state and city registries, and self-report
- **Specimens:** Upper respiratory specimens obtained for central RT-qPCR testing and sequencing

IVY

INVESTIGATING RESPIRATORY VIRUSES IN THE ACUTELY ILL

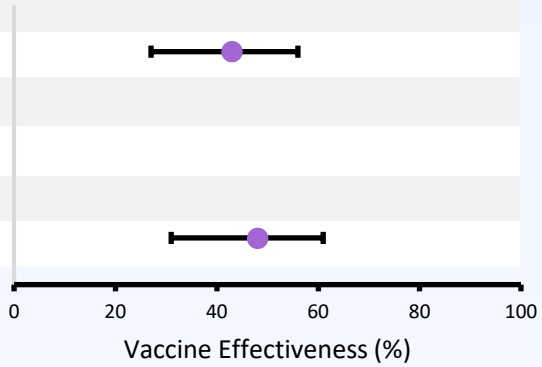


*ARI is defined as presence of any one of the following: fever, cough, shortness of breath, chest imaging consistent with pneumonia, hypoxemia

IVY: VE of *2023-2024 vaccine* against *hospitalization* among immuno*competent* adults aged ≥18 years, by age group

September 2023 – January 2024

COVID-19 dosage pattern/age group	COVID-19 case-patients N (Col %)	COVID-19 control-patients N (Col %)	Median interval since last dose among vaccinated among those vaccinated, days (IQR)	Adjusted VE (95% CI)
≥18 years				
No updated (2023-2024) monovalent dose (ref)	1100 (92)	2570 (88)	645 (387-781)	**Ref**
Updated (2023-2024) monovalent dose, ≥7 days	94 (8)	353 (12)	47 (25-71)	**43 (27 to 56)**
≥65 years				
No updated (2023-2024) monovalent dose (ref)	747 (91)	1284 (84)	573 (375-752)	**Ref**
Updated (2023-2024) monovalent dose, ≥7 days	76 (9)	245 (16)	48 (26-72)	**48 (31 to 61)**



VE estimates adjusted for age, sex, race and ethnicity, geographic region, and calendar time. MMWR to be published February 29, 2024

Conclusions

- Updated (2023-2024) COVID-19 vaccination provided increased protection against symptomatic SARS-CoV-2 infection and COVID-19-associated ED/UC visits and hospitalizations compared to no updated vaccine dose.
- Receipt of updated (2023-2024) COVID-19 vaccine provides protection against JN.1 and other circulating variants
- These are relatively early estimates from all 3 VE studies with no substantial waning; however, waning is expected, and CDC will continue monitoring VE

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