COVID-19 vaccine effectiveness updates

24 February 2023

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Organization of presentation

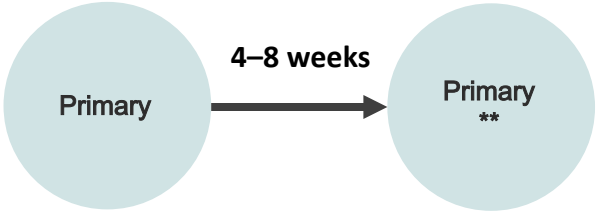
- Preliminary vaccine effectiveness (VE) of monovalent vaccines against *symptomatic infection* in children aged 6 months–4 years (Pfizer-BioNTech) and 6 months–5 years (Moderna)
- Update on VE of bivalent vaccines against *symptomatic infection* in children and adolescents aged 5-17 years and adults aged ≥18 years
- Update on VE of bivalent vaccines against *severe disease* in adults with a focus on adults aged ≥ 65 years

Preliminary Estimates of Effectiveness of Monovalent mRNA Vaccines in Preventing Symptomatic SARS-CoV-2 Infection Among Children Aged 3–5 Years — Increasing Community Access to Testing Program, United States, July 2022–February 2023

Fleming-Dutra KE, Ciesla AA, Roper, LE et al. Preliminary Estimates of Effectiveness of Monovalent mRNA Vaccines in Preventing Symptomatic SARS-CoV-2 Infection Among Children Aged 3–5 Years — Increasing Community Access to Testing Program, United States, July 2022–February 2023. MMWR Morb Mortal Wkly Rep 2023;72:177–182. DOI: http://dx.doi.org/10.15585/mmwr.mm7207a3

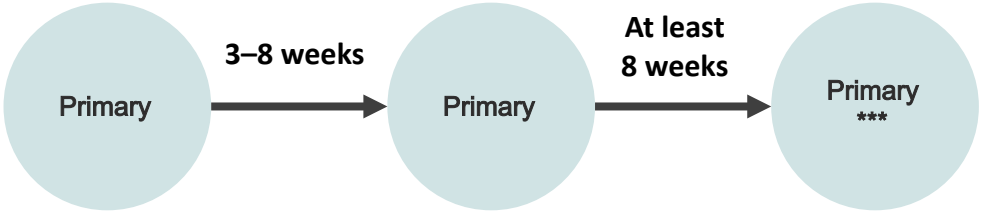
Pediatric COVID-19 Vaccine Primary Series Schedule*: Ages 6 months–5 years (Moderna) and 6 months–4 years (Pfizer-BioNTech)

Ages 6 months–5 years
(Primary Series: **Moderna**)



Earliest date for a child to have a "complete series"= August 1, 2022

Ages 6 months–4 years
(Primary Series: **Pfizer-BioNTech**)



Earliest date for a child to have a "complete series"= September 19, 2022

*On June 18, 2022, ACIP issued interim recommendations for the use of the Moderna COVID-19 vaccine for children aged 6 months–5 years and for the Pfizer-BioNTech COVID-19 vaccine for children aged 6 months–4 years.
** As of December 9, 2022, children who received 2 doses of monovalent Moderna vaccine are recommended to receive a single bivalent booster dose at least 2 months after their last primary series dose.
***As of December 9, 2022, children who received 2 doses of monovalent Pfizer-BioNTech vaccine primary series are recommended to receive a bivalent dose as their third dose.

Percent of people receiving COVID-19 vaccine by age and date administered – United States, December 14, 2020 – February 15, 2023

	<2 yrs	2-4 yrs	5-11 yrs	12-17 yrs	18-24 yrs	25-49 yrs	50-64 yrs	+65 yrs
At Least One Dose	7.7%	10.3%	39.7%	71.9%	81.9%	85.2%	95.0%	95.0%
Completed Primary Series	3.8%	5.5%	32.6%	61.6%	66.5%	72.0%	83.7%	94.2%
Updated (Bivalent) Booster Dose	0.2%	0.3%	4.1%	7.1%	6.7%	11.3%	20.5%	41.0%

https://covid.cdc.gov/covid-data-tracker/#vaccination-demographics-trends

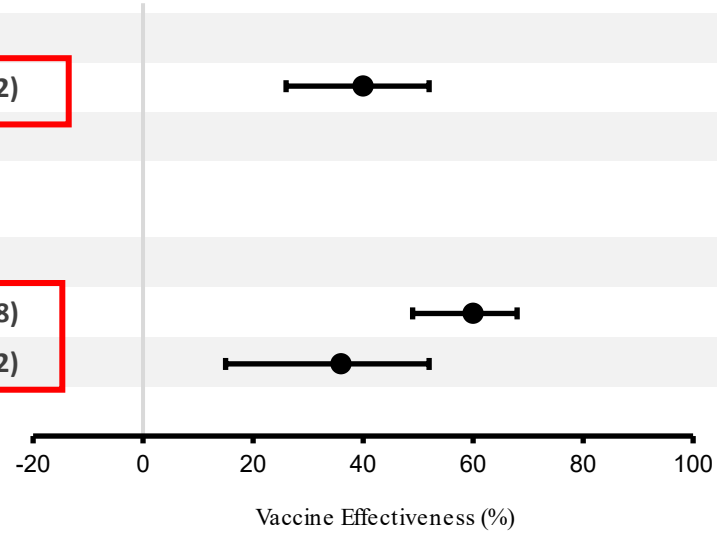
Increasing Community Access to Testing (ICATT) Program: VE of monovalent COVID-19 vaccines against *symptomatic infection* in children aged 3-5 years

- Nationwide community-based drive-through SARS-CoV-2 testing via pharmacies
- Self-reported vaccine history at time of registration for COVID-19 testing
- **Design**: Test-negative, case-control analysis*
- **Population**: Immunocompetent children 3 – 4/5** years with ≥1 COVID-like symptom and nucleic acid amplification testing (NAAT)
- **Period for analysis:**
  - Tested: July 4, 2022*** – February 5, 2023, BA.4/BA.5 predominant period, but includes XBB

*Models adjusted for: age, gender, race, ethnicity, social vulnerability index and HHS region of the testing location, underlying conditions (presence versus absence), pharmacy chain conducting the test, local incidence (cases per 100,000 by individual county and state in the 7 days before test date), and date of testing.
** ICATT testing is generally limited to children ages 3 and up.
***Analysis start date depended on vaccine/dose number being analyzed: Pfizer and Moderna 1st doses started 7/4/2022; Pfizer 2nd dose started 7/25/2022; Moderna 2nd dose started 8/1/2022; Pfizer 3rd dose started 9/19/2022.

ICATT: Preliminary estimates of VE for primary series monovalent Moderna vaccine (children aged 3–5 years) against *symptomatic infection*, July 4, 2022 – February 5, 2023

Vaccination status (months since last dose)	Total tests	SARS-CoV-2 positive, N (%)	Adjusted VE (95% CI)
Moderna, 1 dose (partial series; ages 3-5 years) *July 4, 2022 – February 5, 2023*			
Unvaccinated	34,982	9,523 (27)	**Ref**
1 **monovalent** dose (2 weeks–1 month)*	509	107 (21)	**40 (26 to 52)**
Moderna, 2 doses (complete series; ages 3-5 years) *August 1, 2022 – February 5, 2023*			
Unvaccinated	25,049	5,690 (23)	**Ref**
2 **monovalent** doses (2 weeks–2 months)*	816	81 (10)	**60 (49 to 68)**
2 **monovalent** doses (3–4 months)*	495	58 (12)	**36 (15 to 52)**

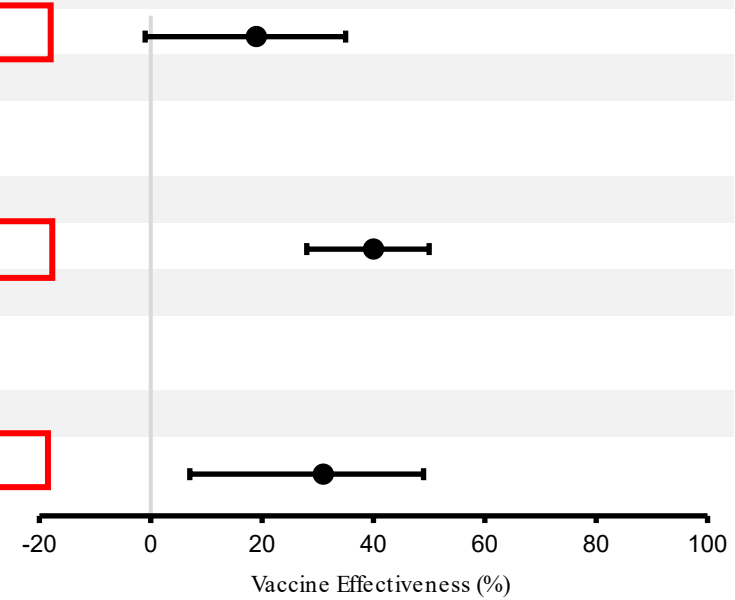


Fleming-Dutra, Ciesla, Roper, et al. MMWR February 16, 2023.

*Test registrants who report receiving COVID-19 vaccines are asked to report the total number of doses and manufacturer(s) of vaccines received and for the most recent dose, month and year of receipt; therefore, the number of months between a vaccine dose and testing is a whole number calculated as the difference between the month and year of testing and the month and year of the vaccine dose. For doses received in the same month or the month before SARS-CoV-2 testing, an additional question was asked to specify whether the dose was received ≥2 weeks before testing, and only doses received ≥2 weeks before testing were included. 17% and 21% of children who received 1 and 2 doses of Moderna, respectively, reported a prior infection >90 days before the current test.

ICATT: Preliminary estimates of VE for primary series monovalent Pfizer-BioNTech vaccine (children aged 3–4 years) against *symptomatic infection*, July 4, 2022 – February 5, 2023

Vaccination status (months since last dose)	Total tests	SARS-CoV-2 positive, N (%)	Adjusted VE (95% CI)
Pfizer, 1 dose (partial series; ages 3–4 years) *July 4, 2022–February 5, 2023*			
Unvaccinated	22,323	6,212 (28)	**Ref**
1 **monovalent** dose (2 weeks–1 month)*	443	114 (26)	**19 (-1 to 35)**
Pfizer, 2 doses (partial series; ages 3–4 years) *July 25, 2022–February 5, 2023*			
Unvaccinated	17,434	4,298 (25)	**Ref**
2 **monovalent** doses (2 weeks–3 months)*	933	137 (15)	**40 (28 to 50)**
Pfizer, 3 doses (complete series; ages 3–4 years)** *September 19, 2022–February 5, 2023*			
Unvaccinated	7,548	1,273 (17)	**Ref**
3 **monovalent** doses (2 weeks–4 months)*	395	53 (13)	**31 (7 to 49)**



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*Test registrants who report receiving COVID-19 vaccines are asked to report the total number of doses and manufacturer(s) of vaccines received and for the most recent dose, month and year of receipt; therefore, the number of months between a vaccine dose and testing is a whole number calculated as the difference between the month and year of testing and the month and year of the vaccine dose. For doses received in the same month or the month before SARS-CoV-2 testing, an additional question was asked to specify whether the dose was received ≥2 weeks before testing, and only doses received ≥2 weeks before testing were included. 18%, 19% and 21% of children who received 1, 2, and 3 doses of Pfizer, respectively, reported a prior infection >90 days before the current test.

**There was insufficient power to stratify Pfizer-BioNTech 3-dose VE estimates by time since vaccination.

Limitations

- Vaccine coverage is low in children ≤5 years. VE estimates may be less stable when vaccine coverage is low.
- Prevalence of prior infection in children is high*; consequently, vaccine effectiveness in this analysis reflects the current situation among young children in the United States.
- Low vaccination coverage in this age group may impact future ability to estimate VE, including against more severe outcomes.

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

Conclusions

- Complete monovalent primary vaccination series helped provide protection for children aged 3–5 years against *symptomatic* SARS-CoV-2 infection for at least the first 4 months after vaccination.
- Waning of monovalent Moderna primary series might occur by 3–4 months after the second dose based on point estimates (although confidence intervals overlapped). This is similar to patterns observed in older children and adults in the first months after vaccination.
  - Waning of monovalent Pfizer-BioNTech VE against symptomatic infection could not be assessed but is also likely based on analyses in older children and adults.
- Children should stay up to date with COVID-19 vaccines, including completing the primary series; those who are eligible should receive a bivalent vaccine dose.
- CDC will continue to monitor VE in this age group, including against severe disease and for bivalent doses.

Updated estimates of bivalent VE against symptomatic infection among children and adolescents aged 5–17 and adults aged ≥18 years

Interpreting absolute and relative vaccine effectiveness

- **Absolute VE:** comparing the frequency of health outcomes in vaccinated and unvaccinated people
  - E.g., comparing outcomes in people vaccinated with an updated bivalent booster versus no vaccine at all
- **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
  - E.g., comparing outcomes in people vaccinated with an updated bivalent booster versus monovalent vaccine only
- In the analyses presented today, relative vaccine effectiveness can be interpreted as the ***additional protection provided by an updated bivalent booster*** among people who already received monovalent COVID-19 vaccines

ICATT: *Relative* VE of bivalent booster against *symptomatic infection* in children and adolescents aged 5–17 years and adults aged ≥18 years

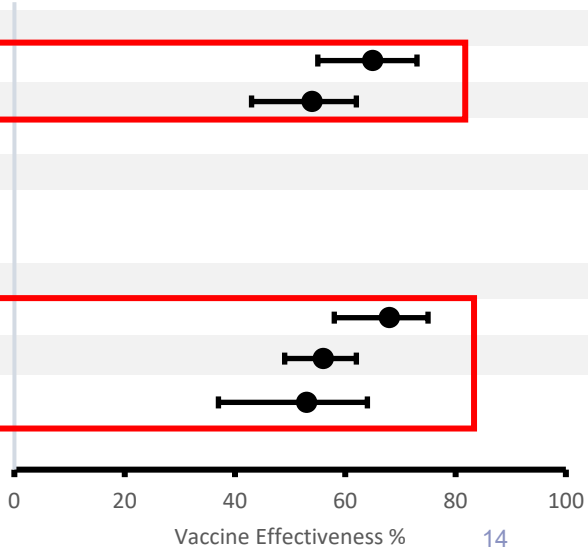
- Nationwide community-based drive-through SARS-CoV-2 testing via pharmacies
- Self-reported vaccine history at time of registration for COVID-19 testing
- **Design**: Test-negative, case-control analysis*
- **Population**: Children and adolescents aged 5–17 years and adults aged ≥18 years with ≥1 COVID-like symptom and nucleic acid amplification testing (NAAT)
- **Exclusion criteria:** Excluded individuals <4 months from last monovalent dose and individuals with immunocompromising conditions
- **Periods for analysis:**
  - Tested: December 1, 2022 – February 13, 2023**
  - Includes periods of both BA.5-related sublineage and XBB/XBB.1.5 sublineage predominance

*Models adjusted for: age, gender, race, ethnicity, social vulnerability index and HHS region of the testing location, underlying conditions (presence versus absence), local incidence (cases per 100,000 by individual county and state in the 7 days before test date), and date of testing

**Analysis is an update of data published in Link-Gelles R, Ciesla AA, Roper LE, et al. Early estimates of bivalent mRNA booster dose vaccine effectiveness in preventing symptomatic SARS-CoV-2 infection attributable to SARS-CoV-2 Omicron BA.5-related and XBB/XBB.1.5-related sublineages among immunocompetent adults—Increasing Community Access to Testing Program, United States, December 2022–January 2023. MMWR Morb Mortal Wkly Rep 2023;72. https://www.cdc.gov/mmwr/volumes/72/wr/mm7205e2.htm

ICATT: *Relative* VE of bivalent booster against *symptomatic infection* in children and adolescents aged 5–17 years, December 1, 2022 – February 13, 2023*

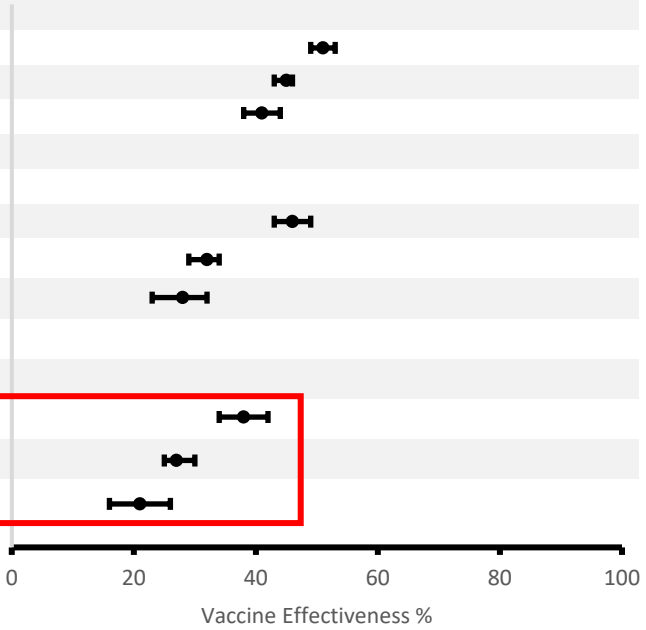
Age group, years/mRNA Dosage Pattern	Total tests	SARS-CoV-2 positive tests, N (row %)	Adjusted VE (95% CI)
5-11 years (*authorized for bivalent booster on October 12, 2022*)			
Received 2-3 monovalent doses only (Ref)	4,855	1,433 (30)	**Ref**
2 weeks-1 month since bivalent booster	600	73 (12)	**65 (55 to 73)**
2-3 months since bivalent booster	881	139 (16)	**54 (43 to 62)**
4-5 months since bivalent booster	58	10 (17)	----
12-17 years *(authorized for bivalent booster on September 1, 2022)*			
Received 2-3 monovalent doses only (Ref)	8,243	3,194 (39)	**Ref**
2 weeks-1 month since bivalent booster	443	73 (16)	**68 (58 to 75)**
2-3 months since bivalent booster	1,122	230 (20)	**56 (49 to 62)**
4-5 months since bivalent booster	283	68 (24)	**53 (37 to 64)**



*Unpublished CDC data.

ICATT: *Relative* VE of bivalent booster against *symptomatic infection* in adults aged ≥18 years, December 1, 2022 – February 13, 2023*

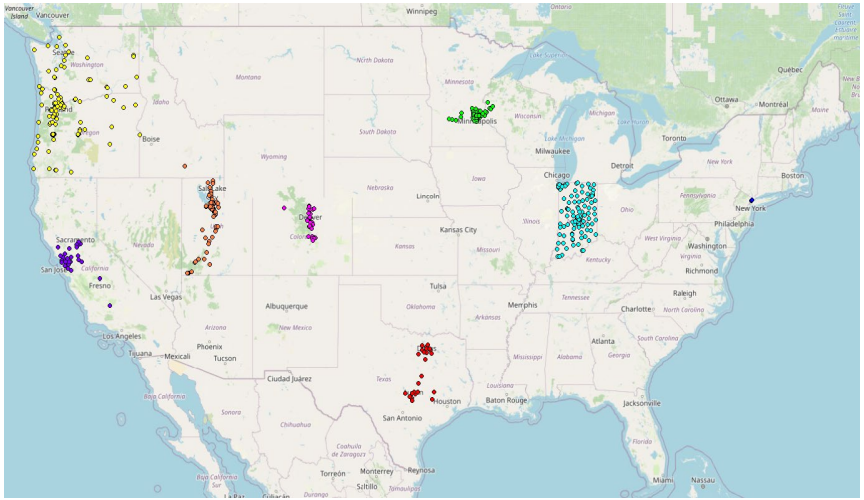
Age group, years/mRNA Dosage Pattern	Total tests	SARS-CoV-2 positive tests, N (row %)	Adjusted VE (95% CI)
18-49 years			
Received 2-3 monovalent doses only (Ref)	182,741	82,043 (45)	**Ref**
2 weeks-1 month since bivalent booster	10,758	3,127 (29)	**51 (49 to 53)**
2-3 months since bivalent booster	32,577	10,206 (31)	**45 (43 to 46)**
4-5 months since bivalent booster	9,197	2,882 (31)	**41 (38 to 44)**
50-64 years			
Received 2-4 monovalent doses only (Ref)	60,822	31,878 (52)	**Ref**
2 weeks-1 month since bivalent booster	6,223	2,331 (37)	**46 (43 to 49)**
2-3 months since bivalent booster	18,399	7,898 (43)	**32 (29 to 34)**
4-5 months since bivalent booster	4,837	2,030 (42)	**28 (23 to 32)**
≥65 years			
Received 2-4 monovalent doses only (Ref)	28,307	14,246 (50)	**Ref**
2 weeks-1 month since bivalent booster	4,579	1,788 (39)	**38 (34 to 42)**
2-3 months since bivalent booster	19,071	8,080 (42)	**27 (25 to 30)**
4-5 months since bivalent booster	5,796	2,431 (42)	**21 (16 to 26)**



*Unpublished CDC data.

Updated estimates of bivalent VE against emergency department/urgent care encounters and hospitalizations among adults aged ≥18 years, VISION Network

VISION Multi-State Network of Electronic Health Records

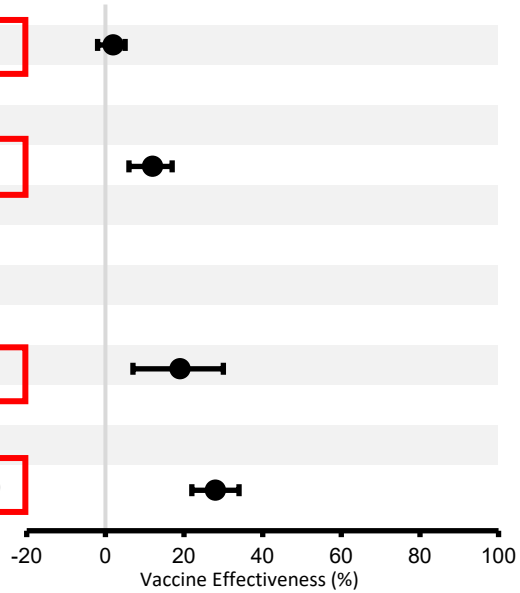


- **Cases**: COVID-like illness (CLI) with positive PCR for SARS-CoV-2 within 14 days before or 72 hours after the admission or encounter
- **Controls**: CLI with negative PCR for SARS-CoV-2

- Variant periods designated for analysis based on time when novel sublineage became predominant at study site
- VE adjusted for age, sex, race, ethnicity, geographic region, calendar time, and local rates of SARS-CoV-2 circulation
- Vaccination documented by electronic health records and state and city registries

VISION: *Absolute* VE of ≥2 monovalent doses against *ED/UC encounters* and *hospitalizations* among adults aged ≥18 years– September 2022 – January 2023*

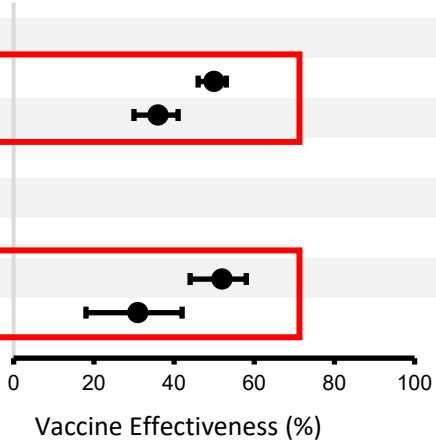
mRNA Dosage Pattern	Total tests	SARS-CoV-2-test-positive, N (%)	Median interval since last dose, days (IQR)	Adjusted VE (95% CI)
Emergency department/urgent care encounters				
Aged 18-64 years				
Unvaccinated (Ref)	56,560	6,632 (12)	—	Ref
Monovalent doses only, last dose ≥2 months earlier	79,203	8,848 (11)	370 (300-508)	**2 (-2 to 5)**
Aged ≥65 years				
Unvaccinated (Ref)	11,277	2,026 (18)	—	Ref
Monovalent doses only, last doses ≥2 months earlier	37,505	5,588 (15)	335 (196-424)	**12 (6 to 17)**
Hospitalizations				
Aged 18-64 years				
Unvaccinated (Ref)	6,213	475 (8)	—	Ref
Monovalent doses only, last doses ≥2 months earlier	7,250	501 (7)	360 (281-502)	**19 (7 to 30)**
Aged ≥65 years				
Unvaccinated (Ref)	4,795	819 (17)	—	Ref
Monovalent doses only, last doses ≥2 months earlier	14,462	1924 (13)	337 (205-439)	**28 (22 to 34)**



*Unpublished CDC data.

VISION: *Relative* VE of bivalent booster against *ED/UC encounters* and *hospitalizations* among adults aged ≥18 years –September 2022 – January 2023*

mRNA Dosage Pattern	Total tests	SARS-CoV-2-test-positive, N (%)	Median interval since last dose, days (IQR)	Adjusted VE (95% CI)
Emergency department/urgent care encounters				
Monovalent doses only, last dose ≥2 months earlier	112,857	13,429 (12)	359 (279-496)	Ref
Bivalent booster, 7-59 days earlier	12,546	948 (8)	33 (20-46)	**50 (46 to 53)**
Bivalent booster, 60-119 days earlier	5,952	617 (10)	76 (67-87)	**36 (30 to 41)**
Hospitalizations				
Monovalent doses only, last dose ≥2 months earlier	28,227	3,187 (11)	348 (243-484)	Ref
Bivalent booster, 7-59 days earlier	2,809	202 (7)	32 (19-45)	**52 (44 to 58)**
Bivalent booster, 60-119 days earlier	1,281	155 (12)	74 (67-85)	**31 (18 to 42)**



*Unpublished CDC data.

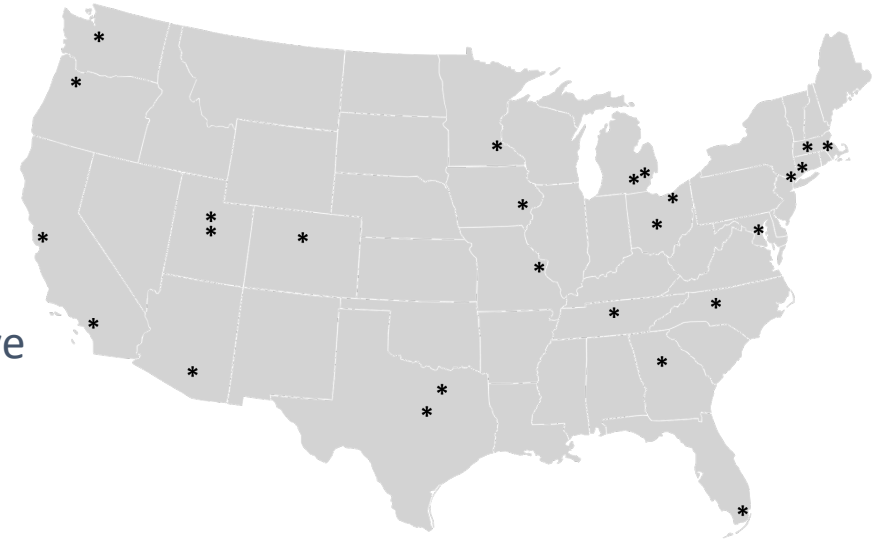
Preliminary estimates of bivalent VE against hospitalizations among adults aged ≥65 years, IVY Network

IVY Network — 24 hospitals, 19 U.S. States

- **Design**: Prospective test-negative, case-control
- **Period**: September 8, 2022–January 30, 2023
- **Population**: Immunocompetent adults hospitalized with COVID-like illness (CLI)
- **Participants have CLI and SARS-CoV-2 test:**
  - **Cases:** SARS-CoV-2-positive by RT-PCR or antigen
  - **Controls:** SARS-CoV-2- and influenza-negative by RT-PCR
- **VE adjustments:** Age, sex, race/ethnicity, admission date (biweekly), and HHS region

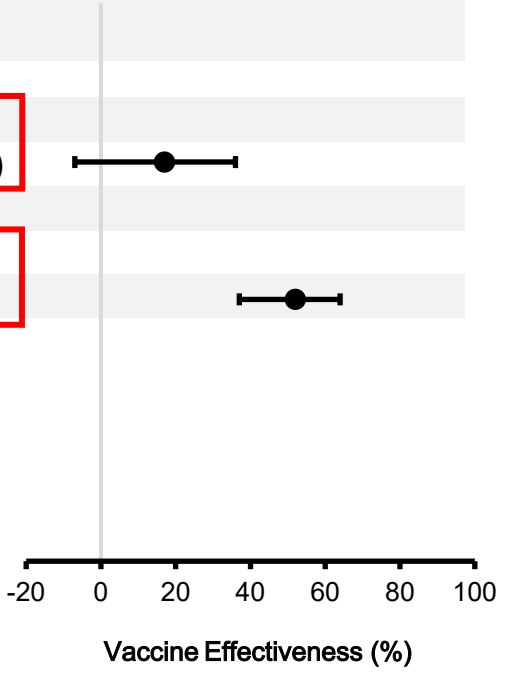
IVY

INVESTIGATING RESPIRATORY VIRUSES IN THE ACUTELY ILL



IVY: *Absolute* VE of ≥2 monovalent doses and *relative* VE of bivalent booster against COVID-19 *hospitalizations* among *adults aged ≥65 years* — IVY Network, September 8, 2022–January 30, 2023*

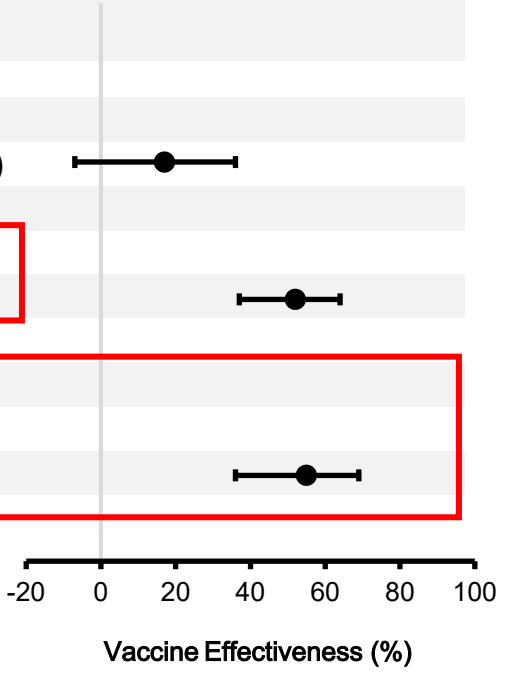
	Vaccinated cases, N/total cases (%)	Vaccinated controls, N/total controls (%)	Median interval since last dose, days (IQR)	Adjusted VE, % (95% CI)
***Absolute* monovalent VE against hospitalization**				
Unvaccinated (Ref)			--	**Ref**
≥2 Monovalent doses, last dose ≥2 months earlier	550/707 (78)	645/810 (80)	352 (224-432)	**17 (-7 to 36)**
***Relative* bivalent VE against hospitalization**				
≥2 Monovalent doses, last dose ≥2 months earlier (Ref)			352 (224-432)	**Ref**
Bivalent booster dose, ≥7 days earlier	108/658 (16)	255/900 (28)	56 (30–84)	**52 (37–64)**



*Unpublished CDC data.

IVY: *Absolute* VE of ≥2 monovalent doses and *relative* VE of bivalent booster against COVID-19 *hospitalizations* among *adults aged ≥65 years* — IVY Network, September 8, 2022–January 30, 2023*

	Vaccinated cases, N/total cases (%)	Vaccinated controls, N/total controls (%)	Median interval since last dose, days (IQR)	Adjusted VE, % (95% CI)
***Absolute* monovalent VE against hospitalization**				
Unvaccinated (Ref)			--	**Ref**
≥2 Monovalent doses, last dose ≥2 months earlier	550/707 (78)	645/810 (80)	352 (224-432)	**17 (-7 to 36)**
***Relative* bivalent VE against hospitalization**				
≥2 Monovalent doses, last dose ≥2 months earlier (Ref)			352 (224-432)	**Ref**
Bivalent booster dose, ≥7 days earlier	108/658 (16)	255/900 (28)	56 (30–84)	**52 (37–64)**
***Absolute* bivalent VE against hospitalization**				
Unvaccinated (Ref)			--	**Ref**
Bivalent booster dose, ≥7 days earlier	108/265 (41)	255/420 (61)	56 (30–84)	**55 (36–69)**



*Unpublished CDC data.

IVY: *Severity of COVID-19 hospitalizations* in bivalent booster VE analysis among adults aged ≥65 years — IVY Network, September 8, 2022–January 30, 2023*

Characteristic	Case-patients, N (%) N = 719**
Hypoxemia	427 (59)
High flow nasal cannula (HFNC)	78 (11)
Non-invasive positive pressure ventilation (NIPV)	51 (7)
Invasive mechanical ventilation (IMV)	47 (7)
HFNC, NIPPV, or IMV	138 (19)
ICU admission	116 (16)
In-hospital death on or before Day 28	38 (5)

- Of all hospitalized cases, 59% had documented hypoxemia
- Approximately 16% of hospitalized cases required an ICU admission
- Some hospitalizations included in the analysis may not represent severe COVID-19 disease

*Unpublished CDC data.
**Data missing for 12% (96/815) of cases due to reporting lag.

Conclusions

Limitations

- For estimates of ***absolute*** vaccine effectiveness, if unvaccinated or vaccinated individuals are significantly different than the rest of the population, estimates may be biased.

- For estimates of ***relative*** vaccine effectiveness, residual protection from prior doses is an important consideration.
  - Particularly important for severe disease, for which residual protection from prior doses may be higher
  - Can be challenging to interpret waning of relative VE

- Limited information on prior infection, although we know rates of prior infection in the U.S. population are high.
- VE against COVID-19 associated hospitalization may underestimate protection against severe COVID-19 disease.

Conclusions

- **Updates to VE of bivalent COVID-19 booster against *symptomatic infection* among children and adolescents aged 5-17 years and adults aged ≥18 years**
  - Bivalent booster provided added protection, though early evidence of waning of relative effectiveness
- **Updates to VE of bivalent COVID-19 booster against *ED/UC encounters* and *hospitalizations* among adults ≥18 years**
  - Bivalent boosters are helping provide additional protection against emergency department/urgent care encounters and hospitalization
  - For most people who received monovalent doses and are eligible for a bivalent booster, more than a year has elapsed since their last monovalent dose. Because of waning, they may have limited remaining protection.

Acknowledgements

CDC COVID-19 Vaccine Effectiveness and Policy Team

- Allison Ciesla
- Monica Godfrey
- Katherine Fleming-Dutra
- Ruth Link-Gelles
- Morgan Najdowski
- Sara Oliver
- Amanda Payne
- Lauren Roper
- Laura Steinhardt
- Evelyn Twentyman
- Megan Wallace
- Ryan Wiegand

PIs and study staff for VE platforms

- Sarah Ball
- Jennifer DeCuir
- Monica Dickerson
- Margaret Dunne
- Eric Griggs
- Matthew Levy
- Patrick Mitchell
- Palak Patel
- Sarah Reese
- Heather Scobie
- Zach Smith
- Diya Surie
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