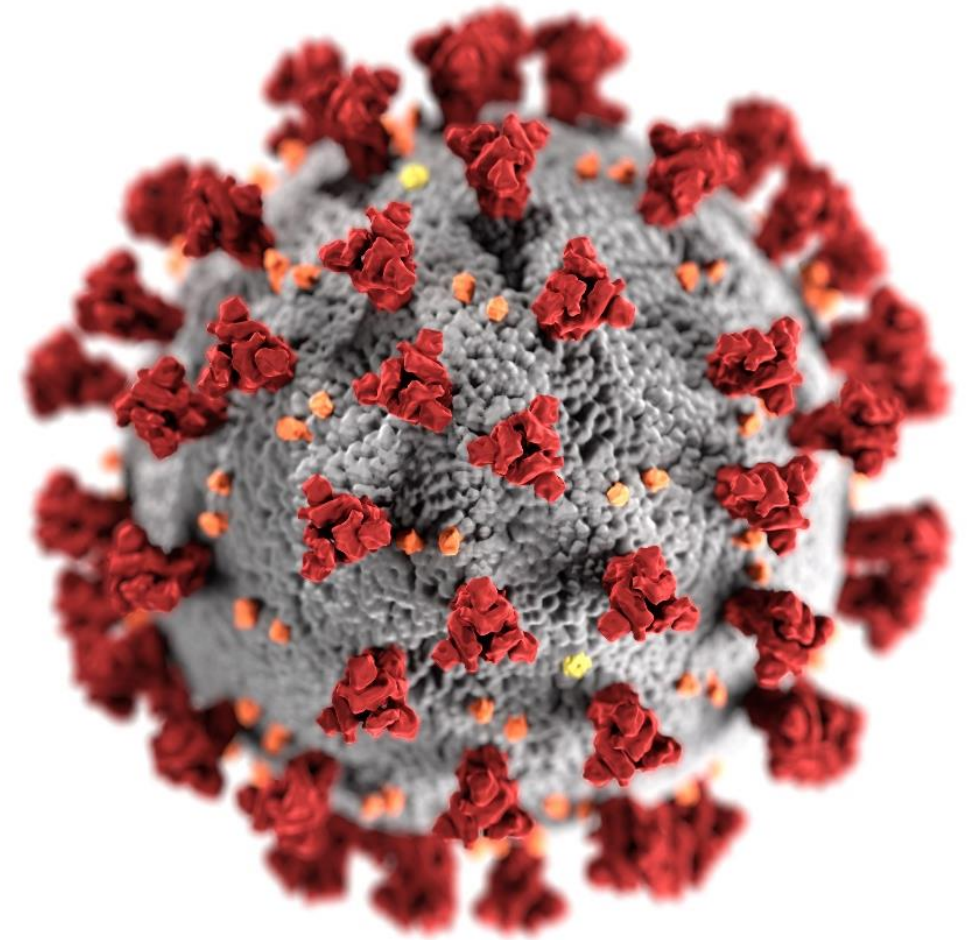


CDC COVID-19 Vaccine Effectiveness Studies

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COVID-19 Response

May 12, 2021



cdc.gov/coronavirus

Need for post-authorization vaccine effectiveness (VE) estimates

- Real-world effectiveness may differ from efficacy under trial conditions due to implementation differences in:
 - Adherence to cold chain requirements
 - Broader population eligible to receive the vaccine
 - For 2-dose regimens, timing and coverage of second dose
- Build on evidence from clinical trials, specifically for:
 - Groups experiencing disproportionate impact of COVID-19
 - Severe disease
 - SARS-CoV-2 infection and transmission
 - Duration of protection



CDC COVID-19 VE policy priorities: results of internal and external input

Timeline after introduction Priority

Immediate

- Does vaccine protect against symptomatic disease as expected?

Subsequent

- VE against key outcomes
 - Severe disease
 - Non-severe disease
 - Infection and transmission
- VE in groups experiencing disproportionate impact of COVID-19
 - Adults aged ≥ 65 years, including those in long-term care facilities (LTCFs)
 - People with key underlying conditions (e.g., immunocompromising conditions, obesity, diabetes)
 - Racial and ethnic minority groups experiencing disproportionate impact
- VE for regimen-related questions for 2 dose products
 - Single-dose and prolonged intervals; mixed-dose schedules (>1 product)
- Viral evolution: Do genome changes impact VE?

Later stage

- Duration of protection
- Comparison of VE across products



COVID-19 mRNA vaccine effectiveness literature globally

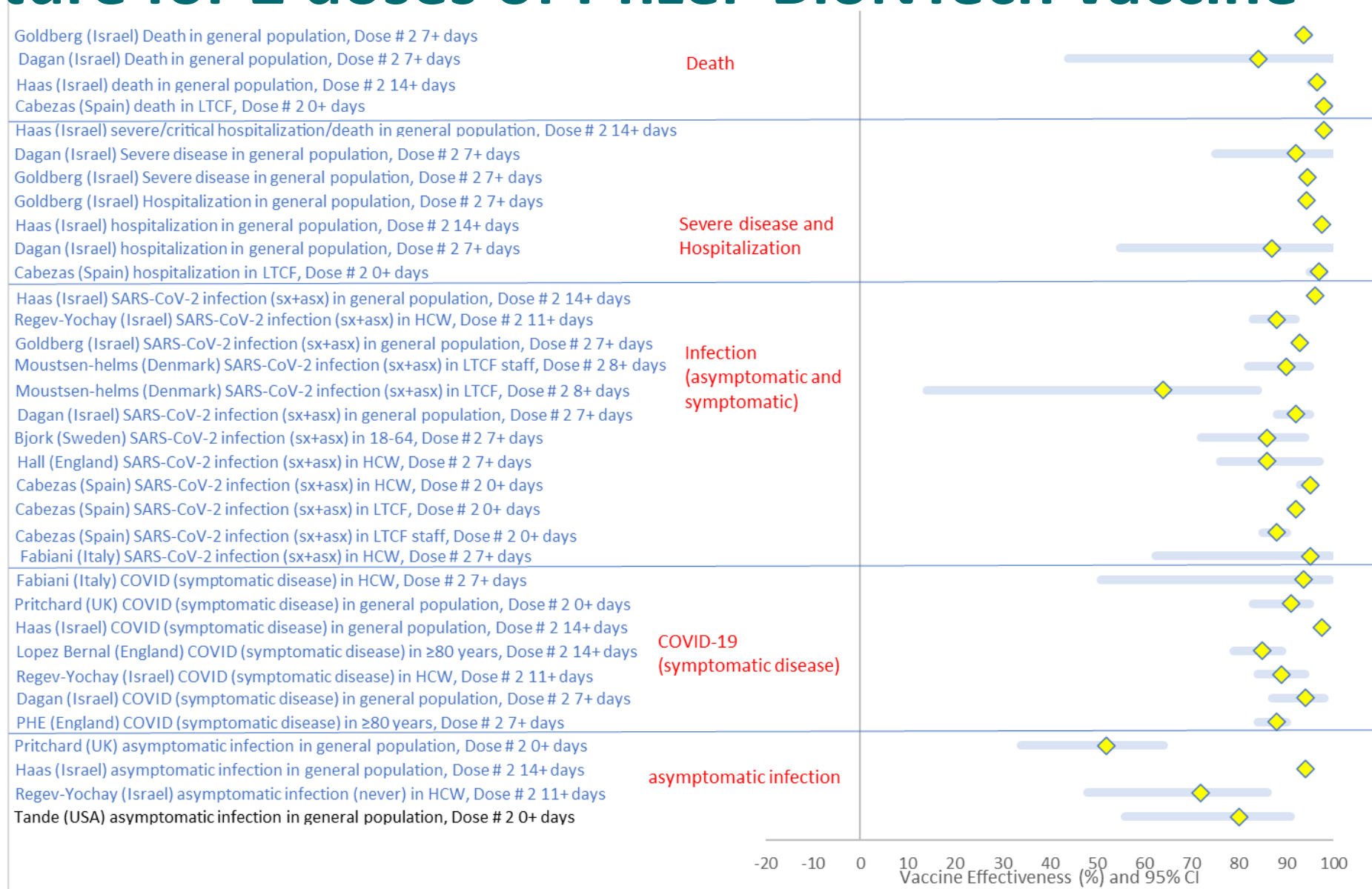


COVID-19 mRNA VE literature caveats

- The literature is rapidly evolving and growing exponentially.
- Wide variety of methods, populations, definitions are used.
- Most literature is currently in pre-print form, with few peer-reviewed publications.
- Quality varies widely.
- Meta-analyses and formal comparisons are not appropriate at this time due to these caveats.



VE literature for 2 doses of Pfizer-BioNTech vaccine



Purple font=in context of P1
 Black font=in context of non VOCs
 Blue font=in context of B.1.1.7



Figure courtesy of Dr. Minal Patel, World Health Organization, Individual studies results only, VOC=variant of concern

VE literature for 2 doses of mRNA vaccine

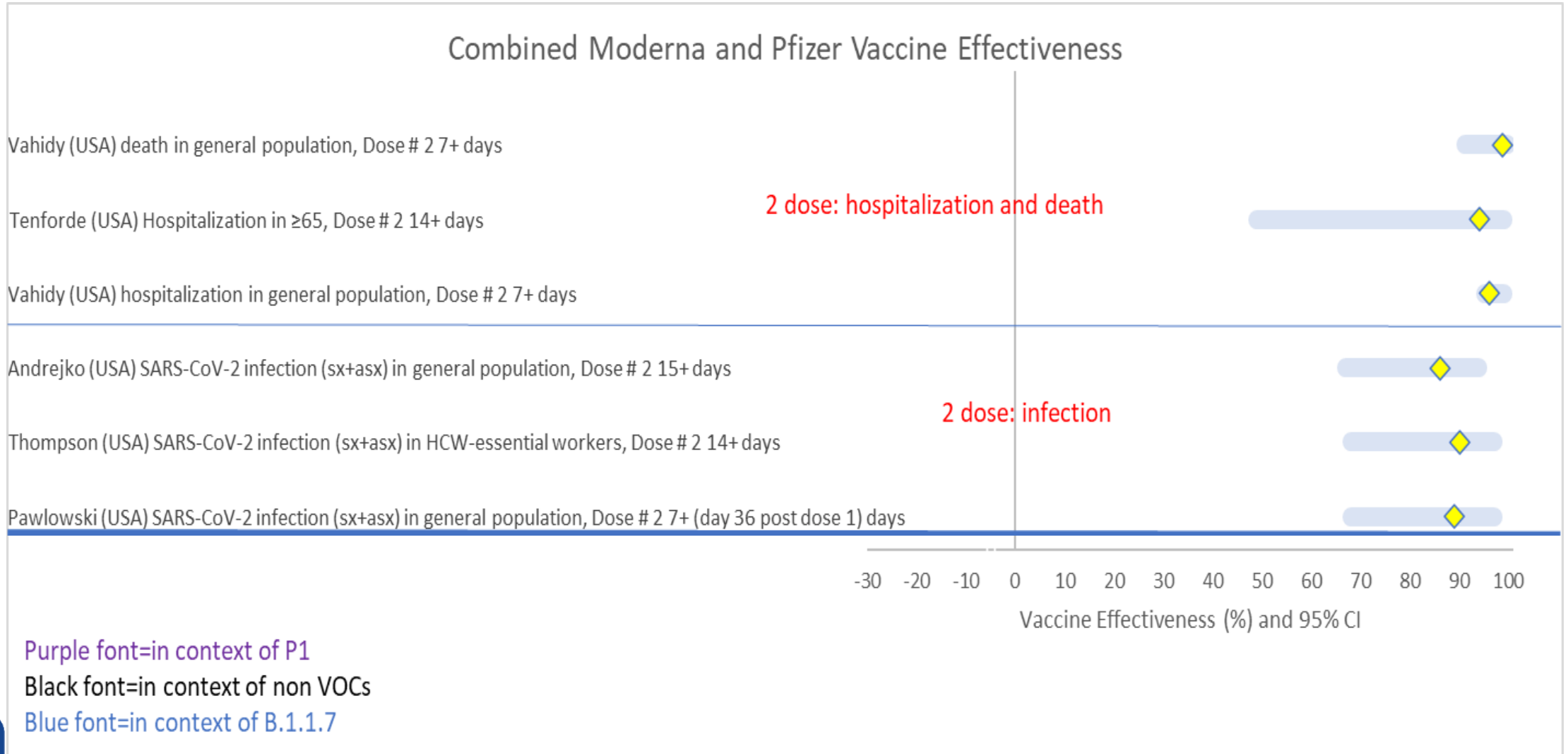


Figure courtesy of Dr. Minal Patel, World Health Organization, Individual studies results only, VOC=variant of concern



CDC vaccine effectiveness studies: Published literature





Effectiveness of the Pfizer–BioNTech COVID–19 Vaccine Among Residents of Two Skilled Nursing Facilities Experiencing COVID–19 Outbreaks — Connecticut, December 2020–February 2021

Weekly / March 19, 2021 / 70(11);396–401

On March 15, 2021, this report was posted online as an MMWR Early Release.

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VE against infection among residents of 2 skilled nursing facilities

COVID-19 immunization status with Pfizer-BioNTech vaccine

Vaccine effectiveness against infection
% (95% confidence interval [CI])

Partially immunized: ≥ 14 days after first dose through dose 2 + 7 days



63 (33–79)

Partially immunized with exclusion of prior SARS-CoV-2 infection



60 (30–77)

Partially immunized: ≥ 14 days after first dose through dose 2 + 0 days

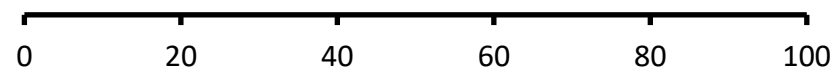


66 (29–83)

Partially immunized: ≥ 14 days after first dose through dose 2 + 14 days



60 (33–77)



Vaccine Effectiveness (%)



https://www.cdc.gov/mmwr/volumes/70/wr/mm7011e3.htm?s_cid=mm7011e3_w

Interim Estimates of Vaccine Effectiveness of BNT162b2 and mRNA-1273 COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Health Care Personnel, First Responders, and Other Essential and Frontline Workers — Eight U.S. Locations, December 2020–March 2021

Weekly / April 2, 2021 / 70(13);495–500

On March 29, 2021, this report was posted online as an MMWR Early Release.

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Interim VE against infection

COVID-19 immunization status with mRNA vaccines

Partially immunized (≥ 14 days after dose 1 through receipt of dose 2)

Fully immunized (≥ 14 days after dose 2)

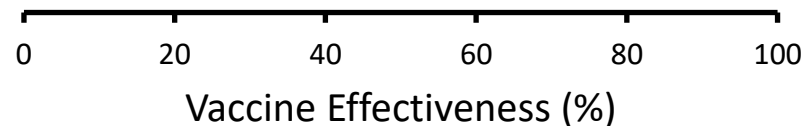
Adjusted vaccine effectiveness against infection^{*,†}
% (95% confidence interval [CI])



80 (59–90)



90 (68–97)



* Vaccine effectiveness was estimated using a Cox proportional hazards model accounting for time-varying immunization status.

† Hazard ratio is adjusted for study site



Effectiveness of Pfizer–BioNTech and Moderna Vaccines Against COVID–19 Among Hospitalized Adults Aged ≥ 65 Years — United States, January–March 2021

Early Release / April 28, 2021 / 70

Mark W. Tenforde, MD, PhD¹; Samantha M. Olson, MPH¹; Wesley H. Self, MD²; H. Keipp Talbot, MD²; Christopher J. Lindsell, PhD²; Jay S. Steingrub, MD³; Nathan I. Shapiro, MD⁴; Adit A. Ginde, MD⁵; David J. Douin, MD⁵; Matthew E. Prekker, MD⁶; Samuel M. Brown, MD⁷; Ithan D. Peltan, MD⁷; Michelle N. Gong, MD⁸; Amira Mohamed, MD⁸; Akram Khan, MD⁹; Matthew C. Exline, MD¹⁰; D. Clark Files, MD¹¹; Kevin W. Gibbs, MD¹¹; William B. Stubblefield, MD²; Jonathan D. Casey, MD²; Todd W. Rice, MD²; Carlos G. Grijalva, MD²; David N. Hager, MD, PhD¹²; Arber Shehu, MD¹²; Nida Qadir, MD¹³; Steven Y. Chang, MD, PhD¹³; Jennifer G. Wilson, MD¹⁴; Manjusha Gaglani, MBBS^{15,16}; Kempapura Murthy, MPH¹⁵; Nicole Calhoun, LMSW, MPA¹⁵; Arnold S. Monto, MD¹⁷; Emily T. Martin, PhD¹⁷; Anurag Malani, MD¹⁸; Richard K. Zimmerman, MD¹⁹; Fernanda P. Silveira, MD¹⁹; Donald B. Middleton, MD¹⁹; Yuwei Zhu, MD²; Dayna Wyatt²; Meagan Stephenson, MPH¹; Adrienne Baughman²; Kelsey N. Womack, PhD²; Kimberly W. Hart²; Miwako Kobayashi, MD¹; Jennifer R. Verani, MD¹; Manish M. Patel, MD¹; IVY Network; HAIVEN Investigators ([View author affiliations](#))



https://www.cdc.gov/mmwr/volumes/70/wr/mm7018e1.htm?s_cid=mm7018e1_w

Interim VE against hospitalization among adults aged ≥65 years

COVID-19 immunization status with mRNA vaccines

Adjusted vaccine effectiveness against hospitalization
% (95% confidence interval [CI])

Full vaccination



94 (44–99)

Partial or full vaccination

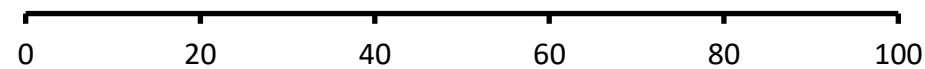


71 (44–85)

Partial vaccination



64 (28–82)



Vaccine Effectiveness (%)



https://www.cdc.gov/mmwr/volumes/70/wr/mm7018e1.htm?s_cid=mm7018e1_w

COVID-19 Outbreak Associated with a SARS-CoV-2 R.1 Lineage Variant in a Skilled Nursing Facility After Vaccination Program — Kentucky, March 2021

Weekly / April 30, 2021 / 70(17);639-643

On April 21, 2021, this report was posted online as an MMWR Early Release.

Alyson M. Cavanaugh, DPT, PhD^{1,2}; Sarah Fortier, MPH²; Patricia Lewis²; Vaneet Arora, MD²; Matt Johnson²; Karim George²; Joshua Tobias, PhD²; Stephanie Lunn, MPH²; Taylor Miller, MPH²; Douglas Thoroughman, PhD^{2,3}; Kevin B. Spicer, MD, PhD^{2,4} ([View author affiliations](#))

[View suggested citation](#)



https://www.cdc.gov/mmwr/volumes/70/wr/mm7017e2.htm?s_cid=mm7017e2_w

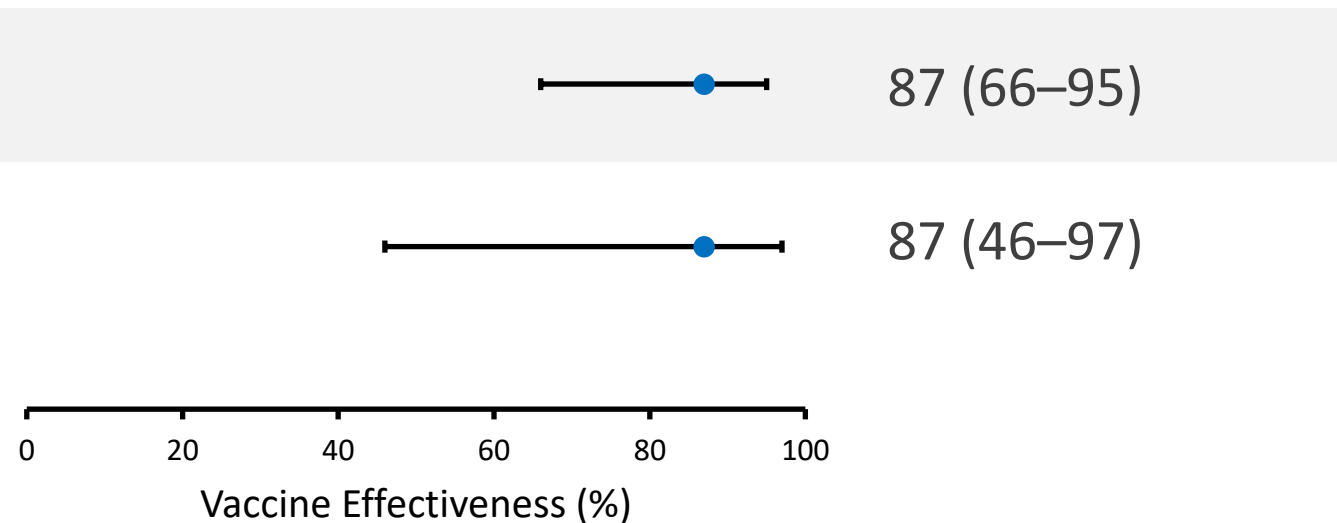
VE against symptomatic disease in a Kentucky skilled nursing facility with a SARS-CoV-2 R.1 lineage variant outbreak

COVID-19 immunization status with Pfizer-BioNTech vaccine

Residents who were fully immunized (≥ 14 days after dose 2)

Healthcare personnel who were fully immunized (≥ 14 days after dose 2)

Adjusted vaccine effectiveness against symptomatic disease
% (95% confidence interval [CI])



https://www.cdc.gov/mmwr/volumes/70/wr/mm7017e2.htm?s_cid=mm7017e2_w

Additional ongoing CDC VE assessments



Current VE assessments

| VE priority | Prospective data collection | Electronic health record (EHR) and claims analyses (coordination across US gov) |
|--|---|---|
| Immediate priority | | |
| Does vaccine work as expected to prevent symptomatic disease? | Test-negative design case-control among healthcare personnel | |
| Subsequent priorities | | |
| Older adults, including residents of long-term care facilities (LTCFs) | Case-control among adults ≥ 65 years (COVID-NET linked to CMS); National Healthcare Safety Network (NHSN) | CMS cohort (FDA, CMS) EHR data sets (CDC, VA, FDA) |
| Infection and transmission | Prospective longitudinal cohorts, including among healthcare personnel and frontline workers; case-ascertained household cohorts for transmission | |
| Severe disease/hospitalization | Test-negative design (for adults and children); conventional case-control using hospitalized controls; screening method | EHR data sets (CDC, VA, FDA); retrospective cohort or test-negative design |
| Non-severe disease | Test-negative design among outpatients | Potentially using EHR data sets |
| Those with key underlying conditions (e.g., immunocompromised) | Captured in above studies | CMS (FDA, CMS); EHR data sets (CDC, VA, FDA) |
| Racial and ethnic groups disproportionately affected by COVID-19 | Captured in above studies; test-negative design in American Indian and Alaska Native populations | CMS (FDA, CMS); EHR data sets (CDC, VA, FDA); exploring IHS EHR (IHS) |
| Vaccine impact | Ecologic analyses of disease incidence/seroprevalence and vaccination coverage; comparisons of expected vaccine impact from models with observed impact | |



Current VE assessments including children

| VE priority | Prospective data collection | Electronic health record (EHR) and claims analyses (coordination across US gov) |
|--|---|---|
| Immediate priority | | |
| Does vaccine work as expected to prevent symptomatic disease? | Test-negative design case-control among healthcare personnel | |
| Subsequent priorities | | |
| Older adults, including residents of long-term care facilities (LTCFs) | Case-control among adults ≥65 years (COVID-NET linked to CMS); National Healthcare Safety Network (NHSN) | CMS cohort (FDA, CMS) EHR data sets (CDC, VA, FDA) |
| Infection and transmission | Prospective longitudinal cohorts, including among healthcare personnel and frontline workers; case-ascertained household cohorts for transmission | |
| Severe disease/hospitalization | Test-negative design (for adults and children); conventional case-control using hospitalized controls; screening method | EHR data sets (CDC, VA, FDA); retrospective cohort or test-negative design |
| Non-severe disease | Test-negative design among outpatients | Potentially using EHR data sets |
| Those with key underlying conditions (e.g., immunocompromised) | Captured in above studies | CMS (FDA, CMS); EHR data sets (CDC, VA, FDA) |
| Racial and ethnic groups disproportionately affected by COVID-19 | Captured in above studies; test-negative design in American Indian and Alaska Native populations | CMS (FDA, CMS); EHR data sets (CDC, VA, FDA); exploring IHS EHR (IHS) |
| Vaccine impact | Ecologic analyses of disease incidence/seroprevalence and vaccination coverage; comparisons of expected vaccine impact from models with observed impact | |



OVERCOMING2: VE against COVID-19 or Multisystem Inflammatory Syndrome in Children (MIS-C) among hospitalized children <19 years

- Based on an intensive care unit (ICU) network assessing influenza VE against critical illness in pediatric patients (aged <19 years)
- During 2020: Overcoming enrolled all MIS-C patients and ICU patients with COVID-19 at ~57 US pediatric hospitals
- Primary objectives:
 - VE against any hospitalized COVID-19 and MIS-C
 - Two control groups (test-negative acute respiratory illness and non-acute respiratory illness hospitalizations)
 - VE by subgroup: variant, vaccine type, age, race/ethnicity, sex, time since vaccination, partial vaccination



Do viral genome changes impact VE?

- Selected prospective platforms will collect specimens from cases, where possible, for whole genome sequencing.
 - Will not be performed in real time
 - May not be powered for variant-specific VE assessments
- Vaccine evaluation unit is assessing vaccine breakthrough cases with hospitalization or death.
 - A collaboration with the Emerging Infections Program comparing the frequency of variants among vaccinated and unvaccinated persons may shed light.
- Work is part of broader CDC efforts to monitor the impact of SARS-CoV-2 variants.



Current VE assessments including genomic characterization

| VE priority | Prospective data collection | Electronic health record (EHR) and claims analyses (coordination across US gov) |
|--|--|---|
| Immediate priority | | |
| Does vaccine work as expected to prevent symptomatic disease? | Test-negative design case-control among healthcare personnel | |
| Subsequent priorities | | |
| Older adults, including residents of long-term care facilities (LTCFs) | Case-control among adults ≥ 65 years (COVID-NET linked to CMS); National Healthcare Safety Network (NHSN) | CMS cohort (FDA, CMS) EHR data sets (CDC, VA, FDA) |
| Infection and transmission | Prospective longitudinal cohorts, including among healthcare personnel and frontline workers; case-ascertained household cohorts for transmission | |
| Severe disease/hospitalization | Test-negative design (for adults and children); conventional case-control using hospitalized controls; screening method | EHR data sets (CDC, VA, FDA); retrospective cohort or test-negative design |
| Non-severe disease | Test-negative design among outpatients | Potentially using EHR data sets |
| Those with key underlying conditions (e.g., immunocompromised) | Captured in above studies | CMS (FDA, CMS); EHR data sets (CDC, VA, FDA) |
| Racial and ethnic groups disproportionately affected by COVID-19 | Captured in above studies; test-negative design in American Indian and Alaska Native populations | CMS (FDA, CMS); EHR data sets (CDC, VA, FDA); exploring IHS EHR (IHS) |
| Vaccine impact | Ecologic analyses of disease incidence/seroprevalence and vaccination coverage; comparisons of expected vaccine impact from models with observed impact | |



Duration of protection from COVID-19 vaccines

- An important VE priority is to understand the duration of protection provided by COVID-19 vaccines.
 - This will inform the question about the need for a booster.
 - It is important to take into account changes in the circulating variants over time.



Current VE assessments including duration of protection

Electronic health record (EHR) and claims analyses (coordination across US gov)

VE priority

Prospective data collection

Immediate priority

Does vaccine work as expected to prevent symptomatic disease?

Test-negative design case-control among healthcare personnel

Subsequent priorities

Older adults, including residents of long-term care facilities (LTCFs)

Case-control among adults ≥ 65 years (COVID-NET linked to CMS); National Healthcare Safety Network (NHSN)

CMS cohort (FDA, CMS)
EHR data sets (CDC, VA, FDA)

Infection and transmission

Prospective longitudinal cohorts, including among healthcare personnel and frontline workers; case-ascertained household cohorts for transmission

Severe disease/hospitalization

Test-negative design (for adults and children); conventional case-control using hospitalized controls; screening method

EHR data sets (CDC, VA, FDA); retrospective cohort or test-negative design

Non-severe disease

Test-negative design among outpatients

Potentially using EHR data sets

Those with key underlying conditions (e.g., immunocompromised)

Captured in above studies

CMS (FDA, CMS);
EHR data sets (CDC, VA, FDA)

Racial and ethnic groups disproportionately affected by COVID-19

Captured in above studies; **test-negative design in American Indian and Alaska Native populations**

CMS (FDA, CMS); EHR data sets (CDC, VA, FDA); exploring IHS EHR (IHS)

Vaccine impact

Ecologic analyses of disease incidence/seroprevalence and vaccination coverage; comparisons of expected vaccine impact from models with observed impact



CDC VE assessments in outbreak settings

- Residents of long-term care facilities
- Incarcerated and detained persons and staff in corrections facilities
- Actively looking for COVID-19 outbreaks in congregate settings to assess:
 - Variant-specific VE
 - VE for Johnson & Johnson's Janssen vaccine
 - VE among adolescents and children once eligible for vaccine



Conclusion

- Initial COVID-19 VE estimates from recently published reports are demonstrating remarkably consistent results across studies with a variety of methods and populations.
- There is an urgent need for VE data to guide vaccine policy.
- A broad approach, including a diversity of projects, methods, bias control, populations, and sample sizes strengthens our understanding of the true real-world performance of these vaccines.



Ensuring COVID-19 Vaccines Work:
<https://www.cdc.gov/coronavirus/2019-ncov/vaccines/effectiveness.html>

COVID-19 Vaccine Effectiveness Research:
<https://www.cdc.gov/vaccines/covid-19/effectiveness-research/protocols.html>

For more information, contact CDC
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TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

