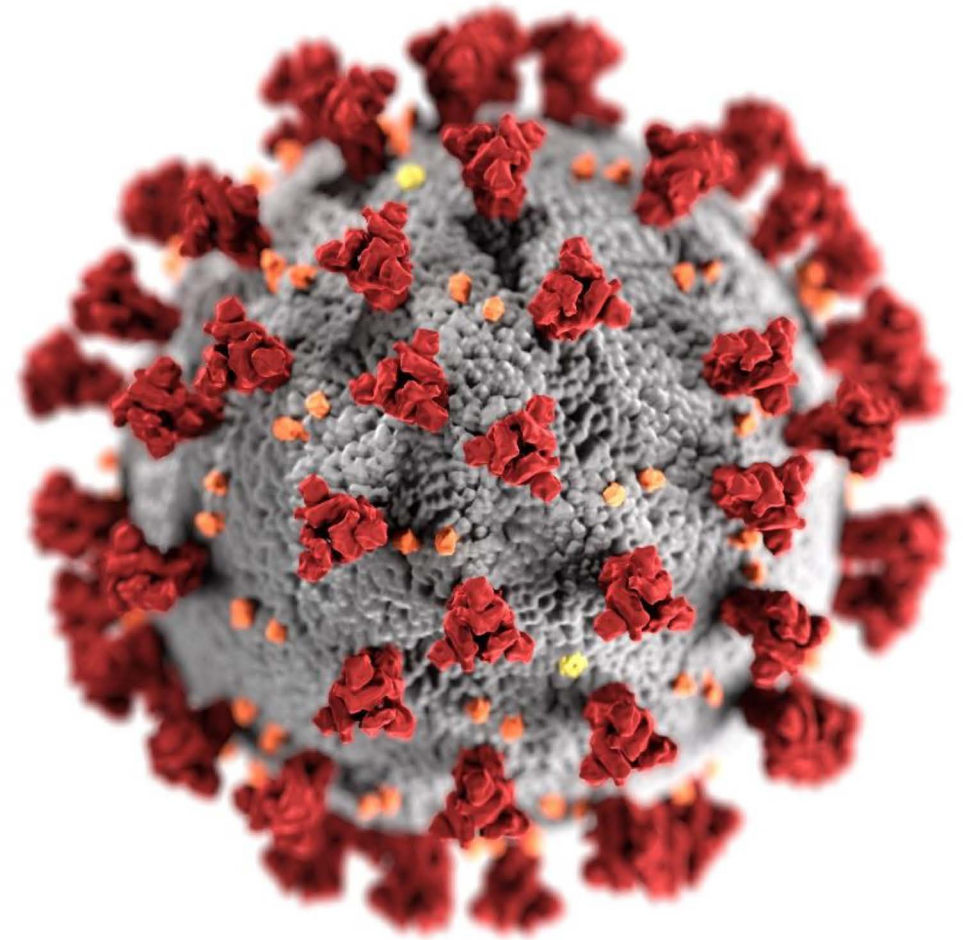


Improving communications around vaccine breakthrough and vaccine effectiveness

July 29, 2021

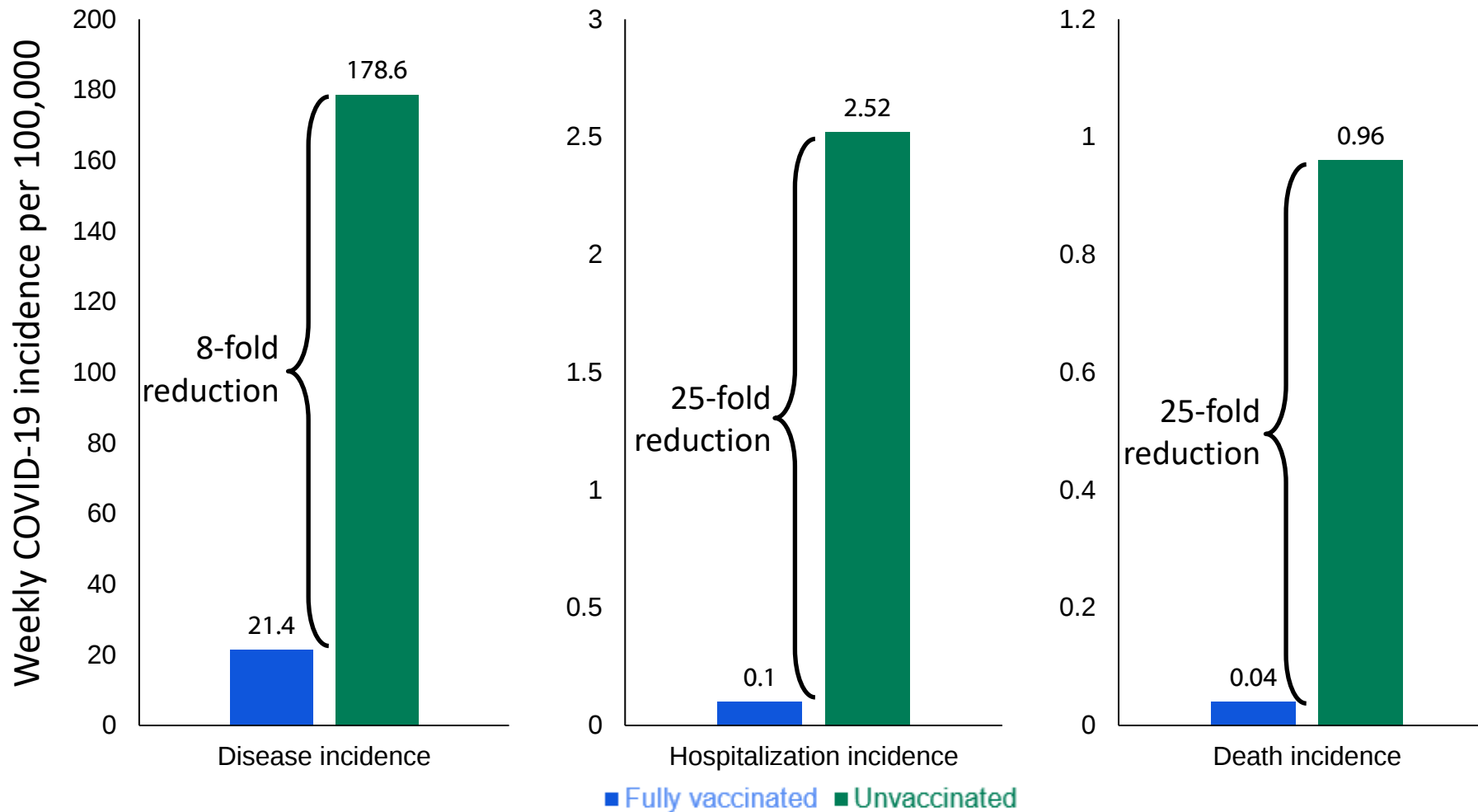


cdc.gov/coronavirus

Vaccine breakthrough cases may reduce public confidence in vaccines

- Vaccine **breakthrough cases are expected** and increase as a proportion of total cases as vaccine coverage increases
- Vaccine breakthrough cases will occur more frequently in congregate settings, and in groups at risk of primary vaccine failure (i.e., immune compromised, elderly, etc.)
- Communication challenges have been associated with increasing proportions of cases vaccinated **even when vaccine effectiveness (VE) remains stable**
 - Concerns from local health departments about VE
 - Public convinced vaccines no longer work/booster doses needed
 - **Important to update communications describing breakthrough cases as “rare” or as a “small percentage” of cases**

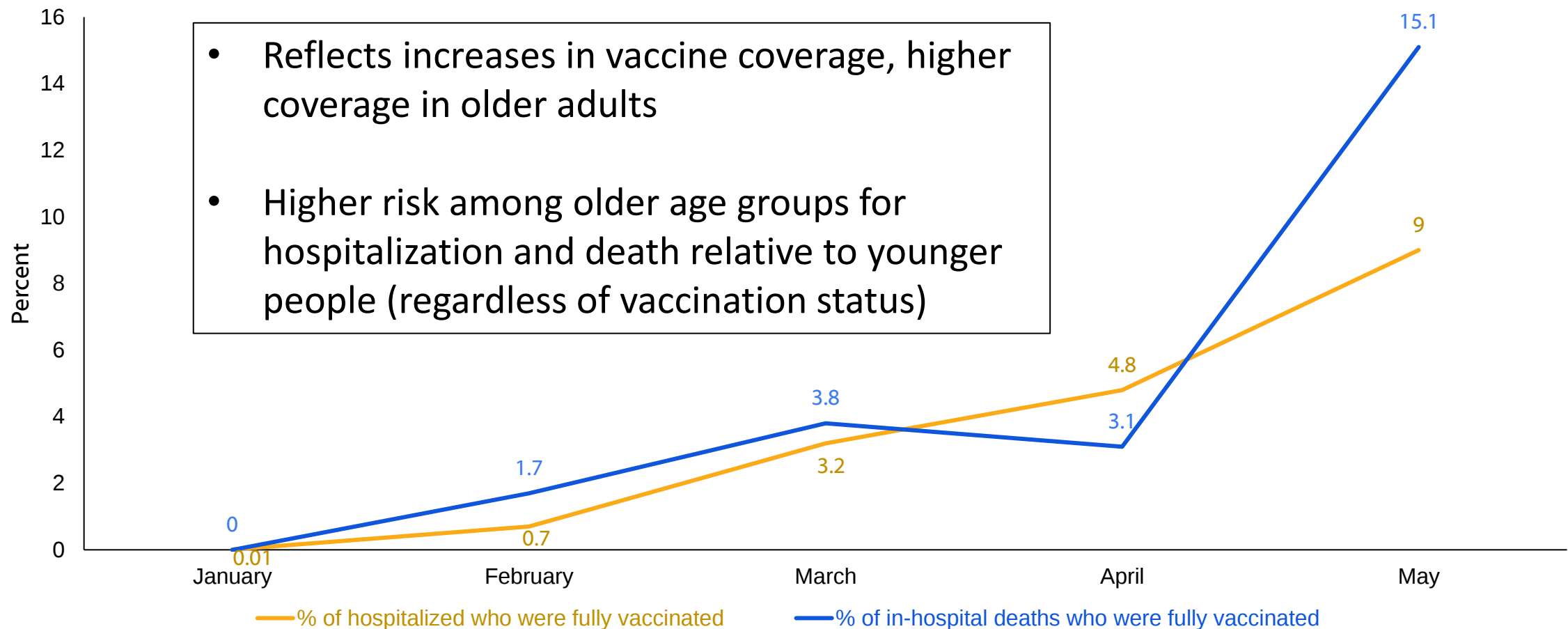
Greater risk of disease, hospitalization and death among unvaccinated vs. vaccinated people: National estimates



**At current incidence,
35,000 symptomatic
infections per week
among 162 million
vaccinated Americans**

Data from COVID Tracker as of July 24, 2021. Average incidence 100 cases per 100,000 persons per week. Vaccine effectiveness against symptomatic illness = 88% (Lopez Bernal et al. [NEJM 2021](#)), where risk is $[1 - VE]$ or 12%. Vaccine effectiveness hospitalization (or death) = 96% (Stowe et al. [PHE preprint](#)), where risk is $[1 - VE]$ or 4%. Rate in unvaccinated = Community rate/ $((1 - \text{fully vaccinated coverage}) + (1 - VE) * \text{fully vaccinated coverage})$. Rate in fully vaccinated = $(1 - VE) * \text{Rate in unvaccinated}$. Fully vaccinated coverage proportions were from COVID Data Tracker as of July 24, 2021 (50% for US,).

Increasing percentage of vaccinated persons among those hospitalized in COVID-NET



(CONFIDENTIAL – preliminary data, subject to change)

CDC uses multiple platforms and study designs to monitor COVID-19 vaccine effectiveness (VE)

VE priority	Design
Infection and transmission	Prospective cohort among healthcare personnel (HCP) & frontline workers; transmissibility evaluation in LTCF and other congregate settings; case-ascertained household cohorts for transmission
Non-severe disease	Test-negative design (TND) case-control among outpatients; Electronic health record (EHR) datasets
Severe disease/hospitalization	TND among hospitalized patients (for adults and children); conventional case-control using hospitalized controls; EHR datasets
Older adults, including nursing home residents	Case-control among adults ≥ 65 years; National Healthcare Safety Network comparison to population coverage estimated through immunization registries; Outbreaks in nursing homes; EHR datasets
Those with key underlying conditions (e.g., immunocompromised)	Captured above
Duration of protection	Captured above
Variant-specific VE	Captured above; outbreaks in congregate settings

VE results



Early evidence in health care providers that vaccination may reduce transmission and attenuate illness (HEROES/RECOVER)

- Period: December 14, 2020 – April 10, 2021
- VE against infection was **91%** (CI 76-97) among fully vaccinated; **81%** (CI 64-90) for partially vaccinated
- Compared to unvaccinated cases, vaccinated cases (full or partial) had:
 - 40% lower mean RNA viral load (2.3 v. 3.8 copies/mL)
 - shorter mean duration of detectable viral RNA (2.7 v. 8.9 days)
 - lower risk of febrile symptoms (25.0% v. 63.1%)
 - shorter mean duration of symptoms (10.3 v. 16.7 days)

Preliminary VE estimates assessing duration of protection for 2 doses of mRNA vaccines

- VISION (test negative design across 8 integrated healthcare systems), data through June 22, 2021
 - VE against hospitalization **88%** (CI 86-90)
 - No evidence of waning immunity to 16 weeks post-2nd dose
- IVY3 (test negative design across 21 hospitals), data through June 2021
 - VE against hospitalization **87%** (CI 85-97)
 - No evidence of waning immunity through 20 weeks post-2nd dose
- Healthcare personnel (test negative design across 33 sites), data to May 31, 2021
 - VE against symptomatic infection **90%**
 - No evidence of waning immunity through 14 weeks post-2nd dose

Lower estimates of VE for mRNA vaccines among immunocompromised populations: Published evidence

- 71% (CI 37-87%) **against SARS-CoV-2 infection** 7-27 days after 2nd dose of Pfizer-BioNTech vaccine among immunosuppressed* people vs. 90% (CI 83-96%) overall¹
- 80% **against SARS-CoV-2 infection** ≥ 7 days after 2nd dose of mRNA vaccine among people with IBD on immunosuppressive medication²
- 75% (CI 44-88%) **against symptomatic COVID-19** 7-27 days after 2nd dose of Pfizer-BioNTech vaccine among immunosuppressed* people vs. 94% (CI 87-97%) overall¹
- 59% **against COVID-19 hospitalization** among immunocompromised ≥ 14 days after 2nd dose of mRNA vaccine³ vs. 91% (CI 86-95%) without immune compromise³

*Immunocompromised conditions (e.g., recipients of hematopoietic cell or solid organs transplant, patients under immunosuppressive therapy, asplenia, and chronic renal failure: advanced kidney disease, dialysis, or nephrotic syndrome)

Lower estimates of mRNA vaccine effectiveness (VE) among nursing home residents

- VE of mRNA vaccines for any infection (including asymptomatic) was **65%–75%** in different locations and platforms during December 2020 – May 2021
 - NHSN: 70% (62-76) for Pfizer-BioNTech, 65% (51-75) for Moderna
 - Signature Healthcare: 74% (54-85) for mRNA vaccines
 - LA County: 75% (43-89) for Moderna

Vaccine effectiveness (VE) and breakthrough example using the screening method

■ Screening method

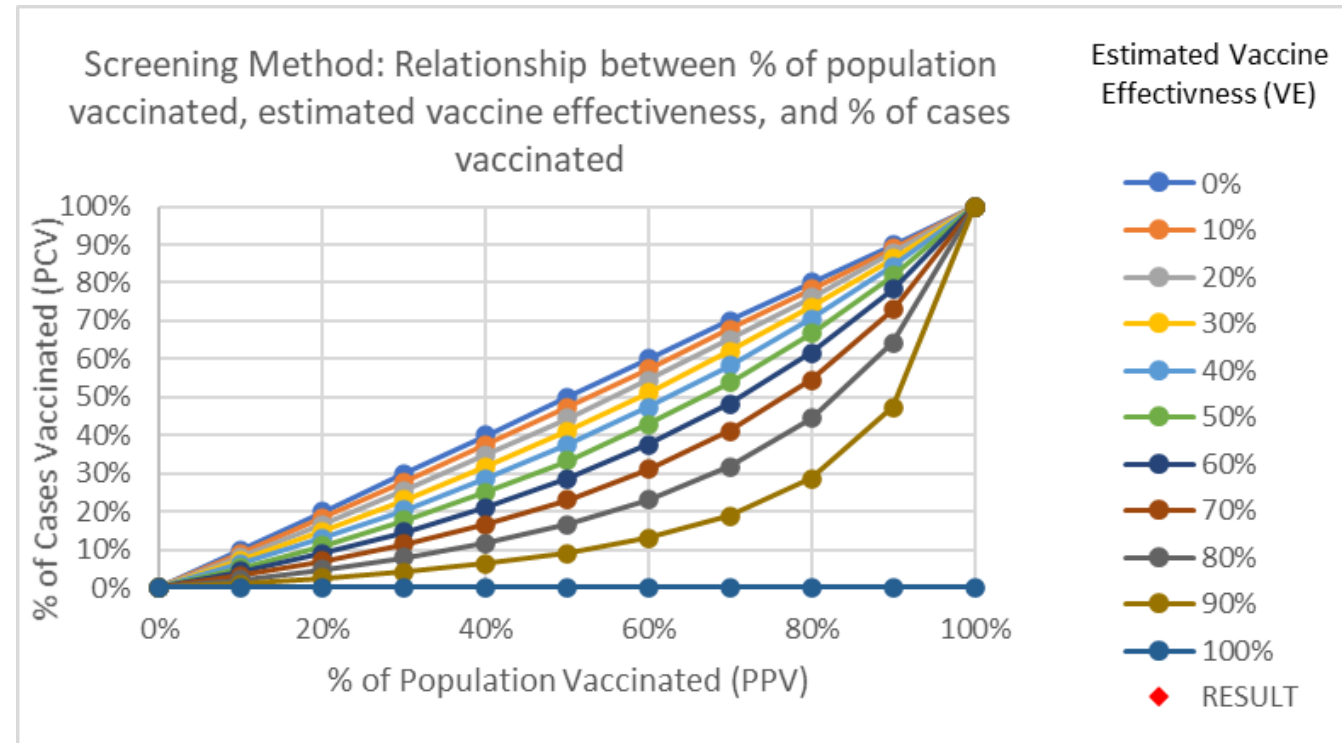
Estimates VE by comparing vaccine coverage in cases to population

$$VE = 1 - [(PCV/(1-PCV))((1-PPV)/PPV)]$$

- PCV=proportion cases vaccinated
- PPV=proportion population vaccinated

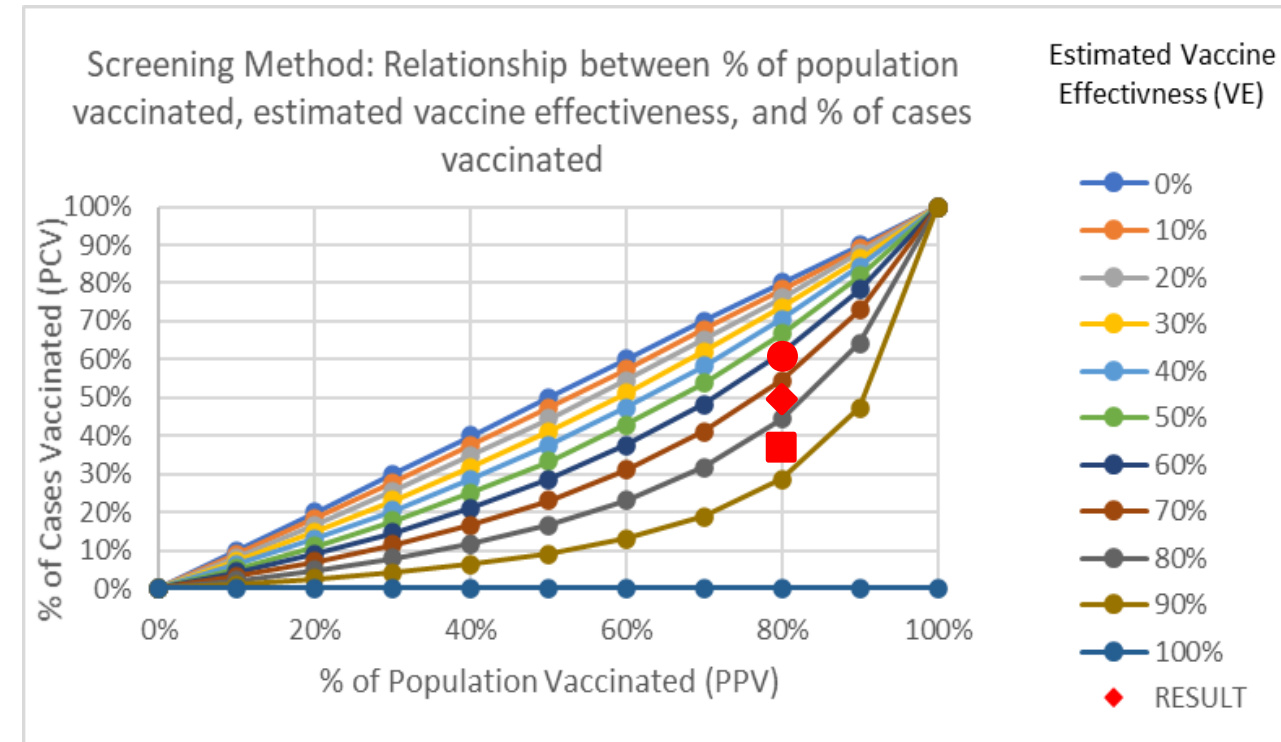
■ Recent nursing home outbreak of Beta variant, VE estimate:

- 61% against infection
- 75% against mild illness
- 85% against severe illness



Vaccine breakthrough in LTCF residents where coverage is 80% nationally

- For infection (VE 61%), 61% of cases vaccinated
- ◆ For mild illness (VE 75%), 50% of cases vaccinated
- For severe illness (VE 85%), 38% of cases vaccinated



Communications challenges around VE and differential risk

- Vaccines more effective against hospitalization/death > illness > infection
 - Important to acknowledge lower VE against infection
- VE estimates represent an average for a group, rather than individual risk
 - Risk modified by age, immunocompromising conditions, etc.
 - Need to clarify messages around individual protection
- How do we communicate this differential risk to the public?
 - Comparisons to unvaccinated that are relatively stable
 - Personal stories
 - Examples from outbreaks

Delta variant

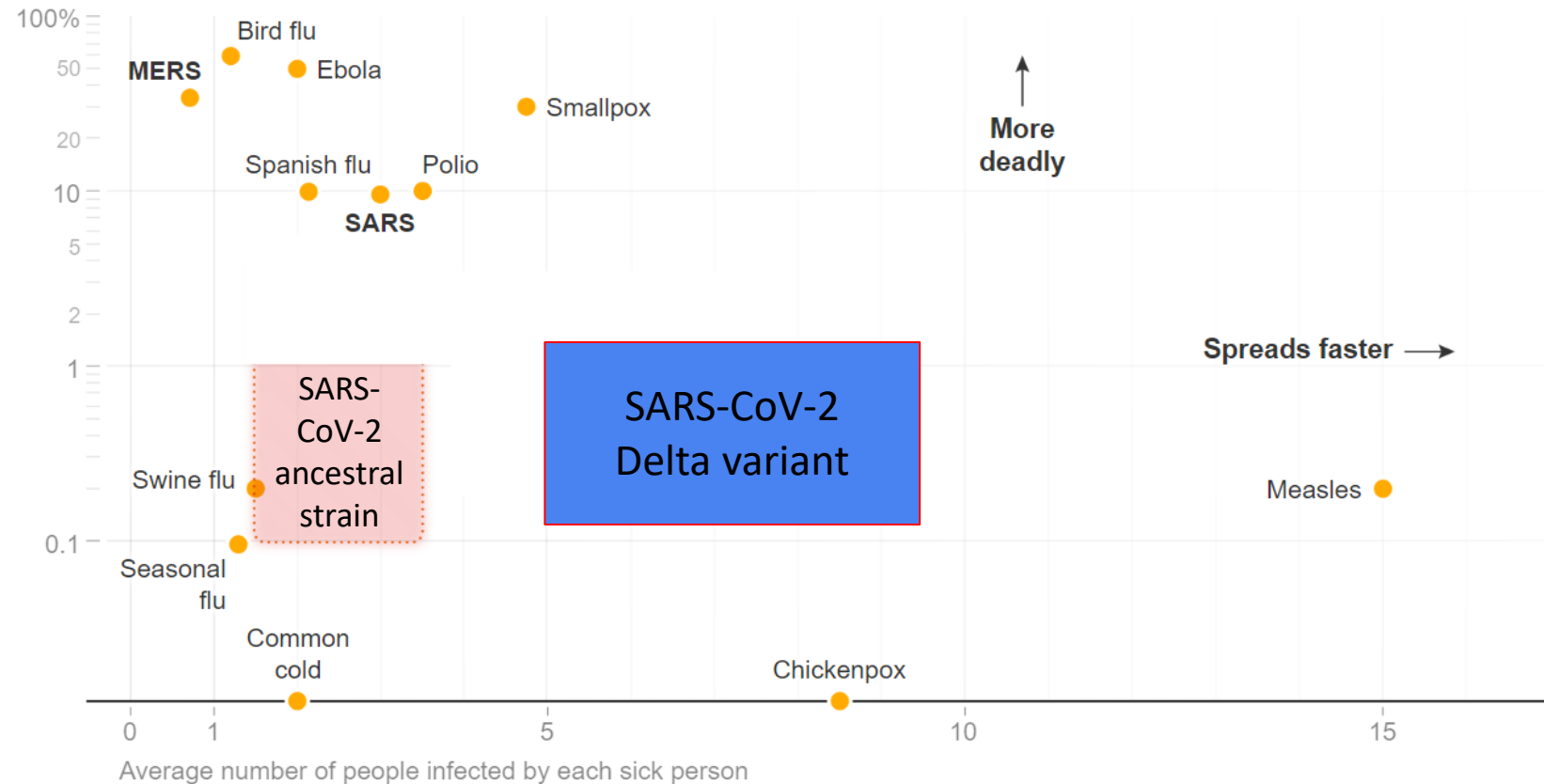


Transmission of Delta variant vs. ancestral strain and other infectious diseases

Fatality rate
(log scale)

The New York Times

Original graph from 2/28/2020.



Delta variant is **more** transmissible than:

- MERS & SARS
- Ebola
- Common cold
- Seasonal flu & 1918 ("Spanish") flu
- Smallpox

Delta variant is **as** transmissible as:

- Chicken Pox

Note: Average case-fatality rates and transmission numbers are shown. Estimates of case-fatality rates can vary, and numbers for the new coronavirus are preliminary estimates.

Delta infections associated with higher viral load and duration of shedding: Published evidence

- India report of lower cycle threshold (Ct) values in Delta breakthrough cases in HCW (n=47, mean Ct 16.5) compared to non-Delta breakthrough cases (n=22, mean Ct 19); also larger cluster size with Delta breakthrough
- Delta infection associated with longer duration of Ct values ≤ 30 [median 18 days vs. 13 days for ancestral strains]
- Risk of reinfection with Delta may be higher [aOR 1.46 (CI 1.03-2.05)] compared to Alpha variant, but only if prior infection ≥ 180 days earlier

Delta variant vaccine breakthrough cases may be as transmissible as unvaccinated cases

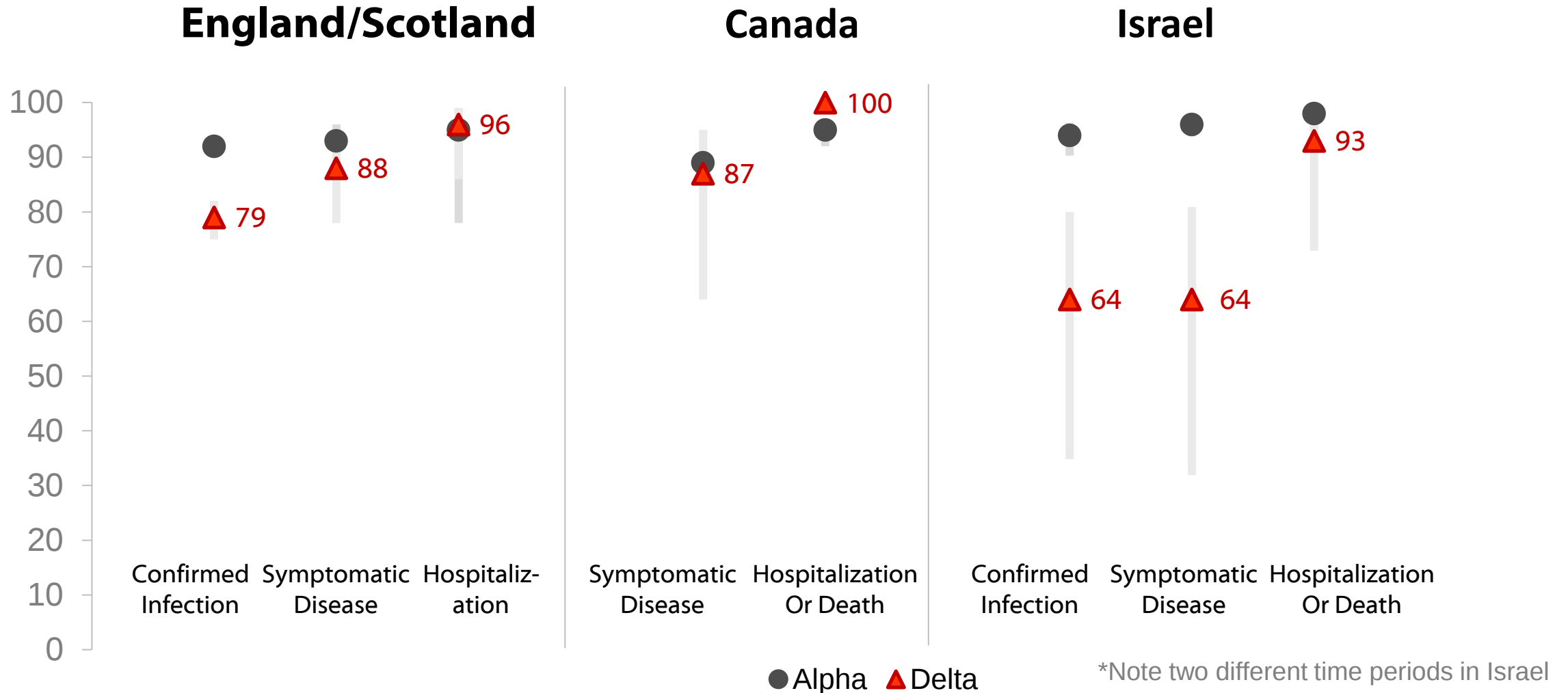
- Breakthrough cases reported to national passive surveillance have lower Ct values by 3 cycles (**~10-fold increase in viral load**) for Delta (Ct=18, n=19) compared with Alpha (Ct=21, n=207) and other lineages (Ct=21, n=251)
- Barnstable County, MA, outbreak: **No difference in mean Ct values in vaccinated and unvaccinated** cases [median among vaccinated (n=80): 21.9; unvaccinated (n=65): 21.5]

Delta variant may cause more severe disease than Alpha or ancestral strains: Published evidence

- Canada: Higher odds of hospitalization [aOR 2.20 (CI 1.93-2.53)], ICU admission [aOR 3.87 (CI 2.98-4.99)], and death [aOR 2.37 (CI 1.50-3.30)]¹
- Singapore: Higher odds of oxygen requirement, ICU admission, or death [aOR 4.90 (CI 1.43-30.78)] and pneumonia [aOR 1.88 (CI 0.95-3.76)]²
- Scotland: Higher odds of hospitalization [HR 1.85 (CI 1.39-2.47)]³

1. Fisman and Tuite, [doi:10.1101/2021.07.05.21260050](https://doi.org/10.1101/2021.07.05.21260050); 2. Ong et al. [doi:10.2139/ssrn.3861566](https://doi.org/10.2139/ssrn.3861566); 3. Sheikh et al. [doi:10.1016/S0140-6736\(21\)01358-1](https://doi.org/10.1016/S0140-6736(21)01358-1)

Pfizer 2-Dose Vaccine Effectiveness for Alpha vs. Delta



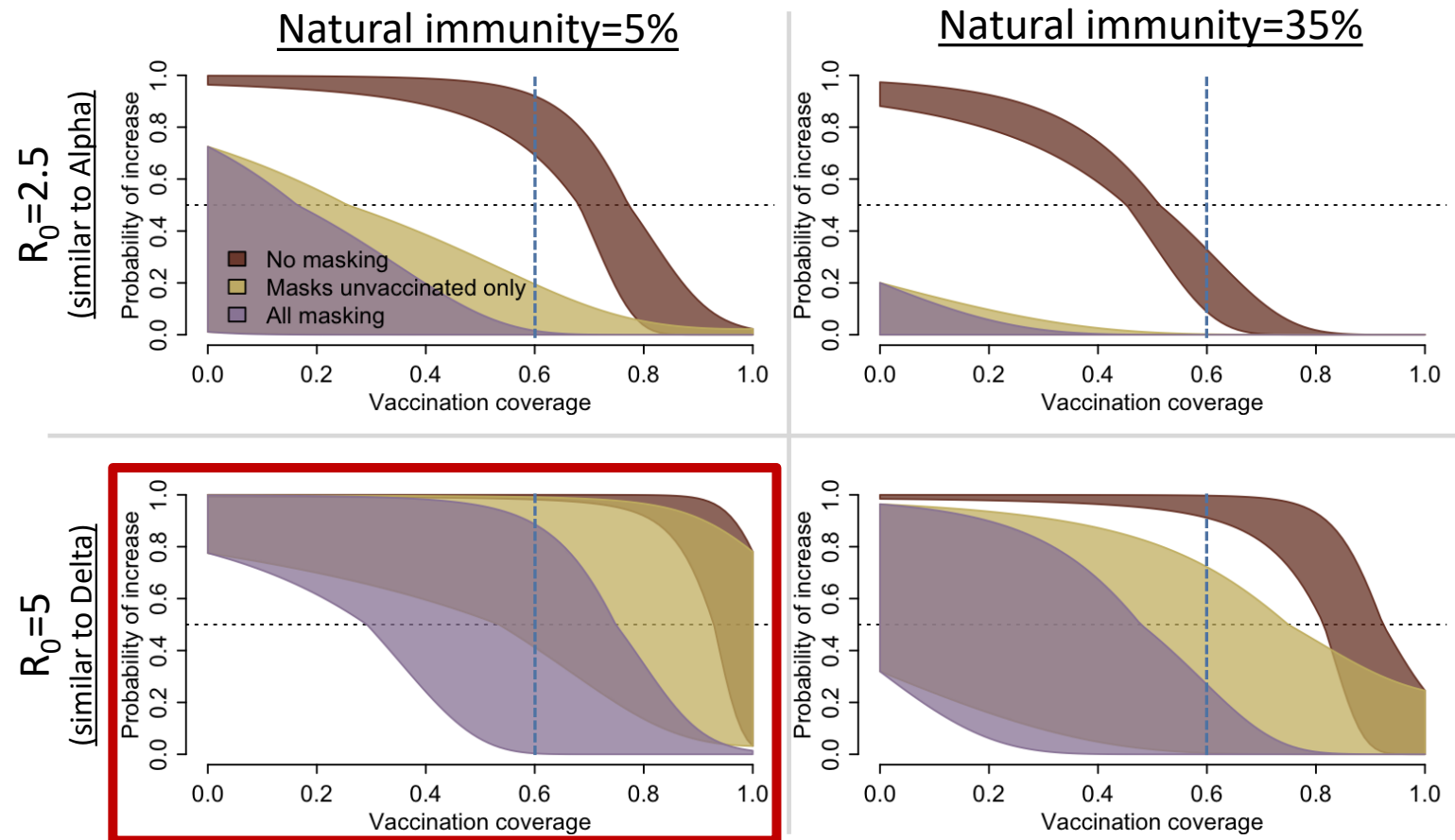
Sheikh et al. Lancet (2021): [https://doi.org/10.1016/S0140-6736\(21\)01358-1](https://doi.org/10.1016/S0140-6736(21)01358-1); Lopez Bernal et al. medRxiv preprint; <https://doi.org/10.1101/2021.05.22.21257658>; Stowe et al. PHE preprint: https://khub.net/web/phe-national/public-library/-/document_library/v2WsRK3ZIEig/view/479607266; Nasreen et al. medRxiv preprint: <https://doi.org/10.1101/2021.06.28.21259420>; <https://www.gov.il/en/departments/news/06072021-04>

Given increased transmissibility, lower VE, and current vaccine coverage, NPIs needed to reduce transmission of Delta variant

Model Assumptions:

- Vaccine effectiveness 75-85%
- 50% infections reported
- Masking:
 - Source control 40-60% effective
 - Personal protection 20-30% effective
- NO ADJUSTMENTS FOR OTHER INTERVENTIONS
 - e.g., no distancing, no isolation, no gathering restrictions

Reported incidence 50 cases per 100,000 per week

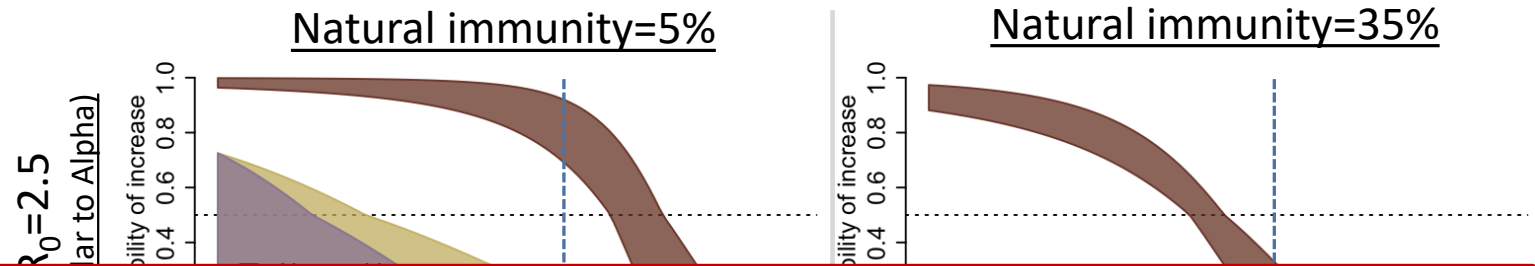


Given increased transmissibility, lower VE, and current vaccine coverage, NPIs needed to reduce transmission of Delta variant

Model Assumptions:

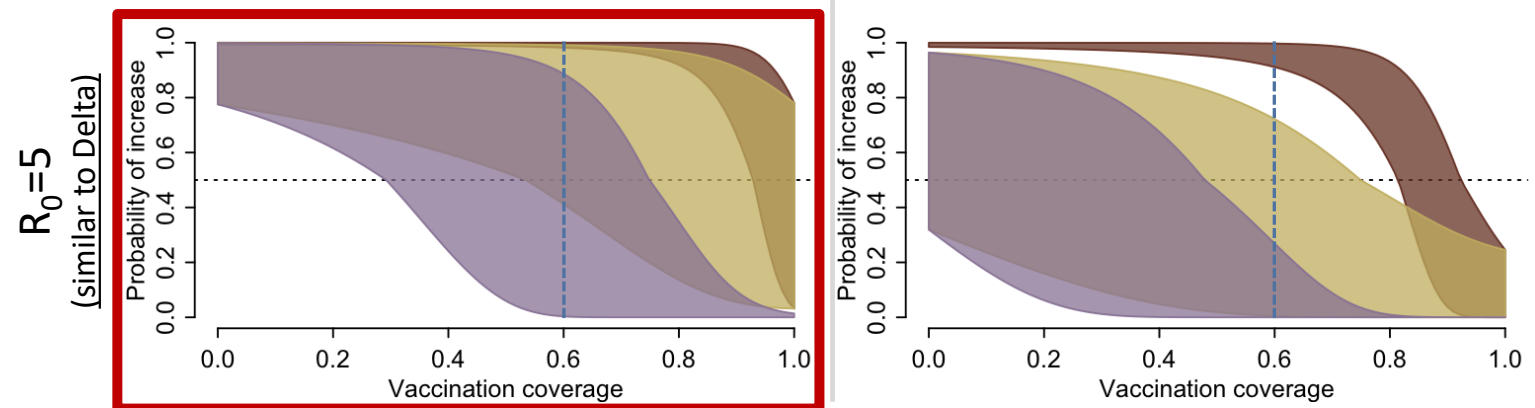
- Vaccine effectiveness 75-85%
- 50% infections reported

Reported incidence 50 cases per 100,000 per week



Given higher transmissibility and current vaccine coverage, universal masking is essential to reduce transmission of the Delta variant

- NO ADJUSTMENTS FOR OTHER INTERVENTIONS
 - e.g., no distancing, no isolation, no gathering restrictions



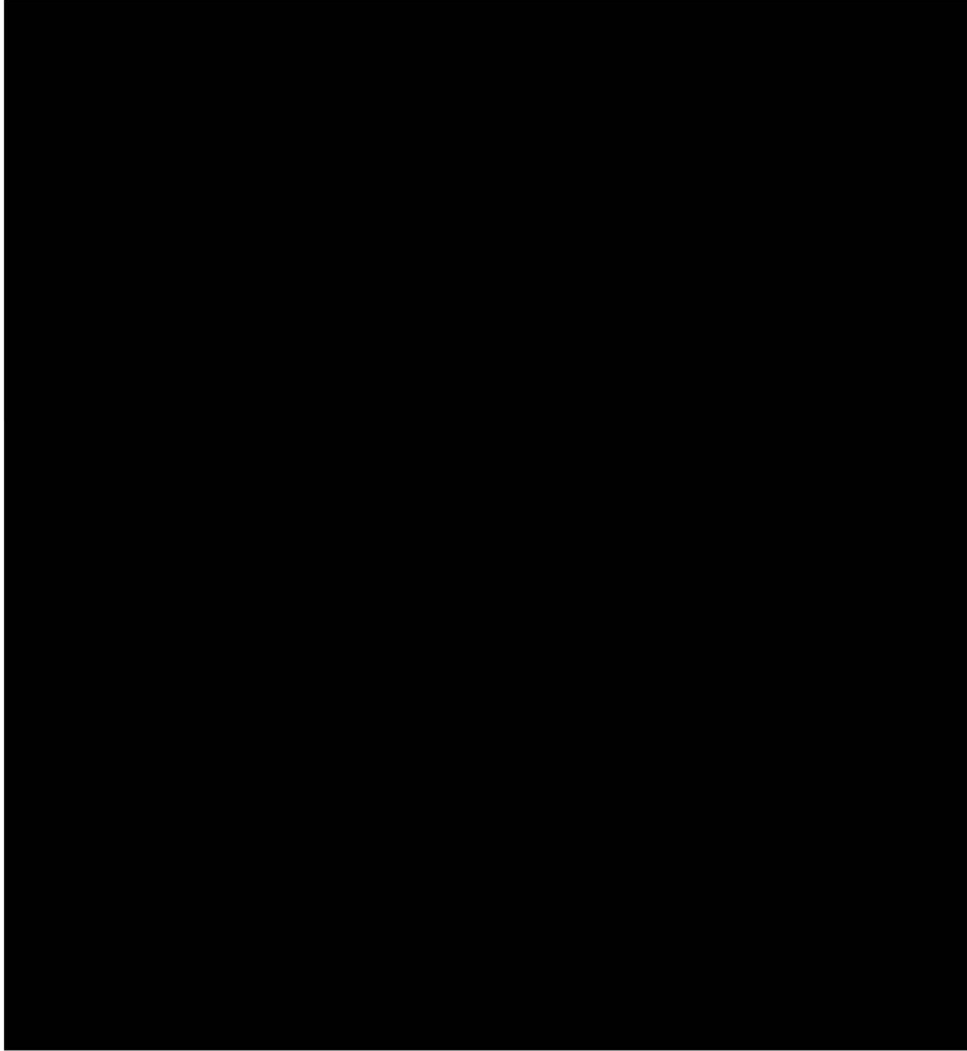
Summary

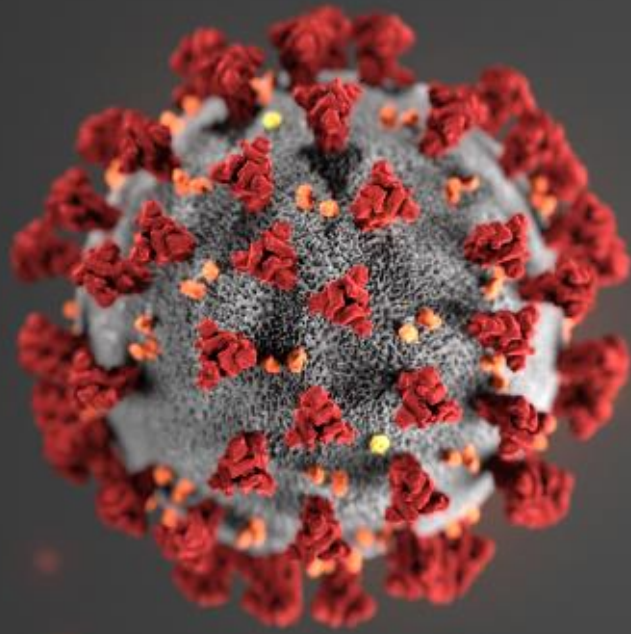
- Delta is different from previous strains
 - Highly contagious
 - Likely more severe
 - Breakthrough infections may be as transmissible as unvaccinated cases
- Vaccines prevent >90% of severe disease, but may be less effective at preventing infection or transmission
 - Therefore, more breakthrough and more community spread despite vaccination
- NPIs are essential to prevent continued spread with current vaccine coverage

Next steps for CDC

- Communications
 - Acknowledge the war has changed
 - Improve public's understanding of breakthrough infections
 - Improve communications around individual risk among vaccinated
 - Risk of severe disease or death reduced **10-fold or greater** in vaccinated
 - Risk of infection reduced **3-fold** in vaccinated
- Prevention
 - Consider vaccine mandates for HCP to protect vulnerable populations
 - Universal masking for source control and prevention
 - Reconsider other community mitigation strategies

Acknowledgements





For more information, contact CDC
1-800-CDC-INFO (232-4636)
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.

