Improving communications around vaccine breakthrough and vaccine effectiveness

July 29, 2021
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-fully vaccinated coverage) + (1-VE)*fully vaccinated coverage). Rate in fully vaccinated=(1-VE)*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

- Reflects increases in vaccine coverage, higher coverage in older adults
- Higher risk among older age groups for hospitalization and death relative to younger people (regardless of vaccination status)

(_CONFIDENTIAL – preliminary data, subject to change)
# CDC uses multiple platforms and study designs to monitor COVID-19 vaccine effectiveness (VE)

<table>
<thead>
<tr>
<th>VE priority</th>
<th>Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection and transmission</td>
<td>Prospective cohort among healthcare personnel (HCP) &amp; frontline workers; transmissibility evaluation in LTCF and other congregate settings; case-ascertained household cohorts for transmission</td>
</tr>
<tr>
<td>Non-severe disease</td>
<td>Test-negative design (TND) case-control among outpatients; Electronic health record (EHR) datasets</td>
</tr>
<tr>
<td>Severe disease/hospitalization</td>
<td>TND among hospitalized patients (for adults and children); conventional case-control using hospitalized controls; EHR datasets</td>
</tr>
<tr>
<td>Older adults, including nursing home residents</td>
<td>Case-control among adults ≥65 years; National Healthcare Safety Network comparison to population coverage estimated through immunization registries; Outbreaks in nursing homes; EHR datasets</td>
</tr>
<tr>
<td>Those with key underlying conditions (e.g., immunocompromised)</td>
<td>Captured above</td>
</tr>
<tr>
<td>Duration of protection</td>
<td>Captured above</td>
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<tr>
<td>Variant-specific VE</td>
<td>Captured above; outbreaks in congregate settings</td>
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</tbody>
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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-2\textsuperscript{nd} 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-2\textsuperscript{nd} 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-2\textsuperscript{nd} dose

*(CONFIDENTIAL – preliminary data, subject to change)*
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%) overall\(^1\)

- **80% against SARS-CoV-2 infection** ≥7 days after 2nd dose of mRNA vaccine among people with IBD on immunosuppressive medication\(^2\)

- **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%) overall\(^1\)

- **59% against COVID-19 hospitalization** among immunocompromised ≥14 days after 2nd dose of mRNA vaccine\(^3\) vs. 91% (CI 86-95%) without immune compromise\(^3\)

*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

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

- **Screening method**
  Estimates VE by comparing vaccine coverage in cases to population
  \[ VE = 1 - \left( \frac{PCV}{1-PCV} \right) \left( \frac{1-PPV}{PPV} \right) \]
  - 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

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

Micchova et al. doi: 10.21203/rs.3.rs-637724/v1
Ong et al. doi:10.2139/ssrn.3861566; PHE technical briefing 19:
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

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Pfizer 2-Dose Vaccine Effectiveness for Alpha vs. Delta


*Note two different time periods in Israel
Given increased transmissibility, lower VE, and current vaccine coverage, NPIs needed to reduce transmission of Delta variant

Reported incidence 50 cases per 100,000 per week

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

\[
R_0 = 2.5 \\
\text{(similar to Alpha)}
\]  

\[
R_0 = 5 \\
\text{(similar to Delta)}
\]
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

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

Reported incidence 50 cases per 100,000 per week

\[
R_0 = 2.5 \quad \text{(similar to Alpha)}
\]

\[
R_0 = 5 \quad \text{(similar to Delta)}
\]
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
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