Update on Emerging SARS-CoV-2 Variants and COVID-19 vaccines

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ACIP Meeting
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Impact of COVID-19 Vaccination
COVID-19 Reported Cases per 100,000 Population (last 7 days) and Percent of Total Population Fully Vaccinated, United States

https://covid.cdc.gov/covid-data-tracker/#vaccination-case-rate (Updated 8/12/21)
DELTA CASES

Two example states with 1 million population and different levels of vaccination coverage (70% vs 30%)
DELTA CASES AND HOSPITALIZATIONS

Two example states with 1 million population and different levels of vaccination coverage (70% vs 30%)

Higher vaccination coverage leads to fewer cases and hospitalizations, but greater % of vaccinated cases and hospitalizations

In both scenarios, cases and hospitalizations are greater among unvaccinated than vaccinated persons.
Emerging SARS-CoV-2 Variants & Vaccines: What do we know now?
## Variants of Concern

### WHO label
- Alpha
- Beta
- Gamma
- Delta

### PANGO Lineage
- Alpha: B.1.1.7
- Beta: B.1.351
- Gamma: P.1
- Delta: B.1.617.2

### First detected
- Alpha: United Kingdom
- Beta: South Africa
- Gamma: Japan / Brazil
- Delta: India

### No. of spike mutations
- Alpha: 10-13
- Beta: 10
- Gamma: 11
- Delta: 11-15

### Receptor binding domain mutations
- Beta: K417N, E484K, K417N
- Gamma: K417T, E484K, N501Y
- Delta: L452R, T478K

### Attributes
- **Alpha**
  - 50% increased transmission
  - **Minimal** impact on neutralization by convalescent or vaccine sera
  - **No impact** on antibody therapies

- **Beta**
  - 50% increased transmission
  - **Significantly reduced** efficacy of some antibodies
  - **Reduced** neutralization by convalescent or vaccine sera

- **Gamma**
  - **Significantly reduced** efficacy of some antibodies
  - **Reduced** neutralization by convalescent or vaccine sera
  - 50% increased transmission
  - Potential reduced antibody efficacy
  - Potential reduced neutralization by vaccine sera

- **Delta**
  - Increased transmission
  - Potential reduced antibody efficacy
  - Potential reduced neutralization by vaccine sera

(*) = detected in some sequences but not all
Estimated Proportions of SARS-CoV-2 lineages in the US

April 25 – July 31, 2021 with NOWCAST

Percent of Viral Lineages

Collection Date, 2-weeks ending

Variants of Concern

- Alpha (B.1.1.7) 2%
- Gamma (P.1) 1%
- Delta (B.1.617.2) 94%
  - Sub-lineages:
    - AY.3 13%
    - AY.2 <1%
    - AY.1 <1%
- Beta (B.1.351) 0%

CDC COVID Data Tracker As of 8/10/21; VOC=Variant of Concern; VOI=Variant of Interest
Types of evidence for monitoring vaccine efficacy

- Antibody neutralization — laboratory
  - Correlate of protection not yet established
  - Good correlation of vaccine efficacy with resulting neutralizing antibody levels
  - Likely first evidence we will get on impact of variants on vaccines

- Vaccine efficacy in clinical trials and real-world effectiveness
  - Greater protection against severe disease > symptomatic illness > confirmed infection (including asymptomatic)
  - Protection against severe disease requires lower antibody levels & less affected by differences in vaccine efficacy

- Vaccine breakthrough infection

Reduced antibody neutralization activity of vaccine sera relative to wildtype/dominant strain by study (n=50)
Duration of immunity

- To date, available data demonstrate antibody persistence at least:
  - 8 months after COVID-19 infection
  - 6 months after 2nd mRNA vaccine dose; 8 months after receiving single Janssen dose

- May maintain long-term protection from severe illness by antigenically similar strain, even if become susceptible to mild infection

- Two studies show combined impact of waning immunity and reduced variant neutralization — ~50% protected against ancestral strain have undetectable neutralizing titers against Beta/Gamma at 6 months after Moderna vaccine
  - Small study 8 months post-receipt of Janssen vaccine — minimal decline in neutralizing titers & improved protection against Beta/Gamma/Delta vs. 1-month post-vaccine

Pfizer vaccine 6-month efficacy

VE against infection: 91% (89, 93)

<table>
<thead>
<tr>
<th>Period after dose 2</th>
<th>% VE (95% CI)</th>
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<tbody>
<tr>
<td>≥7 days to &lt;2 mos</td>
<td>96 (94, 98)</td>
</tr>
<tr>
<td>≥2 mos to &lt;4 mos</td>
<td>90 (87, 93)</td>
</tr>
<tr>
<td>≥4 mos to &lt;6 mos</td>
<td>84 (75, 90)</td>
</tr>
</tbody>
</table>

VE against severe illness: 97% (80,100)

Moderna press release:
93% VE against infection at 6 months (unpublished)

Thomas et al. medRxiv preprint https://doi.org/10.1101/2021.07.28.21261159
Vaccine efficacy and effectiveness (VE) against variants

- **Alpha (B.1.1.7)** — mRNA vaccines >85% real-world VE against confirmed infection in United States and multiple other countries

- **Gamma (P.1)** — mRNA vaccines 84%–88% real-world VE against symptomatic infection and 79% against confirmed infection when P.1 in wide circulation in Canada

- **Beta (B.1.351)**
  - Moderna (96%) & Pfizer (75%) real-world VE against confirmed infection in Qatar
  - Janssen 52% VE against moderate/severe disease in South Africa (vs. 74% in US)
  - **High VE against severe disease** — 96%–100% for mRNA vaccines in Qatar, 73% at ≥14 days and 81% at ≥28 days for Janssen in South Africa

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Abu-Radad and Butt. NEJM (2021); Andrejko et al. medRxiv preprint (Apr 10 2021); Chemaitelly et al. Nature Med (2021); https://doi.org/10.1038/s41591-021-01446-y; Sandoff et al. NEJM (2021); Chung et al. medRxiv preprint (May 28 2021); Yassi et al. medRxiv preprint (May 25 2021); Nasreen et al.medRxivpreprint: https://doi.org/10.1101/2021.06.28.21259420
Delta variant: What we know

- Nearly twice as contagious as previous variants
- Some evidence of increased illness severity vs. previous strains in unvaccinated persons
- Greatest risk of transmission still among unvaccinated people
- Fully vaccinated people with Delta breakthrough infections can spread virus to others
  - However, vaccinated people with Delta appear to be infectious for a shorter period than unvaccinated persons with Delta

Fisman & Tuite. medRxiv; Ong et al. SSRN Journal. 2021; Sheikh et al. Lancet (2021); Daggunar J. medRxiv; Li et al. medRxiv; Lopez Bernal et al. NEJM (2021); Stowe et al. PHE preprint; Riley et al. medRxiv; Micochova et al. Research Square preprint; Musser et al.medRxiv; Brown et al. MMWR (2021); Riemersma et al. medRxiv; Chia et al. medRxiv.
Pfizer & Moderna 2-Dose Effectiveness for Alpha vs. Delta

Differences in COVID vaccination program by country with potential impact on comparability of VE results

<table>
<thead>
<tr>
<th>Country</th>
<th>U.S.</th>
<th>Israel</th>
<th>Qatar</th>
<th>U.K.</th>
<th>Canada</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interval</td>
<td>3-4 weeks</td>
<td>3 weeks</td>
<td>3-4 weeks</td>
<td>12 weeks</td>
<td>16 weeks</td>
</tr>
<tr>
<td>Note</td>
<td>-</td>
<td>Tight cohort</td>
<td>-</td>
<td>Mix-and-match</td>
<td></td>
</tr>
</tbody>
</table>

- Extended intervals between doses (12 weeks) shown to improve immunogenicity and VE for Pfizer and AstraZeneca vaccines compared with standard interval, including ages ≥80 years
- Pfizer has lower mRNA dosage and accelerated schedule (3 weeks) compared with Moderna (4 weeks)

Declines in VE against infection
Preprint and unpublished data from Israel

- Ministry of Health analysis — higher breakthrough rates and lower Pfizer VE against infection for persons vaccinated in Jan–Feb 2021 more recent months for persons aged 16–59 and ≥60 years

- Two retrospective cohort studies of persons vaccinated with Pfizer in large healthcare systems:
  - 2.3-fold increased risk for breakthrough infection among persons vaccinated with Pfizer in January vs. April 2021 (n=1.35 million)
  - Higher breakthrough infection rate (2.4% v. 1.1%, OR=2.2) among those who received 2nd dose ≥5 months ago compared to <5 months ago (n=33,993)
    - Higher magnitude of difference with increasing age

Correlation of SARS-CoV-2 Breakthrough Infections to Time-from-vaccine; Preliminary Study | medRxiv
Elapsed time since BNT162b2 vaccine and risk of SARS-CoV-2 infection in a large cohort | medRxiv
VE against Infection and Hospitalization July vs. Jan-May
Mayo Clinic Health System, Minnesota, n=25,589

SARS-CoV-2 Infection
Moderna: 76% (95% CI: 58%-87%)
Pfizer: 42% (95% CI: 13%- 62%)

COVID-19 Hospitalization
Moderna: 81% (95% CI: 33%-96%)
Pfizer: 75% (95% CI: 24%- 94%)

Delta prevalence increased from 0.7% in May to >70% in July

Puranik et al. medRxiv:
https://www.medrxiv.org/content/10.1101/2021.08.06.21261707v2
U.S. COVID-19 Vaccine Breakthrough Cases

- Despite high vaccine efficacy, vaccine breakthrough cases* are expected
  - Some will be caused by variants, even if vaccine has similar effectiveness against variants
  - CDC monitors nationwide vaccine breakthrough resulting in hospitalization or death

- As of August 2, among more than 164 million fully vaccinated in U.S., there have been 7,101 hospitalizations & 1,507 deaths with vaccine breakthrough reported to passive surveillance**
  - Among hospitalized or fatal breakthrough cases, 74% among persons aged ≥65 years
  - Variants of concern (%) among breakthrough cases similar to national genomic surveillance

- COVID-NET data on COVID-19-associated hospitalizations among aged persons ≥18 years
  — ~32% of all vaccinated cases are immunocompromised vs. 11% of unvaccinated cases

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*Vaccine breakthrough case:* Person with SARS-CoV-2 RNA or antigen detected in respiratory specimen collected ≥14 days after completing primary series of an FDA-authorized COVID-19 vaccine

**CDC website as of 8/5/21; 1,816 hospitalizations and 316 fatal cases reported as asymptomatic or not related to COVID-19. CDC. MMWR (2021); COVID-NET: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covid-net/purpose-methods.html
### Summary of Preliminary Data: Implications of SARS-CoV-2 Variants of Concern on Vaccine Effectiveness

<table>
<thead>
<tr>
<th>Variant</th>
<th>Prevalence in United States</th>
<th>Impact on Vaccine Effectiveness</th>
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<tbody>
<tr>
<td>B.1.1.7  (Alpha)</td>
<td>Low</td>
<td>Minimal impact on VE; attention needed for additional substitutions in receptor binding domain (RBD), e.g., E484K</td>
</tr>
<tr>
<td>B.1.351  (Beta)</td>
<td>Low</td>
<td>Moderate impact on VE against infection, but appear to protect against severe disease</td>
</tr>
<tr>
<td>P.1  (Gamma)</td>
<td>Low</td>
<td>Moderate impact on VE for some vaccines; more data needed</td>
</tr>
<tr>
<td>B.1.617.2  (Delta)</td>
<td>High</td>
<td>Moderate impact on VE for infection, but appear to protect against severe disease; more data needed, especially for Janssen</td>
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Boosters and Second-Generation Vaccines Against SARS-CoV-2 Variants

- Manufacturers conducting booster studies of current vaccines and/or second-generation vaccines against Beta (B.1.351)

- Moderna — preliminary phase 2 results of single 50 µg booster of authorized (mRNA-1273) and variant-specific vaccine (mRNA-1273.351)
  - Both vaccines — acceptable safety; boosted immunity to wild-type, Beta, Gamma

- Pfizer has also submitted preliminary data on booster of original vaccine to FDA

- No Delta-specific booster vaccine studies shared to date

Wu et al. medRxiv preprint (May 6, 2021): [https://doi.org/10.1101/2021.05.05.21256716](https://doi.org/10.1101/2021.05.05.21256716)
Summary

- Currently authorized vaccines offer protection against known variants — important to increase vaccine uptake in eligible populations.
- CDC is closely monitoring real-world vaccine effectiveness and breakthrough infections using multiple methods, populations, and outcomes.
- CDC continues to monitor emerging variants — prevalence and impact on disease incidence, severity, and vaccine breakthrough.
- ACIP will review evidence submitted for boosters and any next-generation vaccines.
- Changing landscape — CDC will communicate promptly about new evidence.
For more information, contact CDC
1-800-CDC-INFO (232-4636)

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.