Overview

• Epidemiology & new data on HIV and COVID
• Vaccines –
  – More data on waning immunity
  – Boosters
• COVID-19 treatment
  – Sotrovimab
  – Paxlovid
Global Trends in COVID-19 Diagnoses & Deaths

>246 Million Confirmed Cases
>3 million cases/week

~5 Million Confirmed Deaths
>50,000 deaths/week

Increase in new cases and deaths since last month’s review
Global Trends in COVID-19 Diagnoses & Deaths

13%↓ Deaths – ↑ Cases Rwanda & Eritrea

4%↓ Deaths – Slowing in decline with increases in parts Caribbean

12%↑ Deaths – High in UK, Russia, Ukraine

10%↑ Deaths

50%↑ Deaths – Case rate and deaths going in opposite directions

4%↓ Deaths – Rates very high in Iran and Iraq
COVID-19 cases/100,000 population, October 25-31, 2021
COVID-19 deaths/100,000 population, October 25-31, 2021
SARS-CoV-2 Variants

Figure 4. Prevalence of Variants of Concern (VOCs) in the last 60 days and historic detections, data as of 2 N

Alpha

Beta

Gamma

Delta

Proportion of VOC among total sequences:
- 0.501 - 1.000
- 0.101 - 0.500
- 0.011 - 0.100
- >0.000 - 0.010

VOC detected, too few sequences to estimate proportion
No new VOC sequences, VOC previously reported**
No presence of VOC reported to WHO
Not applicable
Background: Mu initially seen in Columbia in January 2021. Now in 39 countries. Includes numerous mutations seen in prior variants.

Design: Virus neutralization experiment using pseudovirus with Mu spike and serum from 13 people infected April-Sept 2020 & 14 vaccinated with Pfizer

Outcome: In vitro neutralization

Source: Uriu K. NEJM 2021
• Antibody neutralization of Mu was 9.1-10.6X lower than the initial SARS-CoV2 using both convalescent serum and serum from Pfizer vaccine recipients

Source: Uriu K. NEJM 2021
Background: Waning immunity and DOVID evolution may affect vaccine protection

Design: Cohort study of household contacts to COVID-19

Population: 162 index cases & 231 contacts swabbed daily for 20 days

Outcome: Secondary attack rate in household contacts by index case and contact vaccine status

RESULTS

- Secondary attack rate (SAR) was 38% in unvaccinated and 26% in vaccinated contacts (p=0.14)
  - Consistent with 34% vaccine efficacy
- Time from 2nd dose of vaccine longer in infected than uninfected household contacts (p=0.001)
  - Consistent with waning of immunity
- SAR did not vary by index case vaccine status nor did it vary with time since index case received last vaccine
  - Breakthrough infections are comparably infectious as infections in unvaccinated index cases
- Viral decline rate was faster in vaccinated delta index cases than in unvaccinated delta cases, alpha variant cases, or pre-alpha variant cases
  - Vaccination led to fast clearance in cases - ~3 days vaccinated delta vs. pre-alpha

Source: Sanganayagam A. Lancet ID 2021
Background: Several studies have reported waning of vaccine-induced COVID-19 immunity

Design: Analysis of open-label phase of Moderna trial comparing COVID-19 incidence July-August 2021 among early and late vaccinees (placebo group in initial trial)

Population: ~26,000 persons

Outcome: COVID-19 incidence & severe disease

<table>
<thead>
<tr>
<th>Covid-19 Cases and Age Group</th>
<th>mRNA-1273e Group (N = 14,746)</th>
<th>mRNA-1273p Group (N = 11,431)</th>
<th>Difference in Incidence Rates (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of cases</td>
<td>no. of person-yr</td>
<td>incidence rate per 1000 person-yr</td>
</tr>
<tr>
<td>All cases</td>
<td>162</td>
<td>2102</td>
<td>77.1</td>
</tr>
<tr>
<td>Age 18 to &lt;65 yr</td>
<td>136</td>
<td>1558</td>
<td>87.3</td>
</tr>
<tr>
<td>Age ≥65 yr</td>
<td>26</td>
<td>544</td>
<td>47.8</td>
</tr>
<tr>
<td>Severe cases</td>
<td>13</td>
<td>2102</td>
<td>6.2</td>
</tr>
<tr>
<td>Age 18 to &lt;65 yr</td>
<td>7</td>
<td>1558</td>
<td>4.5</td>
</tr>
<tr>
<td>Age ≥65 yr</td>
<td>6</td>
<td>544</td>
<td>11.0</td>
</tr>
</tbody>
</table>

Difference greater in younger people - unanticipated

Source: Baden LR. NEJM 2021
CDC Booster Guidance

**IF YOU RECEIVED**

Pfizer-BioNTech or Moderna

You are eligible for a booster if you are:
- 65 years or older
- Age 18+ who live in long-term care settings
- Age 18+ who have underlying medical conditions
- Age 18+ who work or live in high-risk settings

When to get a booster:
At least 6 months after your second shot

Which booster should you get?
Any of the COVID-19 vaccines authorized in the United States

**IF YOU RECEIVED**

Johnson & Johnson's Janssen

You are eligible for a booster if you are:
- 18 years or older

When to get a booster:
At least 2 months after your shot

Which booster should you get?
Any of the COVID-19 vaccines authorized in the United States

Who can get a COVID-19 booster vaccine

Booster vaccine doses will be available on the NHS for people most at risk from COVID-19 who have had a 2nd dose of a vaccine at least 6 months ago.

This includes:

- people aged 50 and over
- people who live and work in care homes
- frontline health and social care workers
- people aged 16 and over with a health condition that puts them at high risk of getting seriously ill from COVID-19
- people aged 16 and over who are a main carer for someone at high risk from COVID-19
- people aged 16 and over who live with someone who is more likely to get infections (such as someone who has HIV, has had a transplant or is having certain treatments for cancer, lupus or rheumatoid arthritis)

Which COVID-19 vaccine will I get?

Most people will be offered a booster dose of the Pfizer/BioNTech vaccine or Moderna vaccine.

This means your booster dose may be different from the vaccines you had for your 1st and 2nd doses.

Some people may be offered a booster dose of the Oxford/AstraZeneca vaccine if they cannot have the Pfizer/BioNTech or Moderna vaccine.
**Background:** In the U.S., COVID-19 vaccines are not approved for use in children under 12

**Intervention:** 2 10ug dose 3 weeks apart

**Design:** Analysis of open-label phase of Moderna trial comparing COVID-19 incidence July-August 2021 among and large vaccinees

**Population:** ~2250 children ages 5-<12 years (1518 vaccine recipients)

**Outcome:** COVID-19 >7 days after 2nd dose

**Vaccine efficacy 90.9%**

No cases myocarditis, hospitalization, or death

https://www.fda.gov/media/153409/download
# Pfizer mRNA Vaccine: Risk & Benefits

## Model 1 Million Children – 6 Months

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Prevented Cases</th>
<th>Prevented Hospitalizations</th>
<th>Prevented Deaths</th>
<th>Excess Myocarditis Cases</th>
<th>Excess Myocarditis Hospitalizations</th>
<th>Excess Myocarditis Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence 9/21</td>
<td>45,773</td>
<td>192</td>
<td>1</td>
<td>106</td>
<td>58</td>
<td>0</td>
</tr>
<tr>
<td>Peak incidence</td>
<td>54,345</td>
<td>250</td>
<td>1</td>
<td>106</td>
<td>58</td>
<td>0</td>
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<tr>
<td>Low incidence</td>
<td>2,639</td>
<td>21</td>
<td>0</td>
<td>106</td>
<td>58</td>
<td>0</td>
</tr>
<tr>
<td>9/21 Incidence – 90% VE</td>
<td>58,851</td>
<td>241</td>
<td>1</td>
<td>106</td>
<td>58</td>
<td>0</td>
</tr>
<tr>
<td>High death rate – CDC tracker</td>
<td>45,773</td>
<td>192</td>
<td>3</td>
<td>106</td>
<td>58</td>
<td>0</td>
</tr>
<tr>
<td>Scenario 1 – 50% myocarditis risk</td>
<td>45,773</td>
<td>192</td>
<td>1</td>
<td>53</td>
<td>29</td>
<td>0</td>
</tr>
</tbody>
</table>

https://www.fda.gov/media/153447/download
COVID-19 Vaccination in Children: Guidelines

**CDC**

- **>12 years – 2 doses** Pfizer vaccine 21 days apart
- **Ages 5-11**
  - 1/3 dose vaccine
  - 2 doses 21 days apart
- Vaccines other than Pfizer not currently recommended

**UK**

- **Ages 12-15 years – Single** dose Pfizer vaccine
- 2\(^{nd}\) dose recommended if
  - Child lives with someone at high risk for infection
  - Child has a condition that places them at high risk for COVID-19

Norway, Hong Kong also using a single dose

Discussion of vaccine in children
**Background:** Limited data on COVID-19 vaccines in children

**Intervention:** 2 dose 28 days apart

**Design:** Phase 1/2 trial

**Population:** 72 (phase I) and 480 (phase 2) children in China

**Outcome:**
Immunogenicity and safety

**Vaccine immunogenic:** >97% vaccinated developed antibody – all 3-5 year olds

**Vaccine was safe:**
- common local reactions, fatigue, fever

Source: Han B. Lancet ID 2021
Coronavac in Children 3-17

China to Start Vaccinating Children Over 3 Years Old as COVID-19 Cases Spread

• Coronavac also being used in children ≥6 years in Chile, Cambodia, and Indonesia
• Moderna currently approved in the US only for persons age 18 and over
• Trial children ages 12-17 – TeenCOVE
  • 3,732 participants
  • Vaccine efficacy 100% - press release in May, 2021
  • FDA asked for more safety data in face of concerns related to myocarditis
• Trial 4,753 children 6-11 – 2 x 50ug dose 28 days apart
  • 99.3% seroconversion
  • No data on myocarditis in press release
• Trial children 6 months to 5 years ongoing

Sotrovimab: A New Monoclonal

Background: Sotrovimab is a pan-sarbecovirus monoclonal antibody-targets a highly conserved epitope unassociated with ACE2 receptor binding (unlike many other monoclonals)

Design: Interim analysis RCT

Population: 583 people with symptomatic COVID-19 with >1 risk for severe disease (obesity, age >60, DM, heart disease) within 5 days of symptom onset

Outcome: Hospitalization or death

Adverse events similar in treatment and placebo groups

| Table 2. Efficacy Outcomes through Day 29 (Intention-to-Treat Population). |
|-----------------------------------|------------------|------------------|
| **Outcome**                       | **Sotrovimab (N = 291)** | **Placebo (N = 292)** |
| Primary outcome                   |                  |                  |
| Hospitalization for >24 hr for any cause or death from any cause — no. (%) | 3 (1) | 21 (7) |
| Hospitalization for >24 hr for any cause | 3 (1) | 21 (7) |
| Death from any cause               | 0 (0) | 1 (<3) |
| Alive and not hospitalized — no. (%) | 284 (98) | 270 (92) |
| Data missing — no. (%)             | 4 (1) | 1 (<1) |
| All patients with missing data     | 4 (1) | 1 (<1) |
| Patients with missing data because of withdrawal of consent before receipt of sotrovimab or placebo | 3 (1) | 1 (<1) |
| Relative risk reduction (97.24% CI) | 85 (44–96) | — |
| P value                            | 0.002 | — |
| Other clinical outcomes‡:         |                  |                  |
| Emergency department visit or hospitalization for any cause or death from any cause — no. (%) | 6 (2) | 28 (10) |
| Emergency department visit for any cause§ | 2 (<1) | 8 (3) |
| Hospitalization for any cause      | 4 (1)¶ | 21 (7) |
| Death from any cause               | 0 (0) | 1 (<3) |
| Emergency department visit without hospitalization, or hospitalization for <24 hr for any cause — no. (%)** | 3 (1) | 7 (2) |
| Severe or critical progression — no. (%)†† | 2 (<1) | 19 (7) |
| Low-flow nasal cannula or face mask | 2 (<1) | 11 (4) |
| Nonrebreather mask, high-flow nasal cannula, or noninvasive ventilation | 0 | 5 (2) |
| Invasive mechanical ventilation    | 0 | 2 (<1) |
| Death from any cause               | 0 | 1 (<1) |
| Admission to ICU for any cause — no. (%) | 0 | 5 (2) |
**Background**: There is a need for COVID-19 treatments, particularly orally administered drugs. Paxlovid is a SARS-CoV-2-3CL protease inhibitor

**Design**: RCT

**Population**: 774 non-hospitalized persons with COVID-19 at high risk for severe disease within 3 days of symptom onset – interim analysis

**Outcome**: Hospitalization or death through day 28

<table>
<thead>
<tr>
<th></th>
<th>Hospitalization or Death</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paxlovid</td>
<td>3/389 (0.8%)</td>
<td>0</td>
</tr>
<tr>
<td>Placebo</td>
<td>27/385 (7%)</td>
<td>7</td>
</tr>
</tbody>
</table>

- Similar results of persons treated within 5 days of symptom onset
- Similar adverse events in treatment and placebo groups

Summary

• Epidemiology
  • Some resurgence of epidemic
  • Continued evolution – Mu variant

• Vaccines
  • Vaccine-induced immunity wanes over time – not a new story
  • Evolving consensus supporting boosters – undermines equity
  • New pediatric indications for immunization

• New treatments
  • Sotrovimab – very effective
  • Paxlovid – 2nd oral therapy
Questions and Comments