COVID-19 Clinical Update
I-TECH Videoconference  September 13, 2021

Matthew Golden, MD, MPH
Professor of Medicine, University of Washington
Director, PHSKC HIV/STD Program
Director, UW Center for AIDS and STD
Overview

• Epidemiology

• Vaccines – Focus on Efficacy
  – Impact of Delta Variant
  – Impact of time and waning immunity
Global Trends in COVID-19 Diagnoses & Deaths

>211 Million Confirmed Cases
4.5 million cases/week

~4.4 Million Confirmed Deaths
45,000 deaths/week

Figure 1. COVID-19 cases reported weekly by WHO Region, and global deaths, as of 22 August 2021**
Global Trends in COVID-19 Diagnoses & Deaths

- Highest Rate in Botswana, though declining
- Highest rates in US, but death is higher in Mexico and Brazil
- Highest rates in UK
- Highest rate and death rates in Malaysia
- Highest rate in Thailand. Highest death rate in Indonesia
- Highest rate and death rates in Iran
COVID-19 cases/100,000 population, 16 August – 22 August 2021
COVID-19 deaths/100,000 population, 16 August – 22 August 2021
New CDC Variant Classification System

https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/
Vaccines
Background: Impact of vaccines on transmission not well defined. UK data (reviewed in July) suggested ~50% decreased transmission in households following immunization.

Design: Comparison of periods before and after healthcare workers were vaccinated in UK

Population: 194,362 household members of 144,525 healthcare workers

Outcome: CoV-2 + test and hospitalization in unvaccinated household contacts

Source: Shah A. NEJM 202
Changing Vaccine Effectiveness

**Background:** Numerous studies have suggested that the effectiveness of mRNA vaccines against the delta variant is diminished. Relative impact on different mRNA vaccines uncertain.

**Design & Population:** Retrospective cohort study two cohorts of ~25,000 (vaccinated & unvaccinated) adults with no h/o SAR-CoV2 matched for demographics, date vaccination, h/o PCT testing in the Mayo Health System, MN, USA. Comparison VE 2 vaccines in 5 states of Mayo System

**Outcome:** Vaccine effectiveness against infection & hospitalization.

---

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>VE Infection</th>
<th>VE Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer</td>
<td>76%</td>
<td>85%</td>
</tr>
<tr>
<td>Moderna</td>
<td>86%</td>
<td>92%</td>
</tr>
</tbody>
</table>

Puranik A. MedRxiv 2021
Changing Vaccine Effectiveness

Delta Becomes Dominant June-July

Comparison IRR SARS-CoV2 Infection Moderna vs Pfizer Vaccines, 5 States

<table>
<thead>
<tr>
<th>Timing Vaccination &amp; Time Period</th>
<th>IRR Moderna vs. Pfizer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-7 days after 2\textsuperscript{nd} dose (entire period)</td>
<td>1.1 (0.16-2.2)</td>
</tr>
<tr>
<td>&gt;14 days after 2\textsuperscript{nd} dose (entire period)</td>
<td>0.5 (0.39-0.64)</td>
</tr>
<tr>
<td>&gt;14 days after 2\textsuperscript{nd} dose (July Only)</td>
<td>0.44 (0.32-0.6)</td>
</tr>
</tbody>
</table>

VE July
-Pfizer 42%
-Moderna 76%

Modern vs. Pfizer IRR 0.56 (0.36-0.83)

VE July
-Pfizer 75%
-Moderna 81%

Modern vs. Pfizer IRR 0.57 (0.17-0.1.7)

Puranik A. MedRxiv 2021
**Background:** Israel instituted mass immunization with Pfizer vaccine in 12/20 with >100-fold ↓ in cases. A resurgent epidemic June 2020 (>95% Delta). Uncertain role for waning immunity vs. Delta variant.

**Data & Population:** ~1.3 million Vaccinated Maccabi Healthcare Systems (MHS) patients with no h/o SARS-CoV2

**Design:** Retrospective cohort study persons receiving care through Maccabi Healthcare Systems (an HMO).

**Outcome:** SARS-CoV2 June 1-July 27, 2021

---

### Incidence SARS-CoV-2 6/1/21-7/27/21, by Time of 2nd Vaccine Dose

<table>
<thead>
<tr>
<th>Month</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feb</td>
<td>1.33 (1.21-1.46)</td>
</tr>
<tr>
<td>March</td>
<td>1.65 (1.44-1.89)</td>
</tr>
<tr>
<td>April</td>
<td>2.26 (1.70-3.01)</td>
</tr>
</tbody>
</table>

**Risk of SARS-CoV-2 Among Persons Vaccinated in January 2021 vs. Feb-March**
Waning Vaccine-Induced Immunity: Israel

**Background:** Israel instituted mass immunization with Pfizer vaccine in 12/20 with >100-fold ↓ in cases. A resurgent epidemic occurred in June 2020 (>95% Delta). Uncertain role for waning immunity vs. Delta variant.

**Data & Population:** All PCR+ cases in Israel July 11-31 among ~5 million vaccinated persons

**Design:** Comparison of rates of infection and severe infection among persons vaccinated at different times.

**Outcome:** SARS-CoV2 infection or Severe COVID

Goldberg Y. MedRxiv 2021
Waning Vaccine-Induced Immunity: Israel
Multivariate Analysis

Protection against SARS-CoV2 and Severe COVID-19 compared to persons vaccinated January 16-31, by age group.

Increasing protection among more recently vaccinated on multivariate analysis

Findings Consistent with Waning Immunity with Time from Immunization Over ~6 months

Vaccine Effectiveness Remained High Among Younger People

Goldberg Y. MedRxiv 2021
Association of Antibody Response with Protection

Relationship of Mean Antibody Neutralization Level and Observed Protective Efficacy in COVID-19 Vaccine Trials

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Mean Neutralization Level (Fold Convalescent Sera)</th>
<th>Protective Efficacy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderna</td>
<td><img src="image1.png" alt="Distribution" /></td>
<td>90%</td>
</tr>
<tr>
<td>Pfizer</td>
<td><img src="image2.png" alt="Distribution" /></td>
<td>85%</td>
</tr>
<tr>
<td>Novavax</td>
<td><img src="image3.png" alt="Distribution" /></td>
<td>80%</td>
</tr>
<tr>
<td>AZ</td>
<td><img src="image4.png" alt="Distribution" /></td>
<td>75%</td>
</tr>
<tr>
<td>CoronaVac</td>
<td><img src="image5.png" alt="Distribution" /></td>
<td>70%</td>
</tr>
<tr>
<td>CoronaVac</td>
<td><img src="image6.png" alt="Distribution" /></td>
<td>65%</td>
</tr>
<tr>
<td>CoronaVac</td>
<td><img src="image7.png" alt="Distribution" /></td>
<td>60%</td>
</tr>
</tbody>
</table>

Khoury DS. Nature Med 2021
Estimated Decay in Vaccine Efficacy Based, Time to Need for Booster, and Impact of Variants on Efficacy

Estimated Vaccine Efficacy Over Time Based on Initial Efficacy*

Time for Efficacy to Drop to 50% or 70% Based on Initial Efficacy

Predicted Efficacy Against Variants Based on Observed Decrease in Neutralization

*Based on decline in neutralizing Ab assuming constant relationship to Ab to efficacy

Khoury DS. Nature Med 2021
Waning Vaccine-Induced Immunity: Randomized Trial Data

**Background**: Long-term vaccine effectiveness of COVID-19 vaccines uncertain.

**Data & Population**: 44,165 age >16 and 2,264 age 14-15 participating in a RCT of Pfizer vaccine

**Design**: 6-month follow-up on vaccine effectiveness and safety – cases through March 13, 2021.

**Outcome**: PCR+ SARS-CoV2 infection ≥7 days post 2nd vaccine

Vaccine Remains Efficacious at 6 months
Some Evidence Declining Immunity
Pre-Delta Variant

### Vaccine Efficacy

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥7 days to &lt;2 months after 2nd dose</td>
<td><strong>96.2% (93.3-98.1)</strong></td>
</tr>
<tr>
<td>≥2 months to &lt;4 months after 2nd dose</td>
<td><strong>90.1% (86.6-92.9)</strong></td>
</tr>
<tr>
<td>≥4 months after 2nd dose</td>
<td><strong>83.7% (74.7-89.9)</strong></td>
</tr>
</tbody>
</table>

Thomas SJ. MedRxiv 2021
**Sinovac (Coronavac) Antibody Response**

**Background:** Antibody response may be a good correlate of immunity. The duration of immunity following immunization is uncertain.

**Population:** 185 Thai healthcare workers who completed 2 doses of Sinovac (SV) or AstraZeneca (AZ) vaccine.

**Design:** Prospective cohort study. Ab levels measured at 4 weeks and 12 weeks (SV only) using surrogate viral neutralization test.

**Outcome:** Seroconversion and Ab levels

---

<table>
<thead>
<tr>
<th>Seroconversion Among Thai HCWs at 4 Weeks post 2(^{nd}) Dose Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>% Inhibition ≥68%</strong></td>
</tr>
<tr>
<td>--------------------------</td>
</tr>
<tr>
<td>60.6%</td>
</tr>
<tr>
<td><strong>% Inhibition ≥80%</strong></td>
</tr>
<tr>
<td>SARS-CoV2 total antibody ≥132 U/ml+</td>
</tr>
</tbody>
</table>

*Definition seroconversion **Surrogate for efficacy against variants of concern.  +High titer per US FDA
• Among Sinovac recipients, antibody levels declined between 4 and 12 weeks
• Only 12% met author’s criteria for immunity at 12 weeks
Sinovac (Coronavac) Antibody Response: Boosters

Phase 1/2 RCT Data Follow-up

- Seropositivity declined to 21.5% at 6 months
- 3rd dose was well tolerated and immunogenic

- Coronavac followed by AZ led to higher levels of antibody than 2 doses Coronavac (uncertain when levels measured)

Li M. MedRxiv 2021

Yorsaeng R. MedRxiv 2021
- 3rd immunization at 56 or 208 days increased ab levels

Pan H. MedRxiv 2021
Summary

• **Epidemiology** – 3rd-4th Wave Around the World

• **Vaccines**
  • Vaccine-induced immunity wanes over time (evident in months not years)
  • Immunity from the least effective vaccines likely wanes faster
  • People with lower levels of antibody (e.g., elderly) will become more vulnerable faster
  • Efficacy lower with some variants (e.g., Delta)
  • Impact less on severe disease than infection – vaccines still work!

• How should this impact vaccine policy?
  • Some people will need boosters
  • Boosters in high-income nations could exacerbate global disparities in vaccine access
  • Political pressure to protect the population in high-income nations is likely to be insurmountable
  • Highlights the need to increase vaccine production