Status of COVID-19 Vaccines

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Outline

- Use authorized/licensed COVID-19 vaccines
- Current epidemiology
- Waning immunity and vaccine boosting
- Omicron
COVID-19 Vaccines

Authorized / Approved for Use

- Moderna
  - mRNA
  - FDA EUA Dec 18, 2020
  - FDA EUA Dec 11, 2020
  - FDA licensed Aug 23, 2021

- Biontech / Pfizer
  - mRNA

- AstraZeneca
  - Adenovirus vector
  - MHRA Dec 30, 2020
  - EMA Jan 29, 2021
  - FDA EUA Feb 27, 2021

- Janssen
  - Adenovirus vector

- Novavax
  - Recombinant protein + adjuvant
  - Interim Efficacy; Jan 29, 2021

- GSK / Sanofi
  - Recombinant protein + adjuvant
  - Phase 2/3 in progress
# Authorized and Approved COVID-19 Vaccines

<table>
<thead>
<tr>
<th>Ages Recommended</th>
<th>Pfizer</th>
<th>Moderna</th>
<th>Janssen / Johnson &amp; Johnson</th>
</tr>
</thead>
<tbody>
<tr>
<td>5+</td>
<td>2 doses 21 days apart</td>
<td>2 doses 28 days apart</td>
<td>1 dose</td>
</tr>
<tr>
<td>18+</td>
<td>Everyone &gt; 18 years eligible at least 6 months after the last dose in their primary series.</td>
<td>Everyone &gt; 18 years eligible at least 6 months after the last dose in their primary series.</td>
<td>At least 2 months after the first dose for all people ages &gt; 18 years.</td>
</tr>
<tr>
<td>Booster Dose</td>
<td>Any of the three COVID-19 vaccines can be used for the booster dose.</td>
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Primary Series:

- Moderna x 2:
- Pfizer x 2:
- Janssen x 1:

Boost with Moderna, Pfizer or Janssen

- All combinations safe and immunogenic
- CDC recommendation allows boosting with any FDA authorized COVID-19 vaccine
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Daily New COVID-19 Cases Reported in the United States

![Graph showing daily new COVID-19 cases reported in the United States from February 2020 to December 2021. The graph highlights four distinct peaks: Spring 2020, Summer 2020, Fall/Winter 2020-21, and Late Summer 2021. The data is sourced from Worldometer.]
COVID-19 Deaths in the US

Total Deaths as of December 06, 2021: > 787,000

Daily Trends in Number of COVID-19 Deaths in The United States Reported to CDC

7-Day moving average

https://covid.cdc.gov/covid-data-tracker/#trends_dailydeaths
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Vaccine Effectiveness Studies to Assess Waning Immunity

- US cohorts and systems*:
  - e.g. NHSN, HEROES/RECOVER, IVY, SUPERNOVA, VISION, VA, Mayo Clinic, etc.

- International vaccine effectiveness monitoring
  - e.g. UK, Israel, Qatar, Canada, Finland, Sweden, etc.

https://covid.cdc.gov/covid-data-tracker/#vaccine-effectiveness

Vaccine Effectiveness Against Infection Has Decreased Over Time

- New York State [May - July] (1)
- Mayo Clinic - Moderna [January - July] (2)
- Nursing Home Residents [March - July] (3)
- Mayo Clinic - Pfizer [January - July] (2)

1: Rosenberg, MMWR, August 2021
2: Puranik, medRxiv, August 2021
3. Nanduri, MMWR, August 2021
Rationale for Boosting (Clinical)

- Phase 3 vaccine trials data show a decline in protection vs. symptomatic disease after 6 months; e.g., 95% to 80% or less ( > 4-fold difference in # cases)

- Real-world effectiveness data show a decline in protection vs. symptomatic disease after 6 months; increasing evidence for some decreased protection vs. severe disease

- Delta variant is dominant and highly transmissible – less sensitive to antibodies, and able to infect vaccinated subjects and transmit to others
Rationale for Boosting (Immunologic)

- Increases the level of Antibody and T cell responses
- Increases antibody affinity maturation and thus, breadth of immunity – including to VOC
- Two closely spaced mRNA immunizations (3-4 weeks apart) constitute a strong priming of immune system
- Optimal immunity requires a boost to increase the pool of memory (T and B) cells and solidify long-term memory
- Most effective vaccines use a late boost; e.g. Measles, Hep B, Hep A, Polio, HPV
Durability of Neutralization after Moderna Vaccination

Pegu, Doria-Rose et al, Science, Aug 12, 2021

Half subjects undetectable NAb levels
mRNA Booster Increases Antibody Titers Against Variants of Concern

Immunogenicity After Boosting with Dose of 50ug of Moderna mRNA 1273 (boost given approx. 6 – 7 months after 2nd shot)

First columns: just before 3rd dose
Second columns: 15 days post-3rd dose boost

Reference: Preliminary Analysis of Safety and Immunogenicity of a SARS-CoV-2 Variant Vaccine Booster Wu et al., medRxiv preprint
mRNA Booster Improves the Breadth vs VOC

Neutralization by serum 1 month after primary vaccination series and before and after boosters, as measured by the VSV-based PsVN assay.

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Omicron Spike Mutations

- 37 mutations overall in spike
- 15 RBD mutations
- Mutations at key contact sites for FDA authorized mAbs
- Unclear what all this means without empirical data
  - Epidemiologic surveillance
  - Vaccine sera: 2 vs 3 doses
  - mAbs

Morgane Rolland, WRAIR
SARS-CoV-2 Variants of Concern

- **Alpha**: 10 mutations, 18-Dec-2020
- **Beta**: 12 mutations, 18-Dec-2020
- **Gamma**: 12 mutations, 11-Jan-2021
- **Delta**: 11 mutations, 11-May-2021
- **Omicron**: 37 mutations, 26-Nov-2021

Tongqing Zhou (VRC, NIAID, NIH)
Omicron: Key Information Needed

- Will omicron become the dominant strain worldwide, replacing Delta or co-exist with Delta?
  - Worldwide surveillance and sequencing
  - Clinical effectiveness of current vaccines
  - Laboratory data: Level of neutralization by vaccine sera
- Clinical severity – similar to or different than Delta?
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We will take a short break and reconvene at 3:35 p.m. ET