Status of COVID-19 Vaccines

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National Institutes of Health
Use authorized/licensed COVID-19 vaccines

Current epidemiology

Waning immunity and vaccine boosting

Omicron
<table>
<thead>
<tr>
<th>Developer</th>
<th>Platform</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderna</td>
<td>mRNA</td>
<td>FDA EUA Dec 18, 2020</td>
</tr>
<tr>
<td>Biontech and Pfizer</td>
<td>mRNA</td>
<td>FDA EUA Dec 11, 2020, FDA licensed Aug 23, 2021</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>Adenovirus Vector</td>
<td>MHRA Dec 30, 2020, EMA Jan 29, 2021</td>
</tr>
<tr>
<td>Janssen</td>
<td>Adenovirus Vector</td>
<td>FDA EUA Feb 27, 2021</td>
</tr>
<tr>
<td>Novavax</td>
<td>Recombinant protein + adjuvant</td>
<td>Interim Efficacy; Jan 29, 2021</td>
</tr>
<tr>
<td>GSK and Sanofi</td>
<td>Recombinant protein + adjuvant</td>
<td>Phase 2/3 in progress</td>
</tr>
</tbody>
</table>
# 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>18+</td>
<td>18+</td>
<td></td>
</tr>
</tbody>
</table>

| Primary Series | 2 doses 21 days apart | 2 doses 28 days apart | 1 dose |

<table>
<thead>
<tr>
<th>Booster Dose</th>
<th>Everyone &gt; 18 years eligible at least 6 months after the last dose in their primary series.</th>
<th>Everyone &gt; 18 years eligible at least 6 months after the last dose in their primary series.</th>
<th>At least 2 months after the first dose for all people ages &gt; 18 years.</th>
</tr>
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<td></td>
<td><em>Any of the three COVID-19 vaccines can be used for the booster dose.</em></td>
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NIAID/NIH Mix and Match Study of COVID Vaccines

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
Current epidemiology
Daily New COVID-19 Cases Reported in the United States

- **Spring 2020**
- **Summer 2020**
- **Fall/Winter 2020-21**
- **Late Summer 2021**

Source: Worldometer
COVID-19 Deaths in the US

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

https://covid.cdc.gov/covid-data-tracker/#trends_dailydeaths
Waning immunity and vaccine boosting
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.

CDC COVID Data Tracker
Results of COVID-19 Vaccine Effectiveness Studies: An Ongoing Systemic Review
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

Courtesy A.S. Fauci
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
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.
Omicron
SARS-CoV-2 Omicron (B.1.1.529) Mutations

37 mutations

Tongqing Zhou (VRC, NIAID, NIH)
• 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
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?
NIH ACD Meeting
Dec 9, 2021

Status of COVID-19 Vaccines

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