The Phases of Vaccine Clinical Trials:

Before a vaccine can be tested in humans, researchers must produce robust, compelling laboratory/animal data.

Phase I: Uses a small number of volunteers to evaluate safety and to determine an effective dose that will be used in later phases. Blood tests are used to determine if the vaccine has generated an immune response. As an added safety precaution, phase I trials use healthy volunteers from a narrow age range to reduce the likelihood that other factors could influence results.

Phase II: Uses a larger, slightly more diverse population (i.e. broader age range) to evaluate the safety and efficacy of the vaccine. Researchers study if the vaccine confers protection against the pathogen in question.

Phase III: Pivotal phase that determines if the vaccine will be approved for widespread use. Using tens of thousands of participants, the trial must demonstrate that those that have received the vaccine have significantly lower rates of infection than those who have not. Safety and efficacy data collection continues once the vaccine is in widespread use (post-marketing surveillance).

Emergency Use Authorization (EUA):

Following collection of ‘clear and compelling’ efficacy and safety data from at least one Phase III clinical trial, a vaccine manufacturer may file for EUA. The FDA Vaccines and Related Biological Products Advisory Committee (VRBPAC) will evaluate this data and determine if:

- It is reasonable to believe that the vaccine may be effective in preventing COVID-19.
- The identified and potential benefits of the vaccine outweigh the identified and potential risks.
- There is no adequate, approved, and available alternative for preventing COVID-19.

If all criteria are met, the FDA may then grant EUA. The vaccine can begin to be administered as clinical trials and safety surveillance efforts continue.

Innovations in Vaccine Science:

Two leading COVID-19 vaccine candidates are RNA-based, a revolutionary strategy that uses our body’s own genetic machinery. Traditional vaccines introduce a weakened form of a virus that will train the immune system to recognize and combat viral pathogens. RNA vaccines work by injecting genetic instructions that make viral proteins, giving the body a “preview” of the virus prompting an immune response. RNA vaccines can be rapidly produced and are made without pathogen particles making them safer.

COVID-19 Variants:

- **B.1.1.7**
  - First identified in the U.K., B.1.1.7 has been shown to be ~70% more transmissible with evidence of increased disease severity. Vaccines are still effective against this variant, and there is little evidence of reinfection. According to the CDC, B.1.1.7 is now the dominant COVID-19 strain in the U.S.
  - EUA has been expanded to include adolescents aged 12 to 15. A recent study suggests the vaccine is highly effective against B.1.1.7 and the variant originally identified in India.

- **B.1.351**
  - First identified in South Africa, studies suggest B.1.351 is ~50% more transmissible, with some vaccines shown to be less effective as the virus can escape antibody recognition. There is also some evidence that reinfection with B.1.351 is possible.

- **P.1**
  - First identified in Japan in travelers from Brazil, P.1 is believed to be more transmissible and carry greater risk of reinfection, but more research is necessary. Impact on vaccines is unknown.

- **B.1.427 / B.1.429**
  - First identified in California, B.1.427 and B.1.429 have been shown to be ~20% more transmissible, with some evidence of increased disease severity. Recent research suggests the vaccines are likely to remain effective against these variants.

Five Leading Vaccine Candidates:

<table>
<thead>
<tr>
<th>Developer</th>
<th>BNT162b2</th>
<th>mRNA-1273</th>
<th>Ad26.COV2.S</th>
<th>AZD1222</th>
<th>NVX-CoV2373</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial Phase</td>
<td>Phase II &amp; III Combined</td>
<td>Phase III</td>
<td>Phase III</td>
<td>Phase II &amp; III Combined</td>
<td>Phase III</td>
</tr>
<tr>
<td>Vaccine Type</td>
<td>mRNA-based</td>
<td>mRNA-based</td>
<td>Non-replicating viral vector</td>
<td>Non-replicating viral vector</td>
<td>Protein subunit</td>
</tr>
<tr>
<td>Efficacy</td>
<td>95%</td>
<td>94.1%</td>
<td>72% in U.S. trial</td>
<td>76% in U.S. trial</td>
<td>96.4%</td>
</tr>
<tr>
<td>Cost</td>
<td>$20/dose</td>
<td>$32-37/dose</td>
<td>$10/dose</td>
<td>$3-5/dose</td>
<td>$16/dose</td>
</tr>
<tr>
<td>Production</td>
<td>3 billion in 2021</td>
<td>3 billion by 2022</td>
<td>1 billion in 2021</td>
<td>3 billion in 2021</td>
<td>2 billion in 2021</td>
</tr>
<tr>
<td>Dosage</td>
<td>Two, 21 days apart</td>
<td>Two, 28 days apart</td>
<td>One</td>
<td>Two, 3 months apart</td>
<td>Two, 3 weeks apart</td>
</tr>
<tr>
<td>Storage Temp</td>
<td>36–46°F for five days -4°F for six months</td>
<td>36–46°F for 30 days -4°F for six months</td>
<td>36–46°F for three months -4°F for two years</td>
<td>36–46°F for six months</td>
<td>36–46°F</td>
</tr>
</tbody>
</table>

- 36–46°F and -4°F are standard hospital refrigeration and freezer temperatures, respectively.

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