The COVID-19 Pandemic

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Prepared by:

Health Policy & Public Health COVID-19 Advisory Panel
Department of Health Policy
Vanderbilt School of Medicine

COVID-19 Vaccine: Answers to Questions on the Pandemic's Leading Issue

Vaccines allow us to fight an infection without getting sick. In many cases, once we get a particular infection, our bodies develop the ability to prevent us from getting it again. Vaccines safely teach our immune system to recognize specific infections before they make us sick. This head-start helps our bodies fight off the disease if we are exposed.

How would a COVID-19 vaccine work?

COVID-19 is caused by a virus called SARS-CoV-2. The virus is coated with "spike" protein that allows it to infect cells in the respiratory system. Current vaccine strategies aim to make antibodies that specifically recognize and block the spike protein from attaching to cells.

There is one candidate vaccine against SARS-CoV-2 currently in a clinical trial in the United States. When injected into the body, the vaccine stimulates our cells to make spike protein so that the body can develop antibodies against it. These antibodies should prevent vaccinated humans from becoming infected with SARS-CoV. These individuals would be considered "immune." Importantly, this vaccine would not give you COVID-19 because it does not contain the live virus.

Can a vaccine help end the COVID-19 pandemic?

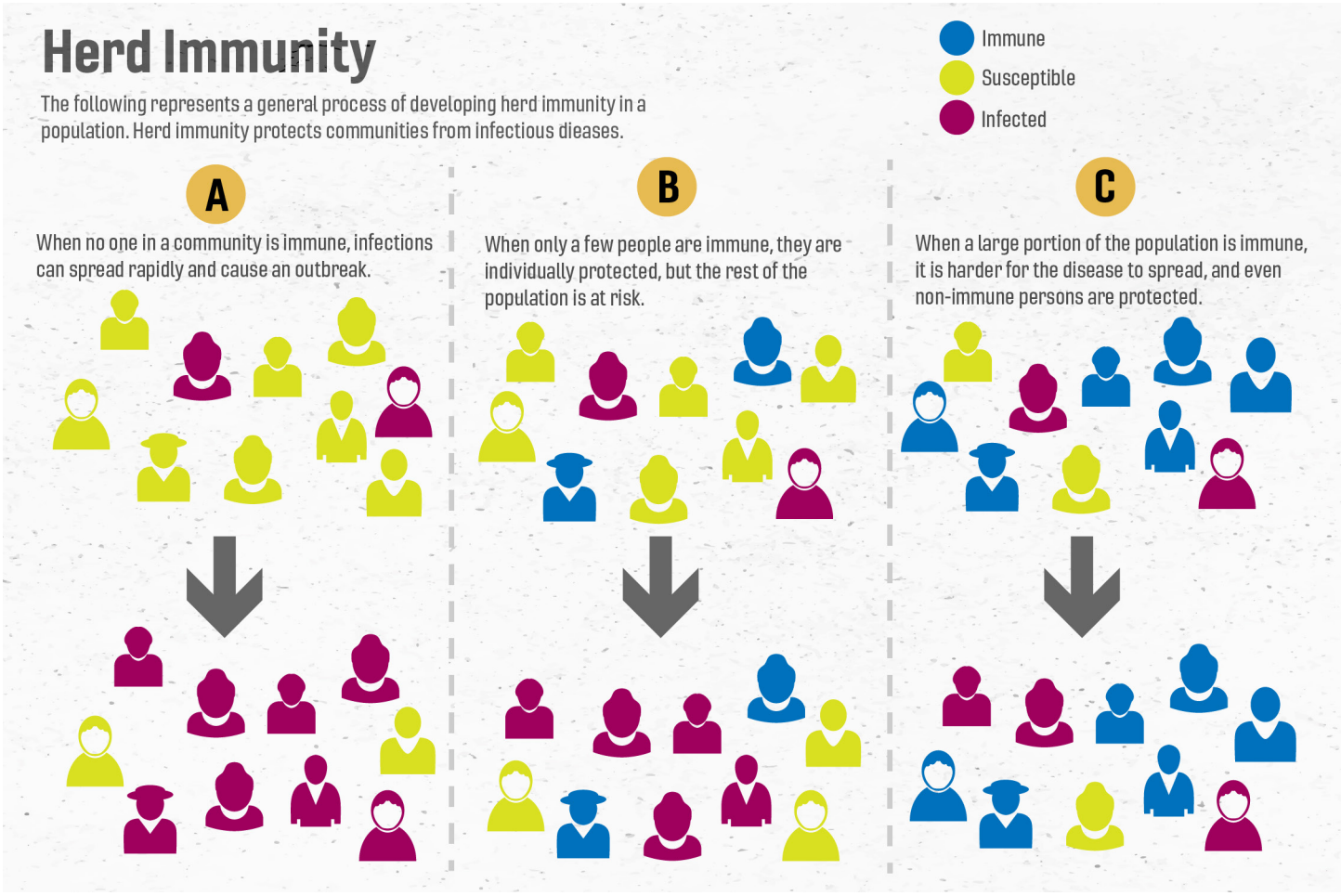
A safe and effective vaccine could end the COVID-19 pandemic. COVID-19 has spread quickly through communities because the SARS-CoV-2 virus is completely new to humans. Since none of us are immune to the virus, it has no trouble finding new people to infect. To slow the spread, we have to make it harder for the virus to find new hosts. Social distancing restrictions reduce the virus' opportunities to spread by keeping us apart, but these restrictions cannot be maintained forever. A more long-lasting solution is to reduce the number of susceptible people by making them immune to SARS-CoV-2. This is the basis of "herd immunity," which makes us all safer **(Figure 1)**. Using a vaccine to generate herd immunity is much better than having the population develop immunity by getting COVID-19, which would result in a large number of sick people and deaths.

What are the steps for developing a vaccine?

Vaccine development goes through several specific stages **(Figure 2)**.

Before being tested in humans, candidate vaccines are tested in many types of animals to determine whether they stimulate protective immune responses and do not cause harm (termed adverse events). This

Figure 1
Herd immunity illustrated.



"preclinical" testing typically occurs over several years, and many potential candidates do not do well enough in this phase to go on to human testing.

Once candidates have been thoroughly tested in animal models, they can proceed to Phase 1 clinical trials, in which small groups of people (50-100) receive the vaccine. **Phase 1** trials are intended to determine whether a vaccine is safe and can stimulate an immune response. However, Phase 1 trials are not designed to test whether the vaccine prevents infections; that occurs in Phase 3.

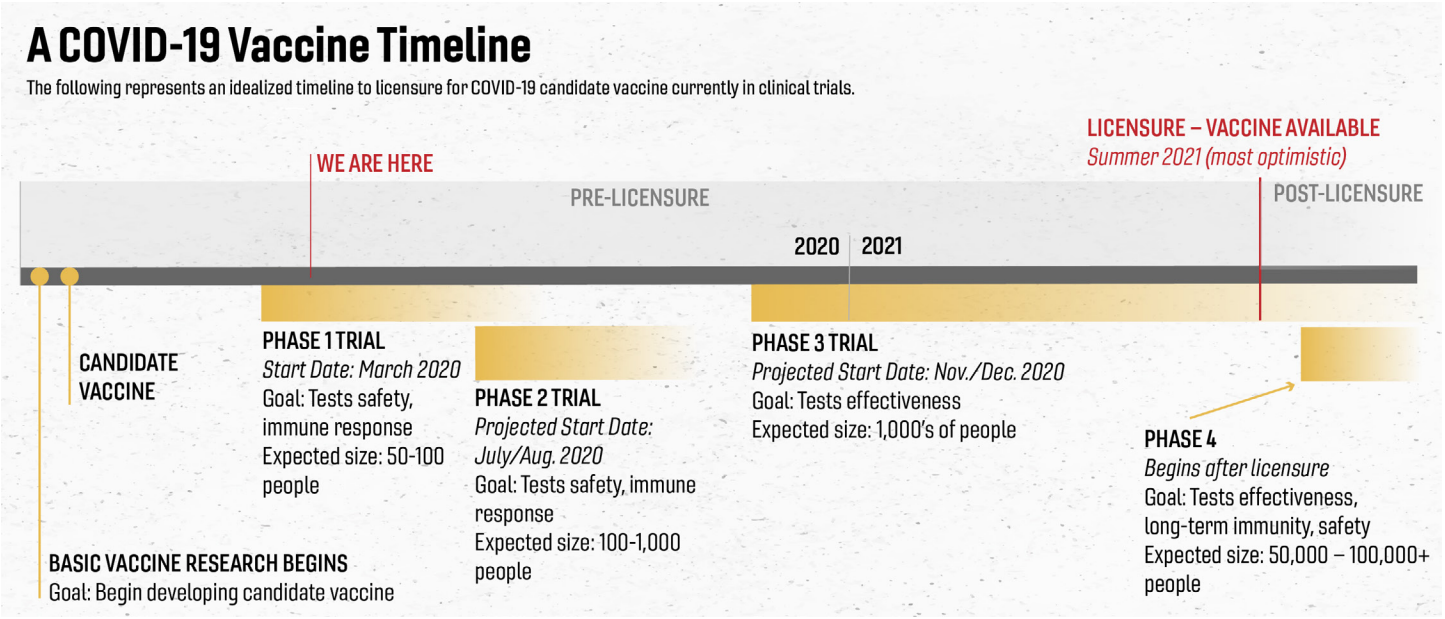
Phase 2 clinical trials have similar goals to Phase 1, but they expand the study into larger, more relevant populations (e.g. into the age group most in need of the vaccine's protection). Phase 2 trials often enroll 100-1,000 participants.

In **Phase 3**, the vaccine is given to large numbers of individuals, allowing researchers to determine whether it is effective at protecting people from disease. Phase 3 trials typically require thousands of participants.

Vaccines deemed safe and effective during these phases are eligible for FDA approval and licensure so they can used routinely.

After approval, most vaccines are monitored with **Phase 4** studies that follow vaccine usage, adverse reactions, and long-term immunity in tens of thousands of people.

Figure 2
An idealized timeline to licensure for COVID-19 candidate vaccine.



Over 90% of vaccines identified in preclinical studies do not make it to licensure. It typically takes years to develop a safe and effective vaccine through this pathway. However, COVID-19 vaccine development has already begun with unprecedented speed, facilitated by recent technological advances and studies of other related coronaviruses. The current vaccine candidate entered a Phase 1 trial just 63 days after the genetic code of the virus was sequenced.

The COVID-19 pandemic is killing people; why aren't we deploying candidate COVID-19 vaccines?

We do need a COVID-19 vaccine urgently to control the pandemic. Researchers are optimistic that the candidate vaccine being tested in the United States will be both safe and effective, but it would not be wise to use it outside of a clinical trial until we know for sure. An unsafe vaccine could harm otherwise healthy people who might never have contracted COVID-19 or who might never have gotten sick. An ineffective vaccine would waste resources on something that does not work and could decrease peoples' trust in other vaccines. Carefully-designed and conducted clinical trials are the only way to know whether the candidate vaccine is safe and effective. The trials of the COVID-19 vaccine are proceeding much faster than usual, and as long as it continues to be safe, the vaccine could be tested in thousands of people before the end of 2020. In the best case scenario, a safe and effective vaccine could be licensed by summer 2021.

Notes: Strategies for combating the spread of COVID-19 and their likely effectiveness, a review of models for forecasting the spread and severity of COVID-19, and other topics will be the subject of additional working papers. The views expressed are those of the advisory group and do not necessarily reflect the views of Vanderbilt University School of Medicine or Vanderbilt University Medical Center. Please see vumc.org/health-policy/covid-19-advisory-memos for those papers.