

AGING AND IMMUNITY:

WHY OLDER ADULTS ARE HIGHLY SUSCEPTIBLE TO DISEASES LIKE COVID-19

Older adults are particularly susceptible to infectious diseases like COVID-19. This disease may also be more severe in older adults than in younger people. Here's why.



RESISTANCE TO INFECTION WANES IN ADULTS OVER 50

- The physical barriers that help fight infection—such as skin, cough reflex, and cilia that push pathogen-laden mucus out of the lungs—weaken with age.
- The cells that prevent infection don't work as well.
- The quantity and quality of antibodies produced is lower than that produced in younger people.
- The body's response of inflammation to fight infection is less regulated.

WHY INFLAMMATION MATTERS

- The impact of immune response in older adults may cause a cytokine storm (in which the body fights its own cells while also fighting the virus) and inflammation, which can have negative consequences.
- Inflammation in the body increases with age as well as with chronic diseases such as diabetes, obesity, hypertension, chronic obstructive pulmonary disease (COPD), heart disease, and dementia. This is amplified in older people with conditions such as influenza, shingles, bladder infection, and pressure sores.
- Inflammation can cause clots, which can lead to heart attack or stroke.
- A severe inflammatory reaction has the potential to cause significant damage in the body, including organ failure.

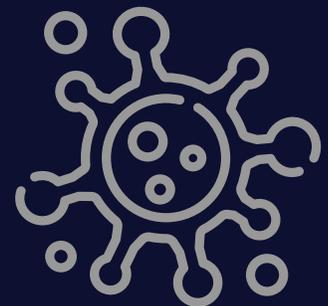


INCREASED LIKELIHOOD OF COMORBIDITIES

- Older adults are more likely to have underlying cardiovascular and pulmonary disease, diabetes, cancer, and other chronic conditions.
- These comorbid conditions increase the risk of contracting infectious diseases and make it harder for people with chronic conditions to survive.

NOTES ABOUT COVID-19

- Chronic conditions such as diabetes, obesity, hypertension, COPD, and heart disease are important risk factors for having severe complications if infected with COVID-19.
- Age is also a risk factor—infected older adults often seem to have worse outcomes than younger people.
- Many older adults, especially women, have recovered from COVID-19, and researchers are trying to understand why some people have better outcomes.
- Infection and death rates for COVID-19 are higher for people who are black or Latino than for whites; this predicament appears to be, at least in part, due to social inequities related to race, income, comorbidities, and access to health care.
- Vaccines are the only way to boost waning immune systems. No vaccines are yet available for COVID-19, although many are in development.
- Testing vaccines on adults aged 60 and older will be an important part of the clinical research to make sure the vaccines can overcome natural waning immunity and protect older people.



THE PROCESS OF DEVELOPING A VACCINE FOR COVID-19

As of May 2020, over a hundred vaccines were in development worldwide for COVID-19; among those vaccines, several are in clinical trials. Typically, it takes over 15 years to develop a vaccine (and the fastest development in the past has been 4 years for Ebola and mumps vaccines). As a matter of urgency, the timeline for COVID-19 vaccine development has been greatly compressed. With focused attention and resources, along with new technology, there is hope that COVID-19 vaccine can be developed quickly; however, several milestones must still be met.

EXPLORATORY STAGE

- Usually takes 2 to 4 years to identify an antigen target for a vaccine to prevent a disease.



PRECLINICAL STAGE

- Addresses whether the vaccine candidate can be produced to scale (efficiently manufactured).
- Investigates whether it is likely that the vaccine will work based on in vitro studies and animal tests.
- Usually takes 1 to 2 years and many candidate vaccines fail because they do not achieve the desired immune response.

CLINICAL TRIALS

The US Food and Drug Administration (FDA) sets standards for 3 phases of clinical trials.

At each phase, the developer's study design and protocol are approved by the FDA, including agreement on specifying endpoints that are considered success. Modern trial design is sophisticated and allows for small shifts depending on results. Developers of vaccines meeting certain criteria may request that the vaccine be fast tracked. After the preclinical stage, drug companies submit an application to the FDA for the investigational new drug. If approved, the vaccine moves to testing in people.

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CLINICAL TRIAL PHASE 1

- Typically takes 1 to 2 years.
- 20 to 100 healthy volunteers.
- Goal is to determine safety.

Question asked during Phase 1:

- Is the vaccine safe?

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CLINICAL TRIAL PHASE 2

- Typically takes 2 or more years.
- Several hundred volunteers ranging in race, ethnicity, and age.
- Goal is to determine proof of concept and vaccine efficacy.

Questions asked during Phase 2:

- What are the most common short-term side effects?
- How are the volunteers' immune systems responding to the vaccine?
- What dose is required to produce immunity? And how many doses are needed?
- Is there evidence that the vaccine doesn't just produce an immune response, but also offers protection?

3

CLINICAL TRIAL PHASE 3

- Typically takes several years plus another 1 to 2 years to analyze the data.
- Thousands or tens of thousands volunteers.
- Goal is to confirm efficacy in large groups of people.

Questions asked during Phase 3:

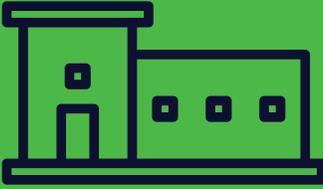
- Does the vaccine continue to be safe? Are any additional side effects reported?
- Is the vaccine effective for preventing the disease? The study is designed to show whether receiving the vaccine prevents disease compared with not receiving vaccine (placebo group). The characteristics of the group studied should be similar to those of the people who could eventually get the vaccine, and the study should be done during the time of year when disease is circulating to make sure the vaccine really works.
- What measures will correlate with vaccine-induced immunity to inform us that a person is protected against infection? Will antibody levels correlate with immunity?

AFTER CLINICAL TRIALS

- If the data indicate that a vaccine is safe *and* effective in preventing disease or producing immunity known to prevent disease, the company developing the vaccine submits a Biologics License Application to the FDA.
- FDA licenses the vaccine if the agency's evaluation of clinical trial results confirms safety and efficacy.
- After a vaccine is licensed, the Centers for Disease Control and Prevention considers whether it should be added to U.S. immunization schedules.



BUILDING VACCINE MANUFACTURING PLANTS



- Manufacturers start making vaccine that they submit to the FDA for safety and quality checks, and their manufacturing facilities are certified or checked for good manufacturing practices.
- Each manufacturing plant is customized with equipment for the process needed to produce a specific vaccine.
- Once manufacturing methods are known, it generally takes about 18 months to build a facility and have it ready for producing vaccine.
- The manufacturing facility has to be licensed, and the FDA monitors the quality of each batch of vaccine before it is released.

HOW THE COVID-19 VACCINE DEVELOPMENT PROCESS IS BEING SHORTENED

- Speeding up clinical development:
 - ♦ The exploratory phase happened within 2 weeks for COVID-19—using both novel (DNA, mRNA, viral-based, and cell-based) and traditional (protein subunits, killed whole virus, and attenuated virus) approaches.
 - ♦ Certain processes can be run simultaneously instead of sequentially. For example, once safety is determined in Phase 1, several COVID-19 vaccine manufacturers plan to move into Phase 2 studies while the previous phase continues to answer other questions. They are calling these Phase 1/2 trials.
- Starting to build manufacturing plants now:
 - ♦ Several organizations have invested in building many kinds of vaccine manufacturing facilities now—knowing that some may never be used—in preparation to have facilities ready once a vaccine gets licensed. Each plant costs approximately \$1 billion to build.
- Creating the National Institutes of Health Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) partnership to:
 - ♦ Develop a collaborative framework for prioritizing vaccine and drug candidates
 - ♦ Streamline clinical trials
 - ♦ Coordinate the regulatory processes
 - ♦ Leverage assets among all partners to rapidly respond to the COVID-19 and future pandemics.



To see all therapies and vaccines in development, visit STAT's COVID-19 Drugs and Vaccines Tracker: <https://www.statnews.com/feature/coronavirus/drugs-vaccines-tracker>

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For more information, visit the CDC website [CDC.gov](https://www.cdc.gov) or the GSA compilation of COVID-19 resources [geron.org/covid19](https://www.geron.org/covid19).

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NATIONAL ADULT VACCINATION PROGRAM
CHARTING NEW FRONTIERS ACROSS THE AGING CONTINUUM

a program of

