Current Vaccines Being Developed and Administered

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What types of COVID-19 vaccines are being developed and tested?

- **Inactivated vaccines**: inactivated vaccines are a common method for designing/creating a vaccine. This involves utilizing an inactive (killed) variant of the disease of interest and using the similarities between the dead form and "real" form to stimulate an immune response. Common examples include influenza and polio vaccines.
  - E.g. Vaccine being developed by **Sinovac**
- **Protein-based vaccines**: these vaccines are designed based on the surface proteins that are on the COVID-19 virus; these proteins are generally how the viruses are recognized.
  - E.g. Vaccine being developed by **CanSino Biologics**
- **Viral-vector vaccines**: these are non-replicating viruses that provide instructions in the form of viral DNA to utilize your body's cells to produce COVID-19 proteins. These proteins then induce an immune response
  - E.g. Vaccines being developed by **University of Oxford** and **Johnson & Johnson**
- **"Genetic"-based vaccines**: these are similar to viral-vector vaccines, but provide the instructions in a different form (mRNA instead of viral DNA)
  - E.g. Vaccines being develop by **BioNTech/Pfizer** and **Moderna**

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“Genetic-based” vaccines were the first two to seek FDA approval

- Gene-based vaccines carry genetic instructions to our cells to produce an antigen that is used to initiate an immune response, just as it would in an actual infection.
  - In the case of coronaviruses, the antigen of interest is the surface spike protein the virus uses to bind and fuse with human cells.
  - Rather than the protein being supplied by the virus itself, the genetic material instructs our cells to make the spike protein necessary for an antibody response
- The approach taken is similar to that used in live-attenuated vaccines for diseases like measles, mumps, and rubella
  - Weakened viruses incorporate their genetic instructions into host cells, causing the body to produce viral copies that elicit an effective antibody response (B- and T-cell responses)
  - In the case of mRNA vaccines—scientists insert genetic instructions from the pathogen of interest to produce antigens in host cells instead of utilizing a virus

Vaccines now available in the USA

- The FDA had previously indicated that it would be willing to approve a vaccine for use that was just 50% effective
  - On November 9th, Pfizer announced their vaccine was up to **94.5% effective in preventing symptomatic COVID-19 disease.**
  - On November 15th, Moderna announced a vaccine that is **95% effective in preventing symptomatic COVID-19 disease.**
  - On February , 27, 2021 Johnson and Johnson announced a single dose vaccine that is **86% effective in preventing severe forms of the COVID-19**
- All of these vaccines rank relatively high in effectiveness compared to other widely used vaccines. For example:
  - 1 dose of the measles vaccine is 93% effective. 2 doses (recommended) increases the effectiveness to 97%
  - For the Seasonal Flu vaccine, the effectiveness usually varies because of the differences in strains that are being transmitted each year, but they have ranged between 10-60% effective 2004-2019
    - Most seasonal flu vaccines are 40-60% effective though.

Pfizer's and Moderna's "gene-based" vaccines

- Both vaccines deliver a molecule known as messenger RNA, or mRNA. While mRNA-based vaccines seem like novel techniques, the research to develop mRNA vaccines began many years before the current pandemic
  - Currently, no other vaccines utilize mRNA
- Pfizer's and Moderna's vaccines have similar results (> 90% effectiveness in preventing symptoms) and use the same technique to activate the body's immune system.
  - The nearly identical effectiveness of the vaccines from Pfizer and Moderna validates the use of mRNA as a vaccination technique.
  - Both vaccines are given in two doses with 3-4 weeks between each dose.
- The vaccines have been generally well tolerated with few side effects lasting more than 48 hours among those who have already received them
  - Side effects reported thus far are mild-moderate , and short lived – similar to other seasonal flu vaccines

Details about Pfizer's study

- Among the US, participants were mostly white:
  - 5.5% Asian
  - 10.1% Black
  - 13.1% Hispanic/Latinx
  - 1.0% Native American
- What does 94.5% effective mean?
  - **This means that those that received the vaccine were 94.5% less likely to exhibit symptoms**
    - It does NOT mean that the vaccine reduces transmissibility.

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The Moderna vaccine

- In Moderna's trial of 30,000 participants, half of study participants (15,000) were given a placebo whereas the other half were given the vaccine.
  - Over several months, 90 of those who received a placebo developed COVID-19, with 11 developing severe forms of the disease.
  - Only five participants who received the vaccine developed COVID-19
- **Moderna’s vaccine appears to have also been protective in important subsets of participants — the elderly and people from racial and ethnic minority groups:**
  - The 30,000-person trial included 11,000 participants from communities of color, making up 37% of the total study population.
  - It also included more than 7,000 participants over the age of 65 and >5,000 people younger than 65 who have chronic health conditions that put them at high risk of suffering from a severe infection (e.g. diabetes, severe obesity and heart disease).

What we do not know about the Pfizer/Moderna vaccines

- For both vaccines, we do not yet know how effective the vaccine is in the long-term… we will not know how long the immunity offered by either of these vaccines last until they begin to wear off.
  - To date, study participants have immune protection for at least 8 months
- This has implications for:
  - How frequently people might have to get boosters shots to maintain immunity
  - The ongoing risk of transmission of SARS-CoV-2
    - The vaccine just prevents people from becoming severely ill, but we are yet to know the extent to which the vaccine reduce transmissibility
    - Some early data suggests the reduction is substantial, but for how long is still unknown

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Moderna’s vaccine has a practical advantage over Pfizer's

- Pfizer's vaccine needs to be kept at -75° Celsius.
- Moderna's vaccine can be kept at -20° Celsius.
  - Other vaccines, such as the one against chickenpox, need to be kept at that temperature.
- Most doctors' offices and pharmacies have freezers that are able to maintain the -20° Celsius temperature needed to store Moderna’s vaccine
- Furthermore, Moderna's vaccine can stored for up to 30 days in the refrigerator, whereas Pfizer's vaccine can last only five days in the refrigerator.

Vaccines take time to become effective and both vaccines require two doses to reach effectiveness over 50%

- COVID-19 vaccines are NOT immediately effective
- Protection from the two vaccines doesn't start until 12 days after the first shot and reaches 52% effectiveness a few weeks later.
- A week after the second vaccination, the effectiveness of both vaccines reaches around 95%.

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COVID-19 Vaccines prevent disease, but disease transmission is still possible

- COVID-19 vaccinations prevent someone from developing COVID-19 disease. They have also been shown to reduce severity of illness in those who still get COVID-19 after vaccination.
- Just because you have immunity from COVID-19, this does not mean you cannot become infected, harbor, and transmit the virus.
- You may still get the virus and be contagious after being vaccinated.
- For this reason, it is important for you to continue physical distancing and wearing a mask to protect others around you.
- **If you come down with the symptoms of COVID-19 after being vaccinated, get tested!**

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Will the Pfizer and Moderna vaccines prevent transmission? We will have to wait to find out

- Currently, we don’t know the extent to which these vaccines will prevent asymptomatic infection. But, we do know that because they reduce symptomatic infection, they should also reduce deaths, hospitalizations, and intubations in those who become infected.
- The trials were conducted with symptomatic endpoints, rather than testing everyone every day or every few days to look for infection, to save resources (let's say 30,000 participants, tested every three days over a course of two months - that’s 600,000 PCR tests that need to be run).
- The hope is that once approved and with widespread use, we will see epidemiologic evidence to show reduction in transmission as well as reduction in symptomatic disease.

Moderna vs Pfizer mRNA Vaccine

During the middle of November 2020, two large biotechnology companies, Moderna Inc and Pfizer, announced interim results of candidate mRNA vaccines that reported 94.5% and 90% efficacy, respectively. These numbers represent a reduction in *syndromic* covid-19 compared to placebo groups. What remains unknown, however, is whether these vaccines ***prevent*** infection and spread, and for how long will it provide protection? (The vaccine uses mRNA vaccine technology that has only recently become feasible and has never been approved for similar purposes). Does the vaccine protect the elderly? Does it protect those with immune system dysfunction? Time will tell.

For more information, as well as daily COVID-19 research / policy updates, visit : https://brief19.com

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Adenovirus vaccines

The Oxford University-AstraZeneca vaccine, Johnson and Johnson , and others *

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What are Adenoviruses?

- **Modified Adenoviruses do not cause illness** and are effective carriers of antigens for infectious diseases
  - Adenoviral vectors act as vaccine carriers when armed with foreign genes and can elicit specific antibody and T-cell responses.
    - Adenovirus-based vaccines generally have few side-effects, like other vaccines.
- **These types of vaccines are used against a wide variety of pathogen including *Mycobacterium tuberculosis*, human immunodeficiency virus (HIV), and *Plasmodium falciparum*.**

The Oxford-AstraZeneca vaccine

- The results reported on November 23rd from Oxford-AstraZeneca come from their Phase III trials involving 23,000 participants in Britain and Brazil.
- The Oxford-AstraZeneca vaccine uses an adenovirus (a weakened version of a common cold virus) with genetic material for the characteristic spike protein of the coronavirus that causes COVID-19.
- Like the other vaccines discussed thus far, the spike protein from the vaccine primes the immune system to attack the coronavirus if it later infects the body.
  - **The weakened version of the virus used in the vaccine has been genetically changed so that the virus is unable to replicate or cause illness in humans.**

The Oxford-AstraZeneca vaccine

- A half-dose of the vaccine followed by a full dose at least one month later was found to be 90% effective.
  - A second regimen using two full doses one month apart was 62% effective.
  - The combined results showed an average efficacy rate of 70%.
  - Questions have been raised about the half dose regime which was not intentional and turned out to be serendipity
- The extent to which the vaccine induces strong antibody and T cell immune responses among elderly populations has yet to be determined because the half dose-full dose regimen was not tested in older participants.

How the three vaccines compare

Company	Type	Doses	Storage
Oxford Uni-AstraZeneca	Viral vector (genetically modified virus)	x2	Regular fridge temperature
Pfizer-BioNTech	RNA (part of virus genetic code)	x2	-70C
Moderna	RNA	x2	-20C

Source: Respective companies, WHO

BBC

Johnson and Johnson Vaccine

The one dose vaccine approved for Emergency Use Authorization on February 27, 2021

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Johnson and Johnson vaccine: How does it work

- J&J is another adenoviral vectored vaccine.
  - For this vaccine, a harmless adenovirus — from a large family of viruses, some of which cause common colds — has been engineered to carry the genetic code for the SARS-2 spike protein.*
- Once the adenovirus enters cells, they use that code to make spike proteins (similar to how the Pfizer and Moderna vaccines).
- J&J employs this same approach to make an Ebola vaccine that has been authorized for use.

Johnson and Johnson vaccine is very effective against severe disease

- J &J is a single dose vaccine administered to those 18 years of age and older
  - An early exploratory trial of the vaccine tested two shots against one and found no measurable difference in immune response. For this reason, one shot was deemed to be sufficient at this time. Whether or not a booster will be recommended in the future depends on the long - term effectiveness of the vaccine and its response to emergent variants
- The vaccine is reported to be 66% effective against moderate to severe/critical COVID-19 disease 4 weeks after inoculation based on a multi country trial.
  - The vaccine was found to be 72% protective in the United States.
  - 66% protective in South America
  - 57% protective in South Africa **where the dominant strain was the B.1.351 variant**

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Johnson and Johnson is not an inferior vaccine when it comes to preventing severe disease and hospitalization

- **Notably, the vaccine offered 86% protection against severe forms of the COVID-19**
  - **In the J&J trial there were no individuals who developed COVID-19 severe enough to be hospitalized after a 28-day period in which immunity developed.**
- **However, there is no evidence, reported to date, that the J&J vaccine is effective against asymptomatic infection.**

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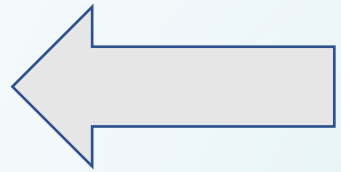
Advantages of adenovirus vaccines

- Adenoviral vaccines can be stored in standard refrigerators, rather than needing freezers.
  - The AstraZeneca-Oxford vaccine and Johnson and Johnson can be transported under "normal refrigerated conditions" of 36°F to 46°F
- The Johnson and Johnson one dose vaccine has obvious advantages in terms of roll out to hard –to- reach populations, and increased rates of vaccine compliance due to easier logistics
  - On the other hand, a disadvantage of the J & J vaccine is that some people many see this vaccine as less effective than two dose vaccines and an inferior product which is not an accurate reading of the data on severe illness
- The Oxford-AstraZeneca vaccine is cheaper than the Pfizer and Moderna vaccines as well.
  - AstraZeneca, *which has pledged not to make a profit on the vaccine during the pandemic*, has reached agreements with governments and international health organizations that put its price at about $2.50 a dose.
  - Pfizer's vaccine costs around $20 a dose while Moderna's vaccine costs between $15 to $25 a dose, and Johnson and Johnson about $10 a dose based on the agreements between the companies and the U.S. government

APPROVED COVID-19 VACCINES

IDAHO DEPARTMENT OF HEALTH & WELFARE	Pfizer-BioNTech	Moderna	Janssen (Johnson & Johnson)
Emergency Use Authorization (EUA) date in the US	Dec. 11, 2020	Dec. 18, 2020	Feb. 27, 2021
Number of doses	Two doses, 21 days apart	Two doses, 28 days apart	Single dose
Type of vaccine	**mRNA** Genetic code teaches immune system how to make part of virus that triggers immune response	**mRNA** Genetic code teaches immune system how to make part of virus that triggers immune response	**Adenovirus vector** Modified virus tells body how to make part of virus that triggers immune response
Disease prevention	**95%** (trials conducted *before* variants widely circulating)	**95%** (trials conducted *before* variants widely circulating)	**66%** (trials conducted *after* variants widely circulating)
Hospitalization & death prevention	**> 90%** (based on clinical trials)	**> 90%** (based on clinical trials)	**> 90%** (based on clinical trials)
Recommended age	People 16 years and older	People 18 years and older	People 18 years and older

More information: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines.html March 11



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The three vaccines approved for use in the USA should not be compared because they tested different outcomes in different populations

- Pfizer's and Moderna's trials tested for slightly different criteria
  - Pfizer counted cases from seven days after receipt of the second dose of vaccine
  - Moderna waited till day 14 to start counting cases.
  - Both tested for any symptomatic COVIDinfection.
- J&J was designed to determine whether one dose of its vaccine protected against moderate to severe COVID illness — defined as a combination of a positive test and at least one symptom such as shortness of breath, beginning from 14 or 28 days after the single shot.

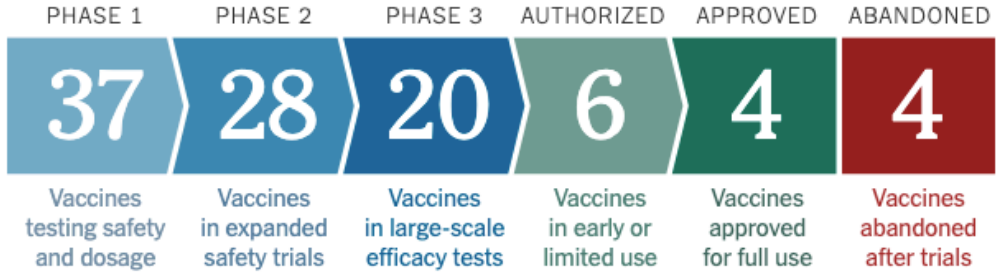
The three vaccines should not be compared because they tested different populations

- The three vaccines were not tried on similar groups of people at the same time
  - The vaccines were tested in different locations at different times
  - Different strains may have been more prevalent in different locations.
    - For example, the Johnson & Johnson's vaccine was tested in South Africa, where the dominant strain was the B.1.351 variant believed to be far more contagious
- In order to compare the three vaccines
  - A trial would have to be conducted where one group got placebo, one group got Pfizer, one group got Moderna, and one group got Johnson & Johnson
    - Such a trial has not taken place

Vaccines currently under development

Coronavirus Vaccine Tracker

By Carl Zimmer, Jonathan Corum and Sui-Lee Wee Updated Feb. 18, 2021



Vaccines typically require years of research and testing before reaching the clinic, but in 2020, scientists embarked on a race to produce safe and effective coronavirus vaccines in record time. Researchers are currently testing **70 vaccines** in clinical trials on humans, and 20 have reached the final stages of testing. At least 89 preclinical vaccines are under active investigation in animals.

Leading vaccines

Developer	How It Works	Phase	Status
Pfizer-BioNTech	mRNA	2 3	Approved in several countries. Emergency use in U.S., E.U., other countries.
Moderna	mRNA	3	Approved in Switzerland. Emergency use in U.S., U.K., E.U., others.
Gamaleya	Ad26, Ad5	3	Early use in Russia. Emergency use in other countries.
Oxford-AstraZeneca	ChAdOx1	2 3	Emergency use in U.K., E.U., other countries.
CanSino	Ad5	3	Limited use in China.
Johnson & Johnson	Ad26	3	
Vector Institute	Protein	3	Early use in Russia.
Novavax	Protein	3	
Sinopharm	Inactivated	3	Approved in China, U.A.E., Bahrain. Emergency use in Egypt, other coutries.
Sinovac	Inactivated	3	Approved in China. Emergency use in Brazil, other countries.
Sinopharm-Wuhan	Inactivated	3	Limited use in China, U.A.E.
Bharat Biotech	Inactivated	3	Emergency use in India.

What is the current status of COVID-19 vaccines for children?

- Children (age 18 and under) account for 1/5 of the population of the U.S. (~73 million individuals). Additionally, 3.7 million infants are born each year. This pool of unvaccinated people would still be at risk for COVID-19 disease and could contribute to its transmission
  - Herd immunity can not be established without vaccinating them.
- Children's immune systems differ from adolescents.
  - There are certain vaccines that work better in children than adults. And there are certain vaccines that work less well in children compared to adults.
- So far, COVID-19 vaccine has only been fully tested on adults.
  - In September 2020, Pfizer began including teenagers as young as 16 in an ongoing trial, and most recently received authorization for use in 12- to 17-year-olds in 2021
  - In January, Moderna began recruiting new trials including children as young as 12 using the exact same vaccine at the same dose and at the same interval as the vaccine given to adults.
  - In the UK, a small trial has been under way for youth age 6-17 using the AstraZeneca vaccine