Preferred Therapy Solutions

COVID-19 VACCINES: **THE FACTS**

Two vaccines have now received FDA Emergency Use Authorizations (EUAs)

- **Pfizer/BioNTech (BNT162b2)**
  95% effective (manufacturer data). Approved for use in people over the age of 16
- **Moderna (mRNA-1273)**
  94.5% effective (manufacturer data). Approved for use in people over the age of 18

VACCINE COMPOSITION

Pfizer-BioNTech COVID-19 Vaccine(BNT162b2): 95% effective: is a white to off-white, sterile, preservative-free, frozen suspension for intramuscular injection.

- The vaccine contains
  - Active Ingredient: A nucleoside-modified messenger RNA (modRNA) encoding the viral spike glycoprotein (S) of SARS-CoV-2
  - Lipids
    - (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis (ALC-3015)
    - (2- hexyldecanoate),2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159)
    - 1,2-distearoyl-snglycero-3-phosphocholine (DPSC)
    - Cholesterol
  - Salts: also knows as phosphate buffered saline (PBS) that keeps the pH or acidity of the vaccine close to that of a person's body
    - Potassium chloride
    - Monobasic potassium phosphate
    - Sodium chloride
    - Basic sodium phosphate dihydrate
  - Sucrose: acts as a cryoprotectant to safeguard the nanoparticles when they're frozen and stop them from sticking together
- The Pfizer-BioNTech COVID-19 Vaccine, BNT162b2 (30 µg), is administered intramuscularly (IM) as a series of two 30 µg doses (0.3 mL each) 21 days apart.
- Vaccine must be stored at -112 degrees Fahrenheit to remain effective and can only be stored for 5 days

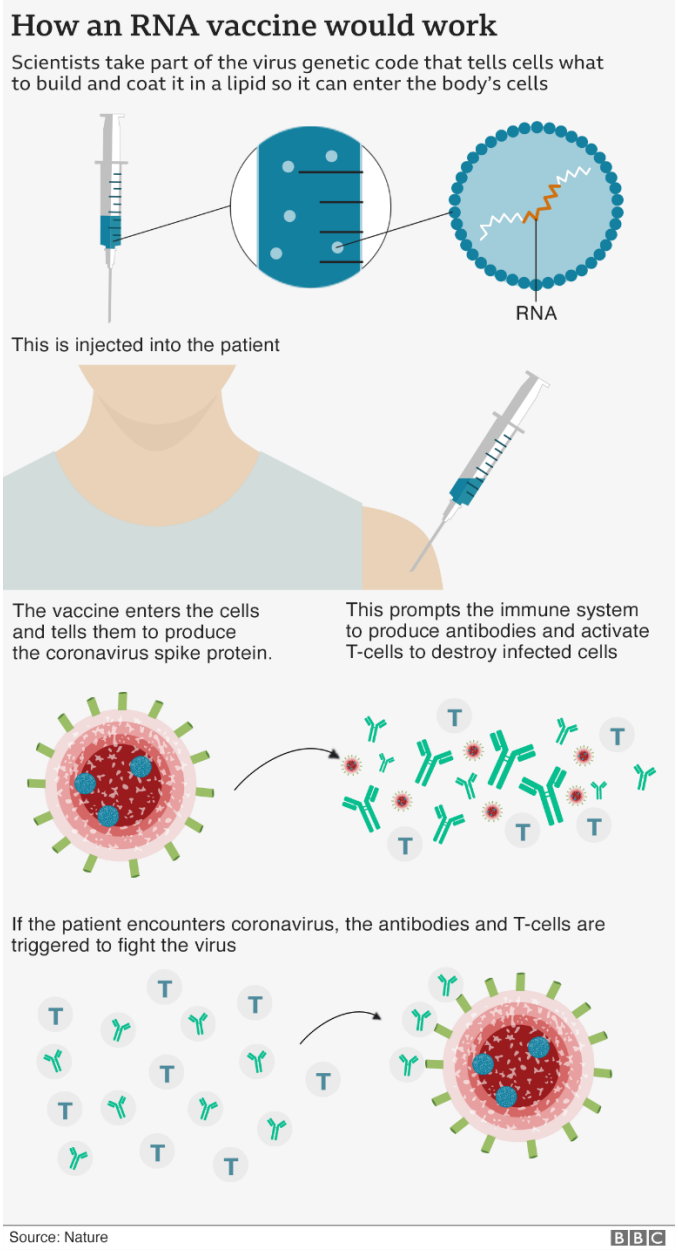
Moderna (mRNA-1273) – 94.5% effective (manufacturer data)

- Vaccine has similar chemical composition with slightly different lipid composition from Pfizer, which allows it to be stored at 36-45 degrees Fahrenheit for nearly 6 months, at refrigerated conditions for up to 30 days and at room temperature for up to 12 hours.

mRNA COVID-19 Vaccines

- COVID-19 mRNA vaccines carry genetic material that teach our cells how to make a harmless piece of what is called the "spike protein." The spike protein is found on the surface of SARS-CoV-2, the virus that causes COVID-19. Our immune systems recognize that the protein doesn't belong there and begins building an immune response and making antibodies, which are what protect us from getting infected when the real SARS-CoV-2 virus enters our bodies.
- mRNA technology has been studied for decades in vaccine trials for influenza, Zika, rabies, and cytomegalovirus. Beyond vaccines, cancer research has used mRNA to trigger the immune system to target specific cancer cells.
- The mRNA is produced by an enzyme that copies DNA that contains the protein to be produced
- Lipid nanoparticles protect and encase the fragile mRNA molecules and help it slide inside cells

- The cationic lipid, which is the main functional component is proprietary to each company.
- Genetic material from the vaccine, mRNA, is destroyed by our cells once copies of the spike protein are made and the mRNA is no longer needed
- The mRNA does not enter the cell nucleus, so it does not affect or interact with our DNA in any way



OTHER IMPORTANT FACTS

- One advantage of mRNA vaccines is that they are not made from the live virus that causes COVID-19. Therefore, there is no chance of getting the disease from the vaccine.
- Another big advantage is that mRNA vaccines can be developed in the laboratory using readily available materials, unlike traditional vaccines, which are grown in cells or eggs.
- People can experience side effects, such as fever, after receiving the vaccine, especially after the 2nd dose.

- This is because the first shot primes the immune system, helping it recognize the virus, and the second shot strengthens the immune response.

- These side effects are normal and are signs that the body is building immunity. It also typically takes a few weeks for the body to build immunity after vaccination therefore it is possible a person could be infected with the virus that causes COVID-19 just before or just after vaccination and get sick as the vaccine may not have had enough time to provide protection.

- COVID-19 mRNA vaccines will not cause you to test positive on COVID-19 viral tests.
  - If your body develops an immune response, which is the goal of vaccination, there is a possibility you may test positive on some antibody tests. Antibody tests indicate you had a previous infection and that you may have some level of protection against the virus.

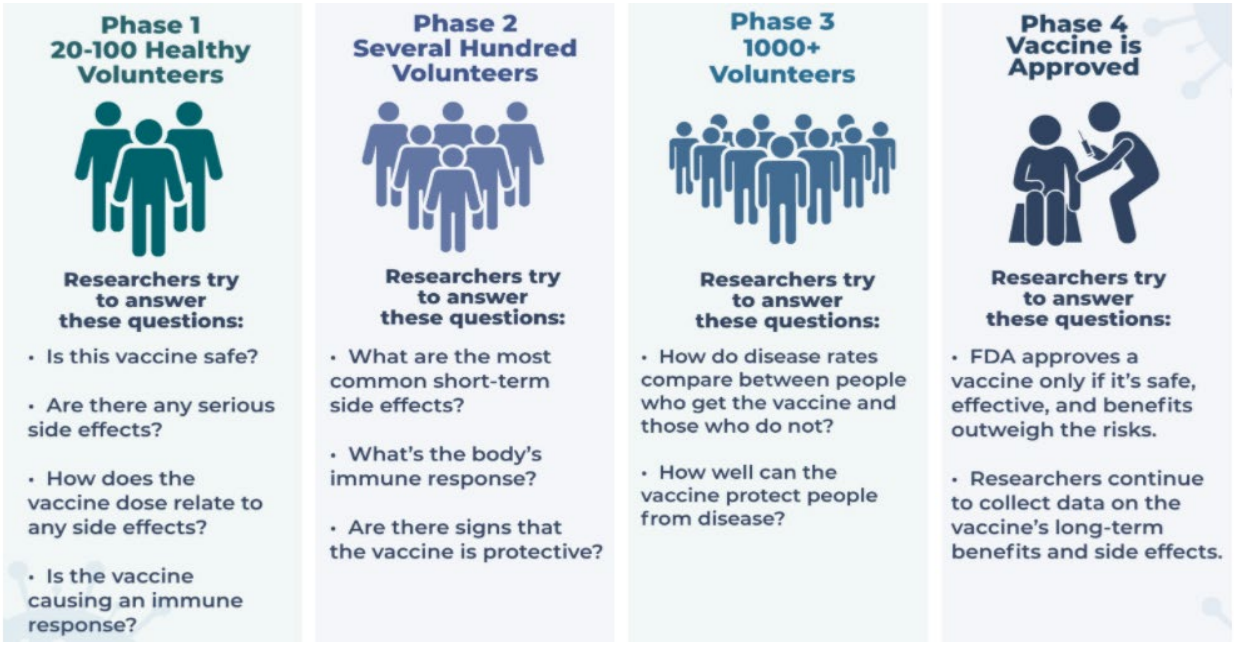
- People may be advised to get a COVID-19 vaccine even if they have already had the virus. This is because a person can catch the virus more than once.

- At this time, experts do not know how long someone is protected from getting sick again after recovering from COVID-19. The immunity someone gains from having an infection, called "natural immunity," varies from person to person.

WHY SO FAST?

- These vaccines were fast tracked because researchers used existing clinical trial networks, like those that study HIV treatments and vaccines, to quickly conduct COVID-19 vaccine trials.
- Global effort with the world's leading scientists focused on a single task
- The U.S. government and vaccine manufacturers invested millions of dollars to scale up vaccine production while clinical trials were in progress, greatly reducing the amount of time between vaccine authorization and vaccine implementation.
  - Because of the great financial risk, the investment in manufacturing normally doesn't happen until later in the development process.
- mRNA vaccines are faster and cheaper to produce because they use ready-made materials.

THERE ARE FOUR PHASES OF CLINICAL TRIALS



CLINICAL TRIAL DATA AS OF NOV 30, 2020:

PFIZER/BIOTECH:	MODERNA
43, 931 enrolled in study 150 clinical sites • 39 US states Racial/ethnic distribution • 13% Hispanic • 10% African American • 6% Asian • 1% Native American 45% ages 56-85	30,350 enrolled in study 89 clinical sites • 32 US states Racial/ethnic distribution • 20% Hispanic • 10% African American/Black • 4% Asian • 3% All others 64% ages 45 and older • 39% ages 45-64 • 25% ages 65+

SAFETY

COVID-19 vaccines are being held to the same safety standards as other routine vaccines.

- **An Emergency Use Authorization (EUA)** for a vaccine is based on the need to use a vaccine quickly to save lives during a public health emergency
  - EUA is a shorter process **but no steps are skipped in the safety evaluation process**
  - The FDA will assess if the vaccine known and potential benefits outweigh the known and potential risks
  - **An EUA does NOT imply that the authorization was done too quickly or that the vaccine is not safe**

- For a preventive COVID-19 vaccine to be potentially administered to millions of individuals, including healthy individuals, data adequate to inform an assessment of the vaccine's benefits and risks and support issuance of an EUA would include meeting the pre-specified success criteria for the study's primary efficacy endpoint, as described in the guidance for industry entitled "Development and Licensure of Vaccines to Prevent COVID-19"

- An EUA request for a COVID-19 vaccine should include all safety data accumulated from studies conducted with the vaccine
  - Data from phase 1 and 2 focused on serious adverse events, adverse events of special interest, and cases of severe COVID-19 among study participants.

  - Phase 3 safety data should include characterization of reactogenicity (common and expected adverse reactions shortly following vaccination) in a sufficient number of participants from relevant age groups and should include a high proportion of enrolled participants (numbering well over 3,000) followed for serious adverse events and adverse events of special interest for at least one month after completion of the full vaccination regimen.

  - The phase 1 and 2 safety data likely will be of a longer duration than the available safety data from the phase 3 trial at the time of submission of an EUA request and thus, are intended to complement the available data from safety follow-up from ongoing phase 3 studies.

- Data from phase 3 studies should include a median follow-up duration of at least 2 months after completion of the full vaccination regimen to help provide adequate information to assess a vaccine's benefit-risk profile.

  - From a safety perspective, a 2-month median follow-up following completion of the full vaccination regimen will allow identification of potential adverse events that were not apparent in the immediate post vaccination period.

- Adverse events considered plausibly linked to vaccination generally start within 6 weeks of vaccine receipt. Therefore, a 2-month follow-up period may allow for identification of potential immune-mediated adverse events that began within 6 weeks of vaccination.

- **Before ANY** vaccines receive authorization or approval, FDA carefully reviews all the safety data from clinical trials.
  - Two **independent advisory committees** reviewed the results of these vaccines trials. Members and experts of these committees have no conflict of interest and are not associated with any vaccine manufacturers
    - The Vaccine and Related Biological Products Advisory Committee (VRBPAC) that advises the FDA
    - The Advisory Committee on Immunization Practices (ACIP) that advises the CDC

- **After ANY** vaccines are authorized and in use, both FDA and CDC continue to monitor the safety of vaccines.

- Monitoring vaccine safety is a regular, ongoing part of vaccine development and these systems have been in place for decades to ensure the safety of routine vaccines. These systems are complementary and work together to monitor vaccine safety. Components include:
  - VAERS, which collects and analyzes reports of adverse events that happen after vaccination
  - The Vaccine Safety Datalink and the Post-Licensure Rapid Immunization Safety Monitoring System, which are networks of healthcare organizations that actively analyze the healthcare information of millions of people
  - The Clinical Immunization Safety Assessment, or CISA, which is a collaboration between CDC and 7 medical research centers. CISA assists healthcare providers with complex vaccine safety questions and conducts clinical research studies to better understand vaccine safety
  - FDA's Biologics Effectiveness and Safety System, or BEST, which is a system of electronic health record, administrative, and claims-based data for active surveillance and research
- Additional systems and data sources are also being developed to further enhance safety-monitoring capabilities. One example is v-safe—an active surveillance system that uses text messaging to initiate web-based survey monitoring.

- Further considerations around use of COVID-19 vaccines in pregnant or breastfeeding HCP will be provided once data from phase III clinical trials and conditions of FDA Emergency Use Authorization are reviewed.

SIDE EFFECTS

Side effects that have been reported with the Pfizer-BioNTech COVID-19 Vaccine include:

- Injection site reaction
- Fatigue
- Headache
- Muscle pain
- Chills
- Joint pain
- Fever
- Injection site swelling
- Injection site redness
- Nausea
- Feeling unwell
- Swollen lymph nodes

There is a remote chance that the Pfizer-BioNTech COVID-19 Vaccine could cause a severe allergic reaction. A severe allergic reaction would usually occur within a few minutes to one hour after getting a dose of the Pfizer-BioNTech COVID-19 Vaccine. Signs of a severe allergic reaction can include:

- Difficulty breathing
- Swelling of your face and throat
- A fast heartbeat
- A bad rash all over your body
- Dizziness and weakness (lymphadenopathy)

Moderna side effects:

- Injection site pain
- Fatigue
- Headache
- Muscle pain
- Joint pain
- Chills

Severe side effects

- Intractable nausea, vomiting
- Facial swelling
- Bell's Palsy (4 study participants)

PFIZER: SERIOUS ADVERSE EVENTS REPORTED

Deaths: A total of six (2 vaccine, 4 placebo) of 43,448 enrolled participants (0.01%) died during the reporting period from April 29, 2020 (first participant, first visit) to November 14, 2020 (cutoff date). Both vaccine recipients were >55 years of age; one experienced a cardiac arrest 62 days after vaccination #2 and died 3 days later, and the other died from arteriosclerosis 3 days after vaccination #1. The placebo recipients died from myocardial infarction (n=1), hemorrhagic stroke (n=1) or unknown causes (n=2); three of the four deaths occurred in the older group (>55 years of age). All deaths represent events that occur in the general population of the age groups where they occurred, at a similar rate.

Non-fatal SAEs: In the all-enrolled population of (total N=43,448), the proportions of participants who reported at least 1 SAE during the time period from Dose 1 to the data cutoff date (November 14, 2020) were 0.6% in the BNT162b2 vaccine group and 0.5% in the placebo group. The most common SAEs in the vaccine group which were numerically higher than in the placebo group were appendicitis (0.04%), acute myocardial infarction (0.02%), and cerebrovascular accident (0.02%)

MODERNA: SERIOUS ADVERSE EVENTS REPORTED

Deaths: As of December 3, 2020, 13 deaths were reported (6 vaccine, 7 placebo). Two deaths in the vaccine group were in participants >75 years of age with pre-existing cardiac disease; one 43 Moderna COVID-19 Vaccine VRBPAC Briefing Document participant died of cardiopulmonary arrest 21 days after dose 1, and one participant died of myocardial infarction 45 days after dose 2. Another two vaccine recipients were found deceased at home, and the cause of these deaths is uncertain: a 70-year-old participant with cardiac disease was found deceased 57 days after dose 2, and a 56-year-old participant with hypertension, chronic back pain being treated with opioid medication died 37 days after dose 1 (The official cause of death was listed as head trauma). One case was a 72-year-old vaccine recipient with Crohn's disease and short bowel syndrome who was hospitalized for thrombocytopenia and acute kidney failure due to obstructive nephrolithiasis 40 days after dose 2 and developed complications resulting in multiorgan failure and death. One vaccine recipient died of suicide 21 days after dose 1. The placebo recipients died from myocardial infarction (n=3), intra-abdominal perforation (n=1), systemic inflammatory response syndrome in the setting of known malignancy (n=1), COVID-19 (n=1), and unknown cause (n=1). These deaths represent events and rates that occur in the general population of individuals in these age groups.

Non-fatal Serious Adverse Events: Among participants who received at least one dose of vaccine or placebo (N=30,351), the proportion of participants who reported at least one SAE from dose 1 to the primary analysis cutoff date (November 25, 2020) was 1% in the mRNA-1273 group and 1% in the placebo group. The most common SAEs occurring at higher rates in the vaccine group than the placebo group were myocardial infarction (0.03% in vaccine group, 5 cases vs. 3 cases in placebo group), cholecystitis (0.02% in vaccine group, 3 cases vs. 0 cases in placebo group), and nephrolithiasis (0.02% in vaccine group, 3 cases vs. 0 cases in placebo group). The small numbers of cases of these events do not suggest a causal relationship. The most common SAEs occurring at higher rates in the placebo arm than the vaccine arm, aside from COVID-19 (0.1% in placebo group), were pneumonia (0.05% in placebo group) and pulmonary embolism (0.03% in placebo group). Occurrence of other SAEs, including cardiovascular SAEs, were otherwise balanced between treatment groups.

AS YOU CONSIDER TO VACCINATE OR NOT, KEEP THIS IN MIND

BEFORE	DURING	AFTER
• Learn about COVID-19 vaccines • See if COVID-19 vaccination is recommended for you	• Read the fact sheet that tells you about the specific COVID-19 vaccine you receive • Receive a vaccination record card	• With most COVID-19 vaccines, you will need two shots • Expect some side effects • Enroll in v-safe • Continue using all the measures to protect yourself

IN SUMMARY - REMEMBER THESE POINTS

- mRNA vaccines are expected to produce symptoms after vaccination, especially after the 2nd dose of vaccination.
  - Most side effects occur within 6 weeks of vaccination
  - Side effects mean your body is doing its job and making antibodies
    - These side effects are normal, common and expected
  - Side effects may include fever, headache, and muscle aches. These are similar to side effects you may experience after other adult vaccines like the flu vaccine and the shingles vaccine.

- The clinical trials did not reveal any significant safety concerns
  - At least 8 weeks of safety data were gathered in the trials, and it is unusual for side effects to appear more than 8 weeks post vaccination

- You must get the second dose because the vaccine will not protect you if you only receive one dose
  - It is important to get the same vaccine as the first dose
  - Protection occurs 1-2 weeks after the second dose

- To be more cautious, the FDA (Food and Drug Administration) requires 8 weeks of safety monitoring of the COVID-19 vaccines.

- We will most likely not know how long the vaccine will be protective once we receive it. We will know more as more time passes in the current research.

- May need to have vaccine shots for COVID-19 on a regular basis (like the flu shot)

- Similar to other vaccines, a large number of people in the community will need to get vaccinated before transmission drops enough to stop the use of masks.

- It is safe to get the COVID-19 vaccine even if you have had COVID-19

- Even if you have positive antibodies, you should get the COVID-19 vaccine
  - The vaccine could give you longer or better protection against the disease

As part of the healthcare system, you are on the front lines of this pandemic and are at high risk of exposure. You can also potentially transmit the virus that causes COVID-19 to populations at higher risk for severe COVID-19 infection, including older adults and those with certain medical conditions.

LEARN MORE

It is important to get information from reliable sources (CDC, AMDA, medical directors, and providers) **Social media is full of misinformation and opinions based on that misinformation**

Here are some links to information:

- CDC: https://www.cdc.gov/vaccines/hcp/covid-conversations/answering-questions.html
- CDC: About COVID-19 vaccines: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/about-vaccines.html
- CDC: Provider Resources for COVID-19 Vaccine Conversations with Patients and Answering Patients' Questions: https://www.cdc.gov/vaccines/hcp/covidconversations/https://www.cdc.gov/coronavirus/2019-ncov/vaccines/index.html
- https://www.pfizer.com/science/coronavirus/vaccine
- https://www.modernatx.com/cove-study
- www.clinicaltrials.gov
- Understanding and Explaining mRNA COVID-19 Vaccines | CDC
- https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19/clinical-considerations.html
- For the latest information about authorized vaccines, visit www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines.
- Source: https://covid19community.nih.gov/resources/understanding-clinical-trials
- https://www.fda.gov/media/144434/download