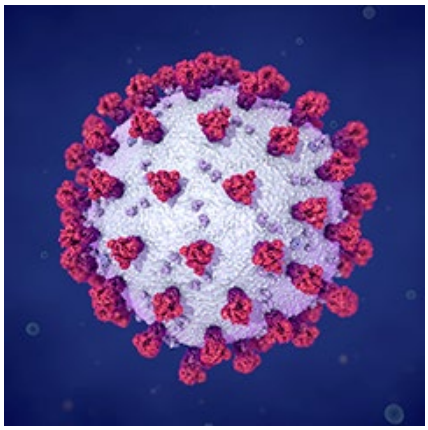
How does each of the available Covid-19 vaccines work?



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What do we know about each vaccine's efficacy?

Both vaccines are remarkably effective. In large clinical trials (Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. opens in new tab by L.R. Baden et al., and Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. opens in new tab by F.P. Polack et al.) that enrolled tens of thousands of people, the vaccines lowered the chance of developing Covid-19 by around 95% as compared with placebo injections. As summarized quite accurately in this XKCD cartoon. opens in new tab, sometimes data are so strong we don't even have to do a statistical analysis — that's what happened with both of these clinical trials. The results were that good.

Although we consider data from randomized, placebo-controlled trials to be the strongest form of clinical evidence, additional details make the results even more compelling. First, the vaccines prevented not only any disease due to SARS-CoV-2, but — quite importantly — severe disease. Prevention of severe disease could convert Covid-19 from the global threat it is now into more of a nuisance, like the common cold. Second, the studies enrolled participants who were quite representative of the U.S. population — age, sex, race, and ethnicity all broadly included. Third, while both vaccines are given as two doses, some protection became apparent just 10 to 14 days after the first dose. The efficacy noted after the first dose has raised questions about whether we should be vaccinating twice as many people with one dose rather than giving people the full two-dose schedule. opens in new tab. However, the 95% vaccine efficacy results come after the *second* dose, which boosts the immune response and is likely to make it more durable. For now, in the United States, the Centers for Disease Control and Prevention (CDC) and Food and Drug Administration (FDA) recommend proceeding with the two-dose schedule whenever possible.

Overall, these impressive results put the two mRNA vaccines up there with our most effective vaccines to date — more like measles than influenza vaccines, at least in the short term. The protection is far better than anyone anticipated, which is why many of us specialists in infectious diseases, virology, immunology, and public health become downright giddy when asked to discuss the vaccine's efficacy. (Last reviewed/updated on 11 Jan 2021)

How long will the vaccines work? Are booster doses required?

Since the vaccines have been tested only since the summer of 2020, we do not have information about the durability of protection. Data from the phase 1 trial of the Moderna vaccine suggested that neutralizing antibodies persisted for nearly 4 months. opens in new tab, with titers declining slightly over time. Given the absence of information on how long the vaccines will be protective, there is currently no specific recommendation for booster doses. (Last reviewed/updated on 11 Jan 2021)

Do the vaccines prevent transmission of the virus to others?

Many commentaries on the results of the vaccine clinical trials cite a lack of information on asymptomatic infection as a limitation in our knowledge about the vaccines' effectiveness. Indeed, this is a theoretical concern, since up to 40% of people who get infected with SARS-CoV-2 have no symptoms but may still transmit the virus to others.

So, until we know whether the vaccines protect against asymptomatic infection, we should continue to emphasize to our patients that vaccination does not allow us to stop other important measures to prevent the spread of Covid-19. We need to continue social distancing, masking, avoiding crowded indoor settings, and regular hand washing.

There are several good reasons to be optimistic about the vaccines' effect on disease transmission. First, in the Moderna trial. opens in new tab, participants underwent nasopharyngeal swab PCR testing at baseline and again at week 4, when they returned for their second dose. Among those who were negative at baseline and without symptoms, 39 (0.3%) in the placebo group and 15 (0.1%) in the mRNA-1273 group had nasopharyngeal swabs that were positive for SARS-CoV-2 by PCR at week 4. These data suggest that even after one dose, the vaccine has a protective effect in preventing asymptomatic infection.

Second, findings from population-based studies now suggest that people without symptoms are less likely to transmit the virus to others.

Third, many of the vaccines in wide use powerfully protect against both disease and transmission, so much so that infection control is one of the main motivators behind some vaccine policies. opens in new tab.

Since originally posting these comments, some of my colleagues have reminded me that certain vaccines allow asymptomatic colonization, and no doubt this will sometimes be true about the Covid-19 vaccines. Plus, the protective effect will never be 100%, which is why while case numbers are still high, we still recommend the use of social distancing and masking in public. These caveats notwithstanding, the likelihood that these vaccines will reduce the capacity to transmit the virus to others remains excellent. (Last reviewed/updated on 20 Jan 2021)

What do we know about each of the vaccines' short-term safety?

Overall, both mRNA vaccines are quite safe — that's the good news, and it should be the dominant message for our patients. But no vaccine (actually, nothing in medicine) is 100% safe.

Before discussing side effects, we need to acknowledge that the safety of Covid-19 vaccines will be in the spotlight for some time — these are new vaccines for a new disease. Rare events will appear in the news, amplifying attention and worry disproportionate to the actual risk. Our task will be to put these uncommon events into perspective, underscoring that these risks are far lower than the risk of getting sick with Covid-19.

These first two vaccines are classified as "reactogenic" — meaning that they will cause some side effects in most people who receive them, reflective of the brisk immune response they generate. In clinical practice, we should put these vaccines in the same side-effect category as the recombinant shingles vaccine (Shingrix) rather than the annual flu vaccine.

The most common side effect is pain at the injection site, especially in the 12 to 24 hours after administration. Around 1% of participants in the trials categorized the pain as "severe." Fatigue and headache are other relatively common side effects; high fevers are less common. These side effects generally resolve within a couple of days and are responsive to acetaminophen or a nonsteroidal antiinflammatory drug such as ibuprofen. In general, side effects are more common in younger vaccine recipients than in older ones, with the second shot inducing more side effects than the first.

Bell's palsy was reported more frequently in vaccine recipients than in controls, but there was not a sufficiently large number of cases to conclude that this was beyond what would naturally be observed in populations of this size by chance. There were no cases of Guillain–Barré syndrome or transverse myelitis.

Although hypersensitivity occurred equally in the placebo and vaccine groups in both trials, after distribution of the vaccines in the United Kingdom and the United States, reports emerged of vaccine recipients experiencing severe allergic reactions (anaphylaxis) shortly after receiving their first dose. opens in new tab. The current leading suspect in causing these reactions is polyethylene glycol, a compound present in both vaccines. Because of these rare events, administration of the vaccines includes a period of 15 minutes of observation after vaccination — 30 minutes for those with a history of severe allergic reactions of any sort.

It's critically important to emphasize that these allergic reactions are uncommon — the current estimate is that anaphylaxis will occur at approximately 1 in 100,000 doses. opens in new tab. Although this rate of severe allergic reactions is higher than that with other vaccines, it is substantially lower than the rate reported with penicillin, which is estimated to be 1 in 5000. But since severe penicillin allergies don't turn up as news stories, our challenge will be to contextualize this risk. (Last reviewed/updated on 11 Jan 2021)

What do we know about the vaccines' long-term safety?

The remarkably fast pace of vaccine development means that we have only months, not years, of follow-up. (Both mRNA clinical trials started in the summer of 2020.) But with other immunizations, severe reactions typically occur within days or weeks after administration. Long-term side effects with vaccines are fortunately quite rare, with putative associations later debunked by carefully done population-based studies.

Further safety data on both vaccines will be reported to the Vaccine Adverse Event Reporting System (VAERS). opens in new tab. This program is an existing national early warning system that was set up to detect possible safety problems in any licensed vaccine and has been in operation since 1990. In addition, the CDC has its own smartphone-based tool, which uses texting and a Web-based survey to collect information right after patients receive their Covid-19 vaccine. (Last reviewed/updated on 11 Jan 2021)

VACCINE AVAILABILITY

How and when are the vaccines being made available?

After careful review of all the primary safety and efficacy data from the phase 3 clinical trials, the FDA granted both vaccines Emergency Use Authorization (EUA). opens in new tab — the Pfizer/BioNTech vaccine on December 11, 2020, and the Moderna vaccine on December 18. Although this is not technically the full licensure that drugs and vaccines typically get, the director of the branch of the FDA that oversees vaccines says that the scrutiny of the data for emergency use was similar to what's needed for full approval.

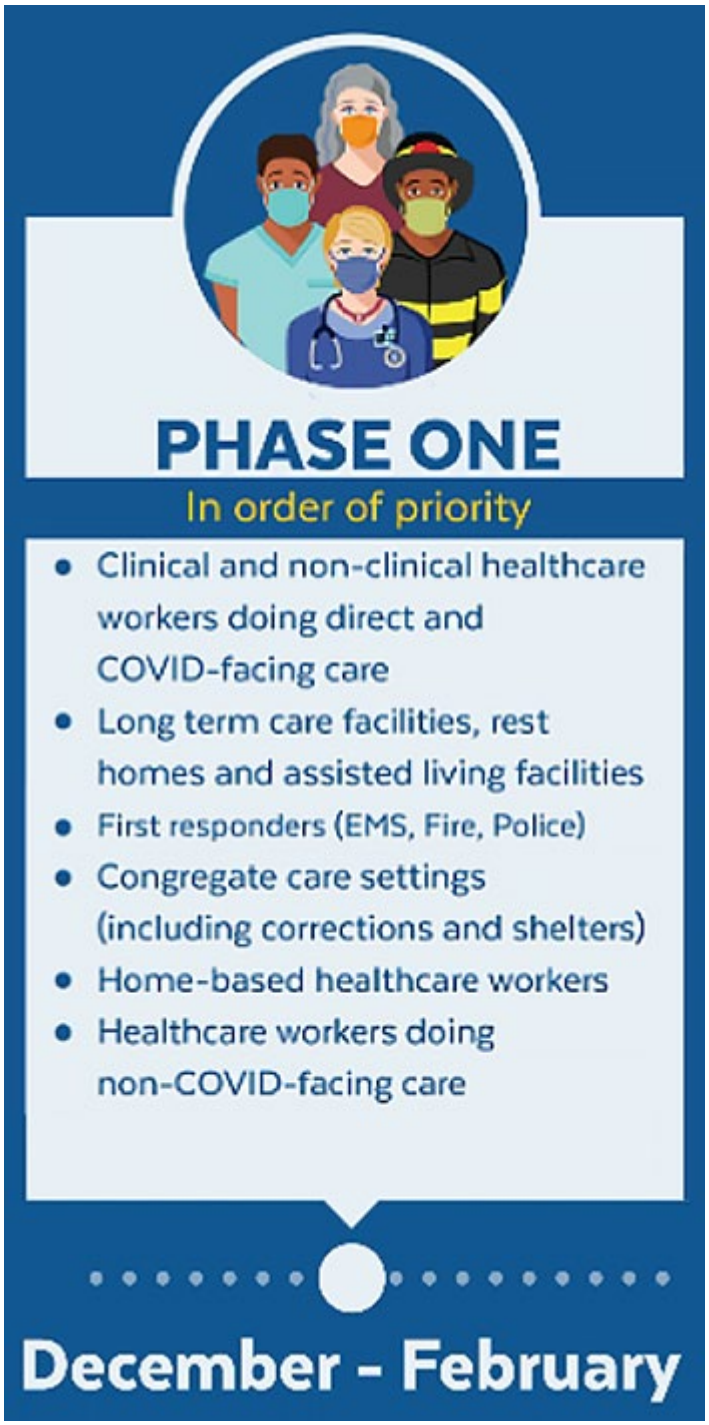
Shipments of the vaccines are sent to the states on the basis of population and are coordinated by the federal government. The states implement a strategy for distributing them, using criteria adapted from guidelines issued by Advisory Committee on Immunization Practices (ACIP). opens in new tab. The ACIP is the group charged with making recommendations to the CDC on immunizations and includes a broad range of experts in vaccines and public health. Its deliberations are summarized on the CDC website. opens in new tab; in addition, the actual meetings were taped and can be viewed on YouTube, in case you want something to watch in place of cute puppy videos.

Vaccine allocations and policies differ from state to state. However, they mostly follow the ACIP recommendations to prioritize (1) health care personnel and (2) residents of long-term care facilities in the initial phase of the Covid-19 vaccination program. A broad overview of each state's distribution plan is summarized at the National Academy for State Health Policies website. opens in new tab; for more details, individual state departments of public health have additional information.

It is important to note that "health care personnel" includes more than just clinicians. It also includes the many people who work in health care facilities who may be exposed to Covid-19 at the workplace or who interact with patients at any time, including staff in dietary, transport, laundry, engineering, and other services. (Last reviewed/updated on 11 Jan 2021)

How do I arrange for administration of the vaccine to my patient?

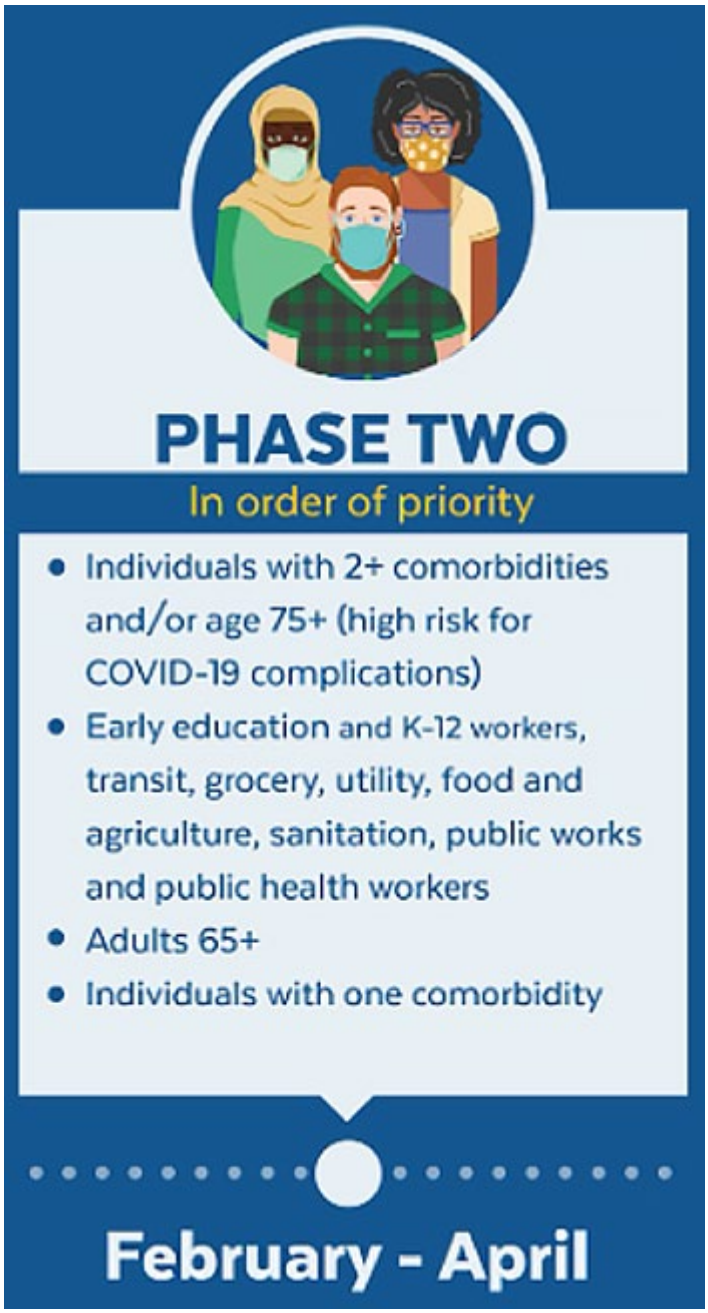
Since policies on distribution of Covid-19 vaccines vary by state, the answer differs depending on your site of practice. For example, in Massachusetts we are currently in Phase 1 of vaccine administration, which limits Covid-19 vaccines to these groups. opens in new tab:



As a result, in Massachusetts we cannot at present call our patients and advise them on exactly when and where to go for their vaccine.

Things may be different in your state — check your state's department of public health for local policies. Here's the policy in Missouri. opens in new tab, to choose one random example.

On the basis of predicted supply — and potential approval of other vaccines — the projected timeline for offering the vaccine to additional patients in my state, Massachusetts, will begin in February 2021, with prioritization of patients who are at highest risk for adverse outcomes from Covid-19 and certain other essential workers:



By April, the supply of vaccine should be sufficient for the general population. But again, because policies and distribution of Covid-19 vaccines vary by state, your timeline may differ depending on your site of practice. Check with your state and local departments of health. (Last reviewed/updated on 11 Jan 2021)

VACCINATION — WHICH PATIENTS

Are the recommendations the same for each of the available vaccines?

From a general perspective, recommendations are quite similar for both mRNA vaccines — each is two shots, and they are applicable to mostly similar populations.

But despite having similar mechanisms of action, safety, and efficacy, the two vaccines differ in certain important ways. As has been widely publicized, both require special attention to maintaining an extremely low temperature during distribution, with the Pfizer/BioNTech vaccine having particularly stringent cold-storage requirements. Indeed, the requirement for −70° C shipping and storage for the Pfizer/BioNTech vaccine means that it will not be suitable for sites that lack ultracold freezers. After thawing, it must be used within 5 days. The Moderna vaccine, by contrast, can be shipped at a comparably balmy −20° C and is stable at refrigerator temperature for 30 days.

An additional challenge for some areas is the minimum shipment size for the Pfizer/BioNTech vaccine, which is 975 doses. This may be too many for certain hospitals or skilled nursing facilities, especially in sparsely populated regions. By contrast, the Moderna vaccine is shipped in 100-dose batches.

These differences have little impact on physicians, however, unless they are involved with acquisition or distribution of the vaccines. More relevant for those in patient care are that Pfizer/BioNTech's vaccine is authorized for ages ≥16 years and Moderna's vaccine for ≥18 years. Studies in children are planned, but neither vaccine should be administered to children at this point.

Both vaccines required two doses for a complete series; 21 days separate the doses with the Pfizer/BioNTech vaccine, versus 28 days with the Moderna vaccine. The schedule does not need to be precise; a "grace period" of 4 days around the 21- or 28-day interval for the second dose is considered valid. If a patient misses this grace period for the second dose, no length of interval between the first and second dose for either vaccine invalidates the first dose. In other words, there is no need to start over; just give the second dose as soon as possible after the 21- or 28-day target. (Last reviewed/updated on 11 Jan 2021)

Is one vaccine preferable to the other for specific patients?

The Pfizer/BioNTech vaccine is authorized for ages ≥16 years, and Moderna's for ≥18 years. Aside from this age difference, there is no target population better suited to one vaccine or the other. In these times of limited supply, we should be advising our eligible patients to get the vaccine that's made available to them. It has already become common for people to ask others about which vaccine they have received, but the efficacy and safety findings in trials of both vaccines were strikingly similar. It is not a status contest, despite what this British vaccine recipient implies after receiving the "Oxford" vaccine. opens in new tab! (The Oxford–AstraZeneca Covid-19 vaccine is not yet available in the United States, though it may be soon.)

However, once the vaccine series has started, it should be completed with the same vaccine on the recommended schedule. There are no safety or efficacy data on using one vaccine for the first dose and a different vaccine for the second. I can't think of a reason why this would be problematic if it happens by accident, but it's not recommended. (Last reviewed/updated on 11 Jan 2021)

Are there contraindications to any of the vaccines?

The only absolute contraindication to these vaccines is known hypersensitivity to the vaccine components. Specific CDC recommendations regarding contraindications list the following:

- Severe allergic reaction (e.g., anaphylaxis) after a previous dose of an mRNA Covid-19 vaccine or any of its components
- Immediate allergic reaction of any severity to a previous dose of an mRNA Covid-19 vaccine or any of its components (including polyethylene glycol [PEG])
- Immediate allergic reaction of any severity to polysorbate (due to potential cross-reactive hypersensitivity with the vaccine ingredient PEG)

Note that anaphylaxis in reaction to any other vaccine or injectable therapies is not a contraindication to these Covid-19 vaccines, but persons with this history should be observed for at least 30 minutes after they receive their dose.

If a person experiences a severe reaction (in particular anaphylaxis) to the first shot, the person should not receive the second. People who experience severe pain will need to make an individual decision about whether to proceed with the second shot — it is not contraindicated, but side effects tend to be worse with the second dose. One potential strategy is to administer acetaminophen or ibuprofen as soon as the pain starts after the second dose. The CDC does not recommend prevaccine administration of these drugs, since theoretically they could blunt vaccine-induced antibody responses.

Monoclonal antibodies or convalescent plasma for treatment of Covid-19 could theoretically reduce the efficacy of the vaccines. Anyone who has received these treatments should delay receiving the vaccine for at least 90 days, a duration that factors in both the known half-life of these therapies and the low likelihood that someone with Covid-19 will experience reinfection in this time period. Further discussion of the rationale behind this recommendation has been added to the clinical considerations from the CDC guidance. opens in new tab. (Last reviewed/updated on 11 Jan 2021)

Can a patient with a history of an allergic reaction receive the vaccine?

Someone with a history of allergies can definitely receive the vaccine — it doesn't matter whether it's an allergy to other vaccines or medications or to bee stings or food or pollen. However, people with these histories should be observed for 30 minutes after receiving the vaccine, rather than the usual 15 minutes.

As has been widely reported, there have been rare cases of severe allergic reactions to the first dose. When this occurs, the second dose should not be given. It is not known whether these people would have allergic reactions to other experimental Covid-19 vaccines that do not use the mRNA mechanism of action. (Last reviewed/updated on 11 Jan 2021)

Should immunocompromised patients receive the vaccine?

The CDC considers immunocompromised patients to be at increased risk for severe Covid-19. opens in new tab. This is broadly defined as patients with histories meeting the following criteria, which are not 100% inclusive:

- Cancer
- Bone marrow transplant
- Solid-organ transplant
- Stem cells for cancer treatment
- Genetic immune deficiencies
- HIV
- Use of oral or intravenous corticosteroids or other medicines called immunosuppressants that lower the body's ability to fight some infections (e.g., mycophenolate, sirolimus, cyclosporine, tacrolimus, etanercept, rituximab)

The American Society of Hematology and the American Society for Transplantation and Cellular Therapy has a similar list with additional details. opens in new tab. Because of the heightened risk of severe Covid-19 in this population, immunocompromised patients should receive the Covid-19 vaccines if there are no contraindications. That's the easy part.

What's more challenging is estimating the safety, and particularly the efficacy, of the vaccines in this population, since neither clinical trial included large numbers of people in these individual categories. Since the Pfizer/BioNTech and the Moderna vaccines don't include live virus, there is no risk of virus dissemination. Whether the antigens in the vaccine will trigger either an increased risk of rejection (for transplant patients) or autoimmune disease (for those with rheumatologic or other autoimmune conditions) is unknown, but it is reassuring that such adverse effects are infrequent with other vaccines. Furthermore, the clinical trials did not see a difference in the occurrence of autoimmune conditions or inflammatory disorders in study participants who received the vaccine as compared with placebo.

Vaccine effectiveness depends on an intact host response; as a result, immunization might be less effective in immunocompromised hosts than in the general population. When immunizing immunocompromised patients for Covid-19, we should counsel them about this potential difference and hence about the continued importance of other prevention measures, such as mask wearing, social distancing, avoidance of crowds, and hand washing. Household members of those with weakened immune systems should also be immunized if possible.

Clinicians may wonder about delaying or stopping immunosuppressive therapies or chemotherapy before starting the Covid-19 vaccine series and then resuming once the two shots have been administered. Although such strategies have theoretical appeal, no general guidance can currently be given applicable to this diverse group. We will need to consider holding or delaying immunosuppression on a case-by-case basis, depending on the seriousness of the underlying condition and the urgency of its treatment.

Both clinical trials included small numbers of clinically stable people with HIV who were on antiretroviral therapy — 120 and 176 in the Pfizer/BioNTech and Moderna trials, respectively. Although these numbers are too small to make any conclusions about safety and efficacy in people with HIV, there is no theoretical reason why someone with well-controlled HIV should have problems with these vaccines, and immunization is recommended. For people with HIV who are not on antiretroviral therapy, especially those with low CD4 cell counts, my opinion is that prioritization of HIV treatment over Covid-19 vaccination is warranted — both for prevention of HIV-related complications and to improve vaccine responsiveness. (Last reviewed/updated on 11 Jan 2021)

Should pregnant or breastfeeding women receive the vaccine?

Although pregnant and breastfeeding women were not enrolled in the Covid-19 vaccine trials and as a result there are limited data about safety, the CDC advises that pregnant and lactating women should be offered the vaccine and may choose to be vaccinated. opens in new tab. This view is shared by the American College of Obstetricians and Gynecologists. opens in new tab and the Society for Maternal–Fetal Medicine. opens in new tab. It's nice when all these groups agree! There is no theoretical reason why mRNA vaccines would be harmful to the mother during pregnancy, to a developing fetus, or to a breastfeeding infant. Also reassuring is that gestating rats receiving the Moderna vaccine did not demonstrate any safety concerns related to fetal or embryonal development.

Pregnant women should be informed that observational studies show that pregnancy is a risk factor for severe illness due to Covid-19, much as it is for influenza. On the basis of this information and the likelihood they have of Covid-19 exposure, along with information about the limited safety data available to date, pregnant women can make an educated decision about whether to accept the vaccine. However, it's important to emphasize that the vaccine should be offered to them — much as we do the flu vaccine — and that they should be given a chance to have their questions addressed. An emergency department doctor or nurse may choose to receive the vaccine, while a person working from home with very few social interactions may choose not to do so, awaiting further data. (Last reviewed/updated on 11 Jan 2021)

Are there minimum or maximum ages for patients to receive the vaccine?

The Pfizer/BioNTech vaccine is authorized for patients ≥16 years and the Moderna vaccine for ≥18 years. Studies in children are planned, but neither vaccine should be administered to children at this point. There is no maximum age restriction. Given the disproportionate toll that Covid-19 has taken on the elderly — essentially every study finds that older age is a risk factor for severe disease — older people should be strongly encouraged to be immunized. (Last reviewed/updated on 11 Jan 2021)

VACCINE ADMINISTRATION — MONITORING, PATIENT INSTRUCTIONS

What capabilities need to be immediately available when the vaccine is administered?

The key capability is to have resources available to manage anaphylaxis — both human resources (for example, nurses or pharmacists or doctors) and equipment. The CDC lists emergency supplies and equipment. opens in new tab that should be available at all sites (epinephrine, H1 antihistamines, blood pressure cuffs, and stethoscopes) and items that should be available if feasible (pulse oximeter, oxygen, IV fluids, and intubation kit).

Since Covid-19 can spread from people who are without symptoms, it is important to ensure that all providers and those receiving the vaccines adhere to best infection-prevention practices during the vaccine appointment. These practices include wearing masks, minimizing time in close contact with others, and avoiding crowded indoor spaces with poor ventilation. The CDC provides guidance on safe immunization practices during the Covid-19 pandemic.. opens in new tab (Last reviewed/updated on 11 Jan 2021)]

How should early side effects be managed?

Analgesics and antipyretics such as acetaminophen or ibuprofen are effective in managing post-vaccine side effects including injection-site pain, myalgias, and fever. However, the CDC does not recommend prevaccine administration of these drugs, as they could theoretically blunt vaccine-induced antibody responses.

Because of the small risk of anaphylaxis, sites that administer the vaccines must have on hand strategies to evaluate and treat these potentially life-threatening reactions. The CDC has issued recommendations on how sites should prepare. opens in new tab. (Last reviewed/updated on 11 Jan 2021)

Should acetaminophen or nonsteroidal antiinflammatory drugs be taken prior to vaccination to prevent postvaccination symptoms?

Although these drugs could decrease subjective side effects, theoretically they could also blunt immune response and make the vaccines less effective — hence they are not recommended before vaccination. They are useful, however, in diminishing side effects once they occur. Acetaminophen is preferred for pregnant women. (Last reviewed/updated on 11 Jan 2021)

What instructions should I provide to a patient after vaccination?

We are accustomed to providing patients with a vaccine information statement (VIS) for each vaccine we administer, but VISs are not yet available for Covid-19 vaccines. I expect they will be developed once the vaccines are formally approved by the FDA. In place of a VIS, we

should provide the Emergency Use Authorization (EUA)-authorized fact sheet. opens in new tab to all vaccine recipients. The fact sheet provides the following information:

- Basic information on Covid-19, symptoms, and what to discuss with a health care provider before vaccination
- Who should and should not receive the vaccine
- Recipients' choice to receive the vaccine
- Vaccine series information
- Potential and known risks and benefits of the vaccine, including common side effects
- Information on reporting side effects to the Vaccine Adverse Event Reporting System (VAERS)
- An explanation of what an EUA is and why it is issued
- Any approved available alternatives for preventing Covid-19
- Additional resources

(Last reviewed/updated on 11 Jan 2021)

What is "v-safe"? Should my patients enroll?

After receiving the Covid-19 vaccine, patients have the option of enrolling in v-safe. opens in new tab. This CDC smartphone-based tool provides automated check-ins after Covid-19 vaccination, allowing people to report side effects using a secure online site. For those reporting severe or notable side effects, a CDC official may call to collect more details about what happened. In addition to collecting this information, v-safe will also send reminders about receiving the second vaccine.

Although enrolling in v-safe is voluntary, my opinion is that we should encourage our patients to participate. We are in the midst of the greatest pandemic in over a century, and the vaccines are a key strategy for getting it under control. Collecting as much information as possible about the safety of the vaccines is critically important in the weeks and months ahead. (Last reviewed/updated on 11 Jan 2021)

Is there anything I need to watch for or report after administration of a vaccine? How do I report it?

Anticipated side effects do not need to be reported unless they are so severe that they trigger hospitalization or an emergency department visit. The most common side effect is pain at the injection site, especially in the 12 to 24 hours after administration. Around 1% of study participants categorized the pain as "severe." Fatigue and headache are other relatively common side effects; high fevers are less common. These side effects generally resolve within a couple of days and are responsive to acetaminophen or a nonsteroidal antiinflammatory drug such as ibuprofen. In general, side effects are more common in younger vaccine recipients than in older recipients, with the second shot inducing more side effects than the first.

Clinicians must report *severe* adverse effects through the Vaccine Adverse Event Reporting System (VAERS). opens in new tab. This should be done whether you think the side effect was related to the vaccine or not. The FDA defines a severe adverse effect as one or more of the following:

- Death

- A life-threatening adverse event
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant incapacity or substantial disruption of normal life functions
- A congenital anomaly or birth defect
- An important medical event that (on the basis of appropriate medical judgment) may jeopardize the person and may require medical or surgical intervention to prevent one of the outcomes listed above
- Multisystem inflammatory syndrome
- Cases of Covid-19 that result in hospitalization or death

Given how quickly the vaccines went through development and clinical trials, health care providers are strongly encouraged to report to VAERS any clinically significant adverse event that follows vaccination, even if the provider is unsure if the event is related to the vaccine. For example, if a 75-year-old man with a history of cardiac disease sustains a myocardial infarction between the first and second Covid-19 vaccines, this should be reported — even though the vaccine may not have caused the MI. It is through accumulation of such data that potential associations can be identified.

Similarly, many of us are hearing about delayed reactions of unclear significance — examples from my experience include diffuse rashes, vertigo, and late-onset discomfort at the injection site. In all these situations, the relationship to the vaccine is unknown, though plausibly connected (especially the injection-site discomfort). To broaden the safety data available for these new vaccines, I have suggested that each of the people experiencing these issues report them on their v-safe account or to VAERS. opens in new tab. (Last reviewed/updated on 11 Jan 2021)

After people receive the vaccine, should there be any testing to determine whether the vaccine worked?

People vaccinated with the Covid-19 vaccines develop antibodies to the spike protein of SARS-CoV-2. However, there is currently no recommendation for postimmunization serologic testing. This may change in the future if results of these tests correlate with protection from infection, especially if they dictate whether booster immunizations are required. It's important to note that not all available antibody tests assess for anti-spike antibody — the package insert for the antibody test should give this information. (Last reviewed/updated on 11 Jan 2021)

SECOND DOSES OF VACCINE

Are there systems in place to make sure a patient receives the second dose?

At the time of the first immunization, you should provide the patient with a vaccination card that includes information on the vaccine the patient received and the scheduled date of the second dose. The second dose should be scheduled as close as possible to the recommended 21

days (for Pfizer/BioNTech) and 28 days (for Moderna) after the first. If that date is not possible, it is better to delay the vaccine for a few days than to give it early.

If patients choose to enroll in the v-safe program, they will receive a reminder about their second dose by text message. (Last reviewed/updated on 11 Jan 2021)

Can the second dose be given sooner than 21 or 28 days if that will help to ensure it is received?

Vaccine sites should not routinely offer the second dose of the vaccine earlier than the recommended time interval between shots. However, if a person arrives early for the second dose of vaccine, the day of arrival is within the 4-day grace period, and the person cannot return on the designated day (day 21 for Pfizer/BioNTech, day 28 for Moderna), then the vaccine should be given to ensure that the two doses are received. In other words, better to give the second vaccine dose a little early than not to give it at all. (Last reviewed/updated on 11 Jan 2021)

Can the second dose be given later than 21 or 28 days and still be effective?

The goal of the first vaccine is to “prime” the immune response; the second “boosts” it. Although most participants in the trials received their second dose on or close to the scheduled time, there is no biological reason why receiving the second dose late would diminish the effectiveness of the vaccine, provided it’s received before too long an interval. In practice, the second dose should be given as soon as possible after the missed scheduled dose (Last reviewed/updated on 11 Jan 2021)

Should vaccination be delayed if a patient has any symptoms or is actively ill?

Vaccination should be deferred in people with acute illness, preferably until after they recover. However, people with chronic diseases and stable symptoms are eligible to receive the vaccine; examples would be people with COPD and dyspnea on exertion or those with inflammatory bowel disease and gastrointestinal symptoms. Many of the participants in the phase 3 clinical trials had underlying medical problems, and although they were not acutely ill, some presumably had symptoms from their diseases — that’s the nature of chronic medical conditions. (Last reviewed/updated on 11 Jan 2021)

Does the second inoculation need to be the same vaccine?

Although the mechanism of action of the two vaccines is the same, they are not identical, and the second shot should be from the same vaccine as the first. There are no data to indicate that receiving a different vaccine as a second shot would be unsafe or less effective, but the vaccines have not been studied this way and such hybrid dosing strategies should be avoided. (Last reviewed/updated on 11 Jan 2021)

PATIENTS WITH COVID-19 OR POSSIBLE COVID-19

Should a patient who was exposed to Covid-19 receive the vaccine in order to prevent the disease?

Currently there are no data to support use of the Covid-19 vaccines acutely to prevent disease after a known exposure to an active case. Since the incubation period for Covid-19 averages around 5 days, it is unlikely that the vaccine would elicit an immune response quickly enough to block infection. As a result, people who have been exposed to Covid-19 should finish their 10- to 14-day quarantine before undergoing immunization. Since some vaccines for other diseases (notably varicella) are effective in preventing infection after exposure, it is possible that this will be a future recommendation for Covid-19 vaccination, but currently it is not. (Last reviewed/updated on 11 Jan 2021)

Should patients who have recovered from Covid-19 receive the vaccine?

Yes, they should receive the vaccine. Some of the people who participated in the clinical trials had evidence of prior SARS-CoV-2 infection (based on a positive antibody test), and the vaccines were safe and effective in this group.

Since re-infection after recovery from Covid-19 is rare in the first 90 days, some people may wish to defer immunization for this long — however, if they wish to be immunized sooner, there is no contraindication. Patients who were treated with monoclonal antibodies or convalescent plasma should wait this long, however. These treatments might inactivate the vaccines, making them less effective. Deferral of immunization for 90 days after treatment with monoclonal antibodies or convalescent plasma is recommended. (Last reviewed/updated on 11 Jan 2021)

Should a patient who is diagnosed with Covid-19 shortly after the first dose still receive the second scheduled dose?

The vaccine begins to generate protective immunity 10 to 14 days after the first shot. As a result, it is not surprising that some people have experienced Covid-19 shortly after their first immunization, and they naturally wonder whether they should proceed with the second shot as originally scheduled.

The current recommendation is that people with current infection should wait until they have recovered from the acute illness and are eligible to discontinue isolation. opens in new tab. These recommendations apply both to those who developed Covid-19 before their first injection and to those who developed it after starting the vaccine series. On the basis of this guidance, some people in the latter group may be able to proceed with their scheduled second shot and others will need to wait. Treatment of Covid-19 with either monoclonal

antibodies or convalescent plasma should delay receipt of the vaccine by 90 days, since these treatments could theoretically make the vaccine less effective. (Last reviewed/updated on 11 Jan 2021)

Should a patient who received an antibody treatment, convalescent serum, or both for Covid-19 receive the vaccine?

Eventually yes, but not right away. Monoclonal antibody treatments for Covid-19 and convalescent plasma might interfere with the vaccine-induced immune response, making them less effective. Deferral of immunization for 90 days is recommended. (Last reviewed/updated on 11 Jan 2021)

How does the vaccine affect the evaluation of a patient and diagnostic testing for possible Covid-19?

The Covid-19 vaccines will not influence the results of PCR or antigen testing for the disease. The vaccines do generate antibodies to SARS-CoV-2, which are directed at the spike protein. Some available serologic assays test for this antibody; others do not. The manufacturers of the individual antibody tests should be able to provide this information, and it is often listed in the package insert. (Last reviewed/updated on 11 Jan 2021)

Other Resources

- **Accreditation Council for Continuing Medical Education**COVID-19 — Learn to Vaccinate: Educator Resources. opens in new tab
- **Vaccine Adverse Event Reporting System. opens in new tab**Report an Adverse Event.. opens in new tab
- **Centers for Disease Control and Prevention. opens in new tab**COVID-19 Vaccines.. opens in new tab

World Health Organization. opens in new tab