COVID-19 and vaccination

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Introduction

The approval of COVID-19 vaccines in December 2020 signifies a major milestone in the battle against the coronavirus SARS-CoV-2. Coronavirus disease 2019 (COVID-19) is defined as illness caused by a novel coronavirus now called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; formerly called 2019-nCoV). This was declared a global pandemic by the World Health Organization in March 2020[1]. It has since caused 1.85 million deaths and 85 million infections worldwide up to the end of 2020[2].

In the fight against SARS-CoV-2, the United Kingdom was the first country to approve a COVID-19 vaccine that has been tested in a large clinical trial. On 2 December 2020, the Medicines and Healthcare Regulatory Agency (MHRA) granted emergency-use authorisation to the Pfizer/BioNTech vaccine. This was followed by the approval of the vaccine developed by Oxford University and AstraZeneca on the 30 December 2020. In the US, the Food and Drug Administration (FDA) gave emergency use authorisation to the Pfizer/BioNTech vaccine on 11 December 2020 and another vaccine produced by Moderna on 18 December 2020. In the UK, the Moderna vaccine was given regulatory approval by the MHRA on the 8 January 2021[4].

The arrival of these SARS-CoV-2 vaccines will be met with hope, but also anxiety. Many will be thinking of whether to have the vaccine or not. This article presents the current scientific information and guidance available on the SARS-CoV-2 vaccine.

What are vaccines?

Vaccines are material that contain weakened or inactive parts of a particular organism such as virus or bacteria and it triggers an immune response within the body.

In response to the material in vaccines called the antigen, the immune cells (B-cells) start to make proteins (antibodies) to fight the virus or bacteria. The immune cells in the body (T-cells) may also be activated to act against the bacteria or virus.

The process of receiving a vaccine is known as vaccination or immunisation. This is a way to prevent certain serious and life-threatening infections. As the vaccine is made up of a weakened

or inactive part of the bacteria or virus, it will not cause disease in the person receiving the vaccine, but it will prompt the immune system to respond much as it would have on its first reaction to the actual infection. It is with this same principle that vaccines will be one of the important ways to control the COVID-19 pandemic.

Why vaccinate?

When a person is vaccinated, they are very likely to be protected against the bacteria or virus by production of antibodies or activation of immune cells. However, there is no vaccine that provides 100% protection.

In addition, not everyone can be vaccinated. There are certain conditions where a vaccine is not suitable for a person. For example, people who have severe allergies to some vaccine components may not be able to receive certain vaccines.

These people may still be protected if they live amongst others who are vaccinated. When a significant number of people in the population are vaccinated, it becomes more difficult for the infection to be passed around. As such, those who are unable to receive the vaccine will have a lower risk of being exposed to the harmful bacteria or virus.

This is known as herd immunity and those who are unable to be vaccinated will receive substantial (but not full) protection against the infection. So vaccination provides protection both for the person receiving it and also for those in the population are unable to be vaccinated. This is why if you are eligible and able to, you should receive the vaccine.

Can I get COVID-19 from the vaccine?

You cannot get COVID-19 from the vaccine.

All vaccines that are presently under development specifically for COVID-19 are non-live vaccines that cannot give you the disease.

Some people worry the vaccine actually contains the virus that causes COVID-19. The COVID-19 vaccines contain parts of the virus such as the genetic code, protein or inactivated portions of the virus. These components are made from a virus, but it is weakened so it will not make a person sick.

The vaccine cannot transfer infection to you, nor can they change your genetic information. The aim of the vaccine is to prepare the immune system and provide protection against future infection from the SARS-CoV-2 virus.

Which COVID-19 vaccines are available?

The genetic sequence of SARS-CoV-2 was published on 11 January 2020, and was followed by the rapid research and development of vaccines. At the end of 2020, there were over 60 COVID-19 vaccines in human clinical trials[5].

It is important to have a range of different vaccines available as manufacturing has to be scaled up to meet the race against time to supply vaccines for the global population.

The vaccines have been given rapid approval with government funding and early review of the data. People who are hesitant to get a COVID-19 vaccine should be reassured that the approval process has been independent and robust[4].

There are currently three types of COVID-19 vaccines that have or are soon to start Phase 3 clinical trials. The types of COVID-19 vaccines are:

- mRNA vaccines

  These vaccines contain genetic code for the virus that gives instruction to our cells to make proteins that resemble part of the virus, in this case the S (spike) protein of the SARS-CoV-2. It is not made up of any part of the COVID-19 pathogen (live or dead).

  The genetic code is called messenger ribonucleic acid (mRNA) and uses this new technology that is different from other vaccines we had before. The mRNA is not integrated into the host DNA. The genetic code from the vaccine is destroyed when the proteins are made.

  The harmless protein produced is recognised by immune cells (B and T cells) and protection is developed against future infection from COVID-19. The vaccine shows the body's immune system what the virus looks like so it can remember the next time it's infected.

  mRNA vaccines do not contain the virus, so there is no risk of the vaccination causing COVID-19.

  Using the mRNA platform, the vaccine can be developed quickly. It has a low to medium manufacturing speed.

- Viral vectors

  These vaccines contain the genetic material of SARS-CoV-2 and are inserted into a weakened version of a non-related virus. This is called a viral vector. When the viral vector is inside our cells, the genetic material instructs cells to make proteins that stimulate an immune response from B and T cells that will remember how to react against the virus if we get infected in the future. It has a medium development speed and high manufacturing scale.

- Protein subunits

  These vaccines contain proteins from the virus that cause COVID-19. These harmless proteins cannot cause the infection and are given as a vaccine. Once inside cells, the immune cells recognise the proteins and begin making antibodies and T-cells. These immune cells will confer protection against future infection with COVID-19. It has a medium to fast development speed and high manufacturing scale.

There are also other platforms being developed such as DNA vaccines for the INO-4800 (Inovio) COVID-19 vaccine[6].

The list of COVID-19 vaccines is shown here:

BNT-162b2 (Pfizer, BioNTech)

First approved in the United Kingdom on December 2, 2020 and in the USA on December 11, 2020. This vaccine is a mRNA vaccine that encodes the SARS-CoV-2 receptor-binding domain antigen. It is thus a genetic-code vaccine.

The mRNA molecule is unstable and this is why it needs to be stored at very low temperatures, otherwise the molecule can break down. It is stored ultra-cold at -70ºC. Once thawed it can be kept refrigerated for up to 5 days. The vaccine comes in a liquid injection and is given as 2 injections, 21 days apart.

The vaccine contains natural tiny oily particles called lipid nanoparticles and these microscopic spheres contain the mRNA molecule. The small droplets are the same structure as the cell membranes, so they can fuse with the membrane allowing the mRNA to enter the cells. The lipids also stabilise the mRNA molecule. Once inside the cells, the mRNA produces the spike (S) protein. The immune system then recognises this as a foreign entity and attacks it using antibodies and T-cells. The immune system learns and remembers how to destroy the spike protein, so if the virus enters the body, it will recognise and destroy it.

mRNA-1273 (Moderna)

Emergency use authorisation by FDA on December 18, 2020[7]. Approved by MHRA for use in the UK on January 8, 2021. This is also an mRNA vaccine. It is a lipid-nanoparticle-encapsulated mRNA vaccine expressing the prefusion-stabilised spike glycoprotein. This vaccine encodes the S-2P antigen.

There are some differences compared to the Pfizer/BioNTech vaccine in the composition of the lipid spheres. There are four types of lipid nanoparticles used to hold the mRNA. The ratios of these lipids, as well as whether they are positively or negatively charged, is what differentiates the mRNA vaccines. This also means they require different storage conditions. The vaccine is stored at -20°C. Once thawed it can be stored in the refrigerator (2-8°C) for 30 days. It is given as 2 injections, 28 days apart.

AZD-1222 (ChAdOx1 nCoV-19, AstraZeneca; Oxford University)

Approved by MHRA for use in the UK on December 29, 2020. This is a viral vector vaccine. The Oxford/AstraZeneca vaccine uses a vector from a common cold virus (adenovirus) from a chimpanzee (ChAd). It is a harmless chimpanzee cold virus that has been genetically changed and cannot grow inside human cells. This replication-deficient chimpanzee adenoviral vector vaccine contains the full-length SARS-CoV2 spike protein genetic sequence.

It delivers into the host cells the surface glycoprotein antigen (spike protein) gene. The gene (DNA) is shuttled into cells and makes the cell produce proteins that will prime the immune system. It elicits antibodies to attack the SARS-CoV-2 virus if it later infects the body. It is more stable and can be stored with refrigeration. It is given as 2 injections, 28 days apart.

Ad26.COV2.S (Johnson & Johnson)

This is a viral vector vaccine. It is an adenovirus serotype 26 (Ad26) recombinant vector-based vaccine (JNJ-78436735; Johnson & Johnson). It can be stored in the refrigerator. Phase 3 trial (ENSEMBLE) ongoing[8]. Second phase 3 trial (ENSEMBLE 2), to study effects of 2 doses.

NVX-CoV2373 (Novonax)

This is a protein subunit vaccine. It is engineered using recombinant nanoparticle technology from SARS-CoV-2 genetic sequence to generate an antigen derived from the coronavirus spike protein. This is combined with an adjuvant (Matrix-M). It is given as 2 injections, 21 days apart. Phase 3 trial in the United Kingdom ongoing. Results from the phase 1 clinical trial December 2020[9]

How effective are these vaccines?

BNT-162b2 (Pfizer, BioNTech)

In the multinational (150 trial sites across 6 countries) phase 3 trial reported[10], it included participants 16 years and older who were randomly assigned to receive vaccine or placebo by injection; 43,448 participants received vaccine or placebo (vaccine group, 21,720; placebo group, 21,728).

People with autoimmune conditions were included in the trial of the Pfizer / BioNTech vaccine if their condition had been stable for 6 weeks before.

Overall, it was 95% effective against clinically evident COVID-19 infection 28 days after 1st dose and was well tolerated across all subgroups. There were 170 confirmed COVID-19 cases (placebo group, 162; vaccine group, 8), 10 severe cases after 1st dose (placebo group, 9; vaccine group, 1). There was consistency across age, sex, race and ethnicity. It was not evaluated for asymptomatic infection/carriage.

Short-term mild-to-moderate pain at the injection site was the most commonly reported reaction, and severe pain occurred in less than 1% of participants across all age groups. Some patients reported fatigue (3.8%) and headache (2%). When the UK vaccine programme started, two people with a history of severe allergy had allergic reactions to the Pfizer /BioNTech vaccine and these cases are being investigated. People with a history of severe allergy will not be given the vaccine at present.

After seven months from the start of clinical trials, the vaccine has been rolled out to care home staff and residents as well as front-line workers in the UK. Phase 3 trials in individuals 16 years and older are ongoing. The Joint Committee of Vaccination and Immunisation (JCVI) advises that the second dose of the PfizerBioNTech vaccine may be given between 3 to 12 weeks following the first dose[11].

mRNA-1273 (Moderna)

The COVE study started in July 2020 and included 30,420 patients. The average age of the participants was 51 years.

Participants received 2 100-µg doses or matched placebo on days 1 and 29. 196 cases of symptomatic COVID-19 occurred at least 14 days after participants received their second dose (185 cases in the placebo group, and 11 in the vaccine group).

It was 94.1% effective in preventing symptomatic COVID-19 in Phase 3 studies[12].

There were no cases of severe COVID-19 in the study and no significant safety concerns. About half of the participants who received the vaccine reported fatigue, muscle aches, joint pain and headache, after the second dose. Most adverse events resolve within 20 days. Severe illness (30 cases) was only in the placebo group, including 1 death. US phase 3 trial (COVE) is ongoing. A phase 2/3 trial in adolescents 12-17 years begun in December 2020 is expected to enroll 3,000 participants.

AZD-1222 (ChAdOx1 nCoV-19; Oxford University, AstraZeneca)

Results of an interim analysis of the phase 3 clinical trial in the United Kingdom, Brazil, and South Africa have been published [13]. One dosing regimen (n = 2741) showed vaccine efficacy of 90% when given as a half dose, followed by a full dose at least 1 month later. Another dosing regimen (n = 8895) showed 62% efficacy when given as 2 full doses at least 1 month apart. The combined analysis from both dosing regimens (N = 11,636) resulted in an average efficacy of 70.4%. There were 131 COVID-19 cases from 21 days after 1st dose and 10 hospitalisations, all in the placebo group (2 classified as severe and 1 death).

The phase 3 efficacy trial in the United States is ongoing. The Oxford/AstraZeneca vaccine was approved by the Medicines and Healthcare Regulatory Agency (MHRA) on December 30, 2020. The MHRA has now approved two full doses, spaced up to 12 weeks apart. It is hoped that this will allow as many people as possible to have some level of protection in a short time period. The JCVI advises that the second dose of the AstraZeneca vaccine may be given between 4 to 12 weeks following the first dose.

All three leading vaccines have probably beaten the goal of achieving 50% efficacy, and all seem to be safe, on the basis of the clinical-trial data so far. The Joint Committee of Vaccination and Immunisation (JCVI) has not advised a vaccine preference for any specific population.

Other vaccines

There are many other vaccines that are being tested and these include:

Ad26.COV2.S (Johnson & Johnson)

In a Phase 1/2a study, antibodies to SARS-CoV-2 observed after a single injection. 99% were positive for neutralising antibodies against SARS-CoV-2 at day 29 and strong T-cell responses and a T_H1 response were also noted[14].

NVX-CoV2373 (Novavax)

Phase 1 data in healthy adults showed that the adjuvant vaccine induced neutralisation titers that exceeded responses in convalescent serum from mostly symptomatic patients with COVID-19[15]. Phase 1/2 trials were initiated in May 2020. The phase 3 trial in the United Kingdom has completed enrollment of 15,000 participants, including more than 25% who were older than 65 years.

When will I be able to get a vaccine?

The rollout of the COVID-19 vaccine is based on age and clinical risk. The Joint Committee of Vaccination and Immunisation (JCVI) ranks priority groups according to risk, largely based on prevention of COVID-19-specific mortality[16]. Many people considered clinically extremely vulnerable (CEV) are in the oldest age groups.

The priority groups are ranked as follows:

1 Residents in a care home for older adults; staff working in care homes for older adults
2 Those 80 years of age and over; frontline health and social care workers
3 Those 75 years of age and over
4 Those 70 years of age and over, CEV individuals (not including pregnant women and those under 16 years of age)
5 Those 65 years of age and over
6 Adults aged 16-65 years who are in an at-risk group
7 Those 60 years of age and over
8 Those 55 years of age and over
9 Those 50 years of age and over

Should I receive the COVID-19 vaccine if I am on immunosuppressants?

The approved COVID-19 vaccines are recommended by the JCVI for immunosuppressed patients. This includes individuals receiving immunosuppressive or immunomodulating biological therapy including, but not limited to, anti-TNF, rituximab, and individuals treated with steroid-sparing agents such as cyclophosphamide and mycophenolate mofetil. This group also includes individuals treated with systemic steroids for more than a month at a dose equivalent to prednisolone at 20mg or more per day (any age).

These patients may have a diminished immune response to the vaccines. Given the level of risk seen in this group as a whole (clinically extremely vulnerable or CEV), this group should be offered the vaccine alongside those aged 70-74 years (priority group 4). CEV people are at high risk of severe illness from COVID-19 and are in a clinical risk group which should receive the vaccine. Any patients who change CEV status during the roll out of the programme should be called in in their appropriate age cohort, or in priority group 6[17].

Should I stop or pause my treatment to receive the COVID-19 vaccine?
There is currently no evidence to stop or pause your immunosuppressive treatment to receive the vaccine[18]. However, further guidance from the JCVI will be given so this advice can be updated. Vaccinations should preferably be given when the disease is in a quiet phase and it is also preferred to vaccinate before planned immunosuppression if feasible[19]. For patients receiving Rituximab, where clinically possible, COVID-19 vaccines should be given four weeks or more before the treatment.

Which vaccine should I receive?

The first one you are offered.

Both the Pfizer/BioNTech and AstraZeneca/Oxford vaccines aim to carry the message for the spike (S) protein to activate our immune cells and produce memory against future infection from SARS-CoV-2. The Pfizer/BioNTech vaccine contains Polyethylene Glycol (PEG). Known allergy to PEG is rare, but would be a contraindication to this vaccine. The AstraZeneca/Oxford vaccine does not contain PEG and will be a suitable alternative.

Are there any contraindications to having the vaccine?

The vaccine should be avoided in those who have had a previous systemic allergic reaction (including immediate-onset anaphylaxis) to a previous dose of the same COVID-19 vaccine or any component (excipient) of the COVID-19 vaccine. The excipients are available for review prior to receiving the vaccine.

Do I still need the vaccine if I have had COVID-19?

Yes. Experts recommend getting vaccinated even if you have had COVID-19 in the past. People who get COVID-19 do develop antibodies that likely provide some protection against getting infected again. But it is not known exactly how long antibodies last after a person recovers.

Do children need to get the COVID-19 vaccine?

COVID-19 vaccines are not routinely recommended for children and young people under 16 years of age currently. There are some exceptions, including those with neurological conditions[20]. There is limited data on safety and immunogenicity in children and young people as vaccine trials have only just begun. This group has a very low risk of COVID-19, severe disease or death compared to adults. One of the available vaccines in the United States can be given to people 16 years of age or older. The other can be given to people 18 or older. Eventually, younger children will be able to get a vaccine after the initial rollout phase and once experts have studied this more to make sure it is safe.

What if I am pregnant?

Although the available data do not indicate any safety concern or harm to pregnancy, there is insufficient evidence to recommend routine use of COVID-19 vaccines during pregnancy. Experts are also still studying the safety of the COVID-19 vaccine during pregnancy.

JCVI advises that, for women who are offered vaccination with the Pfizer-BioNTech or AstraZeneca COVID-19 vaccines, vaccination in pregnancy should be considered where the risk of exposure to SARS-CoV2 infection is high and cannot be avoided, or where the woman has underlying conditions that put them at very high risk of serious complications of COVID-19[19].

Can I breastfeed after receiving the vaccine?

Yes, you can. There is no known risk associated with giving non-live vaccines whilst breastfeeding. The JCVI advises that breastfeeding women may be offered vaccination with the Pfizer-BioNTech or AstraZeneca COVID-19 vaccines.

Will I need a booster after the initial 2 vaccine doses?

This is not recommended at the moment as further research is needed to know if it is needed and the timing of boosters has not yet been determined.

If I get the vaccine, can I stop social distancing and wearing a mask?

Even though vaccines work very well to prevent COVID-19, it is still possible to get the infection. It will also take some time to learn exactly how long immunity lasts after a person gets a vaccine. Experts also need to learn more about how many people are getting vaccinated and how this is affecting the spread of COVID-19. Until this is known, it is recommended that social distancing, hand washing and wearing a mask continues after being vaccinated.

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