COVID19 Vaccine Explainer and Hoaxbusting

Indian Scientists' Response to COVID19

Here, we have provided a condensed version of information on COVID vaccines currently in use anywhere in the globe. We have tabulated the information for easy comparison. India has arguably the most expansive vaccine roll out plan. Ministry of Health & Family Welfare had released a FAQ document, their answers to some of the questions on COVID19 vaccination in India. Similarly, the ICMR, on its website has information on COVID vaccine candidates. Government's press release (dated Jan 3, 2021) announced "restricted emergency approval" of vaccination in the country. However, there is crucial information on authorisation of vaccine candidates in India, as well as information on the efficacy of the various vaccine candidates that has been wanting in the official versions. Below the Table, we collate these questions and their answers based on information available in the public domain.

Vaccine Name	BNT162b2	mRNA-1273	Covishield	Covaxin	CoronaVac	Sputnik V	NVX-CoV2373	Janssen COVID-19 vaccine
Organization	Pfizer & BioNtech	Moderna	AstraZeneca & University of Oxford	Bharat Biotech & ICMR	Sinovac Biotech	Gamaleya Center	Novavax	Johnson & Johnson
Manufactured in	USA	USA	UK & India (Serum Institute)	India	China	Russia & India (Dr. Reddys's)	USA & India (Serum Institute)	USA
Vaccine Type	mRNA enclosed in lipid	mRNA enclosed in lipid	Chimpanzee adenovirus containing spike protein of sars-cov-2	Inactivated sars-cov-2 virus	Formalin inactivated sars-cov-2 virus with alum adjuvant	Human adenovirus containing sars-cov-2 gene	Full-length pre-fusion spike protein	Adenovirus containing sars-cov-2 spike-protein gene
Administration	Intramuscular injection	Intramuscular injection	Intramuscular injection	Intramuscular injection	Intramuscular injection	Intramuscular injection	Intramuscular injection	Intramuscular injection
Dosing strategy	2 doses, 21 days apart	2 doses, 28 days apart	2 doses, 4-6 weeks apart	2 doses, 28 days apart	2 doses, 2-4 weeks apart	2 doses, 21 days apart	2 doses, 21 days apart	Single dose
Dosing Volume	0.3ml - 0.3ml	0.5ml-0.5ml	0.5ml-0.5ml	0.5ml-0.5ml	0.5ml-0.5ml	Both doses are different (Ad26 in 1st dose and Ad5 in 2nd dose)	0.5ml-0.5ml 5 mcg (microgram) of protein and 50 mcg of adjuvant	0.5ml

Storage	-80ºC to -60ºC	-25°C to -15°C	2°C to 8°C	2°C to 8°C	2°C to 8°C	2°C to 8°C (freeze dried) -18°C (liquid)	2°C to 8°C	Two years at -20°C; at least three months at 2-8°C
Clinical Trials (CT) in India	NO	NO	YES	YES	NO	Yes, awaiting approval for phase 3	NO	NO
Approval status in India	Rejected as Pfizer refused to conduct bridging trials in India	Not applied	Approved	Approved	Not applied	Not applied	Not applied	Not applied
Phase 1	✓ published	✓ published	✓ published	✓ published	✓ published	✓ Published	✓ Published	✓ Published
Phase 2	✓	✓	✓ published	✓ Not peer-reviewed yet *	✓ published	✓Published	✓Published	✓Published
Phase 3	✓ published	✓ published	✓ published	In process	Un-published	✓ Published	In process	In process
Current phase 3 process	Follow up of phase 3 participants	Follow up of phase 3 participants	Follow up of phase 3 participants	Recruitment of phase 3 participants in process	Follow up of phase 3 participants	Follow up of phase 3 participants	Follow up of phase 3 participants	Follow up of phase 3 participants
Efficacy	95% published	94.1% published	70.42% Un-publishe	No data	~50% Un-publishe	91.6% Published	89.3% Un-published	66-85% Un-published

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Side Effects	injection site pain, fatigue, headache, muscle pain, chills, joint pain, fever, injection site swelling, injection site redness, nausea, malaise, and lymphadenopathy	pain at the injection site, fatigue, headache, myalgia, arthralgia, chills, nausea/vomiting, axillary swelling/tenderness, fever, swelling at the injection site, and erythema at the injection site.	Tenderness, pain, warmth, redness, itching, swelling or bruising where the injection is given Generally feeling unwell Feeling tired (fatigue) Chills or feeling feverish Headache Nausea, vomiting Joint pain or muscle ache A lump at the injection site Fever Flu-like symptoms, such as high temperature, sore	Pain, swelling, itching, fever, Malaise, weakness, rash, nausea/ vomiting	pain, redness, swelling,	Muscle ache, headache, dizziness, shivering	Not documented	Not documented

			throat, runny nose, cough and chills Feeling dizzy Decreased appetite Abdominal pain Enlarged lymph nodes Excessive sweating, itchy skin or rash					
Age	16 and above	18 and above	18 and above	12 and above	18 and above	18 and above	18 and above	18 and above
Available for use in India	NO	NO	Restricted emergency use	Restricted emergency use	NO	NO	NO	NO
Cost (per dose)	$20	$33	$3	$3	$10	$10	$16	$10
References	(Polack et al., 2020; Walsh et al., 2020)	(Anderson et al., 2020; Baden et al., 2020; Jackson et al., 2020)	(Folegatti et al., 2020; Ramasamy et al., 2020; Voysey et al., 2021)	(Ella et al. 2021) * Ella et al. *Medrxiv*	(Zhang et al., 2020)	(Logunov et al., 2020; Jones & Roy, 2021)	(Keech et al., 2020)	(Sadoff et al., 2021)

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- Emergency use authorisation (EUA) of Pfizer-BioNtech vaccine | FDA
- MODERNA- US FDA https://www.fda.gov/media/144637/download

Section 1: Unanswered questions related to authorization of COVID vaccines in India

1. **What are the different phases of vaccine approval under normal (non-pandemic) situation? What are the parameters to gauge success at each stage?**

A vaccine is a preparation that contains one or more pathogens in inactivated (also known as avirulent) form. Alternatively, the preparation may contain only some part of disease-causing organism or it may comprise artificial substance that mimics a pathogen.

The main purpose of any given vaccine is to generate immune response in the recipient that are sufficient enough to provide protection against a particular disease. This leads to priming of the recipient's immune system against the foreign pathogen. If this particular pathogen is encountered by the recipient in future, the recipient's immune system will be able to act more swiftly and effectively against the pathogen and hence protection is ensured in the recipient.

In general, accessibility to a new vaccine spans a period of 10-15 years, beginning from the discovery of a new vaccine candidate to the licensure of the vaccine formulation. The overall process of vaccine development is rigorous, involving careful study design and continuous monitoring throughout to efficiently determine the final vaccine formulation and analyse whether the vaccine is safe, tolerable and does not outweigh the benefits of protection. The various phases involved in the research and development of a vaccine are mentioned below:

1. Exploratory phase and pre-clinical studies

Aims:

- To identify a novel vaccine candidate
- To evaluate safety and potential to prevent the ‘disease in question’

Tested in: Animals like mouse, hamster, rabbit, rat, monkeys, etc. that mimic the targeted human disease. The testing involves ‘challenge experiments’ to analyse the level of protection by the vaccine candidate against a virus (or another pathogen).

Outcome: A suitable vaccine candidate is identified which is then taken forward to Phase I clinical trials in humans. The pre-clinical phase allows decision making for further development of vaccines. If the immune response elicited is insufficient, the vaccine candidate is abandoned.

Approval methodology: The vaccine candidate must not be toxic, should generate binding and neutralizing antibodies against the target pathogen. The tests include toxicity analysis, and immunoassays, like, ELISA, virus neutralization assays.

2. Phase I clinical trials

Aims:

- To evaluate whether the vaccine is safe for use in humans
- To confirm if it generates an immune response in the recipients
- To estimate the appropriate dosage and route of administration of the vaccine

Tested in: Small numbers of healthy adult volunteers, who are preferably enrolled and observed at a tertiary care hospital. The reason for such preference is to ensure immediate health care service, just in case any adverse reaction post-vaccination occurs.

Outcome: Vaccine safety, tolerability and dosage is identified.

Approval methodology: Antibodies and other parameters of immunity generated as a result of vaccine are assessed. The vaccine must not be toxic. It must be able to generate antibodies that bind and neutralize the pathogen, thereby exhibiting effective protection against the pathogen. Apart from this, T-cell immune responses are also assessed by highly sensitive and robust immunological techniques.

3. Phase II clinical trials

Aims:

- To further assess the immune responses generated by vaccine. This includes evaluation of types and magnitude of immune responses
- To determine the exact dose and immunization schedule

Tested in: Larger numbers (compared to Phase I) of volunteers having characteristics (like age, health conditions, etc.) similar to target population (people more likely to be affected by disease in question; for instance now, COVID19). In this phase, vaccines are administered in some of the volunteers. The non-recipients form the control (or placebo) group, who receive a shot of saline instead of the vaccine formulation.

Outcome: Comparative analysis of vaccine effects on recipients and non-recipients.. Efficacy end points and immunogenicity are determined.

Approval: Generation of sufficient levels of neutralizing antibodies against the target pathogen. Achievement of expected seroconversion rates (time period for antibody development).

4. Phase III clinical trials

Aims: To assess the efficacy and safety of the vaccine so as to progress towards registration and marketing of vaccine.
Tested in: Thousands of individuals representing the targeted population are enrolled. Similar to phase II, vaccine is administered in some, while others form the control group.

Outcome: This phase generates more conclusive data regarding the effects of vaccine in the targeted population. In other words, the vaccine efficacy and final formulation is determined based on the results of phase III trial.

Approval: The success of phase III trial is dependent on the vaccine efficacy. Vaccine efficacy is defined as the percent reduction in incidence (of an infection) among vaccinated individuals. It is calculated by the following formula:

(IU-IV/IU)*100= (1-IV/IU)*100 %=(1-RR)*100%

Where, IU-Incidence in placebo (=number who get disease amongst placebo / total number of placebo or control); IV-Incidence in vaccinated population (= number who get disease amongst vaccinated /total number given vaccine); RR-Relative Risk.

The results of all the clinical trials are carefully reviewed to evaluate the efficacy and safety of the vaccine. This follows application for regulatory and public health policy approvals and subsequent production and roll-out for public use.

5. Phase IV post marketing surveillance

Aims:

- To monitor adverse events; and
- To study long-term effects of the vaccine

Outcome: This enables determination of effectiveness of the vaccine in routine use setting. Since, this phase involves vaccine administration in larger numbers of individuals with varied clinical/health features than in the previous phases, the actual assessment of the vaccine-enabled protection is possible.
References:

- Key steps in vaccine development
- Guidelines on clinical evaluation of vaccines: regulatory expectations
- Vaccines & immunisation | WHO
- Public health activist Dinesh S. Thakur on efficacy data for CoviShield & Covaxin

2. **How is the vaccine development and approval process different in pandemic times?**

   Traditional vaccine development consists of a discovery phase, which include an exploratory phase and pre-clinical stage. In the exploratory phase vaccines are designed (time taken is in years), followed by preclinical experiments which include exploratory as well as formal preclinical experiments and toxicology studies as mentioned here.

   Please see previous question for phase trials in normal (non-pandemic) times.

   In the case of SARS-Cov2 vaccine development during COVID-19 pandemic, the discovery phase is in months because of knowledge gained from vaccine development in case of SARS-CoV, and MERS- CoV. During the clinical development phase, there has been overlap of phases 1, 2 and 3 clinical trials, and the overall clinical trials time is in months, followed by large scale production (large scale vaccine production) . This is followed by vaccine license application and approval (1-2 months). The vaccine is approved in a pandemic only if it is safe, efficacious and the benefits outweigh the risks, as mentioned here. Thus the traditional time of vaccine development during the pandemic is reduced from 15 years to 10-18 months.

3. **What does emergency use authorization (EUA) mean and how is EUA different from "approval" for vaccine candidates ?**

   In the USA, during an emergency, like a pandemic, it may not be possible to have all the evidence that the Food and Drug Administration (FDA) would usually have before approving a vaccine. When there is a declared emergency, such as during a pandemic, the FDA can make a judgment that it is worth releasing a vaccine for broader use even without all the evidence that would fully establish its effectiveness and safety. If there is evidence that strongly suggests that patients have benefited from a treatment or test, the agency can issue an EUA to make it available. EUA is different from "approval", in that it authorizes FDA to facilitate availability of an unapproved product, or an unapproved use of an approved product, during a declared state of emergency.

4. **What does "restricted use" mean, since approval for COVID vaccines in India has been granted as "*restricted use* in emergency situation"?**

   This concern has also been raised in a recent Lancet report. There is no definition provided by the Government, but in a press conference DCGI explained that, "India's first indigenous vaccine against COVID-19 has been approved for restricted use.

This means it should not be given to everyone. Only those in extreme need of it based on his/her medical condition will be given the vaccine." Later on, it was noted that children, pregnant women, the elderly, or persons with co-morbidities should not be given the vaccine.

5. **In the Indian regulatory system, is there a provision for EUA?**
   According to news reports published in Hindustan times, Times of india, Press release on EUA for Serum institute, Bharath Biotech vaccines, along approval for Cadila Healthcare Vaccine Phase 3 trials, there is no mention of the phrase 'Emergency Use Approval' or EUA in the Indian regulatory system. However, in the New Drugs and Clinical Trials Rules 2019, in the Second Schedule under 2) A) a), there is a provision for granting accelerated approval in special situations ("Accelerated approval process may be allowed to a new drug for a disease or condition, taking into account its severity, rarity, or prevalence and the availability or lack of alternative treatments, provided that there is a prima facie case of the product being of meaningful therapeutic benefit over the existing treatment").

Section 2: Basic questions on vaccines: efficacy and safety

1. **What is a vaccine and how does it prevent/reduce disease for an individual, and for a population?**
   When a person is infected by a pathogen for the first time, their immune system gradually learns to recognise it, and then potently and specifically neutralise it. But this process takes one to two weeks, in which time, the person suffers from the disease, and produces many copies of the pathogen, potentially infecting other people. A vaccine is a non-infectious, inactivated version of a pathogen, or part of a pathogen can be injected into a person's body to train their immune system to recognise the wild, harmful pathogen and rapidly neutralise it. This ability to quickly recognise and neutralise future infections or *immune memory* prevents severe disease in the individual, and also reduces chances of spreading the disease to others. As more and more people in a population have an immune memory to quickly fight off a particular infection, the chances of it spreading get lower and lower. A population reaches *herd immunity* for a disease when each infected person spreads the disease to less than one other person, on average. The chances of disease spread depend on biological factors such as the pathogen's virulence but also societal factors, such as physical distancing measures. Vaccinating as many people in a population as possible is one important way to reduce infection spread. But it is just as important to maintain physical distancing and other measures to reduce spread, especially to end the COVID19 pandemic.

2. **What is "efficacy" for a vaccine, and why do we need phase 3 trials to estimate it?**

The efficacy of a vaccine is the percentage reduction in disease incidence in a vaccinated group, as compared to a control group under optimal conditions such as a randomized controlled clinical trial.

As outlined in Qs. 1 of the previous section, the objective of trials at phase 1 and 2 is to determine side effects, safety, dosage, and immunogenicity. It is only during the phase 3 trial, where it can be calculated how effective a vaccine candidate is, as there is a placebo/control arm that consists of volunteers to whom the test vaccine is not given, and the test arm consisting of volunteers to whom the vaccine is given. The disease incidence can be calculated in both groups and compared to calculate efficacy of the vaccine. Such a trial is also needed to determine efficacy in different target populations.

If the efficacy of a vaccine is even 50%, it means 50% fewer or half as many vaccinated individuals got severe disease, as compared to people given placebo or in the control arm. So even if the efficacy of a vaccine is lower than 90%, as reported for some of the most efficacious COVID19 vaccines (Moderna and Pfizer), there is still significant benefit to the population from individuals getting vaccinated.

Before being authorised for general use, or even for emergency authorisation, a vaccine candidate must first pass phase 3 clinical trials (see note on approval process above). The vaccine candidate needs to be administered to tens of thousands of volunteers, to make absolutely sure it is safe. Also, these volunteers then need to be tracked for some months, to make sure they are protected from getting infected in real world conditions (see note above on phases of clinical trials).

Around the world, and also in India, vaccine candidates have been authorised for emergency use after clearing phase 3 clinical trials. Such clearance is typically accompanied by publication and release of phase 3 trial data. Concerns have even been raised over emergency use approval for COVID vaccines. Bharat Biotech's Covaxin candidate has been authorised for emergency use while simultaneously being in Phase 3 clinical trials. This is inconsistent with established policy on vaccine candidate approval (Hindu article, see note on approval above).

3. **How is vaccine safety estimated and how safe are the COVID19 vaccines? (SK)**

Covishield and Covaxin both have no safety concerns as they have done well in phase 1 trials. Immunogenicity is also clear from phase 2 trials (section above on clinical trial phases describes how safety is assessed). ChAdOx1 nCov-19 (the vaccine from Oxford University-AstraZeneca which is manufactured as Covishield by Serum Institute India) was subjected to randomised phase1 clinical trials in UK. 1077 participants took part of which 537 were given the Covid vaccine.Here a small set of 56 participants who got the vaccine also received paracetamol as part of the study. Fatigue and headache were the most commonly reported symptoms. Other adverse reaction included muscle ache, malaise, chills and feeling feverish. The severity and intensity of local and systemic reactions

was highest on day 1 after vaccination. ChAdOx1 nCoV-19 was safe, tolerated, and immunogenic, while reactogenicity was reduced with paracetamol. Covaxin underwent randomised phase 1 clinical trials involving 375 participants of whom 300 were given the vaccine andec 75 the placebo. It was found that the most common adverse event was pain at the injection site, followed by headache, fatigue, and fever. The overall incidence of solicited local and systemic adverse events in the study was 14–21% in the vaccine treated cases.

Reported side effects of the vaccines

Common side effects include redness, tenderness, pain at the site of injection, the feeling of being sick/unwell, fatigue, headache, chills or feeling feverish, nausea, muscle pain/ body pain/joint pain, other flu-like symptoms, including runny nose. Uncommon side effects are dizziness, decreased appetite, abdominal pain, excessive sweating, itchy skin. Any untoward medical event after vaccination is considered an Adverse Event (AE) and must be reported to the concerned officials. If the AE is related to the vaccine it is called as an Adverse Drug Reaction (ADR). A cross-sectional online survey was done involving 5396 people that included questions pertaining to the immediate post vaccination experience in India. As was reported “Tiredness, myalgia and fever were most commonly reported. These symptoms were consistent with an immune response commonly associated with vaccines, and correlated with the findings from previously published phase 2/3 trials. In 90% cases, the symptoms were either milder than expected or meeting the expectation of the vaccine recipient. No serious events were reported. Symptoms were more common among younger individuals. There was no difference in symptoms among those who had a past history of COVID-19.”

Useful links:

Maintaining Safety with SARS-CoV-2 Vaccines | NEJM - nejm.org
Product characteristics | Covaxin | CDSCO
Product characteristics |Covishield | CDSCO

4. **How effective are current vaccines against new COVID-19 virus variants?**

Over time, viruses naturally accumulate changes in their genetic sequence. The more they multiply in number, the higher the chances of mutations. While most changes (mutations) are of little to no consequence, sometimes the virus acquires a mutation that gives it an advantage over its original form (variant), making it more transmissible or more infectious. The chances of new virus variants emerging are higher if more people are infected, as it is multiplying more. The SARS-CoV-2 virus uses its Spike protein to enter the host body by binding to a specific protein on human cells called the ACE2 receptor. Thus, mutations in the gene for the

Spike protein can potentially facilitate better affinity or binding and enable easier entry into the host cell, as was the case with the D614G mutation (which has been the globally prevalent SARS-CoV-2 variant in circulation for the majority of the year 2020).

Mutations that enhance viral fitness need to be identified and monitored to check if the available Covid-19 vaccines are effective in raising an immune response in the human host. The currently approved vaccines raise a host immune response against multiple parts of the virus. So, even if one of the parts of the virus changes due to a new mutation, the vaccine will identify the other parts. This decreases the chances of newer variants escaping the vaccine. Even as the vaccination process has now been initiated globally, the current vaccines need to be evaluated for their potential against the new viral mutations as they arise.

Variants that are of the greatest concern currently include those that have changes (mutations) in the Spike that causes immune escape or the Spike mutations N501Y (located in the viral receptor binding site for cell entry and increasing binding to the human receptor) and/or E484K (reduced susceptibility to neutralization by antibodies), shared by variants that were first identified in the United Kingdom, South Africa and Brazil (called as 501Y.V1, 501Y.V2 and 501Y.V3 respectively).

A key factor with the new mRNA based vaccines (Pfizer's and Moderna's) is that they appear to produce a heightened immune response, such that a drop in the level of neutralization antibody detected with these variants may not be highly worrisome, and they may still provide effective immunity. Pfizer's vaccine shows reduction in neutralization against engineered mutations found in variants of concern, however the degree of reduction is variable in serum from different individuals and is not very huge. Moderna has also demonstrated reduced but still significant neutralization against the variants following mRNA-1273 vaccination. They are however looking to develop booster shots and/or altered vaccines for emerging variants; the mRNA vaccines may probably be the fastest to tweak and redesign (possibly within a few weeks).

The vaccines by Johnson & Johnson and Novavax may also be less effective against some of the new variants, especially the variant identified in South Africa, although new data are being released at a rapid pace. Novavax released data from clinical trials showing that its experimental vaccine, designed to combat the original virus, was about 89% effective against the current COVID-19 virus strain, 85% effective against the variant identified in the United Kingdom, but less than 50% effective against the one identified in South Africa. Bharat Biotech has also released information showing that their vaccine works against the variant seen in the UK - still in a clinical trial mode though approved in India, the vaccine was found to be fully effective against the N501Y mutation. The Serum Institute of India, currently offering the Oxford-AstraZeneca vaccine that may have lower efficacy with emerging variants, is planning to conduct trials to bring a second vaccine called Covovax (which is based on Novavax) that may be more effective against them; adenovirus vector based vaccines are also relatively easy to update, though they may take longer than the mRNA based ones.

Evidence shows that **most of the vaccines will confer some degree of protection** from the currently evolved variants, though the combination of mutations carried in a particular variant, its prevalence in a region and the host immune response, will ultimately decide the final efficacy of any vaccine.

The following studies document some of the tests conducted by the various companies for vaccine efficacy against the new variants:

Pfizer - BNT162b2 vaccine

A. Impact of SARS-CoV-2 B.1.1.7 Spike variant on neutralisation potency of sera from individuals vaccinated with Pfizer vaccine BNT162b2 (pre-print, not peer reviewed)
B. Neutralization of N501Y mutant SARS-CoV-2 by BNT162b2 vaccine-elicited sera (pre-print, not peer reviewed)
C. Neutralization of SARS-CoV-2 spike 69/70 deletion, E484K and N501Y variants by BNT162b2 vaccine-elicited sera

Moderna - mRNA-1273 vaccine

A. Moderna COVID-19 Vaccine Retains Neutralizing Activity Against Emerging Variants First Identified in the UK and the Republic of South Africa
B. mRNA-1273 vaccine induces neutralizing antibodies against spike mutants from global SARS-CoV-2 variants (pre-print, not peer reviewed)

Novavax - NVX-CoV2373

A. Novavax offers first evidence that COVID vaccines protect people against variants
B. SARS-CoV-2 variant B.1.1.7 is susceptible to neutralizing antibodies elicited by ancestral Spike vaccines (pre-print, not peer reviewed)

Bharat Biotech - Covaxin

A. Neutralization of UK-variant VUI-202012/01 with COVAXIN vaccinated human serum (pre-print, not peer reviewed)

Oxford/Astra-Zeneca - AZD1222

A. Efficacy of ChAdOx1 nCoV-19 (AZD1222) Vaccine Against SARS-CoV-2 VOC 202012/01 (B.1.1.7)

5. Is it worth taking the vaccines now if new variants are emerging?

The best way to prevent further mutations from arising and accumulating is to avoid giving the virus a chance to replicate, i.e. reducing the number of infected. This can be safely achieved by vaccinations, hence the rise of worrying mutations should not be a deterrent for vaccination programs. A possible lowered efficacy to new variants will still provide some degree of protection against the disease and also help stop viral transmission in the population. A recent pre-print has shown that the N501Y mutation in the variant seen in the UK can be neutralised by both convalescent sera (serum from an individual who has overcome a recent COVID-19 infection) as well as post-vaccination serum (serum from a vaccinated individual who has mounted an immune response to the COVID-19 vaccine).

Of greater concern is the so-called South African variant that escapes convalescent serum antibodies. It also reduces neutralizing abilities (~6 fold) of mRNA vaccine evoked serum antibodies, but significant neutralization activity still remains. South Africa has paused the roll-out of the AstraZeneca vaccine, following concerns regarding poor efficacy against the variant identified there. Recent work, however, highlights the importance of mRNA vaccines even against such emerging variants. The WHO has released a statement on 8th February, 2021 regarding vaccine efficacy concerns in the light of immune escape variants, affirming that "we need to adjust to the SARS-CoV-2 viral evolution, including potentially providing future booster shots and adapted vaccines, if found to be scientifically necessary". However, the statement also highlights the **need to prioritize the vaccination of high-risk groups everywhere in order to ensure maximum global protection against new strains and minimize the risk of transmission.**

Useful links:

SARS-CoV-2 501Y.V2 escapes neutralization by South African COVID-19 donor plasma

Comprehensive mapping of mutations to the SARS-CoV-2 receptor-binding domain that affect recognition by polyclonal human serum antibodies

6. Does being vaccinated prevent people from infecting others?

The COVID19 virus infects the wet, soft, mucosal tissues first, as it enters the body through the nose, mouth or eyes. At first, the virus replicates in the upper passages of the nose and throat, not causing severe disease for a few days. The infected person

releases these replicated viruses into the air around them, by coughing, speaking or even just breathing, potentially infecting others around them. Only over a period of days, in a second phase, does the virus then spread into the lungs, where severe disease might be caused. So viral replication and spread happens early on and in a different part of the body from severe disease.

Many of the vaccines that have been authorised around the world have released phase 3 clinical trial data; but these have only been tested for efficacy at preventing severe disease (see also study results for Moderna, Pfizer, AstraZeneca vaccines) ie. we know they prevent the second phase of the infection, in the lungs. But they could still cause the first phase of infection, in the upper respiratory mucosa. In fact, we know that vaccines injected into the arm make the body produce a type of antibodies (IgGs) that circulate in the blood, and are effective at protecting the lungs. But they do not reach mucous tissue. For protection there, we would need another class of antibodies (IgA), which are elicited by different, nasal vaccines. We know that when a person gets infected with COVID19, their body's first defensive response is IgA production in mucosal tissues, followed later on by IgG in the blood. In fact, among people vaccinated with the Oxford - AstraZeneca vaccine (Covishield in India), a study found 67% fewer people had virus in nasal swabs as opposed to un-vaccinated people. But even among the vaccinated, people still produced the virus and could potentially spread the infection.

The good news is that the new COVID19 vaccine injections we will get in our arms will give us protection from severe disease in our lungs, potentially for years. But we might still get mild or symptom-free infections in the mucous tissue in our noses and throats and spread the virus to others. So even after getting vaccinated, we need to continue to wear masks and physically distance until population infection numbers come down.