



Commentary

## **COVID vaccination: Myths and hesitancy, and impact on vaccine drive worldwide**

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### **Introduction**

The world is still grappling with the COVID-19 pandemic, which began sometime in December 2019. The World Health Organization (WHO) reports that, as of May 10, 2021, there have been 157,897,763 cases and 3,287,082 deaths arising from COVID-19 globally (WHO, 2021b). Virtually all the countries of the world have had their share of respiratory disease, with the United States, India, Brazil, France, and Russia being the worst hit in terms of number of cases. United States, Brazil, Mexico, India, and the United Kingdom have recorded deaths in hundreds of thousands (WHO, 2020). India, for example, with the onset of the second wave, has crossed all the countries in hitting the maximum number of daily cases and deaths. The current worldwide estimate of mortality percentage is 3.4% as per WHO data (Worldometer, 2021); however, the

mortality rate is quite different among different countries. Many countries are currently facing the 3rd wave, including United Kingdom, France, Italy, Spain, etc. (Baibhawi, 2021; BBC News, 2021a).

To contain the spread of the pandemic from the mid-2020, all the countries primarily focused on developing the COVID-19 vaccine. Vaccine development was a challenge because the virus is rapidly mutating. Vaccine trials took much time, considering the urgency of the need. Previously the fastest vaccine developed was Mumps' vaccine within four years; COVID-19 vaccine development however took just about a year (Cohen, 2020). For COVID Vaccines 'emergency use listing' was issued by WHO in February 2021 (Jeong, 2021).

Currently, major vaccines that have been developed and approved worldwide are included in Table 1 (BBC News, 2021c; WHO, 2021a). The mRNA-based vaccines have been proven to have lesser side effects and more efficacious, but their production and storage can be expensive. Biosafety is not an issue with mRNA vaccines because no viral culture/ cultivation is required (Verga, 2021).

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Table 1. Major COVID-19 vaccines approved for usage around different countries

Name of vaccine	Country of origin	Description of vaccine	Dose and recommendation	Remarks
SPUTNIK V	Russia	A vector virus to carry the Spike-protein of COVID-19 virus	Complete vaccination includes two shots 21 days apart	Adenovirus serotype 26 is used for first dose, and serotype five is used for the second dose
Pfizer	American corporation called Pfizer in New York and BioNTech, a German biotechnology company	Messenger RNA of the COVID-19 virus	includes two doses, three weeks apart, that can be administered in people 16 years or above	The demerit of this vaccine is that it needs to be stored at a temperature lower than -60°C (CDC, 2021c).
Moderna	United States	messenger RNA (m-RNA-1273) of the COVID-19 virus	Two shots of the vaccine are given four weeks apart and approved for 18 years	suffered a setback due to reported side effects in few volunteers of phase1 trial
Johnson & Johnson	Janssen Vaccines in Leiden, Netherlands,	Modified cold virus vaccine	the only single shot is needed, approved for people of age more than 18 years.	Rare but severe blood clot reported
COVAXIN	Bharat Biotech in collaboration with the ICMR -NIV in India (Bharatbiotech, 2021).	An inactivated vaccine and is made of killed coronaviruses	Two intramuscular doses 28 days apart	Recently trials have been started in Indian children
Oxford-Astra Zeneca	United Kingdom	a recombinant vaccine made using aChAdOx1 as a vector that carries S-gene of SARS-CoV-2 virus	Two doses of vaccine were given 8 to 12 weeks apart. The minimum gap recommended currently is 12 weeks.	Recent reports of blood clots in young people have led to withholding in trials
COVISHIELD - Oxford – Astra Zeneca	Oxford – Astra Zeneca vaccine produced locally by the Serum Institute of India.	ChAdOx1 nCoV-19 Corona Virus Vaccine		Thrombosis with Thrombocytopenia Syndrome (TTS), involving unusual and severe blood clotting events associated with

ICMR-Indian Council of Medical Research; NIV - National Institute of Virology

CDC - Centre for Disease Control and Prevention

COVAXIN is an inactivated vaccine and is made of killed corona viruses developed by Bharat Biotech in collaboration with the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV) in India (Bharatbiotech, 2021). Whole-Virion is developed in the Vero Cell line and then inactivated by treating with beta-propiolactone (Corum and Zimmer, 2021).

Oxford - Astra Zeneca vaccine is made from a weakened version of adenovirus from chimpanzee ChAdOx1 which has lost its capacity to replicate. This virus acts as a vector for carrying the gene coding for the Spike glycoprotein of the SARS-CoV-2 virus. Following administration, the S-glycoprotein of SARS-CoV-2 gets expressed locally, stimulating neutralizing antibody and cellular immune responses. (Serum Institute of India, 2021). COVISHIELD is Oxford - Astra Zeneca vaccine manufactured in India. Recently WHO has recommended an increase in the gap between the two doses of this vaccine (Serum Institute of India, 2021). A considerable number of healthcare workers have already received the vaccine doses at the 4-week gap. Evidence needs to be generated about what to be done for such individuals. Need of booster dose is needed or not.

Novavax, a US based firm has developed a vaccine NVX-CoV2373, which is a protein-based COVID-19 vaccine candidate. It contains prefusion spike protein produced by recombinant nanoparticle technology and saponin-based Matrix-M™ adjuvant. It has been tested on about 30000 participants has exhibited a 90.4 % overall efficacy in Phase-3 clinical trials. This is a new development among COVID-19 vaccines and is the first vaccine showing efficacy against the UK and South Africa Variants of COVID-19. Serum Institute of India hopes to introduce US firm Novavax's Indian version of the Covid-19 vaccine - 'Covovax'(ANI, 2021).

Composition, development, and trial results can convince general people. The efficacy of different vaccines is an essential issue among people. All these vaccines have different efficacies according to current knowledge - Covishield (76%), Covaxin (close to 100% for severe infection), Sputnik (91.4%), Moderna (95%), Pfizer (95%), Johnson & Johnson (66%)(BBC News, 2021c; Jeong, 2021; Terry, 2021).

Recently, many countries have started vaccinating the pediatric population against COVID-19. Pfizer and Moderna vaccines are being administered to children in the western world. In India, Covaxin is on trial in the pediatric population in AIIMS Delhi. ZyCov-D is the second indigenous vaccine to be tried on children. The Covovax trial has been planned to start by July (PTI, 2021; Sen, 2021; Yengkhom et al., 2021).

### Vaccine hesitancy and myths

Vaccines have in history saved many lives. They work by training and preparing the body's immune system by recognizing and fighting off their target's micro-organisms. Vaccines are considered critical in fighting the spread and devastations caused by the COVID-19 pandemic. However, this is not the first time vaccines are greeted with ambivalence or outright refusal by sections of the population, both in the developed and developing worlds.

Vaccine hesitancy according to the WHO Strategic Advisory Group of Experts (SAGE) refers to "a delay in acceptance or refusal of vaccination despite availability of vaccination services" (MacDonald, 2015). It is said to be affected by three factors: confidence, complacency, and convenience, as per the 3Cs model. Confidence includes the effectiveness and safety of vaccines, reliability and competence of the healthcare system in providing the vaccine, and

motivations of the policy-makers who decide on the needed vaccine. Vaccination complacency exists when the perceived risks of the disease in question are low, and vaccination is not deemed a necessary preventive measure. This happens, for example, after successful vaccination outcomes in a population. Paradoxically, due to the decrease occurrence of the disease in question due to immunization against it, people consider vaccines a more significant risk than the disease. Vaccination convenience may include different factors like availability, affordability, geographical accessibility, ability to understand the appeal for the immunization services (Mac Donald, 2015). Vaccine refusers can be driven by their religious or philosophical beliefs as well (Miller, 2015). Vaccine hesitancy was cited as one of the top ten threats to global health in 2019 (WHO, 2020b).

In the earliest days of vaccine development in England, compulsory vaccination against smallpox was met with stiff opposition, especially by the working class and the poor (Callendar, 2016). Similarly, in 1902 (Boston, Massachusetts, United States), the State filed a lawsuit against one Mr. Jacobson, who had refused vaccination because such a directive contravened his rights to decide what was best for his body (Callendar, 2016; Schwartz, 2012). In more recent times, people have been reluctant to receive vaccination against Measles (in Canada, Europe, and the United States) and polio (in Nigeria). However, the refusal of the respective vaccine has not been without its own consequences; they have made many vulnerable to diseases and led to outbreaks, which otherwise could have been prevented (Afolabi & Ilesanmi, 2021; Callendar, 2016).

As the cliché goes, ‘there can be no smoke

without fire’, vaccine hesitancy is usually underlined by different beliefs and arguments. Many of these beliefs are the products of ignorance and mere irrationality, whereas others may be based on reasonable distrust of the government and genuine concerns about human safety (Arnold-Forster and Gainty, 2020). In the case of the smallpox vaccine mentioned earlier, the opposition was primarily informed by the (quite understandable) perception of the less privileged and working-class that the compulsory vaccination directive (and the attendant consequences of non-compliance) was a disguised attempt by the government at subjugating the already marginalized groups (Arnold-Forster and Gainty, 2020; Schwartz, 2012). Moreover, given that governments and scientists had many times been found culpable in unethical conduct of human subject's research (for example, the notorious Tuskegee Syphilis study), some fear about vaccines is natural among the common people (Arnold-Forster and Gainty, 2020). Vaccine refusals have also been informed by more radical and unfounded beliefs such as Measles, Mumps, and Rubella (MMR) vaccine leading to childhood autism and irritable bowel syndrome- in the United States, Canada, and Europe (Callender, 2016; Schwartz, 2012); and polio vaccine leading to infertility in Northern Nigeria, especially (Afolabi and Ilesanmi, 2021). According to Centre for Disease Control and Prevention (CDC), medical and scientific evidence suggest the benefits of vaccines far outweigh the risks (CDC, 2020). Table 2 enlists some of the controversies related to a safety concern encountered in the past and measures taken to safeguard the recipients. We can always learn from our past experiences (CDC, 2020).

Table 2. Vaccine controversies in the past and remedies

Vaccines Controversies	Scientific investigations and Measures taken
Guillain Barré Syndrome (GBS) following vaccination with a swine flu vaccine	Following a thorough scientific study, the IOM decided that those who got the 1976 swine influenza vaccine had a higher risk of acquiring GBS, albeit the reason for this could not be determined. The CDC evaluates the safety of seasonal and pandemic flu vaccines regularly, and any potential safety issues are considered by the ACIP.
Hepatitis B vaccination might be linked with multiple sclerosis (MS)	IOM committee found no such link.
RotaShield vaccine, some Infants developed intussusception	The results of the investigations by CDC showed that RotaShield vaccine caused intussusception in some healthy infants younger than 12 months of age, who usually have low risk. ACIP withdrew its recommendation. The vaccine was withdrawn from the market
Meningococcal vaccine Menactra causing GBS	Two studies including more than 2 million adolescents concluded no such relation exists.
Haemophilus influenzae type b vaccine recall	Hib vaccine was withdrawn due to concerns about potential contamination with bacteria called <i>B. cereus</i> . No such contamination was found after thorough investigation.
H1N1 influenza vaccine and Narcolepsy	CDC scientists analyzed and published vaccine safety data on adjuvanted pH1N1 vaccines (arenaprix -AS03, Focetria -MF59, and Pandemrix -AS03) from 10 global study sites. No such associations were detected.

IOM- Institute of Medicine; ACIP- Advisory Committee on Immunization Practices

### COVID-19 vaccine hesitancy and myths

As mentioned earlier, vaccine refusal is a phenomenon that predates the COVID-19 era. Never the less, one question we may want to ask is, what peculiar reasons, in the case of COVID-19, underline vaccine refusal? The existence and origin of the corona virus disease remain a subject of debate in some quarters. Many still believe that COVID-19 is a sham, and even among those convinced of its existence, some are convinced it is a ‘manufactured’ disease (Oyetunji et al., 2021). Therefore, these beliefs

about the origin and legitimacy of the disease outbreak are expected to lead to a negative disposition towards the COVID-19 vaccine. At the base of all these are conspiracy theories, which are being propagated via social media by public figures, including religious leaders and politicians. Some of the issue's peculiar to the COVID-19 vaccine hesitancy are highlighted below:

#### Tanzania: Skepticism and political solidarity

According to the British Broadcasting Corporation (BBC), the President of

Tanzania, John Magufuli, who declared his country COVID-19-free in June of 2020 (even when there was evidence suggesting the contrary) has made reports, implying skepticism about the vaccine developers, as he asks them not to use his countrymen as 'guinea pigs' (BBC News, 2021b).

### **Conspiracy theories**

According to the South African Medical Research Council (SAMRC), big pharmaceutical companies have been accused of creating the virus to make a fortune from the vaccine, which they had developed beforehand (SAMRC, 2021). Also, there seems to have a curious competition amongst the companies, apparently due to the economic gains involved (Money Show, 2020). There are also concerns that the COVID-19 vaccine is a tool by Bill Gates to execute a perennial population control plan by implanting microchips in the COVID-19 vaccine, which will then be used to kill Africans (SAMRC, 2021).

### **Questionable safety**

As earlier stated, some are genuinely concerned about the safety of the COVID-19 vaccines for human use, especially as, in the opinion of many, the vaccine development process was hurried. Consequently, as the CDC reports, many have expressed concerns about the vaccine leading to infertility, alteration of DNA, or even risk of COVID-19 infection (CDC, 2021a, 2021b).

### **Side effects**

Most vaccines' common side effects include fever, muscle aches, fatigue, headache, chills, muscle pain, and injection site pain. Side-effects are more pronounced, especially after the second dose. 'COVID arm' is a red, itchy, swollen, or painful rash at the injection site

and is not contraindicated for the 2nd shot. Severe allergic reactions-also known as anaphylaxis-are not very common but are major concerns that must be monitored. Epinephrine injection is administered in a hospital setup for treating patients with these reactions. In case of a severe allergic reaction after getting the first shot of a COVID-19 vaccine, CDC recommends avoiding the second shot of that vaccine (CDC, 2021b). Evidence of severe side effects like lymphadenopathy, acute myocardial infarction, encephalitis, nerve involvement, etc., are increasing the apprehension (CDC, 2021c).

There could be possible side effects of the vaccines in the long run, as feared in previously used vaccines for other diseases. Thus, adequate trials and studies should be done to eliminate any such fear related to COVID-19 vaccines.

### **Trials**

Vaccines have been developed in a brief period. Their efficacy and side effects, in the long run, are questionable, as mentioned earlier. Trials were conducted rapidly and taking a smaller number of participants, and vaccines were also approved for administration into the adult population on an emergency basis. WHO issued an Emergency Use Listing (EULs) procedure to streamline how new or unlicensed products can be used during public health emergencies (WHO, 2020a).

### **Perceived need for a vaccine**

Mortality related to COVID-19 was earlier predicted to be 1-2%. Most of the patients recover. So, the general notion was that if a person is vaccinated, they might not really be getting any added advantage. Even after receiving a total dose of vaccines, many individuals have contracted the disease.

Previous ICMR survey showed that a more significant chunk of the population in India has already developed antibodies. It was hoped that vaccines would provide at least some protection for newer strains, which appears to be not the case in currently used vaccines worldwide. Currently, trials have been started on the pediatric population in India. With the dilemma about the prediction of the third wave of COVID-19, and all the controversies around vaccination, people are not sure about the requirement and safety of the vaccination to their kids.

### Political battle

The vaccines have become an issue for political battles among leaders. Cost of vaccination is high, especially for developing countries. Investing so much in the development of vaccines has become more of a concern for many countries in the current economic State.

### Steps being taken to promote the vaccine drive

- ◆ Free vaccines are being provided to the public by certain governments world wide.
- ◆ Vaccine campaigns are being run on a war scale to cover as much population as possible within the shortest possible time. Periodic updates are released on government sites, indicating the rapidity with which the vaccines are being administered.
- ◆ The economy of the country is majorly impacted by the vaccine, storage, transport, registration, administration, etc. all steps need infrastructure and a huge workforce, which is difficult to manage amidst the current pandemic scenario. The international economy is also impacted by purchasing vaccines from other countries. Large-scale

planning and implementation are needed and are being done at national and international levels. Stake holders are working on decreasing the financial impact of these vaccination drives in various nations.

### What do we need to do for the vaccine to be more acceptable to the general public?

- ◆ More efficient trials including more study populations will help in relatively increased generalizability and acceptance. More robust evidence about vaccine safety and efficacy needs to be generated.
- ◆ Head-to-head trials between different vaccines need to be done. For example, the Pfizer vaccine vs. the Astra Zeneca vaccine can be compared. The same comparison can be made between other vaccine companies.
- ◆ Identifying demographic groups that are more vulnerable to believing conspiracy theories regarding the COVID-19 vaccine and providing targeted behavioral change communication interventions would be very useful for busting the myths around the vaccine, there by increasing its acceptability.
- ◆ Public health authorities should embark on aggressive orientation and education interventions both on social and traditional media to tackle unfounded and misleading information that may prevent the populace's uptake of the COVID-19 vaccine.
- ◆ Queries of the general public regarding COVID-19 vaccine such as safety for children, whether protective against newer variants, precautions after vaccination, age and co-morbidity-related queries regarding vaccination, advantages of getting vaccinated, etc., should be well addressed, so that even a layman is well informed (WHO, 2020a).

## Conclusion

Even though polls have shown that globally, those who would refuse to take the COVID-19 vaccine are in the minority, the controversy surrounding the vaccine remains a significant threat to the fight against the pandemic. Subsequent in-depth research is essential for generating more evidence regarding long-term safety concerns of COVID-19 vaccines.

Questions regarding COVID-19 vaccine safety in long run need to be answered for increasing acceptance among general public. Other queries like - What is the vaccine efficacy against newer variants? Should vaccine be mandatory for individuals already infected with COVID-19? What is the risk, if such individuals receive a vaccine? Should antibody titer be done before administration of the vaccine? Does a suitable antibody titer negate the need for vaccination? etc. should be addressed and made more clarified for improving acceptance of the COVID-19.

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