

# SARS-CoV-19: Vaccine Efficacy and Administration of the vaccine for all its variants

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## Abstract

*The efficacy of different designed drug for SARS-CoV-2 has been much of debate from the approval and till date after roll out. The data released from WHO, CDC, PHE and ICMR is used to analysis and compare the effectiveness of the UK and Indian made vaccine. The mentioned vaccine differs in raw material and fall under different category in preparation. The immune response of various vaccines over the mutant strains was assessed from the data of public domain. Attempt was made to correlate the effectiveness, mechanism of triggering antibodies and age factor for vaccination based on the vaccine type. The better effectiveness of certain vaccines like Covaxin, Pfizer and AstraZeneca (Covidshield) and the administration of vaccination differences with age factor of over approved vaccines asserted inductively.*

**Keywords:** Corona virus, Variants, Vaccine, Effectiveness, Age factor, Immunization.

## Introduction

The novel human corona virus which has been labeled as SARS-CoV-2 was firstly transpired in late 2019 in Wuhan, China causing respiratory disease called COVID-19. This virus has roll out swiftly around the globe. The worldwide threat of contagious infection, corona virus infectious disease (COVID-19) pandemic globally is related with "severe acute respiratory syndrome" majority of the world population is suffering from this SARS-CoV-2 virus since December 2019.

Corona viruses are a group of associated RNA viruses is a source for respiratory span infections that can lead from mild to fatal. Mild illnesses comprise of, the common cold (which is also brought about by certain other viruses, especially rhinoviruses), while more mortal varieties can cause SARS, MERS, and COVID-19. Corona viruses are enfolded positive sense RNA viruses arraying from 60 nm to 140 nm in diameter with spike like prognosis on its surface.

The inoculation period ranges from 2 to 14 d [median 5 d]. Studies have recognized angiotensin receptor 2 (ACE2) as the receptor through which the microbe enters the respiratory mucosa<sup>4</sup>. The basic case reproduction rate (BCR) is estimated to range from 2 to 6.47 in various modeling studies. In contrast, the BCR of SARS was 2 and 1.3 for pandemic flu H1N1 2009.

## Family

The corona viruses (CoVs) pertain to the group corona virus, the family Coronaviridae, and the order Nidovirales. They are enfolded and have a single- stranded, positive sense ribonucleic acid (ssRNA+), non-fragmented as their nuclear material. The RNA group of viruses is classified into order of three that include the order Nidovirales, which is additionally classified into four families: the coronaviridae, Mesoniviridae, Roniviridae and arteriviridae. The coronaviridae family is further sub-divided into two families: Cronavirinae and Torovirinae. The cocronavirinae sub family comprises four genera of viruses (Alpha Corona viruses, Beta Corona viruses, Delta corona viruses and Gamma corona viruses.

The recent outbreak of this virus is its mutants in spite of the number of mutants of this particular virus some variants shows catastrophic and severe syndrome to the humans. SARS-CoV-2 Interagency Group (SIG) from US government developed a Variant Classification Scheme that elucidates three classes of SARS-CoV-2 variants: Variant of Interest, Variant of Concern and Variant of High Consequence. As of now there is no data, no variants of high consequence.

Among various variants, the Delta variant is a variant of concern that WHO is trailing and monitoring around the world. It's a variant of concern because of its increased transmissibility. This has been revealed by several countries globally. It is known that the Delta variant is identified, it swiftly takes off and spreads among the people more efficiently than even the Alpha variant which was first identified around December, January 2021. It is expected that Delta variant will continue to spread, which was reported in 96 countries as of now. Various factors are responsible for the increased transmission around the world.

## Types of Variant

SARS-CoV-2 variants of concern and variants under investigation in England. The current VOC, VUI, and variants in monitoring as of 21 July is stated below in the table 1

**Table 1: Variant Lineage and Designation as of 21 July 2021**

WHO nomenclature as of 19 July 2021	Lineage	Designation	Status
Alpha	B.1.1.7	VOC-20DEC-01	VOC
Beta	B.1.351	VOC-20DEC-02	VOC
Gamma	P.1	VOC-21JAN-02	VOC
Delta	B.1.617.2, AY.1 & AY.2	VOC-21APR-02	VOC
Zeta	P.2	VUI-21JAN-01	VUI
Eta	B.1.525	VUI-21FEB-03	VUI
	B.1.1.318	VUI-21FEB-04	VUI
Theta	P.3	VUI-21MAR-02	VUI
Kappa	B.1.617.1	VUI-21APR-01	VUI
	B.1.617.3	VUI-21APR-03	VUI
	AV.1	VUI-21MAY-01	VUI
	C.36.3	VUI-21MAY-02	VUI
Lambda	C.37	VUI-21JUN-01	VUI

	B.1.621	VUI-21JUL-01	VUI
	B.1.1.7 with E484K	VOC-21FEB-02	*Monitoring
Epsilon	B.1.427/B.1.429		Monitoring
	B.1.1.7 with S494P		Monitoring
	A.27		Monitoring
	B.1.526		Monitoring
	B.1.1.7 with Q677H		Monitoring
	B.1.620		Monitoring
	B.1.214.2		Monitoring
	R.1		Monitoring
	B.1 with 214insQAS		Monitoring
	AT.1		Monitoring
	Lineage A with R346K, T478R and E484K		Monitoring
	Delta like variant with E484A		Monitoring
	P.1 + N501T and E484Q		Monitoring
	B.1.629		Monitoring
	B.1.619		Monitoring
	C.1.2		Monitoring

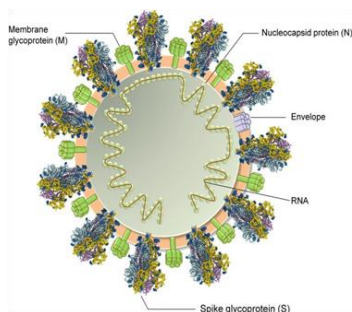
Note that provisionally extinct variants are excluded from this table.

\*VOC-21FEB-02 (B.1.1.7 with E484K). This specific subgenus of B.1.1.7 with E484K has not been identified in England since 1 March 2021. There is an evident transmission outside the UK based on international series data. It is still included in the data update but monitoring of international data continues.

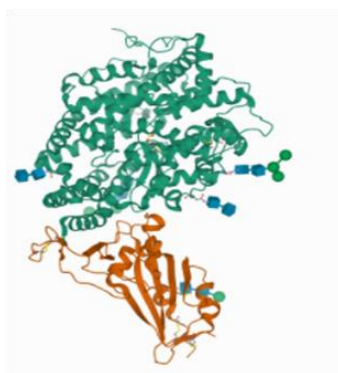
### Structures of Various Variants SARS-CoV-19

Electron microscopy identified that the corona virus-specific morphology of SARS-CoV-2 with virus particle sizes arraying from 70 to 90 nm seen under a large variety of intracellular organelles, most particularly in cavity (Park et al. 2020). Due to high order similarity, the structure of SARS-CoV-2 is hypothesized to be the same as SARS-CoV (Kumar et al. 2020). The surface viral protein spike, envelope, and membrane of corona virus are enclosed in host membrane-extracted lipid bilayer encapsulating the helical nucleocapsid containing viral RNA. Figure.1

- (a) (Finlay et al. 2004). Protease of SARS-CoV-2 (Zhang et al. 2020) and the structure of spike (Yan et al. 2020) have been resolved, which provides a chance to evolve a newer class of medication for treatment of COVID-19. Figure.1(b) Structure of SARS-CoV-2 spike receptor-binding domain complexes with high affinity ACE2 mutant 3N3912.



**Figure 1: (a) Structure of SARS-CoV-2**



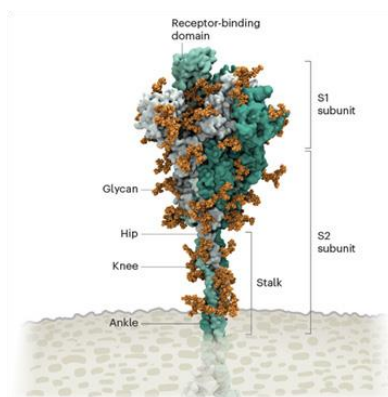
**Figure 1: (b) Structure of SARS-CoV-2 spike-receptor-binding domain complexes with high Affinity ACE2 mutant 3N39**

### **Delta Variant Structure**

Early in the pandemic, researchers established that the RBDs of SARS-CoV-2 spike proteins attach to a known protein called the ACE2 receptor, which embellish the outside of most human lung cells and throat. This ACE2 receptor is also the docking station for SARS-CoV, the microbe that causes severe acute respiratory syndrome (SARS). But compared with SARS-CoV, SARS-CoV-2 sticks to ACE2 two to four times more strongly than estimated, because several changes in the RBD sustain its virus-binding hotspots. The most transmissible variant which is now spreading around the world, the Delta variant where hosts multiple mutations in the subunit- S1, including three in the RBD that seems to improve the RBD's capability to stick

to ACE2 and elude the immune system.

The Delta variant (B.1.617.2) has brought forth a number of sub-lineages called 'Delta Plus' variants that carry most of its property mutations but are different in ways. One of these sub-lineages, AY.12, has all the features of Delta mutations except one. The functional impact of the changes between Delta and AY.12 is not known but the two appear to be very similar at a molecular level.



**Figure 2: (a) A Hidden Spike: The spike protein of SARS-CoV-2 is coated in sugar molecules, or glycans, which disguise it from the immune system. It can hinge at three points on the stalk, giving it flexibility<sup>17</sup>**

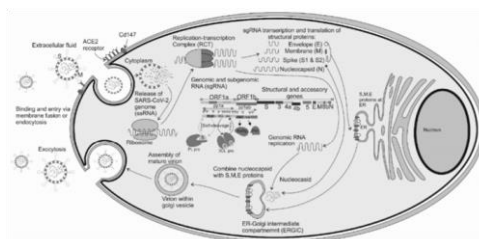


**Figure 2: (b) SARS-CoV-2 Spike D614G variant, minus RBD<sup>18</sup>**

### Mechanism of Virus with Protein

Proteases and receptors on the surface of the host cells play a significant role in the pathophysiology of SARS-CoV-2. For SARS-CoV-2 the best-known receptor is angiotensin-converting enzyme 2 (ACE2). An alternative entry receptor for the virus is a trans-membrane glycoprotein CD147, usually known as an extracellular matrix metalloproteinase inducer (EMMPRIN) or basic immunoglobulin (Basigin) Qiao et al. spotted the appearance of CD147 in mouse brain cell lines and human. Based on studies on other CoVs (SARS-CoV, HCoV-229E) it can be assumed that SARS-CoV-2 uses other receptors, i.e. ENPEP (glutamyl aminopeptidase), AGTR2 (angiotensin II receptor type 2) & ANPEP (alanyl aminopeptidase). Regardless, there is strong proof only for ACE-2 as a required functional receptor protein. Upon cell entry, the

ectodomain of SARS-CoV-2 RBD, situated at the S1 subunit of the S protein forms a complex with a glycosylated domain (sites 5 and 7) of the hACE2 extracellular peptide region. Figure 2. Mechanism of SARS-CoV-2 infection of human cells via the interaction of spike glycoprotein, the ACE2 receptor protein, and the CD147 receptor. Genomic structure and proteins encoded by SARS-CoV-2.



**Figure 3: Mechanism of SARS-CoV-2 infection of human cells**

### Transmissible Rate

The Delta variant is more transmissible than Alpha and nearly twice as transmissible as the original SARS-CoV-2 strain was reported. As per the report given by a Chinese study that viral loads in Delta variant infections were nearly 1,000 times higher than those in infections brought about by other variants. World Health Organization (WHO) considers Delta as “the fastest and fittest” variants so far based on the response of various reports.

### Materials and Methods

Vaccines contain tiny segments of the disease-causing structure or the blueprints for producing the tiny fragments. They also comprise of other constituents to keep the vaccine effective and safe. Or the antigen is the key ingredient in a vaccine. It's either a weakened, non-dangerous version or a tiny part of disease-causing organism, so our body can assimilate the distinct way to fight it without getting ill.

All vaccines consist of an active component (the antigen) which gives rise to an immune response, or the design for producing the active component. The antigen may be a tiny fragment of the infectious disease-causing structure, like sugar or protein, or inactive form, or it may be the whole weakened organism. The constituents of certain vaccines are given below to analyse their effectiveness over variants of SARS-CoV-2.

### Covaxin (BBV152)

The vaccine is developed using Whole-Virion Inactivated Vero Cell derived platform technology. Inactivated vaccines do not replicate and are therefore unlikely to revert and cause pathological effects. They contain dead virus, incapable of infecting people but still able to instruct the immune system to mount a defensive reaction against an infection BSL-3 (Bio-Safety Level 3).

### Pfizer (BNT162b2)

This vaccine consists of nucleoside-modified messenger RNA (modRNA) encoding the viral spike glycoprotein (S) of SARS-CoV-2. The Pfizer vaccine, like one from Moderna, uses lipid nanoparticles to enclose the RNA. The nanoparticles are generally, minute greasy spheres that defend the mRNA and help to slide inside the cells. These nanoparticles are about 100 nanometers around. Interestingly, that's about the same size of the coronavirus.

### Astrazeneca (ChAdOx1 nCoV-19)

The composition of Covidshield includes inactivated adenovirus with segments of corona virus, along with this certain other constituents are Aluminium hydroxide gel, L-Histidine hydrochloride Monohydrate, L-Histidine, Polysorbate 80, ethanol, Magnesium Chloride hexahydrate, sodium chloride, sucrose and EDTA.

### **Janssen (Viral Vector)**

This vaccine is developed with an active ingredient of Recombinant, replication-incompetent Ad26 vector, encoding a stabilized variant of the SARS-CoV-2 Spike(S) protein.

### **Efficacy of Various Vaccines**

The difference vaccine effectiveness was much smaller among persons who had fully vaccinated. In any vaccine analysis, the effectiveness of vaccine was 87.5% with alpha variant and with delta variant it is 79.6%. A small statistical difference that can be seen within the vaccine seen in BNT162b2 vaccine is seen to be 93.7% with alpha variant and for delta variant it seems to be 88%. In same manner ChAdOx1 nCoV-19 vaccine shows smaller difference with BNT162b2 vaccine are that 74.5% effectiveness with alpha variant and 67% with delta variant.

The Oxford–AstraZeneca and Pfizer–BioNTech COVID-19 vaccines are effective against the highly infectious Delta variant of SARS-CoV-2, a study of infections in the United Kingdom has concluded that their shielding effect drops away over time period. The vaccine produced by Pfizer in New York City and BioNTech in Mainz, Germany, was 92% productive at keeping public from emerging a high viral load - a high concentration of the virus in their test specimen -fourteen days after the second dose. But the vaccine's efficacy drop to 90%, 85% and 78% after 30, 60 and 90 days, respectively. The vaccine developed by Oxford and the pharmaceutical company AstraZeneca in Cambridge, UK, was 69% effective against a high viral load 14 days after the second dose, dropping to 61% by 90 days. The results were also published in a preprint on 19 August 2021, insists that both vaccines are effective against delta variant after two dose, but the protection decrease with time.

Seventeen mutations of the genome of the UK-variant were found, among this eight has found in spike receptor-binding domain (RBD) arbitrating the extension of the virus to the angiotensin transforming enzyme 2 (ACE2) receptor on the surface of human cells. Therefore, it seems to be that the predominance of the vaccine candidates, being either recombinant or particularly targeting the single antigenic determinant of original D614G genomic spike series, might not be able to cause an efficient immune reaction against the new variants. The hCoV-19/India/20203522 SARS-CoV-2 (VOC) 202012/01 from UK returnees in India with all signature mutations of the UK-variant were successfully isolated and characterized. The study markedly highlighted comparable neutralization activity of vaccinated individuals' sera against variant as well as heterologous SARS-CoV-2 strains. Importantly, sera from the vaccine recipients could neutralize the UK-variant strains discounting the uncertainty around possible escape. It was reassuring from the PRNT50 data generated in their laboratory that the primitive BBV152/COVAXIN™, following its roll out in vaccination program, could be expected to work against the new UK-variant. It is likely that the mutation 501Y would be able to drench the potential benefits of the vaccine in concern. Effectiveness of various vaccine against variants and recommended age groups for vaccination data sheet collected from WHO, CDC, ICMR and PHE for is presented in the table 2 and 3 respectively.

**Various Types of Vaccines and their Effectiveness is Presented in Table 2**

Name of the vaccine	Percentage of effectiveness (sars-cov-2)	Percentage of effectiveness (delta variant)
AstraZeneca (AZD1222)	63.09%	69%
Covaxin (BBV152)	77.80%	65%
Janssen (Ad26. COV2.S)	85.40%	67%
Moderna (mRNA-1273)	94.10%	66-97%
Pfizer(BNT162b2)	95%	42 -96%
Sputnik (Gam-covid-vac)	91.60%	81%

**Types of Vaccines and their Effectiveness with Age Factor is Produced in Table 3**

Name of vaccine	Countries	Age	percentage of efficacy
Pfizer–BioNTech vaccine	Israel	85 Years	94%
Pfizer–BioNTech and Oxford–AstraZeneca vaccines	UK	>70 Years	80%
Pfizer–BioNTech and Moderna	Cambridge	12–15 Years	100%
Sputnik	Russia	>60	90%
Pfizer–BioNTech and Moderna	Cambridge	12–17 Years	93%
Covaxin	India	> 18 years	81%

**Significance and Consequence of Breakthrough Infections with Vaccinated and Unvaccinated**

Taken together, these data support the significance of full dose vaccination against SARS-CoV-2, but report reveals of lowered vaccine efficacy against Delta variant further examination into breakthrough infections and the probability of vaccine booster shots. Genomic analysis of spotted from 63 vaccine progressed infections in India (not yet peer reviewed) let out that B.1.617.2 was the main lineage in groups who were partially and fully vaccinated with either Covaxin or AstraZeneca.



In late July, 2021, the CDC published a data assessing outbreaks of SARS-CoV-2 that were correlated with large public meetings in Barnstable County, Massachusetts. Out of the 469 recognized cases of COVID-19, 346 or 74% of them were progress infections that transpired in public whowere fully vaccinated with two doses of Moderna or Pfizer, or one dose of Janssen (J&J) vaccine. Genetic analysis revealed that Delta variant was responsible for 90% of the 133 series breakthrough infections. This statics prompted the CDC to endorse the use of masks in indoor public spaces, nevertheless of vaccination status, in areas where COVID-19 communication is high. Further research into breakthrough infections that occur after COVID-19 vaccination is essential.

### Discussion

With lot of limitations in our analyses we found that distinction in the effectiveness of the vaccine against the variants varies according to the dose. But the efficacy is seems to be prominent after fully vaccinated. From various study it seems that the effectiveness between BNT162b2 and ChAdOx1 nCoV-19 (Covidshield) vaccine has remarkable efficacy against alpha and delta variants. One of the studies from India reported that neutralization data in the comprehensive B.1.617 variant group proposed that recovering serum samples from individuals with Covid-19 and from recipients of the BBV152 vaccine (Covaxin) has an ability to neutralize variants in the B.1.617 lineage. As contrast with recent findings from Qatar on the effectiveness of the BNT162b2 vaccine against the alpha and beta variants.

Various countries like UK, US, Israel and somany countries extended their research to enhance the effectiveness of vaccine on variants and administration for smaller age groups. We used two different approaches in our analysis that effectives of various vaccines and administration of vaccine for smaller age groups with alpha and delta variant which has been reported previously. Our findings put forth that effectiveness against the variants after a full vaccination course lies somewhere between these three. It is also found that BNT162b2 vaccines also continues to be available under emergency use authorization (EUA), for individuals 12 – 15 years of age and also recommended for the administration of a third dose in certain immune compromised individuals. Certain vaccines show remarkable effectiveness against age group of 85 years and above. By amplifying the on-going clinical trials and research analysis the efficacy rate could be enhanced and made available for all the individuals regardless the age factor.

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