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Review article

A Concise Review on Current Omicron Variants and Subvariants (SARS-Cov-2) and Effective Vaccines against them

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ABSTRACT

In late 2002 and early 2003, the SARS coronavirus and a new variant of the virus emerged in China and quickly spread around the globe. These viruses were easy to cultivate in tissue culture, which made it possible to study their genomic structure which were significantly different from human and animal coronavirus. The Covid-19 outbreak is a Group 2B Coronavirus. The genomic sequence of SARS-CoV-2 isolated from humans showed a similarity to SARS of 79.5%. The D614G mutation in the SARS-CoV-2 spikes was discovered at the beginning of March 2020. In the second wave of the SARS-COVID-2 epidemic in 2021, a number of novel COVID variants have been reported since the 2020 COVID outbreaks. The Omicron Variants, which were reported after the second wave in late 2021, is one of them. This concise review reports about Classification of new COVID-19 variants, Omicron variants and subvariants and their differences, and current vaccines in use against the newly mutated variants.

Keywords: *Covid-19; SARS-CoV-2; Omicron variants; BW.1 variant; BQ.1 variant; XBB variant; XBB.1.5 (Kraken)*

Introduction

In late 2002 and early 2003, the SARS coronavirus and a new variant of the virus emerged in China and quickly spread around the globe. These viruses were easy to cultivate in tissue culture, which made it possible to study their genomic structure. It was discovered that these viruses' genomic structures were sufficiently distinct from those of human and animal coronaviruses, and they thus formed a new group of viruses that were thought to have originated from Himalayan palm civets. According to genomic architecture, Coronavirus is a member of the subfamily Coronavirinae of the family Coronaviridae and the order Nidovirales. This subfamily is further classified into alpha, beta, gamma, and delta coronaviruses based on phylogenetic grouping. While Gamma and Delta-coronaviruses have evolved from avian and swine gene pools, Alpha and Beta-coronaviruses have their origins in bats [1]. The new SARS-CoV-2 virus type is more contagious and has been found all across the world. The Covid-19 outbreak is a Group 2B Coronavirus. The genomic sequence of SARS-CoV-2 isolated from humans showed a similarity to SARS of 79.5%. The D614G mutation in the SARS-CoV-2 spikes was discovered at the beginning of March 2020. It quickly spread over the world and took control during the following few months. By September 2020, a new variant, later identified through viral genome sequencing in the United Kingdom as SARS-CoV-2 VUI 202012/01 (Variant Under Investigation, the year 2020, month 12, variant 01), had been discovered. This variant was eventually identified by many spike protein alterations. The potential vaccines for SARS-CoV-2 variations that have been suggested by the WHO were explored by Shahab et al. in 2021 [2]. In the second wave of the SARS-COVID-2 epidemic in 2021, a number of novel COVID variants have been reported since the 2020 COVID outbreaks. The Omicron Variants, which were reported after the second wave in late 2021, is one of them.

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Classification of new COVID-19 variants

On November 26, 2021, the WHO designated the B.1.1.529 strain of COVID-19 (originally detected in South Africa) as a potentially dangerous variation and gave it the new moniker Omicron. Furthermore, the World Health Organization (WHO) recognised Omicron as a Variance of Concern (VOC) because of the potential for it to promote transmission or cause a negative shift in COVID-19's epidemiology [3].

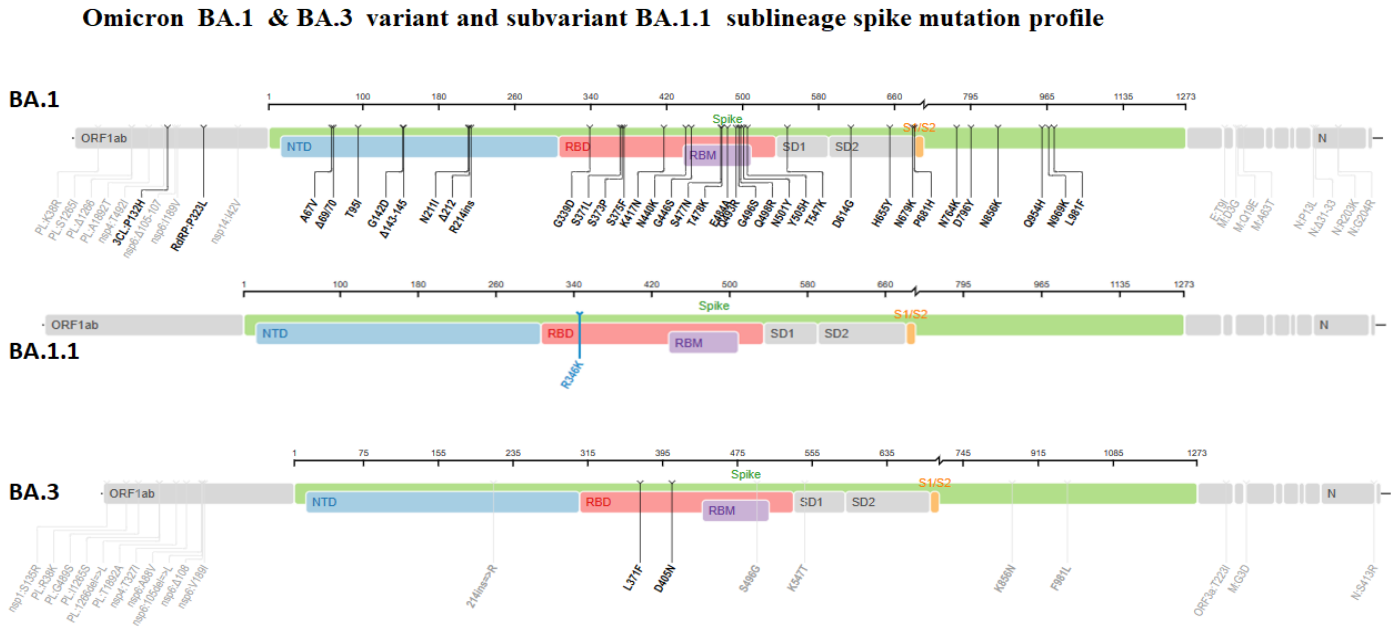

Figure 1(a): Omicron variants and subvariants sub-lineage spike mutation profiles. Source; SARS-CoV-2 Variants - Omicron BA.1 - Stanford Coronavirus Antiviral & Resistance Database (CoVDB).

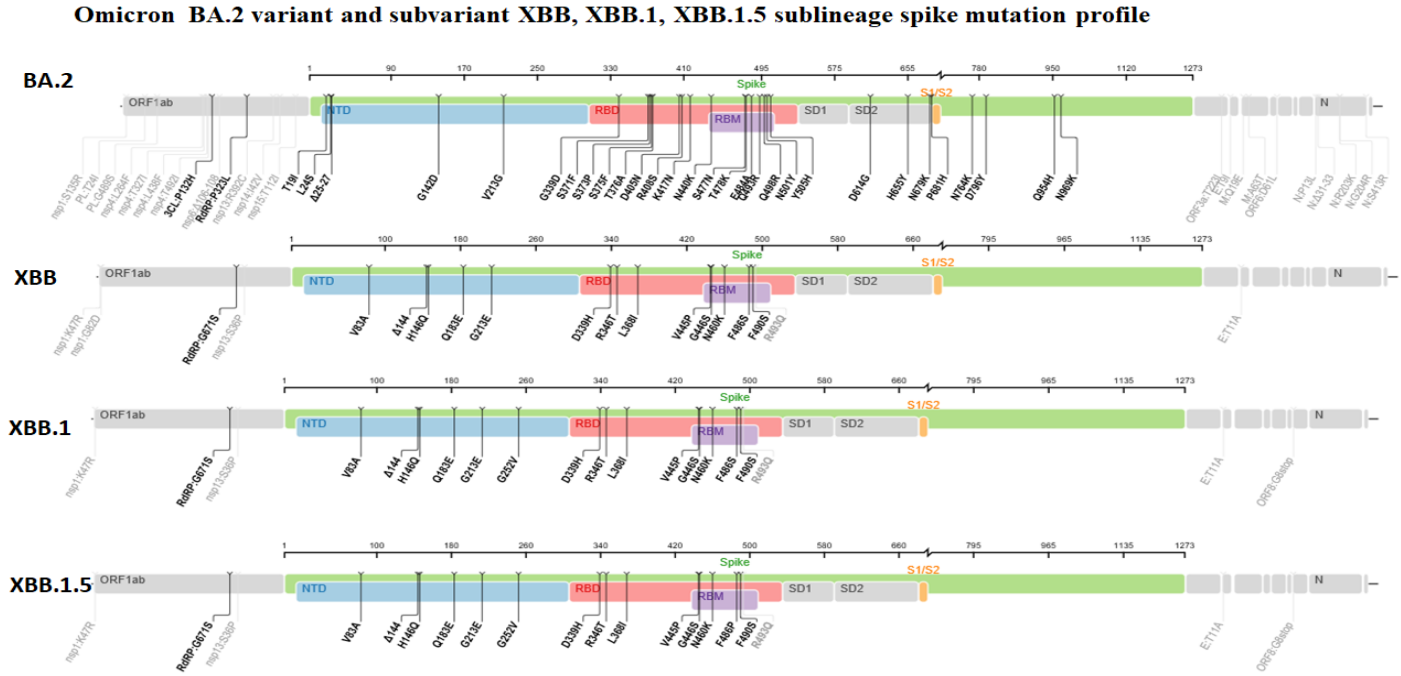

Figure 1(b): Omicron variants and subvariants sub-lineage spike mutation profiles source: SARS-CoV-2 Variants - Omicron BA.2 - Stanford Coronavirus Antiviral & Resistance Database (CoVDB)

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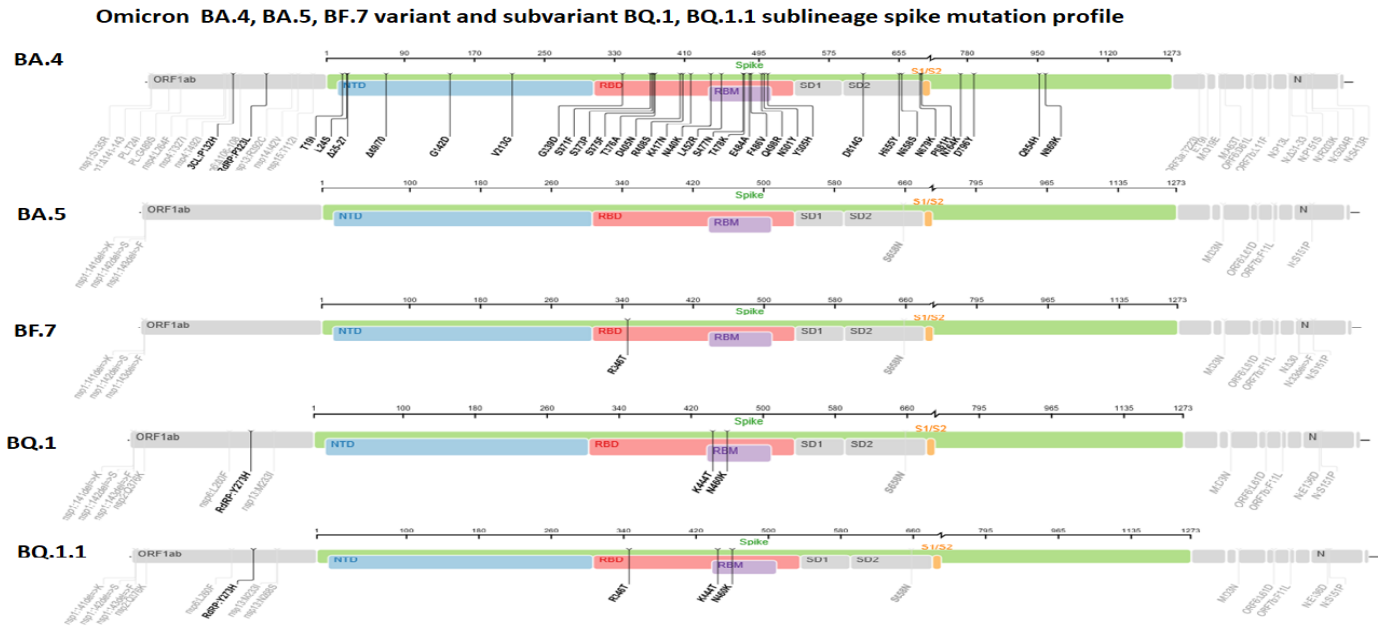

Figure 1(c): Omicron variants and subvariants sub-lineage spike mutation profiles source: SARS-CoV-2 Variants - Omicron BA.4/5 - Stanford Coronavirus Antiviral & Resistance Database (CoVDB).

Omicron variants

On November 24, 2021, researchers in South Africa and Botswana reported a new version of the severe acute respiratory syndrome coronavirus 2 they had named "Omicron" to the World Health Organization (WHO). similar to B.1.1.529, rapidly disperses, and on November 26, 2021, was designated by the WHO as a variation of concern (VOC). Several discrepancies in their genomes have led to the conclusion that the Omicron variant did not originate from an earlier known variant. Stealth evolution in a population with little sequencing, long-term evolution in one or a few humans with chronic infection, and evolution in other animals, especially rodents, are all hypothesised to have contributed to the emergence of the Omicron variant. It is important to note that the Omicron variety did not remain a single strain but rather split into three distinct branches: BA.1, BA.2, and BA.3. Historically, BA.1 was the most common strain worldwide; however, BA.2 is gradually displacing BA.1 in a number of countries. There have been little more than a few hundred confirmed cases of BA.3 transmission worldwide [4]. As a result of its infectious nature and the mutations that make it immune to vaccines, the Omicron variety has sparked worldwide worry and anxiety. Upwards of 60 mutations have been found in the BA.1 lineage thus far, with as many as 38 of them located in the spike (S) protein, 1 in the envelope (E) protein, 2 in the membrane (M) protein, and 6 in the nucleocapsid (N) protein. [5]. There are 57 mutations in the BA.2 lineage, 31 of which are found in the S protein, which has a very different N-terminus from the BA.1 lineage. According to a recent study, people who have overcome infections with more common strains are at increased risk of contracting the Omicron strain [6]. This data demonstrates that Omicron mutations circumvent immunity resulting from a prior infection. Omicron, as described by Kumar et al. in 2022, is a mutation beast with 30 mutations in the spike protein, of which 50% are located in the RBD [7]. The Omicron variant has 60 mutations, in contrast to the original Wuhan variety's [8]. There are 50 non-synonymous mutations, eight synonymous mutations, and two non-coding mutations. A total of 30 mutations [9] have been found in the spike protein, the primary antigenic target of antibodies generated in response to infections and increasingly employed in vaccines. Also, the B.1.1.529 (Omicron) strain of SARS-CoV-2 has been reported from multiple countries, including South Africa, Scotland, England, and Canada, to be more contagious than earlier strains but milder in their effects. As time went on, other Omicron subvariants began to predominate. 5 It is still difficult to put a number on the inherent severity of these novel subvariants [10]. As reported by the WHO Recently emerged VOCs have mostly supplanted previously co-circulating SARS-CoV-2 subtypes. Omicron complex viruses have been evolving since their classification as a Variance of Concern VOC by WHO on November 26, 2021, and as a result, there are now several descendant lineages with unique mutational patterns as depicted in Figures 1a, 1b and 1c.

Omicron subvariants

The World Health Organization (WHO) has established a new subcategory to its variation tracking system called "Omicron subvariants under surveillance" to alert public health agencies around the world as to which VOC lineages may need heightened attention and monitoring [10]. The primary focus of this subfield is on learning whether or not these lineages present a unique danger to public health around the world in comparison to other types of viruses already in circulation. The Omicron form, designated BA.1, was initially discovered in South Africa in November 2021 and rapidly spread across the globe. Multiple "Omicron" subvariants exist today; these include B.1.1.529, BA.1, BA.1.1, BA.2, BA.3, BA.4, BA.5, and BF.7, as well as BQ.1, XBB, and BW.1 as depicted in fig.1b,1c. The variants BA.1 and BA.3 are grouped together under the B.1.1.529 subtype, while BA.1.1 and BA.2 are placed in their own category [11, 12]

Differences between Omicron subvariants

As recorded by WHO, multiple lineages and sublineages have developed since the Omicron variant's initial outbreak. These days, BA.1, BA.1.1, BA.2, and BA.2.12.1 are the most widely used ones. In comparison to BA.1, the BA.2 variation has an effective reproduction number that is 1.4% greater. The virus is so successful because of 53 mutations, 29 of which are located in the spike protein. Infection with BA.2 produces symptoms that are similar to those of BA.1 in that they are upper respiratory system based. Patients often also report stomach issues alongside their vaguer complaints (eg, muscle aches, headache, nasal congestion, and fatigue). The most common variety in the United States was BA.2.12.1, which showed the S704L and L452Q spike mutations in addition to the BA.2 background [13, 14].

In addition, two other variants, known as BA.4 and BA.5, appeared. These variants were detected in South Africa as well as in Europe, and the World Health Organization has classified them as Variants of Concern Lineages Under Monitoring. Both BA.4 and BA.5 seem to be substantially more contagious than previously known (pre-Omicron) variations, which is consistent with the findings regarding other Omicron subvariants. Thankfully, it appears that BA.4 and BA.5 do not induce a condition that is any more severe than its earlier variations [15]. In addition to being a subvariant of BA.5, BQ.1 also contains a number of its own constituent subvariants. XBB is a recombinant subvariant of BA.2.10.1, and BA.2.75 was first found in Singapore, which contributed to a surge in the incidence of the disease in that nation. BF.7, which is an abbreviation for the longer form BA.5.2.1.7, is a sub-lineage of the omicron variety BA.5 and is highly transmissible; as a result, it can cause infection to spread. Because of how quickly it goes into the infectious stage, it is more likely to infect people, even those who have been immunised against it. Following its first discovery, the Omicron BF.7 strain has now been identified in a number of countries, including China, the United States of America, the United Kingdom of Great Britain and Northern Ireland, Belgium, Germany, France, and Denmark [16]. The BF.7 variant of COVID-19, believed to be driving the recent surge of cases in China, was first identified in India as far back as July. Reports from China indicate BF.7 has the strongest infection ability (opens in new tab) out of the omicron subvariants in the country, being quicker to transmit than other variants, having a shorter incubation period, and with a greater capacity to infect people who have had a previous COVID infection, or been vaccinated, or both [17]. Recent reports of new subvariants include:

BW.1 variant

As of late, a novel subvariant, the BW.1 (BA.5.6.2.1) strain, has been described; it is an Omicron subvariant with BA.5.6.2 ancestry. Similar to the BQ.1 variety, the SARS-CoV-2 BW.1 has acquired mutations that facilitate immune evasion. Genetic changes like S:K444T, S:L452R, S:N460K, and S:F486V are seen in BQ.1, one of the most quickly spreading lineages. Because of this, it can evade the protection afforded by vaccination or previous infection. Despite its genetic connection to the Omicron lineage BA.5.6, the BW.1 variant has a lot of similarities with the BQ.x variants. Its is due to the fact that the BA.5 ancestor is shared by both the BW.1 and BQ.x families[18, 19, 20].

BQ.1 variant

Mutations like S:K444T, S:L452R, S:N460K, and S:F486V are seen in BQ.1, one of the most quickly spreading lineages. It's a branch off of BA.5 with alterations at K444T and N460K, two highly conserved antigenic sites. An additional spike mutation at an important antigenic location has been found in the BQ.1.1 sublineage, which is present in addition to the aforementioned mutations (i.e. R346T). Based on sequences submitted to GISAID during Epidemic Week 40 (3-9 October), BQ.1* was found to have a prevalence of 6% and has been identified in 65 countries. Without human data on severity or immune escape, it is

important to keep an eye on BQ.1* because it is demonstrating a large growth advantage over other circulating Omicron sublineages in several contexts, including Europe and the United States. There is likely an increased risk of reinfection due to the fact that these extra mutations have given the virus an immunological escape advantage compared to other circulating Omicron sublineages [21,22].

XBB variant

XBB is a sublineage that came from the mixing of BA.2.10.1 and BA.2.75. XBB* was first found in Singapore. It is found in 1.3% of the world's population and has been found in more than 35 countries, including India. In regional genomic surveillance, there has been a general rise in the number of people with XBB, but this hasn't been linked to a rise in new infections yet. Even though more research needs to be done, the data we have now don't show that there are big differences in how bad XBB* infections are [23]. There are, nevertheless, early signs that the risk of reinfection is significantly greater than with other Omicron sublineages in circulation.

XBB.1.5 (Kraken)

A new strain of XBB, XBB.1.5 (also known as "Kraken"), has recently been identified. This strain is a descendant of XBB.1.1, which is a cross between BA.2.10.1 and BA.2.75. In 2023, XBB.1.5, a great-grandchild of Omicron, is widely regarded as a global security threat, especially in the United States and Europe. To date, the XBB.1.5 subvariant has been found to be the most contagious [20], as reported by WHO. In addition, 5288 Omicron XBB.1.5 sequences were reported from 38 countries between October 22, 2022, and January 11, 2023. The United States (82.2%), the United Kingdom (8.1%), and Denmark (2.2%), account for the majority of these sequences. It is possible that XBB.1.5 is a factor in rising case incidence worldwide due to its genetic traits and preliminary growth rate estimates. No data on the assessment of severity is still being conducted [24].

Current vaccines available and effective for the Omicron variants

The mRNA vaccines developed by Pfizer-BioNTech and Moderna, the viral vector vaccines developed by Johnson & Johnson-Janssen and AstraZeneca, and the purified protein vaccine developed by Novavax were all designed to prevent disease caused by the ancestral strain[25]. Several vaccines have been approved for the new variant of Omicron subvariant BA.1, including.

Pfizer and BioNTech

With BioNTech's unique mRNA technology as the foundation, Pfizer and BioNTech developed the COVID-19 Vaccines (COMIRNATY®). The Food and Drug Administration has authorised Bivalent (Original and Omicron BA.4/BA.5) for use in individuals 5 years of age and older as a single booster dose administered at least two months after: After receiving a booster dose of the Omicron BA.4/BA.5-adapted bivalent COVID-19 vaccine, neutralising antibodies against BA.4.6 increased 11.1-fold (95% CI: 7.1, 17.3), while antibodies against BA.2.75.2, BQ.1.1, and XBB.1 increased 6.7-fold (95% CI: 4.4, 10.2), 8.7-fold (95% CI: 5.7, 13.3), and 4.8-fold (95% CI: 3.3 The neutralising antibody titers against BA.4.6, BA.2.75.2, BQ.1.1, and XBB.1 increased 2.3-fold (95% CI: 1.9-2.8), 2.1-fold (95% CI: 1.7-2.5), 1.8-fold (95% CI: 1.6-2.2), and 1.5-fold (95% CI: 1.3-1.8), respectively, after receiving a booster dose of the original COVID-19 vaccine from the companies. Overall, the bivalent booster resulted in a greater rise in neutralising antibodies against emerging Omicron sublineages compared to the initial Pfizer-BioNTech COVID-19 immunisation [26].

Moderna

Despite using the same mRNA technology as the competing product from Pfizer-BioNTech and having identical efficacy in preventing symptomatic sickness at the time the companies submitted for authorization, the FDA approved the Moderna vaccine; the vaccine must also be maintained at freezer temperatures. It targets the first SARS CoV-2 strain, as well as the Omicron BA.4 and BA.5 sublineages. In a November [27] press release, Moderna stated that its latest bivalent booster also stimulates the body to make more antibodies against BA.4 and BA.5. After three doses of mRNA-1273, the Vaccine Effectiveness (VE) against infection with BA.1 was high and reduced slowly [28,29]. However, the VE against infection with more recent omicron subvariants, such as BA.2, BA.2.12.1, BA.4, and BA.5, decreased more rapidly.

Novavax

In the United States, Novavax was the fourth COVID-19 vaccine administered (also known by the brand names Nuvaxovid and Covovax). Studies showed that this protein adjuvant immunisation was approximately as successful as the initial mRNA vaccines [30]. Phase three trials using the protein nanoparticle vaccine NVX-CoV2373 showed a 90% effectiveness against symptomatic infections and a 100% effectiveness

against severe coronavirus illness (COVID-19). In addition, only 13–50% of plasma samples from people who had received two doses of AD26.COV2.S showed neutralising activity against the Omicron subvariants, while all plasma samples from those who had received three doses of the NVX-CoV2373 or BNT162b22 vaccination showed neutralising activity against the Omicron subvariants [31]. A study published at the end of November 2021 found that compared to Novavax's first coronavirus vaccination [32], NVX-CoV2515 induced 1.6 times as many neutralising antibodies in previously unexposed individuals.

Johnson & Johnson

The SARS-COPV-2 vaccine sold under the Janssen brand name was approved by the US Food and Drug Administration in February 2021. The virus used in this immunisation is not a replicating strain. This vaccine is reserved for patients who cannot get any of the other available COVID-19 vaccines [33] due to medical reasons.

In order to prevent disease, a bivalent booster shot is recommended by the CDC. That's because the bivalent boosters from Pfizer-BioNTech and Moderna provide immunity against both the wild-type SARS-CoV-2 and the Omicron variants. It's implied, but with a caveat [34]. No data is available yet on how well it performs against Omicron variants.

Discussion

Since its appearance, the Omicron variety has been the subject of intense study because of the numerous changes that have greatly improved its transmissibility and immune evasion. SARS-CoV-2 mutations continuously introduce new variants. The VOC causes severe infection waves, which may persist with Omicron. Investigations are underway to determine the SARS-CoV-2 Omicron variant's infectivity, prevalence, and severity to help avoid a future outbreak. Experts are divided on whether or not the Omicron variant may easily evade a person's humoral immune response, which would significantly up the odds of reinfection. Globally expanding omicron subvariants BA.2.12.1 and BA.4/5 BA.2.12.1 is only 1.8-fold more resistant to sera from vaccinated and boosted people than the BA.2 subvariant that dominate the global pandemic. BA.4/5 resists 4.2-fold more. Among the subvariants, XBB.1.5 is the most worrisome because it is spreading rapidly and has already infected some persons who were previously immunised against it. Therefore, it is necessary to conduct additional trials of these vaccinations and improve existing vaccines.

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Conflict of Interest

The author declares no conflict of interest.

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