



Evolution of COVID-19 Practices and Overview of Current Variants of Concern

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Received: August 08, 2022**Published:** August 23, 2022© All rights are reserved by **Robert W Buckingham and Brittany Adams.****Abstract**

COVID-19 is an ever-evolving virus. Quickly appearing and disappearing variants make it difficult to keep up with necessary changes in response. In 2021, WHO created a new naming system to help distinguish different variants. It has been crucial in identifying the many subvariants of Omicron, including the now majority BA.5. Vaccine manufacturers have been working to create boosters that are more effective against variants that have proven evasive of immunity provided by current vaccines. Scientists are divided about the best path forward for these new vaccines, especially concerning future unknown variants. It is impossible to know how long Omicron will be around or if, even in a few weeks, we will have a new variant taking its place.

Keywords: COVID-19; Omicron; Variants; Vaccines; WHO; FDA**Abbreviations**

VOIs: Variants of Interest; VOCs: Variants of Concern; WHO: World Health Organization; FDA: Food and Drug Administration; PANGO: Phylogenetic Assignment of Named Global Outbreak Lineages

Introduction

As predicted from the beginning, COVID-19 has continued to mutate and evolve. While deaths and hospitalizations have remained relatively low compared to pre-vaccination surges, the virus has developed new spike proteins that allow it to evade immunity garnered from both vaccinations and previous infection [1]. There was also significant confusion surrounding the many different variants, primarily due to the Phylogenetic Assignment of Named Global Outbreak Lineages (PANGO) naming system. PANGO is identifiable by its number-based system that includes names like B.1.1.7 or BA.2. Scientists developed PANGO in April of 2020, early on in the pandemic, and scientists and researchers are still using it to track COVID-19 variants [2]. PANGO is not very inclusive of the general public, however. As researchers discover more variants, the numbers become more confusing than before. WHO responded

by bringing together a team of scientists in May 2021 to decide on a better naming system. The agreed-upon system was the Greek alphabet, e.g., Alpha, Beta, Delta, Omicron [3].

This evolution of COVID-19 communication represents an essential facet of pandemic response that, as more variants arise, scientists and governments should not forget. The virus will continue to evolve, and our response to it should evolve in turn. Supposing we want to maintain a level of normalcy in day-to-day activities, we must maintain practices to keep COVID-19 transmission low, including mask-wearing and social distancing when necessary and continued evolution of public health communication and medical innovation.

COVID-19 public health communication

With so many circulating variants at once, WHO realized not only the need for an easier, more uniform way to label variants but also a better system to inform the public about which variants are more severe. Alongside the Greek alphabet system, WHO also announced working definitions to describe the three levels of concern regarding COVID-19 variants.

Emerging variants are precisely that. They have recently been discovered and are likely beginning to circulate in a particular area of the world. Scientists know very little about these variants but will keep close track of them to determine if they belong in one of the following categories.

Variants of Interest, or VOIs, are variants that scientists are studying intently to determine if they have the characteristics of more concerning variants. The working definition provided by WHO for VOIs is a variant

- With genetic changes that are predicted or known to affect virus characteristics such as transmissibility, disease severity, immune escape, diagnostic or therapeutic escape; AND
- Identified to cause significant community transmission or multiple COVID-19 clusters, in multiple countries with increasing prevalence alongside increasing number of cases over time, or other apparent epidemiological impacts to suggest an emerging risk to global public health [3].

An example of a VOI that never reached a more concerning level was B.1.621, which began circulating in Colombia in January 2021. It was declared a VOI in August of 2021 [4]. B.1.621 was a part of the Mu lineage, an entire lineage of COVID-19 that did not make much of an impact compared to other variants. Nevertheless, B.1.621 managed to make it all around the world. As illustrated in figure 1, though, it infected very few people along the way and provided significant immunity after infection [5]. All these factors ensured that B.1.621 would likely never be a severe variant of concern. WHO demoted it from a VOI to the category of previous VOI in March 2022 [4].

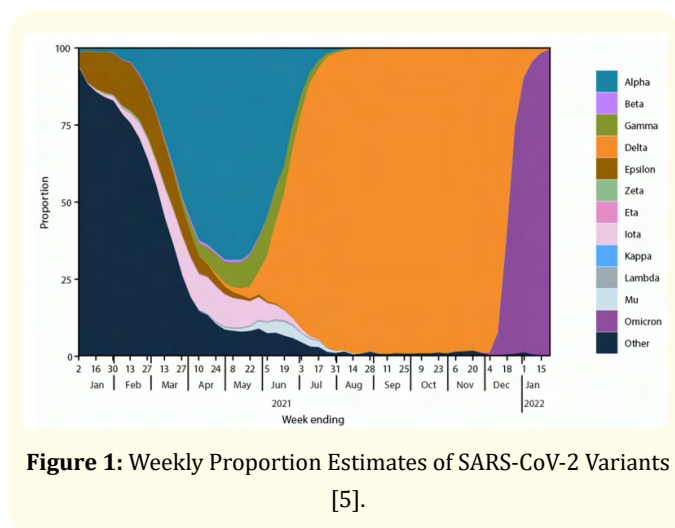


Figure 1: Weekly Proportion Estimates of SARS-CoV-2 Variants [5].

Variants of Concern, or VOCs, on the other hand, are the variants that have surpassed the level of VOI and are labeled to notify the public and the scientific community of the significant concerns surrounding them. The working definition provided by WHO indicates that a VOC is a variant that is associated with one or more of the following on a global scale:

- Increase in transmissibility or detrimental change in COVID-19 epidemiology; OR
- Increase in virulence or change in clinical disease presentation; OR
- Decrease in effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics [3].

This working definition is a fantastic representation of the circumstances under which one would need to worry about a variant. When a variant changes the previous understanding of COVID-19 so significantly, our previous procedures, diagnostics, and medical innovations are at risk of being left in the past. Symptoms change, infection times change, and immune responses change. If the world does not continue to evolve alongside these variants, we will be at a standstill again. The current circulating VOC is Omicron [4].

Under VOCs are subvariants under monitoring. Omicron has many subvariants, still labeled only by their PANGO lineage number. For example, BA.1 would have been Omicron’s first subvariant and BA.2 the second. These subvariants all stem from their parent variant, Omicron, and are mostly similar, with some notable differences. The working definition from WHO is as follows:

- A variant that, according to phylogenetic analysis, belongs to a currently circulating VOC; AND
- Shows signals of transmission advantage compared to other circulating VOC lineages; AND
- Has additional amino acid changes that are known or suspected to confer the observed change in epidemiology and fitness advantage as compared to other circulating variants [3].

Current status of VOCs BA.4 and BA.5

As of July 2022, BA.4/5 are the two most prominent subvariants under monitoring, with more emphasis on BA.5 [6]. Scientists first detected both variants in South Africa in early 2022 [1]. They are most similar to their sister variant BA.2 from 2021, but they

have significant differences that allow them to evade previous immunity better [7]. Like other Omicron subvariants, BA.4/5 cases have risen rapidly, but the number of deaths and hospitalizations have remained more stable [7]. This trend is primarily due to a combination of vaccination coverage and less disease severity overall. As of July 16, 2022, BA.5 made up approximately 80% of all cases in the United States, and BA.4 made up about 13% [6]. With genome sequencing lagging behind rapid variant changes, scientists worry that some cases of BA.5 may be labeled as BA.2 or BA.4 [7]. Mislabeling means that cases of BA.5 are likely being undercounted. This undercount is on top of the already concerning issue that, with the rise of home tests, most testers might not be reporting positive tests. Overall, the case count of COVID is likely significantly higher than the general population is seeing.

The impact that BA.4/5 has been having on individual countries is quite different depending on where you look. The impact has been more severe in countries like Portugal, where the population age trends older. In the long run, the impact will depend mainly on the country’s specific immunity profile and age distribution, meaning how many people have some level of immunity from vaccinations or previous infection and how old their population is on average [7]. BA.5’s ability to evade immunity might also prove concerning for individuals who will rely on their immunity garnered from infection with BA.5. It is possible that even after being infected with BA.5, immunity will not last as long as with previous variants.

Though BA.5 is more competent at invading immunity from any source, this is likely only for infection; meaning vaccinations will still protect from severe COVID-19, hospitalizations, and death.

Scientists base this hypothesis on the research of previous Omicron subvariants, which followed the same patterns [8]. Doctors and scientists highly recommend keeping up to date with vaccinations and boosters to provide the most protection possible [8].

Evolving vaccinations

With the changing conditions around COVID-19, vaccine manufacturers are looking out for the waning protection provided by their first round of vaccinations. The FDA recently indicated that manufacturers should be looking to include a BA.4/5-specific spike protein component in future doses to create a more effective vaccine [9]. Unfortunately, the problem comes down to timing. While preliminary data exists on new vaccines that will include a BA.1 spike protein, vaccine manufacturers have not submitted it to the FDA [10]. This is important because the FDA has required submission of this BA.1-specific data before submitting any data on BA.4/5-specific boosters [9]. Currently, the goal is to have a BA.1-specific booster by late August.

To put this into perspective, as illustrated by figure 2, BA.2, which made up over half of circulating subvariants in April 2022, is wholly undetectable in the population now [6]. By the time a BA.4/5 vaccine gets released, these subvariants will probably also be undetectable. Tight timing does not mean variant-specific vaccines are not worth the manufacturer’s time, however. BA.4/5 and future Omicron subvariants have plenty in common with each other. It is likely that a vaccine simply focused on any Omicron subvariant will provide significantly greater protection than current vaccines. It is a necessary step toward evolving alongside COVID-19, which is essential to protect the global community.

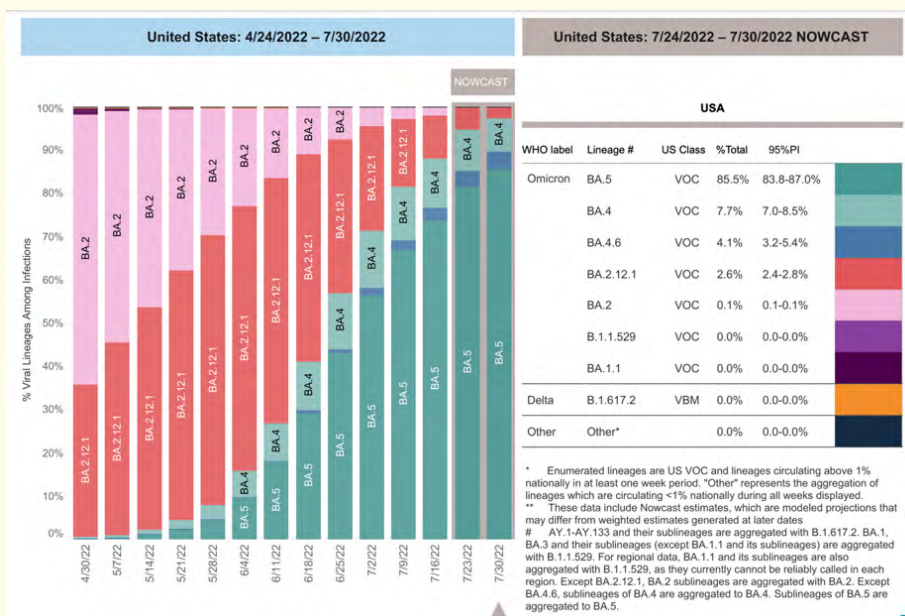


Figure 2: Variant Proportions by Week in U.S. [6].

The optimism surrounding vaccines does not mean scientists are not concerned about the future. Many scientists argue that a subvariant-specific vaccine is too narrow and that a broader scope is likely to be more effective [11]. Some experts insist that instead of having a BA.1 vaccine, manufacturers should instead focus on incorporating as many different aspects of each variant as possible to ensure more comprehensive protection. On the other hand, many scientists are also concerned about manufacturers' intense focus on Omicron. In a Nature article, Penny Moore, a virologist at the University of Witwatersrand in South Africa, stated, "My concern is that there's this huge focus on Omicron and the assumption that Omicron is what we will be dealing with in the future. We have a strong track record of getting that wrong" [11].

Like any other scientific innovation, evolving COVID-19 vaccines are not cut and dry. Instead, it will constitute a process of trying things out, seeing what works best, and then adapting again. COVID-19 will be around for the foreseeable future, and so should adapting protections.

The future of COVID-19 variants

COVID-19 will continue to evolve. New variants and subvariants will arise, some worthy of concern, some not. BA.2.75, first found in India in July 2022 and now in 15 countries, including the United States, could be a subvariant of future concern [4]. So far, experts know that BA.2.75 is spreading faster than any variant before, including the highly infectious BA.5 [12]. Despite this, experts warn that this is laboratory evidence. Evidence deduced in the lab is the first step in identifying variants, and it should not be used to make conclusive decisions about whether a variant is of crucial concern. BA.2.75 is still too new to be labeled concerning [12]. In the United States, as illustrated in figure 2, BA.2.75 is not on the radar [6].

On the other hand, BA.4.6, which U.S.-based scientists began detecting in early June 2022, has already begun to make its mark [6]. As of the week ending on July 30, BA.4.6, an Omicron sublineage of BA.4, made up approximately 4.1% of total cases [6]. It is still too early to know what BA.4.6 shares in common with other members of its lineage and what has changed. As of August 5, 2022, BA.4.6 is not a subvariant under monitoring, but it is likely that in the weeks to come, with its increasing case rates, the CDC will name it as such. Again, it is too early to know if this variant will be of serious concern, but it is one to consider.

As previously discussed, another concern is that soon, Omicron might not be the major VOC. At any point, another variant could emerge. This new variant could be more or less infectious, could cause more or less severe disease, and could more or less evade previous immunity. These uncertainties are why continual improvements to COVID-19 procedures, vaccinations, and communications are critical to ensuring the safety of the global population.

Discussion and Conclusion

BA.5 is a public health emergency. While hospitalizations and deaths are not rising in concordance with cases, it indicates the ability of COVID-19 to quickly mutate in a way that evades the protection measures that governments have put in place. Experts worry that focusing too heavily on variant-specific boosters might not be the solution that many people expect it to be. Vaccinations are not necessarily made to prevent illness. Therefore, no matter how specific the booster is, there will still be people getting infected, and they will still need to isolate. The precautions implemented at the beginning of the pandemic are still effective and should not necessarily be eliminated. It is simply necessary that these precautions be updated to fit with what scientists now know about current variants. Lastly, new variants will continue to emerge. Scientists, governments, and individuals should work to be united in improving our response to these mutations to maintain a level of normalcy for the world.

Conflict of Interest

The authors declare that there is no conflict of interest or financial interest.

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