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Editorial

What is Currently Known About the SARS-CoV2 Variants of Concern

The following four variants of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) are currently spreading worldwide and are labeled as Variants of Concern (VOC) according to the World Health Organization (WHO): the B.1.1.7 (also called 501Y.V1 or "SARS-CoV-2 VUI-202012/01") variant detected in the United Kingdom (UK) in September 2020, the B.1.351 (also called 501Y.V2) variant discovered in August 2020 in South Africa, the P.1 (also called B.1.1.28.1) variant discovered later in December 2020 in Brazil and Japan, and the B.1.617 variant discovered in India being the most recent addition to the list [1]. The three VOC from UK, South Africa and Brazil can have two mutations in common: the N501Y and E484K spike protein mutations, with the latter being more prevalent in the B.1.351 and P.1 variants [1]. According to the WHO, as of April 20, 2021, the presence of the UK, the South African and the Brazilian variants was reported respectively in 125, 67, and 43 countries, and as of May 2021, the Indian variant was recorded in 44 countries [1]. Moreover, the VOC phylodynamics are continuously updated on animated maps on the Global Initiative on Sharing All Influenza Data website. On top of these VOC, there are several additional variants of interest that are currently being investigated at national and international levels including the P.2 variant (also called B.1.1.28.2) detected in Brazil, and the CAL.20C (also called B.1.427/B.1.429) variant discovered in California [1].

The UK and South African variants seem to spread more easily than the original virus, with an increased transmissibility of up to 70% and 50% respectively [2]. The emergence of these VOC in the US has urged the Centers for Disease Control and Prevention to update their guidance on face masking in February 2021. The agency endorsed double masking or fitting a single mask tighter on the face, while the WHO has not issued a statement yet to support this position [3]. No other new precautions have been proposed.

Based on published analyses from Imperial College London, Public Health Scotland, Public Health England, and University of Exeter, the British government stated in February 2021, that being infected with the B.1.1.7 variant is correlated with an increased risk of hospitalization and death compared to the original COVID-19. However, the absolute risk of death per infection remains low [4]. According to the U.K.'s Office for National Statistics, the symptoms described in people infected with the UK variant as well as the incubation period seem to be similar to those of the original virus [5].

The U.S. Food and Drug Administration warned in January 2021, that any molecular testing method for COVID-19 can yield false negative results if a mutation occurred in the virus' genetic sequence detected by the test [6]. However, there are no major concerns regarding the polymerase chain reaction testing which is less affected by genetic variations due to its ability to detect multiple viral genetic sequences. A recent study concluded that the UK and South African variants have minor or no impact on the sensitivity of COVID-19 genetic testing protocols [7].

The UK variant is modestly more resistant to neutralization by sera from individuals who have received the vaccine against SARS-CoV-2 or have recovered from the disease [8]. However, the South African variant was poorly cross-neutralized by convalescent plasma from individuals infected with the original virus, with a 15.1-fold reduced efficacy compared to neutralization of the variant by plasma from individuals infected with this variant [9]. The UK variant maintained *in vitro* susceptibility to several monoclonal antibodies that are currently available and used against SARS-CoV2, where as the South African and Brazilian variants showed a marked reduction in *in vitro* susceptibility to bamlanivimab since they possess the E484K mutation. Imdevimab effectively neutralized South African lineage pseudoviruses containing the mutations N501Y, K417N, and E484K, whereas casirivimab, partially neutralized them [10]. In addition, Gilead has announced that remdesivir, the antiviral drug that has been used against the SARS-CoV-2, should remain effective against the VOC from UK [11].

Most of the currently developed vaccines, including Pfizer, Moderna, AstraZeneca, Johnson & Johnson, and Novavax, target the spike protein of the virus, the location of most of the variants' concerning mutations. It seems unlikely that COVID-19 could mutate to escape T cell recognition. T cells stimulated by the current vaccines against SARS-CoV-2 that should be able to protect against these new variants, as T cells recognize different parts of the virus. Since COVID-19 vaccines create an immune response to the totality of the spike protein, vaccines should theoretically still be efficacious despite some alterations of antigenic sites in the SARS-CoV-2 variants [12]. The UK variant showed a ~2-fold increase in resistance to vaccinee sera (Pfizer and Moderna), while the South African variant demonstrated an increase in resistance of ~6.5 to 8.6-fold, threatening the

protective effectiveness of current vaccines [13]. The BioNTech-Pfizer (BNT162b2) vaccine is slightly less effective against the UK and South African variants, but remains effective against the Brazil variant, and it demonstrated a powerful T-cell response against these variants after patients received the two doses [14]. In addition, a study on the highly vaccinated population of Qatar showed that the Pfizer vaccine remained active against the UK and South African variants with respective estimated effectiveness of 89.5% and 75.0% [15]. The Moderna vaccine (mRNA-1273) vaccine can offer protection against the UK variant and is believed to be protective against the South African variant [14]. The neutralization of many variants by the Pfizer and Moderna vaccines is largely preserved. However, the variants carrying the mutations K417N/T, E484K, and N501Y (Brazil and South African variants) are significantly more resistant to neutralization, even in fully vaccinated individuals [16]. The E484K mutation has also been noted in the UK variant conferring an estimated six-fold decrease in sensitivity to immune sera from individuals who received the Pfizer vaccine [17]. The AstraZeneca- University of Oxford (AZD1222) vaccine is effective against the UK and Brazil variants but not against the South African variant, which is why South Africa suspended the use of this vaccine after a study doubted its efficacy against the B.1.351 variant [14]. Novavax vaccine achieved 86% efficacy against the UK variant in a phase III trial, but 49.4% efficacy against the South African variant in another trial [18]. Johnson & Johnson vaccine trials resulted in efficacy of 72% in the US, 66% in Latin America, and 57% in South Africa, where the new South African variant is the most prevalent [19]. The SinoVac Vaccine (Coronavac) is effective against the UK and South African variants [14]. The Indian vaccine (Covaxin) is effective against the UK variant [14]. The SinoPharma vaccine (BBIBP-CorV) is effective against the South African variant [14].

Redesigning the vaccines currently being rolled out worldwide might be required. In fact, several COVID-19 vaccine manufacturers such as Moderna and Johnson & Johnson are looking into updating their vaccines to match spike mutations in the South African variant. Moderna and Pfizer are also exploring the idea of creating booster shots to improve protection against most variants. COVID-19 vaccines might necessitate periodic updates, as is the case for influenza vaccines. Fortunately, even if a new variant escapes current vaccination efforts, most of the available vaccines are relatively easy to repurpose for new variants [20].

CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

AUTHORS' CONTRIBUTION

TS and JRH contributed equally in designing and writing the manuscript. SSK supervised and edited the manuscript.

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