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Editorial: The 2022 World Health Organization (WHO) Priority Recommendations and Response to the Omicron Variant (B.1.1.529) of SARS-CoV-2

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Abstract The omicron variant of SARS-CoV-2, B.1.1.529, was included in the World Health Organization (WHO) list of variants of concerns (VOC) on 26 November 2021. Within only three months, omicron has spread rapidly to become the dominant variant in many countries. Studies have begun to evaluate the virulence, transmissibility, and degree of immune protection from current SARS-CoV-2 vaccines or previous of infection with the omicron variant. On 21 January 2022, the WHO published its seventh technical update and recommendations for priority actions in response to the omicron SARS-CoV-2 variant and cautioned that the overall risk from omicron remains high. At the start of this third year of the global COVID-19 pandemic, this editorial aims to summarize the evidence that supports the current priority recommendations and response from the WHO regarding the omicron variant of SARS-CoV-2, B.1.1.529.

Keywords: COVID-19 • SARS-CoV-2 • Variant of Concern • Omicron • Editorial

The omicron variant of SARS-CoV-2, B.1.1.529, was added to the World Health Organization (WHO) list of variants of concerns (VOC) on 26 November 2021 [1-3]. The WHO Technical Advisory Group on Virus Evolution identified omicron as a divergent SARS-CoV-2 variant with 26 to 32 mutations in the viral spike (S) protein [3,4]. These mutations involve the receptor-binding domain (RBD) and in the N-terminal domain (NTD) and may result in more efficient entry into the host cell, increased infectivity, and evasion of the immune response [4]. Notably, the omicron variant comprises four Pango lineages that include B.1.1.529, BA.1, BA.2, and BA.3 [3]. Diagnostic genomic testing using the polymerase chain reaction (PCR) identifies a 69-70 S protein deletion that causes a negative signal, known as S-gene target failure (SGTF) [5]. However, because SGTF is a diagnostic marker highly suggestive of the omicron variant, sequencing for at least a subset of SGTF samples should be performed because this deletion may be found in other VOCs [5].

Within three months, the omicron variant of SARS-CoV-2, B.1.1.529, has become the dominant variant in many countries and is still rapidly spreading. The symptoms and signs of COVID-19 from infection with the omicron variant of SARS-CoV-2, B.1.1.529, differ from previous variants [6,7]. Omicron affects the nasopharynx rather than the lungs, and the symptoms are milder, but the virus is highly transmissible [6,8].

The four main questions regarding the severity of the omicron variant of SARS-CoV-2, B.1.1.529, include: how transmissible omicron is; how much immunological protection occurs from previous infection and current vaccines; how virulent the omicron variant is when compared with other SARS-CoV-2 variants; and how should governments and populations understand these risks and follow public health and social measures [3,9].

On 21 January 2022, the WHO published its seventh updated technical brief and recommended priority actions and response to the omicron SARS-CoV-2 variant [9]. In this latest report, the WHO advises that the overall risk associated with the omicron variant remains high [9]. The main concern is that omicron has a significant advantage over the delta variant due to its increased transmissibility [9]. Infection with the omicron variant does carry a lower risk of severe COVID-19 and reduced mortality than previous SARS-CoV-2 variants, but the exceptionally high transmission levels result in a significant increase in hospitalization [9]. Therefore, there is still a concern that health care services will be overwhelmed, and there will be high levels of morbidity, hospitalizations, and possibly mortality in vulnerable individuals and the unvaccinated [9]. Several recent studies support the concerns expressed by the WHO regarding the omicron variant of SARS-CoV-2, B.1.1.529, and the other lineages [9].

First, clinical research supports the transmissibility of the omicron SARS-CoV-2 variant, B.1.1.529. A study in the UK showed that the omicron variant has a significant replication advantage, with higher secondary infection rates and a significantly higher observed reproduction (R) number when compared with the delta variant [10]. Other factors that may increase transmission rates are shorter serial infection intervals and an increased prevalence of asymptomatic infections [11]. Data from the Republic of Korea showed a serial interval for omicron infection of 2.22 days (95% CI, 1.48-2.97) when compared with 3.26 days (95% CI, 2.92-3.6) for the delta variant [11]. A study of vaccine trial participants in South Africa supports the possible contribution to increased transmission by high rates of asymptomatic infection with the omicron variant [12].

Second, there is evidence that the omicron SARS-CoV-2 variant, B.1.1.529, may escape from the effects of current vaccines and therapeutic neutralizing antibodies [13,14]. Modeling studies have shown that the omicron variant may be between 2-8 to >10 times more infectious than the delta variant [14]. Analysis of three-dimensional antibody-RBD complexes indicates that the omicron variant may escape the immune response from current vaccines [14]. Immune evasion, or re-infection risk, after past infection or vaccination, has a significant role in the rapid spread of the omicron variant [15]. Meta-analysis of antibody neutralization studies on convalescent sera conducted up to December 2021 showed a 20-fold drop in antibodies to the omicron variant [15]. However, individuals previously infected with omicron who then had two or three vaccine doses showed a 7-fold reduction in antibodies [15]. Reduced antibody titers to the omicron variant could increase the risk of re-infection [15]. However, preserved cellular immunity following omicron infection may prevent severe COVID-19, reduce hospitalization, and reduce mortality following infection with the omicron variant [16]. Limited studies from the UK, Denmark, Canada, and South Africa have evaluated only four SARS-CoV-2 vaccines, with early findings showing reduced infection prevention with the omicron variant compared with the delta variant [17,18]. Currently, the WHO has advised caution regarding early data on the efficacy of vaccines for infection with the omicron variant, which may be subject to observational bias [9]. Because of these concerns, the WHO is evaluating the efficacy of current vaccines by establishing a repository of data from animal models, antibody neutralization, and cellular immunity studies [19]. In January 2022, the WHO also established the Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) to evaluate the public health implications of the effectiveness of vaccines and emerging SARS-CoV-2 VOCs [20].

Third, preclinical and clinical studies have raised concerns regarding the virulence and pathogenic effects of the omicron

SARS-CoV-2 variant, B.1.1.529. A recent in vitro study published in *Nature* in January 2022 showed reduced replication of the SARS-CoV-2 B.1.1.529 variant in cultured human respiratory epithelial cells compared with other variants [21]. Mechanistic studies showed that this could be explained by reduced dependency on the transmembrane serine protease 2 (TMPRSS2) host protein that facilitates viral entry into the cell, compared with other variants [21]. Studies in K18-hACE2 transgenic mice, which express the human angiotensin-converting enzyme 2 (ACE2) receptor, showed reduced replication of the SARS-CoV-2 B.1.1.529 variant in the upper and lower respiratory tract and reduced lung damage, loss of body weight, and mortality [21].

Fourth, epidemiological studies have shown the severity of COVID-19 in terms of symptoms and hospitalizations may be less than for the alpha and delta variants. However, comparisons between countries and populations at this time have been challenging due to varying vaccination status, age, and comorbidity rates between populations. As of late January 2022, global infection rates for omicron remain high, but countries such as the UK that have implemented successful vaccination programs and achieved reduced rates of hospitalization and mortality from COVID-19, have begun to ease government-mandated social restrictions. However, it may be premature to assume that the omicron variant of SARS-CoV-2, B.1.1.529, causes mild disease or that there are no more emerging variants of SARS-CoV-2 with increased transmissibility, pathogenicity, or the ability to evade vaccine-induced immune responses. In their technical brief and recommendations for the omicron variant, the WHO has made the following recommendations: continued surveillance, monitoring, and testing using PCR-based screening methods; the rapid acceleration of vaccination programs for at-risk populations in all countries; the continued use of public health measures that include masks, physical distancing, crowd avoidance, indoor ventilation, and hand hygiene [9].

Conclusions

During 2022, local, national, and global initiatives, including from the WHO, will continue to evaluate the main concerns regarding the omicron variant of SARS-CoV-2, B.1.1.529, including disease severity, transmissibility, cellular and humoral immune responses to infection and vaccines, and the effectiveness of public health and social measures. It is clear that the global COVID-19 pandemic is far from over and that further variants of SARS-CoV-2 will continue to emerge. For these reasons, the WHO priority recommendations and response to the omicron VOC provide a vital global public health resource.

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