

## Editorial



# The Emergence of SARS-CoV-2 B.1.1.7 and the Future of Mega Sport Events: Is This the Tipping Point from Pandemic to Endemic?

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to cause significant morbidity and mortality globally. The emergence of new variants presents a new challenge in global public health and containment of the pandemic. Since the onset of the SARS-CoV-2, several new variants of concern have emerged, including Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.617.2), and most recently, Omicron (B.1.1.529) (1). The Omicron variant was first reported to the WHO by South Africa on November 24, 2021, and since then, it has rapidly spread to become the dominant variant worldwide. Reduction in neutralization efficacy against Omicron has raised concerns over waning of vaccine-elicited immunity, indicating altered pathogenesis and clinical severity of the disease (1).

More than 50 mutations have been associated with the Omicron variant (2), 32 (compared to 9 in the Delta variant) of which pertain to the virus spike (S) protein, the mediator of host cell entry (3). At least 15 spike protein mutations reside within the receptor-binding domain, enhancing angiotensin-converting enzyme 2 (ACE2) binding affinity and entry efficiency (4). A study by Chen J et al. (5) analyzed the relationship between receptor-binding domain mutations of the Omicron variant and viral infectivity and efficacy of existing vaccines or

antibody drugs. The study revealed that Omicron is about ten times more infectious than the original virus or twice as infectious as the Delta variant. Additionally, it revealed that Omicron's vaccine-escape capability is about twice as high as the Delta variant. Omicron may significantly reduce the efficacy of the Eli Lilly antibody cocktail and may also reduce susceptibility to monoclonal antibodies (mAbs). In this way, a study from Hong Kong indicated that Omicron SARS-CoV-2 infects and multiplies 70 times faster than Delta variant and original SARS-CoV-2 in the human bronchus, explaining the high transmissibility (6).

Biological evidence analysis suggests that the Omicron variant is evolving toward lower virulence relative to previously emerged variants of SARS-CoV-2. TMPRSS2, a protein in lung cells, appeared to engage less efficiently with the Omicron variant, provoking a localized, less severe upper respiratory tract infection (7). A retrospective multicentre cohort study in the USA signified a lower risk ratio of emergency visits (RR: 0.30, 95% CI: 0.28-0.33), hospitalization (RR: 0.44, 95% CI: 0.38-0.52), ICU admission (RR: 0.33, 95% CI: 0.22-0.48) and mechanical ventilation (RR: 0.16, 95% CI: 0.08-0.32) linked with Omicron as compared to the Delta variant (8). In South Africa, a study of a large cohort (n = 16,753) indicated a 59% reduced risk

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of death during Omicron's fourth wave compared to previous waves (9).

Data so far indicates that mRNA vaccines induce a remarkable neutralizing humoral and cellular immunity and have proven effective in tumbling infections, hospitalizations, and mortality. However, the vaccine alone has proven to be ineffective in preventing Omicron SARS-CoV-2 infection in many countries, leading to a high rate of reinfection. Data from Danish registers in December 2021 showed that the Omicron variant, compared to the Delta variant, has a 1.17 times higher secondary attack rate for the unvaccinated, 2.61 times higher for fully vaccinated, and 3.66 times higher for booster-vaccinated individuals (10). A study conducted by Imperial College London (11) revealed a high rate of reinfection associated with the Omicron variant (5.4 times higher than Delta), implying low post-infection protection compared to the SIREN cohort study of UK healthcare workers (19% vs. 85%). The study also estimated vaccine effectiveness against symptomatic Omicron infection between 0% and 20% after two doses and between 55% and 80% after a booster dose. Likewise, in Ontario, Canada, a recent preprint reported vaccine effectiveness following two doses of the coronavirus disease 2019 (Covid-19) vaccine to be 37% (95% CI: 19–50%) against Omicron infection as compared to 93% (95% CI: 92–94%) against the Delta variant (12).

Evasion of humoral response by Omicron variant has prompted researchers to shift their focus to the tendency of T-cell mediated immunity to protect against severe disease. A higher T cell response was observed amongst those receiving three doses of vaccine (two primary and one booster) or post-infection (+/- two doses of mRNA vaccines) as compared to participants receiving two doses of mRNA vaccines without infection (13). Research showed that up to 80% of T-cell reactivity (CD8+ and CD4+) against the Omicron variant is preserved (14). Pfizer and BioNTech indicated that a third dose of BNT162b2 increased the neutralizing antibody titer by 25-fold compared to two doses against the Omicron variant. In addition, a third dose also strongly increased CD8+ T cell levels against multiple spike protein epitopes that correlated with protection against severe disease (15). It has also been shown that vaccine effectiveness against symptomatic disease is lower for Omicron than for Delta, with

waning immunity by ten weeks after the third dose. The risk of hospitalization for symptomatic Omicron was reduced by 68% compared to unvaccinated ones following three doses of vaccines (16). Accordingly, Christensen et al. (17) revealed substantially increased vaccine breakthrough signals for the Omicron variant (51.4%). The author reported that 10.7% of the population had a breakthrough infection after receiving a booster dose (17), bringing about a debate on developing an Omicron-specific vaccine.

The present picture of the SARS-CoV-2 crisis is clouding the future of the pandemic. Even though Omicron may seem anecdotally milder than Delta or other variants of concern, the global exponential surge of heavily mutated Omicron variants will likely lead to more lethal strains as the virus mutates. Furthermore, it remains impossible to accurately characterize the full impact of the Omicron variant on the current vaccines. The degree of waning immunity depends on numerous factors, including vaccine product, target population, individual characteristics, duration of immunity, circulating virus, prior infection, vaccination, and public health measures. Current evidence about severity and hospitalization comes mostly from countries with high levels of population immunity. However, insufficient data is available for populations with different vaccination coverage and prior infections. Alternatively, optimism is growing that as the virus continues to circulate, widespread/herd immunity will be achieved, either through vaccination or natural infection, moving the path toward endemicity. However, for that to happen, the infection rate needs to stabilize over the years, rather than the current global image pointing toward continuous outbreaks.

Globally, COVID-19 continues to pose significant political, socioeconomic, scientific, and public health challenges. Large-scale mass gatherings, such as sporting, musical, and religious events, have historically been a significant source of infectious disease transmission and remain primarily a key challenge to global health (18-22).

In response to the current situation, major sporting events calendars, most notably the upcoming FIFA World Cup Qatar 2022, should consider more rigorous infection prevention and control measures intended for early detection, contact tracing, and isolation to contain the virus's spread.

Numerous examples of relevant research studies (23, 24) suggested the implementation of substantial public health policies such as mandatory complete vaccination ( $\pm$  booster dose) and/or COVID-19 recovery proof within the last six months and/or immunoglobulin-G antibodies showing protective immunity along with a negative COVID-19 RT-PCR certificate within the last 72 hours prior to departure. Additionally, the authors advised requiring fans, personnel, players, and media attending the stadium to provide evidence of a negative COVID-19 Rapid Antigen Test taken within 72 hours of the match. Moreover, they emphasized the efficiency of the bubble system when combined with stringent public health policies, which are regarded as the fundamental preventative measure concerning the multinational group of athletes.

Indeed, we believe that such robust measures and health care strategies are very important, much more so if, by the time a major sporting event such as the World Cup begins, a more lethal strain of COVID-19 has evolved. Meanwhile, if this was not the case and we no longer see deadly epidemics, the stated mandates may soon be rolled back in a reasonably safe manner, allowing fans and players to enjoy football.

Regardless of both scenarios, we know that the virus will continue to challenge our healthcare system. The pandemic looks like it will turn into an endemic, but it is still far from being over. Although epidemiological and clinical studies remain scarce, significant evidence points to the increased transmissibility of the Omicron as compared to previous variants.

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Despite preliminary evidence of immune escape and lower antibody neutralization in both convalescent and vaccinated sera, data on the impact of the Omicron variant on the effectiveness of COVID-19 vaccines, including booster doses, is still limited. However, vaccination is anticipated to continue to offer protection against hospitalization and death.

This is a loud wake-up call to public health authorities to ensure they have a preparedness plan and strengthen their healthcare system in preparation for “the worse.”

Accelerated booster vaccination campaigns and accessible public health measures, including mask-wearing, handwashing, surveillance, and quarantine, are essential to mitigate the surge of COVID-19. Global vaccine inequity remains the world’s most significant obstacle to ending this pandemic.

Further research is needed to understand better the relative impact of Omicron on vaccine effectiveness, breakthrough infections, the need for administering booster dose vaccines, and the severity and clinical outcomes associated with this variant.

## CONFLICT OF INTERESTS

The authors declare that the research was conducted without any commercial or financial relationships that could be constructed as a potential conflict of interest.

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