

## LETTER TO EDITOR

## SARS-CoV-2 outlook in 2023: what lies ahead?

*Panorama del SARS-CoV-2 en 2023: ¿qué nos espera?***Juan S. Serna-Trejos<sup>1</sup>, Stefanya G. Bermudez-Moyano<sup>2</sup>, Diego Prado-Molina<sup>3</sup>, Esteban Agudelo-Quintero<sup>3</sup>**

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**To editor:**

The global health contingency generated by SARS-CoV-2 has caused global effects in various spheres of human development, from alterations in the social, political, and ideological fields, to disorders in the biological sphere with high repercussions on human health, conditioning the appearance of high rates of morbidity and mortality associated with the virus. However, on the other hand, it also meant the creation of viable alternatives for pandemic control in historical time and, therefore, positive impacts on health generated by SARS-CoV-2<sup>(1)</sup>.

According to the World Health Organization (WHO), in the last bimester of 2022, the lowest mortality rates have been reported since March 2020, and they also foresee the presence of subsequent waves or peaks of the pandemic this year due to the Ómicron sub-variant and even other variants related to the virus of public health concern. However, in this last section discussed, they place special emphasis on the great preparation that was achieved globally, given the high rates of immunization, preventing the complications of severe infection. The WHO attributes the success of the different immunization programs of the different nations to immunization or coverage of the Wuhan variants (epicenter of the pandemic) and the Ómicron variant, as well as immunization of more sensitive and vulnerable populations (people over 60 years old and those with comorbidities and/or severe chronic illnesses)<sup>(2)</sup>.

Regarding the use of biological agents or immunizations associated with new immunization schemes, the efficacy of the use of a fourth dose for the mRNA vaccines BT162b2 and mRNA-1273 (Pfizer-BioNTech and Moderna) was considered low, given the predominance of the current variant of interest (Ómicron). However, the use of a fourth booster dose resulted in a reduction in the rates of morbidity and mortality associated with severe complications secondary to SARS-CoV-2 infection. Considerable progress has been made in Latin America in terms of immunization, given that population vaccination rates above 70% with a complete scheme (more than 2 doses) have been achieved. In Peru, a percentage of 83.3% of complete schemes is estimated (Figure 1)<sup>(3)</sup>.

It is necessary to mention that, previously, a drop in immunity was evidenced in the use of a third dose after six months of complete vaccination with any mRNA molecule (messenger RNA), meaning more possibilities of infection or reinfection, later secondary to the appearance of variant B.1.1.529 (Ómicron), which made it necessary to establish a fourth booster dose. Additionally, it was recorded that the use of successive doses did not mean the appearance of adverse reactions, nor was there any increase in local reactions related to the inoculation of the biological product, or constitutional symptoms after immunization<sup>(4,5)</sup>. The main circulating variants of interest for SARS-CoV-2 are listed in Table 1<sup>(6)</sup>.

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**Figure 1.** COVID-19 Observatory in Latin America and the Caribbean in the last century<sup>(1)</sup>

Arbel et al, through an observational study conducted in Israel that included approximately 564,000 patients, evaluated the use of a fourth dose of BNT162b2 in patients over 60 years of age during a certain period of infection with the Omicron variant or predominant strain. The study found that the use of the fourth dose resulted in low protection against short and uncertain duration of infection (approximately 3-8 weeks), but with lower rates of severe disease (75% efficacy against mortality compared to the use of a third dose)<sup>(7)</sup>.

To address the development of new biologics and their availability, it is necessary to remember the precedent of the first immunizing agents, which are developed using a novel mRNA technology (Pfizer and Moderna) targeting the S protein of SARS-CoV-2, and to a lesser extent, AstraZeneca, which used recombinant technology using adenovirus to express the S protein as the mechanism of action. Both vaccines were focused on the Wuhan strain. The Omicron variant of global interest is directly related to this, and therefore, using these classical agents developed by Pfizer, Moderna, and AstraZeneca more frequently, with aspects of revaccination, is not an effective measure for controlling this new variant. Hence, it is necessary to develop new dual strategies regarding strains that should contain the classic Wuhan strain and the Omicron variant, which harbors around 50 mutations. This is in line with the latest vaccination developments, and as a result, the FDA and EMA have approved the development of bivalent technologies adapted to the new variants, i.e., mRNA vaccines with the Wuhan strain and the Omicron variant. This bivalent technology is now part of the COVID-19 vaccination recommendations in some European countries such as Spain, but it has not been fully adapted as more regulatory entities demand safety studies on the use of these vaccines, such as commercialization and pharmacovigilance studies<sup>(8,9)</sup>.

**Table 1.** Main SARS-CoV-2 variants in circulation according to year of appearance

WHO designation	Pango Lineage	Main samples documented
Ómicron*	B.1.1.529	Various countries November 2021
Ómicron*	BA.4#	South Africa, January 2022
Ómicron*	BA.5#	South Africa, January 2022
Ómicron*	BA.2.12.1	USA, December 2021
Ómicron*	BA.275**	India, May 2022
Alfa	B.1.1.7	United Kingdom, September 2020
Beta	B.1351	South Africa, May 2020
Gamma	P.1	Brazil, November 2020
Delta	B.1.617.2	India, October 2020
Epsilon	B.1427; B.1427	USA, March 2020
Dseta	P.2	Brazil, April 2020
Eta	B.1525	Various countries, December 2020
Zeta	P.3	Philippines, January 2021
Iota	B.1526	USA, November 2020
Kappa	B.1.617.1	India, October 2020
Lamnda	C.37	Peru, December 2020
Mu	B.1.621	Colombia, January 2021

Taken and adapted from: WHO. Tracking of SARS-CoV-2 Variants<sup>(6)</sup>.

The objectives for 2023 are clearly focused on controlling strains derived from the Wuhan serotype, such as Omicron and its mutations. It also involves the use of new therapies such as nasal vaccines, the use of dual vaccines for SARS-CoV-2 and influenza, the prudent use of respiratory masks, the use of new antiviral biologics aimed at inhibiting the 3CL protease present in the classic strain and Omicron (Ensirelvir, Ensovibep, and Aplidin), as well as the treatment of complications generated in the post-COVID-19 stages (Long COVID Syndrome)<sup>(10-12)</sup>.

### Author's contribution

All authors have contributed in the conception, drafting of the final manuscript, revision and approval of the manuscript.

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