

# Surfing the third wave

*Surfando a terceira onda*

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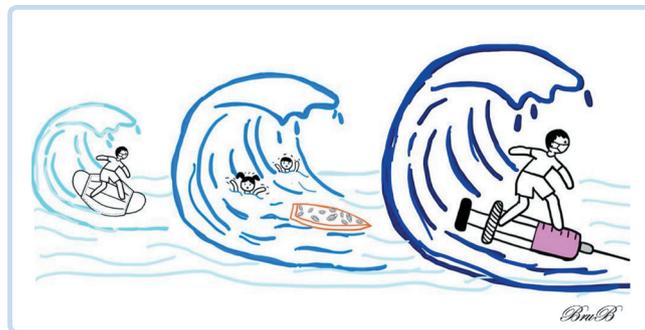
The COVID-19 pandemic reaches two years in March with the staggering figures, officially reported, of more than 400 million infections and about 6 million lives lost in all parts of the world.<sup>1</sup> In Brazil, 28 million infections and 650 thousand deaths have been confirmed so far, in addition to possible underreporting.<sup>1</sup> It will take a few decades to have a more realistic perception of the impact of the pandemic on public health, the economy and society, as well as the changes triggered by COVID-19 in our lives.

Health professionals and scientists have never studied, learned and worked so hard before. In PubMed, the term “COVID-19” was identified in 230 thousand publications, corresponding to more than 300 manuscripts per day. Many questions were answered and much knowledge gained. The well-deserved recognition also came, including the appreciation of Clinical Immunology and Allergy.

However, facing the pandemic also has its obscure pages written by: politicians who are not up to the challenges and demands required by the pandemic;

opportunistic and irresponsible people; crooks who invent and spread false information; criminals who appropriate funds earmarked for health; among other evil forces. It is very sad and exhausting the energy wasted on unfruitful discussions, but they are

necessary to better guide the population about the fact that COVID-19 is not only a “little flu”, that many of the medicines used in the acute phase of the disease do not have scientific evidence, and that vaccines are safe and effective.



The influence of socioeconomic inequality and the heterogeneity of health systems was also evident on the outcomes of the pandemic. We analyzed the presence of antibodies against SARS-CoV-2 in healthcare workers with no previous history of infection and who were providing care to patients with COVID-19 during the first wave of the pandemic. We observed a seroprevalence of 14%. Factors statistically associated with higher seropositivity were: lower schooling (aOR of 1.93), use of public transport to travel between home and work (aOR of 1.65) and cleaner professionals or hospital security (aOR of 10.1).<sup>2</sup> Another study showed that

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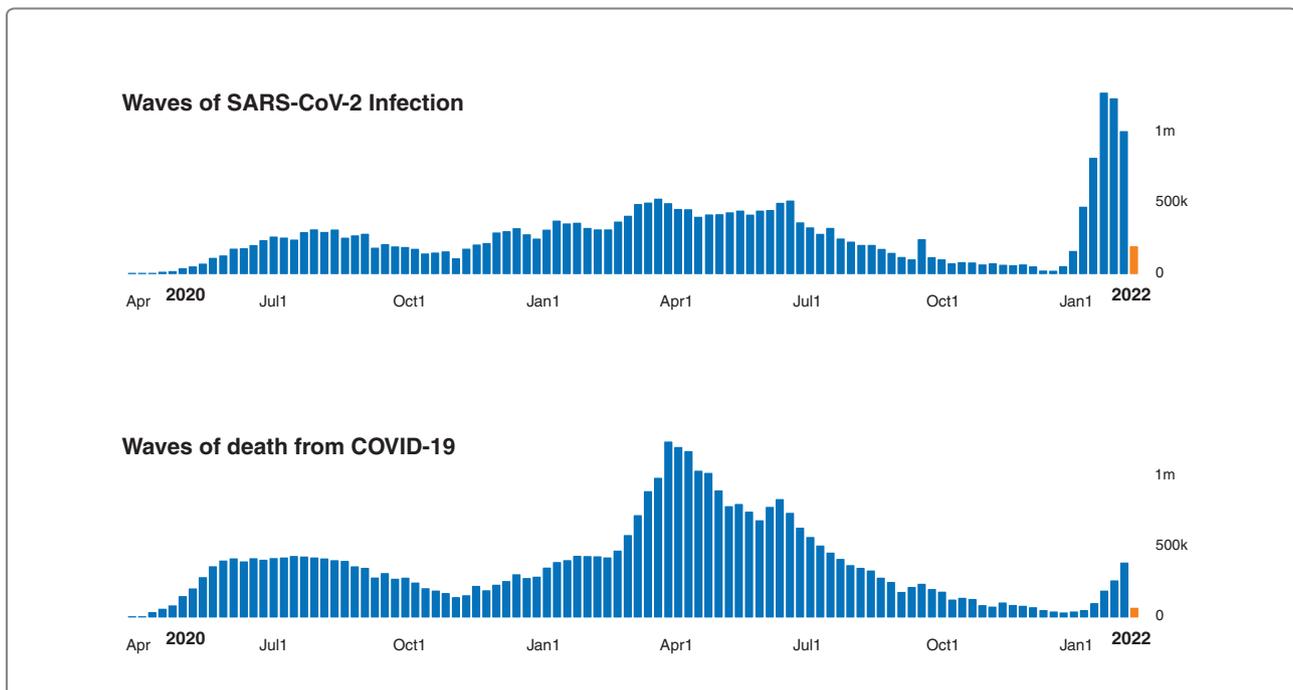
mortality from COVID-19 in Manaus in people over 70 years old was double and triple compared to those observed in Rio de Janeiro and São Paulo, respectively.<sup>3</sup>

In the beginning, hygiene and social distancing measures were the interventions that contributed to the control of the pandemic. Subsequently, the anti-SARS-CoV-2 vaccination became the turning point in the fight against COVID-19. About 10 billion doses of vaccines have been administered worldwide, although heterogeneously distributed among different countries, with the lowest vaccination rates observed in Africa. In Brazil, approximately 75% of the population is fully vaccinated and 10% others received at least the first dose.<sup>4</sup>

As the months passed, but before the pandemic completed a year, we found that we would have more than one wave of coronavirus infections. At least three factors contribute to the resurgence of COVID-19 and with the increase in cases: decrease in hygienic habits and social distance; decreased immune response over time after natural SARS-CoV-2 infection or vaccination; and, mainly, the emergence of variants of the virus. While the vast majority of countries faced

four distinct waves, in Brazil we are experiencing our third wave as a result of infections with the Omicron variant (Figure 1).<sup>1</sup> Here there was a combination of infections caused by more than one variant, in addition to observing greater circulation and impact of the Gamma variant (P1) in relation to Delta, during our second wave.

As with other viruses, SARS-CoV-2 undergoes random mutations of its genome and continually adapts to changes in the environment through the process of natural selection. Most mutations are neutral or harmful to the virus; however, few mutations can provide advantages, such as increased transmissibility, escape from the immune system of a host previously activated by vaccination or previous infections, resistance to antivirals, escape from diagnostic detection, among others. The World Health Organization (WHO) calls these SARS-CoV-2 variants with such characteristics as variants of concern (VOCs). Variants that have specific genetic mutations that can translate into adaptive advantages to the virus need to be monitored and are called variants of interest (VOIs). The WHO system decided to name variants after letters of the Greek alphabet in order



**Figure 1**

SARS-CoV-2 infections and COVID-19 deaths per week from 2020 to 2022

m = million, k = thousand.

Source: WHO (<https://covid19.who.int/>)

to facilitate the sharing of research knowledge with a wider audience, but also provide a platform to enable uniform global discourse around VOIs and VOCs, and avoid stigmatization of places where variants were discovered.

The Omicron variant of SARS-CoV-2 (B.1.1.529) was identified in Africa in late 2021. Compared to the other four previously identified VOCs (alpha, beta, gamma and delta), the Omicron variant is the strain with the highest number of mutations, with 97 mutations accumulated throughout the genome, including at least 33 mutations in the spike protein. Studies have shown that the different mutations of this variant confer increased infectivity with greater affinity of the virus for the ACE2 receptor and immune escape compared to the wild-type initial strain and the other VOCs.<sup>5</sup> Changes in viral antigenicity causes significant coronavirus evasion to the therapeutic monoclonal and polyclonal neutralizing antibodies induced by the original two-dose vaccine schedule. A third dose with mRNA vaccine rescues and extends neutralization.<sup>6</sup> The Omicron variant has become the dominant strain, accounting for record new infections per day worldwide, and brings additional challenges to the prevention and control of COVID-19.

Fortunately, we observed that, despite the rapid increase in new cases of SARS-CoV-2 infection with the circulation and dominance of the Omicron variant, there is not a proportional increase in the number of deaths. Scientific evidence in experimental animal models suggests that this variant has some intrinsic characteristics that make it less virulent, pathogenic and lethal. The Omicron variant has a lower capacity to cleave the spike protein and to bind to the human TMPRSS2 receptor, two properties that help in viral invasion, in addition to a lower activity of inducing multinucleated syncytia in host cells.<sup>5,6</sup> Consequently, there is less tissue damage compared to other variants, especially in human cells that express the TMPRSS2 receptor, such as pneumocytes.<sup>2</sup>

Which factor differentiates the third wave of COVID-19 from others? This time the virus is facing a population with some degree of immunity triggered by vaccination and/or previous infections by other variants. A study by the VISION network showed

that the efficiency of mRNA vaccines in preventing infections by the Omicron variant that lead to hospitalization reaches 91% during the first two months of the third vaccine doses, and 78% after four months.<sup>7</sup> According to CDC data, at the end of 2021, the risk of individuals aged 18 years and over without vaccination of having a fatal infection with SARS-CoV-2 was 68 times greater than in those vaccinated with three doses.<sup>8</sup> Therefore, what is the main message to be highlighted and disseminated? Keep the vaccination for COVID-19 up to date to minimize the risks of contracting the disease and its serious evolutions.

## Acknowledgment

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