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## Review Article

# COVID-19 and isolation: Risks and implications in the scenario of new variants



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## ABSTRACT

With the emergence of new variants of SARS-CoV-2, questions about transmissibility, vaccine efficacy, and impact on mortality are important to support decision-making in public health measures. Modifications related to transmissibility combined with the fact that much of the population has already been partially exposed to infection and/or vaccination, have stimulated recommendations to reduce the isolation period for COVID-19. However, these new guidelines have raised questions about their effectiveness in reducing contamination and minimizing impact in work environments. Therefore, a collaborative task force was developed to review the subject in a non-systematic manner, answering questions about SARS-CoV-2 variants, COVID-19 vaccines, isolation/quarantine periods, testing to end the isolation period, and the use of masks as mitigation procedures. Overall, COVID-19 vaccines are effective in preventing severe illness and death but are less effective in preventing infection in the case of the Omicron variant. Any strategy that is adopted to reduce the isolation period should take into consideration the epidemiological situation of the geographical region, individual clinical characteristics, and mask for source control. The use of tests for isolation withdrawal should be evaluated with caution, due to results depending on various conditions and may not be reliable.

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## Introduction

COVID-19 is a highly contagious disease caused by the SARS-CoV-2 virus, which had the first documented cases in Wuhan, China, in December 2019.<sup>1</sup> In Brazil, the first case was reported on February 26, 2020, and the pandemic state was declared by the World Health Organization (WHO) in March 2020.<sup>2</sup>

Since then, cases and deaths have accumulated and, according to the WHO panel (<https://covid19.who.int/>), more than 595,219,966 cases and 6,453,458 deaths have been confirmed worldwide.<sup>3</sup>

As the pandemic progressed, new variants emerged, which changed the global epidemiological scenario and challenged the health systems in terms of identification, transmissibility, impact on healthcare and hospitalizations, input supply, and availability of human resources in all regions of the world.<sup>4,5</sup>

On the other hand, one of the greatest scientific achievements during this period was the accelerated development of several safe and effective vaccines against this infection. Vaccines against COVID-19 started to be available in December 2020, and Brazil started vaccination in January 2021.<sup>6</sup>

Robust data support that COVID-19 vaccines are effective in protecting people from severe disease and death.<sup>7-9</sup>

**Table 1 – Previous and current main circulating VOCs.**

WHO nomenclature	Lineage	First documented sample	Date of designation as VOC
Alfa	B.1.1.7	United Kingdom, September 2020	12/18/2020
Beta	B.1.351	South Africa, May 2020	12/18/2020
Gama	P.1	Brazil, November 2020	1/11/2021
Delta	B.1.617.2	India, October 2020	5/11/2021
Omicron (currently circulating)	B.1.1.529; BA.1; BA.2; BA.3; BA.4; BA.5	Multiple countries, November 2021	11/26/2021

VOC, Variants of Concern.  
Source: Adapted from WHO – Tracking SARS-CoV-2 variants.<sup>4</sup>

However, vaccines alone will not be enough to stop the pandemic, partly because of the emergence of new and more transmissible variants, considering that the objective of the vaccines is to protect against severe outcomes and death.

The more the virus circulates, the more opportunities it has to evolve. Since the virus will continue to adapt and new variants may be more transmissible, infections can become more or less severe, and/or develop immune breakthrough properties.<sup>10,11</sup>

In the context of the predominant circulation of the Omicron variant<sup>12</sup> in a population that has already been partially exposed to infection and/or vaccination, some proposals have been made to reduce COVID-19 isolation periods both by international and national guidelines.<sup>13,14</sup>

However, some concerns have been raised about the implications of these measures, and to clarify these issues, a collaborative task force was developed among the scientific societies<sup>5</sup> and other experts to review and compile the main information available in a non-systematic way.

For presenting this review, the contents were divided into the following topics: SARS-CoV-2 variants, COVID-19 vaccines, isolation and quarantine periods, the applicability of laboratory testing for ending the isolation period, and the use of masks as mitigation measures.

## SARS-CoV-2 variants and their impact

All viruses, including SARS-CoV-2, mutate over time, with many of these mutations having little or no impact on virus characteristics. However, some mutations may affect their properties, such as their ease of spread, the severity of the associated disease, or the performance of vaccines, drugs, diagnostic tools, or other social and public health measures.<sup>4</sup>

The WHO, in collaboration with partners, expert networks, national authorities, institutions, and researchers, is monitoring and assessing SARS-CoV-2 evolution since January 2020. Towards the end of 2020, the emergence of variants that posed an increased risk to global public health led to the characterization of Variants of Concern (VOCs) and Variants of Interest (VOIs) to prioritize global monitoring and research and ultimately contribute to the ongoing COVID-19 pandemic response [Table 1](#).<sup>4</sup>

With the widespread transmission of the Omicron VOC worldwide and the subsequent expected increased viral diversity, WHO has added a new category to its variant screening system, called “VOC Lineages Under Monitoring” (VOC-LUM) to signal to public health authorities globally

which VOC lineages may require prioritized attention and monitoring. The current main VOC-LUMs are described in [Table 2](#).<sup>4</sup>

The Omicron variant has 34S protein mutations, compared to nine mutations in the Delta variant,<sup>15</sup> and can partially evade immunity generated by vaccines or previous infection.<sup>16,17</sup> The risk of reinfection in patients previously infected with COVID-19 is evident, indicating high transmissibility.<sup>18</sup>

The transmissibility of the Omicron variant was assessed in the province of Gauteng, South Africa, using a mathematical inference model. This model included underreporting, seasonality, nonpharmaceutical interventions, and vaccination estimating the Omicron variant to be 100.3% (95% CI 74.8%–140.4%) more transmissible than the ancestral strain and 36.5% (20.9%–60.1%) more transmissible than the Delta variant.<sup>19</sup>

Evidence shows that the disease induced by the Omicron variant is milder at the population level.<sup>12,20,21</sup> However, even with the minor consequences of Omicron infection, its high transmissibility may still contribute to an enormous impact on the population and healthcare institutions even if a smaller proportion of infected patients is hospitalized, not to mention the possibility of the emergence of new VOCs.<sup>22</sup>

As for clinical presentation, while circulating the Omicron variant, one study identified a lower hospitalization rate (42.3% vs. 69%) and need for oxygen therapy (17.6% vs. 74%), less intensive care admission (18.5% vs. 29.9%), shorter mean

**Table 2 – Omicron subvariants under monitoring.**

Lineage	Relationship to circulating VOC lineages	Earliest documented samples
BA.4	BA.1 and BA.2 sister lineage	South Africa, Jan-2022
BA.5	BA.1 and BA.2 sister lineage	South Africa, Jan-2022
BA.2.12.1	BA.2 sublineage	United States of America, Dec-2021
BA.2.9.1	BA.2 sublineage	Multiple countries, Feb-2022
BA.2.11	BA.2 sublineage	Multiple countries, Feb-2022
BA.2.13	BA.2 sublineage	Multiple countries, Feb-2022
BA.2.75	BA.2 sublineage	India, May-2022

Source: Adapted from WHO – Tracking SARS-CoV-2 variants.<sup>4</sup>

length of stay (3 vs. 8 days), and a higher proportion of unvaccinated hospitalized patients (66.4% vs. 24.2%).<sup>23</sup>

In a comparative analysis of the transmissibility period, Omicron infection had a shorter duration of 9.87 days (8.83–10.9) compared to 10.9 days for Delta-infected individuals (9.41–12.4).<sup>24</sup>

Regarding incubation period and transmissibility, a study conducted in Japan using quantitative RT-PCR and viral isolation of 83 respiratory samples from 21 patients infected with the Omicron variant, found that viral RNA quantification peaked at 3–6 days after diagnosis or symptom onset, which then gradually declined over time, becoming more pronounced after 10 days of diagnosis or symptom onset. Positive viral isolates showed a trend similar to the one with viral RNA quantification and no infectious virus was detected in the respiratory samples 10 days after diagnosis or symptom onset (Table 3).<sup>25</sup>

Despite the small size of the sample that made it impossible to derive robust conclusions or extend the results to other realities, these findings raise the hypothesis that vaccinated subjects infected with the Omicron variant are unlikely to spread the infectious virus after 10 days of symptom onset.

### Considerations on the impacts of vaccination on COVID-19

The impact of a vaccine can be measured by assessing its effects directly on the vaccinated subject, indirectly on the unvaccinated community (collective immunity), on the epidemiology of the pathogen (such as differences in circulating variants or prevention of epidemic cycles), and the additional benefits from health improvements.<sup>26</sup> Vaccine efficacy refers to its performance in a carefully controlled clinical trial, and vaccine effectiveness is its performance in real-world observational studies.<sup>27</sup>

According to definitions proposed by US Centers for Disease Control and Prevention (CDC), people are up to date with their COVID-19 vaccination when they have received all doses in the primary series and all boosters recommended, when eligible.<sup>28</sup>

COVID-19 vaccines seem to have high efficacy against severe diseases and death, but low efficacy against infection.<sup>29</sup> Some studies have shown that fully vaccinated people have shorter symptom durations, less severe disease, and lower mortality, and when they have COVID-19, the protective antibody levels are significantly higher than those in unvaccinated subjects who have experienced SARS-CoV-2 infections.<sup>30</sup> Although fully vaccinated people remain at risk of infection with SARS-CoV-2, if infected, they are likely to have shorter periods of contagiousness than unvaccinated individuals.<sup>31</sup>

In Vaccine Efficacy (VE) studies, COVID-19 vaccines were shown to prevent infections in a fully vaccinated population by 85% (71%–93%), and by 84% in symptomatic laboratory-confirmed COVID-19 in adults aged  $\geq 18$  years (70%–91%). The efficacy in preventing hospitalization was 85% (70%–92%) and nearly 100% in preventing death. In addition, the vaccine reduces transmission by 48% (45%–52%) in vaccinated people.<sup>30</sup>

A document from the Vigivac Project, conducted at Fundação Oswaldo Cruz (Fiocruz), published in December 2021 analyzed the four vaccines administered in Brazil (Coronavac, AstraZeneca, Pfizer, Janssen) between January and October of the same year and pointed out that all of them greatly reduced the risks of infection, hospitalization, and death by the disease. The analysis used information from the national vaccination campaign database, flu syndrome notifications (e-SUS Notifica), and Severe Acute Respiratory Syndrome (SARS) notifications (SIVEP-Gripe). Protection ranged from 83% to 99% with all immunizers considering severe outcomes (hospitalization or death) in people aged 20–80 years.<sup>32</sup>

Meta-analyses of real-life studies conducted before the emergence of the VOCs indicated that the effectiveness of approved vaccines ranges from 85% to 95% seven or more days after the full regimen.<sup>33</sup>

Concerning the efficacy of the mRNA-1273 vaccine against infection and hospitalization comparing Delta and Omicron variants, after the third dose, VE for Delta was 86.0% (78.1%–91.1%)  $> 60$  days, and for Omicron VE was 47.4% (40.5–53.5)  $> 60$  days. As for hospitalization prevention, the VE of the second and third doses were both  $\geq 99\%$  for Delta

**Table 3 – Number and percentage of viral RNA detected by RT-PCR or positive viral isolation in cultures of respiratory samples during SARS-CoV-2 (Omicron variant) infection, Japan.**

Interval in days	Number (n) and percentage (%) of RT-PCR positive samples	Number (n) and percentage (%) of positive viral isolation	Number (n) and percentage (%) of positive viral isolation in RT-PCR-positive samples
Since symptom onset	Symptomatic cases only; n (%)		
1–2 days	15/16 (93.8)	2/16 (12.5)	2/15 (13.3)
3–6 days	8/8 (100)	4/8 (50)	4/8 (50)
7–9 days	16/16 (100)	3/16 (18.8)	3/16 (18.8)
10–13 days	7/12 (58.3)	0/12 (0)	0/7 (0)
14 days or more	4/10 (40)	0/10 (0)	0/4 (0)
Since positive RT-PCR test	Asymptomatic cases only; n (%)		
0–5 days	6/6 (100)	3/6 (50)	3/6 (50)
6–9 days	3/4 (75)	0/4 (0)	0/3 (0)
10 days or more	1/10 (10)	0/10 (0)	0/1 (0)

Source: Adapted from the National Institute of Infectious Diseases (NIID) and the Centers for Disease Control and Prevention within the National Center for Global Health and Medicine (NCGM/DCC).<sup>25</sup>

and 84.5% (23.0%–96.9%) and 99.2% (76.3%–100%) for Omicron infections, respectively.<sup>34</sup>

A narrative review study comparing COVID-19 vaccines against SARS-CoV-2 and VOCs in a fully vaccinated population showed effectiveness against symptomatic infection for mRNA vaccines of 88%–100% for Alpha variant, 76%–100% for Beta/Gamma, and 47.3%–88% for Delta. AstraZeneca (AZ) vaccine effectiveness against the disease was 74.5% for Alpha and 67% for Delta in the UK. CoronaVac effectiveness was 36.8%–73.8% against Alpha/Gamma/D614G strain in Chile and Brazil. Effectiveness against hospitalization and death was 87%–94% for not sequenced strains, 89%–95% against Alpha, 95% against Beta/Gamma, 96% against Alpha/Delta, and 80%–95% against Delta for mRNA or AZ vaccines. CoronaVac was very effective against hospitalization (87.5%) and mortality (86.3%) and the Janssen vaccine had an effectiveness of 60%–85% against Delta.<sup>35</sup>

Protective antibodies has been reported to be present 6–8 months after complete vaccination and may change in the presence of variants.<sup>33,36,37</sup> Observational studies identified decreasing effectiveness at 4–6 months (42%–57%) for mRNA vaccines and 47.3% for AZ against Delta infection. The effectiveness against hospitalization remained high (77%–93%) for mRNA vaccine and AZ (70.3%) at 4–6 months after full vaccination and 68% at > 28 days after full immunization for Janssen vaccine.<sup>35</sup>

A recent study conducted in Qatar has shown that hybrid immunity (recent mRNA vaccination and prior infection) enhances protection against symptomatic infection by the Omicron BA.1 and BA.2.<sup>38</sup> These findings reinforce the importance of vaccination, even among previous COVID-19 cases.

The period of contagiousness in immunocompromised people seems to be longer than that in immunocompetent people.<sup>39</sup> The immunogenicity and efficacy of COVID-19 vaccines also seem to be lower in immunocompromised individuals as compared with the general population. Liver, kidney, and heart transplant recipients demonstrated reduced responses to the messenger RNA (mRNA)-based vaccine, with neutralizing antibodies detected in only 47.5%, 37.5%, and 49% of patients after vaccination, respectively.

As for the Omicron variant, a recent analysis showed that the VE for infection in immunosuppressed patients was only 29.4% (0.3%–50.0%) after the third dose of mRNA-1273, indicating the possible need for additional doses.<sup>34</sup>

To date, while in the immunocompetent population there is information available on the effectiveness of vaccines that encourage reduced isolation time, in immunosuppressed patients there is no adequate data to support this recommendation, and the guidelines already established should remain.<sup>13,40,41</sup>

## Isolation and quarantine considerations in COVID-19

While isolation is the separation of infected from uninfected individuals during the period of disease transmissibility, quarantine is a preventive measure recommended to restrict the movement of people, who have been exposed to a contagious disease, during the period in which they can become ill.

Both are essential public health strategies to protect the population and prevent the spread of contagious diseases such as COVID-19.<sup>13</sup>

The Brazilian Ministry of Health considers a COVID-19 contact a person who had close contact with a confirmed case during its transmissibility period (48 h before through 10 days after the onset of signs and/or positive test), considering a person who: (a) Was at a distance of less than one meter from a confirmed case for at least 15 min without both wearing face masks or wearing incorrectly; (b) Had direct physical contact with a confirmed case; (c) Is a healthcare professional who provided care to a COVID-19 case without wearing Personal Protective Equipment (PPE) as recommended or while wearing damaged PPE; or, (d) Is a household contact of a confirmed case.<sup>13</sup>

Epidemiological studies conducted at the beginning of the pandemic identified a mean incubation period that ranged from 4.0 to 5.1 days to 12.5–14 days.<sup>42–45</sup> The transmissibility period starts 1–2 days before the onset of symptoms and it reaches peak viral load approximately at day 4,<sup>46</sup> after which it declines, with the recovery of viable virus in culture up to eight days after the onset of symptoms in mild cases<sup>47</sup> and 15–20 days in severe/critical cases or severely immunosuppressed patients.<sup>39</sup> Although transmission is possible from asymptomatic individuals,<sup>48</sup> it is more common from symptomatic or pre-symptomatic individuals and can occur even before and after peak transmission.<sup>13,49</sup>

In the early pandemic, the isolation period recommended by the WHO for symptomatic patients was 14 days and at least 72 h without fever with no use of antipyretics, as well as improvement in respiratory symptoms.<sup>50</sup> Subsequently, this period was shortened to 10 days with three asymptomatic days.<sup>51</sup>

As knowledge about the disease was built, isolation duration was stratified according to case severity and presence of immunosuppression and the CDC recommended 10 days for mild, asymptomatic, and non-immunosuppressed cases, and 20 days for severe and immunosuppressed cases, which was incorporated by the Brazilian Health Surveillance Agency (ANVISA).<sup>41</sup>

The asymptomatic status of a significant portion of reinfected patients fully vaccinated against COVID-19 and the fact that they have reduced viral load compared to non-vaccinated patients have been a basis for the possibility of reducing the isolation period, as long as the guidelines for distancing, hand hygiene, and mask use are strengthened, as proposed by the CDC in January 2022.<sup>33,36</sup>

By this guideline, the isolation period was reduced to five days for asymptomatic individuals or those showing symptom improvement, provided they continue to wear masks well-fitted to the face for another five days,<sup>14</sup> based on the concept that most infections are transmitted one to two days before the onset of symptoms, with a peak on day 4 and a decline thereafter.<sup>46</sup>

In addition, the quarantine recommendations for the general population exposed to COVID-19 were updated according to the vaccination status. A quarantine of five days and an additional five days of wearing masks was recommended for unvaccinated individuals or after six months from vaccinating without a booster dose, and no quarantine was necessary

(only mask use for 10 days) for those who had received the booster dose. As a best practice, it is also recommended that a diagnostic test for SARS-CoV-2 be performed after the fifth day of exposure.<sup>14</sup>

However, despite the evidence that people vaccinated against COVID-19 transmit less the disease, there are still no consistent data available on the duration of transmission time with either two or three vaccine doses, especially with enough information contextualized in the current scenario of new variants predominance in Brazil and worldwide for an adequate conclusion on isolation time reduction in infected vaccinated individuals.<sup>52</sup>

The main risk identified in reducing isolation time is the potential increase in SARS-CoV-2 transmission due to potentially infectious residual viral load associated with non-adherence to the recommended mitigation measures.<sup>41,53</sup>

The high transmissibility of the Omicron variant associated with vaccine breakthrough may potentially impact the expected absolute number of moderate to severe cases, affecting not only the demand for health services, but also the workforce, infection control actions, and the quarantine and isolation of infected cases.<sup>53–55</sup>

In health services, the greatest expected risks would be for hospitalized patients in vulnerable situations, at the time of visiting family members or companions who may still be transmitting, and for health professionals in resting and eating areas, i.e., in places where the professionals remove their masks, favoring transmission.<sup>56</sup>

Thus, understanding that the isolation and quarantine period after infection or confirmed exposure depends not only on the incubation and transmissibility period but also on the subjects compliance with the additional measures to mitigate the risk of viral transmission, official recommendations should consider different scenarios and local data to establish the most appropriate rules, constantly monitoring the effects on the epidemiological progression of the pandemic.

In Brazil, the recommendations on the isolation period were updated by the Ministry of Health which reduced the interval to seven full days if the initially symptomatic patient is already without fever for 24 h with no use of antipyretics and no respiratory symptoms, provided maintaining mask use until the tenth day. For asymptomatic patients, the isolation period has been updated to five days if RT-PCR or Rapid Antigen Test (RAT) is negative on day 5, also maintaining the use of masks until day 10.<sup>13</sup>

For hospitalized patients, ANVISA has maintained the recommendation of 10 days of isolation for asymptomatic or mild/moderate cases in non-immunosuppressed patients and 20 days for severe/critical cases or in immunosuppressed patients if there has been no fever for 24 h and the related symptoms have improved.<sup>41</sup>

## Considerations on the use of tests for ending isolation/quarantine

The gold standard test for COVID-19 diagnostic confirmation is RT-PCR. The sensitivity of this test varies according to the type of sample (nasopharyngeal/oropharyngeal secretion, saliva, feces, etc.), collection procedure, transport/

conservation, number of targets (genes) used for identification, and collection period concerning symptom onset.<sup>57</sup>

The standardized sample in most countries is nasopharyngeal secretion, and sampling recommendations include transport in saline or specific media, as well as refrigerated/frozen preservation to ensure better virus recovery. Ideally, RT-PCR reactions should have at least two targets in different genes, and the sample should be collected after 1–3 days of symptom onset.<sup>57</sup> Considering these variables, the diagnostic sensitivity can be higher than 95%. The specificity of the RT-PCR assay is approximately 100%, which may be compromised in occasional cases of contamination during reaction or analytical problems.<sup>58</sup>

As for the period in which viral RNA can be detected by RT-PCR, most clinically recovered individuals show no detectable SARS-CoV-2 RNA in upper respiratory tract samples after an average of 14 days from symptom onset.<sup>46</sup> However, in some cases, this period may extend to up to 60 days, not necessarily indicating contagiousness to other people.<sup>59</sup> Some sub-genomic RNA fragments associate strongly with intracellular vesicles that protect them from degradation by host enzymes, which may explain these persistently positive tests.<sup>60</sup>

Some individuals may have negative RT-PCR results in two consecutive samples and subsequently test positive again. These persistent viral RNA detections are usually associated with higher Ct (cycle threshold) values (i.e., fewer RNA copies) than those found in RT-PCR results from samples collected just before or during the clinical disease phase.<sup>53</sup>

People who are moderately or severely immunocompromised may have longer periods of transmission,<sup>39</sup> and the recommendation is to extend the isolation period to 20 days or more. Viral excretion is reduced to undetectable levels when viral RNA load is low and serum neutralizing antibodies are present.<sup>39</sup> Therefore, some strategies using laboratory tests can help determine an appropriate time of isolation and precautions in immunosuppressed patients in selected cases and with specialist evaluation as recommended by CDC.<sup>40</sup>

RT-PCR values close to the cutoff point (Ct > 34) may mean that the individual is no longer transmitting the disease.<sup>59</sup> Although some authors have encouraged the disclosure of the Ct value in quantitative RT-PCR tests, there is no standardization; therefore, they are not recommended in the routine evaluation of the transmissibility of an individual. However, serial Ct values may be useful in specific contexts of infection in immunocompromised or severely ill patients as a complement while assessing infection resolution.<sup>59</sup>

Another diagnostic test that has been used for COVID-19 diagnostic confirmation is the Rapid Antigen Test (RAT), which is based on an immunochromatographic reaction. Its advantages include low cost, fast release time (around 20 min), and specificity close to 100%.<sup>61,62</sup> However, its main disadvantage compared to RT-PCR testing is a lower diagnostic sensitivity, due to limitations in the methodology.

A positive nasal antigen test requires a larger amount of viral genetic material in the sample, and this condition is often observed until seven days after symptom onset.<sup>41</sup> For this same reason, after an acute infection, the RAT turns out negative before RT-PCR in the same sample. Additionally, its sensitivity, similarly to that of RT-PCR, may be affected by the pre-analytical factors previously listed.<sup>63</sup>

For these reasons, the use of RT-PCR or RAT testing to define the period of isolation may be questionable.

### Considerations on the use of masks for reducing COVID-19 transmission

The use of masks is an essential tool in public health to prevent COVID-19 dissemination, emphasizing that any mask is better than no mask. According to CDC recommendations, everyone should wear the best mask they can, if it is comfortable and allows for proper and consistent use (close adjustment to the face, without spaces, and covering the nose and mouth). Additionally, using a highly effective mask may be important for high-risk situations or for people who are at increased risk of severe disease.<sup>64</sup>

Masks and respirators (i.e., specialized filtering masks such as PFF2/N95) can provide different protection levels depending on their type and the way they are worn. Single-layer fabric masks provide the least protection, whereas those with multiple layers (ideally three layers) offer more protection. Tightly sealed disposable surgical masks and KN95s offer even more protection, and well-fitted respirators such as PFF2/N95 masks offer a higher protection level.<sup>64</sup>

To select the best mask suited to different situations, some considerations about COVID-19 transmission should be reviewed.

In general, respiratory viruses can be transmitted via respiratory secretions by different independent and simultaneous routes (contact with contaminated objects, droplets, and aerosols). Discussions on particle size (droplets and aerosols) in SARS-CoV-2 and influenza transmission have been encouraged by researchers, as a better understanding of the contribution of these different modes of transmission is important to measure the effectiveness of nonpharmaceutical interventions in the population.<sup>65</sup>

Situations in which droplet-based respiratory precautions are required demand surgical masks and physical distancing to prevent transmission, whereas situations that generate aerosols require masks better fitted to the face and efficient filtration, such as the PFF2 or N95.<sup>41</sup>

To date, evidence on the effectiveness of PFF2 or N95-type respirators versus surgical masks in healthcare settings is still limited to five observational studies that have important methodological limitations and inconsistent findings on whether or not respirators decrease the risk of SARS-CoV-2 infection.<sup>66–70</sup>

These studies were conducted before the emergence of the Delta and Omicron VOCs and the use of COVID-19 vaccines increased. The protective efficacy of respirators compared with surgical masks in environments without aerosol exposure remains a critical research question not fully answered in the context of SARS-CoV-2 transmission.

New analyses have been proposed to investigate this issue in a scenario of more transmissible variants.

A recent *in vitro* study used Monte Carlo modeling to estimate viral emissions in the fine aerosol size range and used data on viral loads of the SARS-CoV-2 variants associated with information on air exchange and CO<sub>2</sub> concentration and a hypothetical definition for the Omicron variant in two

scenarios (10 and 100 × greater viral load than Delta), in addition to considering population mask use efficiency as 40% due to inadequate adaptation to the face. The study included no data on vaccination. In this model, the results pointed to the possibility of a much higher proportion of individuals infected with new variants considered as super-emitters: 1 in every 1,000 infected individuals was a super-emitter with the ancestral virus; 1 in 30 with the Delta variant; and, 1 in 20 or 1 in 10 with the Omicron variant, depending on the viral load estimate used. The study also predicted that the use of surgical masks might not be enough in the scenario of new variants, depending on the environmental situations considered in the model (offices, restaurants, nightclubs, and public transportation), due to the lack of complete adaptation to the face and impossibility of maintaining distance in poorly ventilated environments, whereas PFF2/N95 masks would remain effective since they filter 94%–95% of the inhaled aerosols, in addition to better adapting to the face.<sup>71</sup>

In October 2021, the WHO published updated recommendations for the use of masks by healthcare professionals, maintaining the recommendation to use a surgical mask along with other personal protective equipment as part of droplet precaution in caring for patients with suspected/confirmed COVID-19, in addition to the use of PFF2 and N95 respirator-type masks to perform aerosol-generating procedures on patients with confirmed COVID-19, which occurs most frequently in intensive care and emergency room settings.<sup>72</sup>

The WHO additionally recommended that PFF2 or N95-type respirators could be used, when available, even in the absence of aerosol-generating procedures, based on the values and preferences of health care professionals regarding the perception of the greatest possible protection to prevent SARS-CoV-2 infection.<sup>72</sup>

As for the general public, the recommendations called non-pharmacological preventive measures (avoiding travel, limiting physical contact with people outside the household, keeping a distance of 1–2 meters from others in public, and wearing a mask) should be maintained at this time of the pandemic. As for the type of mask, the recommendation is to select the one with a greater possibility of protection that is well-fitted to the face and comfortable to allow consistent use.<sup>73</sup>

As a source control for people with confirmed SARS-CoV-2 infections, both a surgical mask and a PFF2/N95 mask can be used,<sup>13</sup> provided they have no expiratory valves.<sup>41</sup>

A case-control study conducted by the California Department of Public Health on individuals tested for SARS-CoV-2 between February 24 and November 12, 2021, identified situations of increased risk for developing an infection after ≤14 days of exposure before testing that included high-risk household exposure, durations ≥3 h, and being unvaccinated. Wearing a mask showed greater benefits in unvaccinated and partially vaccinated participants and in interactions or contacts involving people not living in the same household without physical contact. Wearing a face mask reduced the chance of infection by 50% when participants were exposed to a confirmed or suspected case.<sup>74</sup>

A study by Wagner et al.<sup>75</sup> used aerosol dispersion analytical modeling to assess the relative risk of infection and the impact of other parameters, including physical distance,

ventilation, and masks, on this relative risk. The lowest risk was for longer distances, open air, increased ventilation, shorter exposure duration, and emission rate. Surgical mask and respirator models prevented higher maximum risk impacts (33-fold and 280-fold, respectively) than fabric masks (4-fold).

Non-pharmacological COVID-19 control, and prevention measures are adopted at individual and collective levels. The use of masks, hand hygiene, appropriate social distancing, and reduced participation in activities outside the household are highlighted as individual actions, whereas travel restrictions, home isolation, the closing of educational institutions, and prohibition of public meetings and non-essential commercial activities are collective measures.<sup>76</sup>

In this context, a study that analyzed data from 53 European countries through the World Health Statistics 2020 and the Institute for Health Metrics and Evaluation (IHME) showed that prevention and control measures implemented for the population had an impact on changing the Rt value, which expresses the average number of secondary cases from a person infected with SARS-CoV-2, having the restriction of mobility as the main factor, in addition to the proportion of physicians per capita and hospital beds per capita, with significant impacts on morbidity and mortality by COVID-19.<sup>76</sup> In this publication, the authors confirm that population prevention and control measures implemented by the government had an impact on the Rt value, and the component with the greatest effect on personal prevention was mobility.

A Brazilian study evaluated adherence to non-pharmacological measures through a questionnaire administered to 1,296 health professionals. This investigation showed adherence of 73% to the use of masks on all occasions when these professionals were not at home and that they never or rarely removed their masks. It also indicated 61% adherence to handwashing > 6 times per period (e.g., morning, afternoon) when not in their workplace.<sup>77</sup>

Thus, in addition to the impact of mobility-related measures implemented by government agencies, behavioral factors, and self-perception of risk can also influence adherence to non-pharmacological measures and the rate of transmission/infection.

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## Conclusions

The emergence of COVID-19 Variants of Concern (VOC) is an expected phenomenon, especially in high transmissibility scenarios. The Omicron variant is a VOC with Spike (S) protein mutations that partially affect the immunity generated by vaccines or prior disease. The disease induced by Omicron seems to be milder and with a lower hospitalization rate and shorter duration compared to the Delta variant. However, despite the minor consequences, the variant is highly transmissible and can have an impact on both the general population and health institutions.

COVID-19 vaccines have high efficacy for preventing severe disease and death, but low efficacy against acquiring infections, including the ones caused by the Omicron variant. Fully vaccinated people seem to have shorter durations of

symptoms, less severe disease, and lower mortality. Although fully vaccinated people remain at risk of SARS-CoV-2 infections, if infected, they are likely to have shorter periods of contagiousness than unvaccinated people.

Isolation or quarantine period should be based on knowledge of the incubation period and transmissibility of the disease. Given the data published on Omicron to date, if a strategy to end the period of isolation is adopted based on the duration of symptoms, the consideration of 10 days for mild cases and 20 days for severe/critical cases or in immunosuppressed patients is valid, without the need for testing. In any other contingency situation in which the isolation period needs to be reduced in case of mild or asymptomatic infections, there is a formal recommendation to wear masks that can make adequate source control until 10 days after the onset of symptoms, provided that the patients are already afebrile, and they show symptom improvement.

COVID-19 transmissibility is best defined by viral culture. However, this test is not applicable in practice. Qualitative information provided by RT-PCR is not adequate to define isolation time. Although quantitative information related to RT-PCR Ct is useful to predict the possible viral load, this information is not usually disclosed in the test report and there is no reliable standardization for its use as a parameter to determine contagiousness and isolation time. There may be false-negative RT-PCR and RAT results due to sample collection time and conditions, considering the natural period of disease progression and time since symptom onset. Therefore, the utility of a testing strategy in reducing isolation time is questionable and should be carefully evaluated.

The indication of the type of mask should consider the route of SARS-CoV-2 respiratory transmission, both by droplets and aerosols with a smaller proportion of transmission by contact. Masks with multiple layers (ideally three layers) offer better protection. The protection may vary according to the fabric, and it decreases over time with repetitive washing. Well-sealed disposable surgical masks and KN95s offer even better protection, and well-fitted respirators such as PFF2/N95 masks provide a higher level of protection. The use of a surgical mask well-fitted to the face or a KN95/PFF2/N95 mask without an exhalation valve can be a mitigation measure for source control in individuals with reduced isolation time.

To access the official recommendations in Brazil for the general population and health professionals, please consult the documents of the Ministry of Health<sup>13</sup> and the ANVISA.<sup>41</sup> To access the legal requirements for workers in general, please consult the Interministerial Ordinance n° 14 of the Ministry of Labor and Welfare and the Ministry of Health.<sup>78</sup>

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## Conflicts of interest

The authors declare no conflicts of interest.

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