



## Herd immunity threshold for SARS-CoV-2 and vaccination effectiveness in Brazil

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### TO THE EDITOR,

Estimating the herd immunity threshold for COVID-19 in the midst of the pandemic is a challenge. This threshold, defined as the percentage of people to be vaccinated in order for improvements in disease indicators and pandemic control, is being modified as the virus mutates, leading to immune escape from vaccines and from immunity due to previous infection itself.<sup>(1)</sup>

In the history of human diseases caused by infectious agents, only smallpox has been eradicated. Smallpox can be transmitted by close contact and through droplets and respiratory secretions containing the infectious agent. Indirect contagion over longer distances, through aerosols, is much less common. The reproduction rate of the virus was equal to 5, meaning that each person with smallpox could infect another five people. The disease caused lesions to the patient's skin, making it easier to locate and isolate an infected person; furthermore, once sick or vaccinated, the possibility of reinfection was remote.<sup>(2)</sup> The eradication of smallpox took approximately 184 years, from the emergence of an effective vaccine to the complete disappearance of the disease.

The literature has shown that there are differences between the two diseases. The first is that many asymptomatic people infected with COVID-19 can continue to spread the virus and, therefore, it is more difficult to fight COVID-19 than smallpox. The second is that there are non-human reservoirs, and the third is that those who have had the disease can become infected again, and immunity against this new virus (SARS-CoV-2) is still not entirely understood.<sup>(3)</sup>

The objective of the control measures was not primarily to fight SARS-CoV-2 but to gain time to develop vaccines and, more recently, to vaccinate the entire population. However, control measures were to be adjusted according to the epidemic situation and evolution of the virus, which constantly undergoes mutations.<sup>(4)</sup>

In this sense, understanding the calculation of the herd immunity threshold is essential to establish new vaccination goals. This threshold is based on the basic reproduction rate ( $R_0$ ) of the virus, assuming that the percentage of the vaccinated population is evenly distributed across all age groups and that vaccine efficacy is close to 100%.<sup>(5)</sup> The calculation of the reproduction rate of the virus that emerged in the city of Wuhan, China, yielded an  $R_0$  close to 3. Therefore, the calculation of  $[1 - (1/\text{Virus Reproduction Rate})] * [1/\text{Vaccine Efficacy}]$  was considered. For SARS-CoV-2, using an  $R_0$  value of 3 and vaccine efficacy

equal to 100%, the calculation would be:  $[1 - (1/3)] * (1/1)$ , thus,  $[1 - (0.3)] * 1$ , i.e.,  $[0.70] * 1$ , which would result in a proportion of 70% of the population required to attain herd immunity.

However, no vaccine is 100% effective, and mutations in the virus can also make it more transmissible and modify its reproduction rate. In COVID-19, such increment in transmissibility occurred with the Alpha, Gamma, and, more recently, the Delta variant of SARS-CoV-2, the latter identified in mid-2021, showing a significant increase in its spread to a reproduction rate equal to seven ( $R_0 = 7$ ).<sup>(6)</sup>

Brazil used different vaccines with distinct levels of efficacy. Considering the two main vaccines used so far, AstraZeneca/Fiocruz and CoronaVac/Butantan, the calculations need to be modified. A search evaluating the effectiveness of the two immunizers in 75,919,840 people vaccinated in the country after a full two-dose regimen of the AstraZeneca/Fiocruz vaccine found an overall effectiveness of 72.9% protection against infection, 88% against hospitalization, 89.1% against ICU admission, and 90.2% against death. People with the complete CoronaVac/Butantan vaccination regimen had a 52.7% lower risk of infection, 72.8% lower risk of hospitalization, 73.8% lower risk of going to the ICU, and 73.7% lower risk of death (Table 1).<sup>(7)</sup>

The calculations considering the different vaccine effectiveness levels and the impact of increasing the reproduction rate from 3 to 7 are shown in Table 1. It can be noted that it is probably impossible to reach a herd immunity threshold with the new variants of SARS-CoV-2 since they are more transmissible, and it would be necessary to vaccinate more than 95% of the population. Non-pharmaceutical interventions, such as physical distancing and the use of masks and antiseptic solutions, will continue to play an important role in keeping COVID-19 cases low regarding morbidity and mortality. The primary goal will be to reduce the number of hospitalizations and deaths due to the disease rather than break the path of viral transmission, although the latter would help reduce the spread of new variants.

With the emergence of new variants and the potential reduction of immunity against infections, new COVID-19 outbreaks appear.<sup>(8,9)</sup> The long-term perspective for the pandemic is that it will probably become an endemic disease, much like influenza. It is unlikely that the vaccine will completely stop the spread of SARS-CoV-2. Nonetheless, even without reaching the threshold of collective immunity, vaccination reduces hospitalizations and deaths due to COVID-19.<sup>(5)</sup>

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**Table 1.** Herd immunity threshold values for the AstraZeneca/Fiocruz and CoronaVac/Butantan vaccines considering the effectiveness of the two in Brazil and the impact of the increase in the virus reproduction rate ( $R_0$ ) from 3 to 7.

	AstraZeneca/Fiocruz			CoronaVac/Butantan		
	Effectiveness (%) <sup>*</sup>	Threshold rate (%)		Effectiveness (%) <sup>*</sup>	Threshold rate (%)	
		$R_0=3$	$R_0=7$		$R_0=3$	$R_0=7$
Infection	72.9	91.4	117.5	52.7	127.0	163.0
Hospitalization	88.0	75.7	97.4	72.8	92.0	118.0
Death	90.2	73.9	95.0	73.7	90.0	116.0

<sup>\*</sup> Cerqueira-Silva T. et al., 2021.

Currently, in Brazil, the prevalence of immunization coverage and absence of non-rigid pharmacological actions favor stationary permanence in scenarios of virus conflagration or coexistence. In these scenarios, viral circulation is reduced, but there is a frequent occurrence of local virus transmission, and outbreaks may occur mainly in the unvaccinated and immunosuppressed population.<sup>(4)</sup>

Both SARS-CoV-2 infection and COVID-19 vaccination induce an immune response that initially confers high levels of protection against symptomatic disease by COVID-19.<sup>(10)</sup> One of the present limitations is that there is not enough data to extend the findings related to infection-induced immunity to children or people with very mild or asymptomatic infection. In addition, the herd immunity threshold formula is used to predict the short- and long-term impacts of vaccination programs alone, to justify them economically, and to understand the nature of vaccine-induced immunity.

Therefore, the institution of a genomic surveillance program is essential to monitor mutations and the emergence of variants, especially those that evade the immune system. The revision of the herd immunity threshold with the expansion of complete vaccination coverage rates by age group, mainly in the most at-risk population, and studies that assess the duration of immunity, whether conferred by the disease or the vaccine, are essential for us to plan future vaccine booster campaigns.

#### AUTHOR CONTRIBUTIONS

ELNM, PCS, JPC, TC, and CMMS contributed to the conception and planning of the study, as well as the interpretation of data, writing and reviewing the preliminary and definitive versions, and the approval of the final version.

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