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Editorial

Analyzing COVID-19 vaccine efficacy in vulnerable communities: efforts beyond addressing vaccine inequity

What does it mean to be vulnerable in the context of COVID-19? At the level of the individual, age and underlying medical conditions are part of the answer. In a population, however, vulnerability to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is influenced by other factors. Masks, hygiene precautions, and physical distancing are the cornerstones for preventing the transmission of SARS-CoV-2 within a population. These prevention measures may be unavailable or unachievable in impoverished populations. This worrisome statement reflects the longstanding and closely linked relationship between public health and poverty. The virus spreads rapidly in communities and social groups in which people live side by side, where there is a shortage of (functional) masks, and where hygiene precautions are difficult to implement. Multigenerational housing in these communities place elderly individuals at risk for severe COVID-19 disease in close contact with individuals who may be at high risk due to unavoidable occupational exposure. These communities are highly vulnerable to outbreaks. Notably, underlying medical conditions are also frequently present in these populations, and access to health care providers is limited. Non-governmental organizations, researchers, and health officials have called for evidence-based strategies to prevent both the spread of infection and COVID-19 in migrants and refugees, fragile and conflict-affected regions, and other vulnerable communities [1].

Vaccination is *the* evidence-based strategy against COVID-19, and its efficacy is proven in clinical trials [2,3]. Again, the availability of COVID-19 vaccine differs considerably between high-income, lower middle-income and low-income countries [4]. Among 25 countries that hosted COVID-19 vaccine clinical trials, zero were conducted in low-income and three in lower middle-income countries [5]. A systematic review and meta-analysis by Lui et al. [6] investigated the vaccine effectiveness in 32 studies. All of them were performed in high-income countries. Conversely, studies have shown that the willingness to take a COVID-19 vaccine is higher in low- and middle-income than in high-income countries [7].

From a social and psychological perspective, the inequity of vaccine availability and the discrepancy in vaccine acceptance is a bit more complex than simply explained by the income-based categorization and binary labelling of populations that are either for or against a vaccine. For example, according to the World Bank database, Brazil is an upper middle-income country [8]. The favelas of Rio de Janeiro, however, are impoverished and high-density

communities, and hence, it is more accurate to consider them as low-income settings. Also, vaccine hesitancy may depend on the type of the vaccine. For instance, unfavorable lay press coverage influenced the reputation of the Oxford–AstraZeneca ChAdOx1-nCoV-19 vaccine (Cambridge, UK). The vaccine faced critique of being inefficacious in older people or of being associated with an increased risk for thromboembolic events [9]. Several countries paused the use of the ChAdOx1-nCoV-19 vaccine. On the other hand, UNICEF reported in November 2021 that ChAdOx1-nCoV-19 was the most donated vaccine through the COVAX initiative [10]. These observations insinuate that certain health authorities from high-income countries may have considered the vaccine as a second-choice option prior to awaiting results from clinical trials. ‘Generously’ donating vaccine purchases to COVAX may be the easier way than campaigning with counterarguments against vaccine skepticism that derives from an undifferentiated view. In the meantime, large placebo-controlled trials performed in the United States, Chile, Peru, Brazil, South Africa, and the United Kingdom demonstrated that two doses ChAdOx1-nCoV-19 vaccine are safe and have efficacy of 70% to 76% in preventing symptomatic COVID-19 [3,11]. Additional analysis suggested vaccine effectiveness of approximately 80% if the time interval between the two vaccine doses was ≥ 3 months [12]. Although, the setting of clinical trials may not necessarily apply to vulnerable communities. In high-density populations, there is a considerable risk of infection with SARS-CoV-2 between the first vaccine injection and the vaccine-induced antibody response, or between the first and second vaccine dose. Taken together, current research on COVID-19 vaccine effectiveness should move to areas where data is lacking, namely to low-income high-density communities.

In a group of favelas (“Complexo da Maré”) of Rio de Janeiro, Brazil, a COVID-19 vaccination campaign was initiated in January 2021. Nine months later, the campaign achieved an applaudable coverage with two doses of ChAdOx1-nCoV-19 vaccine in 93.4% of the adults. In this issue of *Clinical Microbiology and Infection*, Ranzani et al. [13] report their research results after investigating the vaccine effectiveness in this community with a test-negative design study. The authors utilized the results of a community-wide testing program available free of charge at three different regions within the favela groups during periods of time when the Gamma and Delta variants were dominant. The authors analyzed 10 077 test results and calculated an adjusted vaccine effectiveness against symptomatic COVID-19 of 31.6% (95% CI, 12.0–46.8) 21 days after the first dose and of 65.1% (95% CI, 40.9–79.4) 14 days after the second dose. These vaccine effectiveness results are within the same

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range of those in clinical trials [3,11] and other test negative case-control studies investigating the vaccine effectiveness in older adults in Brazil [14,15].

The authors should be commended for the following reasons. First, the authors have demonstrated how a successful a campaign of delivering vaccines to a low-income setting can be simultaneously combined with a study evaluating its effectiveness. Although it is generally acknowledged that assessment of vaccine efficacy is required among multiple different subgroups, efforts for the subgroup ‘favelas’ have been focusing on vaccine coverage but not on effectiveness. Second, these data provide evidence of vaccine effectiveness in a setting that unfortunately reflects the reality for hundreds of millions of people living in poverty around the world. Unfortunately, the pandemic itself will dramatically increase the number of people living in poverty [16]. Accordingly, the importance of vaccine effectiveness data within this population will continue to grow. Third, this study evaluated the Oxford–AstraZeneca ChAdOx1-nCoV-19 vaccine, which is the vaccine available to much of the global poor through the COVAX program. Effectiveness data on this vaccine will continue to be needed to counteract the negative reputation of this vaccine put forth within the media. There are differences in vaccine effectiveness when scientifically comparing various vaccines [17]. However, the nonscientific narrative of “superior” or “inferior” vaccines is detrimental to the global fight against COVID-19.

Efforts that address vaccine inequity both on an international (i.e., low-income countries) and local level (i.e., vulnerable community within a country) must be continuously supported and commended. Although, these efforts need to be taken one step further. Studies are needed to analyze vaccine effectiveness within a vulnerable population. Currently, the aforementioned vaccine inequity goes alongside even a stronger data inequity when reviewing real-world data on vaccine effectiveness. Combining a vaccine campaign with free of charge PCR testing in vulnerable communities, as shown by Ranzani et al. [13], is one example how providers can evaluate the performance of COVID-19 vaccines in these under-investigated subpopulations.

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