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Opinion

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The challenge of conducting epidemiological research in times of pandemic and denialism: 1-year anniversary of the EPICOVID-19 project in Brazil

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As of 20 May 2021, Brazil was the country with the second-highest number of COVID-19 deaths and the third-highest number of COVID-19 cases in absolute numbers in the world. In relative numbers, on 20 May 2021, the 7-day daily rolling average of deaths was 9.08 per million people in Brazil. From the beginning of the pandemic until 20 May 2021, the Brazilian cumulative mortality rate was 2078 per million inhabitants. In late 2020, Manaus, a state capital in the heart of the Amazon region, experienced chaos as oxygen supplies were depleted and intensive care unit (ICU) occupancy exceeded 100%, generating waiting lists. A couple of months later, all remaining 25 states in Brazil experienced the same problem, with waiting lists for ICU beds and shortages of medical supplies. The surge of a new variant (P.1.) in the country in late 2020 partially explains this chaotic situation, but the variant was actually both a cause and a consequence of Brazil's monumental failure at responding to the pandemic, as variants are more likely to emerge in places where the virus is circulating widely. Fifteen months into the pandemic, and despite these frightening numbers, Brazil has adopted neither national- nor state-level lockdowns, and the president himself fails to wear a mask at public gatherings. As scientists, we attempt to counterattack by disseminating evidence-based policies implemented in other countries and by conducting much-needed research, as we describe below.

The date of the first COVID-19 case reported in Brazil was 26 February 2020. Only 19 days later, on 16 March, our team of epidemiologists had already outlined projects for two large-scale population-based serological studies (EPICOVID19-RS and EPICOVID19-BR) to monitor the spread of the virus in our home state of Rio Grande do Sul (population 11.3 million) and in the whole country of Brazil (211 million), respectively. The research design

followed our 35 years of experience with population-based surveys in low- and middle-income countries; the research design ended up being similar to a protocol developed at the same time by the World Health Organization.[1] Briefly, our study used consecutive population-based serological surveys to monitor the progression of the pandemic, with the ultimate goal of helping policymakers to build evidence-based strategies for the pandemic response. The project was also aimed at analysing compliance with social-distancing measures and the prevalence of COVID-19 symptomatology. The urban areas of nine regional hubs in the state of Rio Grande do Sul, and of 133 cities in Brazil's 26 states and in the Federal District of Brasilia, were included in the samples. The total sample sizes for each survey round were 4500 individuals tested in the state survey and 33 250 in the national survey. The nationwide sample covered a geographic spread of ~4000 km from north to south and 4200 km from east to west.

The project's logo depicted an iceberg, based on the notion that the number of cases reported in official statistics represents only a small fraction of the real number of people infected with SARS-CoV-2 in the population. To highlight the importance of population-based data, there were 10 156 reported cases and ~633 deaths in Italy[2] as of 10 March 2020; if these case numbers were correct, the infection fatality rate would be 6.2%. Over the following months, serological studies from around the globe revealed that the real number of infections tended to be much higher than those officially reported.[3,4] Based on these types of surveys, current estimates of the infection fatality rate range from 0.23% in a typical low-income country with a young population structure to 1.15% in high-income countries with older populations.[5]

The protocols of our statewide and nationwide surveys were published in April and July 2020, respectively.[6,7] One of our main challenges at that time was to obtain the appropriate tests to measure the prevalence of infection. We initially decided not to use reverse transcription–polymerase chain reaction (RT–PCR) testing, as our goal was to estimate cumulative prevalence, rather than presence of the virus on the date of the interview. However, few serological tests were available in Brazil at that time, especially those that did not require venipuncture, which would be prohibitive for such large-scale surveys. We then learned that the Ministry of Health had received a donation of 5 million point-of-care antibody tests and we managed to obtain 150 000 tests for our studies. Due to lack of local data on the validity of the test, we rapidly conducted a validation study to assess its sensitivity and specificity in our context.

In our validation study,[8] we were able to confirm the >80% sensitivity and >98% specificity reported by the manufacturer for recent SARS-CoV-2 infections. However, in the next few months, the literature described decays in antibody titres over time with different types of antibody tests[4]—trend that we also observed in our prevalence data for some of the most highly affected cities in the first round of the study.[3] This prompted us to shift to a dried blood spot ELISA-based test developed in Brazil, which, like the rapid test, did not require venipuncture, but retained a high sensitivity to detect infection even after several months.[9,10]

The first months of EPICOVID-19 proceeded surprisingly smoothly, although the fieldwork was quite challenging, given mobility restrictions and safety concerns. The statewide survey gained the full support of the state government, with private institutions securing funding for the first four rounds of data collection. A network of 13 public and private universities, spread across all regions of the state, guaranteed the logistic and academic support needed for the survey. Nationally, the Ministry of Health secured funding for the first three rounds of EPICOVID19-BR. Between April and June 2020, we conducted five statewide and three nationwide rounds of surveys. Our goal of supporting government policy-making was met when data from EPICOVID19-RS began to be used in the 'Controlled Distancing Model', a colour-coding strategy aimed at defining how much each region of the state would be allowed to relax social-distancing measures, which was launched by the state government in May 2020.

There were some incidents during the first round of the nationwide study that deserve to be mentioned. Due to poor communication between the Ministry of Health and local health authorities, our interviewers arrived in many cities unannounced. The proliferation of fake news on social networks about criminal elements disguised as researchers led our fieldworkers to being interrogated and, on some occasions, arrested by local police, even suffering violence at the hands of the population in a few cities. These problems were largely solved once the communication issues were resolved, particularly through the engagement of local authorities, so that subsequent rounds ran smoothly.

In July 2020, however, we began to face what became the major challenge during the first year of our national study: scientific denialism and retaliation by the federal government. The Minister of Health, who initially funded three rounds of the national study, had resigned due to a divergence of opinion with the president on how to handle the pandemic; a second minister was appointed who also resigned in less than a month for the same reasons, and we then had to deal with a third administration in the ministry. Our findings of a high prevalence of infection among

indigenous populations were censored by this administration during the official presentation of results in Brasilia.

When we disseminated this important finding in the national press, funding for our study was discontinued. Tellingly, during the interview in which this decision was announced, the interim minister stated that new epidemiological studies would replace EPICOVID19-BR in the near future. After 11 months, none of these studies has seen the light of day.

In August 2020, we secured additional funding from the private sector and from a state funding agency to continue the nationwide study, thus supporting our intention to continue this series of surveys with or without governmental support. The fourth survey took place in late August 2020. At the same time, the statewide survey was up and running—10 rounds of this survey have been completed since April 2020, thus characterizing the longest series of population-based serological surveys anywhere in the world.

Findings from EPICOVID19-RS and EPICOVID19-BR have been reported in a steady stream of publications. Using data from the first three rounds of the statewide survey (April to May 2020), we showed that the epidemic was at an early stage in the Rio Grande do Sul and that, unlike in other parts of Brazil, compliance with social distancing was high.[11] Using data from the first two rounds of the nationwide survey (May to June 2020), which included >56 000 participants, we showed that seroprevalence of antibodies against SARS-CoV-2 increased from 1.9% to 3.1%.[3] This study also showed that 11 of the 16 cities with the highest prevalence values in the first survey were found along a stretch of the Amazon river, becoming one of the first studies to draw attention to the dramatic COVID-19 crisis in this region. The prevalence of SARS-CoV-2 infection among indigenous peoples was 6.4% compared with 1.4% in the White population. The prevalence in the poorest socio-economic quintile was 3.7%, compared with 1.7% in the wealthiest. The prevalence of infection reported in our surveys was on average 6-fold higher than the number of officially reported cases.[3]

A key feature of EPICOVID-19 was that, given the state of emergency, preliminary results were announced in press conferences only a few days after each round of data collection was completed. We felt that it would be unethical to wait until articles were written, submitted and accepted in scientific journals to disclose information that demanded immediate action. Given the dearth of population-based data on COVID-19 in the state and country, these press conferences have attracted and continue to attract massive media coverage.

As time went by, the federal government expanded their output of anti-science statements and actions, including those that have been widely reported in the international press.[12] Denials include the pandemic, but are not restricted to it: climate change and deforestation are also affected. In relation to the pandemic, denialism includes repeated refusals to implement social-distancing measures, denial of the importance of wearing face masks, promotion of ineffective 'early treatment' (with hydroxychloroquine, ivermectin and other drugs) and repeated anti-vaccination statements that led to failure in procuring sufficient doses of vaccine for the population. Along with the Brazilian scientific community, our group has played an active role in criticizing such statements and demanding that science-based policies be implemented in response to the pandemic. EPICOVID-19 thus became one of the voices of the pro-science movement, which led to vicious personal attacks on our team[13] by supporters of the present government and by government officials themselves. A global ranking by an Australian institute has singled out Brazil as the worst of 98 nations analysed in terms of response to the pandemic.[14]

In February 2021, we carried out the ninth round of EPICOVID19-RS. Ten months of consecutive surveys show an increase in the prevalence of antibodies to SARS-CoV-2 from nearly zero in the first survey to 10% in the last study. Rio Grande do Sul is currently a hotspot for COVID-19 mortality in Brazil with 22 000 deaths, nearly 200 deaths per 100 000 inhabitants. By comparison, Belgium, a country with the same population (11.4 million), has comparable cumulative mortality (23 000 COVID-19 deaths), despite its much older population (25.5% aged ≥60 years, compared with 15.9% in Rio Grande do Sul).

As we write this, we have just completed data collection for the 10th round of the statewide survey, for which results will be made available as soon as blood assays are completed. We are currently conducting the fifth phase of the nationwide survey using a modified protocol, in which ~115 000 participants have provided blood samples. We continue to pursue funding to conduct further rounds of the national study, which is of particular importance in light of the rapid spread of the P.1. variant throughout the country. Future rounds of the survey are essential for evaluating the real-life effectiveness of the vaccines in use in Brazil against the new variants.

On the one hand, sustaining good epidemiology in this hostile environment is challenging but, on the other, it is more important than ever. A key lesson from the current situation is that public funding for science and technology needs to be secured and managed by the state, and not by the government. Otherwise, any anti-science government might promote budget cuts and jeopardize scientific progress in the country. As we enter the second year of EPICOVID-19, we would like to focus our energy on fighting the virus rather than battling denialism. Attacking science and scientists will certainly not help Brazil to

overcome the monumental failure of its government's response to the COVID-19 pandemic.

Conflicts of interest

None declared.

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