

1 Population-level seropositivity trend for SARS-Cov-2 in Rio Grande do  
2 Sul, Brazil: results of 10 repeated surveys of the EPICOID19-RS study

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19 ABSTRACT

20 **Background:** Rio Grande do Sul, the southernmost state in Brazil, had a slow start in the pandemic  
21 compared to other regions of the country, but the number of new cases rose sharply in December  
22 2020, with a huge spike in March 2021, when the number of new cases was close to 800 per million  
23 people. In this article, we describe the pandemic in the State through the lens of 10 consecutive  
24 surveys conducted between April 2020 and April 2021.

25 **Methods:** We used a sentinel city approach, covering all regions of the State. In each city we selected  
26 50 urban census tracts with probability proportional to size. In each tract, 10 households were  
27 selected using a systematic approach. Within each selected household, all residents were listed, and  
28 one was selected randomly. In the first rounds of the study, we used the rapid point-of-care lateral-  
29 flow WONDFO SARS-CoV-2 Antibody Test (Wondfo Biotech Co., Guangzhou, China). In rounds nine  
30 and 10, we used an in-house direct ELISA test that identifies the presence of IgG to the viral spike (S)  
31 protein from dried blood spot samples (S-UFRJ). In terms of social distancing, individuals were asked  
32 three questions, from which we generated an exposure score through principal components analysis.

33 **Findings:** Antibody prevalence in early April 2020 was 0.07 (95% CI 0.01-0.32), increasing to 10.0%  
34 (95% CI 9.1-11.0) in February 2021, and to 18.2% (95% CI 16.9-19.5) in April 2021. Self-reported  
35 whites showed the lowest seroprevalences (9.3%, 95% CI 8.3–10.4 in round 9 and 17.3%, 95% CI  
36 15.9–18.8 in round 10), while indigenous individuals presented the highest levels (20.0%, 95% CI 8.5–  
37 40.3 in round 9 and 44.4%, 95% CI 22.5–68.7 in round 10), followed by blacks (14.4%, 95% CI 11.3–  
38 18.1 in round 9 and 21.6%, 95% CI 17.4–26.4 in round 10). We found an increase in seropositivity in  
39 relation to our exposure score; the most exposed 10% of the population presented a 40% higher  
40 seropositivity.

41 **Interpretation:** The proportion of the population already infected by SARS-Cov-2 in the State is still  
42 far from any perspective of herd immunity, suggesting that herd immunity will only be achieved  
43 through vaccination.

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45 Instituto Cultural Floresta, UNIMED Porto Alegre, “Todos pela Saúde” Group, Instituto Serrapilheira,  
46 Brazilian Collective Health Association (ABRASCO) and the JBS S.A. initiative “Fazer o Bem Faz Bem”.

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## 49 Research in context

### 50 Evidence before this study

51 A large systematic review was published recently, summarizing studies on seroprevalence.<sup>1</sup> It  
52 showed that despite the large number of studies found, most are of low quality. Only 45 (11% of all)  
53 were based on random samples to assure population representativity. The review also presents a  
54 wide variation of seroprevalence estimates for SARS-CoV-2, between studies and across world  
55 regions. The average seropositivity found in population-based studies was 8.0% (95% CI 6.8–9.2), but  
56 in individual studies it ranged from zero to more than 40%.

### 57 Added value of this study

58 From April 2020 to May 2012, we conducted 10 rounds of statewide population-based studies of  
59 seroprevalence of SARS-CoV-2 antibodies in the southernmost Brazilian state of Rio Grande do Sul,  
60 each round covering 4,500 subjects in nine sentinel cities. We documented an increase in  
61 seroprevalence from 0.1% to nearly 20% in the most recent survey. Seropositivity was always higher  
62 among indigenous and black subjects than among whites. We created an exposure score based on  
63 levels of adherence to social distancing measures; and we found a clear association at the individual  
64 level between the exposure score and seropositivity, especially in the last two rounds, when the  
65 prevalence of antibodies to SARS-CoV-2 increased markedly. Although our state has had so far nearly  
66 30 thousand deaths due to COVID-19, fewer than one in five inhabitants showed antibodies.

### 67 Implications of all the available evidence

68 In the southern region of Brazil where Rio Grande do Sul is located, the COVID-19 pandemic was  
69 delayed in comparison to the rest of the country, with low prevalence of antibodies in 2020 and a  
70 drastic increase in infections from January 2021 when the P.1 variant reached the state. Our  
71 analyses show clear association between levels of adherence to social distancing measures and  
72 antibody seropositivity, pointing to the importance of establishing confinement policies, as the  
73 rhythm of vaccination is still very low. Our results suggest that the federal government's emphasis  
74 on reaching herd immunity through natural infection would results in an unacceptable number of  
75 deaths.

## 76 INTRODUCTION

77 In Brazil, the first case of COVID-19 was reported on 27 February 2020 in the city of São Paulo, and by  
78 mid-May 2021 the country has had more than 15 million confirmed cases and more than 420  
79 thousand deaths, the second highest cumulative mortality in the world. In March 2021, Brazil had a  
80 spike in cases and deaths that brought health services to the brink of collapse, with oxygen and  
81 respirators lacking in the North region. The daily number of new cases reached nearly 80 thousand,  
82 some 360 new cases per million people. However, different from other countries who had huge  
83 spikes in cases, like Italy, the USA and the UK who had up to 880 new cases per million people, Brazil  
84 did not have a sharp fall after the spike. Compared to these countries, only the US had had more  
85 cases per million people than Brazil.

86 Rio Grande do Sul, the southernmost state in Brazil, and all the Southern region, in general, had a  
87 slow start in the pandemic compared to other regions of the country, but the number of new cases  
88 rose sharply in December 2020, with a huge spike in March 2021, when the number of new cases  
89 was close to 800 per million people. This increase coincided with dissemination of the P.1 variant.  
90 Since then, the number of new cases has declined, but remains high at around 350 new cases per  
91 million, close to the country's average. These indicators were summarized from the Brazilian Ministry  
92 of Health (<https://covid.saude.gov.br/>) and the State Secretary of Health  
93 (<https://ti.saude.rs.gov.br/covid19/>) on 11 May 2021.

94 It is widely recognized, however, that the number of confirmed cases is much lower than the total  
95 number of infections in the population, making studies, like the EPICOV19-RS, that monitor the  
96 percentage of the population that has already been infected with SARS-Cov-2 essential to understand  
97 the pandemic dynamics. Only a few nationwide seroprevalence studies have been reported, mostly  
98 in European countries during the first months of the pandemic. In April 2020, 0.8% (0.6-1.0) tested  
99 positive for SARS-CoV-2 antibodies in Iceland,<sup>2</sup> and 0.33% (0.12-0.76) in Austria.<sup>3</sup> In Spain, 5.2% (4.9-  
100 5.5) of the populations were seropositive in June 2020.<sup>4</sup>

101 In Brazil, we reported seroprevalence levels of 1.9% (1.7-2.2) for May 2020 and 3.1% (2.8-3.4) for  
102 June 2020, from a national seroprevalence study.<sup>5</sup> A study done in the state of Maranhão, in  
103 northern Brazil, collecting data in selected areas, found a much higher seroprevalence of 38.1%  
104 (34.8%-41.1%).<sup>6</sup> Another study based on samples from blood donors in the city of Manaus in the  
105 state of Amazonas estimated that between 44% and 66% had already been infected with SARS-Cov-2  
106 by July 2020.<sup>7</sup> This raised the possibility that the city was close to reaching herd immunity, but this  
107 was soon dismissed by another spike in cases, as discussed by the same research team.

108 Overestimation of the population seropositivity that was based on blood donors, population mobility

109 and the appearance of coronavirus variants in the population were possible explanations for the  
110 second wave.<sup>8</sup> Since then, hopes for an end to the epidemic through herd immunity – an idea  
111 repeatedly suggested by Brazil’s president<sup>9</sup> – seem to have waned.

112 With the intent of monitoring the population level of seropositivity we started the EPICOV19-RS  
113 study in April 2020, and by September we had conducted eight rounds of the study. Seroprevalence  
114 was estimated using the Wondfo rapid test, increasing from 0.03% in round 1 to 1.89% in round 8.<sup>10</sup>  
115 However, with time, it became clear to us that the test’s sensitivity could not be as high as initially  
116 believed and that it decreased over time.<sup>11</sup> Therefore, we sought for a better test and for ways to  
117 correct the estimates already available.

118 After a 5-month pause since the eighth round of the EPICOV19-RS study, we carried out a ninth  
119 round now using a new ELISA test,<sup>12</sup> alongside the Wondfo rapid test, and soon after a tenth round.  
120 The aims of these rounds were to estimate the population prevalence of seropositivity for SARS-Cov-  
121 2 for the whole sample and for populations subgroups defined by age, sex, ethnicity, and wealth. We  
122 also studied social distancing measures and vaccination status, results of which we report here.

123

## 124 METHODS

125 The EPICOV19-RS study started only 18 days after the first COVID-19 death in the state, to monitor  
126 population level infection by SARS-Cov-2. So far, 10 rounds of the population-based survey were  
127 completed, the first in April 2020, and the last in April 2021. A similar sampling methodology was  
128 used in all rounds. We used a multistage sampling approach based on nine sentinel cities (details in  
129 the supplemental material and published elsewhere).<sup>13</sup>

130 In the first nine rounds of the study, we used the rapid point-of-care lateral-flow WONDFO SARS-  
131 CoV-2 Antibody Test (Wondfo Biotech Co., Guangzhou, China) which can detect both IgM and IgG  
132 antibodies. The Wondfo test manufacturer rates the test sensitivity and specificity at 86.4% and  
133 99.6%, respectively (URL: [https://www.bilcare.com/SARS-CoV-  
134 2%20Antibody%20Test%20\(Lateral%20Flow%20Method\).pdf](https://www.bilcare.com/SARS-CoV-2%20Antibody%20Test%20(Lateral%20Flow%20Method).pdf), accessed 11 May 2021) . We  
135 conducted two separate validation studies on this test. In the first, we estimated a sensitivity of  
136 84.8% with recently diagnosed patients.<sup>13</sup> In the second, we enrolled 133 patients who had positive  
137 RT-PCR results ranging from a few days up to six months before. Here we found sensitivities varying  
138 from around 80% (among subjects diagnosed in the previous two months) to 42% for the earliest  
139 diagnosed patients.<sup>11</sup> The test sensitivity observed in the previous validation for recent infections  
140 was confirmed, but it was clear that sensitivity decreased with time. We therefore developed a  
141 method to adjust the seroprevalences obtained with the Wondfo test starting by using the number  
142 of deaths as an indicator of the temporal distribution of the epidemic (data available from the state  
143 of RS COVID-19 information committee). The second step was to estimate a function describing the  
144 sensitivity decay for the Wondfo test. This calibration procedure ensures the sensitivity function is  
145 more coherent with field estimates of sensitivity, which may differ from estimates in the validation  
146 study. To calculate the adjusted Wondfo prevalence estimates in rounds 1-8, sensitivity was  
147 calculated as the average of the sensitivity function weighted by the daily number of deaths up to the  
148 date of each survey. Details of the correction procedure are described in the supplemental material  
149 and elsewhere.<sup>14</sup>

150 In round nine, we also used an in-house direct ELISA test that identifies the presence of IgG to the  
151 viral spike (S) protein from dried blood spot samples (S-UFRJ) in parallel with the Wondfo test. The  
152 developers estimated the test specificity to be 98.6%, and sensitivity 95.0% (binomial 95%CI 92.3–  
153 97.0).<sup>15</sup> Our own validation of this test, only with participants that were positive in a RT-PCR test  
154 diagnosed up to six months before the study, revealed a sensitivity of 92.5% (95% CI 86.6–96.3).<sup>11</sup>  
155 Given the small impact of correcting for these values of sensitivity and specificity at this prevalence  
156 level, we opted for presenting the unadjusted ELISA estimates. The ELISA test was processed in our  
157 own laboratory according to the developer specification. In round ten, only the ELISA test was used.

158 In both rounds, as soon as the ELISA analyses were completed, the participants were informed of  
159 their own results.

160 A short questionnaire including information on sex, age, schooling, self-reported skin color and  
161 compliance with social isolation measures was applied after testing. Schooling was recorded as the  
162 highest year completed successfully. The IBGE categories were used to classify subjects by their skin  
163 color (or ethnicity). Individuals were asked to self-classify into white, brown (“pardo” in Portuguese),  
164 black, yellow or Asian, or indigenous. Ownership of a series of assets was recorded as a means to  
165 assess household wealth from round four.<sup>16,17</sup> The assets were: automobile for personal use,  
166 desktop or notebook computer, color TV, air conditioning, cable internet, cable TV, number of  
167 bathrooms and number of bedrooms in the house. Using these assets, we performed principal  
168 components analysis to extract the first component score and used it to classify households in terms  
169 of wealth, dividing them into five equally sized groups, the wealth quintiles (the first including the  
170 20% poorest participants, up to the fifth which includes the 20% richest).<sup>16,18</sup> The combined sample  
171 for the nine cities was used for deriving the asset score in each round.

172 In terms of social distancing, individuals were asked three questions: i) “To what extent are you  
173 managing to follow the social distancing guidance from the health authorities, i.e., staying at home  
174 and avoiding contact with others?”; ii) “What have your routine activities been?” with alternatives  
175 about the frequency of going out; and iii) “Thinking about the household routine, who has been in  
176 the house?” with alternatives related to the presence of relatives and friends and its frequency. The  
177 complete questions and possible answers are presented in the supplemental material.

178 Given that the three questions about individual and household routine inform on the level of  
179 exposure of each participant, we used principal components analysis with the three variables to  
180 extract the scores for the first component that was used to indicate the individual level of exposure.  
181 Score cut-offs were calculated to create 10 equally sized groups of participants, with the first group,  
182 D1, including the 10% least exposed, up to D10 with the 10% most exposed participants.

183 In rounds nine and ten we also asked about vaccination against SARS-CoV-2 – the participants  
184 intention to be vaccinated or whether they had already been vaccinated. The date of vaccination and  
185 the brand of the vaccine was also recorded.

186 All analyses took the sample design into account. Pooled seroprevalence estimates for cities and  
187 populations groups were not weighted by the size of each city and represent the average across the  
188 nine cities. For the last two rounds, seropositivity was based on the ELISA test, with the prevalence  
189 estimated directly from the observed results. For rounds one to eight, we used a correction strategy

190 to adjust for fact that the Wondfo test presents a much lower sensitivity when the infection occurred  
191 more than three months before.

192 For the last two study rounds, where the ELISA test was available, we assessed the association  
193 between seroprevalence and the exposure score using a logistic regression model with the  
194 continuous exposure score, thus imposing a logit-linear relationship between the score and the  
195 outcome. Only unvaccinated individuals were used for fitting this model, which goodness of fit was  
196 assessed through the Hosmer-Lemeshow test. All the analysis were carried out with Stata (StataCorp.  
197 2019. *Stata Statistical Software: Release 16*. College Station, TX: StataCorp LLC.) and with R (R Core  
198 Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical  
199 Computing, Vienna, Austria).

200 All interviewers were tested for COVID-19 and only those with negative results and absence of any  
201 symptom worked in the field. In the last two rounds, interviewers who had been vaccinated or had  
202 COVID-19 more than a month before and had a negative RT-PCR test in the previous 30 days were  
203 also allowed to work. They all used individual protection equipment (masks, face shields, gloves, and  
204 aprons) that was discarded after visiting each household. Ethical approval was obtained from the  
205 Brazilian's National Ethics Committee (30415520.2.0000.5313), and we obtained written informed  
206 consent from all participants. A separate informed consent form was used to obtain permission of  
207 parents or legally authorized representatives for minors. If the respondent was a child under age 12  
208 or an older adult unable to answer the questionnaire, it was applied to the respondent's legal  
209 guardian. Positive cases were reported to the statewide SARS-CoV-2 surveillance system.

210

## 211 RESULTS

212 Along the 12 months and ten rounds of the study we observed fluctuations in the sociodemographic  
213 characteristic of the samples. Despite the statistical significance of some differences - given the large  
214 sample size, 44,611 in total - these fluctuations were not marked (Table 1). Consistently, females  
215 accounted for approximately 60% of the sample in all rounds. Children and adolescents were  
216 underrepresented, largely due to refusals likely caused by the finger prick. Apart from this, the  
217 percentages within each age group were stable. Most of the sample had incomplete or complete  
218 higher education. The ethnic composition of the sample was also stable along the rounds, with most  
219 participants self-classifying as white, followed by brown (“pardo”), and black. There were small  
220 numbers of individuals in the yellow or indigenous groups.

221 The estimates of seropositivity (crude and adjusted) observed in the ten study rounds are presented  
222 in Table 2, along with the dates, type of test and sample sizes. Antibody prevalence in early April  
223 2020 was below 0.3% (0.26, 95% CI 0.03–1.00), having increased over time to 9.97% (95% CI  
224 9.06-10.95) in February 2021, and to 18.16% (95% CI 16.90-19.49) in April 2021. We also present the  
225 cumulative number of deaths per million people along the time in Table 2. A graphical representation  
226 of the seropositivity time trend is presented in Figure1.

227 We present a comparison of seropositivity between population subgroups according to vaccination  
228 status in Table 3, based on the ELISA results in the last two rounds. As expected, the prevalence of  
229 seropositive individuals is systematically higher among those who were already vaccinated. These  
230 differences are more marked the round 10, with a larger proportion of the population already  
231 vaccinated and with more time for antibodies to develop. Among individuals aged 80+ years we  
232 found 34.0% (95% CI 26.3–42.7) of seropositivity among those vaccinated, compared to 12.5% (95%  
233 CI 1.7–53.8) among the unvaccinated. Similarly high seropositivity was found among age groups 20-  
234 39 and 40-59 which concentrate health professionals that were among the first groups to receive the  
235 vaccine. Overall, in round 10, 22.5% (95% CI 20.1–25.2) of the vaccinated individuals were  
236 seropositive compared to 16.6% (95% CI 15.2–18.1) of the unvaccinated. For round 9 these  
237 proportions were 21.9% (95% CI 14.8–31.2) and 9.7% (95% CI 8.8–10.7) respectively.

238 The last round of the study took place 12 weeks after the start of COVID-19 vaccination. The priority  
239 groups for vaccination included front line health workers, indigenous people, and the elderly, in  
240 decreasing order of age. Nearly 95% of the elderly aged 80 or more years were already vaccinated by  
241 early April with at least one dose, as did two thirds of those aged 60-79 years (Table 3). Indigenous  
242 people were also included in the priority groups, although only 33.3% (95% CI 16.1–56.5) of the 18  
243 individuals in the sample reported having been vaccinated.

244 Across subgroups, the only notable differences are related to ethnicity based on skin color. In  
245 round 9 we see that unvaccinated indigenous and black individuals present much higher  
246 seropositivity compared to whites. In round 10 we see a similar pattern (although the differences are  
247 no longer significant). Among the vaccinated indigenous individuals in round 10 we found the highest  
248 seropositivity in all groups, 83.3% (95% CI 36.9–97.7), albeit with a very wide confidence interval  
249 given there are just six vaccinated individuals here).

250 The exposure score that was generated by PCA had a mean of zero (by construction) that represents  
251 the average value of exposure along the study period, with a standard deviation of 1.25. The first  
252 component used to derive the score explained 52% of the total variability of the three social  
253 distancing indicators. Figure 2 shows a rapid increase in exposure from the first to the fourth round  
254 of the study, covering the first five months of the pandemic. After that we see a slower but steady  
255 increase in the exposure score until January 2021, when decreases to a value close to zero, the  
256 average level of exposure observed in the study. This final decrease in exposure followed the huge  
257 spike of cases and deaths observed in February and March. We also found a clear association at the  
258 individual level between the exposure score and seropositivity at during the last two rounds (Figure  
259 3). Using the continuous exposure score as the predictor, we used a logistic regression model to  
260 predict the seroprevalence for the average scores in each decile for the last two rounds. Based on  
261 the model, the probability of being seropositive increased from 7.8% to 13.0%, from the lowest to  
262 the highest exposure level for round 9 and from 13.5% to 21.7% for round 10. The Hosmer-  
263 Lemeshow goodness of fit test yielded a p value of 0.7518 indicating the model is adequate, with no  
264 suggestion of non-linearity or interaction in the logit-linear model.

265

## 266 DISCUSSION

267 Our study, to our knowledge is the longest series of surveys carried out on the same population,  
268 covering 10 rounds over 13 months of the COVID-19 pandemic. Earlier results for phases 1-8 were  
269 published elsewhere.<sup>10</sup> At the time of the early rounds of the study, the only rapid test available in  
270 large amounts in the country was the Wondfo lateral-flow test, which had been imported by a  
271 Brazilian mining conglomerate and donated to the Ministry of Health. A set of early validation  
272 studies, including our own, suggested that the test had sensitivity above 80% in subjects who had  
273 been recently diagnosed using RT-PCR – given that as of April 2020 all cases in the country were  
274 recent. Over time, the literature started showing that the sensitivity of several different antibody  
275 tests declined with time since the infection, and we decided to carry out a second validation study in  
276 which such a decline was confirmed. This second study provided parameters for adjusting results  
277 from the original antibody test,<sup>14</sup> and to allow a comparison with a recent ELISA test developed in  
278 Brazil which showed consistently high sensitivity over time since the diagnosis.<sup>11</sup>

279 As observed in previous studies, some population groups are much more vulnerable to COVID-19,  
280 especially indigenous and black participants. This reinforces the very different vulnerability of ethnic  
281 groups, that most likely is related to macro determinants such as living conditions, family structures  
282 and social norms. Surprisingly, there were no important differences across wealth quintiles, despite  
283 indigenous and blacks being, on average, poorer than other ethnic groups. In previous analyses, we  
284 found decreasing levels of seropositivity with wealth,<sup>19,20</sup> but at a much lower level, less than 3% at  
285 the time, between May and June 2020. The higher seropositivity allied with the changing pattern of  
286 exposure may have masked this difference in a crude analysis. On the other hand, the higher  
287 seropositivity observed among indigenous and black people has been consistent across the  
288 studies.<sup>19,20</sup>

289 We found a clear increase in seropositivity in relation to our exposure score, highlighting the  
290 importance and effectiveness of social distancing that has been questioned by some activist groups.  
291 The most exposed 10% of the population presented a 40% higher seropositivity suggesting that if we  
292 could, at a minimum, reduce the exposure to the level of the 10% least exposed, thousands of cases  
293 and deaths could be avoided.

294 The limitations of our analyses include the low participation of children, including adolescents, with  
295 only 6.5% individuals 0-19 years in the round 10 sample, probably due to children's reluctance to  
296 undergo a finger prick. Also, strictly speaking, our sampling design does not present results that are  
297 representative of the state population. However, using the main cities in each subregion of the state  
298 certainly gives us a precise idea of seroprevalence levels, especially that we did not observe

299 important differences across sites. The decaying sensitivity of the rapid test is also an important  
300 limitation that we dealt with through the adjustment process that seems to have produced better  
301 and credible results, when analyzed over time.

302 Our results should be used to inform policy. We show that antibody prevalence increased from under  
303 1% in April 2020 to 18% by April 2021. Rio Grande do Sul state was relatively preserved in the early  
304 stages of the pandemic in comparison with most other states in the country, and the increase in  
305 seroprevalence mirrored the rise in mortality rates (Figure 1). Federal government policy in Brazil has  
306 not been evidence-based. Whereas virtually all scientists recommend social distancing, selective  
307 lockouts and use of face masks in public, President Bolsonaro has repeatedly stated that there is no  
308 need for such measures, and that the natural solution to the pandemic is to allow infections to  
309 spread until natural herd immunity is reached. Although initial estimates of R zero had set a level of  
310 60-70% prevalence as needed for herd immunity, the appearance of new, more infective variants  
311 such as P.1 and more recently an India-originated one, the recognition that immunity does not last  
312 too long and vaccines have efficacies that may be relatively low, has led to upward corrections in the  
313 level of prevalence required for controlling transmission, to 80% or higher.<sup>21</sup> Whatever the required  
314 level, our results show that the proportion of the population already infected by SARS-Cov-2 in the  
315 state is still very far from any perspective of herd immunity. With about 16% of the unvaccinated  
316 population infected, there had already been about 2,000 deaths per million, totaling over 20  
317 thousand deaths in a state with 11.3 million inhabitants. In a simple calculation - ignoring the  
318 protection afforded by vaccination - in order to reach 80% antibody prevalence one would need to  
319 multiply the number of deaths by five, with a cumulative total of 100 thousand deaths. Even if this  
320 simple calculation based on seroprevalence fails to take into account other sorts of immune response  
321 – including cellular immunity – the numbers are staggering. The cost in terms of lives lost of a  
322 permissive “natural herd immunity policy” as favored by the federal government is clearly  
323 unacceptable.

## 324 Declaration of interests

325 The authors declare that they have no known competing financial interests or personal relationships  
326 that could have influenced the work reported in this paper.

## 327 Data sharing statement

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## 333 Contributors

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336 Mesenburg, Nadège Jacques, Claudio J Struchiner, Odir A Dellagostin and Pedro C Hallal contributed  
337 to the conception and design of the work, analysis, and interpretation of data and the drafting of the  
338 manuscript. Flávia R Brust, Marinel M Dall'Agnol, Ana Paula L Delamare, Carlos Henrique R François,  
339 Maria Letícia R Ikeda, Débora C P Pellegrini, Cézane P Reuter, Shana G da Silva, Andréia R M Valim  
340 and Liliana P Weber contributed to the acquisition of data. All authors have read and approved the  
341 submitted version and have agreed to be personally accountable for the author's own contributions  
342 and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in  
343 which the author was not personally involved, are appropriately investigated, resolved, and the  
344 resolution documented in the literature.

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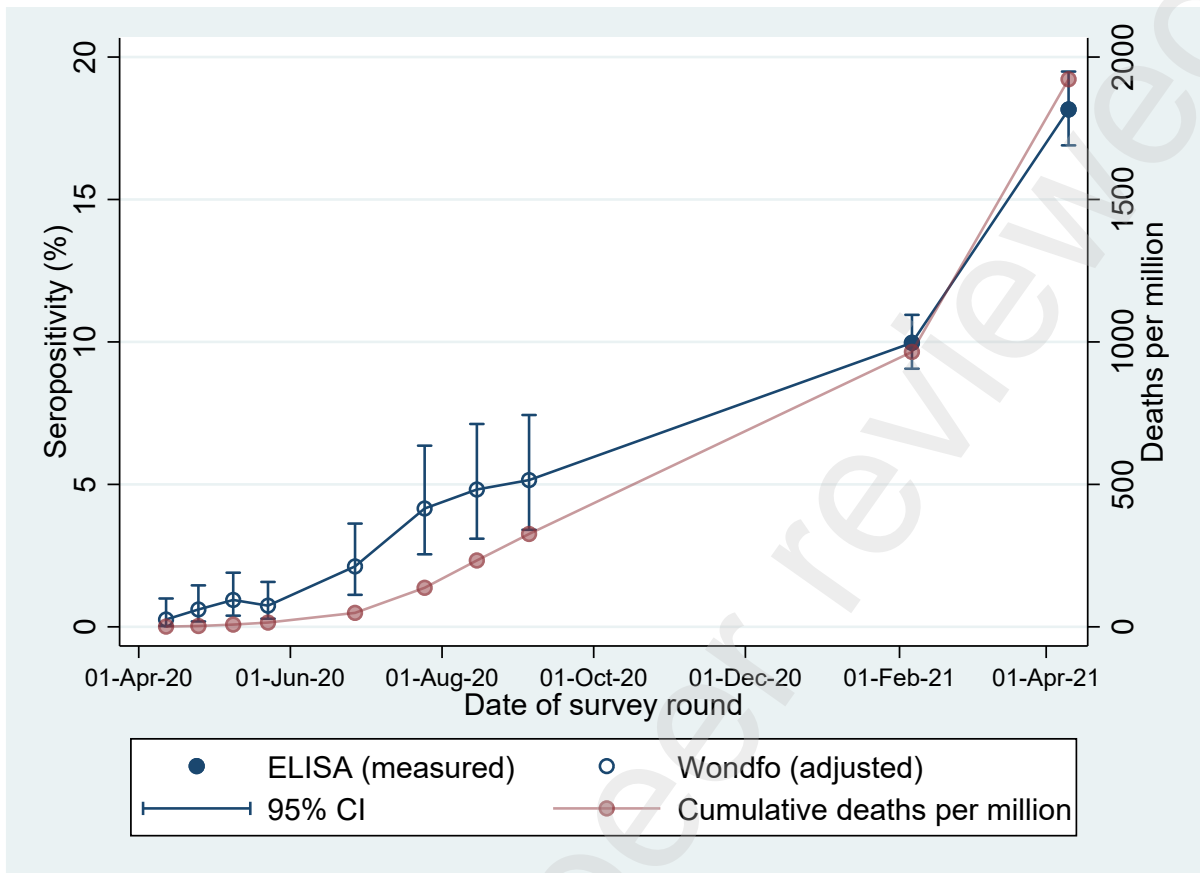
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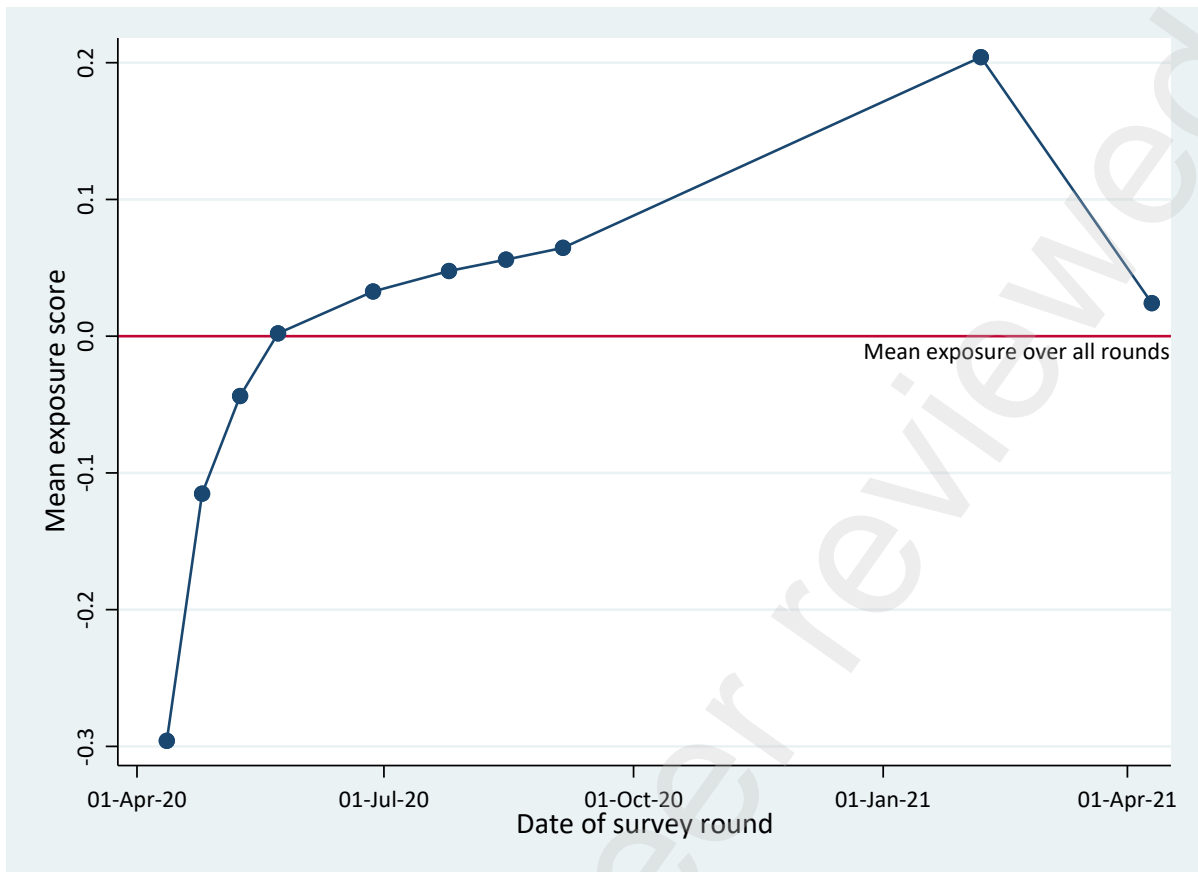
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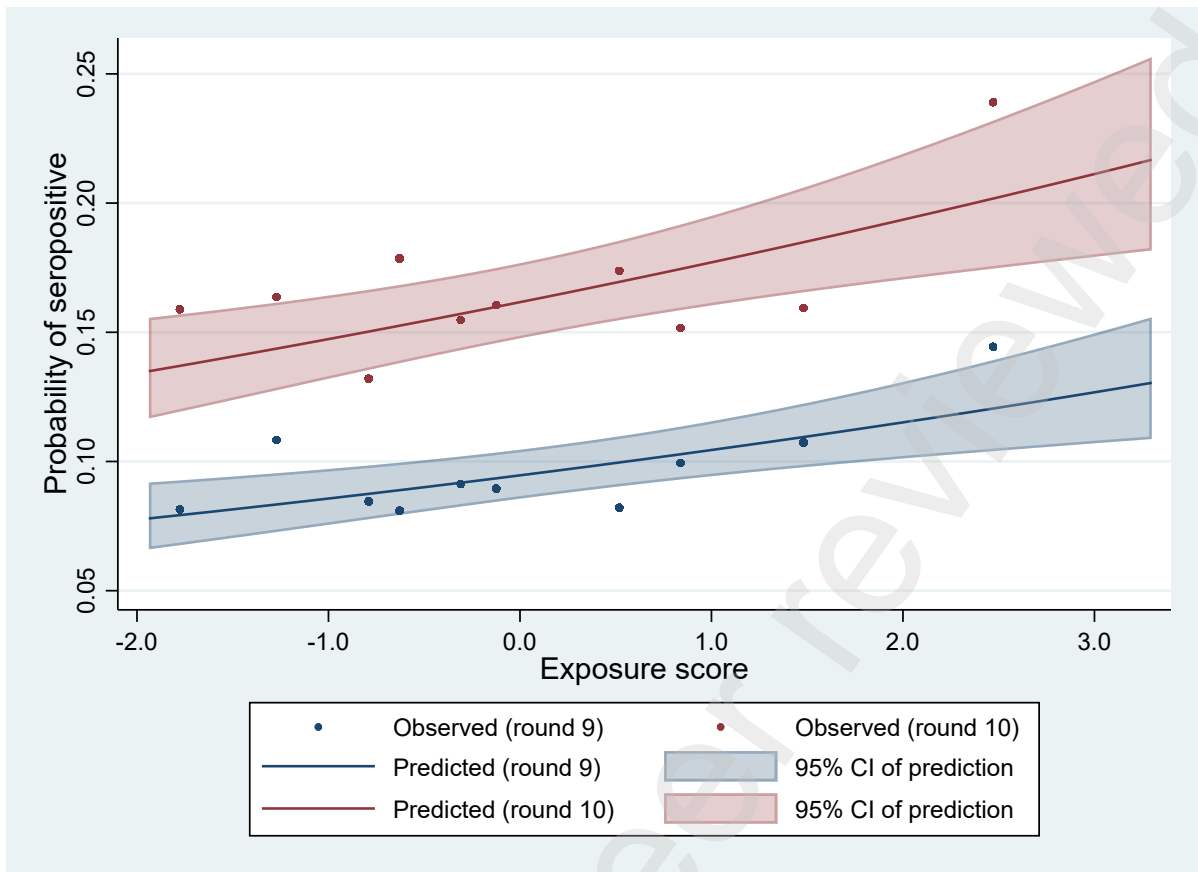
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413  
 414 Figure 1 – Seropositivity for the ten rounds of the EPICOV19-RS study. Source: EPICOV19-RS  
 415 study, Brazil, 2020-21.  
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417  
418 Figure 2 – Mean exposure score for the ten rounds of the EPICOV19-RS study. Source: EPICOV19-  
419 RS study, Brazil, 2020-21.  
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421  
 422 Figure 3 – Probability of being seropositive according to the exposure score, estimated through a  
 423 logistic regression model (7.8% to 13.0%, from the lowest to the highest exposure for round 9 and  
 424 from 13.5% to 21.7% for round 10). The observed percentage of seropositives for each exposure  
 425 decile are presented as dots. Source: EPICOV19-RS study, Brazil, 2020-21.

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428 TABLES

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430 Table 1 – Description of the sample in the ten survey rounds, April 2020 to April 2021, with  
 431 rounds 1-8 presented together. Source: EPICOID19-RS study, Brazil, 2020-21.

Variables	Survey round					
	1-8		9		10	
	N*	%	N*	%	N*	%
<b>Sex (p = 0.0054)</b>						
Male	14,327	40.2	1,731	38.5	1,725	38.3
Female	21,284	59.8	2,770	61.5	2,774	61.7
<b>Age (years) (p &lt; 0.0001)</b>						
0-9	687	2.6	98	2.2	88	2.0
10-19	1,449	5.5	225	5.0	200	4.5
20-39	7,379	27.8	1,111	24.7	1,299	28.9
40-59	8,796	33.1	1,503	33.4	1,563	34.8
60-79	7,218	27.2	1,334	29.7	1,182	26.3
80+	1,055	4.0	228	5.1	159	3.5
<b>Schooling (p &lt; 0.0001)</b>						
Primary (0-4 years)	1,758	4.9	232	5.6	187	4.6
Primary (5-9 years)	3,586	10.1	493	11.9	389	9.5
Secondary	4,530	12.7	586	14.1	535	13.1
Higher (incomplete)	9,804	27.6	1,223	29.4	1,290	31.6
Higher (complete)	15,907	44.7	1,626	39.1	1,688	41.3
<b>Skin color (p = 0.0073)</b>						
White	26,578	76.1	3,291	74.4	3,269	74.0
Brown ("pardo")	5,455	15.6	708	16.0	716	16.2
Black	2,453	7.0	371	8.4	384	8.7
Yellow or Asian	262	0.8	29	0.7	28	0.6
Indigenous	173	0.5	26	0.6	18	0.4

432 \* Unweighted sample size for each subgroup.

433

434 Table 2 – Seropositivity in ten rounds of the EPICOV19-RS study, along with dates, serologic  
 435 test used, type of seropositivity estimation and sample size. Source: EPICOV19-RS study,  
 436 Brazil, 2020-21.

Study round	Median date	Sample size	ELISA	Wondfo rapid test		Cumulative deaths per million
			Crude	Crude	Adjusted <sup>b</sup>	
1	12-Apr-20	4,141		0.05 (0.01-0.19)	0.26 (0.03–1.00)	1
2	25-Apr-20	4,460		0.13 (0.06-0.30)	0.61 (0.19–1.45)	3
3	09-May-20	4,500		0.22 (0.12-0.41)	0.94 (0.39–1.90)	8
4	23-May-20	4,500		0.18 (0.09-0.35)	0.74 (0.28–1.58)	15
5	27-Jun-20	4,500		0.47 (0.30-0.72)	2.12 (1.12–3.62)	49
6	25-Jul-20	4,500		0.96 (0.71-1.29)	4.15 (2.55–6.36)	137
7	15-Aug-20	4,500		1.22 (0.93-1.60)	4.82 (3.09–7.12)	233
8	05-Sep-20	4,500		1.38 (1.06-1.79)	5.15 (3.40–7.43)	326
9	06-Feb-21	4,501	9.97 (9.06-10.95)	2.04 (1.64-2.52)	—	965
10	10-Apr-21	4,499	18.16 (16.90-19.49)	—	—	1,922

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439 Table 3 – Seroprevalence based on the ELISA test, by sentinel city and by population subgroups. Source: EPICOV19-RS study, Brazil, 2020–21.

	Round 9			Round 10		
	% vaccinated*	Vaccinated*	Unvaccinated	% vaccinated*	Vaccinated*	Unvaccinated
<b>City</b>		P = 0.2729	P = 0.4824		P = 0.7264	P = 0.2908
Canoas	1.4	28.6 (7.2–67.4)	12.4 (9.4–16.1)	22.2	20.4 (12.9–30.6)	18.4 (14.1–23.7)
Caxias do Sul	0.8	25.0 (3.3–76.3)	9.3 (7.0–12.3)	22.4	24.3 (17.4–32.9)	15.2 (11.6–19.6)
Ijuí	1.8	55.6 (25.1–82.4)	9.4 (7.0–12.4)	27.8	23.2 (17.0–30.8)	16.2 (12.1–21.2)
Passo Fundo	2.4	25.0 (8.8–53.4)	10.9 (8.2–14.2)	25.9	22.0 (15.5–30.4)	16.2 (11.5–22.2)
Pelotas	2.6	15.4 (4.0–44.3)	8.7 (6.4–11.6)	29.6	23.0 (16.5–31.0)	13.8 (10.1–18.5)
Porto Alegre	3.4	5.9 (0.8–32.3)	8.4 (6.4–11.0)	27.2	23.5 (17.1–31.4)	15.4 (11.9–19.8)
Santa Cruz do Sul	2.2	27.3 (9.0–58.6)	7.9 (5.8–10.7)	26.4	28.2 (20.2–38.0)	14.0 (11.0–17.8)
Santa Maria	2.2	22.2 (5.6–58.0)	10.0 (7.6–13.0)	27.6	16.4 (11.1–23.7)	19.2 (15.6–23.3)
Uruguaiana	2.8	14.3 (3.8–41.0)	10.4 (7.3–14.5)	25.6	21.6 (14.1–31.6)	21.0 (16.8–25.9)
<b>Sex</b>		P = 0.2405	P = 0.2440		P = 0.0620	P = 0.1115
Male	1.3	13.0 (4.3–33.6)	9.0 (7.8–10.5)	22.3	19.2 (15.7–23.3)	15.4 (13.5–17.5)
Female	2.7	24.7 (16.3–35.5)	10.1 (8.9–11.5)	28.4	24.2 (21.0–27.7)	17.4 (15.7–19.4)
<b>Age (years)</b>		P=0.1825	P=0.2533		P=<0.001	P=0.5704
0-10	0	–	9.2 (4.9–16.7)	0	–	21.8 (14.3–31.8)
11-19	0	–	9.8 (6.5–14.4)	0.5	100	17.4 (12.8–23.1)
20-39	4.1	18.2 (9.2–32.7)	11.3 (9.5–13.4)	11.0	31.9 (23.9–41.2)	17.2 (14.9–19.8)
40-59	2.5	32.4 (19.7–48.4)	10.0 (8.5–17.8)	6.0	37.4 (27.6–48.3)	16.4 (14.4–18.4)
60-79	0.9	8.3 (1.2–41.4)	8.4 (7.0–10.1)	66.5	16.8 (14.3–19.7)	14.3 (11.2–18.1)
80+	1.3	0.0	7.7 (4.8–12.3)	94.3	34.0 (26.3–42.7)	12.5 (1.7–53.8)

440

441 Table 3 – Continued.

	% vaccinated*	Round 9		% vaccinated*	Round 10	
		Vaccinated* P=0.0783	Unvaccinated P=0.0262		Vaccinated* P=0.0036	Unvaccinated P=0.1768
<b>Skin color</b>						
White	2.3	17.8 (10.7–28.2)	9.1 (8.1–10.2)	27.7	21.8 (19.1–24.8)	15.6 (14.0–17.2)
Brown (“pardo”)	2.3	37.5 (18.9–60.8)	10.3 (8.2–12.9)	20.7	21.4 (15.4–28.9)	18.9 (15.7–22.6)
Black	1.9	16.7 (2.3–63.2)	14.3 (11.3–18.1)	21.4	29.6 (20.4–40.9)	19.4 (15.0–24.6)
Yellow or Asian	0	—	6.9 (1.7–24.1)	32.1	33.3 (11.1–66.7)	10.5 (2.6–33.8)
Indigenous	3.9	100	16.7 (5.6–40.2)	33.3	83.3 (36.9–97.7)	25.0 (8.0–56.1)
<b>Schooling</b>		P=0.4534	P=0.0258		P=0.1321	P=0.3821
Primary (0-4 years)	0	—	8.7 (5.7–12.9)	59.4	12.8 (7.7–20.6)	18.7 (11.0–29.8)
Primary (5-9 years)	0.6	50.0 (5.9–94.1)	8.0 (5.7–11.1)	38.3	23.1 (17.0–30.7)	13.5 (9.8–18.3)
Secondary	0.3	0.0	11.9 (9.4–14.9)	26.5	21.3 (15.3–28.8)	16.2 (12.8–20.3)
Higher (incomplete)	2.0	34.8 (18.4–55.8)	11.4 (9.7–13.3)	22.2	25.4 (20.7–30.8)	18.6 (16.2–21.3)
Higher (complete)	3.1	22.0 (12.7–35.3)	8.5 (7.2–10.0)	22.8	22.6 (18.1–27.7)	16.7 (14.5–18.9)
<b>Wealth quintiles (IEN)</b>		P=0.0228	P=0.9245		P=0.3003	P=0.3028
Q1 (poorest)	1.4	15.4 (3.9–45.1)	9.6 (7.8–11.8)	34.4	21.8 (17.6–26.6)	18.6 (15.7–21.9)
Q2	1.8	17.7 (5.8–42.8)	10.1 (8.4–12.1)	22.4	27.6 (21.5–34.7)	16.7 (13.9–19.7)
Q3	2.4	50.0 (28.5–71.5)	10.0 (8.1–12.3)	20.8	21.9 (16.5–28.4)	14.5 (11.9–17.6)
Q4	2.1	15.8 (5.2–39.2)	10.0 (8.1–12.3)	25.3	23.4 (18.2–29.5)	17.6 (14.9–20.7)
Q5 (richest)	3.4	11.1 (3.6–29.7)	8.9 (7.0–11.3)	25.6	18.5 (13.5–24.6)	15.7 (13.0–18.9)

442

443 Table 3 – Continued.

Exposure score (deciles)	% vaccinated*	Round 9		% vaccinated*	Round 10	
		Vaccinated* P=0.2686	Unvaccinated P=0.0393		Vaccinated* P=0.2759	Unvaccinated P=0.2207
D1 (least exposed)	1.0	0.0	8.1 (5.4–12.0)	45.9	19.8 (14.5–26.3)	15.9 (11.3–21.9)
D2	1.3	0.0	10.8 (7.7–15.0)	36.3	23.6 (17.4–31.1)	16.4 (12.6–21.0)
D3	1.0	0.0	8.5 (6.4–11.2)	29.2	25.8 (19.0–33.9)	13.2 (9.8–17.7)
D4	0.6	0.0	8.1 (6.1–10.7)	28.3	20.5 (13.8–29.4)	17.9 (13.8–22.8)
D5	0.7	0.0	9.1 (6.2–13.3)	27.0	20.4 (13.4–29.9)	15.5 (11.6–20.4)
D6	1.9	30.0 (10.0–62.4)	9.0 (6.8–11.7)	23.0	18.9 (12.6–27.2)	16.1 (12.8–20.0)
D7	3.1	12.3 (3.1–38.7)	8.2 (6.0–11.1)	21.1	26.4 (18.8–35.7)	17.4 (13.8–21.7)
D8	3.0	18.8 (6.2–44.8)	9.9 (7.6–12.9)	21.6	22.7 (15.7–31.6)	15.2 (11.9–19.1)
D9	3.6	42.1 (22.8–64.1)	10.7 (8.3–13.7)	17.2	19.8 (12.3–30.3)	15.9 (12.6–19.9)
D10 (most exposed)	4.2	27.8 (12.4–51.1)	14.4 (11.6–17.8)	18.5	39.1 (25.9–54.2)	23.9 (18.3–30.6)

444 \* Vaccinated with one or two doses of any of the SARS-CoV-2 vaccines.

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