SARS-CoV-2 seroprevalence and social inequalities in different subgroups of healthcare workers in Rio de Janeiro, Brazil

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Summary

Background COVID-19 has exacerbated health inequalities worldwide. Yet, such a perspective has not been investigated in specific healthcare workers and their resulting inclusion as a priority group for vaccination have been an important focus of political and social discussion. This study aimed at investigating whether SARS-CoV-2-seropositivity in healthcare workers in a public hospital in Rio de Janeiro, Brazil, was influenced by social determinants of health and the social vulnerability in subgroups of workers.

Methods A serological survey was conducted in 1,154 healthcare workers in June and July 2020. The association between the serological test results for detection of IgG antibodies to SARS-CoV-2 and socioeconomic, occupational characteristics and transportation used by the workers to commute was assessed using the Pearson’s chi-square test and Cramer’s V.

Findings Overall, the serum prevalence for the virus in the healthcare workers was 30% (342/1141). Non-white workers (208/561) with lower income (169/396) and schooling (150/353), as well as users of the mass transportation system (157/246) showed the highest infection rates. Importantly they mostly corresponded to hospital support workers (131/324), in particular the cleaning personnel (42/70). Accordingly, income, schooling and work modality appeared as negative predictors, as ascertained by forest plot analysis.

Interpretations The data clearly illustrate the inequality in SARS-CoV-2 infection in the Brazilian population, comprising even healthcare workers of the Brazilian unified health system.

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Keywords: healthcare workers; healthcare professionals; support workers; SARS-CoV-2 seroprevalence; COVID-19; social determinants of health; inequality

Introduction The COVID-19 pandemic is unprecedented in world history, despite global efforts to prevent its spread.1 Although the novel coronavirus was initially viewed as democratic and nondiscriminatory, the disease has exacerbated existing inequalities, as observed in various studies,2–4 demystifying a widely spread but false
Articles

Research in Context

Evidence before this study

Health inequalities involve, not only disparities in income and wealth, but also differences in opportunities, based on ethnicity, race, gender, schooling, occupational exposure, disabilities, sexual orientation, and even geographic location. Despite important strides in overall health indicators, Brazil is still among the ten most unequal countries in the world. In respect to COVID-19, various studies recently investigated seroprevalence to SARS-CoV-2 in healthcare workers, considering this group to be more exposed than the general population.

Added value of this study

Our study used a cohort of health workers and clearly shows the inequities of the COVID-19 pandemics in relation to social determinants. Overall, the serum prevalence for the virus in the healthcare workers was higher in non-white workers with lower income and schooling as well as users of the mass transportation system. Importantly, they mostly corresponded to hospital support workers, in particular the cleaning personnel. Accordingly, income, schooling and work modality appeared as negative predictors, as ascertained by forest plot analysis.

Implication of all the available evidence

The non-democratic distribution of SARS-CoV2 infection is clearly shown even in a population of healthcare workers as the one revealed herein. Population vulnerability is related to social and economic parameters, bypassing biological susceptibilities. These results can drive public policies for the protection and vaccination of the most vulnerable group, especially given situations of shortages of inputs and vaccines.

Evidence before this study

Health inequalities involve, not only disparities in income and wealth, but also differences in opportunities, based on ethnicity, race, gender, schooling, occupational exposure, disabilities, sexual orientation, and even geographic location. Despite important strides in overall health indicators, Brazil is still among the ten most unequal countries in the world. In respect to COVID-19, various studies recently investigated seroprevalence to SARS-CoV-2 in healthcare workers, considering this group to be more exposed than the general population.

Methods

A cross-sectional study was performed in the National Institute of Women, Children, and Adolescent Health “Fernandes Figueira” (IFF), a public tertiary hospital unit specializing in maternal and child healthcare in the framework of the Oswaldo Cruz Foundation (FIOCRUZ), located in the city of Rio de Janeiro.

Data were collected through the dataset generated with a questionnaire, and blood samples were designed in the study entitled “Clinical and immunological characteristics of children, adolescents, and adults with COVID-19 diagnosis: COVID-19 Kids Project”, which was submitted to the Institutional Review Board of IFF (CER/IFF) under identification number 30487120.2.0000.0008 and approved under review number 4.100.148. There was no discrimination in the selection of research subjects or exposure to unnecessary risks.

Study population

In June and July 2020, an invitation to participate was sent to all hospital workers, including both healthcare professionals and support workers. Symptomatic workers were on sick leave and did not participate in the study. Data collection considered every healthy worker who responded to the questionnaire. All the workers were residents in the state of Rio de Janeiro.

Serology

SARS-CoV-2 IgG antibodies were detected with ELISA as previously published. The serological test was performed in a blood sample for semiquantitative investigation of SARS-CoV-2 IgG antibodies with commercial kits manufactured by Euroimmun, with 99.4% sensitivity and 99.6% specificity and according to the manufacturer’s instructions. Plates were read in the spectrophotometer at 450nm for recording the optic density (O.D) of each sample, which was then divided...
by the calibrator’s average O.D. This calculation identifies positive IgG results for values above 1.1, negative IgG for values below 0.8, and indeterminate results for values between 0.8 and 1.0.

**Blood sample collection**
Voluntary serological testing was offered to workers during their working hours, maintaining safety protocols and distancing. Interested individuals scheduled their testing and appeared at the testing facility. The blood sample collection team was prepared technically, and samples were stored at adequate temperature. Prior to blood sample collection, workers completed an online self-administered questionnaire with sociodemographic data (race, gender, schooling, income, health insurance, and number of residents in the household); and work data (department or area of work in the hospital, type of work, workweek, shift, existence of other employment, and job performed). Moreover, data were later collected in terms of the means of transportation for commuting to and from the hospital. Workers were allowed not to answer any specific questions, which led to variation in the number of answers for each item.

**Data survey**

**Sociodemographic data.** For purposes of the data analysis, for the race variable, indigenous, brown, and black individuals were grouped as “non-whites”, resulting in only two groups: whites and non-whites. For the sex variable, although it was an open question, the only answers were “female” and “male”, although some subjects left this item blank. For schooling, we grouped the answers into complete high school, complete undergraduate university, and more than complete undergraduate university. For income, the question was related to the person’s income in multiples of the monthly minimum wage (MW), with one monthly minimum wage being equivalent to approximately US$ 220.00. We grouped individuals into ≤ 3 MW; 4-5 MW, >5 and ≤ 10 MW, and > 10 MW. Having a private health plan was dichotomized as yes or no. As for the number of residents in the household, we grouped the open answers as follows: living alone, 2 to 4 residents, and 5 to 8 residents.

**Data on work at the hospital.** We classified workplaces according to time in contact with patients as follows: high exposure as places in direct clinical contact with patients (in-patient and out-patient departments); medium exposure as places with indirect contact with patients (reception, gates, kitchen, information technology (IT), maintenance, and engineering); and low exposure, places without contact with patients (administrative staff, management, classroom, laboratories, waste disposal). Of note, this hospital does not have a specific area for treating COVID-19 patients. Workweek was grouped as: <30 hours, 30-40 hours, and >40 hours. As for job position, workers were grouped as healthcare professionals, including all professions with specific training in health (physicians, nurses, nurse technicians, physical therapists, psychologists, speech therapists, occupational therapists, nutritionists, pharmacists, social workers, etc.) and support workers, including the other hospital workers (administrative staff, maintenance staff, drivers, cleaning workers, IT staff, etc.). Work modality was classified as daily versus on-duty shift work. Shifts were classified as daytime or night-time. As for the existence of other employment, workers were asked whether they worked in another hospital besides the study site.

**Statistical analysis**
The descriptive analysis presented the absolute and relative frequencies of the target variables. Pearson's chi-square test was used to verify the association between SARS-CoV-2 seroprevalence and sociodemographic, work, and commuting characteristics. The analyses were performed with SPSS, version 22, with statistical significance set at 5%.

To analyze the correlation between the variables, Pearson's chi-square test was performed and the level of correlation was calculated using Cramer's V. To ascertain the predictive power of the variables together and their respective importance, a forest plot was carried out using the variables race, sex, schooling, income, private health plan, number of residents, work modality, workweek, shift, other employment, occupation, and type of means of transport used.

**Role of the funding source**
The funders had no role in data collection, analysis, or interpretation; trial design; patient recruitment; or any aspect pertinent to the study.

**Results**
During the first phase of SARS-CoV-2 serological testing at IFF/Fiocruz in June-July 2020. Specific serology for SARS-CoV2 identifies individuals who have been previously infected, regardless of symptomatology. A total of 1,154 workers were tested, of whom 11 yielded indeterminate results and 2 did not have this information. Of the remaining 1,141 IgG results, 30.0% (342) of the workers tested positive and 70.0% (799) tested negative, still in the first quarter of the pandemic in Brazil.
As for the study population’s sociodemographic data (Table 1), 50.3% of the workers (568) self-identified as whites and 49.7% (561) as non-whites. For gender, 74.6% (848) were women and 25.4% (289) were men. As for schooling, 31.2% (353) had only studied up to high school. For income from wages, 36% (396) reported income less than or equal to 3 minimum wages (approximately US$ 660.00 per month). Most of the workers, 79.2% (879), had private health plans. Only 11.8% (116) of the workers lived alone. The number of infected versus non-infected individuals was slightly higher in individuals living with SARS-CoV2 positive (63.2% pos X 37.8% neg) or suspected positive pals (55.9% pos X 44.1% neg).

As for the characteristics of the work performed (Table 2), the workers were evenly split between 48.5% (492) daily work and 51.5% (522) on-duty shifts. Of all the workers, 71.6% (735) reported workweeks greater than 40 hours. Daytime shifts were reported by 86.1% (945) of shift workers, 69.8% (748) of the total were healthcare professionals, and two-thirds or 67.8% (713) occupied job positions with high exposure to SARS-CoV-2.

Concerning workers’ commuting from home to the hospital and back (Figure 1), 79.2% (499) used a single means of transportation. Among the types of high-density public transportation, buses (46%) were the most widely used by the workers.

As shown in Table 3, when analyzing the socioeconomic variables and the types of work activities performed in relation to ELISA results, race, schooling, income, job position, and type of exposure were significantly associated with the SARS-CoV-2 test result. For race, 37.1% (208) of non-whites tested positive, compared to 23.1% (131) of whites. Level of schooling was inversely associated with SARS-CoV-2 seropositivity, as was income. Even though no statistically significant association was found between number of residents in the household and the work modality in relation to the serological results, there were higher proportions of positive tests in households with 5 to 8 residents (38.9%) and in on-duty shift workers (34.3%).

The results indicated that having another job did not increase the test positivity, since 32% of workers without another job tested positive, compared to 25.5% in workers who did have another job. As for job positions, we observed that 40.4% (208) of support workers tested positive for SARS-CoV-2 IgG antibodies, compared to only 25.0% (187) of healthcare professionals. Concerning the level of potential exposure to SARS-CoV-2, 40.9% (47) of workers with medium exposure tested positive, compared to 27.5% (194) and 26.8% (59) in workers with high and low exposure, respectively.

In the different categories of support workers (Table 4), 60.6% (44) of cleaning workers tested positive, compared to only 25% (18) of healthcare professionals. Among the means of transportation for commuting between home and the hospital and back, all types of
transportation showed statistically significant associations with the serological results (Table 5). Workers that used mass transportation (train, subway, and bus) showed significantly higher positive test results than those using other means of transportation. Workers that used lower density commuting (walking, car, motorcycle, taxi) showed lower rates of positive test results than those commuting by other means of transportation.

All analyzed variables were correlated with at least one other variable demonstrating some degree of dependence between them. The variable with the lowest number of correlations was the number of residents (1 correlation) and the one with the highest number of correlated variables is schooling that correlates with shift and with 10 other variables analyzed (Figure 2A).

To assess whether, when analyzed together, these variables would have predictive power, we observed that, despite the high total efficiency of 0.8125, the positive predictive power value was 0.00 and the negative predictive power value was 1.00, demonstrating a high power for negative but not for positive cases. The most important variables for this prediction are income, followed by schooling and work modality, and the ones of less importance are shifts, followed by occupation and number of residents in the house (Figure 2B).

**Discussion**

We report here the prevalence of SARS-CoV-2 IgG antibodies in a sample of healthcare workers in a public hospital in Rio de Janeiro, which is not a referral hospital for COVID-19. Higher seroprevalence was not only associated with exposure in the workplace but was aggravated mainly by social inequalities within the group, with higher seroprevalence being associated with non-white race, lower salary income, lower schooling, and commuting by mass transportation.

Compared to the largest seroprevalence study with 2,857 voluntary and asymptomatic blood donors in the city of Rio de Janeiro in April 2020, the weighted prevalence using the population of Rio de Janeiro in 2020 was 3.3%. In Spain, a national population-based cohort study in April-May 2020 showed 4.6% seroprevalence in the domiciled population. Our survey of healthcare workers in June-July 2020 showed much higher prevalence, namely 30%. Differing from the domiciled Spanish population study, healthcare workers are considered one of the social groups most exposed to the virus. In this respect, the 30% prevalence (342/1141) seen in the current study corroborates other studies of healthcare workers in New York, Birmingham, London, and Bukavu, with rates of 27.0% (137/500), 24.4% (126/516), 31.64% (634/2004), and 41.2% (148/359), respectively.

 Contributing factors to the increased exposure of healthcare workers may include patient-worker transmission and worker-worker transmission, especially in referral hospitals for COVID-19, or high exposure during commuting to and from work. Meta-analyses of SARS-CoV-2 seroprevalence in healthcare workers and the general population showed that the prevalence rates vary greatly, with healthcare workers presenting the highest rates. In the former, the highest prevalence rate was reported by studies in North America (12.7%) compared to Europe (8.5%), Africa (8.2%), and Asia (4%). Differently, the meta-analysis that excluded populations at greatest risk revealed SARS-CoV-2 seroprevalence rates varying from 0.37% to 22.1%. These differences may reflect the samples, level of exposure, and testing period, besides the regions’ political and economic conditions that affect availability and access to tests. We believe that the higher prevalence observed in our study may reflect a combination of workplace and community exposure, since the population we analyzed consisted of healthcare workers residing in the city of Rio de Janeiro.
| Variables                                      | Serological test | p-value       |
|-----------------------------------------------|------------------|---------------|
|                                               | Negative n | %     | Positive n | %       |
| Race                                          |              |            |            |         |
| White                                         | 437          | 76.9%    | 131        | 23.1%   | < 0.001* |
| Non-white                                     | 353          | 62.9%    | 208        | 37.1%   |          |
| Sex                                           |              |            |            |         |
| Female                                        | 604          | 71.2%    | 244        | 28.8%   | 0.158    |
| Male                                          | 193          | 66.8%    | 96         | 33.2%   |          |
| Schooling                                     |              |            |            |         |
| Complete secondary or less                    | 203          | 57.5%    | 150        | 42.5%   | < 0.001* |
| Complete undergraduate university             | 225          | 72.6%    | 85         | 27.4%   |          |
| More than undergraduate university            | 363          | 77.6%    | 105        | 22.4%   |          |
| Income                                        |              |            |            |         |
| ≤ 3 MW                                        | 227          | 57.30%   | 169        | 42.7%   | < 0.001* |
| 4-5 MW                                        | 109          | 69.40%   | 48         | 30.6%   |          |
| More than 5 and ≤ 10 MW                       | 202          | 76.50%   | 62         | 23.5%   |          |
| More than 10 MW                               | 232          | 82.30%   | 50         | 17.7%   |          |
| Private health plan                           |              |            |            |         |
| No                                            | 154          | 66.7%    | 77         | 33.3%   | 0.226    |
| Yes                                           | 624          | 71.0%    | 255        | 29.0%   |          |
| Number of residents in the household          |              |            |            |         |
| Living alone                                  | 83           | 71.60%   | 33         | 28.4%   | 0.068    |
| 1 to 4 residents                              | 529          | 71.20%   | 214        | 28.8%   |          |
| 5 to 8 residents                              | 77           | 61.10%   | 49         | 38.9%   |          |
| Work modality                                 |              |            |            |         |
| Daily                                         | 351          | 71.3%    | 141        | 28.7%   | 0.058    |
| On-duty shift                                 | 343          | 65.7%    | 179        | 34.3%   |          |
| Workweek                                      |              |            |            |         |
| <30 hours                                     | 86           | 67.7%    | 41         | 32.3%   | 0.785    |
| 30-40 hours                                   | 115          | 69.7%    | 50         | 30.3%   |          |
| >40 hours                                     | 520          | 70.7%    | 215        | 29.3%   |          |
| Shift                                         |              |            |            |         |
| Daytime                                       | 669          | 70.8%    | 276        | 29.2%   | 0.183    |
| Nighttime                                     | 100          | 65.4%    | 53         | 34.6%   |          |
| Other employment                              |              |            |            |         |
| No                                            | 512          | 68.0%    | 241        | 32.0%   | 0.030    |
| Yes                                           | 269          | 74.5%    | 92         | 25.5%   |          |
| Job position                                  |              |            |            |         |
| Healthcare professionals                      | 561          | 75.0%    | 187        | 25.0%   | < 0.001* |
| Support workers                               | 193          | 59.6%    | 131        | 40.4%   |          |
| Workplace exposure to SARS-CoV-2              |              |            |            |         |
| Low exposure                                  | 161          | 73.2%    | 59         | 26.8%   | 0.010    |
| Medium exposure                               | 68           | 59.1%    | 47         | 40.9%   |          |
| High exposure                                 | 511          | 72.5%    | 194        | 27.5%   |          |

Table 3: Socioeconomic variables and types of work activities among hospital workers according to ELISA results for SARS-CoV-2 IgG antibodies.

* Pearson chi-square test; significant result: p-value < 0.05.

** One monthly minimum wage = BRL 1,045.00 or US $220.00.
Rio de Janeiro and outlying cities, one of the most populous regions of Brazil.\textsuperscript{17}

We observed that race was significantly associated with SARS-CoV-2 seropositive status, with higher prevalence in non-whites (black, brown, and indigenous individuals) (37.1%) than in whites (23.1%). These data are corroborated by previous studies both in healthcare workers and in the general population, confirming the racial inequality in SARS-CoV-2 prevalence.\textsuperscript{2,3,10,25} The reasons for this is probably related to lower socioeconomic status, and/or living in areas with higher population density and crowding, thus increasing exposure and risk of infection.\textsuperscript{21,26}

A study in the United States evidenced racial/ethnic predisposition as a determinant condition for SARS-CoV-2 seropositivity in healthcare workers in New York\textsuperscript{21}, with a crude odds ratio of 2.42 (95\%CI 1.3 - 4.5; p = 0.005) for Hispanics, and 2.55 (95\%CI 1.3-5.02; p = 0.006) for Blacks, when compared to Caucasians, what is much probably related to social aspects than race itself.

Another finding from the present study was that lower schooling and income were associated with higher seropositivity (42.5\% and 42.7\%, respectively. Data from a seroprevalence study in the city of São Paulo, Brazil, in June-July 2020 showed higher SARS-CoV-2 seropositivity in residents of low-income neighborhoods (22\%) compared to residents of high-income neighborhoods (9.4\%). In addition, individuals who had not finished primary school showed 22.5\% seroprevalence, compared to 12\% in those with university education,\textsuperscript{27} in accordance to our results.

The higher prevalence (40.7\%) in workers that used mass transportation to commute to and from work was another important finding in this study, reinforcing the hypothesis that SARS-CoV-2 transmission may be influenced by social inequality and community exposure.\textsuperscript{28,29}

Previous studies have analyzed SARS-CoV-2 seroprevalence in healthcare professionals, but without taking into account the support workers. In our study, COVID-19 seroprevalence rates varied according to occupational activity. Hospital support workers had higher SARS-CoV-2 seroprevalence (40.4\%) than healthcare professionals (25\%). According to subgroups of jobs, cleaning workers, followed by security guards and doormen, administrative staff, maintenance staff, and healthcare professionals had

\begin{table}
\centering
\begin{tabular}{|l|c|c|c|c|}
\hline
Categories of hospital workers & Serological test & p-value & \\
& Negative & Positive & \\
& n & % & n & % & \\
\hline
Cleaning workers & 28 & 40.0\% & 42 & 60.0\% & < 0.001\* \\
Security guards and doormen & 31 & 60.8\% & 20 & 39.2\% & \\
Administrative staff/mangement & 105 & 65.2\% & 56 & 34.8\% & \\
Engineering and maintenance & 29 & 69.0\% & 13 & 31.0\% & \\
Healthcare professionals & 561 & 75.0\% & 187 & 25.0\% & \\
\hline
\end{tabular}
\caption{Categories of support workers and healthcare professionals according to SARS-CoV-2 IgG ELISA results.\* Pearson’s chi-square test; significant result: p-value < 0.05.}
\end{table}

\begin{table}
\centering
\begin{tabular}{|l|c|c|c|c|}
\hline
Train/subway & Serological result & p-value & \\
& Negative & Positive & \\
& n & % & n & % & \\
\hline
No & 376 & 72.7\% & 141 & 27.3\% & < 0.001\* \\
Yes & 67 & 59.3\% & 46 & 40.7\% & \\
Bus & 264 & 77.6\% & 76 & 22.4\% & < 0.001\* \\
No & 179 & 61.7\% & 111 & 38.3\% & \\
Yes & 207 & 63.9\% & 117 & 36.1\% & < 0.001\* \\
Walking/car/motorcycle & 236 & 77.1\% & 70 & 22.9\% & \\
No & 207 & 63.9\% & 117 & 36.1\% & < 0.001\* \\
Yes & 236 & 77.1\% & 70 & 22.9\% & \\
Uber/Taxi & 401 & 69.0\% & 180 & 31.0\% & < 0.001\* \\
No & 42 & 9.5\% & 7 & 3.7\% & \\
Yes & 236 & 77.1\% & 70 & 22.9\% & \\
\hline
\end{tabular}
\caption{Means of transportation is related to the frequency of health works tested positive for the presence of anti-SARS-CoV-2 IgG antibodies.}
\end{table}
seropositive rates of 60%, 39.2%, 34.8%, 31%, and 25%, respectively supporting the interpretation that exposure occurs more in the community than within the hospital. This finding is in keeping with the study that reported higher prevalence of SARS-CoV-2 infection in cleaning workers at a hospital in the city of São Paulo.30 A study in the United Kingdom tested 9,958 university hospital employees, and 10.7% tested positive for SARS-CoV-2 IgG antibodies, with doormen and cleaning workers having the highest rates (18.6%), and administrative personnel the lowest proportion (7.2%).9 It is likely that cleaning workers not only have high exposure to the virus at work and lower knowledge about the virus and its transmission mechanisms, but also belong to lower socioeconomic classes and live under conditions that can expose them to crowding.

Three European studies confirmed higher prevalence in high-risk versus low-risk environments (34.7% vs 22.6%, 21% vs 9%, and 7.19% vs 4.45%). However, the study in São Paulo showed that working in dedicated in-hospital COVID-19 units was not associated with higher seropositivity.30 This is an interesting finding, reinforcing the notion that healthcare workers in direct contact with patients are not necessarily more susceptible to infection despite being more exposed to the disease than hospital workers with little or no contact with patients. Again, we reinforce that the hospital herein reported was not specifically a referral unit for COVID-19 care, although it frequently received COVID-19 patients.

Finally, although we observed a clear association between seroprevalence and race, income, schooling, work activity, type of exposure, and use of mass transportation, we were not able to distinguish between the effects of occupational exposure and community exposure on SARS-CoV-2 seropositivity. Still, given the shortage of vaccines at the testing period reported herein, this study...
points clearly what the more vulnerable subgroups within the group of healthcare workers. These more vulnerable subgroups should be a priority in the immunization process under Brazil’s national policies, and can be useful as a basis for other latinamerican countries.

Conclusion
SARS-CoV-2 transmission in healthcare workers occurs between patients and workers, between workers and workers, or due to high exposure during commuting to and from work. Our study further stresses that social determinants of health influence the infection rates in healthcare workers. In addition to the high prevalence of infection in the studied population, non-white workers, those with less income and schooling, and users of mass transportation were the most affected. Moreover, hospital support workers and especially cleaning workers had higher seroprevalence rates than healthcare professionals. Income, followed by schooling and work modality were the main factors in the negative prediction for contamination. Also, community exposure appears to prevail over transmission inside the hospital.

Acknowledging social determinants and work conditions as aggravating factors in the profile of SARS-CoV-2 transmission in the pandemic allows identifying and prioritizing groups with high vulnerability, in addition to orienting and adapting interventions, such as priority for immunization.

Declaration of interests
The authors declare no conflict of interest.

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Author contributions
Conceptualization, RFC., ZV, EA; Methodology, RFC, ZFVM, ACCC, RGG; DCBCM, SCGJ.; Validation, RFC, ACCC, RGG, ZFVM, EA ; Investigation, RFC, ZFVM; Resources, RFC, ZFVM, MPCI, MCCZ, WS, ACB, EA.; Data Curation, RFC, ZFVM; Writing—Original Draft Preparation, RFC; Writing—Review and Editing, RFC, ACCC, RGG, DCBCM, SCGJ, WS, ACB, ZFVM, EA; Supervision, RFC, ZFVM, EA; All authors have read and agreed to the published version of the manuscript.

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