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Mitigation of Socio-Economical Inequalities on the Profile of Healthcare Workers Infected with SARS-CoV-2 upon Vaccination: The Experience of a Brazilian Public Healthcare Institution during the Omicron Wave

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Abstract: Background: COVID-19 increased health inequalities worldwide. Even among healthcare workers, social-economical features enhanced the risk of infection (having positive serology) during the first outbreak. The Omicron variant changed the pandemic course and differs from previous variants in many aspects (molecular, clinical, and epidemiological). Herein, we investigated if the profile of our hospital SARS-CoV-2-positive workers during the Omicron outbreak was the same as the first COVID-19 wave. Methods: Socio-demographics, previous infection, and vaccine status of 351 healthcare workers from our institution during the Omicron outbreak were compared between SARS-CoV-2-negative and -positive workers, using chi-square tests. These data were confronted with the profile observed at the beginning of the pandemic. Results: Compared to the original COVID-19 wave, higher odds of SARS-CoV-2 positivity in highly exposed workers in our hospital and a loss of impact of public transportation and other socio-demographic features in SARS-CoV-2 transmission were observed. Conclusions: Our data suggest the current phase of the pandemic is associated with a reduction of social inequalities among healthcare workers in Rio de Janeiro, possibly due to vaccine-associated protection. Therefore, a worldwide effort to advance vaccination coverage, especially for healthcare workers in developing countries, should be reinforced.

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

1. Introduction

A new variant of SARS-CoV-2, B1.1.52c Omicron, was first identified in South Africa in November of 2021 [1]. The Omicron variant contains over 30 mutations in its spike protein, compared to the Wuhan-Hu-1 strain [2]. The World Health Organization (WHO) designated this variant as the fifth variant of concern (VOC), as it is highly transmissible and has the ability of immune escape [3]. An important fraction of individuals who developed antibodies against the Alpha, Gamma, or Delta variants, either by natural infection or by the complete vaccination schedule, are unable to neutralize the infection by the Omicron variant [4]. Nevertheless, the clinical severity of COVID-19 disease caused by Omicron seems to be reduced compared to other variants [5–7].

During the first SARS-CoV-2 wave of infection, we conducted a serological survey in 1154 workers of our institution to monitor SARS-CoV-2 infection in our staff and hospital environment. We observed a 30% prevalence of SARS-CoV-2 positivity and the highest infection rates in non-white workers, with lower income and schooling, and users of the mass transportation system. This group was composed mainly of hospital support workers, particularly the cleaning personnel. These data clearly depict Brazilian high inequality, even amongst healthcare workers [8].

Epidemiological studies on the profile of healthcare workers with higher vulnerability for infection are essential for the development of strategies to improve worker safety whilst maintaining effective health services. Moreover, these studies are valuable to the design of public policies for the protection and vaccination of healthcare workers, especially in situations of vaccine shortage.

However, while the Omicron variant changed the pandemic's course and is different from previous variants in many aspects (molecular, clinical, and epidemiological), it is currently unknown if these inequalities also impact infection among workers. Moreover, the impact of COVID-19 vaccines in this scenario is also yet to be estimated. Herein, we investigated if the profile of our institution's workers who tested positive for SARS-CoV-2 during the Omicron outbreak (December 2021 through March 2022) resembles the one from the first infection wave in 2020.

2. Materials and Methods

2.1. Study Population

This is a cross-sectional study performed in the National Institute of Women, Children, and Adolescent Health "Fernandes Figueira" (Instituto Fernandes Figueira—IFF), one of the Oswaldo Cruz Foundation (Fundação Oswaldo Cruz—Fiocruz) institutes located in the city of Rio de Janeiro. The present study is part of a broader institutional COVID-19 monitoring initiative entitled "Clinical and immunological characteristics of healthcare workers after vaccine against COVID-19: the LEGEND study", which was submitted to the Institutional Review Board of IFF (CEP/IFF) under identification number 42988721.6.0000.5269 and approved under review number 4.536.586 on 18 February 2021.

Data regarding workers from our institution who tested for SARS-CoV-2 during the Omicron outbreak (from December 2021 through March 2022) were collected and analyzed. Inclusion criteria were (1) being a worker in our Institution, (2) having participated in the original serological study (having answered to the inquiry and having a valid serological test result), and (3) having tested for SARS-CoV-2 during the Omicron wave. Workers who did not fulfill all criteria were excluded from the study population. Socio-demographic information was obtained through a questionnaire, which workers answered when they joined the serological survey of all workers from IFF conducted in 2020. The vaccination status of workers was obtained through the vaccine database of our public healthcare system (ConecteSUS). As vaccination data are dynamic, for the purposes of the current study, only jabs taken before the day of the SARS-CoV-2 test during the Omicron outbreak were considered. Based on these criteria, a total of 351 workers were included in the present study. It is important to notice that our hospital is not a COVID-19 reference center.

A timeline of the study depicting related pandemics events and number of workers in each inclusion criteria is provided in Figure 1.

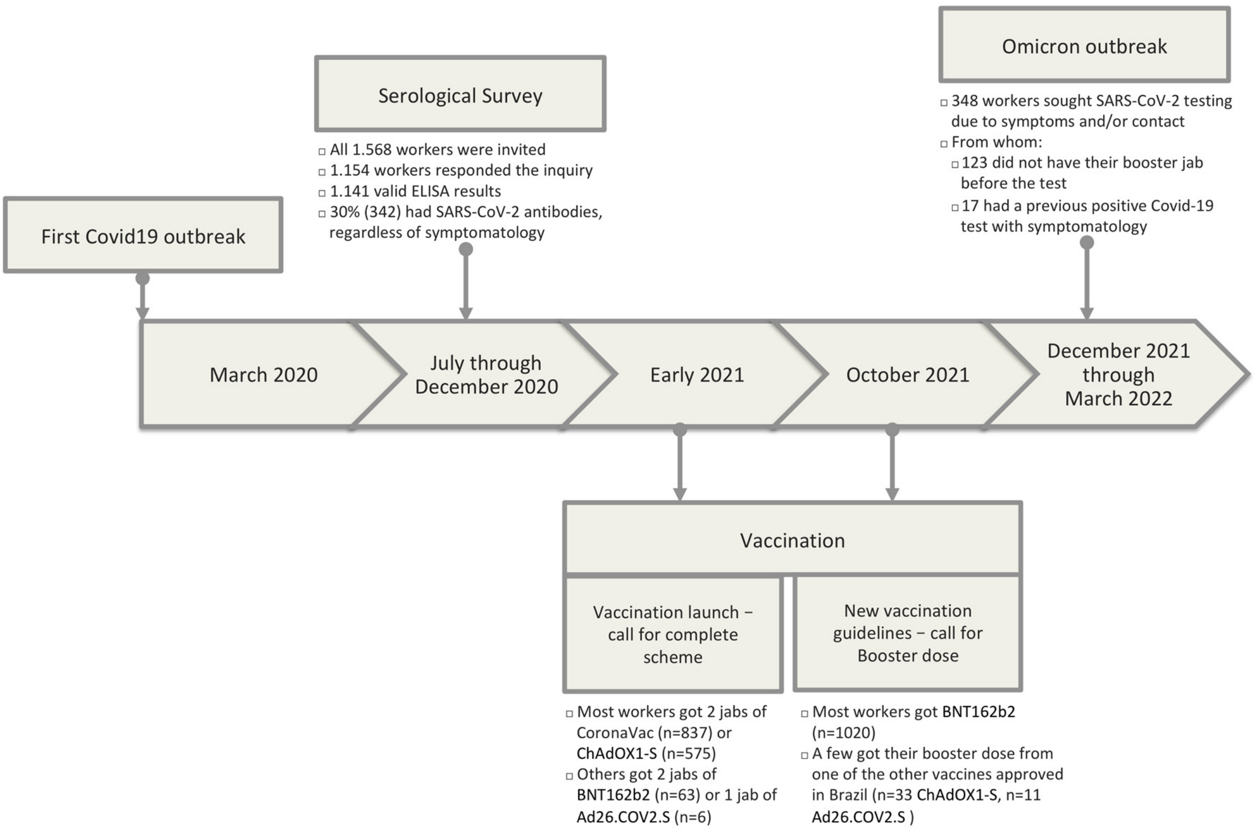

Figure 1. Study timeline depicting related pandemic events and number of workers in each inclusion criteria.

2.2. *SARS-CoV-2 PCR Test*

The real-time PCR technique was performed using RNA extracted from nasopharynx swab samples. Samples were collected between three and seven days after the onset of symptoms. Next, one-step qRT-PCR was performed in the BDMAX system, based on the protocol developed by scientists from Charité University of Berlin [9]. Primers and probes are listed in Table 1. The cycling conditions were: first incubation at 50.0 °C for 30 min, second incubation at 95.0 °C for 5 minutes (qScript), 45 times at 95.0 °C for 15 min, and 60.0 °C for 1 minute (Table 1).

Table 1. Primers and Probes for the SARS-CoV-2 E gene.

Gene	Oligonucleotide	Sequence (5′-3′)	Concentration
E	E_Sarbeco_F	ACAGGTACGTTAATAGTTAATAGCGT	400 nm
	E_Sarbeco_P1	FAM-ACACTAGCCATCCTTACTGCGCTTCG-TAMRA	200 nm
	E_Sarbeco_R	ATATTGCAGCAGTACGCACACA	200 nm

2.3. *SARS-CoV-2 Antigen Test*

SARS-CoV-2 S antigen was detected with a Rapid test performed in a nasal sample with commercial kits manufactured by Bio-Manguinhos//Fiocruz-RJ (Rio de Janeiro, Brazil), according to the manufacturer's instructions (TR COVID-19 Ag Bio-Manguinhos). Samples were collected, and the SARS-CoV-2 antigen, when present in the samples, was enabled to react with the gold conjugate coupled to the SARS-CoV-2 monoclonal antibody, followed by reaction with anti-SARS-CoV-2 monoclonal antibodies immobilized on the test stand. The results were interpreted by visual reading: negative samples presented only the control line, and positive samples presented the control line and the test line. If the control line was not shown, the test was considered invalid.

2.4. SARS-CoV-2 IgA and IgG ELISA

SARS-CoV-2 IgA and IgG antibodies were detected with ELISA as previously described [8]. Briefly, the serological test was performed in a blood sample for semiquantitative investigation of SARS-CoV-2 IgA and IgG antibodies with commercial kits manufactured by Euroimmun, with 99.4% sensitivity and 99.6% specificity, according to the manufacturer's instructions. Plates were read in the spectrophotometer at 450 nm to record each sample's optic density (O.D), which was then divided by the calibrator's average O.D. This calculation identifies IgG as positive for values above 1.1, negative for values below 0.8, and indeterminate for values between 0.8 and 1.1.

2.5. Data Categorization

For purposes of data analysis, variables were categorized as follows:

2.5.1. Socio-Demographic Data

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". Individuals were also categorized into age groups as 18–30 years old, 31–45 years old, 46–60 years old, and 61 years old or above.

2.5.2. Data on Work at the Hospital

Individuals were also categorized according to their occupation as healthcare professionals (all professions with specific training in healthcare, such as physicians, nurses, nurse technicians, physical therapists, psychologists, speech therapists, occupational therapists, nutritionists, pharmacists, and social workers, among others) or support workers (the other hospital workers, such as administrative staff, maintenance staff, drivers, cleaning workers, and information technology staff, among others). Regarding the level of workplace exposure to SARS-CoV-2, individuals were categorized as working in high exposure (environments with direct clinical contact with patients, in-patient and out-patient sectors), intermediate exposure (environments with indirect contact with patients, such as reception, gates, kitchen, information technology, maintenance, and engineering), or low exposure (environments with no contact with patients, such as administration, management, classroom, laboratories, and waste disposal), as previously described [8].

2.5.3. Data on SARS-CoV-2 Test Result

For the current study, we also categorized individuals as negative or positive according to (1) their SARS-CoV-2 infection test result (either PCR or Antigen) taken during the Omicron outbreak (between 1 December 2021 and 31 March 2022) and (2) their SARS-CoV-2 antibody status, as of evaluated during the first COVID-19 wave in 2020 (as previously described [8]). Patients with inconclusive results were not included in the statistical analyses.

2.5.4. Data on Vaccination Status at the Time of SARS-CoV-2 Testing

Individuals were also categorized according to their COVID-19 vaccination status at the time of their SARS-CoV-2 test during the Omicron wave. Vaccination status was defined as: unvaccinated—individuals who did not have any jab at the time; partially vaccinated—individuals who had one jab of CoronaVac (Sinovac), ChAdOX1-S (Oxford-AstraZeneca), or BNT162b2 (Pfizer-BioNTech); fully vaccinated—individuals who had one jab of Ad26.COV2.S (Janssen) or two jabs of CoronaVac, ChAdOX1-S, or BNT162b2; or fully vaccinated with a booster dose.

2.6. Statistical Analysis

Pearson's chi-square test (2×2 Tables) [10] or Fisher's Exact Test (3×2 Tables) [11] were used to investigate the association between SARS-CoV-2 positivity during the Omicron outbreak and socio-demographic, work, and vaccination status characteristics. Logistic regression was used to verify the independent predictive value of these characteristics [12]. SARS-CoV-2 positivity was considered as the event. For all estimates of odds, a 95% confidence interval alongside the respective p-value is given. The analyses were performed with SPSS, version 22, or JASP, version 0.14.1. Association between the investigated categorical features and SARS-CoV-2 positivity was considered statistically significant when p-value < 0.05.

3. Results

3.1. Socio-Demographic Features

Socio-demographic data from the 351 workers tested for SARS-CoV-2 by our institution's surveillance program during the Omicron wave: regarding race, 165 declared themselves as white and 186 as non-white (indigenous, brown, or black). Consistent with the fact that our workforce is mostly composed of women, there were 272 women and 79 men. Regarding age, most workers who sought COVID-19 testing during the Omicron wave were aged 31 to 45 years (149/348). Absolute numbers and percentages are depicted in Table 2.

Table 2. Socio-demographic data on IFF/Fiocruz healthcare workers tested for SARS-CoV-2 during the Omicron wave.

Variable	n	% *
Total	351	100%
Race		
White	165	47%
Non-white	186	53%
Gender		
Female	272	77.5%
Male	79	22.5%
Age		
18–30	38	8.0%
31–45	149	42.8%
46–60	135	38.8%
Over 60	26	7.4%
Income		
≤3 MW	110	33%
4–5 MW	46	14%
More than 5 and ≤10 MW	92	27%
More than 10 MW	85	26%

* Percentages calculated excluding cases with missing information. One monthly minimum wage (MW) = BRL 1045.00 or USD 195.00.

Considering the nature of their jobs, 198 individuals were classified as healthcare professionals and 151 as support workers. We also categorized workers according to the level of their workplace environment exposure to SARS-CoV-2. A total of 65 individuals were classified as working under low exposure, 12 as medium exposure, and 130 as high exposure. Absolute numbers and percentages are depicted in Table 3.

During the first COVID-19 outbreak in 2020, we evaluated the IgA and IgG anti-SARS-CoV-2 antibody status of our workforce [8]. From the 351 workers who sought SARS-CoV-2 testing during the Omicron wave, nearly half (n = 176) had antibodies against the virus (Table 4). This data is consistent with the 30% positivity found in our previous study comprising most of our workforce (1154 individuals). Regarding vaccination status, nearly 2/3 of workers had taken their first booster dose before getting tested during the Omicron wave (225/351). Almost all booster doses were BNT162b2 (Table 4).

Table 3. Types of job activities performed by healthcare workers in IFF/Fiocruz.

Variable	n	% *
Occupation		
Healthcare professionals	198	56.7
Support workers	151	43.3
Level of workplace exposure to SARS-CoV-2		
Low exposure	65	31.4
Medium exposure	12	5.8
High exposure	130	62.8

* Percentages calculated, excluding cases with missing information.

Table 4. Statuses of SARS-CoV-2 IgA/IgG before vaccination and vaccine scheme at the time of SARS-CoV-2 test in healthcare workers from IFF/Fiocruz.

Variable	n	% *
Total	**351**	**100%**
SARS-CoV-2 Antibody Status before vaccination **		
Negative	*175*	*49.9*
Positive	*176*	*50.1*
COVID-19 vaccination scheme status ***		
Unvaccinated	*4*	*1.1*
Incomplete	*5*	*1.4*
Complete	*342*	*97.4*
CoronaVac	178	52.0
ChAdOX1-S	144	42.1
BNT162b2	10	2.9
Ad26.COV2.S	1	0.3
Unavailable	*9*	*2.6*
Complete without booster	*117*	*34.2*
CoronaVac	39	33.3
ChAdOX1-S	71	60.7
BNT162b2	6	5.1
Ad26.COV2.S	1	0.9
Complete with a booster dose	*225*	*65.8*
ChAdOX1-S	9	4.0
Two doses CoronaVac	1	0.4
Two doses ChAdOX1-S	8	3.6
BNT162b2	216	96.0
Two doses CoronaVac	138	61.3
Two doses ChAdOX1-S	65	28.9
Two doses BNT162b2	4	1.8
Unavailable	9	4.0

* Percentages calculated, excluding cases with missing information. ** Antibody status evaluated through ELISA during the first COVID-19 outbreak in 2020. *** Vaccination scheme status was classified as unvaccinated (individuals who did not have any jab at the time), incomplete (individuals who had one jab from CoronaVac, ChAdOX1-S or BNT162b2), complete (individuals who had one jab from Janssen or two jabs from CoronaVac, ChAdOX1-S or BNT162b2), and complete with a booster dose.

3.2. Socio-Demographic Profile of SARS-CoV-2 Positivity during the Omicron Outbreak

Next, we evaluated if socio-demographic characteristics and types of work activity were associated with the result of the SARS-CoV-2 test during the Omicron wave (Table 5). Race was not significantly associated with SARS-CoV-2 infection (p-value = 0.119). Surprisingly, the female gender was associated with a positive test for SARS-CoV-2 (p-value = 0.033). Being a female increased the risk of testing positive by almost 2-fold. Regarding work activity, being a healthcare professional per se did not associate with testing positive (p-value = 0.219). Instead, working in high-exposure sectors had over 2-fold added risk of testing positive (*p*-value = 0.032). Of note, the type of commute to work, which increased the risk of being exposed to COVID-19 in our previous study, was not associated with an increased risk of testing positive for SARS-CoV-2 during the Omicron wave (Table S1).

Table 5. Socio-demographic variables and types of work activities of IFF/Fiocruz healthcare workers, according to SARS-CoV-2 test result.

Variables	**SARS-CoV-2 Test Result**				***p*-Value**
	Negative		**Positive**		
	n	**%**	**n**	**%**	
Total	128	36.7	221	63.3	
Race					
Non-white	68	41.2	97	58.8	0.119
White	60	32.6	124	67.4	
Gender					
Female	91	33.6	180	66.4	0.033 *
Male	37	47.4	41	52.6	
Income					
≤3 MW	44	40.0	66	60.0	0.254
4–5 MW	10	21.7	36	78.3	
More than 5 and ≤10 MW	33	35.9	59	64.1	
More than 10 MW	32	38.6	51	61.4	
Occupation					
Healthcare professionals	67	33.8	131	66.2	0.219
Support workers	61	40.4	90	59.6	
Workplace exposure to SARS-CoV-2					
Low exposure	31	47.7	34	52.3	0.032 *
Medium exposure	6	50	6	50	
High exposure	39	30	91	70	

* Pearson's chi-square test (2 variables) or Fisher's Exact Test (3 or more variables); significant result: *p*-value < 0.05. One monthly minimum wage (MW) = BRL 1045.00 or USD 195.00.

To further understand the association between women and highly exposed workers to SARS-CoV-2 test positivity, we questioned if this gender association coincided with women working in high-exposure sectors (Table 6). Indeed, we observed that in our cohort, most women do work in high-exposure environments (*p*-value = 0.010). In addition, most of our healthcare professionals are women (*p*-value = 0.004). Moreover, in the multivariate analysis, gender was not significantly associated with SARS-CoV-2 positivity (*p*-value = 0.355), but high workplace exposure was (*p*-value = 0.016). Logistic regression is depicted in Table S2. These data are consistent with the fact that women account for 70% of healthcare professionals worldwide [13].

Table 6. Association between gender and types of work activities amongst IFF/Fiocruz workers.

Variables	Gender				*p*-Value *
	Female		Male		
	n	%	n	%	
Workplace exposure to SARS-CoV-2					
Low exposure	46	28	19	44.2	0.010 *
Medium exposure	7	4.3	5	11.6	
High exposure	111	67.7	19	44.2	
Occupation					
Healthcare professionals	165	60.9	33	42.3	0.004 *
Support workers	106	39.1	45	57.7	

* Pearson's chi-square test (2 × 2 Tables) or Fisher's Exact Test (3 × 2 Tables); significant result: *p*-value < 0.05.

3.3. Impact of Previous Infection or Vaccine-Acquired Immunity on SARS-CoV-2 Positivity during the Omicron Outbreak

Concerning acquired immunity, to verify if a previous COVID-19 infection would protect against the Omicron outbreak, we compared the frequency of SARS-CoV-2 infection between personnel with and without antibodies from the original SARS-CoV-2 strand and between personnel with or without a positive PCR test previous to the Omicron outbreak (Table 7). Positive serology for SARS-CoV-2 against the original strand did not protect against infection during the Omicron wave (*p*-value = 0.718) nor did a previous positive PCR test (*p*-value = 0.798). These observations are consistent with previous reports where asymptomatic infections did not protect against a subsequent symptomatic infection; hence, natural immunity may wane after a few months [14].

Similarly, in order to verify if the booster jab would protect against this new variant, we compared the frequency of COVID-19 infection among personnel according to their vaccination status (Table 7). Individuals that declared not having received any COVID-19 vaccine jab (unvaccinated) and subjects that declared having received only one jab from CovonaVac, ChAdOX1-S, or BNT162b2 (partially vaccinated) were considered incompletely vaccinated. Individuals that declared having received one dose of Ad26.COV2.S or two doses of CoronaVac, ChAdOX1-S, or BNT162b2 were considered completely vaccinated. Individuals that declared a complete scheme plus a booster dose were considered completely vaccinated with a booster.

Analogously to having antibodies from the first wave, having received the booster jab did not protect against infection during the Omicron wave (*p*-value = 0.501). This result is consistent with previous data suggesting that a vaccination may protect from disease severity but not from being infected with the virus [14,15]. Indeed, none of the workers who tested positive reported moderate/severe disease. Of note, because our institution is a healthcare facility in Brazil, vaccine acceptance is very high. Hence, very few people did not have a complete vaccination scheme when the Omicron outbreak hit us. This is possibly the reason why an incomplete scheme was not statistically significantly associated with testing positive.

Table 7. Status of SARS-CoV-2 IgA/IgG and vaccine of IFF/Fiocruz workers according to SARS-CoV-2 test result.

Variables	SARS-CoV-2 Test Result				*p*-Value *
	Negative		Positive		
	n	%	n	%	
SARS-CoV-2 Antibody Status before vaccination **					
Negative	59	35.1	109	64.9	0.718
Positive	68	38.6	108	61.4	
SARS-CoV-2 positive PCR before Omicron outbreak					
Negative	112	37.2	189	62.8	0.798
Positive	16	34.0	31	65.0	
COVID-19 vaccination status ***					
Incomplete	2	20.0	8	80.0	0.501
Complete	53	38.7	84	61.3	
Complete with booster	73	36.1	129	63.9	
Complete Scheme—CoronaVac					
Complete	17	37.0	29	63.0	0.970
Complete with booster	48	36.6	83	63.4	
Complete Scheme—Others ****					
Complete	36	40.0	54	60.0	0.867
Complete with booster	24	37.5	40	62.5	
Complete Scheme					
CoronaVac	65	36.7	112	63.3	0.733
Others	60	39.0	94	61.0	

* Pearson's chi-square test; significant result: p-value < 0.05. **Antibody status evaluated through ELISA during the first COVID-19 outbreak in 2020. *** Vaccination scheme status was classified as incomplete (individuals who had one jab from CoronaVac, ChAdOX1-S, or BNT162b2, or who did not have any jab at the time), complete (individuals who had one jab from Janssen or two jabs from CoronaVac, ChAdOX1-S, or BNT162b2), and complete with a booster dose. **** Others: BNT162b2, ChAdOX1-S, or Ad26.COV2.S.

We also investigated the association between CoronaVac, which is an inactivated whole virus vaccine, and the other RNA and adenovirus-based vaccines (BNT162b2, ChAdOX1-S, and Ad26.COV2.S) with SARS-CoV-2 positivity during the Omicron outbreak. As observed in Table 7, there was no statistical association between testing positive and having received a booster for individuals with a complete scheme either from CoronaVac (p-value = 0.970) or the RNA and adenovirus-based vaccines (p-value = 0.867). In addition, there was no significant association between testing positive and having received a complete scheme either from CoronaVac of the RNA and adenovirus-based vaccines (p-value = 0.733). These data suggest that having received the first two jabs from CoronaVac was not predictive of testing positive during the Omicron wave and, therefore, did not increase the risk of a SARS-CoV-2 infection in our workforce.

Lastly, we performed a logarithmic regression to account for all the studied variables. Contrasting to the first outbreak, working in high exposure was more predictive of testing positive for SARS-CoV-2 during the Omicron outbreak than any other socio-demographic variable ($p = 0.037$), as depicted in Table 8.

Table 8. Logistic regression of IFF/Fiocruz workforce according to gender and types of work activities.

Variables	Crude Odds Ratio (95% CI) [a]	Adjusted Odds Ratio (95% CI) [a]	*p*-Value *
Race			
Non-white	1.0	1.0	
White	1.44 (0.93–2.22)	1.48 (0.73–3.01)	0.276
Gender			
Male	1.0	1.0	
Female	1.84 (1.11–3.06)	1.42 (0.67–3.01)	0.358
SARS-CoV-2 Antibody Status before vaccination			
Negative	1.0	1.0	
Positive	0.97 (0.75–1.24)	1.01 (0.68–1.55)	0.952
Income			
≤3 MW	1.0	1.0	
4–5 MW	0.44 (0.19–1.00)	2.43 (0.39–15.00)	0.345
More than 5 and ≤10 MW	0.50 (0.22–1.13)	1.13 (0.21–6.06)	0.890
More than 10 MW	0.48 (0.15–1.53)	0.71 (0.12–4.18)	0.705
Education			
Complete secondary or less	1.0	1.0	0.872
Complete undergraduate university	1.22 (0.62–2.41)	1.28 (0.55–3.01)	0.569
More than undergraduate university	0.90 (0.49–1.64)	1.09 (0.37–3.15)	
Workplace exposure to SARS-CoV-2			
Low exposure	1.0	1.0	
Medium exposure	0.91 (0.27–3.13)	0.95 (0.25–3.61)	0.934
High exposure	2.13 (1.16–3.92)	2.03 (1.04–3.96)	0.037 *

* Significant result: p-value < 0.05. [a] Odds Ratios were adjusted by race, gender, SARS-CoV-2 antibody status before vaccination, income, education, and workplace level of exposure. CI: Confidence Interval.

4. Discussion

In 2020, we conducted a serological survey on 1154 IFF/Fiocruz workers to monitor SARS-CoV-2 infection in a public hospital environment. We observed a 30% prevalence of SARS-CoV-2 positivity, and the highest infection rates in non-white workers, with lower income and schooling and users of the mass transportation system. This group was mainly composed of hospital support workers and cleaning personnel. These data revealed, once more, Brazilian high inequality even amongst healthcare workers. The present study aimed to verify if the healthcare worker profile at risk was the same during the Omicron outbreak.

Before analyzing the results of the present study, it is worthy to establish the differences between our 2020 serological survey and the data presented herein. In the 2020 serological survey, all institutional workforce was invited to participate in the study, and we evaluated the presence of IgA and IgG in a blood sample from workers that accepted to participate, along with the data from a thorough socio-demographic questionnaire each participant answered. In the present study, we relied on the same cohort of workers, but only those individuals tested for SARS-CoV-2 during the Omicron outbreak, hence, those who either sought to test themselves in our employee testing facilities or reported a positive test result from a private laboratory, confirming the infection during the Omicron wave. In general, individuals were either tested through a PCR or with an antigen test. A positive antigen test was enough to consider the individual as infected, but a negative antigen test further required confirmation through PCR. This is important in light of the reduced sensitivity of antigen tests in comparison to PCR, especially upon the emergence of the Omicron variant [16]. We also analyzed the data from the vaccination scheme and status.

Despite these differences, in the present study, the proportion of individuals in each socio-demographic characteristic was equivalent to the overall previous serology evaluation (Table S3) [8]. The sole feature with a noticeable difference was the occupation. The proportion of support workers in the present study is somewhat higher than in the serology study (43.4% versus 30.2%, respectively). The previous serology study accounted for all workers regardless of symptomatology, whereas the present study was directed to subjects who tested for SARS-CoV-2 due to symptoms. These data might suggest that support workers were slightly more prone to seek SARS-CoV-2 testing during the Omicron wave than willing to adhere to the previous serology inquiry during the first COVID-19 wave. Upon the original outbreak, non-essential workers (mainly support staff) worked from home in compliance with social distance mitigation strategies employed at that time. Upon reaching a high proportion of vaccinated individuals in Rio de Janeiro, most support workers returned to work on-site or in hybrid schemes, alternating on-site with home-office work. This increased proportion of support workers that sought SARS-CoV-2 during the Omicron wave might merely reflect the enhanced opportunity and availability of testing because testing was available at their working place. As mentioned above, our institution is not a referral center for COVID-19 treatment but a pediatric and maternal health facility.

Regarding their vaccination status, Rio de Janeiro called healthcare workers for their booster jab in September 2021 [17]. By the time the Omicron wave started, most workers had already received their booster. Consistent with the reality in Brazil [18], most healthcare workers in our institution received either CoronaVac or ChAdOX1-S as the first two vaccine doses. Later, booster doses were mainly of BNT162b2 or ChAdOX1-S, particularly due to the literature indicating more robust protection with either of these vaccines than with CoronaVac [18,19].

During the pandemic's evolution, VOC began to arise. The Alpha variant did not circulate importantly in Brazil, but in December 2020, the Gamma variant (P.1) outbreak in the North region of Brazil began and rapidly spread throughout the country. During the first semester of 2021, Brazil went through the Gamma variant wave, followed by the Delta variant's arrival in the second semester and the Omicron variant in late 2021. From December 2021, COVID-19 cases in Brazil were virtually entirely composed of the Omicron variant (Figure S1) [20].

From December 2021 through March 2022, Brazil, and more specifically, Rio de Janeiro, went through the Omicron wave, which again hit our workforce, with a high number of cases in a short time window. We then analyzed SARS-CoV-2 test results from the 351 healthcare workers from our previous cohort study, tested for SARS-CoV-2 during the Omicron wave. Notably, we observed a different profile of workers with a positive test compared with the initial outbreak in 2020 (Figure 2). As opposed to the first cohort report, socio-demographic features such as race, income, schooling, and use of mass transportation were no longer associated with a positive test. Actually, the profile of a worker with a positive test during the Omicron outbreak was more associated with a healthcare professional working in high exposure (in-patient and out-patient sectors) than any other socio-demographic characteristic. These data suggest a decreased impact of transmission in commuting to work as well as an increased workplace transmission with patient-worker transmission as the most probable scenario.

During the Omicron wave, the professionals more prone to test positive were those working directly with patients, regardless of education, income, and type of commute to work. These data suggest that in the Omicron phase of the pandemic, workers were more exposed to SARS-CoV-2 in the workplace than in the first COVID-19 wave. These data also indicate that different categories of workers are more equally exposed in transportation or personal life.

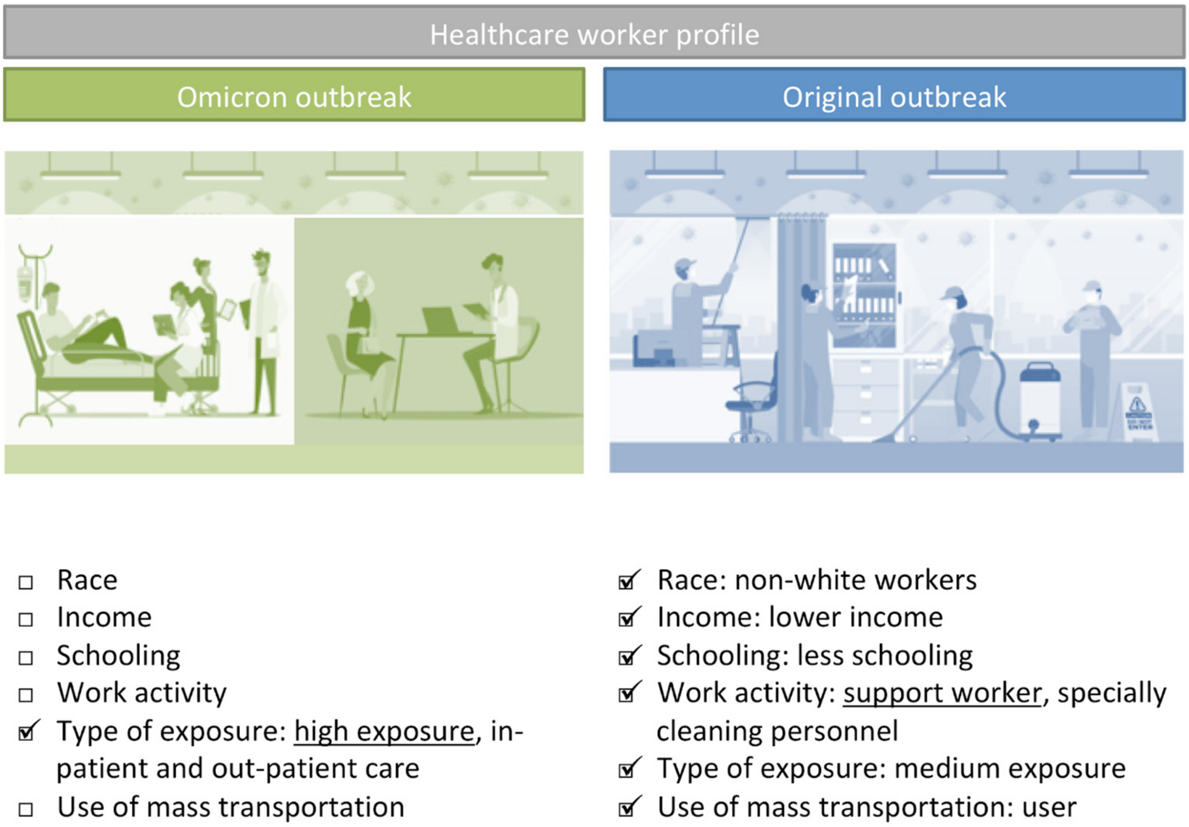

Figure 2. Profile shift from the first SARS-CoV-2 outbreak to the Omicron Era. Comparison between the different profiles of SARS-CoV-2 positive healthcare workers on the Omicron outbreak (green panel) and the Original outbreak (blue panel). ☑ represents statistically significant ($p < 0.05$) characteristics associated with SARS-CoV-2 positivity.

In this regard, a few explanations are possible. Firstly, at the beginning of the pandemic, an unprecedented worldwide effort to mitigate transmission based on non-pharmacological measures was severely employed, such as extreme social isolation and mask-wearing whenever social isolation was not possible. However, after two years into those restrictions imposed by the pandemic and a few vaccine jabs later, individuals were no longer sustaining proper transmission control measures. Thus, one possible explanation is the relaxation of non-pharmacological measures, especially in Brazil. Here, the spread of fake news and the lack of effective government policies to control transmission contributed to generating a significant amount of fear in the general population and healthcare workers from public institutions. Moreover, Brazil also experienced a severe Gamma variant outbreak in late 2020/beginning of 2021, which contributed to maintaining high-stress levels in healthcare workers throughout this period.

Secondly, the advent of vaccination and the positive effect on reducing the severity of the disease, hospitalization, and death due to COVID-19 also caused a sensation of safety, therefore promoting the relaxation of individual efforts to mitigate transmission. In the same way, almost all official restrictions regarding transmission mitigation were lifted during the second semester of 2021 in Rio de Janeiro. The sole public measure still sustained at that time was the use of masks in closed environments and public transportation. Altogether, we believe this combination of fatigue and relaxation of transmission mitigation measures throughout the population, including healthcare workers, may have contributed to this pattern shift.

However, two other reasons may have been especially relevant and related to the fact that we are mainly a children's hospital. First, after over one year of school closure in Brazil, most schools reopened mid-2021. Nevertheless, particularly during the Omicron wave, schools were closed for summer vacations (between December and February). This is consistent with the results of many studies from countries that chose to reopen schools as early as mid-2020, revealing higher infection rates among children during vacation periods than school periods [21].

Furthermore, concerning our in-hospital reality, very few cases were detected during the first year of the pandemic, and this number increased by several folds during the Omicron outbreak. Moreover, the vaccination of children aged 5 to 11 years in Brazil only began by late January 2022, which was already during the Omicron outbreak [22]. Additionally, vaccination for children under five years was not approved until mid-July 2022, when vaccination was authorized for children aged 3 to 4 [23]. Together, these elements may have contributed to an unprecedented number of new COVID-19 cases in patients and their relatives, which in turn highly increased the exposure of children's hospital workers to the virus. Furthermore, consistent with the increased transmissibility of the Omicron variant [24], nearly 50% of tests performed in our testing facilities were positive during this period.

An important added contribution of the current study in comparison to our previous one is the evaluation of vaccination in our workforce. It is important to highlight that immune response to COVID-19 vaccination is dependent on several factors such as age, sex, serostatus, and pre-existing comorbidities [25]. In addition, despite the chronological waning of humoral response post-SARS-CoV-2 vaccination [26], there has been evidence showing that vaccination could confer protection against long COVID-19 development [27]. Regarding the lack of association between the booster jab and positivity, our data should be interpreted cautiously because individuals who sought testing were mainly persons with mild symptoms. Therefore, it does not mean that the complete scheme or the booster jab did not protect against moderate and severe disease. In fact, none of the workers were hospitalized following SARS-CoV-2 positive testing during the Omicron wave, which argues for the effectiveness of vaccination.

Because CoronaVac was one of the first COVID-19 vaccines to be approved in Brazil, hundreds of thousands of healthcare workers received two CoronaVac jabs at the beginning of 2021. A few months later, the number of older adults who received two jabs from CoronaVac was rising among patients admitted to hospitals due to COVID-19 with moderate to severe disease [18]. At the same time, the Delta variant was beginning to strike, and increased protection from a heterologous booster dose with RNA vaccines or ChAdOX1-S was verified [28,29]. As a result, Brazil's first approved booster doses were BNT162b2 and ChAdOX1-S, and started to be offered in September 2021 [17].

In the present study, we were unable to detect a different level of protection against SARS-CoV-2 symptomatic infection during the Omicron outbreak between healthcare workers who were vaccinated and had a booster dose when compared those who had their first two jabs with either CoronaVac to those who were vaccinated with the other vaccines in use in Brazil. These data are reassuring of the increased protection due to the heterologous vaccination schema previously reported [19,28,29].

Several studies have demonstrated the higher prevalence of SARS-CoV-2 in healthcare workers compared to the general population [30–33]. Identifying the profile of infected individuals is important for protecting both the healthcare workforce and the patients; through better designing of safe workplaces, maintaining effective health services, reducing patient exposure to COVID-19, and driving public policies for the protection and vaccination of each group, especially given situations many countries still face of vaccine shortage [34].

Our data highlight the fact that during the Omicron outbreak, in-patient and out-patient hospital workers were more exposed and, indeed, more infected. Furthermore, these data demonstrate the challenge of constantly monitoring disease-spread behavior to efficiently contribute to policy makers about vaccine prioritization and booster schedules in underprivileged countries. Accordingly, the findings reported here might be applied to healthcare facilities in general and highlight the importance of vaccination to mitigate socio-economical inequalities among healthcare professionals regarding SARS-CoV-2 infection.

One limitation of our analyses is that we did not confirm SARS-CoV-2 variant through virus genome sequencing. However, nearly all SARS-CoV-2 genomes sequenced in Brazil during the study period (21 December–22 March) were of the Omicron lineage. We highlight that our institution is part of the Brazilian Network of SARS-CoV-2 Genomic Surveillance, a group of over 20 academic, health, and research institutions in Brazil that monitor SARS-CoV-2 variants' circulation in our country. Almost 200 thousand SARS-CoV-2 genomes have been sequenced from infected individuals all over the country since March 2020. Genomic Surveillance data is depicted in Supplementary Table S2.

Another limitation is that the cohort of this study is very specific: health professionals who work in a maternal and infant institution, where we do not have emergency attendance and we do not receive patients with COVID-19 as a referral center. Thus, we cannot extrapolate our results to the general population. However, our data is valuable for the particular subset of healthcare workers in non-COVID-19 referral centers, which represent the vast majority of healthcare institutions.

Regarding vaccination, we have one of the largest National Immunization Program in the world and very low vaccine hesitancy in Brazil, especially amongst healthcare workers [35,36]. Nearly all health workers had a complete vaccination schedule by the time the Omicron wave hit us. So, we could not detect a statistically significant difference between the vaccinated and unvaccinated groups. Furthermore, our cohort was not large enough to detect a statistically significant difference between the boosted and non-boosted groups.

As for the strengths of our study, we highlight that we are observing this cohort since the beginning of the COVID-19 pandemic and we have information on almost every worker on a large amount of SARS-CoV-2 epidemiological- and laboratorial-relevant features, such as serological characteristics, habits, contamination by SARS-CoV-2, and its consequences. Because of that, we were able to compare the same population in two different time frames of the pandemics: the very beginning and the post-vaccination era.

5. Conclusions

Compared to the first COVID-19 wave, we observed higher odds of SARS-CoV-2 positivity in highly exposed workers at the IFF hospital, together with a loss of impact of public transportation and socio-economical inequalities in SARS-CoV-2 transmission. These data indicate that the reduction of infection as a function of social inequalities among healthcare workers in Rio de Janeiro is likely due to vaccine-associated protection. Therefore, we emphasize the importance of vaccination, especially for those on the front-line, to protect against severe disease, and PPE (personal protection equipment), notably N95 or FFP2-mask-wearing to further minimize the risk of infection. Unfortunately, a large number of individuals worldwide have yet to receive their first jabs. Therefore, our findings highlight the importance of a global effort to advance vaccination coverage, especially for healthcare workers in developing countries, in order to better cope with COVID-19 and its likely endemicity.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/covid3010004/s1, Figure S1: Frequency of occurrence of SARS-CoV-2 relevant variants in the state of Rio de Janeiro; Table S1: Types and number of means of transportation to work used by IFF/Fiocruz workers according to SARS-CoV-2 test result; Table S2: Logistic regression model of IFF/Fiocruz workforce according to gender and types of work activities; Table S3: Socio-demographic and types of work activities data on IFF/Fiocruz healthcare workers tested for SARS-CoV-2 during the Omicron wave and the Original outbreak.

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Data Availability Statement: The data presented in this study are available on request to the corresponding author. The data are not publicly available due to IRB policy.

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References

1. Callaway, E. Heavily mutated Omicron variant puts scientists on alert. *Nature* **2021**, *600*, 21. [CrossRef]
2. Flemming, A. Omicron, the great escape artist. *Nat. Rev. Immunol.* **2022**, *22*, 75. [CrossRef] [PubMed]
3. WHO. Science Brief: Omicron (B.1.1.529) Variant 2021. Available online: https://http://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/scientific-brief-omicron-variant.html (accessed on 15 July 2022).
4. Dejnirattisai, W.; Huo, J.; Zhou, D.; Zahradník, J.; Supasa, P.; Liu, C.; Duyvesteyn, H.M.; Ginn, H.M.; Mentzer, A.J.; Tuekprakhon, A.; et al. SARS-CoV-2 Omicron-B.1.1.529 leads to widespread escape from neutralizing antibody responses. *Cell* **2022**, *185*, 467–484.e15. [CrossRef] [PubMed]
5. Lauring, A.S.; Tenforde, M.W.; Chappell, J.D.; Gaglani, M.; Ginde, A.A.; McNeal, T.; Self, W.H. Clinical severity of, and effectiveness of mRNA vaccines against, covid-19 from omicron, delta, and alpha SARS-CoV-2 variants in the United States: Prospective observational study. *BMJ* **2022**, *376*, 1756–1833. [CrossRef] [PubMed]
6. Nyberg, T.; Ferguson, N.M.; Nash, S.G.; Webster, H.H.; Flaxman, S.; Andrews, N.; Thelwall, S. Comparative analysis of the risks of hospitalisation and death associated with SARS-CoV-2 omicron (B.1.1.529) and delta (B.1.617.2) variants in England: A cohort study. *Lancet* **2022**, *399*, 1303–1312. [CrossRef]
7. Wolter, N.; Jassat, W.; Walaza, S.; Welch, R.; Moultrie, H.; Groome, M.; Cohen, C. Early assessment of the clinical severity of the SARS-CoV-2 omicron variant in South Africa: A data linkage study. *Lancet* **2022**, *399*, 437–446. [CrossRef]
8. Correia, R.F.; Da Costa, A.C.C.; Moore, D.C.B.C.; De Oliveira, M.P.C.; Zuma, M.C.C.; Galvani, R.G.; Artmann, E. SARS-CoV-2 seroprevalence and social inequalities in different subgroups of healthcare workers in Rio de Janeiro, Brazil. *Lancet Reg. Health Am.* **2022**, *7*, 100170. [CrossRef]
9. Corman, V.M.; Landt, O.; Kaiser, M.; Molenkamp, R.; Meijer, A.; Chu, D.K.W.; Bleicker, T.; Brünink, S.; Schneider, J.; Schmidt, M.L.; et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro surveillance* **2020**, *25*, 2000045. [CrossRef]

10. Pearson, K.X. On the criterion that a given system of deviations from the probable in the case of a correlated system of variables is such that it can be reasonably supposed to have arisen from random sampling. *Lond. Edinb. Dublin Philos. Mag. J. Sci.* **1900**, *50*, 157–175. [CrossRef]
11. Fisher, R.A. Statistical methods for research workers. In *Breakthroughs in Statistics*; Springer: New York, NY, USA, 1992.
12. McCullagh, P.; Nelder, J.A. *Generalized Linear Models*, 2nd ed.; Chapman and Hall: London, UK, 1989; Chapters 4 and 5.
13. WHO. Female Health Workers Drive Global Health 2019. Available online: https://http://www.who.int/news-room/commentaries/detail/female-health-workers-drive-global-health (accessed on 15 July 2022).
14. Rahman, S.; Rahman, M.M.; Miah, M.; Begum, M.N.; Sarmin, M.; Mahfuz, M.; Hossain, M.E.; Rahman, M.Z.; Chisti, M.J.; Ahmed, T.; et al. COVID-19 reinfections among naturally infected and vaccinated individuals. *Sci. Rep.* **2022**, *12*, 1438. [CrossRef]
15. Cerqueira-Silva, T.; Oliveira, V.D.A.; Paixão, E.S.; Florentino, P.T.V.; O Penna, G.; Pearce, N.; Werneck, G.L.; Barreto, M.L.; Boaventura, V.S.; Barral-Netto, M. Vaccination plus previous infection: Protection during the omicron wave in Brazil. *Lancet Infect. Dis.* **2022**, *22*, 945–946. [CrossRef]
16. Del Vecchio, C.; Daniels, B.C.; Brancaccio, G.; Brazzale, A.; Lavezzo, E.; Ciavarella, C.; Onelia, F.; Franchin, E.; Manuto, L.; Bianca, F.; et al. Impact of antigen test target failure and testing strategies on the transmission of SARS-CoV-2 variants. *Nat. Commun.* **2022**, *13*, 5870. [CrossRef] [PubMed]
17. Prefeitura do Rio de Janeiro. Rio Tem Uma Das Menores Taxas De Hospitalização Desde O Início Da Pandemia De COVID-19. 2021. Available online: https://prefeitura.rio/saude/rio-tem-uma-das-menores-taxas-de-hospitalizacao-desde-o-inicio-da-pandemia-de-covid-19/ (accessed on 15 July 2022).
18. Cerqueira-Silva, T.; Oliveira, V.D.A.; Boaventura, V.S.; Pescarini, J.M.; Júnior, J.B.; Machado, T.M.; Flores-Ortiz, R.; Penna, G.O.; Ichihara, M.Y.; de Barros, J.V.; et al. Influence of age on the effectiveness and duration of protection of Vaxzevria and CoronaVac vaccines: A population-based study. *Lancet Reg. Health Am.* **2022**, *6*, 100154. [CrossRef] [PubMed]
19. Cerqueira-Silva, T.; Katikireddi, S.V. Vaccine effectiveness of heterologous CoronaVac plus BNT162b2 in Brazil. *Nat. Med.* **2022**, *28*, 838–843. [CrossRef] [PubMed]
20. Fiocruz, R.G. SARS-CoV-2 Genomic Surveillance in Brazil 2020. Available online: http://www.genomahcov.fiocruz.br (accessed on 30 September 2022).
21. Silverberg, S.L.; Zhang, B.Y.; Li, S.N.J.; Burgert, C.; Shulha, H.P.; Kitchin, V.; Sauvé, L.; Sadarangani, M. Child transmission of SARS-CoV-2: A systematic review and meta-analysis. *BMC Pediatr.* **2022**, *22*, 172. [CrossRef] [PubMed]
22. Prefeitura do Rio de Janeiro. Prefeitura Começa A Vacinar Crianças De 5 A 11 Anos Contra A COVID-19. 2022. Available online: https://coronavirus.rio/noticias/prefeitura-comeca-a-vacinar-criancas-de-5-a-11-anos-contra-a-covid-19/ (accessed on 15 July 2022).
23. Prefeitura do Rio de Janeiro. Rio Vacina Crianças De 3 E 4 Anos Contra COVID-19. 2022. Available online: https://coronavirus.rio/noticias/rio-vacina-criancas-de-3-e-4-anos-contra-covid-19/ (accessed on 30 September 2022).
24. Araf, Y.; Akter, F. Omicron variant of SARS-CoV-2: Genomics, transmissibility, and responses to current COVID-19 vaccines. *J. Med. Virol.* **2022**, *94*, 1825–1832. [CrossRef]
25. Notarte, K.I.; Ver, A.T.; Velasco, J.V.; Pastrana, A.; Catahay, J.A.; Salvagno, G.L.; Yap, E.P.H.; Martinez-Sobrido, L.; BTorrelles, J.; Lippi, G.; et al. Effects of age, sex, serostatus, and underlying comorbidities on humoral response post-SARS-CoV-2 Pfizer-BioNTech mRNA vaccination: A systematic review. *Crit. Rev. Clin. Lab. Sci.* **2022**, *59*, 373–390. [CrossRef]
26. Notarte, K.I.; Guerrero-Arguero, I.; Velasco, J.V.; Ver, A.T.; Santos de Oliveira, M.H.; Catahay, J.A.; Khan, M.S.R.; Pastrana, A.; Juszczyk, G.; Torrelles, J.B.; et al. Characterization of the significant decline in humoral immune response six months post-SARS-CoV-2 mRNA vaccination: A systematic review. *J. Med. Virol.* **2022**, *94*, 2939–2961. [CrossRef]
27. Notarte, K.I.; Catahay, J.A.; Velasco, J.V.; Pastrana, A.; Ver, A.T.; Pangilinan, F.C.; Peligro, P.J.; Casimiro, M.; Guerrero, J.J.; Gellaco, M.M.L.; et al. Impact of COVID-19 vaccination on the risk of developing long-COVID and on existing long-COVID symptoms: A systematic review. *Eclinicalmedicine* **2022**, *53*, 101624. [CrossRef]
28. Marra, A.R.; Miraglia, J.L.; Malheiros, D.T.; Guozhang, Y.; Teich, V.D.; da Silva Victor, E.; Pinho, J.R.R.; Cypriano, A.; Vieira, L.W.; Polonio, M.; et al. Effectiveness of heterologous COVID-19 vaccine booster dosing in Brazilian healthcare workers, 2021. *Clin. Infect. Dis.* **2022**. ePub ahead of print.
29. Clemens, S.A.C.; Weckx, L.; Clemens, R.; Mendes, A.V.A.; Souza, A.R.; Silveira, M.B.; da Guarda, S.N.F.; de Nobrega, M.M.; de Moraes Pinto, M.I.; Gonzalez, I.G.; et al. Heterologous versus homologous COVID-19 booster vaccination in previous recipients of two doses of CoronaVac COVID-19 vaccine in Brazil (RHH-001): A phase 4, non-inferiority, single blind, randomised study. *Lancet* **2022**, *399*, 521–529. [CrossRef] [PubMed]
30. Gómez-Ochoa, S.A.; Franco, O.H.; Rojas, L.Z.; Raguindin, P.F.; Roa-Díaz, Z.M.; Wyssmann, B.M.; Guevara, S.L.R.; Echeverría, L.E.; Glisic, M.; Muka, T. COVID-19 in healthcare workers: A living systematic review and meta-analysis of prevalence, risk factors, clinical characteristics, and outcomes. *Am. J. Epidemiol.* **2021**, *190*, 161–175. [CrossRef]
31. Rudberg, A.-S.; Havervall, S.; Månberg, A.; Falk, A.J.; Aguilera, K.; Ng, H.; Gabrielsson, L.; Salomonsson, A.-C.; Hanke, L.; Murrell, B.; et al. SARS-CoV-2 exposure, symptoms and seroprevalence in healthcare workers in Sweden. *Nat. Commun.* **2020**, *11*, 5064. [CrossRef] [PubMed]

32. Iversen, K.; Bundgaard, H.; Hasselbalch, R.B.; Kristensen, J.H.; Nielsen, P.B.; Pries-Heje, M.; Knudsen, A.D.; E Christensen, C.; Fogh, K.; Norsk, J.B.; et al. Risk of COVID-19 in health-care workers in Denmark: An observational cohort study. *Lancet Infect. Dis.* **2020**, *20*, 1401–1408. [CrossRef]
33. Fitzpatrick, V.; Rivelli, A.; Blair, C.; Copeland, K.; Richards, J. Disparities in seroprevalence of SARS-CoV-2 immunoglobulin antibodies in a large midwestern health care system. *Public Health Rep.* **2021**, *136*, 361–367. [CrossRef]
34. Pan, A.; Liu, L.; Wang, C.; Guo, H.; Hao, X.; Wang, Q.; Huang, J.; He, N.; Yu, H.; Lin, X.; et al. Association of public health interventions with the epidemiology of the COVID-19 outbreak in Wuhan, China. *JAMA* **2020**, *323*, 1915–1923. [CrossRef]
35. Domingues, C.; Maranhão, A.G.K. The brazilian national immunization program: 46 years of achievements and challenges. *Cad Saude Publica.* **2020**, *36*, e00222919.
36. Moore, D.C.B.C.; Nehab, M.F.; Camacho, K.G.; Reis, A.T.; Junqueira-Marinho, M.F.; Abramov, D.M.; De Azevedo, Z.M.A.; De Menezes, L.A.; Dos Santos Salú, M.; Da Silva Figueiredo, C.E.; et al. Low COVID-19 vaccine hesitancy in Brazil. *Vaccine* **2021**, *39*, 6262–6268. [CrossRef] [PubMed]

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