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SPECIAL ARTICLE / *ARTIGO ESPECIAL*

Low COVID-19 vaccination coverage and high COVID-19 mortality rates in Brazilian elderly

Baixa cobertura da vacina contra COVID-19 e altas taxas de mortalidade por COVID-19 em idosos no Brasil

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ABSTRACT: ***Objective:*** To investigate the relation between COVID-19 vaccine coverage and COVID-19-related mortality by age groups in Brazil in 2021. ***Methods:*** Secondary data on COVID-19 deaths and vaccination coverage were retrieved to investigate COVID-19 mortality rate (MR) evolution as the vaccination against COVID-19 advanced in Brazil in 2021. Poisson regression with adjustment for age and Brazilian states was used to calculate the MR. ***Results:*** By mid-April 2021, MR increased 2 – 3 times compared with the already high level in January for people aged 60 years or older, reaching the highest epidemic level of 5 – 15 per 100,000 inhabitants in this age group. Despite the following decline trend, by the end of May, the MR level was still about 50% and 80% higher for the age groups of 40 – 79 years and 80 years or older. The coverage concerning the first dose of COVID-19 vaccine reached 80% for people aged 60 – 69 years and exceeded 95% for those aged 70 years or older, but the second dose was only given to 26, 76 and 64% of the age groups of 60 – 69, 70 – 79, and 80 years or older, respectively. The age-standardized average MR over the study period was the highest in northern Brazilian states of Rondônia, Amazonas, Acre, and Roraima (range 6-8.4 per 100,000 inhabitants). ***Conclusions:*** COVID-19 vaccination coverage was below the level necessary to protect Brazilians from rising MR between January and May 2021. Urgent measures are necessary to increase the vaccine supply and the adherence to non-pharmacological protective measures.

Keywords: COVID-19. Mortality. Vaccination coverage. Statistics. Brazil.

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RESUMO: ***Objetivo:*** Investigar a relação entre a cobertura vacinal contra COVID-19 e a mortalidade por faixa etária relacionada à COVID-19 no Brasil em 2021. ***Métodos:*** Foram levantados dados secundários sobre mortes e cobertura vacinal relacionadas a COVID-19, para examinar a evolução da taxa de mortalidade (TM) com avanço da vacinação. Utilizou-se a regressão de Poisson com ajuste para idade e as unidades federadas. ***Resultados:*** Em abril, a taxa de mortalidade aumentou 2 – 3 vezes comparado com começo do ano 2021 em pessoas com 60 ou mais anos de idade (60 +), atingindo o nível recorde de 5 – 15 por 100.000. Apesar do subsequente declínio, no final de maio a taxa ainda estava aproximadamente 50 e 80% mais alta que no começo do ano para faixas etárias de 40 – 79 e 80 + anos, respectivamente. As pessoas com 70 + anos ultrapassaram a cobertura vacinal de 95%, enquanto aqueles de 60 – 69 anos chegaram à 80% da cobertura com a primeira dose da vacina. Porém, a segunda dose foi aplicada a somente 26, 76, e 64% das pessoas com 60 – 69, 70 – 79, e 80 + anos, respectivamente. As mais altas taxas de 6 a 8.4 per 100.000, ajustadas por faixa etária, foram registradas em Rondônia, Amazonas, Acre e Roraima. ***Conclusão:*** Cobertura vacinal contra COVID-19 não atingiu os níveis necessários para proteger os Brasileiros contra crescente mortalidade por esta doença entre janeiro e maio de 2021. É preciso tomar medidas urgentes para aumentar o suprimento das vacinas e aderência às medidas preventivas não farmacológicas.

Palavras-chave: COVID-19. Mortalidade. Cobertura vacinal. Estatística. Brasil.

INTRODUCTION

The dramatic rise of Coronavirus Disease 2019 (COVID-19) cases and deaths in Brazil in 2021[1] coincided with the spread of the P.1 variant[2,3] and a large increase in the proportion of the non-elderly population being hospitalized and even succumbing to the disease. The new variant is more transmissible and more resistant to protective immunity from the previous infection with other variants[3]. The demand for oxygen and intensive care exponentially increased and overreached the installed capacity, with subsequent chaos and many patients waiting to receive adequate medical care for too long. Although this was a nationwide problem, it was particularly critical in the state of Amazonas[4].

By the end of May 2021, almost all Brazilians aged 70 years or older received at least one dose of the vaccine against COVID-19[5], but in the age group of 60 – 69 years this figure was down to 80%. A British simulation study showed that mortality rate (MR) rapidly drops in the vaccinated population compared with the non-vaccinated one, but the latter also benefits from the group immunity, especially after having 50% of the adult population vaccinated[6]. Lengthy vaccination in Brazil passed the 20% mark for the first and about 10% for the second of the two-dose regimen in the last week of May 2021. The objective of this report is to investigate the evolution of COVID-19 MR, taking into account the age distribution in the population, as COVID-19 vaccination advanced in Brazil in 2021, both nationwide and across states.

METHODS

Data sources included a death registry assembled by a non-governmental organization, the data on vaccination assembled by the Brazilian Ministry of Health and published on its website[5], and on the country's population[7]. The former only contained main causes of death aggregated in six broad categories (COVID-19, other serious acute respiratory illness, other respiratory diseases, septicemia, other causes, and unknown causes) as well as the information on state, municipality of residence, sex, age group, and place of death. Any mention of COVID-19 or Coronavirus or New Coronavirus on the death certificate with the codes U07.1 or U07.2 of the International Classification of Diseases, Tenth Revision (ICD-10), led to the diagnosis of COVID-19, either confirmed by laboratory tests (ICD-10 codes B34.2 + U07.1), clinical exam, clinical and epidemiological criteria, or imaging, or suspected (ICD-10 codes B34.2 + U07.2) if these conditions were not met[8]. Such inclusive case definition was made to reduce the impact of the lack of laboratory testing or its long delay even among those suspected to have died from COVID-19[9], thus increasing the sensitivity of epidemiological surveillance at the expense of its specificity. Undetermined causes of death were those from the ICD-10 chapter XVIII. The place of death included a hospital, community health center, other healthcare facilities, home, street, ambulance, or other places. For this study, age was grouped into the bands of 0 – 19, 20 – 39, 40 – 59, 60 – 69, 70 – 79, and 80 years or older.

Data on vaccination contained compatible sociodemographic data (sex, age, state, municipality, race, nationality) along with information on the vaccine (producer, batch number, country of origin, dates of importation and administration, and whether the administered dose was the first, the second, or unique)[10]. Municipality and state population within the same age bands used for the mortality data was retrieved from the Brazilian Institute of Geography and Statistics (*Instituto Brasileiro de Geografia e Estatistica* – IBGE)[7].

Data on both death certificate and vaccination have been daily updated.

The number of deaths from unknown causes that were likely due to COVID-19 (N_a) was estimated by the following formula:

$$N_a = (N_c / N_t)\, N_u \quad (1)$$

where N_c, N_t, and N_u represent the number of reported COVID-19 deaths, the total number of deaths, and the number of deaths from unknown causes, respectively. Thus, the estimated total of COVID-19 deaths (N_{tot}) was

$$N_{tot} = N_c + N_a \quad (2)$$

This equation consists in a standard procedure based on proportional redistribution of unknown causes of death using the proportions of known causes[11,12]. The latter were estimated for each combination of state/Federal District and sex-by-age group.

Poisson regression with COVID-19 death count as the dependent variable was used to evaluate the effects of five distinct periods in the year 2021 (January 1st to March 19; March 20 to March 29; March 30 to April 14; April 15 to May 11; and May 12 to May 27), for the aforementioned age groups and the states/Federal District. Thus, marginal rates were adjusted by age and state-specific MR for each of the analyzed periods. The age adjustment amounts to direct standardization of the MR, with age-group-specific exposure time as an offset. A total of 27 geographical units (26 states and the Federal District) were modeled as fixed effects. For each state/Federal District, age group, and period, the exposure time was calculated by multiplying the corresponding population with the period duration. In the last analyzed period, locally weighted regression ("lowess") related COVID-19 MR, on the one hand, with the coverage of the first and the second dose of vaccine across federal states and, on the other hand, separately for each of the three oldest age groups. Data management and statistics were handled with the Stata software[13].

The date that separates the first period from the second was chosen to mark the achievement of 90% of people aged 80 years or older receiving at least one dose of the COVID-19 vaccine according to the official data[5]. During the second period, social distancing measures were reinforced nationwide to curb the surge of the COVID-19 epidemic and the incapacity of the national health system to provide adequate care to these patients, especially regarding the lack of intensive care units. During the third period, these measures were somewhat relaxed, although their reinforcement widely varied across the country. The fourth and fifth periods represent declining MR related to COVID-19, with the end of the latter period marking 20% of the population receiving at least one dose of the COVID-19 vaccine.

RESULTS

By the last week of May 2021, about 80% of the vaccine doses administered were CoronaVac, produced by Sinovac (China), and 18% were AZD122(ChAdOx1-S), produced by Oxford/AstraZeneca, mostly supplied by the Serum Institute of India. The age groups of 60 – 69, 70 – 79, and 80 years or older had the first dose vaccination coverage of 80, 96, and 99%, respectively (Figure 1). However, the second dose vaccination coverage was only 26, 76, and 64%, in the same order of the age groups. People aged 60 years or older had second-dose vaccination coverage of 46.2%.

Although about 4.3 million Brazilians aged 80 years or older had the highest vaccination coverage, MR in this age group was the highest over the analyzed period (Figure 2). MR rapidly increased over the first period up to mid-April, then significantly decreased for all age groups of 60 years or older. Below 60 years of age, both MR of $< 5/100{,}000$ inhabitants/day and the vaccination coverage of $< 20\%$ may be considered low. Nevertheless, MR among the age group of 40 – 59 years increased about 50% over the analyzed period, from 1 to 1.5 per 100,000 inhabitants/day. The age groups of 60 – 69 and 70 – 79 years showed an increase of similar magnitude, whereas those with 80 years or older suffered a 70% increase over the same time.

Both MR and vaccination coverage showed considerable variation between states (Table 1, Figure 3). The highest age-adjusted average MR per 100,000 inhabitants/day over the study

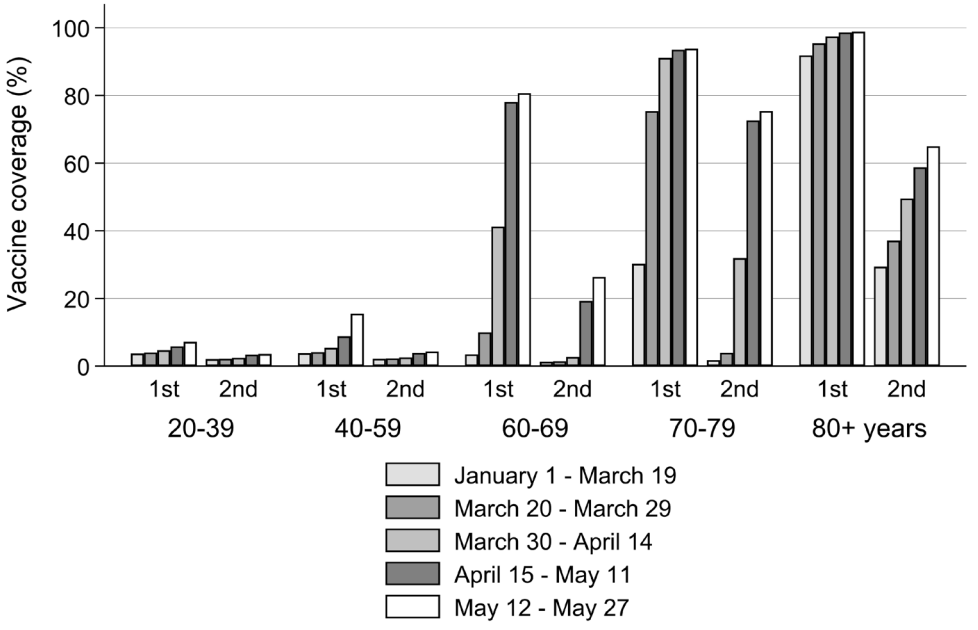


Figure 1. Percentage of people who received the first and the second doses of COVID-19 vaccine by age group and period in Brazil, 2021.

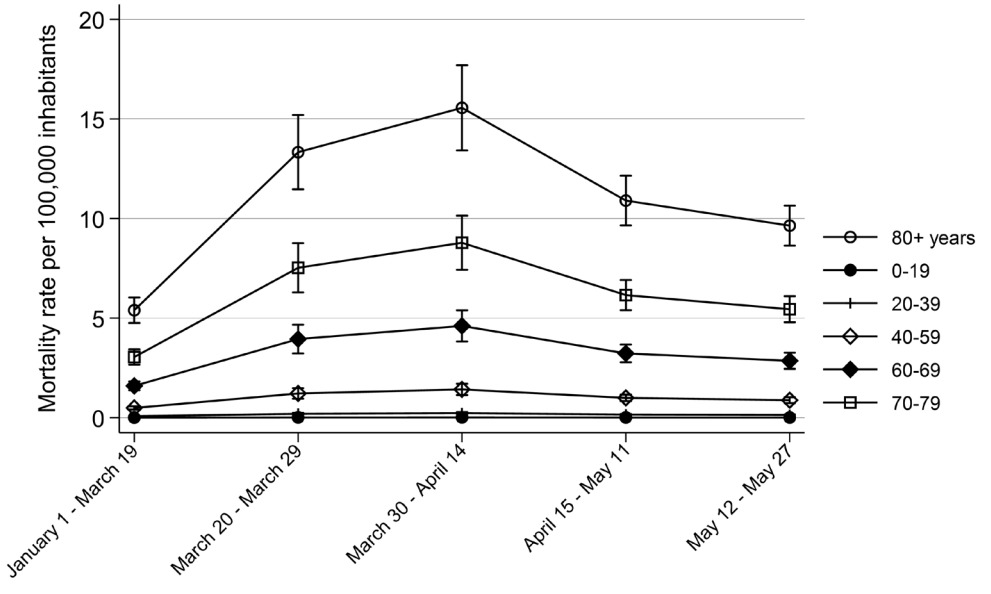
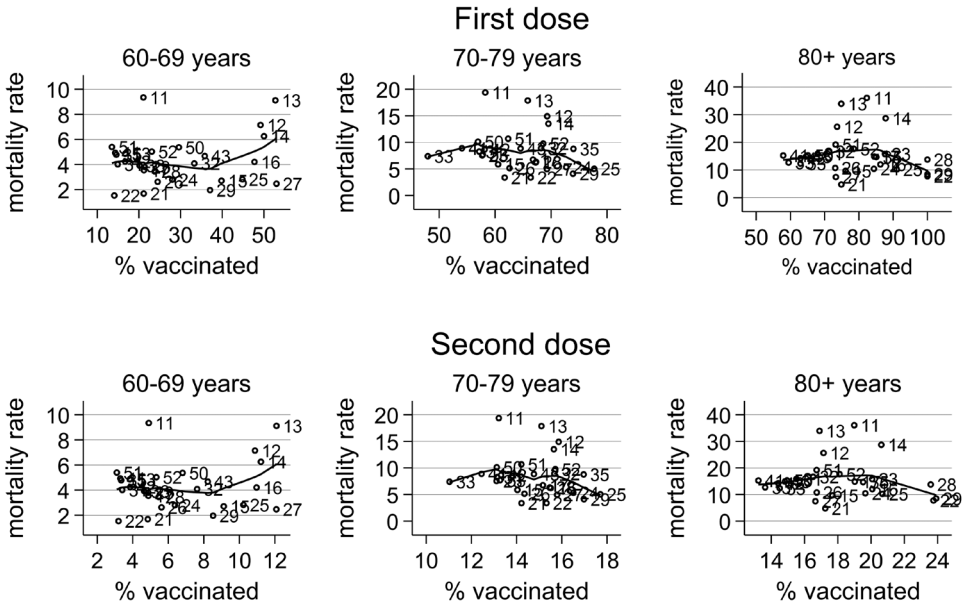


Figure 2. Marginal predicted mortality rate due to COVID-19 by age group and period in Brazil, 2021, derived from Poisson regression. Vertical bars represent 95% confidence intervals.

Table 1. COVID-19 mortality rate per 100,000 inhabitants in Brazil by states between January and May 2021, adjusted for age in Poisson regression.

States/ Federal District	Jan. 1–Mar. 19			Mar. 20–29			Mar. 30–Apr. 15			Apr. 16–May 11			May 11–26			Jan. 1–May 26		
	MR	LB	UB	MR	LB	UB	MR	LB	UB	MR	LB	UB	MR	LB	UB	MR	LB	UB
Rondônia	4.06	3.96	4.17	10.04	9.77	10.3	11.72	11.41	12.02	8.21	7.99	8.42	7.26	7.06	7.46	8.39	8.17	8.60
Acre	3.02	2.88	3.16	7.45	7.10	7.80	8.69	8.29	9.10	6.09	5.81	6.38	5.39	5.13	5.64	6.22	5.94	6.51
Amazonas	3.76	3.69	3.83	9.29	9.10	9.48	10.84	10.62	11.06	7.06	7.44	7.75	6.72	6.57	6.87	7.76	7.61	7.91
Roraima	2.91	2.73	3.09	7.19	6.74	7.63	8.39	7.86	8.91	5.88	5.51	6.24	5.20	4.87	5.52	6.00	5.63	6.38
Pará	1.10	1.08	1.13	2.72	2.66	2.79	3.18	3.10	3.25	2.23	2.17	2.28	1.97	1.92	2.02	2.27	2.22	2.33
Amapá	1.44	1.33	1.54	3.55	3.29	3.80	4.14	3.85	4.44	2.90	2.69	3.11	2.57	2.38	2.75	2.96	2.75	3.17
Tocantins	1.56	1.49	1.63	3.85	3.69	4.02	4.50	4.30	4.69	3.15	3.02	3.29	2.79	2.67	2.91	3.22	3.08	3.36
Maranhão	0.68	0.66	0.70	1.68	1.62	1.73	1.96	1.90	2.02	1.37	1.33	1.42	1.21	1.17	1.26	1.40	1.36	1.45
Piauí	0.71	0.68	0.74	1.76	1.69	1.84	2.06	1.97	2.15	1.44	1.38	1.50	1.28	1.22	1.33	1.47	1.41	1.54
Ceará	1.71	1.68	1.73	4.22	4.14	4.29	4.92	4.84	5.00	3.45	3.39	3.51	3.05	2.99	3.11	3.52	3.47	3.58
Rio Grande do Norte	1.26	1.22	1.29	3.10	3.01	3.19	3.62	3.51	3.73	2.54	2.46	2.61	2.24	2.18	2.31	2.59	2.52	2.67
Paraíba	1.25	1.21	1.28	3.08	2.99	3.16	3.59	3.49	3.69	2.52	2.45	2.59	2.23	2.16	2.29	2.57	2.50	2.64
Pernambuco	1.17	1.15	1.19	2.89	2.83	2.95	3.38	3.31	3.44	2.36	2.32	2.41	2.09	2.05	2.14	2.42	2.37	2.46
Alagoas	1.05	1.02	1.09	2.60	2.51	2.69	3.03	2.93	3.14	2.13	2.05	2.20	1.88	1.81	1.95	2.17	2.10	2.25
Sergipe	1.49	1.44	1.54	3.68	3.55	3.81	4.30	4.14	4.45	3.01	2.90	3.12	2.66	2.57	2.76	3.08	2.97	3.18
Bahia	0.91	0.90	0.93	2.26	2.22	2.30	2.64	2.59	2.68	1.85	1.81	1.88	1.63	1.60	1.67	1.89	1.86	1.92
Minas Gerais	1.81	1.79	1.83	4.48	4.42	4.53	5.23	5.17	5.28	3.66	3.62	3.70	3.24	3.19	3.28	3.74	3.71	3.78
Espírito Santo	1.85	1.81	1.89	4.58	4.48	4.69	5.35	5.23	5.46	3.75	3.66	3.83	3.31	3.24	3.39	3.83	3.75	3.91
Rio de Janeiro	1.68	1.66	1.70	4.15	4.09	4.20	4.84	4.78	4.90	3.39	3.35	3.43	3.00	2.96	3.04	3.47	3.43	3.50
São Paulo	2.04	2.03	2.05	5.04	4.99	5.09	5.88	5.83	5.93	4.12	4.08	4.16	3.65	3.6	3.69	4.21	4.18	4.24
Paraná	2.09	2.07	2.12	5.17	5.09	5.24	6.03	5.95	6.11	4.22	4.17	4.28	3.74	3.68	3.80	4.32	4.26	4.37
Santa Catarina	1.84	1.81	1.87	4.55	4.47	4.63	5.31	5.22	5.40	3.72	3.65	3.78	3.29	3.23	3.35	3.80	3.74	3.86
Rio Grande do Sul	2.07	2.05	2.09	5.12	5.05	5.18	5.97	5.90	6.04	4.18	4.13	4.24	3.70	3.64	3.76	4.27	4.23	4.32
Mato Grosso do Sul	2.24	2.18	2.3	5.54	5.39	5.68	6.46	6.30	6.62	4.53	4.41	4.64	4.00	3.9	4.11	4.63	4.51	4.74
Mato Grosso	2.43	2.38	2.49	6.01	5.87	6.15	7.01	6.85	7.18	4.91	4.8	5.03	4.35	4.24	4.46	5.02	4.91	5.14
Goiás	2.29	2.26	2.33	5.66	5.56	5.76	6.61	6.50	6.72	4.63	4.55	4.71	4.10	4.02	4.18	4.73	4.66	4.81
Distrito Federal	1.82	1.78	1.87	4.51	4.38	4.63	5.26	5.12	5.40	3.68	3.59	3.78	3.26	3.17	3.35	3.77	3.67	3.86
Total	0.52	0.52	0.52	1.28	1.27	1.9	1.50	1.49	1.51	1.05	1.04	1.06	0.93	0.92	0.94	0.78	0.78	0.79

MR: mortality rate; LB: lower bound of the 95%CI; UB: upper bound of the 95%CI.



Solid line represents locally weighted regression trend. State/Federal District codes: 11 Rondônia; 12 Acre; 13 Amazonas; 14 Roraima; 15 Pará; 16 Amapá; 17 Tocantins; 21 Maranhão; 22 Piauí; 23 Ceará; 24 Rio Grande do Norte; 25 Paraíba; 26 Pernambuco; 27 Alagoas; 28 Sergipe; 29 Bahia; 31 Minas Gerais; 32 Espírito Santo; 33 Rio de Janeiro; 35 São Paulo; 41 Paraná; 42 Santa Catarina; 43 Rio Grande do Sul; 50 Mato Grosso do Sul; 51 Mato Grosso; 52 Goiás; 53 Distrito Federal.

Figure 3. COVID-19 vaccination coverage regarding first and second doses and mortality rate per 100,000 inhabitants for Brazilian states/Federal District between May 11 and 27, 2021.

time was observed for the northern states of Rondônia, Amazonas, Acre, and Roraima (range of 6.00 – 8.39), followed by the midwestern states of Mato Grosso, Mato Grosso do Sul, and Goiás (range of 4.63 – 5.02), the southeastern state of São Paulo (4.21), and the southern states of Santa Catarina, Rio Grande do Sul, and Paraná (range of 3.80 – 4.27). Nationwide MR over the study time was 0.78 per 100,000 inhabitants/ day.

For each of the three oldest age groups, the highest level of vaccination coverage with the first and the second doses seems to correspond to a small MR reduction (Figure 3), although no statistical significance could be assigned to this trend. The opposite trend was observed for the age group of 60 – 69 years.

DISCUSSION

Despite advances in the vaccination against COVID-19 in Brazil in 2021, related MR continues to rise, particularly among those aged 80 years or older. A slow pace of vaccination with the first dose left 20% people unvaccinated in the age group of 60 – 69 years.

Moreover, the low uptake of the second dose enhances the lack of protection against severe COVID-19. With social distancing below 50% in most of the country, especially among younger people, the most vulnerable elderly are those who depend on the younger ones for their daily routine. Many elderly are not aware that full protection against COVID-19 is reached at least 3 weeks after receiving the second dose of the vaccines currently administered in Brazil, in such a way the risk of infection is often underestimated after receiving the first dose of the vaccine[14]. A nationwide Brazilian study showed that COVID-19 comorbidities are more prevalent in older people and exponentially increase their risk of death compared with younger individuals[15]. All these elements may explain the seemingly paradoxical finding of the highest level and fast rise in COVID-19 MR in the age group with the best vaccination coverage between January and May 2021.

Only one study published nationwide estimates of COVID-19 deaths (but not MR) in older Brazilians in 2020, but it was restricted to older adults living in long-term care facilities and based on the lethality data from other countries[16]. The authors concluded that over 117,000 deaths occurred in this age group, thus representing almost 45% of all deaths from this cause in Brazil. Another study focused on the first two months of the epidemic in the state of Ceará in 2020, and found a MR 3.6 times higher among the elderly due to comorbidities[17]. The latter were considered main causes of higher COVID-19 mortality in a recent review, together with lower immunity[18]. The present study results corroborate these findings on a nationwide scale in 2021 (Table 1). There was hardly any vaccination coverage to address among people aged below 60 years, and the COVID MR trend was nearly flat in the age group below 40 years. On the other hand, for the population of 60 years or older, for which the first-dose vaccination coverage was close to 90%, there was a significant MR decline since mid-April (Figure 2).

In the Serrana municipality in the state of São Paulo, vaccinating almost 96% of individuals aged 18 years or older with two doses of CoronaVac between February and April 2021 resulted in the reduction of COVID-19 mortality, hospitalizations, and the number of asymptomatic cases by 95, 86, and 85%, respectively[19]. Although the safety and immunogenicity of CoronaVac, the COVID-19 vaccine given to 4/5 Brazilian vaccinees, has already been demonstrated in phase 1/2 clinical trial for the age groups of 18 – 59[20] and 60 years or older[21], the Serrana community trial showed both direct and indirect (group) immunity effects. Another similar study has been currently carried out on the AZD122(ChAdOx1-S) vaccine produced by Oxford/AstraZeneca in partnership with the Oswaldo Cruz Foundation (Fiocruz) in Rio de Janeiro, Brazil[19].

The ecological design of the present study does not allow concluding the vaccine effectiveness, but on a descriptive level, decreasing COVID-19 MR for high vaccination coverage observed in people aged 70 years or older seems intuitive (Figure 3). The opposite tendency for individuals aged 60 – 69 years may be due to prioritizing people with comorbidities and administering a higher proportion of the AstraZeneca vaccine in this age group, thus leaving over a 3-month gap between the first dose and full immunity achieved only several weeks after the second dose. Furthermore, many people in this age group worked outside their

homes and hence had more difficulties adhering to social distancing measures because of the need for using public transport or contacting their clients face-to-face. However, the data available from this study do not allow verifying these hypotheses.

The strengths of the present study include the COVID-19 diagnosis based on medical records (> 90% laboratory-confirmed), covering all age bands, presenting both the first and the second dose vaccination coverage, and relating these to age-standardized COVID-19 mortality rates. Standardization is necessary to adjust for different percentages of older people across the states, associated with more chronic diseases that increase the risk of death as comorbidities. These MR values allow a comparison of the joint impact of state-specific factors such as vaccination coverage, social distancing measures, access to adequate medical care, and non-pharmaceutical measures. However, it is beyond the scope of this study to quantify separate contributions for each of these factors.

Among the study limitations, misdiagnosis[22] and reporting delay[23] for COVID-19 deaths are worth noting. The former heavily depends on the availability of the SARS-CoV-2 tests that widely varies in Brazil, whereas the latter was estimated as two weeks at most for the data source used in the present study[24]. Furthermore, COVID-19 MR underestimation in 2020 was estimated at 20 – 25% nationwide and is likely to have continued in 2021. Furthermore, the choice of dates to separate the analyzed periods was somewhat arbitrary, but it seems unlikely that a different choice would have altered the key results. In addition, the scope and duration of social distancing measures widely varied throughout the country, and so did the adherence to these measures.

Proportional redistribution of unknown causes of death, according to the known causes, assumes that both distributions are equal within state / Federal District and sex-by-age group, but there is no guarantee concerning this assumption. Investigation methods may be preferable[25], though they are not viable with secondary data. Nevertheless, it seems extremely unlikely that not using the aforementioned redistribution would result in less biased estimates, especially considering large state variation in the quality of death registers[25], the novelty of COVID-19, and the lack of its laboratory testing. Hence, the trade-off between sensitivity and specificity bias points to the greater weight of the former.

The rapid spread of the P.1 variant from the northern state of Amazonas[2] to the South[3] and all over Brazil coincided with the rapid surge of new COVID-19 cases and deaths that led to the collapse of the national health system[4]. However, the share of this variant in the increase of COVID-19 mortality in Brazil in 2021 is difficult to apportion with the available data, especially during the period of high viral transmissibility. This is also applied to the effectiveness of COVID-19 vaccines, although a significant reduction in the MR since mid-April coincided with high coverage (about 90%) of the first dose in the population of individuals aged 60 years or older. So far, the second dose coverage has just passed the 10% mark and is probably the most serious pitfall in the vaccination of elderly in Brazil. Without urgent measures to increase the vaccine uptake and non-pharmaceutical protective measures, high COVID-19 mortality is likely to continue.

All in all, COVID-19 vaccination coverage with two doses was below the level necessary to protect Brazilian elderly from rising MR between January and mid-April 2021. By the end of this period, the highest MR per 100,000 inhabitants was registered among people aged 80 years or older, followed by the age groups of 70 – 79 and 60 – 69 years. Urgent measures are necessary to increase the vaccine uptake and the adherence to non-pharmacological protective measures.

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