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**Artigo especial**

# Low anti-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 Brazil

Short title: Low anti-COVID-19 vaccination coverage and high COVID-19 mortality in Brazil

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The individual contribution of each author in the manuscript elaboration

As the only author of the manuscript, the whole work was done by myself.

**Abstract**

Introduction: In 2021, Brazil started a nationwide vaccination against COVID-19 but the emergence of the P.1 variant of SARS-CoV-2, more transmissible and resistant to immunity from the previous infection, rapidly led to a record increase in COVID-19 mortality. Methods: Secondary data on COVID-19 deaths and vaccination coverage were retrieved to examine COVID-19 mortality rate (MR) evolution as anti-COVID-19 vaccination advanced in Brazil in 2021. Poisson regression with adjustment for age and federal states was used to calculate the MR. Results; By mid-April 2021, MR increased 2-3 times compared to the already high level in January for the people of 60 years or older, reaching the highest epidemic level of 5-15 per 100.000 in this age group. Despite a declining time trend followed, by the end of May, the MR level was still about 50% and 80% higher for the 40-79 and 80 years or older. The first dose of anti-COVID-19 coverage reached 80% for the 60-69 years old and exceeded 95% for those of 70 years or older, but the second dose was applied to only 26%, 76%, and 64% of the 60-69, 70-79, and 80 years or older, respectively. The average age-standardized MR over the study time was the highest in northern Brazilian states of Rondônia, Amazonas, Acre, and Roraima (range 6-8.4 per 100.000). Conclusion: Anti-COVID-19 vaccination coverage was below the level necessary to protect Brazilians from rising MR between January and May 2021. Urgent measures are needed to increase the vaccine supply and the adherence to non-pharmacological protective measures.

*Keywords*: COVID-19, Mortality, Vaccination coverage, Statistics & numerical data, Brazil.

**Resumo**

Introdução: Brasil começou vacinar contra COVID-19 em 2021, mas o surgimento da variante P.1 do SARS-Cov-2, mais transmissível e resistente, rapidamente levou a aumento recorde em mortalidade por COVID-19. 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 TM 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 & dados numéricos, 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 increased dramatically and overreached installed capacity, with ensuing 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 of 70 years or older received at least one dose of the anti-COVID-19 vaccine[5] but in the 60-69 years group this figure was down to 80%. A British simulation study showed that the mortality rate (MR) drops rapidly in the vaccinated population compared to the non-vaccinated one, but the latter also benefits from the group immunity, especially after 50% of the adult population has been 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 examine the evolution of COVID-19 MR, taking into account the age distribution in the population, as anti-COVID-19 vaccination advanced in Brazil in 2021, both nationwide and across federal 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 population[7]. The former contained only

principal causes of death aggregated in six broad categories (COVID-19, other serious acute respiratory illness, other respiratory diseases, septicemia, other causes, 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 death certificate with the codes U07.1 or U07.2 of the tenth revision of the International Classification of Diseases (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 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, another health facility, home, street, ambulance, or another place. For this study, the age was grouped into the bands of 0-19, 20-39, 40-59, 60-69, 70-79, and 80 or more years.

The data on vaccination contained compatible socio-demographic data (sex, age, state, municipality, race, nationality) along with the information on the vaccine (producer, batch number, country of origin, the dates of importation and application, and whether the dose applied was the first, the second, or unique). Municipality and state population within the same age bands used for the mortality data was retrieved from the Brazilian Institute of Geography (acronym IBGE in Portuguese)[7].

Both death certificate and vaccination data have been updated daily.

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

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

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

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

Above adjustment is a standard procedure based on proportional redistribution of unknown causes of death using the proportions of known causes[11,12]. The latter were calculated for each combination of state/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 (1 January to 19 March, 20-29 March, 30 March to 14 April, 15 April to 11 May, and 12-27 May), for the aforementioned age groups and the federal states/district. Thus marginal rates were age-adjusted and state-specific MR for each of the periods analyzed. The age adjustment amounts to direct standardization of the MR, with age-group-specific exposure time as an offset. Twenty-seven federal states and the district were modeled as fixed effects. For each state/district, age group, and period, the exposure time was calculated by multiplying the corresponding population with the period duration. In the last period analyzed, locally weighted regression ("lowess") related COVID-19 MR on one hand with the coverage of the first and the second dose of vaccine across federal states on the other hand, separately for each of the three oldest age groups. Data management and statistics were handled with Stata[13].

The date that separates the first period from the second was chosen to mark the achievement of 90% of the people 80 years or older receiving at least one dose of the anti-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 the lack of intensive care units. During the third period, these measures were somewhat relaxed, although their reinforcement varied widely across the country. The fourth and fifth periods represent declining COVID-19 MR, with the end of the latter period marking 20% of the population receiving at least one dose of the anti-COVID-19 vaccine.

## RESULTS

By the last week of May 2021, about 80% of the vaccine doses applied were CoronaVac produced by Sinovac (China), and 18% were AZD122(ChAdOx1-S) of Oxford/AstraZeneca, mostly supplied by the "Serum Institute" in 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 60 years or older had second-dose vaccination coverage of 46.2%.

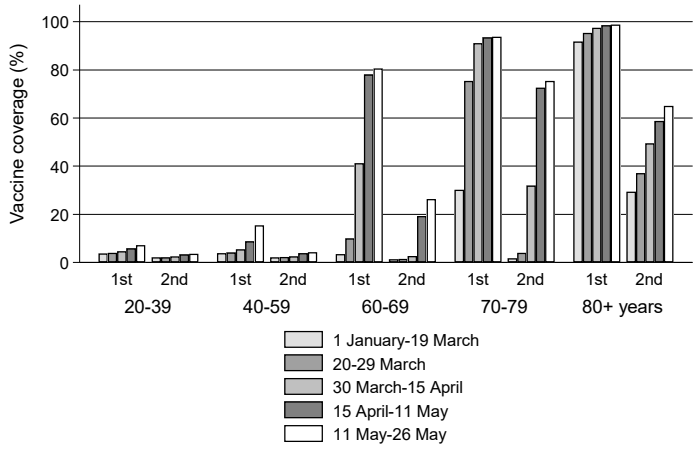



Figure 1. Percentage of the people who received the first and the second dose of anti-COVID-19 vaccine by age group and period in Brazil, 2021.

Although about 4.3 million Brazilians 80 years or older had the highest vaccination coverage, the MR in this age group was the highest over the time analyzed (Figure 2). The MR increased rapidly over the first period up to mid-April, then decreased significantly for all age groups of 60 years or older. Below 60 years of age, both MR of < 5/100.000 100.000 inhabitants per day and the vaccination coverage of <20% may be considered low. Nevertheless, the MR among the 40-59 years old increased about 50% over the time analyzed, from 1 to 1.5 per 100.000 inhabitants per day. The 60-69 and 70-79 years old showed an increase of similar magnitude, whereas those with 80 years or older suffered a 70% increase over the same time.

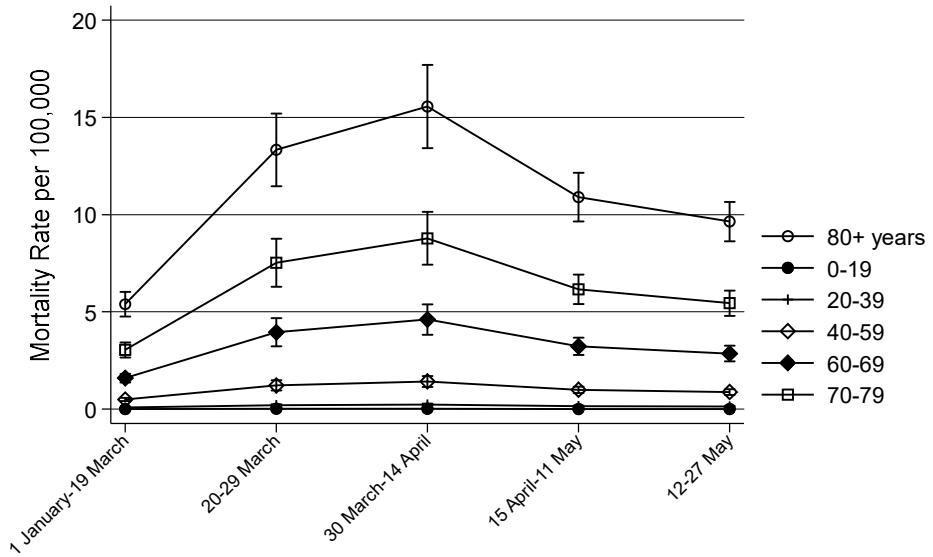



Figure 2. Marginal predicted COVID-19 mortality rate by age group and period in Brazil, 2021, derived by Poisson regression. Vertical bars represent 95% confidence intervals.

Both MR and vaccination coverage showed considerable variation between federal states (Table1, Figure 3). The highest age-adjusted average MR per 100.000 inhabitants per day over the study time was observed for the northern states of Rondônia, Amazonas, Acre, and Roraima (range 6.00-8.39) followed by the midwestern states of Mato Grosso, Mato Grosso do Sul, and Goiás (range 4.63-5.02), a southeastern state of São Paulo (4.21), and the southern states of Santa Catarina, Rio Grande do Sul, and Paraná (range (3.80-4.27). Nationwide MR over the study time was 0.78 per 100.000 inhabitants per day.

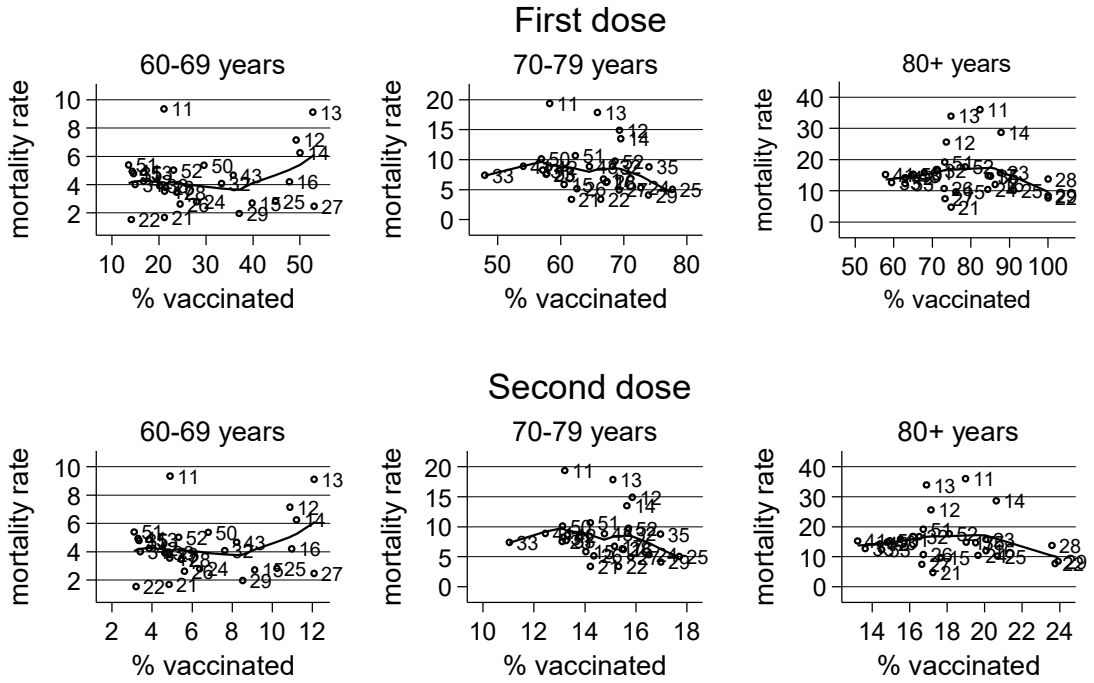
For each of the three oldest age groups, the highest level of vaccination coverage with the first and the second dose seems to correspond to a small MR reduction (Figure 3), although no statistical significance could be assigned to this trend. The opposite trend was observed for the 60-69 years old.

Table 1. COVID-19 mortality rate per 100.000 in Brazil by federal states between January and May 2021, adjusted for age in Poisson regression

| Federal states/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 |
| Espirito 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% confidence interval, UB=upper bound of the 95% confidence interval




Solid line represents locally weighted regression trend. State/district codes: 11 Rondônia, 12 Acre, 13 Amazonas, 14 Roraima, 15 Pará, 16 Amapa, 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 Espirito 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. First and second dose anti-COVID-19 vaccination coverage and mortality rate per 100.000 for Brazilian federal states/district between 11 and 27 of May 2021.

## DISCUSSION

Despite advances in vaccination against COVID-19 in Brazil in 2021, related MR continued to rise, particularly among those of 80 years or older. A slow rhythm of the vaccination with the first dose left 20% unvaccinated in the age group of 60-69 years old. Also, the low uptake of the second dose added to 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 used in Brazil, so 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 increase their risk of death exponentially compared to the younger ones[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 those in long-term care and based on the lethality data from other countries[16]. It 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 the MR 3.6 times higher among the elderly due to comorbidities[17]. The latter were considered principal causes of higher COVID-19 mortality in a recent review, along with lower immunity[18]. The present study results go along with these findings on a nationwide scale in 2021 (Table 1). Below 60 years of age there was hardly any vaccination coverage to speak of, and the COVID MR trend

was nearly flat below 40 years of age. On the other hand, for the population of 60 years or older where 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 São Paulo state, vaccinating almost 96% of the population of 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 anti-COVID-19 vaccine applied to 4/5 Brazilian vaccinees, has already been demonstrated in phase 1/2 clinical trials 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 is in progress with the AZD122(ChAdOx1-S) vaccine produced by Oxford/AstraZeneca in partnership with the Fiocruz Institute 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 those of 70 years or older seems intuitive (Figure 3). The opposite tendency for those of 60-69 years old may be due to prioritizing people with comorbidities and applying 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 obeying social distancing measures because of using public transport or contacting their clients face-to-face. However, the data available in this study do not allow checking 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. The standardization is necessary to adjust for different percentages of the older people across the states, associated with more chronic diseases that increase the risk of death as comorbidities. These MR allow a comparison of the joint impact of state-specific factors, such as the vaccination coverage, social distancing, 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 varies widely in Brazil, whereas the latter was estimated as two weeks at most for the data source used in the present study[24]. Also, 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 periods analyzed was somewhat arbitrary but it seems unlikely that a different choice would have altered the key results. Also, the scope and duration of social distancing measures varied widely across the country, and so did the adherence to these measures.

Proportional redistribution of unknown causes of death according to the known ones assumes that both distributions are equal within state/district and sex-by-age group but there is no guarantee this assumption holds. Investigation methods may be preferable[25] but are not viable with secondary data. Nevertheless, it seems extremely unlikely that not using the aforementioned redistribution would result in less biased estimates, especially keeping in mind 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 data available, especially during the period of high viral transmissibility. The same goes for the effectiveness of the anti-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 60 years or older. So far, the second dose coverage has just passed the 10% mark and is likely the most serious pitfall in the vaccination of elderly Brazilians. Without urgent measures to increase the vaccine uptake and non-pharmaceutical protective measures, high COVID-19 mortality is bound to continue.

In conclusion, anti-COVID-19 vaccination coverage with two doses was below the level necessary to protect the Brazilian elderly from rising MR between January and mid-April 2021. By the end of this period, the highest MR per 100.000 was registered among the people of 80 years or older, followed by the 70-79 and 60-69 years old. Urgent measures are needed to increase the vaccine uptake and the adherence to non-pharmacological protective measures.

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