Analyzing the COVID-19 parameters for large Brazilian municipalities using a model with fuzzy transitions between epidemic periods

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Abstract. *This study investigates the dynamics of the COVID-19 pandemic across the 41 largest Brazilian municipalities from 2020 to 2022. We used a mathematical model with fuzzy transitions between epidemic periods to estimate epidemiological parameters such as basic reproduction number (R_0) and the Infection Fatality Rate (IFR). We provide insights into the trajectory of the pandemic by correlating these parameters with data on social isolation, vaccination efforts, and the emergence of new variants. Our findings highlight the role of social isolation in reducing R_0 in 2020 and the impact of mass vaccination on lowering the IFR in 2022. However, the highest mortality rates recorded in 2021 underscore the complex interplay of various factors observed in that moment.*

1. Introduction

The impact of the COVID-19 pandemic on Brazil was profound, with around 38 million confirmed cases and 711 thousand deaths reported until April 2024 [DATASUS 2020]. Undoubtedly, the virus has spread extensively across the country, affecting every city.

In this research, we delve into the dynamics of COVID-19 across the initial three years, from 2020 to 2022, focusing on the 41 largest municipalities in Brazil. Leveraging a mathematical model with fuzzy transitions between epidemic periods as proposed by Lima et al. [2024], we estimate time-varying parameters such as the *basic reproduction number* (R_0) and the *Infection Fatality Rate* (IFR). Via an extensive analysis, we correlate these model outputs with data concerning social isolation measures, vaccination indices, and the emergence of new coronavirus variants. We aim to offer insights into the factors that influenced the trajectory of the pandemic at the municipal level.

Different studies utilized models to forecast the first COVID-19 wave in the Brazilian context [Bastos and Cajueiro 2020, Melo et al. 2020, Oliveira et al. 2021]. Notably, a work analyzed epidemiological parameters across 29 inner municipalities during the initial wave, emphasizing potential differences in control effectiveness across regions [Almeida et al. 2021]. Our focus is on research exploring the dynamic of epidemiological parameters over time. Other work examined the impact of mobility on the variation of R_0

in various countries [Nouvellet et al. 2021]. Lima et al. [2024] explored the variation of epidemic parameters across time using national data from Brazil. Ferrante et al. [2022] correlated epidemiological parameters with various factors to elucidate the dynamics of the first two waves in the Brazilian city of Manaus/AM [Ferrante et al. 2022].

We note a need for more work that conducted comprehensive pandemic analysis across a more significant period at the municipal level. So, our study contributes by analyzing the pandemic within larger Brazilian cities across three years. Our research provides an understanding of the factors shaping the pandemic trajectory via the correlation of the model outcomes with data on social isolation, vaccination indices, and the emergence of variants. We also examine the cities exhibiting outlier death rates (Cuiabá/MT, Rio de Janeiro/RJ, and Goiânia/GO), contrasted with bottom outliers (Feira de Santana/BA, São Luís/MA, and Florianópolis/SC), which illuminates the diverse drivers behind divergent pandemic outcomes. Our findings give policymakers and public health officials empirically grounded insights, facilitating decision-making for combating future challenges.

The rest of the paper follows this organization: Section 2 details the methodology, Section 3 shows the results and discussion, and we present our conclusions in Section 4.

2. Material and methods

2.1. Data source

This study utilized daily COVID-19 death data from Brazilian municipalities, extracted from the Mortality Information System (MIS) [DATASUS 2022b]. Data collection spanned from the early stages of the pandemic in 2020 until December 31, 2022.

In this work, we concentrated our analysis on a sample of the 41 largest Brazilian municipalities with populations exceeding 500,000 people. We obtained population size data from the 2022 Demographic Census [Instituto Brasileiro de Geografia e Estatística 2022]. The relation with all municipalities in our sample is available in the supplementary material.

For tracking COVID-19 cases in Brazilian municipalities, we accessed data from the Monitoring Panel [DATASUS 2020] and the Severe Acute Respiratory Syndrome (SARS) database [DATASUS 2022a], both provided by the Brazilian Health Ministry.

We examined our results with correlated data on human mobility, vaccination, and COVID-19 variants. To monitor human mobility in Brazilian municipalities, we utilized data from the COVID-19 Community Mobility Report [Google 2020] produced by Google. We used vaccination data for Brazilian municipalities from Cota [Cota 2021], which organized datasets from the Brazilian Health Ministry containing administered doses. Additionally, state-level data on COVID-19 genomic surveillance in Brazil, reported monthly by the Fundação Oswaldo Cruz [Fiocruz 2020], were incorporated.

2.2. Data overview

The average death rate per 100,000 inhabitants in our sample of municipalities on December 31, 2022, is 413 ($\pm$ 89). Figure 1 shows the existence of outlier municipalities in this sample. Cuiabá/MT, Rio de Janeiro/RJ, and Goiânia/GO recorded the highest death rates at 580, 564, and 558, respectively. Conversely, Feira de Santana/BA, São Luís/MA, and Florianópolis/SC reported the lowest rates at 189, 234, and 245, respectively. We highlighted these two outlier groups in our analysis and discussion.

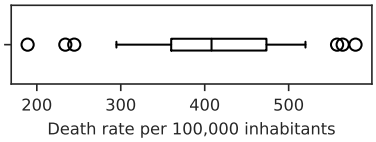

Figure 1. Boxplot illustrating COVID-19 death rate per 100,000 for the 41 largest Brazilian municipalities across 2020-2022. The lower and upper bounds represent the first and third quartiles, respectively. The vertical line within the box indicates the median, while the whiskers extend to the minimum and maximum values within 0.7 times the interquartile range. The points represent the outlier municipalities. Data from DATASUS [2022b].

The highest COVID-19 mortality peaks in Brazilian municipalities occurred between 2020 and 2021. Figure 2a illustrates that top outlier municipalities experienced more frequent and elevated peaks than their bottom outlier counterparts.

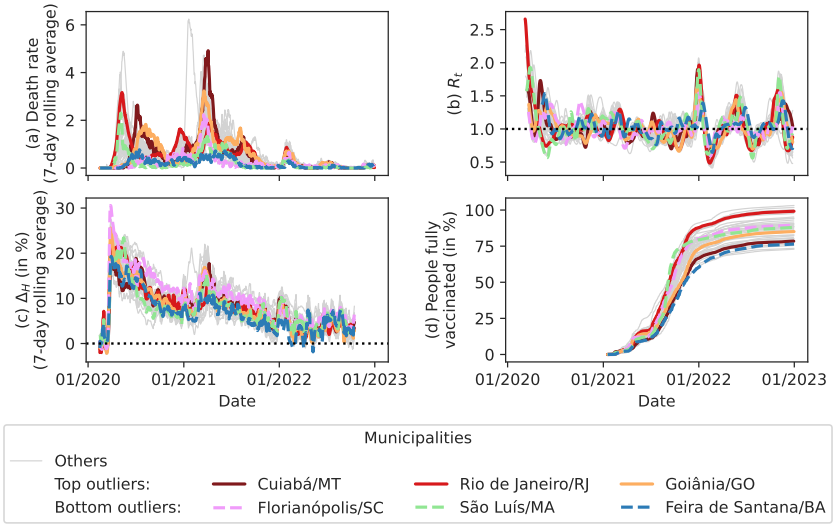

Figure 2. Pandemic data overview for the 41 largest Brazilian municipalities. (a) COVID-19 death rate per 100,000 inhabitants in a 7-day rolling average. Data from DATASUS [2022b]. (b) *Effective reproduction number* (R_t). The dotted horizontal line represents the reference value ($R_t = 1$) used to monitor epidemics. (c) *Stay-at-home index* (Δ_H) reported in a 7-day rolling average. The dotted horizontal line highlights the baseline ($\Delta_H = 0\%$). Data from Google [2020]. (d) Cumulative percentual of individuals fully vaccinated against COVID-19. Data from Cota [2021]. The plots highlight cities with notable deviations from the average death rate, categorized as top outliers (Cuiabá/MT, Rio de Janeiro/RJ, and Goiânia/GO) and bottom outliers (Feira de Santana/BA, São Luís/MA, and Florianópolis/SC).

The *effective reproduction number* (R_t) indicates whether a disease is spreading or diminishing. Values exceeding one signal ongoing transmission, while those below one indicate a decline in transmission. In our examination of COVID-19 within Brazilian municipalities, R_t was computed using the time series of new cases sourced from SARS patients [DATASUS 2022a]. This computation utilized the *epyestim* library, a Python toolkit implementing the methodology proposed by Cori et al. [2013]. The detailed parameter settings for estimating R_t are accessible in the supplementary material.

Figure 2b shows the time-varying behavior of R_t, revealing instances where R_t surpasses one during various periods of the study. Notably, in the initial two years, epidemic periods exhibited some lack of synchronization among municipalities; however, by 2022, three synchronized epidemic periods became apparent.

In the early stages of the pandemic, the primary measures against spreading the virus were adopting non-pharmacological interventions, including social isolation. We observed changes in the mobility behaviors of the population in Brazilian municipalities throughout the pandemic. To monitor these changes, we used data from the COVID-19 Community Mobility Report [Google 2020] generated by Google. This report quantifies the percentage change in time spent at residential locations by Google users, relative to a pre-pandemic baseline, serving as a metric known as the *stay-at-home index* (Δ_H).

We note in Figure 2c a significant change in mobility patterns in March 2020, coinciding with the moment that the country reported its first COVID-19 fatality. During the initial outbreak, most municipalities experienced a notable increase in the Δ_H, gradually trending towards baseline levels, with occasional exceptions observed.

In Brazil, up until 2022, the national health service administered COVID-19 vaccines developed by AstraZeneca, Janssen, Pfizer/BioNTech, and Sinovac [Cota 2021]. The initial vaccination protocol for all these vaccines consisted of two doses, except for the Janssen vaccine, for which only one dose was recommended [World Health Organization 2023]. Consequently, we consider an individual fully vaccinated either after receiving the second dose of AstraZeneca, Pfizer/BioNTech, or Sinovac vaccines or upon receiving the first dose of the Janssen vaccine.

Figure 2d depicts the vaccination timeline in Brazil, indicating that vaccination efforts began in early 2021. However, it was not until around October 2021 that approximately half of the population across Brazilian cities reached complete vaccination status.

Another aspect of understanding the pandemic dynamic is the prevalence of variants. Figure 3 depicts that the Gamma variant became dominant in early 2021, co-occurring with the second wave of infections in the country. Following the peak of cases in 2021, the Delta variant emerged as the predominant strain. Subsequently, coinciding with the onset of the third wave, the Omicron (BA.1) variant swiftly became the prevailing strain. Additionally, throughout 2022, other Omicron subvariants, including BA.2, BA.4, and BA.5, have emerged as the most dominant strains in the country.

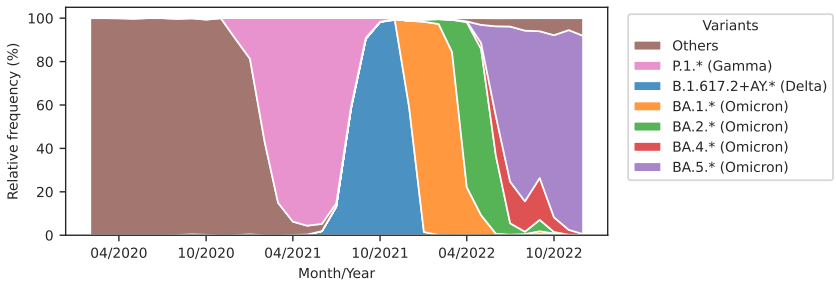

Figure 3. Monthly relative frequency (%) of different coronavirus variants over time in Brazil. Data from Fiocruz [2020].

2.3. Simulations

In our study, we utilized the mathematical model proposed by Lima et al. [2024] to simulate the progression of the COVID-19 pandemic across municipalities. This model uses fuzzy transitions between epidemic periods to depict epidemiological dynamics over time, capturing changes in essential parameters [Lima et al. 2024]. At its core, the model relies on key epidemiological metrics. Firstly, the *recovery rate* (γ), defined as $\gamma = \frac{1}{\textit{infectious period}}$, stands as a fundamental parameter. Additionally, the model discerns between the rapid adjustment of the *contact rate* (β), expressed as $\beta = \frac{R_0}{\textit{infectious period}} = \gamma R_0$, and the more gradual transitions characterizing the *lethality rate* (f) and *immunity loss rate* (ω), represented respectively as $f = \frac{\textit{IFR}}{100}$ and $\omega = \frac{1}{\textit{protected period}}$. Consequently, it provides time-varying estimates for crucial epidemiological indices such as R_0, IFR, and the *duration of protection against reinfection* (Ω). Furthermore, the model generates time series data for population compartments including *Susceptible* (S), *Infected* (I), *Recovered* (R), and *Deceased* (D) [Lima et al. 2024].

The model developed by Lima et al. [2024] relies on epidemic periods to guide its input parameters. In this context, an epidemic period comprises the time between outbreak onsets. To identify the outbreaks for each city, we consider an outbreak the period where a sustained R_t value is above one for at least seven consecutive days. Also, we allowed for a maximum of seven consecutive days below this threshold within the identified outbreak. Each municipality experienced approximately 10.6 outbreaks ($\pm$ 1.5).

The model proposed by Lima et al. [2024] introduces several parameters, including the initial infected population ($I(0)$), recovery rate (γ), lists representing contact rates for different epidemic periods ($\overrightarrow{\beta}$), infection fatality probabilities for different epidemic periods ($\overrightarrow{f}$), immunity loss rates for different epidemic periods ($\overrightarrow{\omega}$), breakpoints for fast transition between epidemic periods ($\overrightarrow{b_{fast}}$), transition days for smoothing fast transitions ($\overrightarrow{\tau_{fast}}$), and breakpoints for slow transition between epidemic periods ($\overrightarrow{b_{slow}}$).

Lima et al. [2024] introduce a fuzzy variable to denote a rapid transition (μ_{fast}) between epidemic periods, with the universe representing the number of days in the simulation. Each epidemic period is represented by a fuzzy partition in this variable, resulting in a total of $|\overrightarrow{b_{\text{fast}}}| + 1$ fuzzy partitions. Additionally, they propose another fuzzy variable, μ_{slow}, to represent a gradual transition between epidemic periods, employing the same universe as the number of days in the simulation. Similar to μ_{fast}, each epidemic period is represented by a fuzzy partition, yielding a total of $|\overrightarrow{b_{\text{slow}}}| + 1$ partitions.

Also, Lima et al. [2024] performs a defuzzification on μ_{fast} by combining it with $\overrightarrow{\beta}$ and $\overrightarrow{\tau_{fast}}$ to obtain a time-varying parameter β. Similarly, μ_{slow} is defuzzificated combining it with $\overrightarrow{f}$ and $\overrightarrow{\omega}$ to derive time-varying parameters f and ω, respectively.

We utilized the stochastic differential evolution algorithm [Storn and Price 1997] to optimize the model parameters. The details about the algorithm application are available in the supplementary material. We minimized the error between the original data and the simulations for both the *death rate per 100,000 inhabitants in the 7-day moving average* (M) sourced from MIS [DATASUS 2022b], and the *effective reproduction number* (R_t), calculated from SARS database [DATASUS 2022a] and presented in Section 2.2. To accomplish this, we formulated a composite objective function as depicted in Equation 1:

$$\frac{\text{MAE}(M, \hat{M})}{\overline{M}} + \frac{\text{MAE}(R_t, \hat{R}_t)}{\overline{R_t}}, \tag{1}$$

where MAE represents the mean absolute error measure. In this context, $\hat{M}$ and $\hat{R}_t$ denote the mortality and effective reproduction numbers estimated by the model, respectively. Additionally, $\overline{M}$ and $\overline{R_t}$ represent the mean values of M and R_t, respectively.

For each outbreak after the initial one, we define a breakpoint b_{fast} to represent fast transitions between epidemic periods. Another innovation proposed by Lima et al. [2024] is the insight that the β could change inside an outbreak. So, we defined, following the criteria proposed by Lima et al. [2024], special breakpoints b^0_{fast} and $b^{'}_{fast}$ to represent the adjustment in the initial outbreak and subsequent outbreaks, respectively. Being $\overrightarrow{b^*_{fast}} = b^0_{fast} \cup \overrightarrow{b_{fast}} \cup \overrightarrow{b^{'}_{fast}}$, we define an initial β and one β for each item in $\overrightarrow{b^*_{fast}}$, along with one τ for each item in $\overrightarrow{b^*_{fast}}$.

To model a gradual transition between epidemic periods, we establish a breakpoint b_{slow} for each subsequent outbreak following the initial one, ensuring that the interval between outbreaks is at least 180 days, as proposed by Lima et al. [2024]. Consequently, in practical terms, $\overrightarrow{b_{\text{slow}}}$ forms a subset of $\overrightarrow{b_{\text{fast}}}$. We initialize both f and ω, along with additional instances of f and ω corresponding to each $\overrightarrow{b_{\text{slow}}}$.

We optimize our model by conducting 25 executions for each municipality in our sample considering parameter bounds presented in Table 1, a population of 100,000 individuals, and the simulation period beginning at the start of the case time series until December 31, 2022. Following Lima et al. [2024] findings, we set $\gamma = 1/8$, i.e., an infectious period of eight days. Additionally, it is crucial to highlight that $\overrightarrow{b_{slow}} \subset \overrightarrow{b_{fast}}$, and optimization of these parameters is unnecessary, as $\overrightarrow{b_{fast}}$ has already been optimized.

2.4. Data analysis

This section outlines the methods employed for analyzing the obtained results. Initially, we evaluated the performance of the Lima et al. [2024] model using data from our municipality sample. This assessment relied on two key metrics: the Sum of Squared Errors (SSE) and the coefficient of determination (R^2).

For each municipality, we conducted a cross-correlation analysis [Shumway et al. 2000] between Δ_H and R_0. Before applying this technique, we performed one transformation on the time series R_0, resulting in $R^{'}_0$, and two transformations on Δ_H, resulting in $\Delta^{''}_H$. These transformations were necessary to ensure the stationarity of $\Delta^{''}_H$ and $R^{'}_0$. Further details about the cross-correlation measurement, time series transformations, and significance thresholds can be found in the supplementary material.

Additionally, we explored the relationship between virus variants and R_0 and the percentage of vaccinated individuals and IFR. We present these analyses in Section 3, which presents our findings and discusses observations regarding outlier municipalities.

Table 1. Model parameter bounds for optimization, adapted from Lima et al. [2024].

Parameter	Description	Minimum value	Maximum value	Reference
$I(0)$	Initial quantity of infected population	$\frac{1}{\text{population}} \times 100,000$	$C[0:56]$	Empirical
b^0_{fast}	Adjusted breakpoint in initial outbreak for fast transition between epidemic periods	Outbreak begin	Outbreak end	Empirical
b_{fast}	Breakpoint for fast transition between epidemic periods	Outbreak begin	At $R_t^{\uparrow}$	Empirical
b'_{fast}	Adjusted breakpoint in subsequent outbreaks for fast transition between epidemic periods	At $R_t^{\uparrow}$	Outbreak end	Empirical
τ	Transition days for smoothing fast transitions between epidemic periods	0	56	Empirical
β_0	Initial contact rate	$\gamma\overline{R_t}$	γR_0	Empirical
β'_0	Adjusted contact rate in initial outbreak	$\gamma R_t^{Q_{0.25}}$	γR_0	Empirical
β	Contact rate	$\max(\inf \beta_{b-1}, \gamma R_t^{\uparrow})$	$\gamma R_t^{\uparrow}/0.3$	Empirical
β'	Adjusted contact rate	$\gamma R_t^{Q_{0.25}}$	$\gamma R_t^{\uparrow}/0.3$	Empirical
f	IFR in probability	$\max(M, 0.0001)$	$\min(\text{CFR}, 0.0133)$	[Verity et al. 2020]
ω	Immunity loss rate	1/365	1/90	[Pulliam et al. 2022]

$C[0:56]$: Case rate per 100,000 inhabitants until the 56^{th} day in the first outbreak.
$R_t^{\uparrow}$: Peak of the effective reproduction number in outbreak.
$\overline{R_t}$: Mean of the effective reproduction number in outbreak.
R_0: Basic reproduction number.
$R_t^{Q_{0.25}}$: First quartile of the effective reproduction number in the period between the current outbreak end and the subsequent outbreak begins.
γ: Recovery rate.
$\inf \beta_{b-1}$: Minimum bound of the previous contact rate.
IFR: Infection Fatality Rate.
CFR: Case Fatality Rate in the epidemic period.
M: Death rate per 100,000 inhabitants in the epidemic period.

3. Results and discussion

Table 2 shows that the model closely matches the observed data about mortality in larger Brazilian municipalities. On the other hand, the R^2 assessed for R_t indicates that the model captures moderately the variance of the actual observations.

Table 2. Results of the COVID-19 simulations for the 41 largest Brazilian municipalities.

Error	SSE		R^2	
	R_t	New death rate	R_t	New death rate
0.278 (0.255-0.320)	0.018 (0.014-0.023)	0.014 (0.010-0.019)	0.600 (0.430-0.678)	0.942 (0.912-0.966)

Note: values are presented as the median with the first and third quartiles in parentheses.
Error: the objective function error, as defined by Equation 1.
SSE: Sum of Squared Error.
R^2: coefficient of determination.
R_t: effective reproduction number.
New death rate: per 100,000 inhabitants.

While the model may not precisely capture the variability of R_t, the overall outcomes suggest that it effectively captures the trend of the original data. As an illustration, Figure 4 depicts the simulation results for Cuiabá/MT, the city with the highest death rate in our sample. The median R^2 for R_t in Cuiabá/MT is 0.55, but still, Figure 4 indicates a reasonable reproduction of the pandemic dynamics. We produced outcome plots for all municipalities in our sample and have them available in the supplementary material.

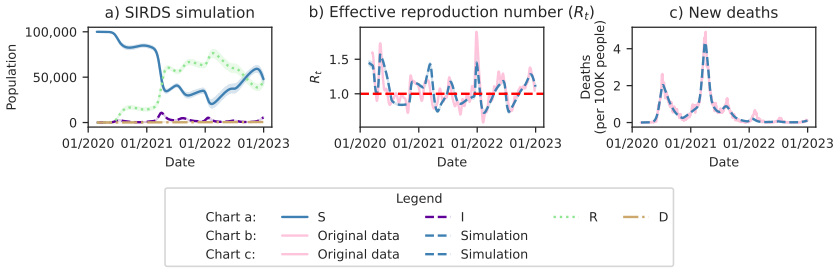

Figure 4. Comprehensive analysis of simulation results for Cuiabá/MT, the municipality with the highest COVID-19 mortality in our sample. (a) Model outcomes for the compartments Susceptible (S), Infected (I), Recovered (R), and Deceased (D). (b) Comparison of the effective reproduction number (R_t) between original data and simulation. (c) New death rate per 100,000 inhabitants comparing original data and simulation. Shaded regions depict the 95% Confidence Interval (CI).

Figure 5 shows the time-varying estimates of R_0, IFR, Ω for the municipalities from our sample. Notably, Ω exhibits the highest uncertainty, aligning with Lima et al. [2024] findings, which reported low sensitivity for this parameter. We note a trend in the cities to reduce R_0 to near the critical value of 1 during the early stages of the pandemic. However, this trend reverses after mid-2020, with the model estimating an increase in R_0, which persists across 2021. 2022 is marked by increased uncertainty in R_0 estimations. Regarding IFR, we note that the highest confusion was in the early stages of the pandemic. In 2021, the model suggests a declining trend in IFR. Notably, the model estimates significantly lower IFR values for municipalities in 2022 compared to the preceding years.

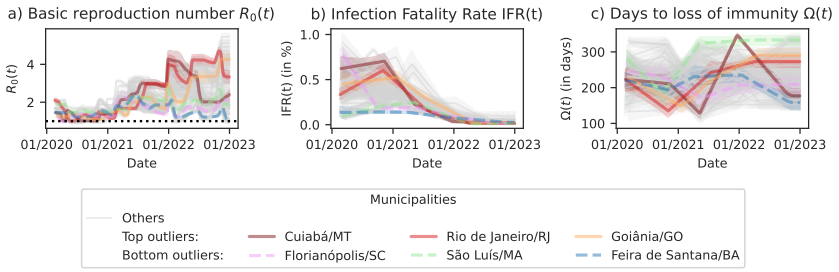

Figure 5. Model parameters varying by time (t) estimated for COVID-19 in the 41 largest Brazilian municipalities from 2020 to 2022. (a) Basic reproduction number (R_0), with a dotted horizontal line representing the reference value ($R_0 = 1$). (b) Infection Fatality Rate (IFR). (c) Days to loss of immunity (Ω). The plot highlights cities with notable deviations from the average mortality rate, categorized as top outliers (Cuiabá/MT, Rio de Janeiro/RJ, and Goiânia/GO) and bottom outliers (Feira de Santana/BA, São Luís/MA, and Florianópolis/SC). Shaded regions depict the 95% Confidence Interval (CI).

Our analysis delved into the cross-correlation between the time series of Δ_H and the time-varying R_0 for municipalities in our sample, as depicted in Figure 6. Across the years, distinct patterns emerged: in 2020, we observed two distinct groups of municipalities where Δ_H inversely led to R_0, which we noted eight municipalities with a lag of around seven days and six municipalities with a lag of around 28 days. Regarding 2021, we note that Δ_H is lagged by R_0 for 13 municipalities, in which 75% of the correlations

were with the lag between one day and seven days. However, in 2022, no notable correlation was observed. These findings shed light on the effectiveness of social isolation measures over time: stringent early stages reduced R_0, while reactive measures in 2021 failed to replicate the same impact. The absence of significant correlations in 2022 indicates that social isolation was no longer the primary measure to combat COVID-19 in municipalities since a large portion of the population was already vaccinated.

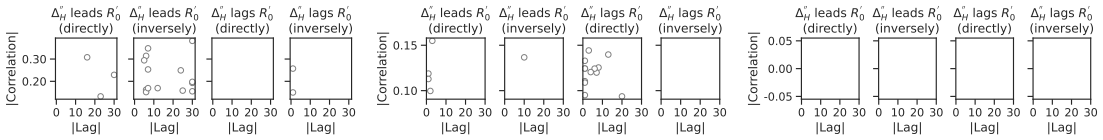

Figure 6. Scatter plots for the correlation absolute coefficients and lag values resulting from cross-correlation analysis between $\Delta_H^{''}$ (stay-at-home index) and COVID-19 $R_0^{'}$ (time-varying basic reproductive number) estimated for the 41 largest Brazilian municipalities in the years (a) 2020, (b) 2021, and (c) 2022. Each point represents the highest significant correlation coefficient observed for a municipality in the respective analysis.

We calculated the median R_0 for each coronavirus variant during the months it predominated in states across the 41 largest Brazilian municipalities. As illustrated in Table 3, the initial dominant variants, categorized as *Others*, exhibited a median R_0 of 1.30. Subsequently, variants such as Gamma and Delta emerged as dominant in 2021, showcasing an R_0 hovering around 2. The Omicron phase marked the period with the highest median R_0, with values exceeding 2.30, except for the BA.4.* subvariant, which reported a lower R_0. These observations underscore the capability of the model to capture the rising trend of R_0 in Brazilian municipalities in response to the emergence of new variants.

Table 3. Basic reproduction number (R_0) for each coronavirus variant during months when it was dominant in states from the 41 largest Brazilian municipalities.

Variant	R_0
Others	1.30 (1.16 - 1.45)
P.1.* (Gamma)	1.95 (1.62 - 2.41)
B.1.617.2+AY.* (Delta)	1.98 (1.66 - 2.36)
BA.1.* (Omicron)	2.53 (1.81 - 3.22)
BA.2.* (Omicron)	2.94 (1.99 - 3.54)
BA.4.* (Omicron)	1.53 (1.24 - 1.81)
BA.5.* (Omicron)	2.32 (1.69 - 3.66)

Note: values are presented as the median with the first and third quartiles in parentheses.

Table 4 illustrates a consistent reduction in the IFR as the percentage of the population fully vaccinated against COVID-19 increases. Our analysis reveals a robust negative correlation between the proportion of fully vaccinated individuals and IFR, with a Spearman correlation coefficient of -0.80.

We analyzed the correlations among the epidemic parameters and the usual interventions against COVID-19, such as social isolation and vaccination. We pay special attention to outlier cities that exhibited notably elevated mortality rates during the study period, exemplified by Cuiabá/MT, Rio de Janeiro/RJ, and Goiânia/GO, as well as those

Table 4. Infection Fatality Rate (IFR) for different ranges of the fully vaccinated population against COVID-19 in the 41 largest Brazilian municipalities.

Population fully vaccinated	Infection Fatality Rate (IFR)
0%	0.32% (0.21 - 0.49)
$> 0\%$ and $\leq 10\%$	0.29% (0.23 - 0.37)
$> 10\%$ and $\leq 20\%$	0.23% (0.17 - 0.29)
$> 20\%$ and $\leq 30\%$	0.18% (0.13 - 0.24)
$> 30\%$ and $\leq 40\%$	0.15% (0.11 - 0.21)
$> 40\%$ and $\leq 50\%$	0.13% (0.10 - 0.19)
$> 50\%$ and $\leq 60\%$	0.11% (0.08 - 0.16)
$> 60\%$ and $\leq 70\%$	0.07% (0.04 - 0.11)
$> 70\%$ and $\leq 80\%$	0.04% (0.02 - 0.06)
$> 80\%$	0.03% (0.01 - 0.05)

Note: values are presented as the median with the first and third quartiles in parentheses.

demonstrating reduced mortality rates, such as Feira de Santana/BA, São Luís/MG, and Florianópolis/SC. Despite our efforts, we did not uncover a definitive explanation for why top outlier cities experienced 2.5 times more deaths than their bottom outlier counterparts.

If Δ_H and vaccination could not clearly explain the pandemic outcome in outlier cities, we note that epidemiological parameters estimated are much more explicit in suggesting the differences between outlier groups. Notably, we noted a contrast between these two groups of cities during the initial two years, with death rates in top outliers being 2.65 times higher than those in bottom outliers. By 2022, however, the death rate in top outliers had reduced to 65% higher than in bottom outliers. Also, we note that all outliers reduced R_0 during the early stages of 2020, as depicted in Figure 5a. Subsequently, in early 2021, R_0 increased for all outliers; however, we note that after the initial rise in R_0, the municipalities from the bottom outlier group were able to maintain a stable R_0, while municipalities such as Cuiabá and Rio de Janeiro experienced R_0 values exceeding 2.5. Finally, the model estimated that the IFR for top outlier municipalities was higher than that observed in bottom outlier municipalities during the initial two years, as illustrated in Figure 5b. However, by 2022, the model indicated a convergence of the IFR in top outliers towards the same pattern observed in bottom outliers, suggesting a mitigating effect of mass vaccination efforts on lethality disparities among cities.

We note limitations in our study. We identify eight cities with vaccination rates exceeding 100% of their population due to noise in the database [Cota 2021]. Also, Google advises caution when using the COVID-19 Community Mobility Report [Google 2020] for comparisons between different locations or periods. Despite this, we assessed that the data remained reasonably reliable and did not damage the analysis conducted in this study.

4. Conclusion

In this study, we conducted COVID-19 simulations for the 41 largest Brazilian municipalities, uncovering several significant insights. Initially, we observed a significant reduction in the time-varying R_0 during the early stages of the pandemic, coinciding with robust social isolation measures. While municipalities implemented preventive social isolation in 2020, a shift to reactive social isolation occurred in 2021, leading to less control over R_0 and increased mortality rates. The emergence of variants Gamma and Delta in 2021 also contributed to elevated R_0 values. However, the simulations revealed

a notable decline in the IFR throughout 2021, coinciding with mass vaccination efforts. In 2022, all municipalities exhibited a convergent pattern of reduced IFR. These findings underscore the effectiveness of social isolation measures in 2020 and the crucial role of mass vaccination campaigns in mitigating the impact of the pandemic. Nonetheless, the issues observed in 2021, characterized by reactive social isolation, variant emergence, and slow vaccination, highlight the need for proactive measures to combat epidemics.

Our study also revealed disparities between cities from the top and bottom outlier groups, which we attribute to differences in the R_0 and IFR. Further work into correlated factors, particularly socioeconomic features, is needed to understand these observations.

Supplementary material

Data, code, and supplementary information are available on GitHub (`https://github.com/helderseixas/covid-brazilian-municipalities`).

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References

Almeida, G., Vilches, T., Ferreira, C., and Fortaleza, C. (2021). Addressing the COVID-19 transmission in inner Brazil by a mathematical model. *Scientific Reports*, 11(1):10760.

Bastos, S. B. and Cajueiro, D. O. (2020). Modeling and forecasting the early evolution of the Covid-19 pandemic in Brazil. *Scientific Reports*, 10(1):19457.

Cori, A., Ferguson, N. M., Fraser, C., and Cauchemez, S. (2013). A new framework and software to estimate time-varying reproduction numbers during epidemics. *American Journal of Epidemiology*, 178(9):1505–1512.

Cota, W. (2021). Vaccination data. Database: GitHub [Internet]. Available from: `https://github.com/wcota/covid19br-vac`. Accessed: 2024 February 27.

DATASUS (2020). Painel de casos de doença pelo coronavírus 2019 (COVID-19) no Brasil pelo Ministério da Saúde. Database: Gov.BR [Internet]. Available from: `https://covid.saude.gov.br/`. Accessed: 2023 November 23.

DATASUS (2022a). Banco de Dados de Síndrome Respiratória Aguda Grave - incluindo dados da COVID-19. Database: Gov.BR [Internet]. Available from: `https://opendatasus.saude.gov.br`. Accessed: 2023 November 23.

DATASUS (2022b). Sistema de Informação sobre Mortalidade – SIM. Database: Gov.BR [Internet]. Available from: `https://opendatasus.saude.gov.br/fa_IR/dataset/sim`. Accessed: 2023 January 23.

Ferrante, L., Duczmal, L. H., Capanema, E., Steinmetz, W. A. C., Almeida, A. C. L., Leão, J., Vassao, R. C., Fearnside, P. M., and Tupinambás, U. (2022). Dynamics of COVID-19 in Amazonia: a history of government denialism and the risk of a third wave. *Preventive medicine reports*, 26:101752.

Fiocruz (2020). Fiocruz's genomics network. Database: Fiocruz [Internet]. Available from: `https://www.genomahcov.fiocruz.br/en/`. Accessed: 02/20/2024.

Google (2020). Google COVID-19 community mobility reports. Database: Google [Internet]. Available from: `https://www.google.com/covid19/mobility/`. Accessed: 2024 February 27.

Instituto Brasileiro de Geografia e Estatística (2022). Censo 2022. Database: Gov.BR [Internet]. Available from: `https://censo2022.ibge.gov.br/`. Accessed: 2023 March 29.

Lima, H. S., Tupinambás, U., and Guimarães, F. G. (2024). Estimating time-varying epidemiological parameters and underreporting of Covid-19 cases in Brazil using a mathematical model with fuzzy transitions between epidemic periods. *PLoS ONE*.

Melo, G. C. d., Duprat, I. P., Araújo, K. C. G. M. d., Fischer, F. M., and Araújo Neto, R. A. d. (2020). Prediction of cumulative rate of COVID-19 deaths in Brazil: a modeling study. *Revista Brasileira de Epidemiologia*, 23.

Nouvellet, P., Bhatia, S., Cori, A., Ainslie, K. E., Baguelin, M., Bhatt, S., Boonyasiri, A., Brazeau, N. F., Cattarino, L., Cooper, L. V., et al. (2021). Reduction in mobility and COVID-19 transmission. *Nature communications*, 12(1):1090.

Oliveira, J. F., Jorge, D. C., Veiga, R. V., Rodrigues, M. S., Torquato, M. F., da Silva, N. B., Fiaccone, R. L., Cardim, L. L., Pereira, F. A., de Castro, C. P., et al. (2021). Mathematical modeling of COVID-19 in 14.8 million individuals in Bahia, Brazil. *Nature communications*, 12(1):333.

Pulliam, J. R., van Schalkwyk, C., Govender, N., von Gottberg, A., Cohen, C., Groome, M. J., Dushoff, J., Mlisana, K., and Moultrie, H. (2022). Increased risk of SARS-CoV-2 reinfection associated with emergence of Omicron in South Africa. *Science*, 376(6593):eabn4947.

Shumway, R. H., Stoffer, D. S., and Stoffer, D. S. (2000). *Time series analysis and its applications*, volume 3. Springer.

Storn, R. and Price, K. (1997). Differential evolution-a simple and efficient heuristic for global optimization over continuous spaces. *Journal of Global Optimization*, 11(4):341.

Verity, R., Okell, L. C., Dorigatti, I., Winskill, P., Whittaker, C., Imai, N., Cuomo-Dannenburg, G., Thompson, H., Walker, P. G., Fu, H., et al. (2020). Estimates of the severity of coronavirus disease 2019: a model-based analysis. *The Lancet Infectious Diseases*, 20(6):669–677.

World Health Organization (2023). Covid-19 vaccine tracker and landscape. Available from: `https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines`. Accessed: 2024 February 27.