Assessing the nationwide impact of COVID-19 mitigation policies on the transmission rate of SARS-CoV-2 in Brazil

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Abstract

COVID-19 is now identified in almost all countries in the world, with poorer regions being particularly more disadvantaged to efficiently mitigate the impacts of the pandemic. In the absence of efficient therapeutics or vaccines, control strategies are currently based on non-pharmaceutical interventions, comprising changes in population behavior and governmental interventions, among which the prohibition of mass gatherings, closure of non-essential establishments, quarantine and movement restrictions. In this work we analyzed the effects of 547 published governmental interventions, and population adherence thereof, on the dynamics of COVID-19 cases across all 27 Brazilian states, with emphasis on state capitals and remaining inland cities. A generalized SEIR model with a time-varying transmission rate (TR), that considers transmission by asymptomatic individuals, is presented. Confirmed COVID-19 cases were used to calibrate the model parameters using non-linear least squares methods. We analyze the changes on the TR and effective reproduction number as a function of both the extent of enforced measures across Brazilian states as well as population movement. The social mobility reduction index, a measure of population movement, together with the stringency index, adapted to incorporate the degree of restrictions imposed by governmental regulations, were used in conjunction to quantify and compare the effects of varying degrees of policy strictness across Brazilian states. Our results show that population adherence to social distance recommendations plays an important role for the effectiveness of interventions, and represents a major challenge to the control of COVID-19 in low- and middle-income countries.

Keywords: Brazil; COVID-19; mathematical modeling; non-pharmaceutical interventions; transmission rate.

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1. Introduction

COVID-19, a disease caused by the SARS-CoV-2 coronavirus, emerged in December 2019 in China and was recognized as a pandemic by the World Health Organization on March 11, 2020 [1]. At that moment, Brazil had already confirmed 53 cases. On March 20, with 972 confirmed cases, the Brazilian Ministry of Health recognized community transmission of COVID-19 throughout the national territory, 24 days after the first confirmed case of COVID-19 was identified [2]. Brazil is a country with 209.5 million individuals and stark socioeconomic disparities throughout its territory. It is the largest country in South America and the fifth largest nation in the world. Accordingly, the many challenges imposed by the COVID-19 pandemic are unprecedented in this country.

The political-administrative organization of Brazil comprises three spheres of governance: The Union (federal government), the 27 states (including the Federal District, where the capital city, Brasilia, is located) and 5,570 municipalities. To reduce the transmission of SARS-CoV-2, federal, state and city governments implemented a series of interventions by means of government decrees [3]. This included recommendations to identify and isolate confirmed cases and contacts; to restrict unnecessary movements; to practice social distancing; to increase hygiene awareness; to follow respiratory etiquette; to widespread use masks, among others. In the absence of more intensive mitigation policies implemented by the federal government (such as lock-downs and movement restrictions), most measures were adopted by local governments (state/municipalities) [3]. However, adherence to these policies varied greatly throughout the country, and while some regions enacted more strict controls, others have been more lax.

Mathematical modeling has been instrumental to inform policies and to evaluate the trends of the COVID-19 pandemic [4, 5, 6, 7, 8, 9]. Here we define the transmission rate (TR) in terms of a generalized SEIR model, that simulates the dynamics of virus spread in a population entirely susceptible to the new virus. In this approach, the TR represents the probability that an infected individual will transmit the disease to a susceptible individual [10]. Therefore, the higher this rate, the greater the number of new cases for a region. Downward changes on the TR are expected with the implementation of mitigation policies such as non-pharmaceutical interventions (NPI), currently the only option to limit the spread of SARS-CoV-2 given the absence of vaccines or effective therapies.

In this work, we comparatively analyze the evolution of the COVID-19 transmission rate and reproductive number in all 27 Brazilian states, with emphasis on state capitals and remaining inland cities, establishing links with measures of governmental restrictions (NPIs) implemented in each region together with the human behaviour response, particularly the adherence to recommendations of social distancing. The varying degree of enforced policies across the country offers an opportunity to study the impacts of interventions, including their breadth and timing, on the TR of SARS-CoV-2 throughout Brazilian states. These findings can be extrapolated to similar settings in other low- and middle-income countries to drive improvements in mitigation policies against subsequent waves of SARS-CoV-2 or other potentially pandemic pathogens.

2. Methodology

Data sources

The number of confirmed cases of COVID-19 for each Brazilian municipality, up to May 22, was obtained from the Ministry of Health, Brazil, and are publicly available at `https://covid.saude.gov.br/` and at `https://brasil.io/datasets/`. Since the capitals of each state present different dynamics and largely concentrate COVID-19 cases in the initial wave of the epidemic, we considered separately the transmission dynamics of capitals and aggregated the remaining state municipalities (which we refer throughout the text as inland cities, although strictly not all of these are distant from the shore).

To evaluate state-wide enforced governmental measures, we relied upon the careful collection of government decrees and resolutions scattered throughout various state government gazettes and other official repositories, since each state uses different platforms to communicate their legislation. We annotated the type of measure enforced, the implementation date, the duration and whether it was valid to the whole state or limited to some regions.

As a proxy of the population adherence to recommendations of social distancing, we used information from InLoco (`https://inloco.com.br/`), a Brazilian technology start-up that developed an index of social mobility, which seeks to help in fight the pandemic in Brazil. Data for the index construction is obtained from the unidentified, aggregated geo-movement patterns extracted from 60 million mobile devices throughout the country. The index ranges from 0 to 100% and measures the proportion of devices from a given municipality that remained within a 450 meter radius from the location identified as home by the device. The higher the index, the greatest the population adherence to social distancing recommendations. The data is available at `https://mapabrasileirodacovid.inloco.com.br`. Examples of other works that used the Social mobility reduction index (SMRI) can be found in [11, 12].

Lastly, historical average daily flux data throughout the country using road/air/fluvial networks were obtained from the Brazilian Institute of Geography and Statistics [13, 14].

Stringency Index

To comparatively evaluate the governmental measures implemented by the Brazilian states, we constructed a stringency index I, similarly to that implemented in [15]. To score each employed policy we adapted the methodology to the Brazilian context by taking into account the specific measures established by the different state governments.

Measures were classified into two categories: Ordinal and cumulative. Ordinal measures, denoted by O, are those in which there is a clear order on the intensity of the restriction, so that there are less possibilities of reclassification. For instance, a decree prohibiting agglomerations of more than 100 people, followed by a second decree restricting to 500 people, belong to the ordered category, where the first is more intense than the second. Cumulative restrictions, denoted by C, are those with no clear order of intensity, allowing for a wide range of possibilities to classify the restriction. For instance, closure of malls and prohibition to accessing parks and beaches have no clear order to which of these measures is more intense and may lead to subjective classification. In this last case we evaluate each measure by a sum of points defined by sub-measures.

The classification varies from 0 (when no measure is applied) to N_i (when the most stringent measure is applied), where i corresponds to the i-th sub-measure adopted. Additionally, to take into account whether the measure was enforced for the whole state or limited to a particular region, each index of classification has a target G_i. If the measure is ordinal, then we consider $G_i = Go_i$, taking the value 0 if the measure is applied for specific areas of the state, and 1 if it is enforced for the whole state. If the measure is cumulative and since the measure will be a sum of the sub-classes, then $G_i = Gc_i$ is the sum of targets for each sub-class, which again is 0 if the sub-class is applied to specific areas or 1 if it is applied to the whole state without exemptions.

In this work we have six classes of measures, that are described in Supplementary Table 1. The summary of the six measures, as well as their sub-classes and targets are presented in Table 1. The index for the ordinal classes is given by

$$Io_i = \frac{O_i}{N_i(2 - Go_i)}.$$

For the cumulative measures the index is defined by

$$Ic_i = \frac{Gc_i + \frac{(C_i - Gc_i)}{2}}{N_i},$$

where C_i are sub-measures. Therefore, the total state index I, for a given day, will be taken as the average of the value of the classes I_i, thus yielding

$$I = 100 \times \frac{\sum_{i=1}^{4} Io_i + \sum_{i=1}^{2} Ic_i}{6}.$$

Only measures declared by state governments were considered, given the lack of availability of centralized information regarding the municipalities, as well as the difficulty of evaluating regulations published by each of the 5,570 Brazilian municipalities. Federal government policies were also not considered, as these affect equally all states.

Table 1: Classification of governmental responses to COVID-19 in Brazil (state-wide).

Measure adopted	**Type**	**Classification index**	**Targeting index**	**N_i**
Cancellation of public events	ordinal	O_1 $(0, 1, 2, 3, 4, 5, 6)$	G_{o1} (0, 1)	6
Closure of schools/universities	ordinal	O_2 (0,1,2)	G_{o2} (0, 1)	2
Home-office for governmental employees	ordinal	O_3 (0,1,2,3,4)	G_{o3} (0, 1)	4
Isolation	ordinal	O_4 (0,1,2)	G_{o4} (0, 1)	2
Closure of non-essential businesses and public activities	cumulative	C_1 (0,1,2,3,4,5,6,7)	G_{c1} (0,1,2,3,4,5,6,7)	7
Transport lock	cumulative	C_2 (0,1,2,3,4,5,6)	G_{c2} (0,1,2,3,4,5,6)	6

The mathematical model

We generalize the usual SEIR model by taking into account the asymptomatic cases. To account for variations in the TR over time, we assume that the TR parameter varies according to

$$\beta(t) = \beta_0 \mathcal{H}(t_1 - t) + \sum_{i=1}^{n-1} \beta_1 \mathcal{H}(t_{i+1} - t)\mathcal{H}(t - t_i) + \beta_0 \mathcal{H}(t - t_n), \qquad (1)$$

where $\{t_1, t_2, \ldots, t_n\}$ represent a set of points in time defining the change on the TR; $\mathcal{H}(t) = lim_{k\to\infty} \frac{1}{1+exp(-2kt)}$ is the Heaviside step function; and β_i are TRs that can be obtained by the fitting of the data to the time interval defined by the t_i's.

The system of differential equations then reads:

$$\frac{dS}{dt} = \frac{-\beta(t)S(I_s + \delta I_a)}{N} \qquad (2)$$

$$\frac{dE}{dt} = \frac{\beta(t)S(I_s + \delta I_a)}{N} - \kappa E \qquad (3)$$

$$\frac{dI_a}{dt} = (1-p)\kappa E - \gamma_a I_a \qquad (4)$$

$$\frac{dI_s}{dt} = p\kappa E - \gamma_s I_s \qquad (5)$$

$$\frac{dR}{dt} = \gamma_a I_a + \gamma_s I_s \qquad (6)$$

In this work we analyze the time intervals (in a daily scale) in which there were observed changes on the TR for each state, capital cities and remaining inland cities, after community transmission of the disease was declared on the state, that is when there is no clear source of origin of the infection in the community.

Here we estimated the β_i's, δ, p and t_i's parameters using non-linear least squares method, while κ, γ_a, γ_s were kept fixed. The key epidemiological model parameters and intervals were informed by the literature and are presented in Supplementary Table 3.

Based on the obtained parameter values we also evaluated the basic reproductive number $\mathcal{R}_0$ and the effective reproductive number $\mathcal{R}(t)$, where the first one, following the notation introduced in [9], is expressed by:

$$\mathcal{R}_0 = \frac{\beta p}{\gamma_s} + \frac{\beta\delta(1-p)}{\gamma_a}. \tag{7}$$

The epidemiological meaning of $\mathcal{R}(t)$ is the same as for $\mathcal{R}_0$, namely, it represents the average number of secondary infections that an individual, who became infected at time t, is able to generate. The series of $\mathcal{R}(t)$ values indicates the current trend of the epidemic and represents the dissemination of the disease in the population. As in our previous work [9], we have:

$$\mathcal{R}(t) = \frac{b(t)}{\int_0^\infty b(t-x)g(x)dx}, \tag{8}$$

where $b(t)$ represents the daily number of new cases and $g(x)$ is the disease probability distribution function for the time interval between the infection of an individual and its secondary cases. The function $g(x)$ receives contributions from the three compartments E, I_a, I_s that impact the evaluation of $\mathcal{R}_0$ and $\mathcal{R}(t)$. For more details, refer to [9].

Aiming at overcoming the fluctuations in the officially confirmed number of cases (which is impacted by testing capacity and its associated increase, even if momentarily, such as when pending tests accumulate over weekends), we present two series of $\mathcal{R}(t)$: The first, evaluated from a 7-day moving average series of the daily number of newly confirmed cases, as informed by local health authorities, while in the second $\mathcal{R}(t)$ series data is replaced by the predictions of the model, which effectively smooths the oscillations produced by the officially confirmed cases, since these values are given by the dynamics of the ODE system.

Data availability

Codes used to produce the results presented herein, and related datasets, are available as supplementary material and in a public GitHub repository [16].

Ethics statement

This study was conducted with publicly available data from the COVID-19 epidemic, published by the Ministry of Health of Brazil or third parties. Therefore, no approval by an ethics committee was required, according to Resolutions 466/2012 and 510/2016 (article 1, sections III and V) from the National Health Council (CNS), Brazil.

3. Results

The entry of SARS-CoV-2 in the Brazilian states

We initially analyzed the relationship between the identification of SARS-CoV-2 in each state and the time interval of the declaration of community transmission by state governments, as well as the connection of virus spread and historical movement patterns of the Brazilian population.

Figure 1a shows the temporal variation of the first reported case and the interval from the first case to the declaration of community transmission in the state. The first confirmed case of COVID-19 in Brazil occurred in the state of São Paulo, southeastern region, on February 26, 2020. Within an interval of seven to twelve days (from March 4 to March 9) the states of ES, DF, BA, AL, RJ and MG (abbreviations given in the caption of Figure 1) had confirmed cases of COVID-19. From March 10 to March 25 the disease spread to the remaining 20 Brazilian states. As depicted in Figure 1b, 40.7% (11/27) of the states took between 0 and 10 days to declare community transmission, 51.9% (14/27) took between 11 and 30 days, while only two states (Tocantins and Roraima), corresponding to 7.5%, took more than 30 days to register the first cases of COVID-19.

In Figure 2a we present the interstate flow network (road, air, fluvial), showing that states where viral spread occurred earlier, such as Rio de Janeiro, Minas Gerais, Distrito Federal and Bahia were more likely to share a large transportation flux with the state of São Paulo. On the other hand, states with the lowest interstate flows, such as Acre, Roraima and Amapá, all located in north region, were among the last to confirm SARS-CoV-2 transmission.

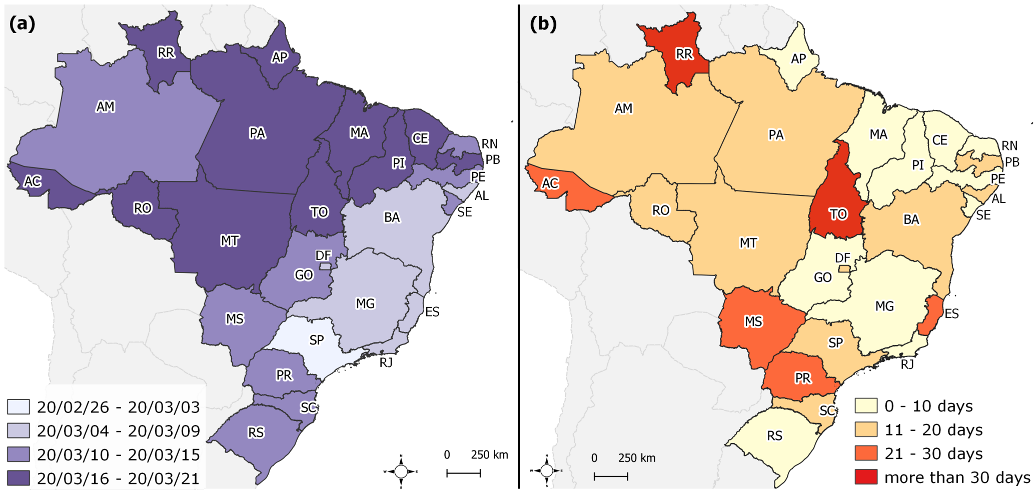

Figure 1: Dissemination of COVID-19 in Brazil. (a) Date of first confirmed COVID-19 case per state and (b) number of days elapsed from the first identified case to the establishment of community transmission in the state. Two-letter state abbreviations are as follows: AC, Acre; AL, Alagoas; AP, Amapá; AM, Amazonas; BA, Bahia; CE, Ceará; DF, Distrito Federal; ES, Espírito Santo; GO, Goiás; MA, Maranhão; MT, Mato Grosso; MS, Mato Grosso do Sul; MG, Minas Gerais; PA, Pará; PB, Paraíba; PR, Paraná; PE, Pernambuco; PI, Piauí; RJ, Rio de Janeiro; RN, Rio Grande do Norte; RS, Rio Grande do Sul; RO, Rondônia; RR, Roraima; SC, Santa Catarina; SP, São Paulo; SE, Sergipe; TO, Tocantins.

Once the entry of the virus was confirmed within each state, the capitals were the most affected cities initially, emerging as the epicenter of the epidemic in each state. Subsequently, SARS-CoV-2 disseminated throughout the inland cities with a different speed, as shown in the top panel plots of Supplementary Figure 1, where the incidence of COVID-19 is reported for the Brazilian states. In Figure 2b we show the average daily flux between all capitals and the remaining inland cities. We can see that the states of the Northeast (Sergipe, Pernambuco, Ceará, Bahia), Southeast (Minas Gerais, Rio de Janeiro) and South (Paraná) regions present a higher historical average daily flux of people compared to the remaining states.

Governmental measures and population adherence

Next, we evaluated the timing of governmental interventions on the number of cases, the breadth of these interventions as measured by the stringency index, and their effects on influencing people's behavior, particularly adhesion to social distancing recommendations.

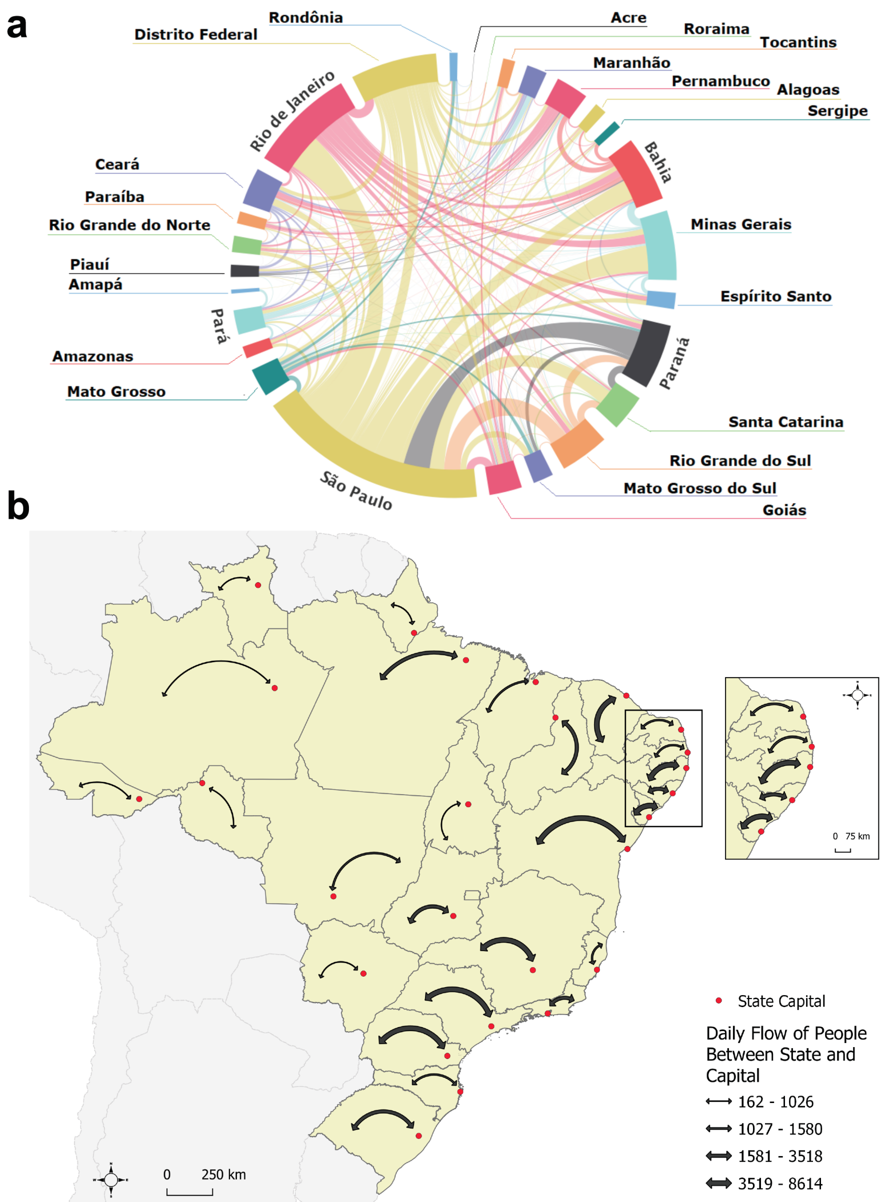

Figure 2: a) Average historical daily flux of people between Brazilian states through road/air/fluvial networks. State and flux colors are used only for the purpose of better identification, but otherwise have no specific meaning. b) Average historical daily flux of people between state capitals (depicted as red dots) and the remaining inland cities within each state. Graphs compiled using data from [13, 14].

A total of 547 regulations published by the 27 Brazilian state governments were annotated according to the methods described to construct the stringency index. Information on each individual regulation, including description, date of enforcement and validity is available in Supplementary Table 2. In contrast to the pattern of disease spread observed through the states, some regions which were first affected by COVID-19 were among those that delayed the implementation of measures to contain viral spread. For instance, São Paulo adopted measures only 2 weeks after the confirmation of the first case, on March 13, the same day of community transmission declaration in the state. A similar scenario occurred in Rio de Janeiro, where the first restriction measures were only implemented in parallel to the declaration of community transmission. Nevertheless, the majority of the state governments (15 out of 27) implemented restriction measures to contain the COVID-19 spread on March 16, many of which weeks before declaring community transmission. Indeed, six of them (TO, RR, PI, PA, MT and AC) adopted measures even before the first registered case.

Among the measures classified in Table 1, strict quarantine measures (only adopted partially in AP, BA, CE, MA and MT) and restrictions on public transportation were the most weakly implemented measures enforced by the states.

Figure 3 shows the variation of the stringency index over time for each state relative to the number of confirmed cases per 100,000 inhabitants. With the exception of Tocantins, Mato Grosso do Sul, Espírito Santo, Paraíba and Piauí, all states reached stringency index values over 50% during the detection period. Espírito Santo and Tocantins were states with the lowest values of the stringency index, ranging from 20% and 30% for an average period of 33 days, and reaching a maximum of about 40% in the remaining period. Mato Grosso do Sul, Paraíba and Piauí presented stringency index values between 30% and a maximum of 45% for most of the period. The remaining states had the index varying between 50% and 75%, with Ceará and Amapá reaching the highest values of 84% (from May 6 to May 31) and 95% (from May 19 to May 31), respectively. However, these were the states with the highest incidence of COVID-19 nationwide.

Variable adherence to social isolation recommendations was seen across the states, with values of the SMRI close to 30% at the beginning of March, followed by a peak to around 60% at the end of that month. This was observed in both state capitals and inland cities. The evolution of the stringency index for each state, as well as the SMRI for capitals and inland cities

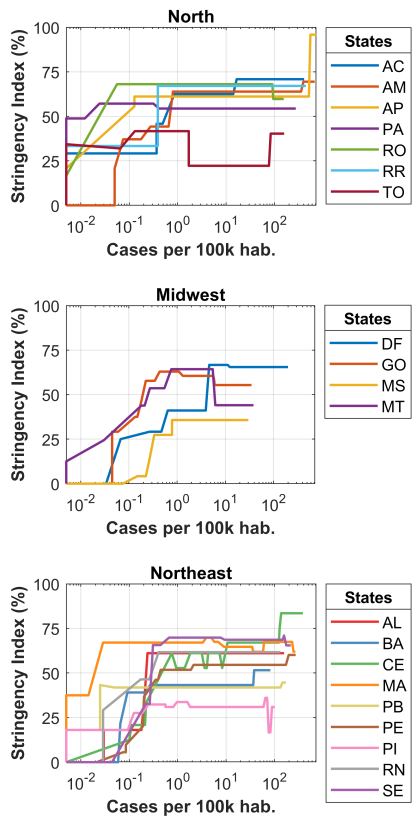

Figure 3: Evolution of the governmental measures adopted for each Brazilian state with respect to COVID-19 incidence. The number of confirmed cases per 100,000 population is shown in logarithmic scale on the x-axis.

is presented in the lower panel plots of Supplementary Figure 1. Used in conjunction, both measures offer a quantitative evaluation of the degree of policies enforced by Brazilian state governments, as well as their effectiveness in reducing the circulation of people. The SMRI peaks in parallel to the enforcement of more strict government measures, a pattern which is observable both in capitals and inland cities (Supplementary Figure 1). Our results showed that, once the SMRI reached its maximum, it was followed by a decreasing trend even with the maintenance of measures by state governments.

With respect to the breadth and intervention period of governmental measures, our results led to the identification of three stringency index patterns: 1) Increase-and-decrease (ID), where the stringency index increases initially, but is followed by the lifting of measures leading to its reduction (such as Santa Catarina in Figure 4a); 2) Increase-and-steady (IS), where stringency measures reach a peak that remains constant over time (depicted by São Paulo in Figure 4b); 3) Increase-and-increase (II), where the stringency index increases successively, probably a mechanism to cope with the accelerated growth of the epidemic in some regions (illustrated by Amapá in Figure 4c). Five states, all located in the North (AC, AP) and Northeast (BA, CE, PE), followed the II pattern, while seven states, distributed throughout the Midwest (GO, MT), South (PR, RS, SC), Southeast (ES) and North (RO) regions conform to the ID pattern. The state of Tocantins is an exception to this general trend, displaying a mixed behavior in which the intensity of measures peaked on March 21, then decreased by 47.2% beginning on April 13 only to be further increased on May 15 (Table 1 and Supplementary Figure 1). The remaining 14 states (AL, AM, DF, MA, MG, MS, PA, PB, PI, RJ, RN, RR, SE and SP), distributed in all regions, followed the IS pattern. In addition, our results indicated that the reduction of the SMRI was smaller in states that followed both IS and II patterns (median reduction of -7.55% and -5.88%, respectively), compared to states that relaxed their measures according to the ID pattern (median reduction of -10.71%) (Figure 4d).

Of note, even in states that promoted relaxation of policies, such as those that followed an ID pattern, a fraction of the population close to 40% still remained in isolation (Supplementary Figure 1).

Varying transmission rates of SARS-CoV-2 in Brazil

Lastly, we sought to comparatively evaluate the effects of governmental measures and population adherence to social distancing recommendations in the TR of SARS-CoV-2 in the Brazilian states.

Table 2 shows the variation of the TR obtained by the SEIR model, the dates when TR changes (β_0, β_1 and β_2 parameters) occurred, and the reproduction number $\mathcal{R}_0$ for each state, capital and inland cities. The majority of states presented a decrease of the TR, mainly determined by a decrease of the TR in their capitals, with the exceptions of Piauí and Tocantins, where capitals presented an increase of the TR. We also observed decreases in the TR throughout inland cities, with the exception of the state of Acre. Mato Grosso do Sul presenting a decrease of the TR in the capital, meanwhile the state and inland cities showed increases. Three out of the 27 states (DF, MT and PR), as well as the inland cities of Bahia, exhibited a different behavior, in which a single change on TR (leading to β_0, β_1 parameters) was

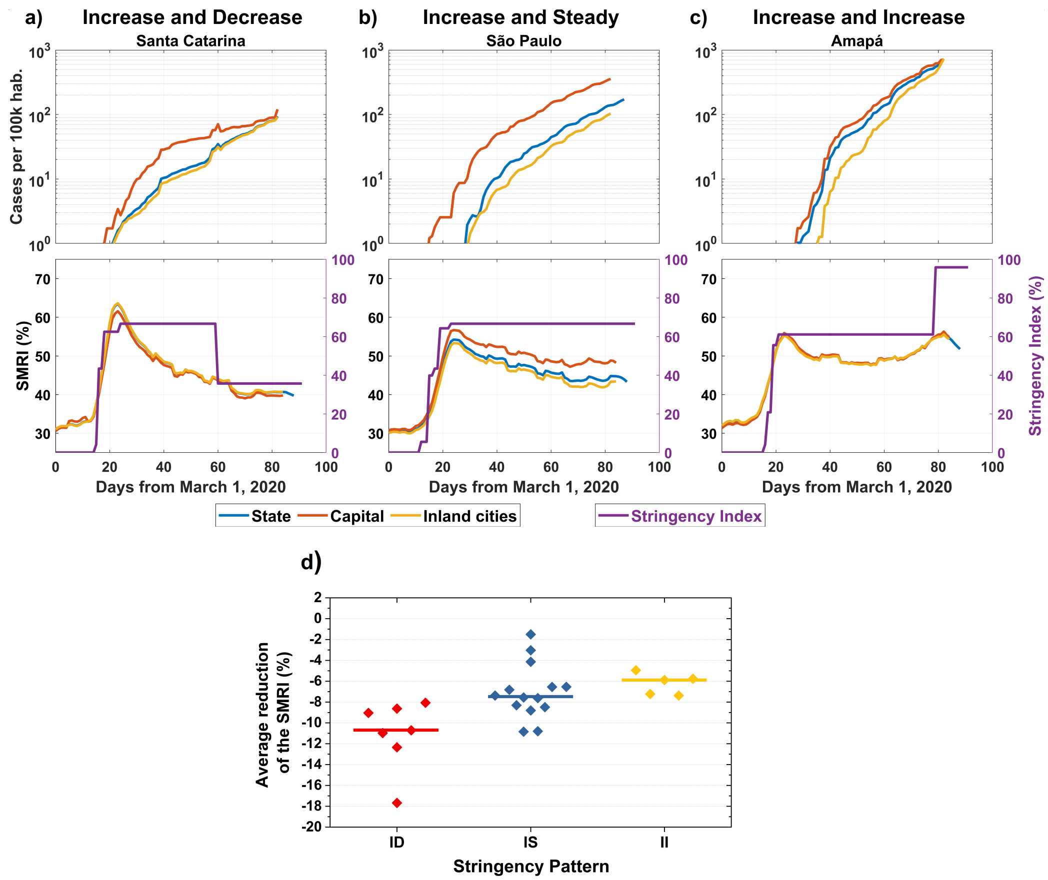

Figure 4: Illustrative examples of a general pattern observed for the behavior of stringency measures over time in Brazil. Upper panels show COVID-19 incidence and bottom panels exhibit the social mobility reduction and the stringency indexes over time for a) Santa Catarina (increase-and-decrease, ID), b) São Paulo (increase-and-steady, IS) and c) Amapá (increase-and-increase, II). The social mobility index is considered separately for capitals, inland cities and the whole state. Plots for the remaining Brazilian states are shown in Supplementary Figure 1. The average reduction in the SMRI according to the stringency pattern for all states (except Tocantins) is shown in panel d. For each category, the median is shown as a solid horizontal bar.

insufficient to accurately fit the model predictions to the observed data. For these regions, we incorporated a third TR parameter over time (β_2), which effectively leads to two events of TR change and possibly represents an underlying feature of the dynamics of SARS-CoV-2 spread in these places. Still in these cases, we see that all regions presented an initial decrease on the TR followed by a small increase.

In 74% of the states (20/27), the changes on the TR in capital and inland cities occurred at the same time or within a 10-days window. In the remaining 36% of the states (AM, AP, TO, CE, MA, PI, RJ), this change was only noticeable 11 days or more after TR changes in capital and inland cities. In addition, although the capitals can be considered the initial route of COVID-19 spread, the results presented in Table 2 reveal that the TR of inland cities is on average 10% higher than that of capitals.

In the North region of Brazil, on the first half of April, Amapá and Amazonas were the states with the highest decline of the TR and also the highest reproduction number, with decreases of 178% and 101% on the TR and $\mathcal{R}_0$ values of 4.23 and 3.25, respectively. Consecutively, Pará and Rondônia presented 37% and 62% drop in the TR on mid-April, with $\mathcal{R}_0$ of 2.30 and 2.29 respectively. The remaining states (TO, AC and RR) had changes on the TR occurring from May 1 to May 13 and with $\mathcal{R}_0$'s between 1.6 and 2.3, with Acre having the lowest variation on the TR of about 9%, mostly affected by the increase of the TR that occurred in inland cities.

In the Northeast region, Ceará and Rio Grande do Norte were the first to show a decrease on the TR of about 319% and 203% respectively, by the end of March. They were the states with the highest basic reproduction number compared to all states in the country, with values of 6.4 and 4.4 respectively. Followed by that, on the first half of April, Maranhão and Bahia had 68% and 61% of decrease on the TR, with $\mathcal{R}_0$'s values of 2.6 and 2.4 respectively. From April 17 to April 30, we observed decreases of the TR in the states of AL, PE, PB and PI ranging from 20% to 92%, with basic reproduction numbers varying from 2.0 to 2.5. Sergipe was the last state in the region to show a reduction on the rate (of around 56%) on May 13 and with $\mathcal{R}_0$ of 2.1.

In the Midwest region, Mato Grosso presented the highest decrease on the TR of 83% on April 6, while Mato Grosso do Sul presented an increase on the TR of 1.6% on April 9. DF and GO exhibited decreases on the transmission on the second half of April, of respectively, 31% and 27%. The reproductive number of all states in the region varied between 1.2 and 2.4, the lowest of the country. The states in South and Southeast regions had changes on the TR early compared to the states of the other regions, varying between March 20 and April 14. The decrease on the TR ranged from 37% to 195%, with MG being the one with highest decrease and PR the one with the lowest reduction. The basic reproductive number varied between 2.05 in PR and 3.96 in SC.

In an interactive, supplementary plot (available at `https://bit.ly/SuppPlotBrazilTR`) we present the fitting of the data to the SEIR model produced in this work, for both capitals and inland cities of each state. We highlight, in each plot, as vertical dashed red lines, the dates of transition from β_0 to β_1 (and β_1 to β_2, when applicable). The blue dashed and full lines represent the evolution of the epidemic with a fixed transmission rate β_0 and with both β_0 and β_1 (where β_2 is included when suitable), respectively. The effective reproductive number is also presented for each state, capital and inland cities. The black line represents the $\mathcal{R}_t$ calculated with reported number of new cases; the blue dashed line represents the $\mathcal{R}_t$ calculated with the new number of simulated cases obtained from the model. The variation of the TR highlights the variations of the trends of the effective reproductive number. These results show that, in spite of the reduction of the TR in all states, in none of the regions the values of $\mathcal{R}_t$ fell below one.

4. Discussion

In this work we evaluated the effects of non-pharmaceutical interventions and social mobility reduction patterns on the spread dynamics of SARS-CoV-2 throughout the 27 Brazilian states, by employing an underlying SEIR model to estimate TRs. Our results show that the measures adopted, combined with the population adherence to restrict circulation, contributed to the decrease of the TR in almost all states, an effect that was perceived in both capitals and inland cities. However, in spite of the continued maintenance of governmental restrictions in most regions, population adherence to isolation recommendations gradually decreased over time, even with the expansion of cases throughout the country. This might have reflected in the $\mathcal{R}(t)$ values, which we observed to have decreased in all states, but still insufficiently to consider SARS-CoV-2 transmission controlled in the country, since it remains above 1 for all Brazilian states. Thus, public cooperation constitutes a particularly important challenge for tackling COVID-19 in low- and middle-income countries.

Although the entry of the virus in Brazil probably occurred as a result of multiple introductions by returning international travelers [17, 18, 19, 20], its subsequent spread has been accelerated by the domestic transportation flows. Our results point that states with historically large transportation fluxes with São Paulo, initial epicenter of COVID-19 in Brazil, were among the first to report cases. The fact that the majority of states did not adopt measures restricting passenger transportation, or did so in a very lax manner, reinforces this observation. In addition, no Brazilian state enforced strict lock-down measures as adopted by other countries. Such restrictive policies have shown to significantly decrease the number of cases, deaths, and viral transmission in other countries [21, 22]. On the other hand, the economical costs imposed by harsher interventions is even more burdensome to developing countries, where large economical segments rely on consumption and services, usually involving physical contact, such as informal workers, tourism, service and retail businesses.

Once the entry of the virus was confirmed within each state, the capitals were the most affected initially. Then, viral spread continued at different rates, with our results revealing that inland cities present increased TR compared to state capitals. This is of worry considering the large inequalities in the access to health services as well as their distribution in Brazil [23, 24], which tend to concentrate near state capitals. We also observed that downward changes on TRs occurred first in the capitals, followed by the remaining cities. These results corroborate the association between population flux and viral spread [25], and highlights the major role of state capitals to its subsequent diffusion towards smaller, inland cities. Capitals also tend to centralize international airports, ports, population density and industries. Accordingly, the TR observed in capitals should also affect that of inland cities, as suggested by a meta-population compartmental model [26], but the possibility of a second-wave of COVID-19 in these smaller cities, particularly with the lifting of measures, should not be ruled out.

We identified common trends in the stringency index that allowed the disclosure of three patterns, with the majority of states conforming to an increase-and-steady pattern, in which the set of governmental policies adopted remained unaltered over time. States that enforced and maintained mitigation measures were likely to observe a less pronounced relaxation of stay-at-home advises by their population, as measured by the SMRI. These results suggest the intimate relationship between the magnitude of governmental measures and the population adherence to such measures, particularly since higher values of stringency implicate in decreased opportunities of public activities. However, individuals throughout all states, in both capitals and inland cities, still reduced their adherence to social isolation in the course of time. The politicization of COVID-19 in Brazil [27] could have had an impact on people's behavior and compliance with sanitary recommendations, particularly when individuals downplay the health risks imposed by SARS-

CoV-2, as has been suggested for a segment of the United States population [28].

We also observed that even in states that conformed to an increase-and-decrease stringency index pattern, at least a part of the population still maintained adherence to isolation. More studies are warranted to evaluate if this trend associates with specific age-groups, such as the elderly, employment status, such as individuals that have the possibility to continue working from home, education level or perception of risks around COVID-19.

Our work has some limitations. First, in order to estimate TRs (and changes thereof) we relied upon a generalized form of the SEIR model which explicitly considers asymptomatic transmission. Thus, albeit the estimates of model parameters (or their respective search intervals) were retrieved from the literature for other countries, they could be different from the reality of the ongoing epidemic in Brazil. However, while the true extent of SARS-CoV-2 transmission by asymptomatic and pre-symptomatic individuals is still debated, current reports conclude that it is an important route of transmission [8, 29, 30]. Also, there are delays on the notification system that may be of different magnitudes throughout the regions in Brazil. This limitation may impact on the perception of the implemented measures as well as compromise the planning of new ones. We used mobility data from mobile phones as proxies of social isolation as measured by the SMRI. In particular, the sample of devices monitored using this technology cannot be considered a representative population sample, as state/cities with superior economic status will probably exhibit increased technology adoption by their populations, leading to better accuracy of the mobility patterns in these regions. This is in contrast to rural areas, for instance, where mobile phone usage is limited [31]. However, considering the general widespread use of mobile phones in the country (with estimates that 60% of adults report owning a smartphone [32]), the general trends observed in our work should not be drastically altered by more accurate measurements of Social mobility reduction.

In sum, our results point to the importance of timely deployment of interventions in curbing the first-wave of the COVID-19 epidemic. Yet, population adherence represents a crucial factor for the success of this effort and represents a major challenge in low- and middle-income countries.

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Authors' contributions

DCPJ, MSR and JFO designed the model and implemented the computational framework, with theoretical input from PIPR, RFSA and STRP. DCPJ, JFO, MSS, PIPR and VAFS performed data analysis. LLC, NBdS, IHS, FACP, STRP, RFSA, PIPR and JFO interpreted the results and worked on the manuscript. All authors provided critical feedback and approved the final manuscript text.

Additional information

Supplementary Table 1. Classification of governmental measures implemented in Brazilian states in response to the COVID-19 spread.

Supplementary Table 2. Brazilian government decrees and resolutions.

Supplementary Table 3. Key epidemiological parameters used in the SEIR model, with their respective value (when fixed) or the search intervals used for parameter estimations.

Supplementary Figure 1. COVID-19 incidence per state, their capitals and remaining inland cities (upper plots). The bottom subplots exhibit the Social mobility reduction index, considered separately for capitals, inland cities and the whole state, and the stringency index, for the state measures, over time.

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Table 2: SARS-CoV-2 transmission landscape throughout 27 Brazilian states.

State	Region	Date of first case	Date of community transmission	β_0	β_1	Date of the first change	β_2	Date of the second change	R_0	SIP
Acre	State	20/03/17	20/04/11	0.95	0.87	20/05/01	-	-	1.70	II
	Capital	-	-	0.62	0.48	20/05/01	-	-	1.78	
	Inland cities	-	-	0.52	1.22	20/04/22	-	-	0.92	
Amazonas	State	20/03/13	20/03/28	1.42	0.71	20/04/04	-	-	3.25	IS
	Capital	-	-	1.45	0.72	20/04/04	-	-	2.89	
	Inland cities	-	-	1.78	1.19	20/05/01	-	-	2.32	
Amapá	State	20/03/20	20/03/20	1.16	0.43	20/04/09	-	-	4.23	II
	Capital	-	-	1.03	0.37	20/04/09	-	-	4.11	
	Inland cities	-	-	1.01	0.83	20/05/01	-	-	1.86	
Pará	State	20/03/18	20/03/30	0.91	0.66	20/04/22	-	-	2.30	IS
	Capital	-	-	1.18	0.72	20/04/17	-	-	2.56	
	Inland cities	-	-	0.56	0.43	20/04/27	-	-	2.35	
Rondônia	State	20/03/20	20/03/31	0.63	0.39	20/04/26	-	-	2.29	ID
	Capital	-	-	0.80	0.50	20/05/01	-	-	2.10	
	Inland cities	-	-	1.53	0.81	20/04/20	-	-	2.63	
Roraima	State	20/03/21	20/05/02	0.94	0.56	20/05/09	-	-	1.60	IS
	Capital	-	-	1.85	1.07	20/05/08	-	-	1.52	
	Inland cities	-	-	1.66	0.88	20/05/11	-	-	1.82	
Tocantins	State	20/03/18	20/04/24	0.89	0.68	20/05/13	-	-	2.06	-
	Capital	-	-	0.96	1.13	20/04/24	-	-	1.42	
	Inland cities	-	-	0.87	0.53	20/05/09	-	-	2.61	
Alagoas	State	20/03/08	20/03/28	0.86	0.48	20/04/29	-	-	2.40	IS
	Capital	-	-	1.45	0.66	20/04/29	-	-	2.33	
	Inland cities	-	-	1.23	1.03	20/04/30	-	-	2.15	
Bahia	State	20/03/06	20/03/26	1.40	0.87	20/04/01	-	-	2.37	II
	Capital	-	-	1.39	1.04	20/04/19	-	-	1.70	
	Inland cities	-	-	0.42	0.34	20/04/11	0.56	20/05/11	1.73	
Ceará	State	20/03/16	20/03/20	1.76	0.42	20/03/24	-	-	6.35	II
	Capital	-	-	1.90	0.49	20/03/26	-	-	5.42	
	Inland cities	-	-	1.15	0.92	20/04/19	-	-	2.18	
Maranhão	State	20/03/20	20/03/30	1.46	0.87	20/04/14	-	-	2.55	IS
	Capital	-	-	2.00	0.98	20/04/18	-	-	2.32	
	Inland cities	-	-	1.37	1.10	20/05/01	-	-	2.21	
Paraíba	State	20/03/18	20/04/05	1.29	1.07	20/04/28	-	-	1.97	IS
	Capital	-	-	0.88	0.57	20/04/30	-	-	1.88	
	Inland cities	-	-	0.72	0.63	20/04/30	-	-	2.27	
Pernambuco	State	20/03/12	20/03/17	1.31	0.68	20/04/17	-	-	2.51	II
	Capital	-	-	0.74	0.40	20/04/18	-	-	2.40	
	Inland cities	-	-	1.17	0.56	20/04/16	-	-	2.95	
Piauí	State	20/03/19	20/03/20	1.15	0.79	20/04/30	-	-	1.96	IS
	Capital	-	-	0.65	1.74	20/03/31	-	-	0.70	
	Inland cities	-	-	0.98	0.60	20/04/26	-	-	2.61	
Sergipe	State	20/03/14	20/03/20	0.68	0.44	20/05/13	-	-	2.07	IS
	Capital	-	-	0.72	0.39	20/05/12	-	-	2.07	
	Inland cities	-	-	0.89	0.73	20/05/03	-	-	2.33	
Rio Grande do Norte	State	20/03/12	20/03/20	1.08	0.35	20/03/28	-	-	4.40	IS
	Capital	-	-	1.09	0.49	20/03/31	-	-	3.08	
	Inland cities	-	-	1.21	0.64	20/03/28	-	-	2.65	
Goiás	State	20/03/12	20/03/15	1.28	1.01	20/04/10	-	-	1.58	ID
	Capital	-	-	0.69	0.49	20/04/11	-	-	1.72	
	Inland cities	-	-	0.80	0.68	20/04/08	-	-	**1.62**	
Distrito Federal	-	20/03/07	20/03/27	0.80	0.27	20/03/30	0.55	20/04/17	2.40	IS
Mato Grosso	State	20/03/20	20/03/31	1.14	0.62	20/04/06	1.01	20/04/27	1.93	ID
	Capital	-	-	0.53	0.24	20/04/05	0.49	20/05/05	2.13	
	Inland cities	-	-	0.79	0.42	20/04/07	0.67	20/04/24	2.07	
Mato Grosso do Sul	State	20/03/14	20/04/04	0.95	0.97	20/04/09	-	-	1.17	IS
	Capital	-	-	0.78	0.70	20/04/26	-	-	1.00	
	Inland cities	-	-	0.90	1.28	20/05/01	-	-	**1.18**	
Espírito Santo	State	20/03/06	20/03/30	1.76	1.02	20/04/14	-	-	2.16	ID
	Capital	-	-	1.07	0.83	20/04/17	-	-	1.62	
	Inland cities	-	-	1.63	1.02	20/04/16	-	-	1.99	
Minas Gerais	State	20/03/08	20/03/17	1.38	0.51	20/03/24	-	-	3.55	IS
	Capital	-	-	2.00	0.31	20/03/20	-	-	7.14	
	Inland cities	-	-	1.11	0.63	20/03/31	-	-	2.39	
Rio de Janeiro	State	20/03/05	20/03/13	1.59	0.83	20/04/01	-	-	2.57	IS
	Capital	-	-	1.43	0.52	20/03/26	-	-	3.73	
	Inland cities	-	-	0.74	0.39	20/04/07	-	-	**2.80**	
São Paulo	State	20/02/26	20/03/12	0.98	0.44	20/04/01	-	-	2.96	IS
	Capital	-	-	0.78	0.34	20/03/31	-	-	2.9	
	Inland cities	-	-	1.17	0.48	20/04/04	-	-	3.37	
Paraná	State	20/03/12	20/04/09	0.70	0.15	20/04/09	0.44	20/04/20	2.05	ID
	Capital	-	-	1.07	0.36	20/04/10	0.79	20/04/26	1.61	
	Inland cities	-	-	1.07	0.51	20/04/09	0.91	20/05/06	1.95	
Rio Grande do Sul	State	20/03/10	20/03/20	1.33	0.50	20/03/20	-	-	3.55	ID
	Capital	-	-	1.36	0.33	20/03/26	-	-	3.34	
	Inland cities	-	-	1.06	0.59	20/03/20	-	-	2.66	
Santa Catarina	State	20/03/12	20/03/27	1.59	0.54	20/03/24	-	-	3.96	ID
	Capital	-	-	1.40	0.58	20/04/02	-	-	2.28	
	Inland cities	-	-	0.97	0.40	20/03/23	-	-	3.39	

SIP, stringency index pattern; ID, increase-and-decrease; IS, increase-and-steady; II, increase-and-increase.