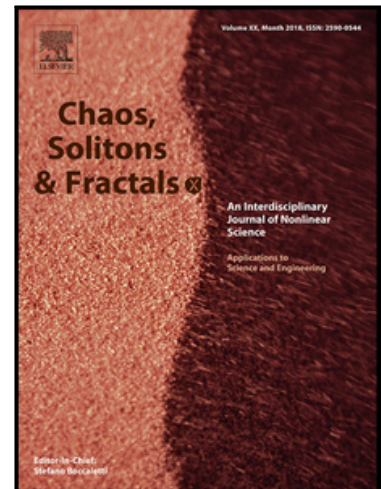


Journal Pre-proof

A data-drive model for COVID-19 pandemic – Evolution of the attack rate and prognosis for Brazil

T.M.Rocha Filho, M.A. Moret, C.C. Chow, J.C. Phillips,
A.J.A. Cordeiro, F.A. Scorza, A.-C.G. Almeida, J.F.F. Mendes

PII: S0960-0779(21)00713-X
DOI: <https://doi.org/10.1016/j.chaos.2021.111359>
Reference: CHAOS 111359



To appear in: *Chaos, Solitons and Fractals*

Received date: 27 July 2021
Accepted date: 11 August 2021

Please cite this article as: T.M.Rocha Filho, M.A. Moret, C.C. Chow, J.C. Phillips, A.J.A. Cordeiro, F.A. Scorza, A.-C.G. Almeida, J.F.F. Mendes, A data-drive model for COVID-19 pandemic – Evolution of the attack rate and prognosis for Brazil, *Chaos, Solitons and Fractals* (2021), doi: <https://doi.org/10.1016/j.chaos.2021.111359>

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2021 Published by Elsevier Ltd.

Highlights:

1. we introduce a compartmental model SEIAHRV (Susceptible, Exposed, Infected, Asymptomatic, Hospitalized, Recovered, Vaccinated) with age structure for the spread of the SARAS-CoV virus
2. we use compartments for individuals vaccinated with one and two doses without vaccine failure and a compartment for vaccinated individual with vaccine failure
3. The model uses known epidemiological parameters and the time dependent probability p_c is obtained by fitting the model output to the series of deaths in each locality and reflects non-pharmaceutical interventions
4. We also estimate the attack rate, the total proportion of cases (symptomatic and asymptomatic) with respect to the total population, for all Brazilian states since the beginning of the COVID-19 pandemic

Journal Pre-proof

A data-drive model for COVID-19 pandemic – Evolution of the attack rate and prognosis for Brazil

T. M. Rocha Filho

*International Center for Condensed Matter Physics and Instituto de Física,
Universidade de Brasília, Brasília – BRAZIL.*

M. A. Moret

*Centro Universitário SENAI CIMATEC and
Universidade do Estado da Bahia, Salvador – Brazil*

C. C. Chow

Mathematical Biology, NIDDK, NIH, Bethesda, Md 20892 – USA

J. C. Phillips

Physics and Astronomy, Rutgers University, Piscataway, NJ 08854 – USA

A. J. A. Cordeiro

*Centro Universitário SENAI CIMATEC, Salvador and
Instituto Federal de Educação e Tecnologia da Bahia, Feira de Santana – Brazil.*

F. A. Scorza

Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo – Brazil

A.-C. G. Almeida

Universidade Federal de São João del-Rei, São João del-Rei – Brazil

J. F. F. Mendes

Departamento de Física and I3N, Universidade de Aveiro, 3880 Aveiro – Portugal

Abstract

We introduce a compartmental model SEIAHRV (Susceptible, Exposed, Infected, Asymptomatic, Hospitalized, Recovered, Vaccinated) with age structure for the spread of the SARS-CoV virus. In order to model current different vaccines we use compartments for individuals vaccinated with one and two doses without vaccine failure and a compartment for vaccinated individual with vaccine failure. The model allows to consider any number of different vaccines with different efficacies and delays between doses. Contacts among age groups are modeled by a contact matrix and the contagion matrix is obtained from a probability of contagion p_c per contact. The model uses known epidemiological parameters and the time dependent probability p_c is obtained by fitting the model output to the series of deaths in each locality, and reflects non-pharmaceutical interventions. As a benchmark the output of the model is compared to two good quality serological surveys, and applied to study the evolution of the COVID-19 pandemic in the main Brazilian cities with a total population of more than one million. We also discuss with some detail the case of the city of Manaus which raised special attention due to a previous report of We also estimate the attack rate, the total proportion of cases (symptomatic and asymptomatic) with respect to the total population, for all Brazilian states since the beginning of the COVID-19 pandemic. We argue that the model present here is relevant to assessing present policies not only in Brazil but also in any place where good serological surveys are not available.

Keywords: Epidemiological model, non-linear ODE, SARS-CoV-2, COVID-19

1. Introduction

The present COVID-19 pandemic initiated in the end of 2019 in the city of Wuhan in China, and was first reported to the World Health Organization in January 2020 as an outbreak of pneumonia of undetermined origin. The etiologic agent was identified as the the new coronavirus SARS-CoV-2 [1]. The resulting disease caused until the present day more than four million deaths in the whole world, with a reported number of 190 million cases [2]. Waves of the pandemic occurred at different moments of time and in all countries, prompting mitigation measures, that were widely adopted, such as social distancing and mask wearing [3]. During the year of 2020 a few vaccines were developed and approved, with only a small number of countries having vaccinated a significant part of the population [4]. Since then an ongoing effort was taken to gain knowledge has been accumulated on how the virus act and how it spreads, with mathematical modeling one of the tools deployed to predict possible future outcomes [5].

The mathematical modeling of infections diseases has a long tradition starting from the seminal work by Kermack and McKendrick that introduced a SIR (Susceptible, Infectious, Recovered) model to estimate for the epidemic outbreak threshold [6]. Different approaches were developed afterwards to study many diseases, emphasizing different aspects of the epidemic evolution [7, 8, 9]. Since the beginning of the COVID-19 pandemic a substantial number of works were devoted at its modeling, ranging from SIR and SEIR mean-field models and variants [10] to agent-based models [11] and meta-population based models [12] (for reviews of different forecasting models used for COVID-19 see [13] and [14]). The main limitation relies in model calibration due to the lack of reliable data resulting from the emergency situation caused by a pandemic [15], mainly during its initial period, that must be used with care [16]. Despite that, models have been a valuable planning tool in predicting possible future scenarios [5].

We present here a SEIARHV (Susceptible, Exposed, Infected symptomatic, Asymptomatic, Recovered, Hospitalized, Vaccinated) model, with age structure, that uses known epidemiological parameters to model the evolution of the COVID-19 pandemic by fitting the time dependent transmission rate using real data available from official sources. We implement the model for the main Brazilian cities (municipalities) and all its 27 states.

Since the beginning of 2021 Brazil has received great attention due to a strong second wave, resulting in overcrowded hospitals, a lack of basic medical supplies for a proper treatment in ICUs, and even people dying asphyxiated with lack of oxygen, as occurred in the city of Manaus [17]. The lack of a centralized coordinated effort to mitigate the pandemic allowed for a rapid circulation of the virus in a country with the sixth largest population in the world, resulting in one more hotbed for variants. After more than a year of pandemic some variants of concern have emerged. The variants of concern currently are [18]: α (B.1.1.7 from the United Kingdom), β (B.1.351 from South Africa), γ (P1 from Brazil), ϵ (B.1.427-9 from the US), and more recently the δ variant, from India, which is now prevalent in India, the UK and other localities. Those variants are more transmissible by a factor from 1.5 to 2.5 than the original strain, and possibly able to reinfect individuals with a former infection by the original variant [19]. This makes the analysis and predictions of possible outcomes even more difficult, as base epidemiological parameters change over time.

The official figures for the total number of cases, and also for the number of deaths although to a lesser extent, are underestimated all over the world [20, 21], and also in Brazil [22] due to a very small number of tests per million inhabitants (253 131), at the 120-th position among all countries [23]. Due to the large proportion of non-identified cases we fit our model using the time series for deaths in each locality, as it is more reliable and representative of the situation of the pandemic at each moment of time. On the other hand, a realistic estimate of the number of people already infected by the virus is of great relevance for implementing and evaluating mitigation policies, such as determining the degree of social distancing and which sectors to close or reopen, as well as for predicting possible outcomes of the pandemic in each locality. For that purpose serological surveys for detecting SARS-CoV-2 antibodies were implemented in many countries worldwide [24]. Among good quality surveys there are two in Brazil: an estimate of the attack rate (proportion of total real number of symptomatic and asymptomatic cases in the population) in the

Email address: marciano@fis.unb.br (T. M. Rocha Filho)

state of Rio Grande do Sul, based on a serological survey in ten municipalities [25], and the SoroEpi MSP in the city (municipality) of Sfo Paulo [26]. The former covered a time span from from April, 1 to May, 11 2020, while the survey in Sfo Paulo reported five surveys from April 2020 to January 2021. We use these two surveys as benchmarks for our model.

The paper is structured as follows: The model, all the required parameters, and how it fitted from data, are presented in Sec. 2. Section 3 contains the benchmark analysis with the serological surveys and the results for the attack rate (proportion of already infected individuals) for all the Brazilian states and cities with a population of over a million inhabitants. We discuss with a greater length the city of Manaus where the pandemic was particularly intense, and present some prognostics for the evolution of the pandemic with the arrival of the δ variant. We close the paper with some discussion and concluding remarks in Sec. 4.

2. Model

The SEIAHRV model (Susceptible, Exposed, Infected, Asymptomatic, Hospitalized Recovered and Vaccinated), is an extension of the model used in [27], with compartments for individuals vaccinated with one and two doses, $V^{(1,k)}$ and $V^{(2,k)}$ for different vaccines, each with a known efficacy with one and two doses, respectively, and a time delay between the two, each vaccine type denote by the superscript, without primary vaccination failure. A compartment $U^{(k)}$ is also introduced for individuals with primary vaccination failure U . The model assumes homogeneous mixing and M age groups with different number of contacts between each group. The variables are given as proportion with respect to the total population at the initial time. The decomposition of the compartments into age groups enables to incorporate the estimated contact structure in a given population, represented here by a contact matrix $C_{i,j}$ with the average number of contacts per day of a single individual of age group j with any individual of age group i . Up to the authors knowledge there is no estimation for the contact matrix in Brazil, so we use the results by Mossong et al. [28] for eight European countries, taking the average of the contact matrix for all countries, and adapting the result to the age distribution for each cities and state considered here. This is a reasonable assumption due to cultural similarities between Europe and Brazil. The age groups represented in the model are: 0 to 9, 10 to 19, 20 to 29, 30 to 39, 40 to 49, 50 to 59, 60 to 69, 70 to 79 and 80 years of age and more. The contact matrix obtained in this way for Braslia (capital of Brazil) is shown in Fig. 3.

Required epidemiological parameters are given in the literature in Refs. [29, 30, 31, 32, 33, 34] and shown in Tables 1 and 2. The transfer diagram for the model is shown in Figs. 1 and 2, and the corresponding non-linear differential equations with time-delay are given by:

$$\begin{aligned} \frac{dS_i}{dt} &= - \left[\lambda_i + \mu' + \nu_i + \frac{1}{p_v} \sum_{k=1}^K d_1^{(i,k)} \right] S_i + \kappa' \delta_{i,1} + \nu_{i-1} S_{i-1}, \\ \frac{dE_i}{dt} &= \lambda_i S_i + \lambda_i \sum_{k=1}^K U_i^{(k)} - \left[\sigma + \mu' + \nu_i + \frac{1}{p_v} \sum_{k=1}^K d_1^{(i,k)} e_1^{(k)} \right] E_i + \nu_{i-1} E_{i-1}, \\ \frac{dI_i}{dt} &= (1 - \chi) \sigma E_i - [\gamma + \mu' + \nu_i] I_i + \nu_{i-1} I_{i-1} - (1 - \chi) \zeta_i \sigma E_i(t - \tau_1), \\ \frac{dA_i}{dt} &= \chi \sigma E_i - \left[\gamma + \mu' + \nu_i + \frac{1}{p_v} \sum_{k=1}^K d_1^{(i,k)} e_1^{(k)} \right] A_i + \nu_{i-1} A_{i-1}, \\ \frac{dH_i}{dt} &= - [\psi + \mu' + \nu_i] H_i \\ &\quad + (1 - \chi) \zeta_i \sigma E_i(t - \tau_1) - (1 - \chi) \theta_i \zeta_i \sigma E_i(t - \tau_2) + \nu_{i-1} H_{i-1}, \\ \frac{dR_i}{dt} &= \gamma I_i + \gamma A_i + \psi H_i - \left[\mu' + \nu_i + \frac{1}{p_v} \sum_{k=1}^K d_1^{(i,k)} e_1^{(k)} \right] R_i + \nu_{i-1} R_{i-1}, \\ \frac{dV_i^{(1,k)}}{dt} &= - [\mu' + \nu_i] V_i^{(1,k)} + \nu_{i-1} V_{i-1}^{(1,k)} + e_1^{(k)} d_1^{(i,k)} - e_1^{(k)} d_2^{(i,k)}, \end{aligned}$$

$$\begin{aligned}
 \frac{dV_i^{(2,k)}}{dt} &= -[\mu' + \nu_i]V_i^{(2,k)} + \nu_{i-1}V_{i-1}^{(2,k)} + e_2^{(k)}d_2^{(i,k)}, \\
 \frac{dU_i^{(k)}}{dt} &= -[\lambda_i + \mu' + \nu_i]U_i^{(k)} + \nu_{i-1}U_{i-1}^{(k)} \\
 &\quad + \frac{(1 - e_1^{(k)})d_1^{(i,k)}S_i}{p_v} - (e_2^{(k)} - e_1^{(k)})d_2^{(i,k)}, \\
 p_v &= S_i + E_i + A_i + R_i,
 \end{aligned} \tag{1}$$

where all variables are calculated at time t except where explicitly indicated. The time delay is due to the average time between first symptom and hospitalization and first symptom and death. In Eq. (1) $d_1^{(i,k)}$ and $d_2^{(i,k)}$ are the number of individual vaccinated per unit of time for the first and second dose, respectively, for the age group i and vaccine type k , $e_1^{(k)}$ and $e_2^{(k)}$ the efficacy of vaccine of type k with one and two doses, respectively, $k = 1, \dots, K$, with K the number of different vaccines. In order to consider the time for a dose to reach full efficacy we assume a linear growth of the protection and suppose the vaccine is given at half this time interval. We also define $\mu' \equiv \mu N/N_0$ and $\kappa' = \kappa N/N_0$, with N_0 , N , κ and μ the initial population, current population, birth and natural mortality rates, respectively, with the mortality rate distributed homogeneously through all age groups. The aging rate from the i -th to the $(i+1)$ -th age group is denoted by ν_i and given by the inverse of the time span of the i -th age group, with $\nu_0 = 0$. The force of infection is given by

$$\lambda_i = \sum_{j=1}^M \beta_{i,j} \frac{I_j + \xi A_j}{n_i}, \tag{2}$$

with

$$\beta_{i,j} = p_c C_{i,j}, \tag{3}$$

is the infection rate matrix, with n_i the proportion of the population in age group i and ξ the infectiousness of an asymptomatic individual with respect to a symptomatic one, p_c the contagion probability per single contact, assumed to be age independent.

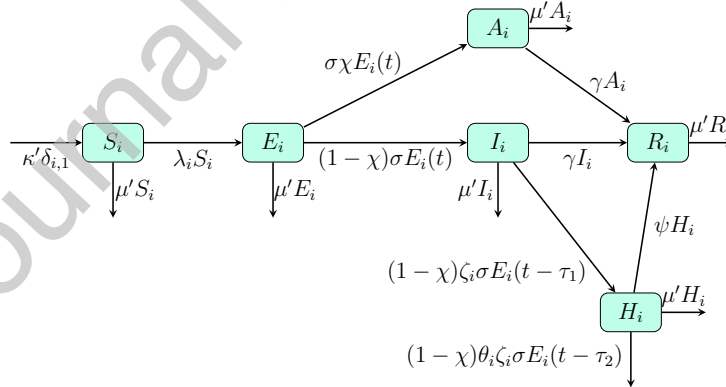


Figure 1: Transfer diagram for the SEIAHRV epidemiological model.

The knowledge of the Infection Fatality Ratio (IFR) $L_i^{(0)}$ according to age-group is central in our approach. We use the values obtained by Linton et al. (see Table 2) from a statistical analysis of data from and outside Wuhan, China up to January, 31 2020 [31]. It is important to notice that this analysis does not consider the proportion of asymptomatic cases and therefore the fatality is relative only to the symptomatic cases, as implemented in our model. An estimate of $\chi = 17.9\%$ for the proportion of true asymptomatic cases was obtained from the follow up of cases on the Diamond

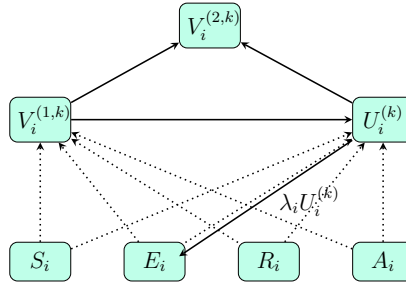


Figure 2: Transfer diagram for the vaccination component of the model in Fig. 1. Dotted lines indicate a flow between different compartments due to vaccination, according to the effectiveness of each vaccine type, with one and two doses.

Parameter	Definition	Value [Ref]
ψ	Recovery rate from hospitalization	$1/17.5 \text{ days}^{-1}$ [29, 30]
σ	Inverse of incubation time	$1/5.0 \text{ days}^{-1}$ [31]
γ	Recovery rate for non hospitalized individuals	$1/3.69 \text{ days}^{-1}$ [32]
θ_i	Fatality rate among hospitalized individuals (see Table 2)	$L_i^{(0)}/\zeta_i$
τ_1	Median time from first symptoms to hospitalization	3.3 days [31]
τ_2	Average time from first symptoms to death	16.8 days [29]
χ	Proportion of asymptomatic cases	17.9% [33]
ξ	Contagiousness of asymptomatic with respect to symptomatic individuals	55% [32]
κ	Average birth rate in Brazil	1.416% [34]
μ	Average natural mortality rate in Brazil	0.608% [34]

Table 1: Epidemiological parameters required by the SEIAHRV model.

Princess cruise ship, as reported in [33]. The passengers were kept quarantined on board of the ship, which allowed a fully controlled groups, which resulted in a more realistic estimate for χ .

As discussed in the introduction, the time series of total deaths reported in each locality is a more reliable data than the number of cases [20, 21, 22], and therefore is better suited for determining the (time dependent) probability of contagion p_c . Different functional forms are possible, and we use here a piece-wise function, with constant values in 14 days intervals and varying among different intervals. These values are determined by minimizing the square error function:

$$\mathcal{E} = \sqrt{\frac{1}{N_{\text{data}}} \sum_{i=1}^{N_{\text{data}}} [D_i^{(m)} - D_i^{(r)}]^2}, \quad (4)$$

where N_{data} is the number of data points to fit, $D_i^{(r)}$ and $D_i^{(m)}$ are the real and model values for the cumulative number of deaths, respectively. The fitted parameters are the values of p_c in each interval and the number of infectious individuals in the older age group at the initial time (which age group represents the seed becomes irrelevant after a few generations). The minimization process is performed using a simplex algorithm with adaptative parameters [35]. The time varying contagion probability is a result of changes in behavior, social distancing, and other mitigation policies.

All COVID-19 data for each municipality in Brazil is publicly available at the Brazilian Health Ministry COVID-

Age group	$L_i^{(0)}$	ζ_i
0 – 9	0.0%	0.00161%
10 – 19	0.2%	0.408%
20 – 29	0.2%	1.04%
30 – 39	0.2%	3.43%
40 – 49	0.4%	4.35%
50 – 59	1.3%	8.16%
60 – 69	3.6%	11.8%
70 – 79	8.0%	16.6%
≥ 80	14.8%	18.4%

Table 2: Infection fatality ratio (IFR) $L_i^{(0)}$ and hospitalization probability ζ_i for each age group as obtained by Linton et al. [31].

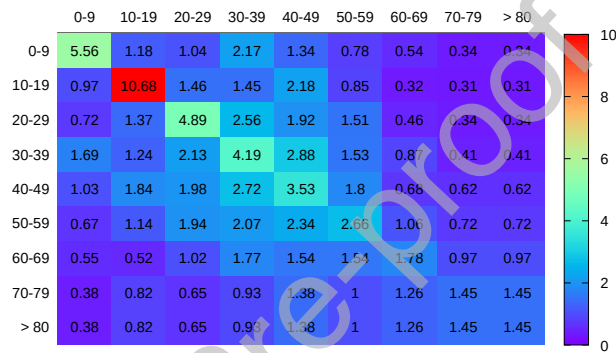


Figure 3: Estimated contact matrix for Brasilia (see supplementary material) with the average number of contacts of an individual of a given age group (column) with any individual of age group j (row).

19 website [36]. Estimates of population by age-group for 2020 are available at the Brazilian Institute for Geography and Statistics [37] and from DATASUS system of the Ministry of Health [34]. Detailed data on each vaccine shot applied in Basil is publicly available on the at Brazilian Health Ministry [38]. All the data considered here span the period from February, 26 2020 (first case in Brazil) up to July, 18 2021.

The fatality ratio in ICUs varied according to the region in Brazil, from 49% to 79% in the southeast and north regions, respectively [39]. The IFR values for each age group are then corrected accordingly, with the IFR in the Southeast region, the one with the best health infrastructure, used as reference and changing the values for other regions accordingly to the proportion of increase reported in [39].

Figure 4 shows the resulting fit for the four more populous Brazilian cities. Although the series for total deaths was used in the fitting, We display the results in the form deaths per week to facilitate the visualization of the quality of the fit. Once the model is fitted to the data, the attack rate is computed from the cumulative number of individual entering the exposed compartment E_i since the beginning of the pandemic.

For a comparison purpose, we also estimate the total number of cases from the average IFR obtained as:

$$L_{avg} = \frac{1}{N_{tot}} \sum_{i=1}^M N_i L_i^{(0)}, \quad (5)$$

where N_i is the population in age group i , N_{tot} the total population and $L_i(0)$ the IFR for age group i . The number of new cases $c(l)$ at day l can then be estimated by

$$c(l) = \frac{1}{L_{avg}} \sum_{m=14}^{22} D(L+M) F_d(m) \quad (6)$$

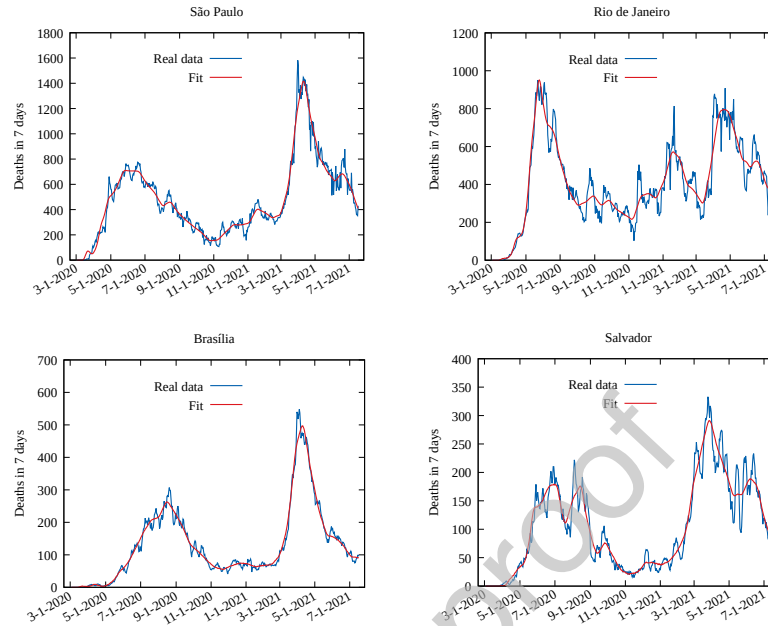


Figure 4: Number of deaths per week from real data and the fitted model data for the four more populous cities in Brazil: So Paulo, Rio de Janeiro, Braslia and Salvador.

where $F_d(l)$ is the distribution for the time between first symptom and death [32] and $d(l)$ the numbers of new deaths in day l .

3. Results

3.1. Comparing model results to serological surveys

As a benchmark for the present approach, we first compare the attack rate obtained from for our model to the surveys for So Paulo and Rio Grande do Sul. The results are shown in Fig. 5, alongside values obtained from official number of cases, the results from the serological surveys, and estimates obtained from the averaged IFR as given by Eq. (6). The serological survey for the Rio Grande do Sul state was obtained from data for the ten largest cities in the state, and is not necessarily representative of the whole state [25], but the attack rate obtained from our model is well within the confidence intervals. We note that the time span considered in this survey corresponds to the very beginning of the pandemic in the state, with a small number of cases and deaths, which resulted in greater estimated errors. In the case the SoroEpi MSP survey in city of So Paulo our model yields a good agreement.

The SEIAHRV model considers explicitly the social contact structure expressed by the contact matrix among individuals of different age groups and thus is a better representative of how the virus spreads than estimates obtained from the IFR average. The difference between the IFR estimate and the surveys is at least in part due to the proportion of asymptomatic individuals. Indeed, a direct computation from the data here presented implies that the result from Eq. (6) would imply a value for the proportion of asymptomatic individuals of $\chi = 23.9\%$, CI 95% (11.1 – 43.4), which is compatible with the result reported in [33] and considered in our model. Emerging variants may result in an increase in mortality, and thence an overestimation of the total number of cases [40, 41, 42]. This is not expected to play a major role in So Paulo up to January 2021, but most certainly the case latter, with the arrival of the γ and other variants. We now extend our analysis to the main cities and all the 27 states in Brazil.

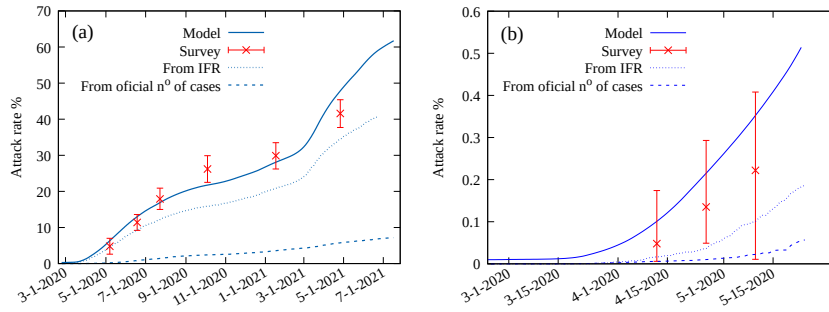


Figure 5: a) Attack rate from the total number of cases (symptomatic and non-symptomatic) as obtained from the epidemiological model (solid line), and data from the SoroEpi MSP serological survey [26]. The dotted line gives the total number of cases estimated from the average IFR using Eq. (S4), and the dashed line is obtained from the official number of cases as reported by the Brazilian Ministry of Health [36]. b) Attack rate for the state of Rio Grande do Sul from the epidemiological model and IFR estimates, official number of cases and serological survey [25].

3.2. Main Brazilian cities

We consider the Brazilian cities (municipalities) with a population of at least one million inhabitants (population between parenthesis): Macei (1018948), Curitiba (1933105), Manaus (2182763), Rio de Janeiro (6718903), Salvador (2872347), So Gonalo (1084839), Fortaleza (2669342), Porto Alegre (1483771), Goinia (1516113), Campinas (1204073), So Lus (1101884), Guarulhos (1379182), Belo Horizonte (2512070), So Paulo (12252023), Belm (1492745), Braslia (3055149) and Recife (1645727). The time evolution of the attack rate obtained for these cities is shown in Fig. 6. The case of the city of Manaus must be considered with more care, and is discussed separately.

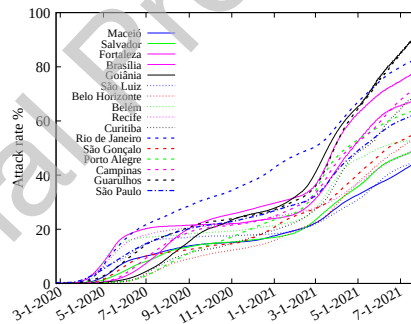


Figure 6: Model estimates for the attack rate for Brazilian cities with more than one million inhabitants (except Manaus).

The attack rate by July, 18 2021 in all cities in the interval from 35% to 90%, showing a great heterogeneity of the current situation. This is mainly due to different adherence to mitigation measures adopted locally. The cases with a very high attack rate, above 70%, must be explained as they are above the herd immunity predicted for SARS-CoV-2. The second wave of the pandemic was very intense in Brazil, with overcrowded hospitals in many localities, resulting in an increase of the IFR, which at its turn implies an overestimation of the total number of cases. Also after more than a year in the pandemic the natural immunity by a previous infection may start to wane, allowing for a substantial proportion of reinfections [43, 44]. Future research for gathering more data is important to clarify this point.

3.3. The case of Manaus

Results for Manaus and the Amazonas state are shown in Fig. 7, with the attack rate for the city of Manaus and for the Amazonas state in July, 18 2021 are 75.1% and 48.2%, respectively. This result must be interpreted with due care. The Amazonas state is the largest state in Brazil, with 1 559 146 Km^2 , 18% of the Brazilian territory, but only 2% of

its population. The state capital Manaus has 2 219 580 inhabitants, a little more than half the population of the state, and the second largest city has a population of only 101 thousand. Almost all medical facilities, including ICUs, are in Manaus. As a consequence most of the critical patients, with a higher probability of dying, are transferred there. This explains why 69% of the deaths in the state occurred in Manaus, while only 46% of the official number of cases were reported there. This flow of critical cases to Manaus was even more pronounced during the second wave, the deadliest observed in Brazil until now, which overwhelmed all medical facilities. Therefore, fitting the model with the time series of deaths in Manaus is unrealistic. The attack rate in the city is most probably closer to the one estimated for the whole Amazonas state. Such peculiarities do not occur, at least not in the same intensity, for the other cities considered here. The occurrence of the P1 variant in the Amazonas state could also explain a higher value of the attack rate due to possible reinfections, as claimed in [42], but not the asymmetry of the number of deaths compared to the total number of cases between Manaus and the rest of the state.

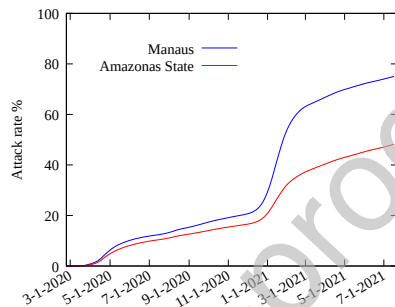


Figure 7: Model estimates for the attack rate for the Amazonas state and Manaus municipality.

A previous estimate by Bussi et al. [45], based on a survey of samples from blood donors, obtained an attack rate in Manaus of 76% in October, 1st 2020. Therefore the important second wave that occurred in January 2021 would imply a high proportion of reinfection among new cases, possibly caused by the more contagious P1 variant. Nevertheless this value for the attack rate is highly at variance with our finding of 25.9% for the whole state and 39.4% for the city of Manaus in January, 15 2021. This significant difference can be explained out by two facts: Bussi and collaborators considered a model for seroconversion with an exponential decay to estimate the expected real number of already infected individuals. Although the results obtained by Bussi et al. for So Paulo are close to those from the SoroEpi MSP survey, we note that small errors are exponentially increased, which could lead to large errors in the estimate, while the SoroEpi MSP survey relied on a blood test with negligible seroconversion during the time span considered. The second fact is that using samples from blood donors introduces a strong bias, which is even more important if one considers that blood donations in the state of Amazonas are only possible in Manaus, and that the family of hospitalized individuals are often asked to donate blood, and that it is a common practice for people from other Amazonas cities to register in the hospital using the address of a relative living in Manaus. As a consequence, many donors in Manaus have been in recent contact with hospitalized individuals from all over the state.

3.4. Brazilian states

We also obtain estimates for the attack rate in each Brazilian state by considering the time series for the cumulative number of deaths for the whole state. Population and COVID-19 data are obtained from the same sources. Results for the attack rate in intervals of four months starting in July, 1st 2020 are shown as heat maps in Fig. 8, where the great impact and rapid increases during the second wave starting by the end of 2020 is clearly visible, but with different intensities in each state.

3.5. Using the model for prognostics

In order to demonstrate how our model can be used to predict future outcomes for the pandemic, we show how to model an increase in the transmission probability p_c due to a more contagious variant. Our intent is not to provide an complete set of possible outcome for the pandemic, but to show how our model can be used to model the evolution

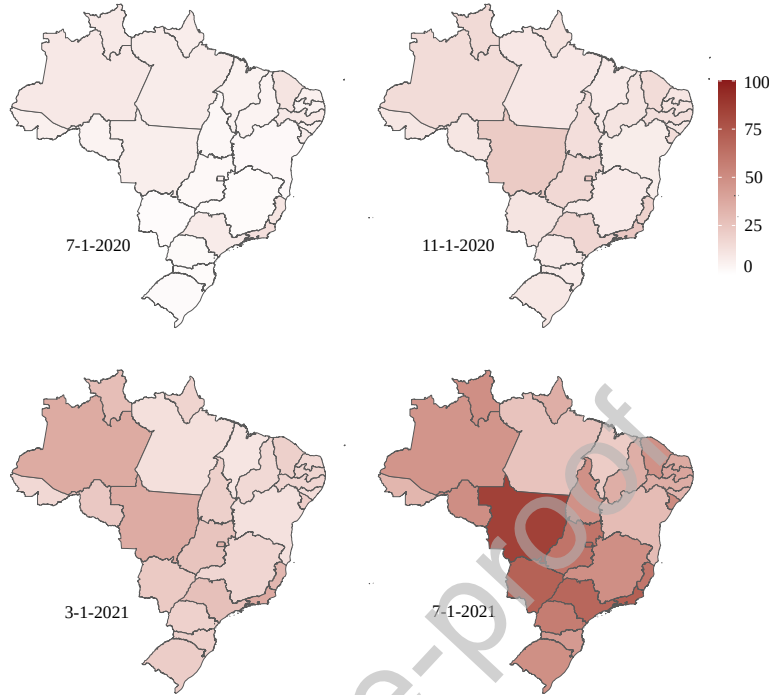


Figure 8: Heat map with the model estimates of the attack rate in % for each Brazilian state for four different dates.

under different circumstances. New variants become dominant in an area only if it is more transmissible than the original strain. In Brazil the currently predominant variant γ is roughly 70% to 140% more contagious than the original strain. The α variant, first observed in the United Kingdom, is 50% to 100% more contagious and the δ variant from India is estimated to be 64% more contagious than the α variant, i. e. roughly 50% more contagious than the Brazilian variant γ [18]. With this estimate, we perform a few prognostics for the evolution of the pandemic in Brazil by considering the current situation in each state as given by the last computed value of the transmission probability p_c in Eq. (3). The δ variant is present in Brazil but not yet dominant, which means that its prevalence will raise in a amount of time that depends on the circulation of the virus, which is high in Brazil in July 2021. we suppose that this results in an increase of p_c given by a logistic function of the form:

$$p_c \rightarrow p_c \left[1 + \frac{\Delta p_c}{1 + \exp(-k(t - t_0))} \right], \quad (7)$$

with $k \approx 0.1$ and $t_0 \approx 68.28$ constants chosen such that at present time (July, 12 2021) the probability p_c increases from $10^{-3}\Delta p_c$ and reaches a value of $0.9\Delta p_c$ after an estimated time of 90 days, which is compatible with what was observed in places where the variant became predominant [46]. Following the discussion above we use the values 0.0 (no increase in p_c , 0.5 and 1.0 for Δp_c . We also suppose that vaccination will proceed in Brazil with a number of doses for each type of vaccine equal to the average during the months of May and June 2021, with 80% of the population in each age-group being fully vaccinated proceeding from from the eldest to the youngest, including children. The results for the epidemic curve (cases per day) and the cumulative number of deaths are shown in Fig. 9. We see that the arrival of the δ variant which is already present in Brazil, can produce another wave with an intensity depending on how much it contagious, and the vaccine coverage, among other factors.

Predicting the future for a pandemic is always an intricate task, as it depends on many factors such as the degree of social isolation, the compliance to mask use and to other measures, the possibility of new yet unknown variants. Despite that, a well calibrate model is an important tools for assessing the current situation, foe evaluations of previous

mitigation measures, and for predicting possible scenarios of evolution that can be helpful for evaluating the effect of different policies for reducing the already immense impact of the current pandemic.

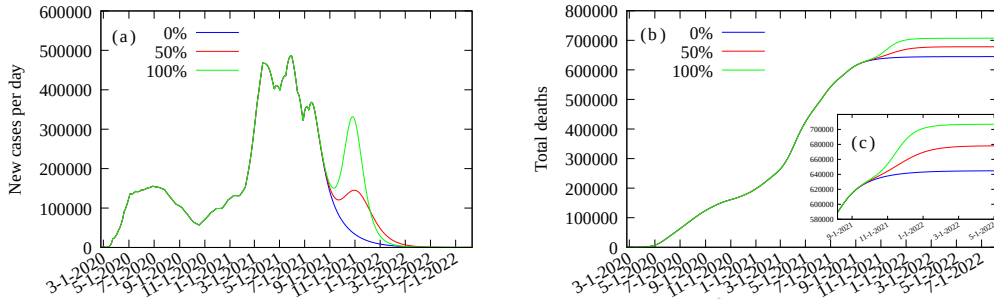


Figure 9: Prognostics for Brazil in three different scenarios: $\Delta p_c = 0$ (no change in current situation), $\Delta p_c = 0.5$ (a 50% increase in the contagiousness) and $\Delta p_c = 1$ (the new variant is twice as contagious as the current dominant γ variant). a) New cases per day; b) Deaths per day; c) Zoom over (b).

4. Concluding remarks

We have shown that the SEIARHV model here introduced can be calibrated with data from the time series for the number of deaths in each locality, with very good results when compared with two good quality serological surveys. For that it is important to have good quality estimates for the infection fatality rate according to the age group, and for the proportion χ of asymptomatic individuals. In fact, our results corroborate the estimate for χ obtained in [33]. An additional complication comes from new variants of the SARS-CoV-2 virus, which are more transmissible and also more lethal, which was overcome by estimating the increase in mortality during the second-wave in Brazil from data for the number of official cases and deaths. Of course, this may lead to a change over time of some of the epidemiological parameters used in our model, and must be taken into account if sufficient information is available. The same applies for new variants as data is gathered on them. A different approach would be to use the series for cases and deaths to determine how the parameters change [15], but then this would require that the data used is reliable which, as discussed above, is not currently the case for the COVID-19 pandemic [20, 21, 22], so one has to choose which information is more appropriate to use for model calibration.

We applied our approach to study the current, and previous, state of the pandemic in Brazil, one of the most attacked countries in the World. Since there was no centralized policy for controlling the pandemic in Brazil, each state and sometimes each municipality had to implement his own mitigation measures. This explains the widely different attack rates in each one, and also shows how the present approach can describe them if properly adjusted. In our case we chose to use the series of deaths as reliable data. The attack rate in most of Brazil is still well below herd immunity, estimated at the initial stages of the pandemic close to 70% [44]. The advent of more transmissible variants raise significantly this value. Some Brazilian states and cities are approaching or even surpassing this value. This fact was properly discussed in the text, but requires more data to be gathered for a more precise interpretation. The attack rate in the cities presented here are higher than in the corresponding states, as the pandemics started in the bigger cities, with the main airports and more intense inter-cities traveling. The pandemic then spread to smaller cities, meaning that more important outbreaks are most likely to be expected there.

It is expected that future results of serological surveys can shed some light on the possibility of a greater proportion of reinfections, and we hope that the present approach can be used as an important tool in this analysis. Our approach can be extended straightforwardly to other cities and countries with reliable data, usually on the number of deaths but not for the number of cases as under-reporting is important almost anywhere [20, 21, 22]. Where good serological surveys are not available the current approach is an alternative tool to assess the current and past situation, and to prepare for what is still ahead. It can also be directly applied to other diseases than are modeled by SEIR type models, such as measles.

The simplifying assumption that the transmission probability p_c is age independent can also be readily improved by considering a probability that depends on the age of the infecting or being infected individual, provided that data on the time series of deaths is publicly available. One can also fit the model with the number of cases if the data is reliable, which is usually not the case by far for the current COVID-19 pandemic.

It is yet not clear how long natural immunity will last, and how much current vaccines protect against transmission. The arrival of more contagious variants casts many doubts on the real relevance of herd immunity. The determination of the attack rate is important for guiding and correcting public policies as a criterion to estimate its results. The model used in the present work is also a useful tool in estimating the evolution of the present pandemic from the current situation, if good estimates for the IFR and for the characteristics of new variants exist.

Acknowledgments

This work received financial support from the National Council of Technological and Scientific Development - CNPq (grant numbers 302449/2019-1 FAS, 309617/2020-0 ACGA, 305291/2018-1 MAM), Bahia State Research Support Foundation (BOL0723/2017 AJAC) (Brazil) and i3N (grant numbers UIDB/50025/2020 & UIDP/50025/2020) - Fundaço para a Cincia e Tecnologia/MEC (Portugal).

References

- [1] Zhu N, Zhang D, Wang W, Li XW, Yang B, Song JD et al. *A novel coronavirus from patients with pneumonia in China*. 2019. *N. Engl. J. Med.* 2020;382:727-733. <https://doi.org/10.1056/NEJMoa2001017>.
- [2] COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). <https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6>. Accessed on July, 19 2021.
- [3] Ayouni I, Maatoug J, Dhoub W, Zammit N, Fred SB, Ghammam R, Ghannem H. *Effective public health measures to mitigate the spread of COVID-19: a systematic review*. *BMC Public Health* 2021;21:1015. <https://doi.org/10.1186/s12889-021-11111-1>
- [4] *The New York Times Coronavirus Vaccine Tracker*. <https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html>
- [5] Vespignani A, Tian H, Dye C, Lloyd-Smith JO, Eggo RM, Shrestha M, et al. *Modelling COVID-19*. *Nat. Rev. Phys.* 2020; 2:279.
- [6] Kermack W, McKendrick AG. *A contribution to the mathematical theory of epidemics*. *Proc. Royal Soc. London Series A*. 197; 115:700.
- [7] Hethcote HW. *The Mathematics of Infectious Diseases*. *SIAM REVIEW* 2000; 42:599.
- [8] Brauer F, Driessche P, Wu J (Eds.) *Mathematical Epidemiology*. 2008 Springer-Verlag Berlin Heidelberg.
- [9] Keeling MJ, Rohani P. *Modeling Infectious Diseases in Humans and Animals*; 2008 Princeton University Press;
- [10] Estrada E. *COVID-19 and SARS-CoV-2. Modeling the present, looking at the future*. *Phys. Rep.* 2020; 869:1.
- [11] Lorig F, Johansson E, Davidsson P. *Agent-based Social Simulation of the Covid-19 Pandemic: A Systematic Review*. *J. Artif. Soc. Soc. Simul.* 2021; 24:5.
- [12] Coletti P, Libin P, Petrof O, Willem L, Abrams S, Herzog SA et al. *A data-driven metapopulation model for the Belgian COVID-19 epidemic: assessing the impact of lockdown and exit strategies* *BMC Infectious Diseases* 2021;21:503.
- [13] Xiang Y, Jia, Chen L, Guo L, Shu B, Long E. *COVID-19 epidemic prediction and the impact of public health interventions: A review of COVID-19 epidemic models*. *Infect. Dis. Modell.* 2021; 6:324.
- [14] Rahimi I, Chen F, Gandomi AH. *A review on COVID-19 forecasting models*. *Neural. Comput. Appl.* <https://doi.org/10.1007/s00521-020-05626-8>
- [15] Roda WC, Varughese MB, Han D, Li MY. *Why is it difficult to accurately predict the COVID-19 epidemic?* *Infect. Dis. Modell.* 2020; 5:271.
- [16] James LP, Salomon JA, Buckee CO, Menzies NA. *The Use and Misuse of Mathematical Modeling for Infectious Disease Policymaking: Lessons for the COVID-19 Pandemic*. *Med. Decis. Making.* 2021; 41:379.
- [17] Taylor L. *Covid-19: Is Manaus the final nail in the coffin for natural herd immunity?* *BMJ* 2021;372:n394. <https://www.bmj.com/content/372/bmj.n394>
- [18] Otto SP, Day T, Arino J, Colijn C, Dushoff J, Li M et al. *The origins and potential future of SARS-CoV-2 variants of concern in the evolving COVID-19 pandemic. To appear in: Current Biology*. <https://doi.org/10.1016/j.cub.2021.06.049>.
- [19] Callaway E. *Delta coronavirus variant: scientists brace for impact*. *Nature*, June 2021. <http://doi.org/10.1038/d41586-021-01696-3>
- [20] Jrahmandad J, Lim TY, Sterman J. *Behavioral dynamics of COVID-19: estimating under-reporting, multiple waves, and adherence fatigue across 92 nations*. *MedRxiv*: <https://doi.org/10.1101/2020.06.24.20139451>
- [21] Docherty KF, Butt JH, de Boer RA, Dewan P, Kober L, Maggioni AP et al. *Excess deaths during the Covid-19 pandemic: An international comparison*. *MedRxiv*: <https://doi.org/10.1101/2020.04.21.20073114>
- [22] Veiga e Silva L, Abi Harb MPA, Santos AMTB, Teixeira CAM, Gomges VHM, Cardoso EHS et al. *COVID-19 Mortality Underreporting in Brazil: Analysis of Data From Government Internet Portals*. *J. Med. Internet. Res.* 2020;22:e21413. <https://doi.org/10.2196/21413>
- [23] *Worldometers*. <https://www.worldometers.info/coronavirus/#countries>. Accessed July, 19 2021.
- [24] Chen X, Chen Z, Azman AS, Deng X, Sun R, Zhao Z et al. *Serological evidence of human infection with SARS-CoV-2: a systematic review and meta-analysis*. *Lancet Glob. Health* 2021;9:e598. [https://doi.org/10.1016/S2214-109X\(21\)00026-7](https://doi.org/10.1016/S2214-109X(21)00026-7)
- [25] Silveira MF, Barros AJD, Horta BL, Pellanda LC, Victora GD, Dellagostin OA et al. *Population-based surveys of antibodies against SARS-CoV-2 in Southern Brazil*. *Nat. Med.* 2020;26:1196-1199. <https://doi.org/10.1038/s41591-020-0992-3>

- [26] SoroEpi MSP: Serial seroepidemiological survey to monitor the prevalence of SARS-CoV-2 infection in the Municipality of So Paulo, SP, Brazil (2020). <https://www.monitoramentocovid19.org/>. Accessed April, 28 2021.
- [27] Rocha Filho TM, Mendes JFF, Murari TB, Nascimento Filho AS, Cordeiro AJA, Ramalho WM et al. WHO vaccination protocol can be improved to save more lives. *Research Square*, January 18, 2021. Preprint Available at <https://www.researchsquare.com/article/rs-148826/v1>
- [28] Mossong J, Hens M, Jit M, Beutels P, Auranen K, Mikolajczyk R, Massari M et al. Social Contacts and Mixing Patterns Relevant to the Spread of Infectious Diseases. *PLOS Medicine* 2008;5:e74. <https://doi.org/10.1371/journal.pmed.0050074>
- [29] Zhou T, Liu Q, Yang Z, Liao J, Yang K, Bai W et al. Preliminary prediction of the basic reproduction number of the Wuhan novel coronavirus 2019-nCoV. *J. Evid. Based Med.* 2020;13:3-7. <https://doi.org/10.1111/jebm.12376>
- [30] Verity R, Okell LC, Dorigatti I, Winskill P, Whittaker C, Imai N et al. Estimates of the severity of coronavirus disease 2019: A model-based analysis. *Lancet Infect. Dis.* 2020;20:669-677. [https://doi.org/10.1016/S1473-3099\(20\)30243-7](https://doi.org/10.1016/S1473-3099(20)30243-7).
- [31] Linton NM, Kobaiashi T, Yang Y, Hayashi K, Akhmetzhanov AR, Jung S et al. Incubation Period and Other Epidemiological Characteristics of 2019 Novel Coronavirus Infections with Right Truncation: A Statistical Analysis of Publicly Available Case Data. *J. Clin. Med.* 2020;9:538. <https://doi.org/10.3390/jcm9020538>
- [32] Lauer SA, Grantz KH, Bi Q, Forrest K, Zheng Q, Meredith HR et al. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. *Ann. Intern. Med.* 2020;172:577-583. <https://doi.org/10.7326/M20-0504>
- [33] Mizumoto K, Kagaya K, Zarebski A, Chowell G. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. *Euro Surveill.* 2020;25:2000180. <https://doi.org/10.2807/1560-7917.ES.2020.25.10.2000180>
- [34] DATASUS. <http://tabnet.datasus.gov.br/cgi/defthtm.exe?popsvs/cmv/popbr.def>. Accessed April, 28 2021.
- [35] Gao F, Han L. Implementing the Nelder-Mead simplex algorithm with adaptive parameters. *Comput. Optim. Appl.* 2012;51:259-277. <https://doi.org/10.1007/s10589-010-9329-3>
- [36] COVID19 Painel Coronavrus Ministerio da Sade da Repblica Federativa do Brasil DATASUS. <https://covid.saude.gov.br/>
- [37] Instituto Brasileiro de Geografia e Estatstica (IBGE). <https://brasilensintese.ibge.gov.br/populacao/>. Accessed April, 28 2021.
- [38] OpenDATASUS - Ministerio da Sade do Brasil.i <https://opendatasus.saude.gov.br/dataset/covid-19-vacinacao>
- [39] Ranzani OT, Bastosi LSL, Gelli JGM, Marchesi JF, Baio F, Hamacheri S, Bozza FA. Characterisation of the first 250 000 hospital admissions for COVID-19 in Brazil: a retrospective analysis of nationwide data. *Lancet Respir. Med.* 2020;9:322-324. [https://doi.org/10.1016/S2213-2600\(20\)30560-9](https://doi.org/10.1016/S2213-2600(20)30560-9)
- [40] Freitas ARR, Lemos DRQ, Beckedorff AO, Cavalcanti LPG, Siqueira AM, Mello CRS, Barros ENC. The increase in the risk of severity and fatality rate of covid-19 in southern Brazil after the emergence of the Variant of Concern (VOC) SARS-CoV-2 P.1 was greater among young adults without pre-existing risk conditions. *medRxiv April 19, 2021. medRxiv* <https://doi.org/10.1101/2021.04.13.2125281>
- [41] Tuite AR, Fisman DN, Oduyayo A, Bobos P, Allen V, Bogoch II et al. COVID-19 Hospitalizations, ICU Admissions and Deaths Associated with the New Variants of Concern. *Science Briefs of the Ontario COVID19 Science Advisory Table.* 2021;1:1-10. <https://doi.org/10.47326/ocsat.2021.02.18.1.0>.
- [42] Bermudi PMM, Lorenz C, Aguiar BS, Failla MA, Barrozo LV, Chiaravalloti-Neto F. Spatio temporal dynamic of COVID-19 mortality in the city of Sao Paulo, Brazil: shifting the high risk from the best to the worst socio-economic conditions. *ArXiv: 2008.02322 [STAT.ap]*, August 5, 2020; [arXiv https://arxiv.org/abs/2008.02322](https://arxiv.org/abs/2008.02322)
- [43] Lavine JS, Bjornstad ON, Antia R. Immunological characteristics govern the transition of COVID-19 to endemicity. *Science* 2021; 371:741.
- [44] Fontanet A, Cauchemez S. COVID-19 herd immunity: where are we? *Nat. Rev. Immunol.* 2020;20:583-584. <https://doi.org/10.1038/s41577-020-00451-5>
- [45] Bussi LF, Prete Jr CA, Abraham CMM, Mendrone Jr A, Salomon T, Almeida-Neto C et al. Three-quarters attack rate of SARS-CoV-2 in the Brazilian Amazon during a largely unmitigated epidemic. *Science* 2021;371:288-292. <https://doi.org/10.1126/science.abe9728>
- [46] Alizon S, Haim-Boukobza S, Foulongne V, Verdurme L, Trombert-Paolantoni S, Emmanuel L, Roquebert B, Sofonea MT. Rapid spread of the SARS-CoV-2 Delta variant in some French regions, June 2021. *Euro Surveill.* 2021; 26:2100573. <https://doi.org/10.2807/1560-7917.ES.2021.26.28.2100573>

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Journal Pre-proof