How fast vaccination can control the COVID-19 pandemic in Brazil?*

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Abstract. The first case of Corona Virus Disease (COVID-19) was registered in Wuhan, China, in November 2019. In March, the World Health Organization (WHO) declared COVID-19 as a global pandemic. The effects of this pandemic have been devastating worldwide, especially in Brazil, which occupies the third position in the absolute number of cases of COVID-19 and the second position in the absolute number of deaths by the virus. A big question that the population yearns to be answered is: When can life return to normal? To address this question, this work proposes an extension of a SIRD-based mathematical model that includes vaccination effects. The model takes into account different rates of daily vaccination and different values of vaccine effectiveness. The results show that although the discussion is very much around the effectiveness of the vaccine, the daily vaccination rate is the most important variable for mitigating the pandemic. Vaccination rates of 1M per day can potentially stop the progression of COVID-19 epidemics in Brazil in less than one year.

Keywords: COVID-19 · Vaccination · SIRD

1 Introduction

The first case of Corona Virus Disease (COVID-19) was registered in Wuhan, China, in November 2019. Quickly, the fast spread of the virus in the Chinese city was characterized as an epidemic, and in February 2020, 8 countries already had cases of the disease. Deeply concerned both by the alarming levels of spread and severity of the disease and the alarming levels of inaction, the World Health Organization (WHO) declared COVID-19 as a global pandemic in March 2020 [18].

Until February 3rd 2021, COVID-19 had already infected more than 104.221M people globally, 9.283M only in Brazil. The global number of deaths has reached

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more than 2.262M, 226,309 only in Brazil [1]. In this context, the world population's best hope is mass vaccination, which is a big challenge for the pharmaceutical industry and national health systems.

According to Li *et al.* [10], vaccines, in a general context and not only for COVID-19, will have prevented 69 million (95% confidence interval) deaths between 2000 and 2030, showing that vaccination is fundamental to mitigate the effect of infectious diseases. The conclusion of the tests for the first vaccines for COVID-19 took place in December 2020. As soon as national regulatory agencies approved them, the vaccines began to be applied to the population according to each country's national immunization plan. By February 3$^{\text{rd}}$ 2021, 83.83M vaccines were administrated globally, 1.09% of its population. In Brazil, the number of vaccine shots administrated is 2.52M, 1.19% of its population. Israel is already experiencing a reduction in hospitalization and transmission rates after the vaccination of 3.3M people (38.11% of its population) [2]. It is known that a rapid vaccination is essential to mitigate the spread of the disease, but the limitations imposed by the productive capacity and a clear definition of a logistics plan for the distribution of the vaccines reduces the potential of application of vaccines in the population, especially in lower-income countries. Particularly in Brazil, by keeping the current rate of vaccinated people per day, it would take more than two years to get 70% of the population vaccinated.

Many researchers have been carrying out studies to model the behavior of viruses computationally. In [12], the authors present a study showing that real-time vaccination following an outbreak can effectively mitigate the damage caused by an infectious disease using a stochastic SIR model. They analyzed the trade-offs involving vaccination and time delays to determine the optimal resource allocation strategies. The earlier a population undergoes mass vaccination, the more effective the intervention, and fewer vaccines will be required to eradicate the epidemic. In [1], the authors estimated the number of clinical cases, hospitalizations, and deaths prevented in the United States that were directly attributable to the 2009–2010 A(H1N1)pdm09 virus vaccination program. They show that early vaccination improves the efficacy of immunization significantly.

There is also a study [11] where the authors try to determine an optimal control strategy for vaccine administration for COVID-19 considering real data from China. This problem was solved using multi-objective and mono-objective Differential Evolution. The mono-objective optimal control problem considers minimizing the number of infected individuals during the treatment. On the other hand, the multi-objective optimal control problem considers minimizing the number of infected individuals and the prescribed vaccine concentration during the treatment.

Many works have dedicated efforts to adjust models for short-term prediction of virus behavior, such as [4], which calibrates a model to estimate the pandemic's behavior in the State of Mato Grosso and Brazil as a whole. To accomplish this objective, the authors proposed an exponential model and time series forecasting

[1] available at https://data.humdata.org/dataset/novel-coronavirus-2019-ncov-cases
[2] available at https://ourworldindata.org/covid-vaccinations

techniques. In [14], the use of a simple mathematical model is proposed, based on the classical SIRD model to adjust and predict the pandemics behavior in the three countries: Brazil, Italy, and Korea, which are examples of very different scenarios and stages of the COVID-19 pandemic [13].

In this work, we extend the model proposed in [14] by adding a new time-dependent variable called immunization rate. This variable is calculated as a linear function that grows as time passes by and depends on the vaccination rate (people/day) and the vaccine effectiveness for simulating different vaccination scenarios. In this context, the main goal of this work is to show that by considering the immunization rate, we can better simulate the evolution of the number of infections and deaths for COVID-19 and forecast when we can expect to overcome the pandemic, considering different scenarios that take into account different vaccine efficiency and vaccination rates. Moreover, this study can raise awareness that even with the vaccination, it will take some time to alleviate the non-pharmacological measures (social distancing, use of masks, among others) to prevent the spread of the disease. Our results show that although the discussion is very much around the effectiveness of the vaccines, the daily vaccination rate is the most important variable for mitigating the pandemic. In addition, our results suggest that Brazil's vaccination should be done more quickly to make it possible to overcome the pandemic.

2 Material and Methods

2.1 Mathematical model

The model used here is an extension of the model presented in [14] which is based on the classic compartmental SIRD model [2, 5, 8, 7, 6] and was kept as simple as possible to reduce the number of unknown parameters to be estimated. The modified model to include the vaccination scheme is described by the following set of equations:

$$\begin{cases} \frac{dS}{dt} &= -\frac{\alpha(t)}{N}(S - v(t)S)I, \\ \frac{dI}{dt} &= \frac{\alpha(t)}{N}(S - v(t)S)I - \beta I - \gamma I, \\ \frac{dR}{dt} &= \gamma I, \\ \frac{dD}{dt} &= \beta I, \\ I_r &= \theta I, \\ R_r &= \theta R, \\ C &= I_r + R_r + D, \end{cases} \tag{1}$$

where S, I, R, D, I_r, R_r, and C are the variables that represent the number of individuals within a population of size N that are susceptible, infected, recovered, dead, reported as infected, reported as recovered, and total confirmed cases, respectively. The term $\alpha(t) = a(t)b$ denotes the rate at which a susceptible individual becomes infected, where $a(t)$ denotes the probability of contact and b the rate of infection. See [14] for further details on the model.

The new term $v(t)$ denotes the rate of immunization and is described by the following equation:

$$v(t) = \begin{cases} 0, & \text{if } t < (t_{vs} + t_{im}), \\ 1 - v_e v_r t, & \text{otherwise.} \end{cases} \quad (2)$$

where t_{vs} is the day when the vaccination program starts; t_{im} is the immunization delay, i.e., the time between the vaccination and the acquired immunization; v_e is the vaccine effectiveness (in %), and v_r is the vaccination rate (the percent of the population vaccinated per day). To simplify the model and due to the lack of data for the Covid-19 vaccines, the following hypotheses are considered: 1) In the lack of numbers for vaccine effectiveness, we use the disclosed range of reported vaccine efficacy (between 50% and 90%); 2) We consider the optimistic scenario, reported in some recent studies [17, 9], where once immunized an individual when in contact with the virus has a significant reduction in the virus load, i.e., once immunized an individual is no longer infectious; 3) we do not directly consider the differences of vaccine effectiveness after a booster dose, i.e., the need of a second dose is implicitly captured by the parameter t_{im}, the immunization delay.

2.2 Numerical Simulations

We started our investigation by adjusting the model variables with available public data for Brazil, using the 78 days and the original model, described in 2.1. The variable adjustments were made using Differential Evolution (DE), using the same approach presented in [14]. Then we applied the modified model (including the vaccination scheme), simulating one year (365 days) using the adjusted parameters and the configurations described in the scenarios below.

- **Scenario 1**: Fixing vaccination rate at 100k p/d and varying vaccine efficacy from 0.5 to 0.9, with an increment of 0.1.
- **Scenario 2**: Fixing vaccination rate at 2M p/d and varying vaccine efficacy from 0.5 to 0.9, with an increment of 0.1.
- **Scenario 3**: Fixing vaccine efficacy at 0.5 and using vaccination rates of 100k, 1M and 2M p/d.
- **Scenario 4**: Fixing vaccine efficacy at 0.9 and using vaccination rates of 100k, 1M and 2M p/d.

To execute the simulations, we consider that the vaccine takes 28 days to trigger the immune response. We also limit the maximum population to be vaccinated to 109.5 Million, which corresponds to the number of people for vaccination, according to the Brazilian Immunization Program [15].

A global sensitivity analysis of the modified mathematical model for vaccination was carried out using Sobol indices [16]. In particular, in this study, only the vaccination parameters such as immunization time, the vaccine efficacy, and vaccination rate were analyzed, since the remaining parameters were investigated previously [14].

3 Results

After applying the methodology described in Section 2, we were able to simulate the proposed scenarios considering different vaccination and efficacy rates. The results of the numerical simulations are depicted in Figures 1, 2, 3 and 4, that illustrate the evolution of active cases and deaths in Brazil. First, it is important to notice some important information that is common to all simulation scenarios. If no vaccination scheme is adopted, we would have approximately 276.614 active cases and 540.674 total deaths after the 365-time span of the simulations. The particular results for each of the proposed scenarios are presented in Sections 3.1 to 3.4. A deeper discussion on the results is presented in Section 4.

3.1 Scenario 1

Figure 1 shows the evolution of active cases and deaths in Brazil, considering the simulation of the numerical method presented in Section 2 using 365 days, with a fixed vaccination rate of 100 thousand people per day and varying the vaccine efficacy rate. From Scenario 1, we observe that the number of active cases after the 365 days would vary from 148.000 with a vaccine efficacy of 50% to 85.135 for a 90% effective vaccine. The total number of deaths would stand between 496.988 and 469.493 considering vaccine efficacy between 50% and 90%, respectively, indicating a reduction in the total number of deaths between 8% and 13%.

3.2 Scenario 2

The results of the numerical simulation of Scenario 2, which considers a fixed vaccination rate of 2 million people per day, Brazilian theoretical vaccine production capacity, and a varied vaccine efficacy rate, are depicted in Figure 2, which shows the variation of active cases and total deaths in 365 days. The number of active cases would vary from 8.387 with a vaccine efficacy of 50% to 201 for a 90% effective vaccine, and the total deaths would stay between 349.564 and 314.201 considering a vaccine efficacy between 50% and 90% respectively. Compared to the number of deaths observed in the simulation without vaccination, the number of deaths considering Scenario 2 represents a decrease of approximately 35% for a 50% effective vaccine and almost 42% for a vaccine with a 90% efficacy rate after 365 days of simulation. It is also important to notice a drastic drop in the number of active cases after day 110, considering Scenario 2 for all the simulated vaccination and vaccine efficacy rates, which reflects a substantial reduction in the expected number of deaths on the following days of the simulation.

3.3 Scenario 3

Differently from the previous scenarios, where the vaccination rate is fixed, in Scenario 3, we investigate the vaccination effects with three different rates (100k,

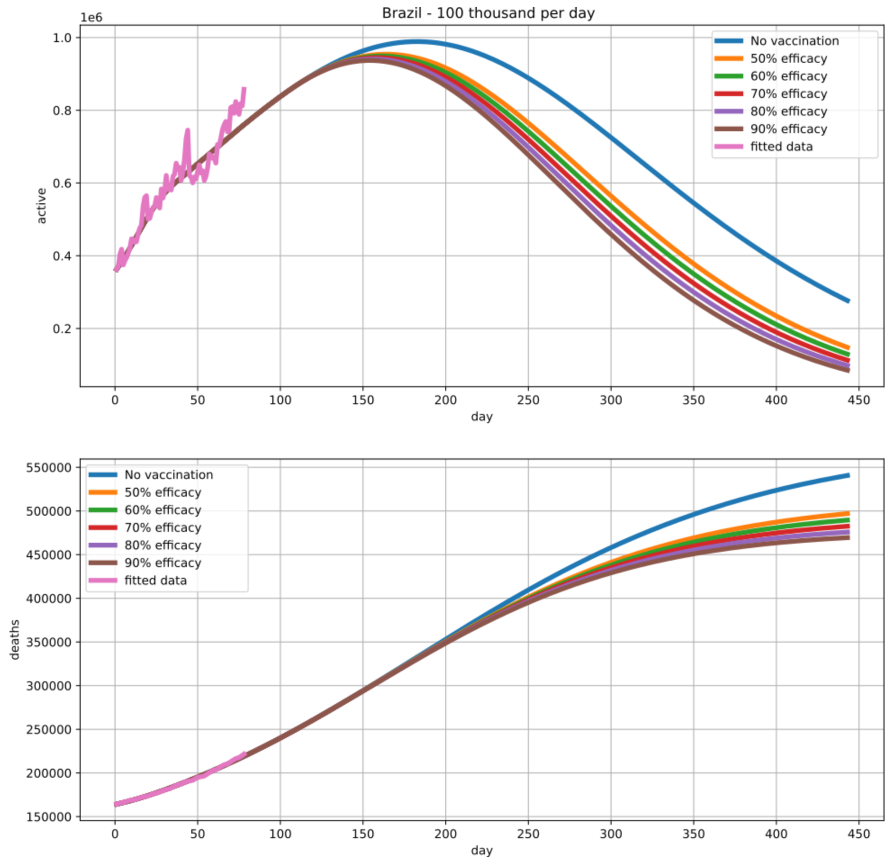

Fig. 1. Fixing vaccination rate at 100k p/d and varying vaccine efficacy from 0.5 to 0.9

1M, and 2M people per day), but fixing the efficacy rate as 50%. Figure 3 presents the number of active cases and the total of deaths for the numerical simulation considering Scenario 3 in the 365 days. The resulting curves for the 1M and 2M people per day simulations show a drastic reduction in the number of active cases around day 110, and in Figure 2 which represents the results for Scenario 2. A less drastic reduction is observed in the number of active cases for the parameterization with a vaccination rate of 100k people per day, which causes the number of deaths to be increasingly high, even after the 365 days.

3.4 Scenario 4

In Scenario 4, the vaccine efficacy rate is fixed, and the vaccination rate is varied in 100k, 1M, and 2M people per day, as in Scenario 3. However, the numerical simulations consider a vaccine efficacy of 90%. Figure 4 shows the number of

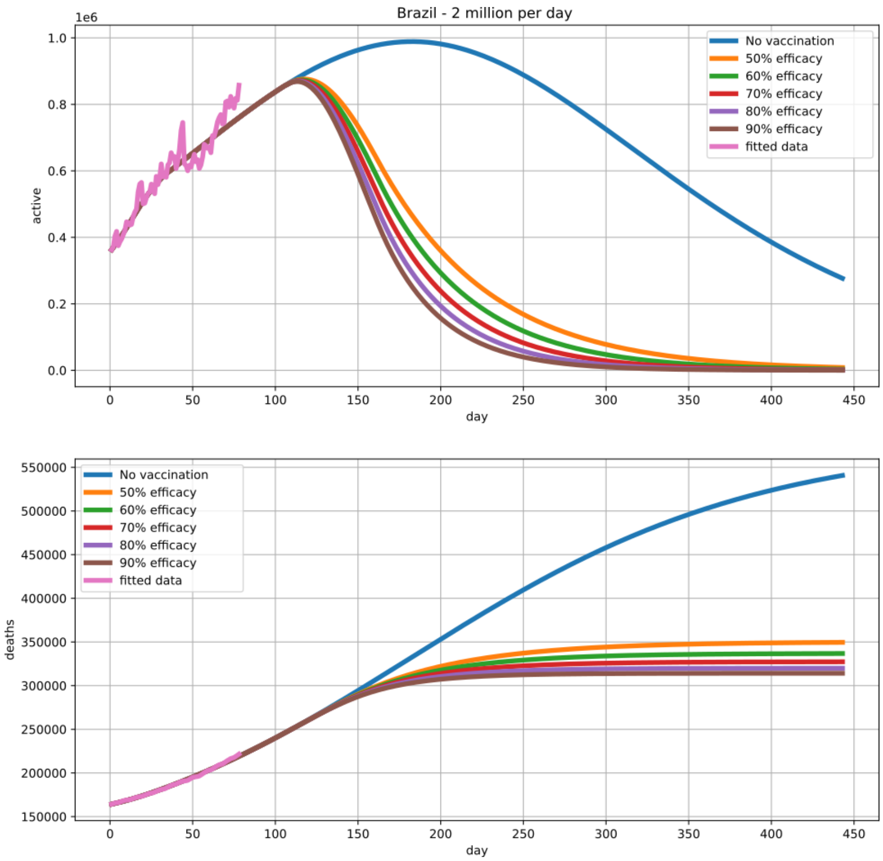

Fig. 2. Fixing vaccination rate at 2M p/d and varying vaccine efficacy from 0.5 to 0.9

active cases and the number of deaths observed for the simulation of the proposed model in 365 days. The peaks of the curves of active cases considering the vaccination of 1M and 2M people per day occur around day 120, while the peak of the curve for the vaccination of 100k people per day occurs after day 150. Moreover, for the curves that represent the total number of deaths considering the vaccination of 1M and 2M people per day, we can observe a steady state after the 365 days time span, while for the vaccination of 100k people per day, the number of deaths still increases even after the 365 days of simulation.

3.5 Sensitivity Analysis

To better understand how the different parameters considered impact the number of active cases and the number of deaths for the model presented in Section 2, this section presents a Sensitivity Analysis (SA) carried out for immunization delay, vaccine efficacy and, vaccination rate. The interval for immunization delay

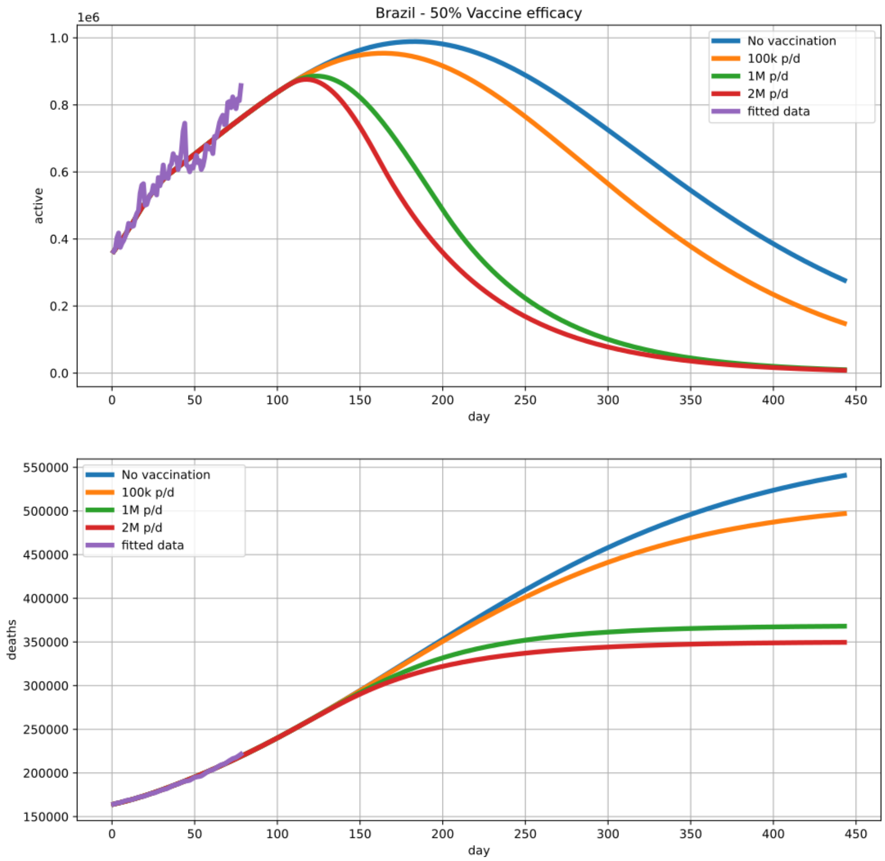

Fig. 3. Fixing vaccine efficacy at 0.5 and using vaccination rates of 100k, 1M and 2M p/d

considers the bounds $[14, 42]$, representing a standard 28 +/− 14 days immunization time. The bounds for the vaccine efficacy, $[0.5, 0.9]$, are the same values used for the experiments, as reported in Section 2.2. The bounds for vaccination rate, $[0.000545107, 0.009371513]$, consider the proportion of the Brazilian population regarding the vaccination rates of 100k and 2M people per day, also reported in Section 2.2.

First, it is essential to mention that the results observed for the curves representing the Sensitivity Analysis regarding the number of active cases and the number of deaths are very similar. Thus, to avoid redundancy, we chose to omit the results of the Sensitivity Analysis for the number of deaths. The Sensitivity Analysis results based on main Sobol indices regarding the number of active cases are presented in Figure 5, which reports the sensitivities in the period after the beginning of vaccination. One can observe that the immunization delay plays an essential role during the vaccination program, whereas the vaccination

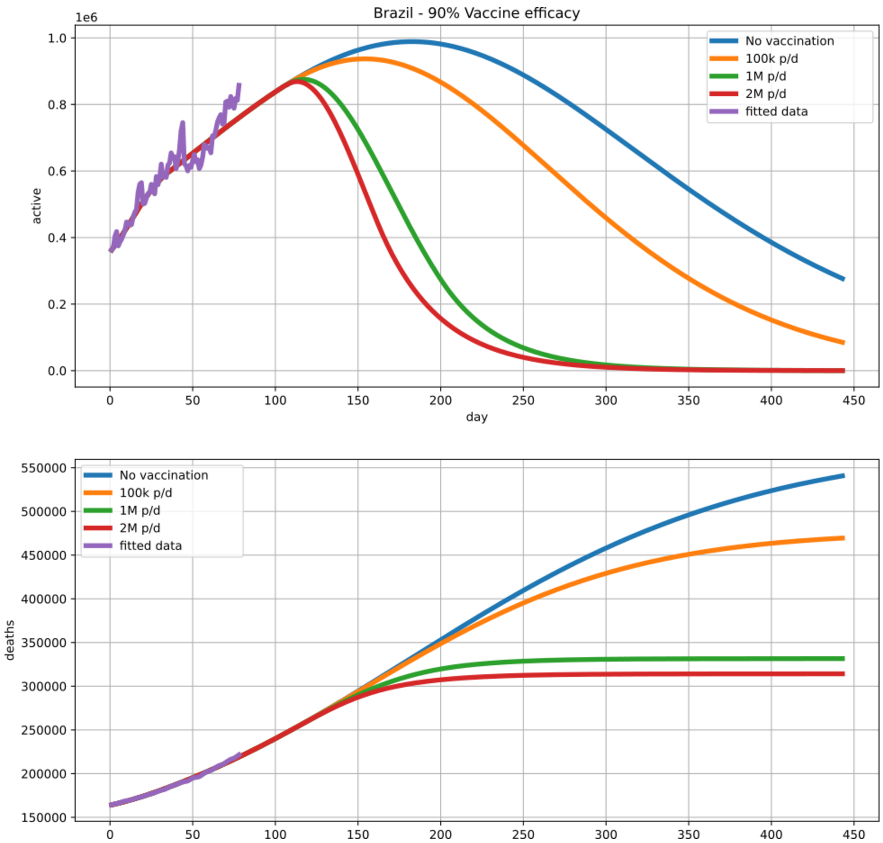

Fig. 4. Fixing vaccine efficacy at 0.9 and using vaccination rates of 100k, 1M and 2M p/d

rate becomes the more relevant parameter to control the number of active cases in the long term. We can also note that the efficacy of the vaccine appears as the least important parameter for controlling the number of active cases.

4 Discussion

By analyzing the results presented in Sections 3.1 to 3.4, it can be seen that, according to the simulations performed in this work, with a vaccination rate of 100 thousand people per day, the disease would not be fully controlled after the 365 time span, regardless of the vaccine efficacy as the number of active cases would still be high (85.135 active cases), even with a 90% effective vaccine. By vaccinating the population at a rate of 2M p/d, the active cases would vary from 8.387, for a 50% effective vaccine to 201, for a vaccine with 90% of efficacy. These results indicate that, at this rate, the pandemic would be controlled, after one year of vaccination, regardless of the vaccine efficacy.

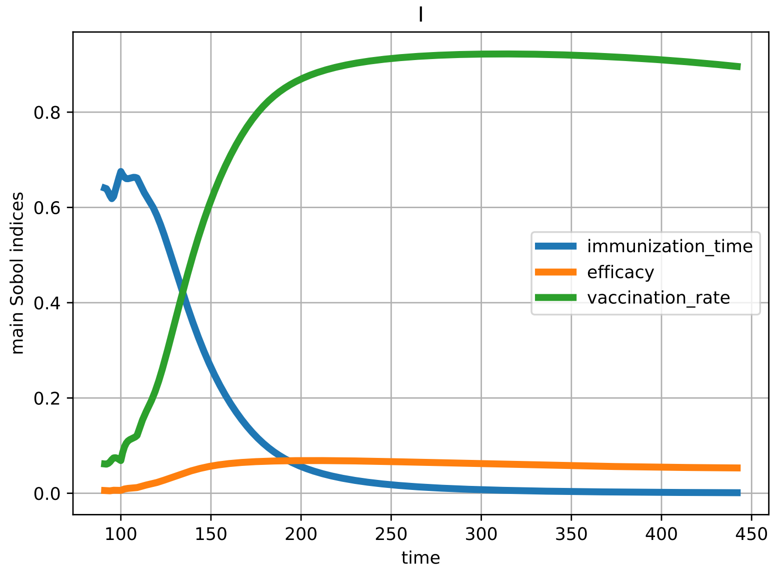

Fig. 5. Main Sobol sensitivities for the number of active cases (I) as a function of time.

By January 28$^{\text{th}}$, 2021, according to the Johns Hopkins University data [3], Brazil had 221.547 deaths caused by COVID-19. Without a vaccination scheme, the number of fatalities can be more than 500 thousand in one year from now, according to the model. Moreover, the number of active cases increases approximately until day 180 of the simulations. It is also interesting to see that, in the simulations for the four scenarios proposed in this work, all the curves overlap until at least day 100, indicating that, in the short-term, the choice of a vaccination scheme, or the lack of it, is irrelevant. However, it is worth observing that, in the long-term, the adoption of immunization policies could substantially reduce the number of deaths due to COVID-19. Even considering a more conservative vaccination scheme with the vaccination of 100k people per day and a 50% effective vaccine, a similar rate to that currently adopted in Brazil, represented in Scenario 1 (Section 3.1), the model predicts 43.686 fewer deaths. The data provided by our simulations also suggests that a solid vaccination scheme could potentially control the pandemics in Brazil in 356 days, and thousands of lives could be saved. If a more assertive vaccination scheme is adopted, considering the vaccination of 2M people per day, taking advantage of the immunization potential of the Brazilian health system, we would have 191.110 less deaths with a 50% effective vaccine, and 226.473 lives could be saved if a 90% effective vaccine was adopted, according to the numerical simulations in the 365 days.

The experiments conducted in this work allow us to better understand an essential issue in the definition of a vaccination scheme for COVID-19: the impact of the vaccination rate and vaccine efficacy in the mitigation of the pandemic. By analyzing the simulation Scenarios 1 (Section 3.1) and 2 (Section 3.2), where the vaccination rate is fixed, it can be observed that the curves that represent the results of the numerical simulation behave very similarly, although the number of deaths and active cases decreases as the vaccine efficacy increases. This suggests that the significance of the vaccine efficacy is limited to define the success of a global immunization effort. When we consider the scenarios where the vaccination rate varies (Scenarios 3 and 4, presented in Sections 3.3 and 3.4 respectively), we can observe a clear distinction between the curve that represent the results of the simulation with a vaccination rate of 100k people per day and the curves for 1M and 2M people per day. According to the simulations performed in this work, regardless of the vaccine efficacy considered (50% for Scenario 3 and 90% for Scenario 4), the vaccination of 1M and 2M can mitigate the spreading of the virus after 365 days, unlike Scenario 1, with the vaccination of 100k people per day, where the curves that represent the number of deaths still increases after 365 days. The observation of the high relevance of the vaccination rate in the success of the immunization efforts for COVID-19 is corroborated by the Sensitivity Analysis (SA), presented in Section 3.5. The Sobol indices observed for the immunization delay, vaccination rate, and vaccine efficacy as a function of time show that, in the long term, the vaccination rate is the most relevant parameter to control the number of active cases and, accordingly, the number of deaths, considering the numerical simulations conducted in this work.

5 Limitations and future works

The model considered in this work, as well as the model in which it is based [14], is able to adjust well to real data, as presented in Section 3. However, it shows a series of limitations, which we intend to discuss in this section.

As the first case of COVID-19 occurred not much more than one year ago, some limitations of our model relate to uncertainties regarding the disease's characteristics, which only recently has been investigated. Currently, there is no consensus on how often reinfections of COVID-19 can occur and how does a recurrent occurrence of the disease could affect the dynamics of its transmission. We still do not understand how different Corona Virus variations can impact the transmission rate in a population and the severity of COVID-19.

Other limitations are imposed by the complex behavior of a population, especially facing a pandemic, due to explicit public policies and guidelines or the self-organization of people. As the pandemic progresses, people harden or soften the social distancing and the adoption of measures like the use of masks and hands sanitation; restaurants, schools, and business places for other economic activities close and open as the occupancy of hospitals change. The variations of the social dynamics are not considered by our model and represent a limitation of our work. Our model also considers the population to be homogeneously spread in the space and a homogeneous contact between people and, these aspects should be considered in future works if we want our model to be more realistic.

The definition of public policies regarding the immunization strategy also involves the stratification of the population in different levels of priority to be vaccinated, according to the risk of severity of COVID-19, in case of infection. For instance, in Brazil, the first individuals to be vaccinated are the most vulnerable to COVID-19 infection, which means that if this kind of information is incorporated into our model in future works, the number of deaths could be reduced in our simulations. To keep it simple, we are also disregarding that a vaccine's efficacy to avoid infections is frequently lower than its efficacy in preventing more severe occurrences of the disease, sometimes almost avoiding the evolution of patients' clinical conditions to death or even the need to use respirators.

Moreover, as more vaccines are developed and approved by regulatory agencies, public and private organizations negotiate their acquisition and improve the strategies for the logistics and the administration of vaccine shots, changing the vaccination rate, which, in this work, remains fixed as a function of time.

As reported in Section 2, the model proposed in this work is intended to be kept as simple as possible. The limitations here described do not prevent us to better understand the effect of the adoption of different vaccination schemes over time, and we intend to consider and solve them in future works.

6 Conclusions

This work presents an extension of the model proposed in Reis *et al.* [14], which simulates the propagation of COVID-19 in a homogeneous population by incorporating the immunization of a portion of the population as a function of time. The model parameters were adjusted to the real data of 78 days before the start of vaccination in Brazil via differential evolution regarding the number of active cases and the number of deaths. Different values for the daily vaccination rate and vaccine efficacy were tested to simulate Brazil's pandemic effects in 365 days. From the numerical simulation results, we investigated the parameters set that would better control the pandemic and how long it would take for a significant reduction in the number of deaths by varying these values. In this context, the observation of the resulting curves from the simulations combined with a Sensitivity Analysis of the parameters allows us to verify that the vaccination rate is much more important than the vaccine's efficacy to mitigate the pandemic.

One of the main issues in the discussion regarding vaccines' acquisition for implementing public policies for immunization is its reported efficacy. However, according to the results of the numerical simulations and the Sensitivity Analysis conducted in this work, considering the parameters adopted for the vaccination and vaccine efficacy rates, it is clear that this should be a secondary topic to be discussed, as the vaccination rate is much more relevant for mitigating COVID-19 than the vaccine efficacy. Thus, considering that the primary purpose of an immunization policy is rapid mitigation of the disease and a substantial reduction in the number of deaths, more attention should be given to adopting vaccines that allow a logistic that enables universal and very fast vaccination of the population.

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