WHO vaccination protocol can be improved to save more lives

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Biological Sciences - Article

Keywords:

Posted Date: January 18th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-148826/v1

Abstract

Coronavirus disease 2019 (COVID-19) pandemic, a virus infection caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, has impacted all countries of the world, and the main 2021's challenge is clearly vaccinating the greater number of persons, in the shortest time span, for a maximal reduction in the number of deaths and in the significant economic impacts. Large-scale vaccination aimed to achieve herd immunity poses many logistic and social difficulties [1], with different vaccine candidates and designs [2,3], and vaccination priorities will determine the evolution of the current COVID-19 pandemic. In this paper we explicitly propose an alternative vaccination protocol that can be more effective than those already being deployed, as the ones in the European Union [4] and in the United States [5]. We report strong evidence based on an epidemiological model for the importance of contact hubs (or superspreaders), having a much larger average number of contacts than in the rest of the population [6-11], on the effectiveness of the vaccination strategy. We show that carefully choosing who will be in the first group to be vaccinated can significantly impact on both health services demand and total death toll, by increasing the overall numbers of lives saved and of hospitalizations. We argue that the approach here considered, which does not coincide with current proposals, and given the current conditions with a lack of basic resources for proper vaccination in several countries, and with a significant reduction in mobility and social isolation restrictions, should be considered by all authorities participating in the design of COVID-19 vaccination with the intent of maximising the number of human lives saved.

Introduction

The first cases of human transmission of SARS-CoV-2 were reported in the Wuhan province in China in December 2019 [12]. By January 2020 the spread became an epidemic and was declared a pandemic on March 11 by the World Health Organization [13]. Since then, the virus has spread over all countries in the world, with more than 93 million total cases and two million deaths [14]. With basic reproduction number R_0 in the range 2.8 – 3.3 [15], a minimum estimate of the herd immunity of 67% [16,17] and an infection fatality rate of 0.657% [18], the natural free evolution would imply a too large death toll, with overcrowded medical facilities, and an even larger economic impact [19-21]. The duration of the disease generated immunity is not yet well known, with the complicating factor that allowing for the SARS-CoV-2 virus to freely circulate can lead to new potentially dangerous mutations [22,23]. As a consequence, a high efficiency vaccine is a sought and important tool in controlling the current COVID-19 pandemic, although, in the current scenario, not the only relevant one in the overall public health response to COVID-19. Thus an efficient immunization strategy will most certainly result in the best payoffs, for the whole health system, for the population well being, and for a proper working economy.

A great amount of effort has been deployed in different countries in developing a vaccine for the SARS-CoV-2 virus, with to the present date three vaccines with some degree of authorization by a national regulatory authority. Large studies of five candidates have been publicly reported in press releases and one in a peer reviewed paper [24], with a total of 56 vaccine candidates in clinical test phase [25]. At the present moment more than 40 countries have approved and started administering COVID-19 vaccines to their populations.

The World Health Organization COVAX initiative, a global vaccine alliance, aims to allocate two billion vaccine doses during 2021 across different participant countries [26], roughly a quarter of the world population, and supposing that another two billion doses can be produced during the year, the number of vaccine doses initially

available will be very limited, and priorities will mandatory to establish who is going to be vaccinated first. The North American CDC vaccination recommendations for the initial phase of the vaccination program are to initiate with healthcare personnel, workers in essential and critical industries, individuals at higher risk for severe COVID-19, and the population with 65 years and older [4]. For the European Union, elderly people, healthcare workers and individuals with certain comorbidities are the first in line [5]. In Brazil, third in number of cases and second in deaths among all countries, the vaccination will start with healthcare workers, 75 years of age and older individuals, long-term care facilities patients with 60 years of age and older, indigenous peoples living in reservations, and traditional communities in river banks, with next phases comprising 60 years of age up to 74 years and individuals with comorbidities [27]. It is possible that general guidelines will be modified as more evidence is gathered on the COVID-19 epidemiology and on the vaccine safety and efficacy for each target group.

A recent survey carried out in Belgium asked 2060 participants, with ages from 18 to 80 who should be vaccinated first, second and so on, reached no consensus [28]. However, depending on the vaccine supply available, a priority ranking can be important as the selected priority groups constitute a considerable fraction of the population. The stage of the pandemic in each country must also be considered, as some vaccine variants may be more effective in reducing the likelihood of severe COVID-19 cases, while others may be effective in reducing transmission [17]. A successful and equitable vaccination strategy will obviously need to take into account all these points, as well as fundamental ethical choices in vaccine allocation already agreed upon.

An important element and the main goal of the present discussion is to bring forward the importance of superspreaders, meaning here individuals with a much higher number of contacts than the average in the population. Possible superspreaders comprise teachers in all levels, public transport workers, supermarket workers, among others social network hubs. Although it is expected that such individuals are to be infected first than the rest of the population, social distancing policies adopted in many countries may have prevented it, at least partially. This kind of population heterogeneity can have relevant effects on the spread of the pandemics and must be considered carefully when designing a vaccination strategy. Previous works on fictional communities arranged in free-scale networks show that the choice of who should be vaccinated first can greatly impact on the evolution of an epidemic [6-11].

In order to evidence the possible role of superspreaders in vaccination plans, we implemented an age-stratified epidemiological model, with homogeneous mixing and compartments for Susceptible (S), Exposed (E), symptomatic Infected (I), Asymptomatic infected (A), Hospitalized (H), Recovered (R), Vaccinated without primary vaccination failure (V) and vaccinated with primary vaccination failure (U). The age groups considered 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 or more years of age, with epidemiological parameters in the literature and fitted using empirical data (see supplementary information for model details and parameter values). All data used here span the period from the beginning of the pandemic up to January, 10 2021. For Brazil the data is available at [29] and for Portugal at [30].

We apply the model for two countries: Brazil and Portugal, which are at the present time at different stages of the pandemic. Brazil is in the start of the second wave, with rising numbers of new cases and deaths, while Portugal is already well ahead on this stage, and allows a comparison of the effects of vaccination in two different contexts. As a simpler approach, we consider that 20% of the age-group with 30 to 39 years is in the superspreaders group, which amounts to 3.2% of the total population of Brazil and 2.5% of Portugal. We also

suppose that due to social distancing superspreaders follow the same contact pattern as other individuals of the same age group, and that at a further time (February, 13 2021 for Portugal and March, 6 2021 for Brazil) they resume to full contacts. We consider superspreaders as having 3 to 10 times (the contact factor) the average number of contacts as the assumed number for the 30-39 years old age group (as given by the contact matrix in Figure 2 of the supplementary information).

Results

We suppose vaccination starts on January 1st 2021 for Portugal and January, 15 for Brazil, with two vaccine efficiencies possibilities of e_v=0.7 and e_v=0.95, with following scenarios: No Vaccination; (Vaccination schedule 1) 60 years and older are the first vaccinated, them the other age groups come next in descending order of age; (Vaccination schedule 2) superspreaders are vaccinated first, then the same as in vaccination schedule 1. We also assume that vaccines protect against the disease and avoid transmission, and that full immunization is attained after 30 days of the first dose and that two doses are required, with a total number of doses of 20 million for Portugal and 250 million for Brazil, available in a time span of one year. The predicted number of deaths for each scenario obtained from our epidemiological model is given in Figs. 1 and 2.

In order to estimate the health care demand we note that the proportion of mild, severe and critical COVID-19 cases is 80.9%, 13.8% and 4.7% among symptomatic individuals [21]. We assume that severe and critical cases require hospitalization and all severe cases demand ICU attention, i.e. 25.4% of the hospitalized individuals [21]. From the hospitalized population as predicted from our model, we obtained the maximum ICU demand in beds projected for the year 2021 for each vaccination scenario and country, and shown in Table 1.

Table 1
Estimated demand of ICU beds for each vaccination scenario

	Vaccination	Scenario I			Vaccination	Scenario II	
	Contact Factor	**e_v**	**ICU beds**		**Contact Factor**	**e_v**	**ICU beds**
Brazil	3	0.7	34939	**Brazil**	3	0.7	35640
	3	0.95	34398		3	0.95	35441
	10	0.7	156884		10	0.7	77765
	10	0.95	141383		10	0.95	36343
Portugal	3	0.7	1316	**Portugal**	3	0.7	1316
	3	0.95	1316		3	0.95	1316
	10	0.7	5033		10	0.7	1316
	10	0.95	4342		10	0.95	1316

We note that starting vaccination by the considered superspreaders population is only effective if their average contact number is a few times that of the average in the population. Using the estimated contact matrix, we obtained the average number of contacts of a single individual with individuals of any age group in Brazil as

15.6 per day and 13.8 per day in Portugal. This implies that a superspreader has roughly 4 to 12 times that figure as obtained from the entries of the contact matrix with a contact factor range from 3 to 10. For the hypothetical scenarios considered here we observe a threshold value for the contact factor such that starting vaccination by the superspreaders and the eldest members of the population is beneficial, in the sense that the death toll and the total number of cases decrease significantly, even more than starting vaccination only by the eldest. This also depends on the current situation of the pandemic in each location, and is more pronounced if it is in an expanding phase, as it is the case for the fitted model used here for Brazil and Portugal, where the present situation is clearly of a new wave with increasing numbers of new cases and deaths. The implied decrease in both these numbers is significant for the strategy here proposed, as seen in Figs. 1 and 2. The reduction in the peak number of ICU beds required is also significant as shown in Table 1, limiting the demand of both health personnel and resources, which at its turn can spare more lives as the consequence of an individual requiring intensive care and not having it is death in most cases.

We also point out that no significant gain is obtained by starting vaccination by other age groups than 60 years of age and more. Indeed, from the contact matrix (see supplementary information) between all age groups, one could argue that vaccinating first the age group of 10 to 19 years of age, the one with the naturally highest number of contacts due to school attendance, could reduce the overall virus transmission. While this is true, the time span required to vaccinate this population would leave the eldest age group exposed to the virus, resulting in a higher overall mortality. Such a scenario was also simulated by the authors (not shown here, with the results just described. Finally, the simpler case considered here of superspreaders being limited to the 30–39 years age group can be extended, by taking into account demographics and data on occupation distribution for each population, in order to have a more realistic estimate of the superspreaders group and the most beneficial vaccination strategy.

Conclusions

In summary, we showed that starting vaccination by the superspreaders group (vaccination schedule 2) at the same time as the elder population (60 years of age and more), and afterwards the remaining age groups in descending age order, is more efficient than current protocols implemented in countries that already started vaccination and similar protocols yet to be initiated. We note that the boundaries of each simulated scenario (given by 3 to 10 times the average number of contacts for the superspreaders age group of 30 to 39 years of age) of the shaded regions in Figs. 1 and 2, corresponding to schedule 2 (in red) has a smaller width than the one for schedule 1 (in green). This implies a lesser dependency on the number of contacts of the superspreaders, which is yet another favourable point for the proposed approach of including superspreaders in the first group to be vaccinated. We also considered here the important issue of the expected number of ICU beds required. For both countries it is significantly smaller for schedule 2 than for schedule 1, in the case superspreaders have a large contact factor close to 10 (see Table 1). These results suggest that vaccination schedule 2 allows greater flexibility in economic activities, since it is less dependent on the existence of superspreaders and its contact structure.

We argue that the present approach for designing vaccination strategies can increase the overall number of lives saved, given the current conditions, considering the lack of basic resources for the vaccination campaigns in several countries, and the reduction in the restrictions on mobility.

Our results can be straightforwardly extended to other countries, and from our studies it is clear that similar results are expected, showing that the benefits of a carefully designed vaccination strategy are evident and should be explored in more detailed studies for each location, for maximal results from a limited number of vaccine doses and limited infrastructure and logistics.

Methods

We use an age-stratified model with homogeneous mixing with compartments and different age groups as described above (see also Supplementary Table 1).

The following parameters are considered in the epidemiological model: average incubation time (5.0 days) [31], average time for recovery (estimated average time the individual remains contagious given by 3.69 days) [34], the time from first symptom to hospitalization (3.3 days) [31], time from first symptom to death (16.8 days) [18], recovery time from hospitalization (17.5 days) [18, 32], proportion of asymptomatic individuals (17.9%) [33], contagiousness of asymptomatic with respect to symptomatic individuals (55%) [34] (see summary of parameters in Supplementary Table 2), and fatality ratios and probability of hospitalization for each age group [18] (Supplementary Tables 3 and 4).

The model relies on a contact matrix with the average number of contacts of an individual of a given age group with any other individual of a given age group. For this purpose we use the contact matrix obtained by Mossong et al. [35] for eight European countries (Belgium, Germany, Finland, Great Britain, Italy, Luxembourg, The Netherlands and Poland). Up to the authors knowledge no such study was performed for either Portugal or Brazil. This difficulty can be overcome by considering that the social contacts structure of the European countries in [35] is similar to that in Portugal as the dispersion for the contact matrices for the countries considered in this study is small, and it is quite reasonable to use it as an estimate for other European countries. For Brazil, where the great majority of the population also live in urban centers, the same supposition stands. This can be better justified by noting that for countries with similar economic structures and cultural setups the number of contacts does not depend significantly on the total population of the country, and is mainly determined by the average over different types of activities of each person (school, work, transportation, etc.). We then compute the average contact matrix for the eight listed countries, and properly consider the different age-groups in the present work. The resulting contact matrix is shown in the Supplementary Fig. 2.

Population per age group for Brazil is obtained from the 2010 census data [29], with the current values estimated using a linear proportion on official estimates for the population in each Brazilian state and the Federal District as available at [29]. Current data for Portugal is available at [30]. In the present work Portugal is considered as a whole, while model parameters for Brazil are separately fitted for each of the 26 states plus the Federal District, and final results are then added to obtain a gross total for the country. COVID-19 data for Portugal was obtained from the World Health Organization Coronavirus Disease (COVID-19) Dashboard [36], and data for each municipality of Brazil from the Brazilian Health Ministry [37]. All data used in the present span the period from the start of the pandemic up to January, 10 2021.

It is a well known fact that the total number of cases is highly underestimated, due mainly to a limited number of COVID-19 tests, and that deaths by COVID are more easily reported, although also subject to some under reporting [38, 39]. As a consequence fitting the model using the data series for the number of deaths yields

results closer to the real situation. The transmission matrix is obtained as the product of the contact matrix multiplied and a time dependent transmission probability P(t). By using a step function for this probability, with 21 days intervals, we minimize the mean square deviation of the time series for the number of deaths over the last seven days and the model output for the same quantity.

Declarations

Competing interests

The authors declare no competing interests.

Table 1

Estimated maximum number of ICU beds required for 2021 for each vaccination scenario (1) and (2), as obtained from our epidemiological model. We use the known hospitalization probability per age group and the average time from first symptoms to hospitalization [18] to determine the number of hospitalized individuals from our epidemiological model. The proportion of hospitalized individuals requiring ICU care is estimated as 25.4% [21], used to estimate the maximum number of hospitalized individuals demanding ICU care is estimated.

Author contributions

T.M.R.F. implemented the computational modeling; All authors discussed the relevant variables and parameters in the model, analyzed the results, wrote and reviewed the manuscript.

Acknowledgements

This work received financial support from National Council of Technological and Scientific Development - CNPq (grant numbers 305842/2017-0 TMRF, 302449/2019-1 FAS, 309617/2020-0 ACGA, 305291/2018-1 MAM), Bahia State Research Support Foundation (BOL0723/2017 AJAC) (Brazil) and i3N (grants numbers UIDB/50025/2020 & UIDP/50025/2020) - Fundação para a Ciência e Tecnologia/MEC (Portugal).

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Figures

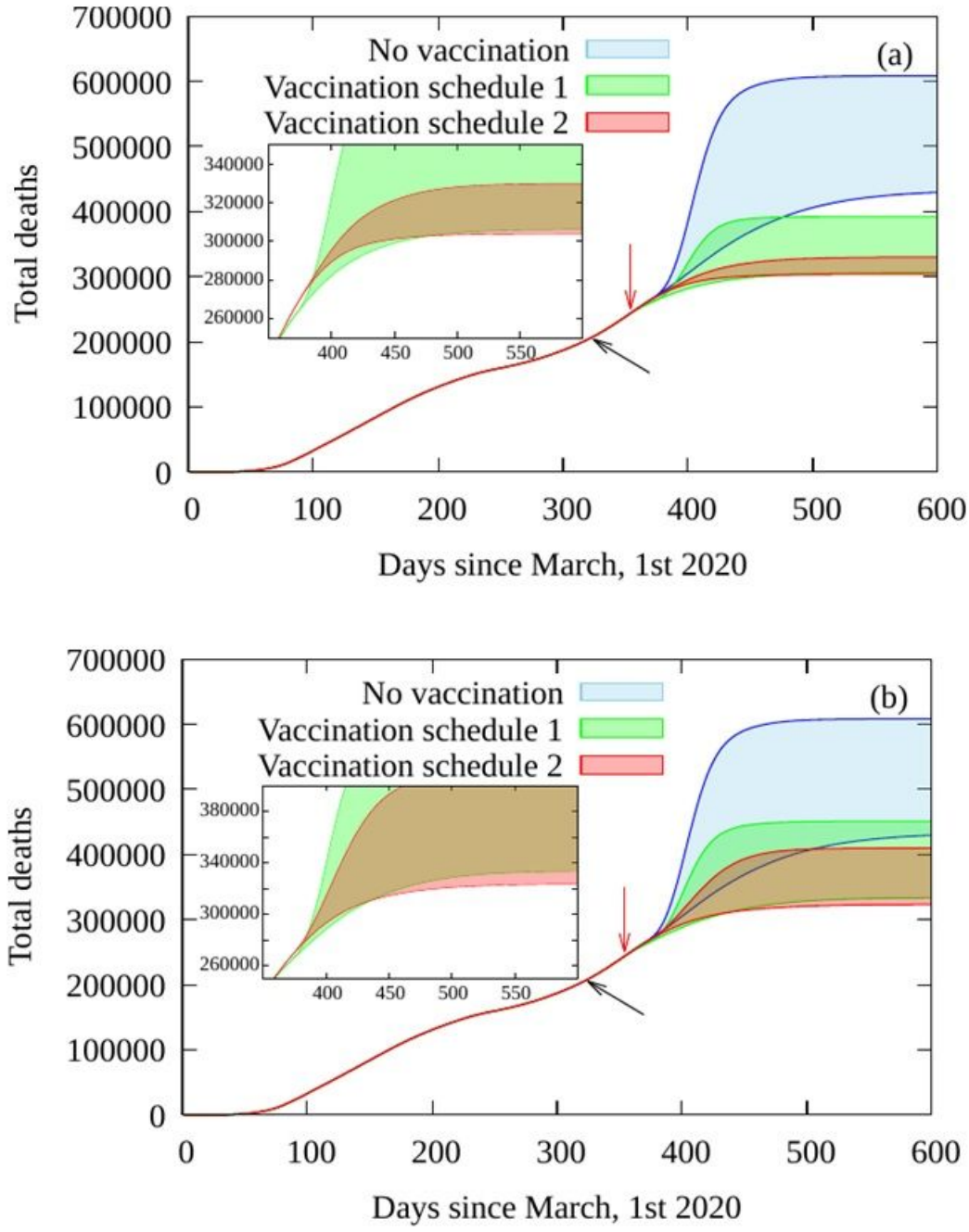

Figure 1

Total number of deaths in Brazil obtained from the fitted model (see supplementary information). The results correspond to the application of the epidemiological model, with two vaccine efficacy scenarios a) ev=95% and b) ev=70%. The black arrow indicates the beginning of each vaccination schedule and the red arrow indicates the moment when the superspreaders return to full activity, with 3 to 10 times more contacts than typically for its age group (30 to 39 years old). The shaded blue area gives the prognostics in the absence of any vaccination, delimited by the contact factors 3 and 10 (see text), which also delimit the green and red regions. The green area gives the prognostics with vaccination starting with 60 years and older individuals and then

vaccinating the remaining population in descending order of age group (vaccination schedule 1). The red region corresponds to the vaccination schedule 2 starting by the superspreaders, and afterwards proceeding in the same order as in the vaccination schedule I. For the prognosis we retained the transmission matrix fitted up to December 15 which corresponds to more stable data and a better fit of the model.

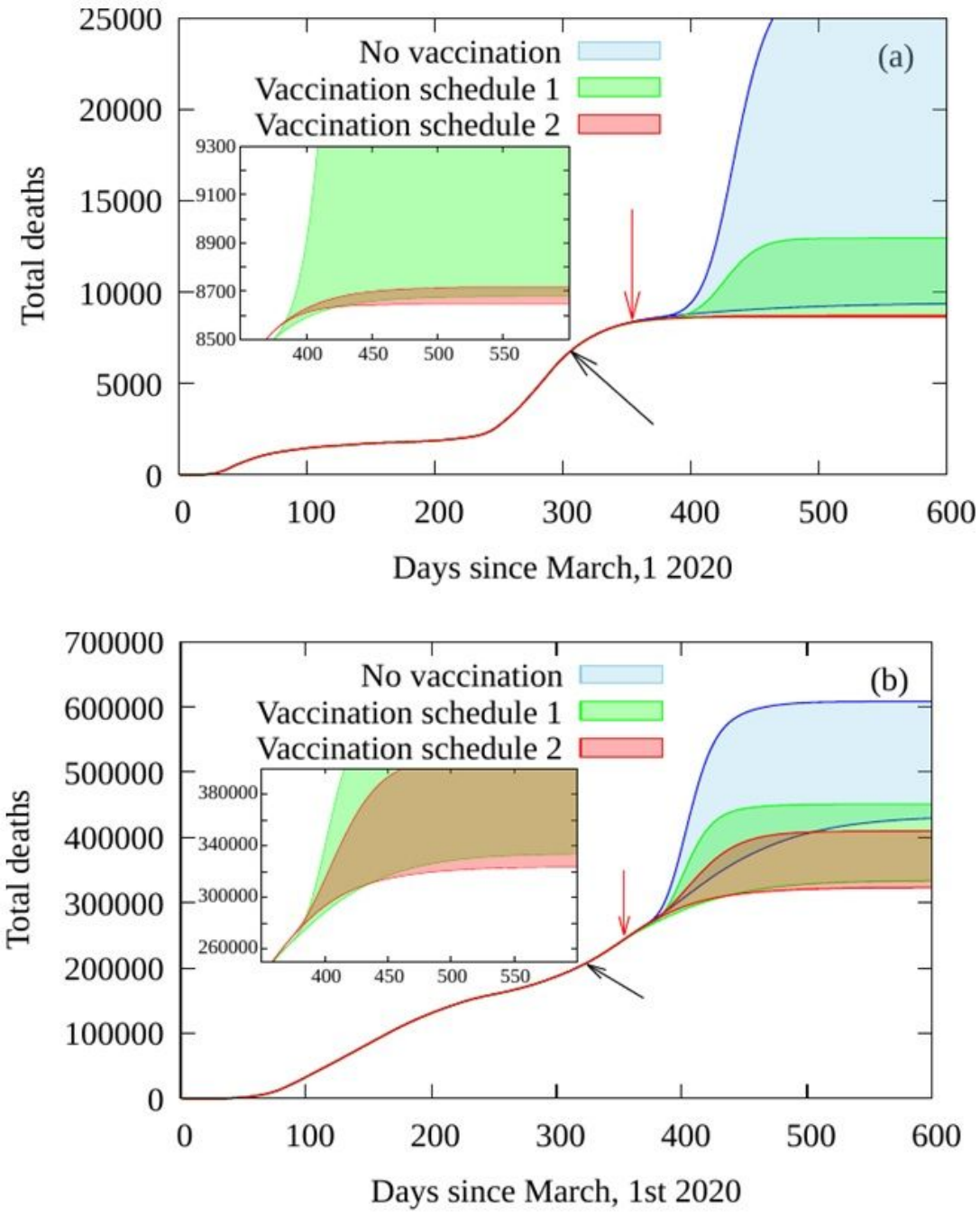

Figure 2

Total number of deaths in Portugal obtained from the fitted model. The results correspond to the application of the model in two vaccine efficacy scenarios a) ev=95% and b) ev=70%. . The shaded areas and arrows follow

the same definitions as in Fig. 1. For performing the predictions we retained the transmission matrix of November, 28, which is closer to the situation in Portugal in January, 10 (see supplementary information).

Supplementary Files

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