AIMS Biophysics

AIMS Biophysics, 11(2): 239–254.
DOI: 10.3934/biophy.2024014
Received: 06 April 2024
Revised: 28 May 2024
Accepted: 17 June 2024
Published: 26 June 2024

http://www.aimspress.com/journal/biophysics

Research article

COVID19 vaccines as boosters or first doses: simulating scenarios to minimize infections and deaths

Omar El Deeb[1,*] and Joseph El Khoury Edde[2]

[1] Department of Mathematics, University of Warwick, United Kingdom
[2] Gilbert and Rose-Marie Chagoury School of Medicine, Lebanese American University, Lebanon

* **Correspondence:** Email: omar.el-deeb@warwick.ac.uk.

Abstract: Public health authorities face the issue of optimal vaccine distribution during the spread of pandemics. In this paper, we study the optimal way to distribute a finite supply rate of COVID-19 doses between either the first or second doses for unvaccinated individuals and the third doses (booster shots) for fully vaccinated individuals. We introduce a novel compartmental model that accommodates the vaccinated populations. This Booster model is implemented to simulate two prototypes of populations: one with a highly infected and highly vaccinated proportion, and another with a lowly infected and lowly vaccinated percentage. We namely use sample data from Russia and Djibouti, respectively.

Our findings show that around one quarter of the vaccines should be employed as booster shots and the rest as first and second doses to minimize the deaths for the first type of population. On the other hand, the second type of population can minimize their number of deaths by mainly focusing on administering the initial two doses, rather than giving any booster shots. The novel Booster model allows us to study the effect of the third dose on a community and provides a useful tool to draw public policies on the distribution of vaccines during pandemics.

Keywords: COVID-19; vaccination; booster shot; compartmental model; simulation

1. Introduction

Throughout history, mankind has faced numerous pandemics, causing health, economic, and political crises around the globe. Although these pandemics resulted in hundreds of millions of deaths,

in hindsight, these catastrophes motivated research that gave rise to major breakthroughs in the related public health and medical fields. The Coronavirus disease 2019 (COVID-19) was proclaimed a global pandemic in March of 2020 after spreading worldwide, starting from China, where the first case appeared in December 2019, then Italy and Iran, and subsequently the whole world. The most common symptoms of infection included fever or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, loss of taste or smell, and so on. This is caused by the airborne SARS-CoV-2 virus, which is responsible for over 692 million confirmed cases and 6.9 million deaths globally as of July 2023 [1]. Governments around the world were obliged to enforce strict measures to mitigate the spread of this contagion, resulting in adverse effects on people's lives and routines. Since the beginning of the COVID-19 pandemic, the SARS-CoV-2 virus has mutated numerous times. In most cases, the changes made to the genetic material led to little to no impact on the properties of the virus itself. However, some mutations may lead to the formation of variants of concern (VOCs), which are classified as mutations of viruses that have proven to increase the transmissibility of the virus, increase the severity of the disease, and decrease the effectiveness of vaccines and other medical treatments [2]. There have been multiple cases of VOCs that originated from different countries around the world at different times, such as the Alpha variant from the United Kingdom in September 2020, the Delta variant from India in October 2020, and the Omicron variant from South Africa in November 2021 [3].

The pharmaceutical industry has developed multiple forms of vaccines approved by the World Health Organization and other national health agencies. Each vaccine uses a specific approach to enhance the immune system's response against the virus. There are genetic vaccines that contain a segment of the virus, inactivated vaccines that contain a killed sample of the Sars-CoV-2 virus, attenuated vaccines that contain a weakened virus, and protein vaccines that contain different protein fragments of the virus [4]. Additional studies are currently investigating different forms of vaccines, such as dry vaccines and antiviral drugs [5]. Previous studies have shown that the effectiveness of the Moderna vaccine is around 93% two weeks after the second dose; similarly, the effectiveness remains around 92% 4 months after full vaccination. While the Pfizer-BioNTech vaccine starts off with 91% efficacy 2 weeks after the second dose, it slightly loses effectiveness with time to reach 77% efficacy 4 months after the second dose. Finally, Johnson & Johnson, which is a one-dose vaccine, was shown to have a 71% vaccine effectiveness two weeks after vaccination, and a 68% effectiveness one month after vaccination [6].

Attempting to predict the number of active cases at any point in the future for any given set of initial conditions is important, since a recent study has shown that approximately 2% of the COVID-19 cases were admitted to the hospital [7]. Therefore, if the number of cases drastically increases, then the number of infected individuals in need of hospitalization due to COVID-19 may exceed the hospital's capacity to admit these patients.

The aim of this study is to predict the spread of infectious diseases, specifically COVID-19, and to explore the optimal use of a limited availability of vaccines by examining various proportions of vaccine doses that can be used for different initial conditions. The study investigates the expected number of active cases, deaths, as well as the number of hospitalized patients due to the COVID-19 pandemic, during which the available vaccines are either administered as boosters for previously vaccinated individuals or as first and second doses for unvaccinated individuals. The results of this study are important, as the world still faces the imminent threat of the emergence of new variants and new viruses that may cause a resurgence in the pandemic, with a limited supply of vaccines that would

ultimately be available to fight them. Prioritizing the administration of vaccines for a specific group or another would be a very important factor to draw public policies by health authorities across the globe.

2. Literature review

Mathematical modeling of infectious diseases is a lively interdisciplinary field of research that brings together researchers from biology, epidemiology, mathematics, statistics, physics, and medicine. These models allow researchers to forecast, predict, and quantify the uncertainty of their forecasts.

The first compartmental model used was the SIR model, created by Kermack and McKendrick in 1929, which splits the population into 3 compartments: Susceptible (S), Infected (I), and Removed (R) [8]. This model was later modified to consider other factors such as undetected infections, environmental factors, traveling, lockdown, non-pharmaceutical treatments, and vaccinations. Environmental factors are incorporated into the model to understand their impact on the viability and transmission of pathogens, thus allowing researchers to simulate seasonal variations in the disease spread. To account for travel effects, SIR models are extended to spatial models, which divides populations into distinct geographical regions and considers patterns of human movement between these areas. This integration of travel data enables the assessment of how population mobility influences the spread of infectious diseases. Moreover, SIR models are invaluable for evaluating the impact of lockdown measures on disease transmission. By modeling interventions such as social distancing, quarantines, and the closure of public spaces, researchers can assess the effectiveness of various strategies in slowing down the spread of the disease. Adjusting parameters, such as contact rates between individuals based on the severity and duration of lockdown measures, allows for the simulation of different scenarios to predict their influence on the epidemic's course [9,10]. Additionally, SIR models are employed to analyze the effects of vaccination on disease dynamics. Researchers can simulate the vaccination of susceptible individuals, thereby altering the parameters to reflect the coverage, efficacy, and timing of vaccination campaigns. This helps assess the potential impact of vaccination in reducing the overall transmission and severity of the disease within the population [11−16].

The issue of optimizing vaccine distribution was considered under several constraining scenarios. In [17], the authors argue that, under sufficient resources, the optimal strategy is to apply the administration of vaccines as quickly as possible to as many people as possible without much regard for nuanced targeting or prioritization, which is also known as the Bang-Bang control strategy. However, with limited resources, they conclude that time-variant vaccinations would be more efficient. Limited vaccines and time delays were also studied in [18], and the tradeoffs were investigated to minimize the severity of the pandemic by prioritizing vaccination to particular sub-populations. Vaccine prioritization studies focused on several key criteria tailored to the disease, vaccines, and the target population. Prioritization typically begins with assessing the risk of severe disease cases and death, favoring groups such as older adults, individuals with underlying health conditions, and those with compromised immune systems [19−21]. Exposure risk plays a significant role, thus prompting prioritization for frontline workers, healthcare personnel, and those in crowded or high-risk settings [22]. The transmission dynamics inform decisions to vaccinate individuals who are more likely to spread the disease, such as school-age children or those with frequent social interactions [23]. Moreover, the healthcare system capacity, ethical principles, public health impact, and vaccine acceptance are integral, guiding decisions to maximize benefits, minimize harm, and promote justice while optimizing vaccine

distribution to achieve the greatest population health outcomes.

The question of optimizing the distribution of a limited flow of vaccines or a limited timely availability was not properly studied in available literature and its formal analysis constitutes a gap that this work aims to fill.

While studying the durability of the vaccine, it was found that those who were successfully immunized after vaccination had a strong resistance to infection for 6 months, or 180 days, after vaccination [24]. For that reason, countries such as the United States and France have introduced a third shot, or a booster shot, to reimmunize those who have lost their immunity [25,26]. Recent studies revealed a dose-dependent reduction in the percentage of infected individuals within the vaccinated population. The simulation results exhibited a close alignment with real-world data on the infected patients, affirming the appropriateness of the model [27].

3. Methods: the booster model

One of the major topics that needs to be studied in detail is the COVID-19 third dose or booster shot. As mentioned previously, the immunity gained through vaccination is not permanent. In this model, it will be taken at 6 months, or 180 days, in accordance with the latest studies.

However, this immunity can be reacquired through the administration of a single booster shot. Our study introduces a novel approach with the objective of minimizing deaths in two distinct population types. Therefore, a new question arises: Which vaccination scheme leads to less deaths: giving unvaccinated individuals 2 doses, or giving double the number of people, a booster shot? Given the huge disparities in the availability of vaccines among different countries, this issue could also be similarly addressed on the global level. For an ideal scenario of global vaccine equity, would it be more efficient to continue supplying booster shots in countries that already achieved high percentages of vaccination, or should we prioritize allocating these resources to spread the first doses among populations that didn't have enough access into them yet?

$$
\begin{cases}
\frac{dS}{dt} = -\beta(I + I_V)S - (1-\tau)vS & (1)\\
\frac{dS_V}{dt} = (1-\tau)(1-ev_i)vS - \beta'(I + I_V)S_V + 2\tau v(1-ev_i)S_L & (2)\\
\frac{dS_L}{dt} = \frac{\gamma_R I + \gamma_{RV} I_V}{T_{II}} + \frac{(1-\tau)ev_i vS + 2\tau v ev_i S_L}{T_{VI}} - \beta'(I + I_V)S_L - 2\tau v S_L & (3)\\
\frac{dE}{dt} = \beta(I + I_V)S - \sigma E & (4)\\
\frac{dE_V}{dt} = \beta'(I + I_V)(S_V + S_L) - \sigma E_V & (5)\\
\frac{dI}{dt} = \sigma E - (\gamma_D + \gamma_R)I & (6)\\
\frac{dI_V}{dt} = \sigma E_V - (\gamma_{DV} + \gamma_{RV})I_V & (7)\\
\frac{dR}{dt} = (1-\tau)ev_i vS + 2\tau v ev_i S_L + \gamma_R I + \gamma_{RV} I_V - \frac{(1-\tau)ev_i vS + 2\tau v ev_i S_L}{T_{VI}} - \frac{\gamma_R I + \gamma_{RV} I_V}{T_{II}} & (8)\\
\frac{dD}{dt} = \gamma_D I + \gamma_{DV} I_V & (9)
\end{cases}
$$

To answer this question, the *Booster* model was introduced. It is a compartmental model made up of the following 9 compartments: Susceptible (S), Susceptible vaccinated (S_V), Susceptible with lost immunity (S_L), Exposed (E), Exposed Vaccinated (E_V), Infected (I), Infected vaccinated (I_V), Recovered (R), and Dead (D). The *Booster* model can be represented with the following system of ordinary differential equations:

where S is the fraction of the population that is unvaccinated and susceptible to the virus, S_V is the vaccinated susceptible population, E and E_V are the exposed unvaccinated and vaccinated individuals who haven't become infectious yet, respectively, I is the unvaccinated infectious population, I_V is the vaccinated infectious population, R is the recovered population, and D is the dead population.

$\beta = R_t * \gamma_R$ is the effective contact rate between the infected individuals ($I + I_V$) and the unvaccinated susceptible individuals S; likewise, $\beta' = R_t * \gamma_{RV}$ is the contact rate between the infected individuals and the vaccinated susceptible individuals $S_V.e$ is the efficiency of the vaccine, v_i is the maximum possible vaccine intake, and v is the abundancy or roll out rate of the vaccine. $\gamma_R = 1/14$ and $\gamma_D = \gamma_R/50$ are the average rate of recovery and death of unvaccinated individuals, respectively. The recovery rate is inversely related to an average of a 14 day infection duration [28], while the death rate amounts to about 2% or 1/50 of the infected individuals [1].

Similarly, $\gamma_{RV} = \gamma_R$ and $\gamma_{DV} = \gamma_D/5$ are the average rates of the recovery and death of vaccinated individuals, respectively. The vaccinated individuals would need a similar time for recovery, while the death rate among vaccinated individuals was about 20% or 1/5 of that among the unvaccinated [29]. σ is the rate at which the exposed individuals become infected, and it is associated to the mean incubation period, which is taken to be $\frac{1}{5.2}$ in relation to a 5.2 day average incubation period [10]. T_{II} = 360 $days$ and T_{IV} = 180 $days$ are the average lengths of immunity after infection and vaccination, respectively [30]. Finally, τ is the proportion of vaccine doses used as booster shots. For example, if τ = 0.75, then three quarters of the vaccines are booster shots, while the remaining 25% are used as either the first or second doses.

Notice that there is $2\tau v S_L$ rather than $\tau v S_L$ in the 3rd and 8th equation. This is because only one dose is required to give the booster shot to people who lost their immunity. Contrarily, 2 doses are needed to fully vaccinate unvaccinated individuals. As a result, half the doses are required to give booster shots; therefore, the rate at which the booster shots are given to the public should be twice the rollout rate to the unvaccinated population, thereby explaining the presence of a factor of 2.

To visualize the interaction between different compartments, we graphically illustrate them in Figure 1.

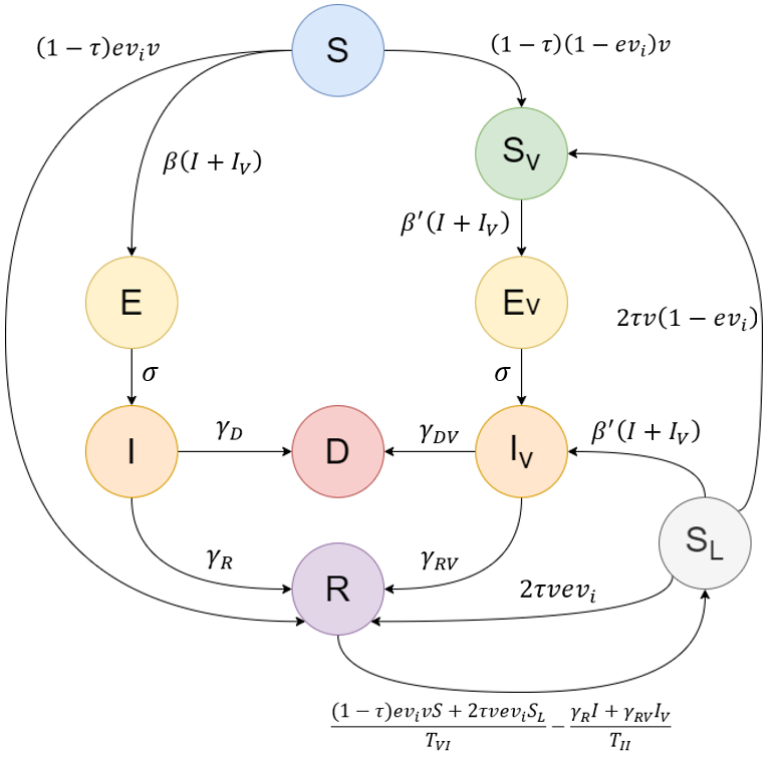

Figure 1. Schematic diagram showing the 7 compartments of the Booster model: Susceptible (S), Susceptible Vaccinated (S_V), Susceptible with Lost immunity (S_L), Exposed (E), Exposed Vaccinated (E_V), Infected (I), Infected Vaccinated (I_V), Recovered (R), and Dead (D) - along with the transfer dynamics between them.

In order to apply the model to real life scenarios, two populations are taken as the prototypes: Russia and Djibouti. Russia is used to simulate the dynamics of COVID-19 in a population with a relatively high infection and vaccination rate, while Djibouti is used to model COVID-19 spread in a population with a low infection and vaccination rate.

Throughout the study, nine vaccination schemes were tested, with vaccine efficacies (e) ranging between 55% and 92% [16], and a vaccine abundancy or rollout rate (v) ranging between 0.1% and 1.5%. The schemes tested were as follows: $e = 92\%$ and $v = 0.1\%$, $e = 92\%$ and $v = 0.3\%$, $e = 92\%$ and $v = 0.5\%$, $e = 72\%$ and $v = 0.3\%$, $e = 72\%$ and $v = 0.5\%$, $e = 72\%$ and $v = 0.7\%$, $e = 55\%$ and $v = 0.7\%$, $e = 55\%$ and $v = 1\%$, and $e = 55\%$ and $v = 1.5\%$, with the vaccine intake assumed to be $v_i = 90\%$ for all scenarios.

4. Results and discussion

In mid-February 2022, there was a total of 2,668,036 active cases in Russia. Therefore, with a total population of 143.4 million, the percentage of the infected individuals was 1.84%. At that time, COVID-19 was the cause of 340,248 deaths in Russia, or 0.23% of the Russian population. In mid-February, there were 71.32 million individuals, or 49.74% of the Russian population, who were fully vaccinated. However, 6 months prior, there were 32.43 million (22.62%) double vaccinated individuals; therefore 22.62% of the Russian population have probably lost their immunity after vaccination,

leaving 27.12% that are currently immune [1].

Table 1. A summary of the parameters used in the model and their numerical values.

Parameter	Description	Value	Source
γ_R	Rate of recovery	$\frac{1}{14}$ day^{-1}	[28]
γ_D	Rate of death	$\frac{1}{50}$ day^{-1}	[1]
γ_{RV}	Rate of recovery of the vaccinated	γ_R	[29,30]
γ_{DV}	Rate of death of the vaccinated	$\frac{\gamma_D}{5}$	[29,30]
σ	Rate of infection of the exposed	$\frac{1}{5.2}$ day^{-1}	[10]
T_{II}	Duration of natural immunity	365 days	[31]
T_{IV}	Duration of acquired immunity	180 days	[31]
e	Vaccine efficacy	$55\% - 92\%$	[16]
v_i	Maximum Vaccine reach	90%	Assumed
ν	Vaccine deployment rate	$0.1\% - 1.5\%$ day^{-1}	Assumed
R_t	Transmission coefficient	1.5	Simulated
τ	Proportion of booster vaccines	0%−100%	Simulated

According to the data obtained in Figure 2, if the vaccination scheme consists of vaccines with a high efficacy (e = 92%), it is better to use all the vaccine doses to fully vaccinate unvaccinated individuals. This can be seen in the top row of the above Figure, as the curve resulting with the lowest number of cumulative deaths was achieved with a value of τ = 0. However, when the efficacy of the vaccine decreases, the significance of the third dose increases. Hence, if a vaccine has a low efficacy (e = 55%), the optimal value of tau is τ = 0.25; if a vaccine has a moderate efficacy (e = 72%), both τ = 0 and τ = 0.25 were equally effective in decreasing mortality.

In addition to that, the Figure also shows that the roll out rate of the vaccine has an important impact on the percentage of cumulative deaths. For any given efficacy of the vaccine, when the rollout rate increases, the cumulative deaths decrease.

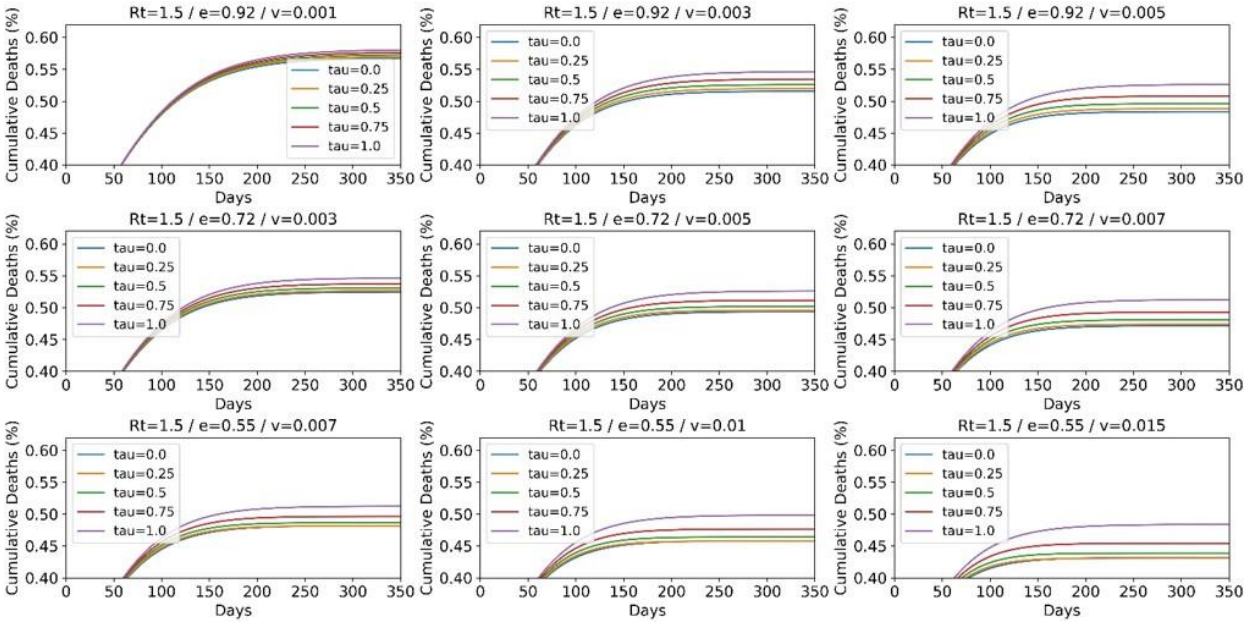

Figure 2. Graphs showing the percentage of cumulative deaths in a population with infection characteristics similar to those of Russia with a transmission coefficient of $R = 1.5$ with initial conditions: 1.84% currently infected and currently exposed, 27.12% currently immune, 22.62% currently susceptible with lost immunity, 0.23% currently dead. Data collected using the following 9 vaccination schemes: e = 92% and $v = 0.1\%, e = 92\%$ and $v = 0.3\%, e = 92\%$ and $v = 0.5\%, e = 72\%$ and $v = 0.3\%, e = 72\%$ and $v = 0.5\%, e = 72\%$ and $v = 0.7\%, e = 55\%$ and $v = 0.7\%, e = 55\%$ and $v = 1\%, e = 55\%$ and $v = 1.5\%$, with $v_i = 90\%$.

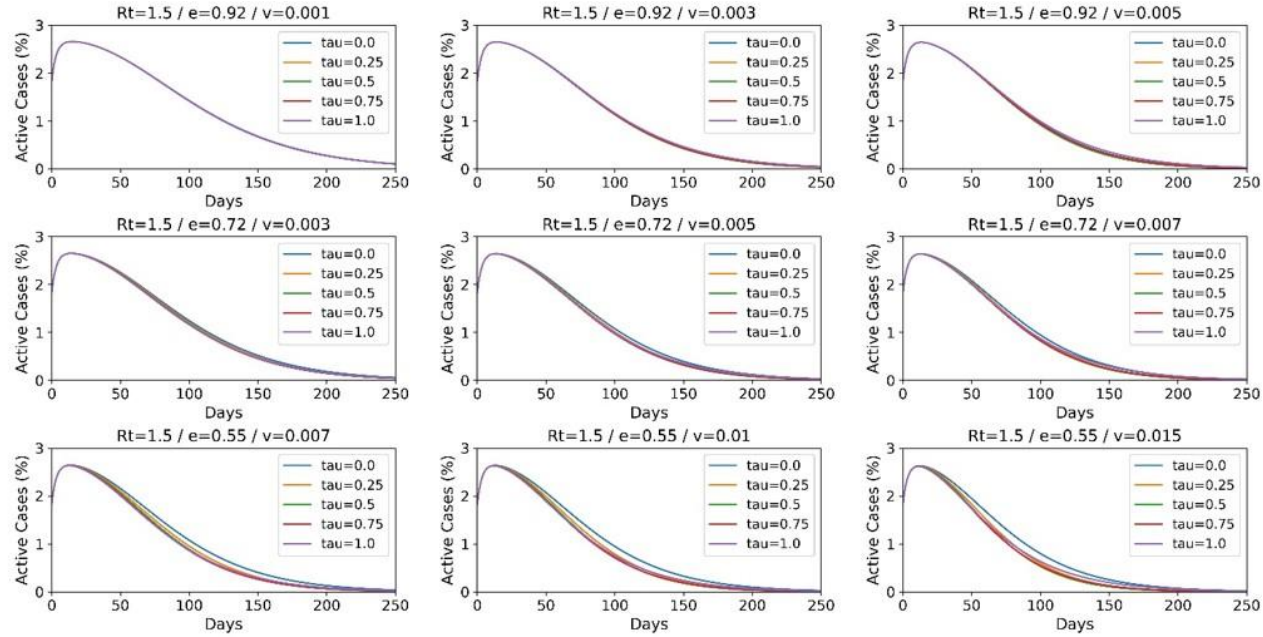

Figure 3. Graph showing the percentage of active cases in a population similar to Russia. Initial conditions and vaccination schemes are the same as those used in Figure 2.

To accurately study the dynamics of the spread of COVID-19 in a population, the percentage of active cases should be measured. By using the same initial conditions used in Figure 2, the percentage of active cases can be predicted in populations with high infection and vaccination rates, similar to Russia.

According to Figure 3, all vaccination schemes reach a peak in the active cases shortly after the start of the simulation, then gradually decrease to reach approximately 0 after nearly 200 days. In order to minimize the number of active cases, the optimal value for tau needed is $\tau = 0.5$. This is interesting since $\tau = 0.5$ does not correspond to the least percentage of cumulative deaths in Figure 2.

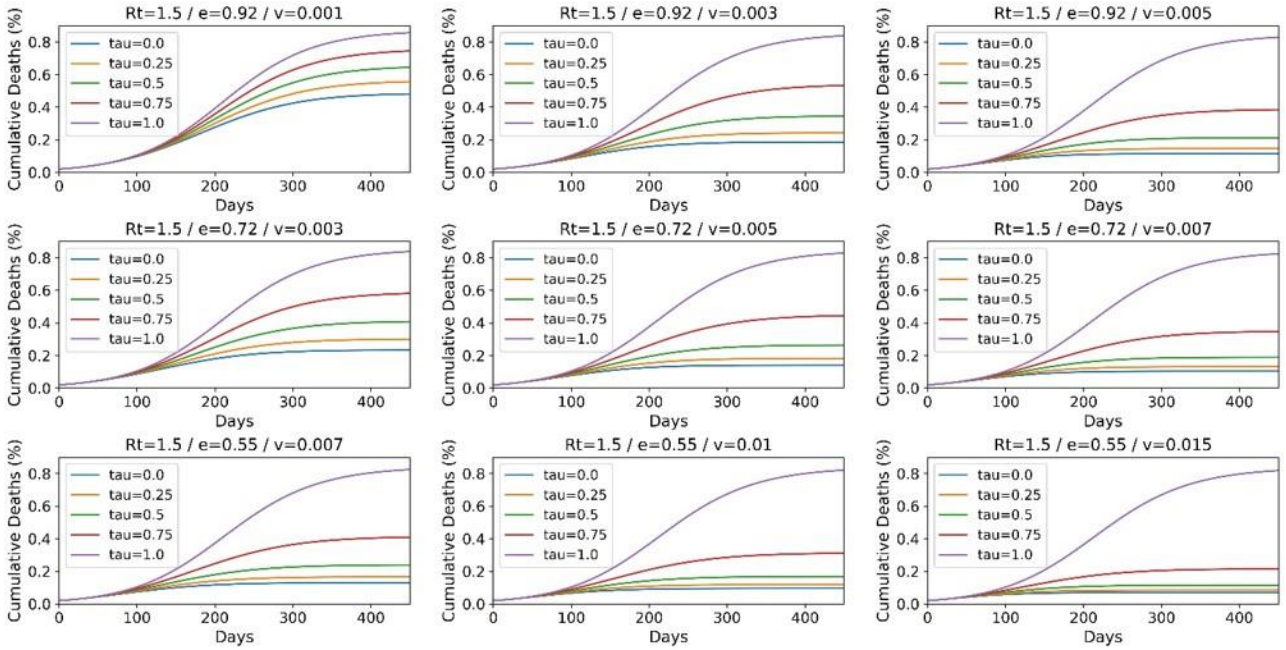

Figure 4. Graph showing the percentage of cumulative deaths in a population similar to that of Djibouti with a transmission coefficient of $R = 1.5$ with initial conditions: 0.18% currently infected and equally currently exposed, 7.64% currently immune, 2.33% currently susceptible with lost immunity, 0.02% currently dead. The data collected was collected using the same vaccination schemes as Figure 2.

In Djibouti, there was a total of 2,017 active cases in early April 2022. Therefore, with a total population of 1.1 million, the percentage of currently infected individuals is 0.18%. At that time, COVID-19 was the cause of 189 deaths in Djibouti, or 0.02% of the population. In April, 9.97% of the population was fully vaccinated. However, 6 months prior, there were 2.33% double vaccinated individuals; therefore 2.33% of the population have probably lost their immunity after vaccination, leaving 7.64% that are currently immune [32].

In contrast to the graphs obtained in Figure 2, all the graphs in Figure 3 show the same trend, which is that when the proportion of vaccine doses used as the third dose decreases, the percentage of cumulative deaths also decreases. Consequently, the optimal value of tau that achieves the lowest percentage of deaths is $\tau = 0$. However, Figures 2 and 3 share one finding, which is that as the roll out rate of vaccines increases, the percentage of deaths decreases.

By graphing the percentage of active cases in a population similar to Djibouti, the following

graphs are obtained in Figure 5.

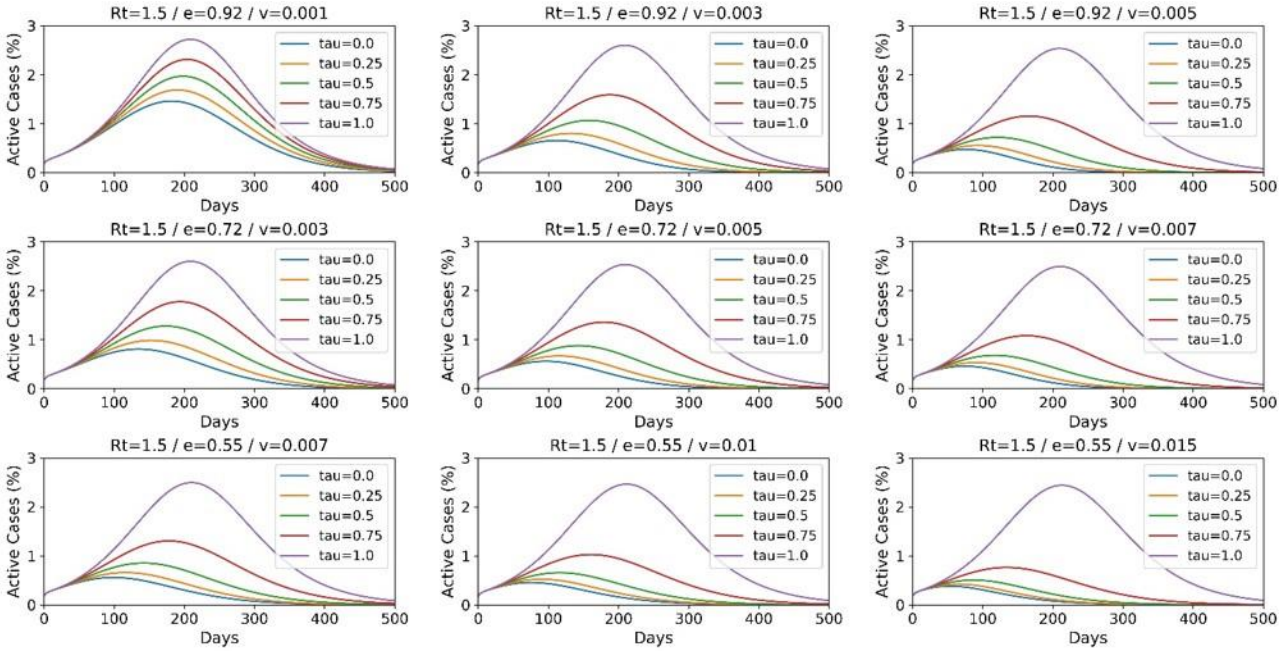

Figure 5. Graph showing the percentage of active cases in a population similar to that of Djibouti. The data collected was collected using the same initial conditions and vaccination schemes as Figure 4.

Figure 5 shows that in all vaccination schemes, the percentage of active cases reaches a peak around 200 days for $\tau = 1$, reaching around 2.5% of the total population. However, as the proportion of vaccines used as the third dose decreases, the peak of the percentage of active cases decreases in amplitude and is shifted to the left. Therefore, it can be concluded that for a population with a low infection and vaccination rate, the optimal way to reduce the active cases is by using all the available doses to give two doses to the unvaccinated individuals.

In addition to that, the roll out rate seems to play an important role in decreasing the peak of active cases. As seen in the bottom-right graph, which corresponds to a vaccination scheme with a 55% efficacy and the highest roll out rate of 1.5%, the peak for the optimal tau value of $\tau = 1$ was obtained at around day 50 with an amplitude of approximately 0.3%.

These findings are crucial in order to minimize the burden of infectious diseases such as COVID-19 on medical care sectors. As previously mentioned, around 2% of the COVID-19 patients were hospitalized [6]; therefore, by decreasing the amplitude of the peaks, there will be fewer hospitalized patients at any given moment.

Many previous studies have analyzed the spread of COVID infections in Russia and, to a lesser extent, in Djibouti. However, they mostly relied on analyzing and forecasting spreads using SIR (Susceptible -Infected-Recovered) and SEIR (Susceptible-Exposed-Infected-Recovered) models without introducing the effects of vaccination [33−36]. With the introduction of massive vaccination campaigns worldwide, including these two countries, the incorporation of vaccination models became essential to understand the spreads. In particular, vaccinations would decrease and may even prohibit the spread, leading to a huge reduction in infection, hospitalization, and deaths. Models incorporating

vaccination dynamics offer a more nuanced understanding of the disease spread compared to traditional compartmental models such as SIR or SEIR. By accounting for vaccination processes, such models can simulate factors such as vaccine efficacy, coverage, and distribution, thus providing a more realistic portrayal of how vaccinations can impact the disease transmission and immunity over time. This adaptability allows policymakers to assess various intervention strategies, from vaccination campaigns to booster doses, and make informed decisions to effectively curb the spread of infectious diseases. Our analysis added another aspect to be considered by policymakers, whether in these two countries or in other countries with similar conditions, which is the optimal allocation of a limited flow of vaccines among those in need for a booster or a first dose.

Sensitivity analysis: In this paragraph, we analyze the sensitivity of our prototype model with respect to variations in the basic reproductive number R_t. In our study, we simulated various spread scenarios under different vaccination schemes, with a moderately reproductive value for $R_t = 1.5 > 1$, which assumed an increased spread pattern. However, the reproductive number representing the average number of secondary infections produced by a single infected individual in a fully susceptible population directly depends on the contact rates and the acquired and natural immunities; hence, it represents a changing parameter that gets influenced by external factors such as mitigation measures, closures, awareness, and vaccination levels.

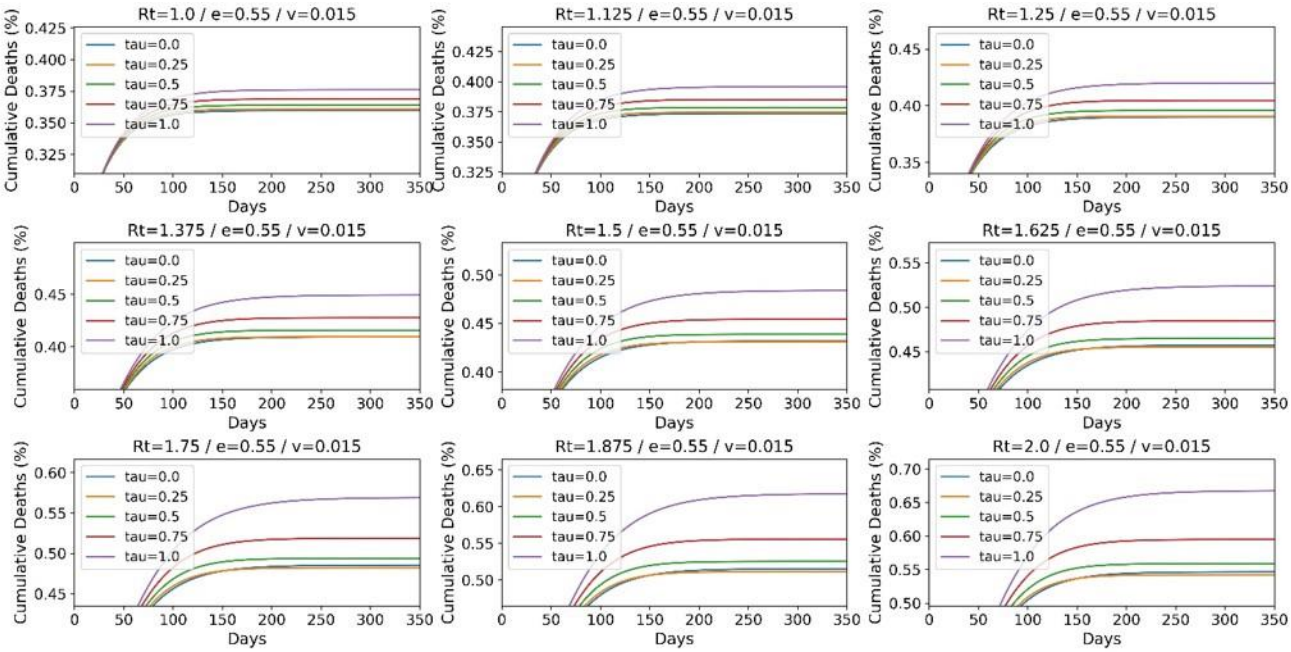

Figure 6. Sensitivity analysis of cumulative deaths with respect to variations in R_t in Russia under the conditions of vaccine efficacy $e = 0.55$ and daily deployment rate $v = 1.5\%$ of population.

To analyze the sensitivity of our model to changes in the reproductive number, we simulated a range of values corresponding to $1 \leq R_t \leq 2$, ranging from the threshold value of spread up to a rapid spreading scenario. We applied this for each country under consideration, namely Russia and Djibouti, while deploying vaccines of efficacy $e = 0.55$ at a deployment rate of $v = 1.5\%$ of the population per day. These results are displayed in Figure 6 and Figure 7, respectively.

The main findings from this sensitivity analysis can be summarized as follows:

1. The number of cumulative deaths in both countries under all considered scenarios were positively correlated to R_t, as expected, with an increased total number of deaths alongside an increased R_t.
2. The second interesting sensitivity result is that in a country with a high number of previous infections and vaccinated people such as Russia, the optimal value of τ, which is the proportion of administered booster doses, depends on the value of the reproductive number. In particular, for smaller values of $(R_t \leq 1.375)$, it would be more optimal to distribute all vaccines as the initial doses. Altenatively, for $R_t > 1.375$, a quarter of these doses would better be assigned as booster shots. The optimal prioritization scheme is sensitive for a changing R_t and the optimal strategy is R_t-dependent.
3. In a country with a low level of infection and vaccinated people such as Djibouti, it would always be better to totally spread the vaccines as first doses, for all values of R_t under consideration. The prioritization scheme is not sensitive to this range of variation in the reproductive number.

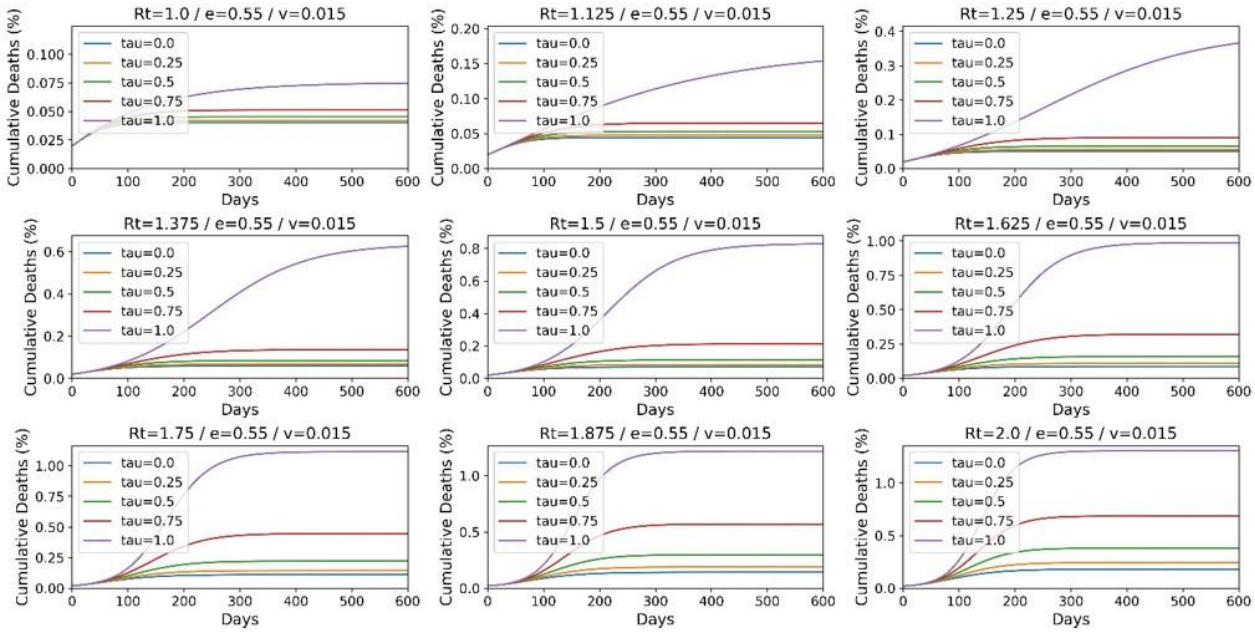

Figure 7. Sensitivity analysis of cumulative deaths with respect to variations in R_t in Djibouti under the conditions of vaccine efficacy $e = 0.55$ and daily deployment rate $v = 1.5\%$ of population.

This sensitivity analysis on the infections and deaths in relation to the basic reproduction number (R_t) in epidemiological models is essential for effective public health planning. It identifies which factors most influence the infection rates and mortality, thus allowing for precise adjustments in response strategies and assists in optimizing interventions, such as vaccinations, to reduce disease transmission and fatalities, ultimately enhancing the effectiveness of public health measures during an outbreak.

The model equations (1−9) and all related Figures (2−7) were coded, solved, and plotted in Python. The codes are publicly available at the following link: https://github.com/JE-1/COVID_codes.

5. Limitations

In this study, we introduced a novel model to simulate the expected results of using vaccine shots as either boosters or as first doses. However, in this *Booster* model, there are still gaps and limitations that stand in the way of this model accurately representing the dynamics of infectious spreads in certain communities.

The maximum possible vaccine intake percentage is an important factor in analyzing and forecasting infection and death scenarios related to COVID19 and its related vaccination programs. In this study, we assumed that we were dealing with populations that would achieve around 90% vaccination rate. Though this was achieved across many countries across the world, it would be important to further continue this study and simulate different values for this parameter. This would account for populations that may be affected by anti-vaccination rhetoric and campaigns, or for poorer countries that may not have the logistics to widely spread the vaccine. A separate simulation for v_i could be the goal of future studies.

Another important factor is that the transmission coefficient is also sensitive on mitigation measures and may vary depending on specific implementations of social distancing, cleanliness, face masks, and other mitigation schemes.

Several limitations and biases may arise due to neglecting individual heterogeneity in the model dynamics. On the transmission dynamics level, differences in susceptibility, infectiousness, and behavior can significantly impact the spread within a population. Intervention strategies that fail to account for individual heterogeneity would not ultimately achieve the intended outcomes. For instance, interventions that target the general population may be less effective than targeted strategies focused on high-risk groups. Population characteristics, such as age distribution, comorbidities, and social networks, can widely vary between populations; failing to account for these differences can lead to models that are less applicable outside of the specific context in which they were developed. Finally, in the realm of vaccine prioritization, tackling specific vulnerable populations, such as the elderly and those carrying chronic diseases, specifically with booster shots in case of limited resources, could also prove effective enough to minimize deaths. This alternative was not addressed in our study.

6. Conclusions

The new *Booster* model allowed us to study the effect of a third vaccination dose on a community. It allowed us to find the optimal percentage of COVID-19 doses that should be administered as booster shots, rather than being used as either first or second shots for unvaccinated individuals.

The obtained results show that for communities with a relatively high number of individuals that have lost their immunity after vaccination or after recovery from infection, allocating around 25% of the vaccines as third doses should lead to the lowest percentage of cumulative deaths. On the other hand, a population with a relatively low portion of individuals with lost immunity would find more benefit from vaccinating the susceptible unvaccinated individuals, rather than reimmunizing those who have received the first and second doses.

Our model and results have important potential for tackling real world problems and informing policy makers on efficient strategies. In our prototype example, we could advise health officials in one country to dedicate a quarter of their vaccine resources for boosters in case there is still need for first doses, while calling for full dedication to first doses in another country with different infection

conditions. In this sense, this model is generic and flexible and could be implemented to reach optimal distribution scenarios under different needs.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Acknowledgments

The authors are grateful for many useful and constructive comments suggested by two anonymous reviewers.

Conflict of interest

The authors declare no conflict of interest.

Author contributions

EE J. performed the simulations and coding and wrote the first draft. ED O. designed the study and wrote the final draft.

References

1. Worldometer, COVID-19 Coronavirus Pandemic, 2023. Available from: https://www.worldometers.info/coronavirus/.
2. CDC, SARS-CoV-2 Variant Classifications and Definitions, Centers for Disease Control and Prevention, 2021. Available from: https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-classifications.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fvariants%2Fvariant-info.html.
3. Pulliam JR, Van Schalkwyk C, Govender N, et al. (2022) Increased risk of SARS-CoV-2 reinfection associated with emergence of Omicron in South Africa. *Science* 376: eabn4947. https://doi.org/10.1126/science.abn4947
4. British Society for Immunology, A Guide to Vaccinations for COVID-19, British Society for Immunology, 2021. Available from: https://www.immunology.org/sites/default/files/BSI_GuidetoVaccinationsCOVID19_Aug21.pdf.
5. Heida R, Hinrichs WLJ, Frijlink HW (2021) I Inhaled vaccine delivery in the combat against respiratory viruses: a 2021 overview of recent developments and implications for COVID-19. 21: 957−974. https://doi.org/10.1080/14760584.2021.1903878
6. Self WH (2021) Comparative effectiveness of Moderna, Pfizer-BioNTech, and Janssen (Johnson & Johnson) vaccines in preventing COVID-19 hospitalizations among adults without immunocompromising conditions—United States, March–August 2021. Morbidity and Mortality Weekly Report 70: 1337−1343. 10.15585/mmwr.mm7038e1

7. Menachemi N, Dixon BE, Wools-Kaloustian, KK, et al. (2021) How many SARS-CoV-2–infected people require hospitalization? Using random sample testing to better inform preparedness efforts. *J Public Health Man* 27: 246–250. https://doi.org/10.1097/phh.0000000000001331
8. Kermack WO, McKendrick AG (1927) A contribution to the mathematical theory of epidemics. *Proceedings of the Royal Society A* 115: 700−721. https://doi.org/10.1098/rspa.1927.0118
9. Giandhari J, Pillay S, Wilkinson E, et al. (2020) Early transmission of SARS-CoV-2 in South Africa: an epidemiological and phylogenetic report. *Int J Infect Dis* 103: 234−241. https://doi.org/10.1016/j.ijid.2020.11.128
10. El Deeb O, Jalloul M (2020) The dynamics of COVID-19 spread: evidence from Lebanon. *Math Biosci Eng* 17: 618−5632. https://doi.org/10.3934/mbe.2020302
11. Kim YJ, Seo MH, Yeom HE (2020) Estimating a breakpoint in the pattern of spread of COVID-19 in South Korea. *Int J Infect Dis* 97: 360−364. https://doi.org/10.1016/j.ijid.2020.06.055
12. Kharroubi S (2020) Modeling the spread of COVID-19 in Lebanon: a Bayesian perspective. *Front Appl Math Stat* 6: 40. https://doi.org/10.3389/fams.2020.00040
13. El Deeb O, Jalloul M (2020) Forecasting the outbreak of COVID-19 in Lebanon. medRxiv https://doi.org/10.1101/2020.09.03.20187880
14. Hattaf K, Yousfi N (2020) Dynamics of SARS-CoV-2 infection model with two modes of transmission and immune response. *Math Sci Eng* 17: 5326−5340. https://doi.org/10.3934/mbe.2020288
15. Abou Hassan F, Bou Hamdan M, Ali F, et al. (2023) Response to COVID- 19 in Lebanon: update, challenges and lessons learned. *Epidemiol Infect* 151: 23. https://doi.org/10.1017/S0950268823000067
16. El Deeb O, Jalloul M (2021) Efficacy versus abundancy: comparing vaccination schemes. *PLoS One* 17: e0267840. https://doi.org/10.1371/journal.pone.0267840
17. Zhou Y, Yang K, Zhou K, et al. (2014) Optimal vaccination policies for an SIR model with limited resources. *Acta Biotheor* 62: 171−181. https://doi.org/10.1007/s10441-014-9216-x
18. Nguyen C, Carlson J (2016) Optimizing real-time vaccine allocation in a stochastic SIR model. *PLoS One* 11: e0152950. https://doi.org/10.1371/journal.pone.0152950
19. Colombo R, Garavello M (2019) Optimizing vaccination strategies in an age structured SIR model. *Mat Biosci Eng* 17: 1074−1089. https://doi.org// 10.3934/mbe.2020057
20. Wang X, Wu H, Tang S (2022) Assessing age-specific vaccination strategies and post-vaccination reopening policies for COVID-19 control using SEIR modeling approach. *B Math Biol* 84: 108. https://doi.org/10.1007/s11538-022-01064-w
21. Campos E, Cysne R, Madureira A, et al. (2021) Multi-generational SIR modeling: determination of parameters, epidemiological forecasting and age-dependent vaccination policies. *Infect Dis Model* 6: 751−765. https://doi.org/10.1016/j.idm.2021.05.003
22. Rao I, Brandeau M (2021) Optimal allocation of limited vaccine to control an infectious disease: Simple analytical conditions. *Math Biosci* 337: 108621. https://doi.org/10.1016/j.mbs.2021.108621
23. Gavish N, Katriel G (2022) The role of childrens' vaccination for COVID-19—Pareto-optimal allocations of vaccines. *PLoS Comput Biol* 18: e1009872. https://doi.org/10.1371/journal.pcbi.1009872
24. Collier AY, Yu J, McMahan K, et al. (2021) Differential kinetics of immune responses elicited by Covid-19 vaccines. *New Engl J Med* 385: 2010–2012. https://doi.org/10.1056/nejmc2115596

25. The Connexion (2021) France to give third Covid vaccine dose to those with immunodeficiency. https://www.connexionfrance.com/article/French-news/France-to-give-third-Covid-vaccine-dose-to-those-with-immunodeficiency
26. Krause PR, Fleming TR, Peto R, et al. (2021) Considerations in boosting COVID-19 vaccine immune responses. *The Lancet* 398: 1377−1380. https://doi.org/10.1016/S0140-6736(21)02046-8
27. Theparod T, Kreabkhontho P, Teparos W (2023) Booster dose vaccination and dynamics of COVID-19 pandemic in the fifth wave: an efficient and simple mathematical model for disease progression. *Vaccines* 11: 589. https://doi.org/10.3390/vaccines11030589
28. Center for Disease Control and Prevention (CDC), Interim Guidance on Ending Isolation and Precautions for Adults with COVID-19, 2021. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html.
29. Lacobucci G (2021) Covid-19: Single dose of Pfizer and Oxford vaccines cuts risk of hospital admission by 80% in over 80s, data suggest. *BMJ* 372: n612. https://doi.org/10.1136/bmj.n612
30. Bernal JL, Andrews N, Gower C, et al. (2021) Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. *BMJ* 373: n1088. https://doi.org/10.1136/bmj.n1088
31. Moghadas SM, Vilches TN, Zhang K, et al. (2021) The impact of vaccination on Coronavirus disease 2019 (COVID-19) outbreaks in the United States. *Clin Infect Dis* 12: 2257−2264. https://doi.org/10.1093/cid/ciab079
32. Mathieu E, Coronavirus (COVID-19) Vaccinations, Our World in Data, 2000. Available from: https://ourworldindata.org/covid-vaccinations.
33. Tomchin DA, Fradkov AL (2020) Prediction of the COVID-19 spread in Russia based on SIR and SEIR models of epidemics. *IFAC-PapersOnLine* 53: 833−838. https://doi.org/10.1016/j.ifacol.2021.04.209
34. Kudryashov N, Chmykhov M, Vigdorowitsch M (2021) Analytical features of the SIR model and their applications to COVID-19. *Appl Math Model* 90: 466−473. https://doi.org/10.1016/j.apm.2020.08.057
35. Sharov K (2020) Creating and applying SIR modified compartmental model for calculation of COVID-19 lockdown efficiency. *Chaos, Solitons Fractals* 141: 110295. https://doi.org/10.1016/j.chaos.2020.110295
36. Takele R (2020) Stochastic modelling for predicting COVID-19 prevalence in East Africa Countries. *Infect Dis Model* 5: 598−607. https://doi.org/10.1016/j.idm.2020.08.005

AIMS Press