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MATHEMATICAL MODELING OF INFECTIOUS DISEASES AND IMPACT OF VACCINATION STRATEGIES

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Abstract

In this work, we consider mathematical time-varying Susceptible, Exposed, Infectious, and Recovered epidemic model to study optimal vaccination strategy to control excess death due to the epidemic. We model the periodic family of vaccination strategies based on vaccination days and gaps between two periods, where we assume that a government aims to vaccinate about 80% of its population within one year. This is a constraint optimization problem, and to find the optimal vaccination strategy we used a numerical analysis approach. The mathematical models are calibrated to COVID 19 situations in Kazakhstan. Findings of the experiments suggest that to control death tolls due to disease, the governments need to offer vaccinations at the maximum possible rate without any breaks until they reach the desired 80% goal.

Keywords: SEIR model, dynamical systems, vaccination, COVID, Optimal strategy, Death toll

Introduction

SARS-CoV-2, a new virus belonging to the Coronaviridae family, causes COVID-19, a Severe Acute Respiratory Syndrome (SARS). The epidemic was initially identified in December 2019 in the Chinese city of Wuhan, and shortly after it lost control turning to the worldwide pandemic. As of May 2022, COVID-19 pandemic has claimed the lives of over 6 million people with more than 500 million confirmed cases. While some countries were reluctant, most world countries reacted fast and implemented various measures to control the spread of the virus in their countries. In particular, various lockdown measures, social distancing rules, and PCR testing requirements are put in action. Yet, aside from partial success the pandemic continued to progress with new variants. Most countries believed that developing new vaccines against the virus would help to overcome the disease and various researchers were developing their version of vaccines and running clinical trials on safety and effectiveness.

In August 2021, the Pfizer–BioNTech vaccine became the first COVID-19 vaccine to be approved by the Food and Drug Administration in the United States. Soon after, various other vaccines including Moderna, AstraZeneca, Johnson & Johnson, Sputnik V, and Sinovac started publishing the effectiveness reports of clinical trials. All these required tremendous work and it was a huge success from researchers' side, and governments were very optimistic to be able to see the light at the end of the tunnel very soon. However, now governments face different tasks: allocating a budget to purchase vaccines, convincing hesitant individuals to get vaccinated, and developing proper vaccination protocols. In other words, once the vaccinations are developed, the main challenge to governments is to establish effective vaccination strategies and programs. In this work, our purpose is to find the best vaccination strategy that minimizes the death toll due to the virus.

Related work

Rapid invasion and widespread coronavirus disease all over the world required the development of vaccines within a short period of time. After a year of investigation, there was significant progress in creating the vaccines in January 2021, and the first trials among Chinese students were tested within 11 days between 5 and 16 January (Chen et al., 2021). As of April 2021, Kumar et al. (2021), in their paper, claimed that more than 300 vaccines were being developed and 9 of them already were approved to apply among the population in different countries showing the promising effectiveness ranged between 50 and 95%. Such a big range can be explained by the following factors: the quality of vaccines, preexposure and age. Hence, to achieve the goals, every government should consider of particular cases of their own countries in choosing a vaccination strategy if it should be selective vaccination in cities with a relatively high population density, or applying two or more vaccines with two-dose schemes with different time intervals from 3 to 9 weeks, or age-specific vaccination which depends on the different categories of population: age, jobs, and preexposure.

Considering the strategy based on agent-based transmission, age characteristics, and demographics, a double shot vaccination model was implemented in Ontario, Canada (Vilches et al., 2021). This article provides an investigation of vaccine efficacy (Pfizer-BioNTech and Moderna vaccines) and its effect on the virus attack, critical cases, and the number of deaths. Vilches studied the relationship between daily contact of vaccinated individuals and the period of time that passed, which resulted in an increased immunity of the population to overcome the disease outbreak through the vaccination process. Furthermore, Vilches analyzed the case of Brazil in another article, with 2 two-dose vaccines which are CoronaVac and Oxford-AstraZeneca with different efficacy levels and time periods between the shots (Vilches et al., 2021). In Brazil, two vaccination strategies were taken into account, with a standard dosage and its double amount, whereas both of them have a positive impact on the further spread of the virus. Following the first strategy, the number of deaths decreases from 122 to 99 for CoronaVac and to 80 for Oxford-AstraZeneca, likewise for the number of critical cases in hospitals. While the second strategy suggests a lower number of deaths by 74.4% and hence considerably stops the infection spread.

Different vaccine efficacy rates (0.75, 0.85, 0.95) were considered in Malaysia through a modified SIR model leading to a slight virus spread, when the rate of vaccination is higher than 0.75 (Wong et al., 2021). According to simulation results, decreasing the reproduction number leads to a low level of an infection graph both with vaccination and without it. However, Wong states that gradual vaccination procedure helps to achieve the herd immunity and make the population susceptible to a removed state.

According to Moghadas et al. (2021), a two-dose vaccination program was implemented for Moderna and Pfizer-BioNTech studying the agent-based model of the Coronavirus case. Regarding the effectiveness of Moderna, it was computed that during a 9-week gap, a maximum can be obtained in contrast to the suggested 4-week gap. While Pfizer-BioNTech was proved to be more effective in a 9-week period instead of recommended 3-week period between the two dosages. By carrying out a suggested campaign and designing a plan with 30 vaccines in one day per 10,000 individuals, this pace corresponds to a goal of 100 million vaccine doses prescribed in the first 100 days. Furthermore, an immunization ratio per day was analyzed for 45 doses per 10,000 people meaning 1.5 million vaccines in the US during on day period. Whereas, the priority was given to healthcare workers who comprised 5% of all individuals, patients with chronic diseases and old people aged 65 or more.

Vaccination implementation strategies in South Korea were reviewed by Shim to control incidence, critical cases, and the number of deaths by constructing the age-based model with respect to the Korean demography situation during the fourth wave of the global pandemic (Shim, 2021). The results of this paper suggested that the proper vaccination approach decreases the virus transmission from 3.9% to 6.9% without offering vaccines in the period of 150 days, whereas the most considerable outcome of 50% was detected among the older population of 50-59 years old. Moreover, vaccines play a significant role in decreasing the number of deaths by 43% and critical cases resulting in hospitals by 45%.

Similarly, the agent-based model was suggested to understand the optimal vaccination strategy by considering two types of vaccines: Moderna and Pfizer-BioNTech with a 28-day gap and 21-day gap between the first and second dosages, respectively (Sah et al., 2021). The results illustrate the substantial decrease in the virus spread according to the parameterized model of accelerating the delivery of both vaccines. Moreover, applying the vaccination efficacy contributes to halting the upcoming COVID-19 waves.

As a result of literature review, this study is guided by the following research question: What is the best vaccination strategy for governments to reduce the death toll due to a virus?

Methodology

Epidemic Model

We consider the SEIR epidemic model which groups the entire population into four compartments, Susceptible (S), Exposed (E), Infectious (I), and Recovered (R). The model flow diagram is given in Figure 1.

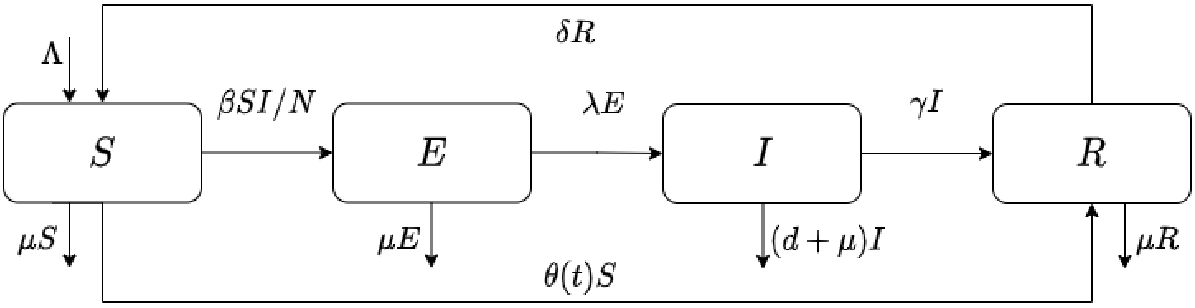


Figure 1. Flow diagram of the epidemic model

It follows that the system of ordinary differential equations (ODE) governing the epidemic dynamics is given by the following system of four equations.

$$\frac{dS}{dt} = \Lambda + \delta R - \beta SI/N - (\theta(t) + \mu)S$$

$$\frac{dE}{dt} = \beta SI/N - (\lambda + \mu)E$$

$$\frac{dI}{dt} = \lambda E - (\gamma + \mu + d)I$$

$$\frac{dR}{dt} = \gamma I + \theta(t)S - (\mu + \delta)R$$

This is a non-autonomous system as we allow the vaccination parameter $\theta(t)$ depending on time. The details of model parameters and their calibrated values are given below in Table 1. When the vaccination rate is taken to be constant, we can provide formulas for basic reproduction numbers. To this end, the disease free equilibrium (DFE) solution is obtained by setting each equation equal to zero and solving yields

$$(\bar{S}, \bar{E}, \bar{I}, \bar{R}) = \left(\frac{\Lambda(\mu+\delta)}{\mu(\theta+\mu+\delta)}, 0, 0, \frac{\Lambda\theta}{\mu(\theta+\mu+\delta)}\right).$$

It follows from next generation matrix method (Van den Driessche & Watmough, 2002) that the basic reproduction number is given by

$$R_0 = \frac{\beta\lambda\bar{S}}{N(\lambda+\mu)(\gamma+\mu+d)},$$

where $\bar{S}$ is given in the previous equation. In particular, when $R_0 < 1$ the DFE is locally asymptotically stable in which case the disease is controlled. On the other hand, when $R_0 > 1$ we have unstable DFE and the infectious disease turns into an epidemic. Since, θ appears in the denominator of the basic reproduction number formula, we see that the disease can be controlled with the increase of the vaccination rate.

Modeling Vaccination Strategies

While there can be various vaccination strategies, we will consider one family of vaccination strategies $\theta(t)$ with three parameters, constant vaccination rate θ, vaccination period π, and gap between two vaccination periods τ. The proposed family of strategies for vaccination is given by

$\theta(t) = \theta$ if $t \in [(\pi+\tau)k, (\pi+\tau)k+\pi]$ for some integer k, and $\theta(t) = 0$ otherwise. Graphically, we have the following periodic function, Figure 2, where $\theta(t)$ is illustrated for $\pi = 30, \tau = 10$, and $\theta = 0.00414$.

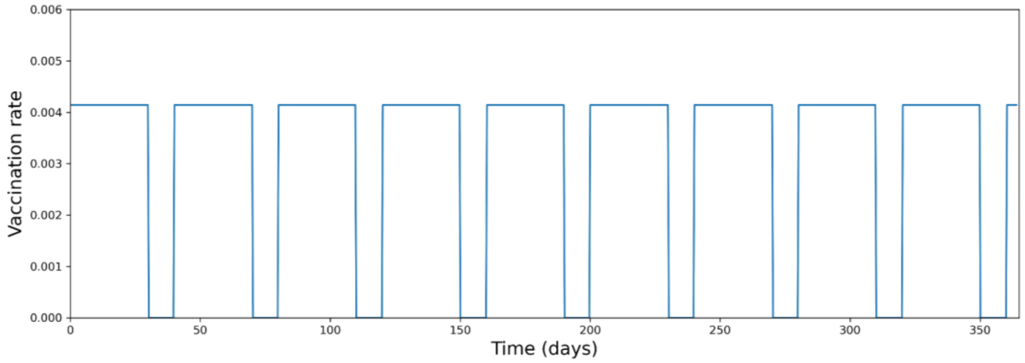


Figure 2. Graph of a vaccination strategy $\theta(t)$ when $\pi = 30, \tau = 10$, and $\theta = 0.003$

Since we want to test the strategies for one year, we restrict t to $[0,364]$. This family of vaccination strategies captures various real life scenarios. For example, taking $\tau = 0$, we get constant vaccination θ which if often the case. If we take $\pi = 5$ and $\tau = 2$, we are assuming that vaccinations are provided during the weekdays and weekends there are no vaccinations.

Model Calibration and Numerical Analysis

In our experimental work, we consider various vaccination strategies for the case of Kazakhstan. To calibrate the model we fix the parameters as described in Table 1.

Parameter	Meaning	Calibration
Λ	Daily birth	1134
μ	Natural death rate	0.000025
β	Transmission rate	0.1
λ	Incubation rate	0.1
d	Death rate due to virus	0.01
γ	Recovery rate	0.07
θ	Vaccination rate	Depends on the strategy
δ	Rate of loosing immunity	0.005

N	Initial total population	18700000
S_0	Initial susceptible population	18500000
E_0	Initial exposed population	171650
I_0	Initial infectius population	17165
R_0	Initial recovered population	160000

Table 1. Model parameters and their values

Kazakhstan started its vaccination program in February 1, 2021. Therefore, in our simulations we take initial time zero as this date. In particular, initial conditions (S_0, E_0, I_0, R_0) reflects the Covid projections from Februrary 1, 2021.

When $\theta = 0$, we see that the basic reproduction number is $R_0 = 3.15$ which is within acceptable range for COVID-19.

Since the SEIR model is nonlinear, it has no closed form solution. Hence, to carry the simulations and find the best strategy to minimize the death toll we implement numerical methods in python.

To make the strategies comparable, for each positive integers π and τ we fix θ so that at the end of one year the total individuals received at least one vaccination is 80%, that is $0.8N$. This is done using bisector method for finding roots of the continuous functions. Here, we can compute the vaccinated individuals $V(t)$ up to date using

$$\frac{dV}{dt} = \theta(t)S.$$

However, θ cannot be too high due to limited vaccination resources at a given time, so we only consider those parameters π and τ for which $\theta \leq 0.02$ which is to say that an entire population cannot be vaccinated in less than $1/0.02 = 50$ days. With these limits for the parameters, finding the best strategy to decrease the death toll can be formulated as

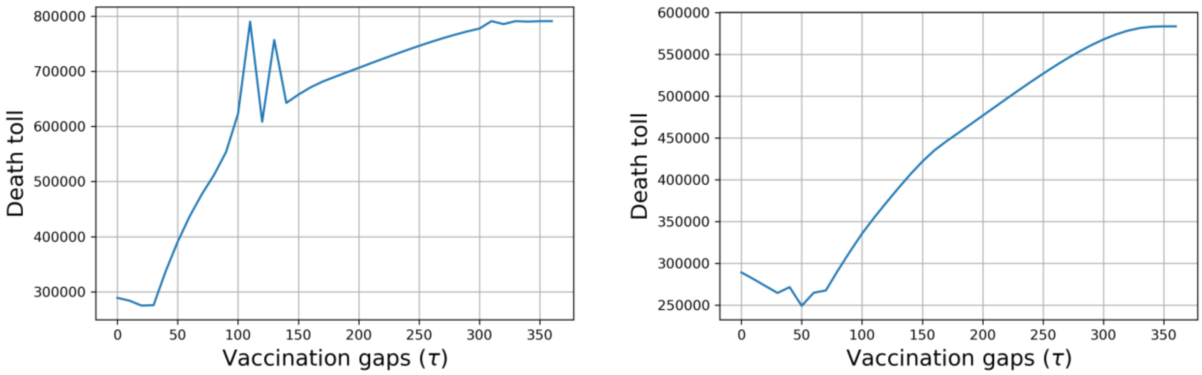
$$arg\ \underset{\pi,\tau}{min} D(365)$$

where $D(t)$ represents the total death due to virus up to time t, given by

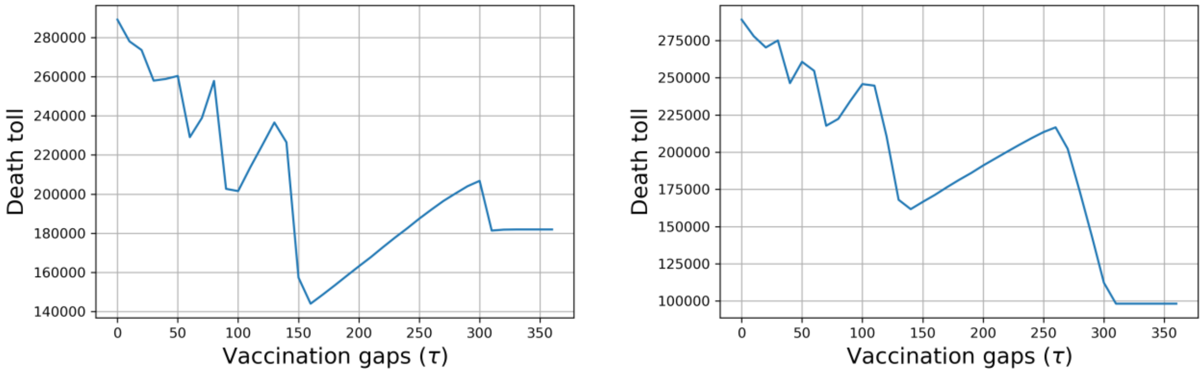
$$\frac{dD}{dt} = dI.$$

Results of experiments

In this section we summarize the findings of the numerical analysis. Figure 3 and 4 provides the graphs of death toll due to the epidemic for various vaccination strategies, where in each graph π is kept fixed and τ is allowed to vary between 0 and 364.



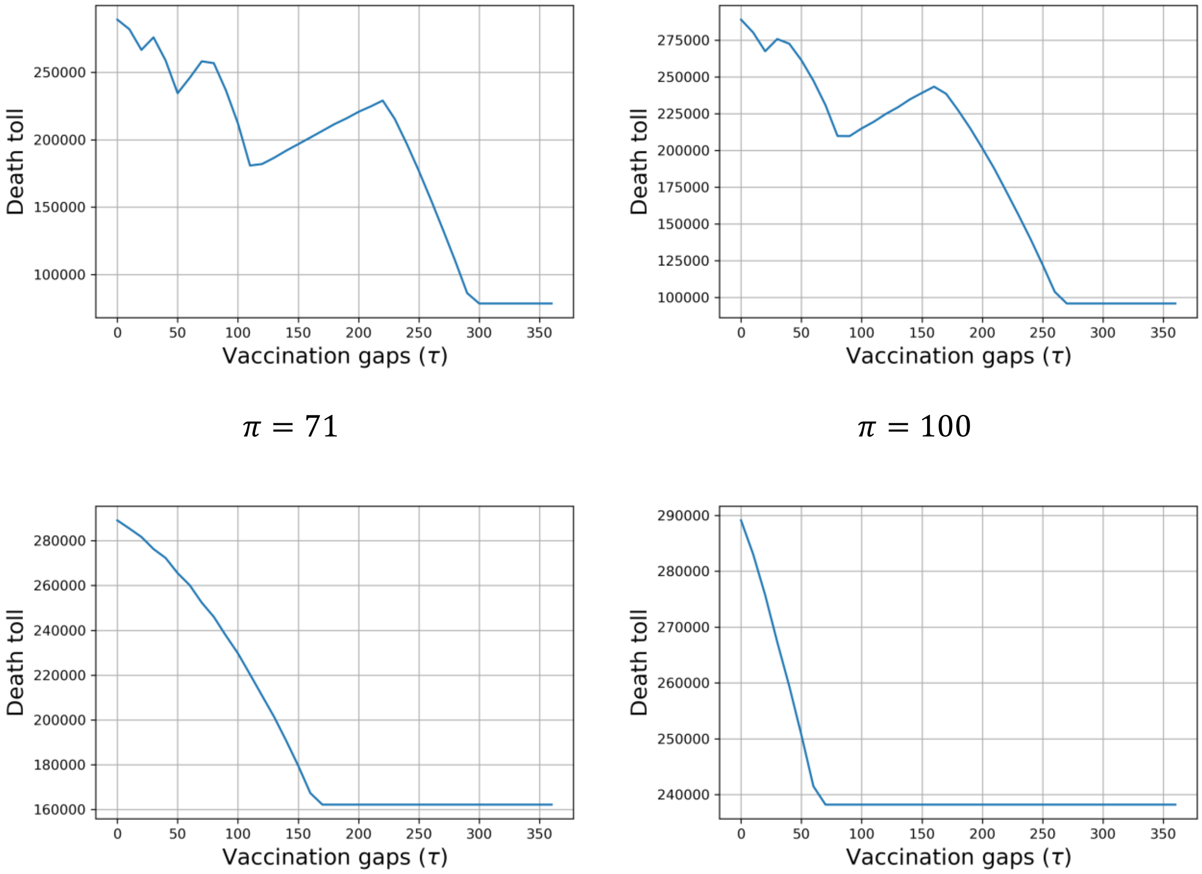
$\pi = 5$ $\pi = 10$



$\pi = 30$ $\pi = 50$

Figure 3. Death toll dynamics for various vaccination strategies with fixed π

Our analysis implemented in Python showed that the optimal strategy is reached with $\pi = 71$ and $\tau = 293$. In this case, vaccination rate reaches maximum allowed $\theta = 0.02$. Figure 4(a) shows how death toll varies with the gaps τ when vaccination day π is kept fixed 71. Indeed, we see that death toll is minimal once τ reaches 293. When the optimal strategy is applied, the death toll remains around 78447.



$\pi = 71$

$\pi = 100$

$\pi = 200$

$\pi = 300$

Figure 4. Death toll dynamics for various vaccination strategies

The death toll of 78447 can be compared for other situations in Figures 3&4. When there is no vaccination, the epidemic dynamics are depicted in Figure 5. In this case, we see that the death toll is exceeding 1 million, showing the important of vaccination.

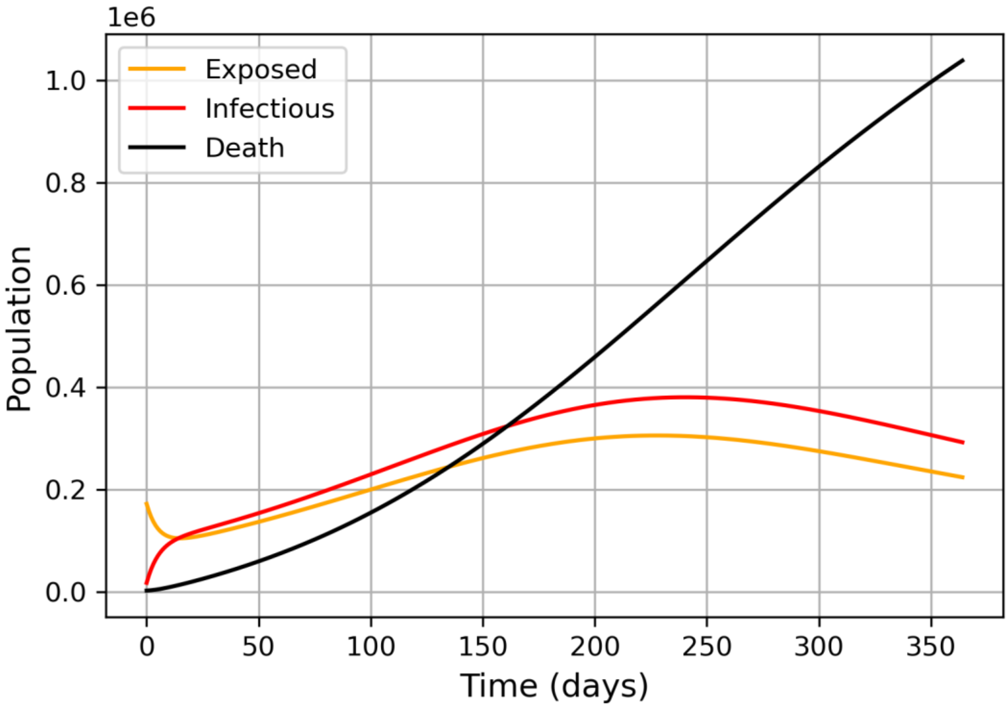


Figure 5. Dynamics without any vaccination, $\theta = 0$

In Figure 6, we illustrated disease dynamics for an arbitrary vaccination strategy, namely, when $\pi = 30, \tau = 10, \theta = 0.00414$. In this occasion, the death toll is 277983 which is clearly better than the case without vaccination. However, compared to the optimal vaccination strategy we see that the death toll is $277983/78447 \approx 3.5$ times higher, while in both situations the total population vaccinated reaches 80% within a year.

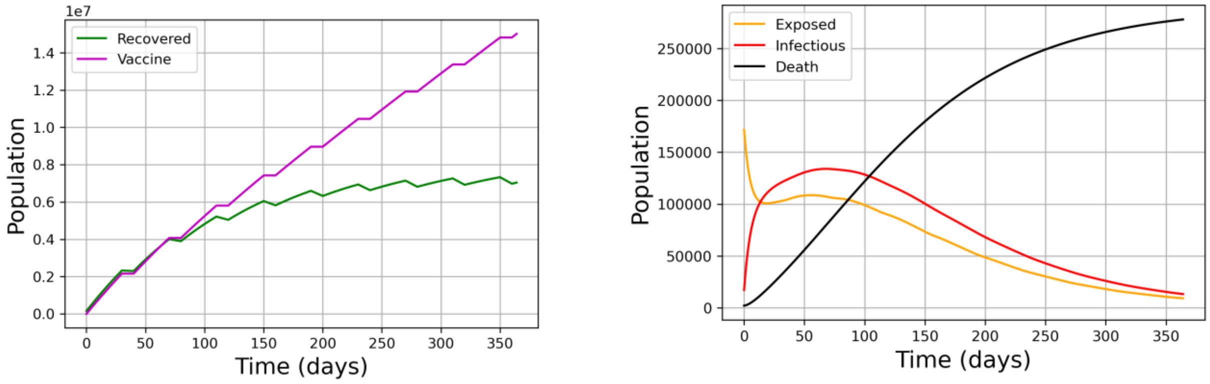


Figure 6. Disease dynamics when $\pi = 30, \tau = 10, \theta = 0.00414$

In Figure 7, we provide the disease dynamics when the optimal vaccination strategy is applied.

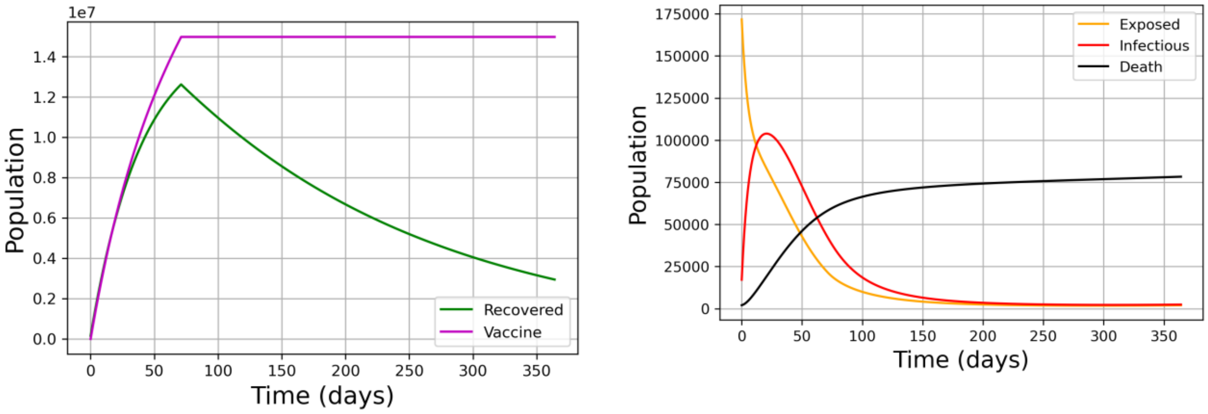


Figure 7. Dynamics with optimal vaccination stargey $\pi = 71, \tau = 291, \theta = 0.02$

Discussion and Conclusion

This paper studies the modified mathematical model of SEIR depending on time to find out the optimal strategy for vaccination during the epidemic to reduce the number of deaths. In order to understand the best vaccination option, periodic family of different strategies was constructed taking into account days of applying the vaccine and period of time between the two doses with the condition that a government has a goal of vaccinating 80% of people during 365 days. Since the given research problem is about a constraint optimization question, the numerical methods tools were applied to control excess death rate. Considering the COVID-19 dynamics in Kazakhstan, the corresponding epidemic model was investigated for computational analysis. With the given constraints, our analysis show that in the first 71 days the individuals should be vaccinated ata daily rate of 0.02 (2%) without any breaks.

While we considered a two parameter family of vaccination strategies, there are other kind of strategies not necessarily periodic ones that governments implemented. For example, age-dependent strategies applied in certain countries, where elderly were given priority to get vaccinated. As a future work, different strategies can be satudied.

In our model, our main goal was to reduce death toll. With limiting ourselves to vaccinate 80% of the people withina year we were implicitly assuming the budget constraints. However, as another future direction, one may try to incorporate government cost with explicit formulas that involves vaccination costs, hospital costs, taxation and so on.

Finally, we point out that there are many other more complex mathematical models that may better explain the epidemic dynamics that may be studied in the future.

As a policy recommendation, the findings suggest that governments should aim to vaccinate people at a maximum rate possible without any brakes such as holidays, weekends, and so on until the number of vaccinated individuals reach 80%.

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