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Estimation of Vaccination Price through Mathematical Epidemic Models to Optimize the Government Cost

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Abstract

These days, humanity is faced with a global Coronavirus pandemic problem, which entails a financial crisis, so the governments want to minimize their financial loss.

In this project work by using the epidemic mathematical model we consider on the basic reproduction number, which is important parameter in the epidemiology and also on the optimization problem about how much should be a discount for the vaccination to optimize the government revenue.

During this study, we get acquainted with the following topics: mathematical modelling, dynamical systems, epidemic models, stability analysis, optimization methods, simulations on software and etc. Initially, we constructed the epidemic model for COVID-19 and separated infectious individuals by two groups, based on the compartmental SIR model and after that by using two different approaches to analyze the model, namely, Linearization (Hartman-Grobman) and Next Generation matrix method, we obtained the most important formula in epidemiology: the basic reproduction number 1.3.

To solve the government cost, we constructed the government cost function which takes into account the cost of vaccination, the cost of treatment, the average wage of citizens. By using the software we solved numerically the system of nonlinear differential equations of our epidemic model, also we optimized the governmental cost function depending on a vaccination discount and obtained the main result of applied part of our project work 1.6, that the government cost is minimized with making the vaccination fully free of charge for citizens.

The study will be useful for the Government of Kazakhstan in predicting the number of infectious individuals as well as in planning the income revenue. By changing the initial parameters in our epidemic model, it is easy compute the basic reproduction number and Government cost function for any country.

Аңдатпа

Қазіргі уақытта адамзат қаржылық дағдарысқа әкеп соқтыратын жаһандық коронавирустық пандемия проблемасымен бетпе-бет келді, сондықтан үкімет өздерінің қаржылық шығындарын барынша жеңілдетуді қалайды.

Бұл жобалық жұмыста эпидемиялық математикалық модельді қолдана отырып, эпидемиологияның маңызды параметрі болып табылатын негізгі репродукция саны туралы, сондай-ақ мемлекеттік кірісті оңтайландыру үшін вакцинацияға қандай жеңілдік болуы қажет екенін қарастырамыз.

Зерттеу барысында біз келесі тақырыптармен танысамыз: математикалық модельдеу, динамикалық жүйелер, эпидемиялық модельдер, тұрақтылықты талдау, оңтайландыру әдістері, бағдарламалық жасақтамада модельдеу және т.б. Бастапқыда біз COVID-19 эпидемиялық моделін құрдық және ауру жұқтырған адамдарды екіге бөліп қарастырдық. SIR бөлімдік моделіне және сол модельді талдау үшін екі түрлі тәсілді, атап айтқанда Linearization (Хартман-Гробман) және Next Generation matrix әдісітерін қолдану арқылы эпидемиологиядағы маңызды негізгі репродукция санының 1.3 формуласын таптық.

Мемлекеттік шығындарды шешу үшін біз вакцинациялау құнын, емдеу шығындарын, азаматтардың орташа жалақысын ескеретін мемлекеттік шығындар функциясын құрдық. Бағдарламалық жасақтаманы қолдана отырып, эпидемиялық модельдің сызықтық емес дифференциалдық теңдеулер жүйесін сандық түрде шештік, сонымен қатар вакцинация жеңілдіктеріне байланысты мемлекеттік шығындар функциясын оңтайландырдық және жобалық жұмысымыздың қолданбалы бөлігінің негізгі нәтижесін 1.6 алдық, мемлекеттік шығындар есебінен вакцинацияны ақысыз ету жобасын қалыптастырдық.

Зерттеу Қазақстан Республикасы үшін жұқпалы аурулардың санын болжауда, сондай-ақ кірістерді жоспарлауда пайдалы болады. Біздің эпидемиялық модельдегі бастапқы параметрлерді өзгерте отырып, кез-келген ел үшін негізгі репродукция санын және Үкіметтің шығындар функциясын есептеуге болады.

Аннотация

В наши дни человечество столкнулось с глобальной проблемой пандемии коронавируса, которая влечет за собой финансовый кризис, поэтому правительства хотят свести к минимуму свои финансовые потери.

В этом проекте мы используем математическую модель эпидемии, для вычисления формулы индекса репродукции, которая является важным параметром в эпидемиология, а также проблему оптимизации о том, какая должна быть скидка на вакцинацию для оптимизации государственных доходов.

В ходе этого исследования мы знакомимся со следующими темами: математическое моделирование, динамические системы, модели эпидемий, анализ стабильности, методы оптимизации, моделирование на программном обеспечении и т. д. Первоначально мы построили эпидемическую модель для COVID-19 и разделили инфицированных людей на две группы на основе компартментальной модели SIR, а затем использовали два разных подхода для анализа модели, а именно: линеаризацию (Хартман-Гробман) и Next-Generation matrix метод, с помошью которых мы получили важнейшую формулу в эпидемиологии: формулу индекса репродукции 1.3.

Для оптимизации государственных затрат, мы построили функцию государственных затрат, которая учитывает стоимость вакцинации, стоимость лечения, среднюю заработную плату граждан. С помощью программного обеспечения мы численно решили систему нелинейных дифференциальных уравнений нашей модели эпидемии, а также оптимизировали функцию государственных затрат в зависимости от скидки на вакцинацию и получили основной результат прикладной части нашей проектной работы 1.6, что государственные расходы минимизированы с проведением вакцинации полностью бесплатно для граждан.

Данное научное исследование может быть полезным Правительству Казахстана при прогнозировании количества инфекционных лиц, а также при планировании доходов. Изменив исходные параметры в нашей эпидемиологической модели, легко вычислить формулу индекса репродукции и так же функцию государственных затрат для любой страны.

Contents

1. Introduction

Nowadays, when the world is facing a lot of challenges, predicting or warning about the upcoming problems is a crucial for the society. By using different mathematical tools it is possible to estimate or evaluate some processes, which surround us. The society has always overtaken and struggled with various diseases and some of them became the epidemic and took away thousands of life, such as the Black Death, Spanish flu, the Plague of Justinian etc. Even now, when the technological process is peaked, we face such decease problems. According to *World Health Organization* about 3.5 million of people dead, due to COVID-19 in the past one and half year, by May 2021. So it is crucial for the scientists and health care organizations, as well as for the government to react immediately and solve such problems.

The first attempts to solve such problems were dated in 1760s when Daniel Bernoulli [1] created a mathematical model which proved the effectiveness of vaccinating against smallpox and increased the life expectancy to about three years.

The next successful of modeling the disease was in 1920s, when Kermack and McKendrick [2] created a compartmental model. They divided the population into three different compartments such as susceptible, infectious and recovery; and described the relationship between them by using the system of ordinary differential equations. The McKendrick and Kermack model also well known as the classic SIR epidemic model, where susceptible, infectious and recovery denoted as S, I and R, respectively. This model is the base for developing other epidemic models. The detailed developing of this model you can find in the section 2.7. The SIR epidemic model was successful in predicting the peak of the disease, which were observed for short period of time in that days.

The SIR epidemic model has as pros as cons, it is too simple, so we can easily analyze it, at the same time it does not take into account the birth rate and the

death rate, so it does not satisfy for describing the long term disease. Vaccination and death due to diseases are also omitted in the model, as the exposed period and so on. The exposed period is important for diseases, where before becoming infectious, there is some period of time during which people are infected, but not infectious. Later, there were developed a lot of epidemiological models, which took into account some of the listed above factors. The most popular of them are: $SIRS$ [3] where people have an immunity only for a short period of time after recovery; SIS where upon recovery there is no immunity; SIV [4] involves vaccinating humans to eradicate the disease; $SEIR$ [5] involves the incubation period. In fact, we can develop any new model with adding all factors which affect, but in that case it will be too complicated to analyze, so our goal is construct the model which will be more realistic, at the same time to be amenable to analysis.

Recently in 19 June 2020, the Arcede, Jayrold P and Caga-Anan, Randy L and Mentuda, Cheryl Q and Mammeri, Youcef published the paper [6], where they divided the infectious compartment by two: reported (symptomatic) and unreported (asymptomatic), since it is actual for the COVID-19, because some infected individuals does not have any symptoms. This work prompted us to develop our epidemic model, analyze it and to estimate of vaccination price through epidemic model to optimize the government cost.

To measure the transfer-ability of disease in epidemiology the most important parameter is basic reproduction number.

Definition 1.1. The basic reproduction number, denoted by $\mathscr{R}_0$, is defined as the average number of susceptible individuals becomes infected by one infectious person during his/her infection period [7].

To make conclusion about the disease such us: the disease will spread exponentially, die out, or remain constant the basic reproduction number helps to do such analyses.

Remark 1.2. If $\mathscr{R}_0 < 1$, then each person infects fewer than one person on average so the disease will die out; and if $\mathscr{R}_0 = 1$, then each person will infect on average exactly one other person, so the disease will become endemic, endemic means: it will move throughout the population, but not increase or decrease. The third case if $\mathscr{R}_0 > 1$, then one infectious person on average infects more than one, so there will be an epidemic [7].

For instance the $\mathscr{R}_0$ for well-known epidemic diseases:

- Ebola [8]: between 1.5 and 2.5
- SARS [9]: between 2 and 4
- COVID-19 [10]: between 2.5 and 6.0
- Influenza [11]: between 0.9 and 2.1

The $\mathscr{R}_0$ may vary depending to the region and country since it depends from the density of population, the health care organization system and so on.

1.1 Problem statement and research objectives

Since the government suffers from the financial losses due to COVID-19, it is crucial to optimize the government costs and revenues to avoid the financial crisis. So our goals are to make suggestions regarding how the government should act in this situation and to find the formula of the basic reproduction number. To make such suggestions, first of all we have to develop the epidemic model and then to do the analysis of the model and finally to solve it numerically and to optimize the government costs. According to the definition 1.1, we see that the basic reproduction number is the crucial parameter in the epidemiology, so we need to calculate it accurately. Regarding to the optimization problem, we have to take into account all the parameters which have an influence on the government cost such us the hospital treatment price, the taxes from the employed part of the population and the price of vaccination. Since all the parameters listed above are in a mutual dependence, it means if the number of infectious individuals increase with that the hospital treatment cost also increase, while the number of employed part of the population decreases the government get less taxes. So the government has to make a decision how to optimize the costs, whether the vaccination should be free for the citizens or it should be paid fully by the citizens or only some part of the price should be covered by the government. To summarize our research objectives are

- To learn about Epidemic Models and develop the model
- To conduct mathematical analysis of the Epidemic Model

- To estimate the discount for vaccination that minimizes the government cost function
- To use software to simulate dynamics

In the following section there is the detailed construction of the SEI_rI_uRD epidemic model.

1.2 Construction of the SEI_rI_uRD Epidemic Model

To build our mathematical model of the COVID-19 disease we used the standard strategy of building the Epidemic Models, with the following assumptions:

1. Homogeneous mixing of the population;
2. The disease has an incubation period;
3. There are both reported (symptomatic) and unreported (asymptomatic) individuals;
4. Susceptible can be infected by reported infected individuals as well as unreported infected individuals, but at different rates;
5. Death due to disease occurs in reported infectious and unreported infectious individuals with the same rate;
6. Recovered individuals have indefinite immunity;
7. Both S and E are vaccinated at a certain rate.

We made the above assumptions to make our model more realistic, since the epidemic of COVID-19 lasts more than a year, we can not take the total number of population as a constant, so we take into account the birth and natural death rate.

We consider on six compartments of the epidemic flow, where S–Susceptible individuals (individuals who are susceptible to the disease, but healthy at time t), E–Exposed individuals, I_r–Reported infectious individuals (Infectious individuals who has been registered officially), I_u–Unreported infectious individuals, R–Recovered individuals (healthy individuals who are immune to the disease),

and D–Dead individuals. All six compartments are the functions where the variable is t (time). As follows from the variable function t, the model is dynamic because of the numbers in each compartment can fluctuate over time.

Figure 1.1 provides the transmission flow diagram of our proposed model.

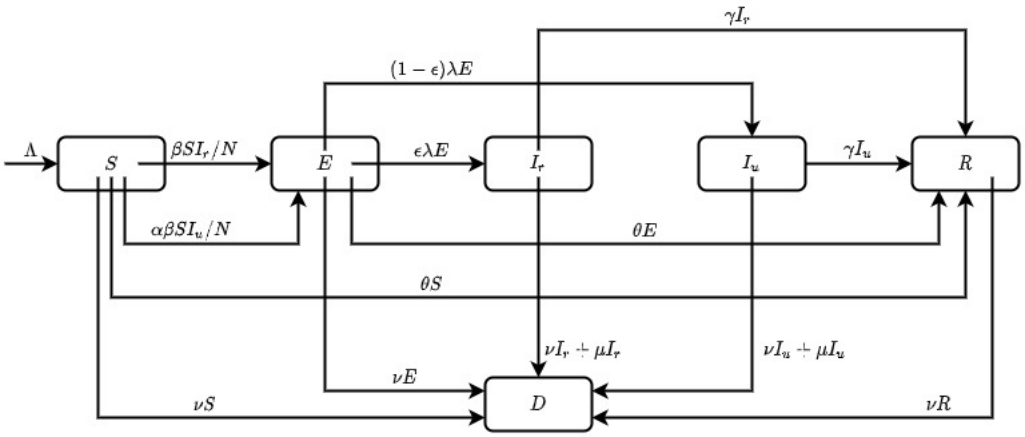


Figure 1.1: SEI_rI_uRD

The dynamics is governed by a system of six ordinary nonlinear differential equations (ODE) as follows:

$$\begin{cases} \dfrac{dS(t)}{dt} = \Lambda - \dfrac{\beta S I_r}{N} - \dfrac{\alpha\beta S I_u}{N} - S(\theta+\nu), \\ \dfrac{dE(t)}{dt} = \dfrac{\beta S I_r}{N} + \dfrac{\alpha\beta S I_u}{N} - E(\theta+\lambda+\nu), \\ \dfrac{dI_r(t)}{dt} = \epsilon\lambda E - I_r(\gamma+\mu+\nu), \\ \dfrac{dI_u(t)}{dt} = (1-\epsilon)\lambda E - I_u(\gamma+\mu+\nu), \\ \dfrac{dR(t)}{dt} = \theta(S+E) + \gamma(I_r+I_u) - \nu R, \\ \dfrac{dD(t)}{dt} = \nu(S+E+I_r+I_u+R) + \mu(I_r+I_u). \end{cases} \tag{1.1}$$

where N is the total number of population at a particular time.

The resulting model consists of the following nine parameters that need to be determined: Λ–daily birth (how many infants were born in that day), β–transmission rate (the intensity of spread the disease during the contact with infected individual), α–infection effect (in how many times the unreported individuals are more infectious than reported individuals), ϵ–proportion of reported Infectious, ν–natural death rate, μ–death rate due to disease, $\gamma = \frac{1}{\text{recovered period}}$,

$\lambda = \frac{1}{\text{incubation period}}$, θ–vaccination rate. The domain for all parameters is positive and some of them are bounded: $0 < \beta < 1$; $0 < \epsilon < 1$; $0 < \nu < 1$; $0 < \mu < 1$; $0 < \theta < 1$.

1.3 The Main results of the Project

As a result of mathematical analysis of the proposed SEI_rI_uRD epidemic model, we obtained two main results of our project:

Theorem 1.3. *The basic reproduction number for the SEI_rI_uRD epidemic model is:*

$$\mathscr{R}_0 = \frac{\beta\lambda\Lambda(\epsilon + \alpha(1-\epsilon))}{(\lambda+\nu+\theta)(\gamma+\nu+\mu)(\nu+\theta)N} \tag{1.2}$$

Remark 1.4. In particular, if $\mathscr{R}_0 < 1$ then the disease free equilibrium, which means the solution of the system when there is no disease, is locally asymptotically stable and it is unstable otherwise, where locally asymptotically stable means that solutions that start close enough to the equilibrium remain close and also eventually converges to the disease free equilibrium.

Remark 1.5. The theorem is obtained by using two different approaches, namely, Linearisation (Hartman-Grobman) and the Next Generation matrix method.

Our next main result is the following:

Theorem 1.6. *The government cost is minimized with making vaccination fully free of charge.*

For details of how we model the government cost, we refer to Chapter 4.

In the following chapter, we review the background information. In the third chapter, we prove our main mathematician result and Theorem 1.3. Then, we consider on the numerical simulation of our epidemic model and prove the main optimization result Thereom 1.6 of our work. Finally, we end with the summary.

2. Background and Literature Review

For example, today it is known that if patient zero becomes infected, then the flu virus progresses very quickly. Let there be data on how many people or children were infected yesterday and today. Questions arise: What will happen next? How many people will become infected tomorrow? Everyone? Or the virus has already ceased to exist on the third day. To study the questions posed, let us indicate what needs to be done.

1. Build a mathematical model of the epidemic development process. It is needed because we cannot analyze thousands of people to see if they can carry the virus or are already immune to it. Therefore, we need to build a model that is both simple and effective so that we can predict the further spread of the virus with the data already available.

2. Solve the model. At this point, we must use all the knowledge of mathematics for its analytical or numerical solution.

3. Investigate the inverse problem of finding the parameters of the model. The model includes several coefficients that cannot be immediately determined. Which complicates the above task a little. Incorrectly found coefficients can show that millions can become infected in a week, although in fact there were only thousands of them. From here we understand how our model can be sensitive to the kind of parameters.

4. Find ways to change the parameters of the model in real life. For example, we can close schools and universities, introduce quarantine, etc. Take any measures in order to reduce the spread parameters, which will ultimately lead to a halt of the epidemic.

The spread of infectious diseases gives rise to a complex appearance with an

abundance of interacting factors. The main role of mathematical epidemiology is to develop models for the spread of pathogens. These models work as a mathematical basis for understanding the difficult dynamics of disease spread.

In this chapter we introduce some basics needed to study epidemic models and review related literature. Also we describe and explore a simple SIR model. To this end, we first start with review of mathematical biology.

2.1 Mathematics in biology

For several centuries, physics and astronomy have been the main sources of mathematical problems. Recently, we can notice that this state of affairs has changed significantly, since such terms as mathematical economics, mathematical biology, mathematical linguistics, mathematical chemistry and so on have already appeared.

This is due to the fact that mathematics is a fundamental science that provides a common language tool to other sciences, such as physics, chemistry, biology, sociology, linguistics, and so on. Thus, it reveals their relationship and contributes to finding the general laws of nature.

The first attempts to use precise quantitative methods for such sciences as biology date back to a rather distant past, for example, in 1680, the work "De Motu Animalium" written by Giovanni Borelli [12] was published in Rome. In this work, the movement of animals and humans was investigated using geometric and mechanical considerations.

We can see that mathematical biology mainly uses mathematical tools such as the theory of differential equations, mathematical statistics and different software programs. One of the first attempts to use mathematical statistics is considered the work of Daniel Bernoulli, entitled as "An attempt at a new analysis of the mortality caused by smallpox and of the advantages of inoculation to prevent it" [13]. In 1766, a scientist compiled an analysis of data on disease and deaths from smallpox to demonstrate the effectiveness of the smallpox vaccination.

Moving on to later times, namely to our century, it is necessary to mention the work of D'Arcy Thompson "On growth and For" (1917) [14], in which the author applied mathematical methods to the study of the growth processes of animals and plant organisms and their geometric forms.

In general, mathematical biology focuses on the use of mathematical models and theoretical analysis to model organic processes and study biological systems.

One way to model biological systems is using dynamical systems. In the next, we briefly review the theory of dynamical systems.

2.2 Dynamical systems

A *dynamical system* is a system that changes according to a fixed evolutionary rule describing the change in the initial state over time.

An *evolutionary rule* is a function that describes the future state of the system, depending on the current state.

For a dynamical system, the concept of a *state* is uniquely defined, which is defined by means of n variables, x_1, x_2,..., x_n, which takes arbitrary real values, and the law of evolution of the initial state over time. In mathematical terms, a dynamical system is:

$$\frac{\mathrm{d}x_i}{\mathrm{d}t} = X_i(x_1, x_2, \ldots, x_n), \qquad (i = 1, 2, \ldots, n)$$

where the variables x_1, x_2 ,..., x_n determine the state of the system at each moment of time.

It is believed by many that starting with a number of theses by Henri Poincare laid the foundation for modern dynamical systems theory. Here are some of Poincare's now classics: his dissertation in 1879 [15], then a series of four memoirs on the qualitative theory of differential equations (1881-1886) [16], a competition memoir on three-body problems (1890) [17], and New Methods of Celestial Mechanics in three parts (1892-1899) [18].

In modern science, the concept of a dynamic system covers systems of almost any nature - physical, chemical, biological, economic, social and others. In this graduation project, we focus on the biological part of dynamic systems, since we are interested in the dynamics of the spread of the virus among the population.

As mentioned above, dynamical systems can be used to mathematically model real life phenomena.

2.3 Mathematical model

Cognition and study of the world around us can be carried out in various ways and methods. There is a whole area of knowledge - methodology, which is specifically concerned with the study of methods of cognition. These days, we are interested in the general scientific method, which is widely used in various spheres of life: in music, linguistics, philosophy, as well as in natural (such as biology, physics, chemistry) or social sciences (such as sociology, economics, political science, psychology) and in engineering disciplines (such as electrical engineering, computer science). This technique is called *mathematical modeling*.

If we briefly characterize modeling, then it consists in replacing a real system (process or phenomenon) with a model that is in some correspondence with it (with them) and is able to explain the system, reproduce the properties or characteristics of a real system that are of interest to the researcher, and also make predictions about its behavior.

So, a person before doing something, thinks about the possible sequence of actions and the possible consequences of these actions, organizing the interaction of many objects in order to get the maximum effect from the activity of such a system.

If expressed in mathematical language, then the *mathematical model* is any operator A that allows setting the output values of the parameters Y of the modeling object according to the corresponding values of the input parameters

$A : X \to Y = AX$.

Depending on the nature of the modeled object,the elements of the sets X and Y can be any mathematical objects. For example, numbers, vectors, functions, sets, and etc. At the same time, the concept of operator A can be interpreted rather broadly. It can be as some function, differential or integral operator, or algebraic operator.

Moreover, mathematical models are classified as:

- Linear vs. nonlinear;
- Static vs. dynamic;
- Deterministic vs. probabilistic (stochastic);

- Explicit vs. implicit;
- Discrete vs. continuous;

When modeling, we may be faced with an overly complex system in which each particular unit can make different changes to the model. Therefore, when building any models, the researcher must identify the most important parts of the system and include them in the model. In this respect, any model is not identical to the real system (process or phenomenon) and is incomplete. The "complete" model will obviously be completely identical to the original.

We think the statement of Nobert Wiener will be the best conclusion to this theme:"The best material model of a cat is another, or preferably the same, cat" [19]. Let us give an illustrative example of the use of mathematical modeling, namely, consider the SIR model. But to better understand this model, we need to introduce new terms, which are described below.

There is no doubt that one of the important areas of mathematical models comes from epidemiology.

2.4 Epidemiology

As we all know, an epidemic is an infectious disease that spreads rapidly among a large part of the population, which can trigger various emergencies. The epidemic process itself consists in the spread of infection in the human community (or population). And for the occurrence of this process, the following factors are sufficient:

1. Source of the causative agent

This source can be both a living infected organism and an inanimate object, which is the natural habitat of pathogens - parasites. For example, a sick person, a sick animal, or a bird, soil or water;

2. Transmission mechanisms

This is a way of transferring an infectious agent from an infected organism to a susceptible one. Existing mechanisms of transmission of infection: aerogenic (airborne), fecal-oral, contact and blood contact (blood, transmissible);

3. And the last factor is the group susceptible to the disease.

Based on human history, epidemics play a large role in the human population. Despite the development in technologies and medicine, we are facing with epidemics that cause unpleasant consequences for our body and everyday life. They can also adversely affect the development of countries, since the costs of prevention, treatment and rehabilitation of infectious patients, even in developed countries of the world, are quite expensive. Consequently, one of the most important research objectives is to protect the population. That is, improving the quality and increasing the life expectancy of a person, reducing mortality and disability from diseases, preventing, limiting the spread and elimination of infectious diseases.

To reduce the impact of epidemics, mathematical models were introduced to simplify the representation of the spread of infection among the population. The work of Kermack W. O. and McKendrick A. G., published in 1927 [2], was the first epidemic work that used a mathematical apparatus and provided a model of the epidemic, which was later called the classical SIR model. Scientists have built a model for one city with a population that does not change in size over time. The entire population of the city under consideration was divided into three groups: individuals who are susceptible to a given disease, but healthy, infected individuals, and healthy individuals who are immune to this disease. The mechanism of infection is realized through meetings of susceptible with infected.

Then, in the mid-70s of the last century, O.V. Baroyan and Rvachev L.A. [20] developed a methodology for mathematical modeling and forecasting of influenza epidemics for the territory of Russia, which was called the Baroyan-Rvachev model. However, in the 1980s, this model began to lose its predictive power, since in some cities the model predicted the time of an influenza epidemic, where, in fact, there were not observed at all. The reason was that the pattern of daily migration of people in different cities affects herd immunity, which behaves differently and in each city the susceptibility to the disease must be assessed differently.

After the agents of the virus enter the body, the immune system turns on its antibodies to fight. It takes a little time for the antibodies to begin to resist the virus. In this short period of time, the virus has time to multiply and cause great damage to the body. When antibodies are involved, they quickly eliminate them. Thanks to antibodies, the body can quickly cope with the virus of this strain. To accelerate antibodies in this position, medicine uses vaccination. At the moment,

we know that vaccinations have helped to get rid of a large number of viruses and not only. Unfortunately, a new strain of viruses appears almost every season, making it difficult to recover quickly. Many people think that vaccination not only helps antibodies, but replaces them, so scientists did not agree on the annual vaccination. There are a large number of people in the world who flatly refuse to be vaccinated, which gives a second chance to long-forgotten viruses.

All this led to the emergence of different variations of the SIR model described in the following literature: Hastings A., "Population Biology" [21]; Dickman, O. and Hesterbeck, J., "Mathematical epidemiology of infectious diseases: Model building, analysis, and interpretation" [22]; optimal control for the epidemic process was discussed in the article by Gubar E., Zhu Q. "Optimal Control of Influenza Epidemic Model with Virus Mutations"[23]. In the work of Kolesin I.D. and Zhitkova E.M. [24] many different models of epidemics are given, including the influenza epidemic.

Among other epidemiological parameters, the basic reproduction number is by way the most important constant. In the next two sections we review two classical ways to compute the basic reproduction numbers.

2.5 Basic reproduction number and linearisation method

One of the possible way to find the basic reproduction number for compartmental epidemic models in epidemiology is to linearize the system of nonlinear ordinary differential equations. In this section we will consider on the linearization method in details [25].

Suppose, we have the system of n nonlinear differential equations:

$$\dot{X}_i = f_i(X),$$

where $X \in \mathbb{R}^n$ and $i = 1, 2, 3, \ldots, n$ and the X_0 is the operating point, where operating is a point through which the system trajectory passes. In other words, $\dot{X} = f_i(X_0) = 0$. In particular, the fixed point (DFE) is also the operating. Let $X = X_0 + \Delta X$ denote the component of a small disturbance from the fixed point. To see weather the disturbance grows or decays, we need to derive differential

equations. Let rewrite the system in column vector form:
$f_i(X) = [f_1, f_2, f_3, \ldots, f_n]^T$, and $X = [X_1, X_2, X_3, \ldots, X_n]^T$.

Definition 2.1. Taylor expansion for multivariable function is defined as: If $f : \mathbb{R}^n \to \mathbb{R}$ be a k-times differentiable at the point $X_0 \in \mathbb{R}^n$. Then there exists $h_\alpha : \mathbb{R}^n \to \mathbb{R}$ such that

$$f(X) = \sum_{|\alpha| \leq k} \frac{D^\alpha f(X_0)}{\alpha!}(X - X_0)^\alpha + \sum_{|\alpha|=k} h_\alpha(X)(X - X_0)^\alpha$$

and $\lim_{X \to X_0} h_\alpha(x) = 0$.

Lets, approximate the system of ODE at the fixed point X_0 using the Taylor expansion formula only for the first two terms, so we obtain:

$$\dot{X}_0 + \Delta\dot{X} \approx f(X_0) + \left[\frac{\partial f}{\partial X}\right]_{X_0} \Delta X,$$

where $A = \left[\frac{\partial f}{\partial X}\right]_{X_0}$ and this matrix A is called the *Jacobian* matrix at the fixed point X_0. Since $\dot{X} = f_i(X_0) = 0$, then the Taylor approximation could be written in the following form:

$$\Delta\dot{X} \approx \left[\frac{\partial f}{\partial X}\right]_{X_0} \Delta X,$$

Lets, redefine the $\Delta X = X$ and finally we obtain the linearized form of our system of nonlinear differential equations:

$$\dot{X} = AX$$

According to work (published in 1943) of Bellman and Richard [26] the solution of any system of linear differential equations can be presented as:

$$X(t) = C_1 e^{\lambda_1 t} + C_2 e^{\lambda_2 t} + C_3 e^{\lambda_3 t} + \cdots + C_n e^{\lambda_n t},$$

where $\lambda_1, \lambda_2, \lambda_3, \ldots, \lambda_n$ are the distinguished eigenvalues and $C_1, C_2, C_3, \ldots, C_n$ are coefficients. So if $\lambda_i < 0$ for $i = 1, 2, 3, \ldots, n$ the solution will converge to zero (finite) since each term of the solution approaches to zero, otherwise if at least one of the eigenvalue is $\lambda_i > 0$ for any i the solution will diverges since at least one term of the solution approaches to infinity.

The linearisation method gives qualitative information about the original ODE system thanks to Hartman-Grobman theorem.

Theorem 2.2 (Hartman-Grobman)**.** *The behaviour of a dynamical system in a domain near a hyperbolic equilibrium point is qualitatively the same as the behaviour of its linearisation near this equilibrium point, where hyperbolicity means that no eigenvalue of the linearisation has real part equal to zero [27].*

For the nonlinear epidemic models to define the basic reproduction number, we have to linearize it and to determine a condition, in which case real parts of all eigenvalues are negative. Finally, that condition will lead to the basic reproduction number for the epidemic model.

2.6 Basic reproduction number and the next generation matrix method

Another possible way to find the basic reproduction number for compartmental epidemic models in epidemiology is the Next Generation Matrix method. This method was developed by van den Driessche, Watmough and Diekmann in 2001 [28]. To use this method the all population is divided into n compartment, where some of them are infected $m < n$. Let x_i, $i = 1, 2, 3, \ldots, m$ be the numbers of infected individuals in the i^{th} infected compartment at time t. So the epidemic model could be written in the following form:

$$\frac{dx_i}{dt} = \mathscr{F}_i(x) - \mathscr{V}_i(x),$$

where $\mathscr{V}_i(x) = \mathscr{V}_i^+(x) + \mathscr{V}_i^-(x)$ and $\mathscr{V}_i^+(x)$ the rate of change of new individuals into the compartment i from all other compartments, $\mathscr{V}_i^-(x)$ the rate of change of individuals from the compartment i and $\mathscr{F}_i(x)$ represents the rate of coming of new infection individuals into compartment i. We can rewrite the the system of ODE into the column matrix, so the model has the following form:

$$\frac{dx}{dt} = \mathscr{F}(x) - \mathscr{V}(x),$$

where $\mathscr{F}(x) = (\mathscr{F}_1(x), \mathscr{F}_2(x), \mathscr{F}_3(x), \ldots, \mathscr{F}_m(x))^T$ and
$\mathscr{V}(x) = (\mathscr{V}_1(x), \mathscr{V}_2(x), \mathscr{V}_3(x), \ldots, \mathscr{V}_m(x))^T$.

Let x^* be the disease free equilibrium (DFE) it means the solution of the system when there is no disease. The *Jacobian* matrices of $\mathscr{F}(x)$ and $\mathscr{V}(x)$ at DFE have the following forms:

$$D\mathscr{F}(x^*) = \begin{pmatrix} F & 0 \\ 0 & 0 \end{pmatrix}$$

and

$$D\mathscr{V}(x^*) = \begin{pmatrix} V & 0 \\ J_3 & J_4 \end{pmatrix},$$

where F and V are $m \times m$ matrices, defined as $F = \dfrac{\partial F_i}{\partial x_j}(x^*)$ and $V = \dfrac{\partial V_i}{\partial x_j}(x^*)$ with $1 \leq i, j \leq m$. Further, F is non-negative, V is a non-singular M-matrix and all eigenvalues of J_4 have positive real part.

The product of F and inverse of V is called the Next Generation matrix and according to the theorem described in [28] the largest eigenvalue of the FV^{-1} is the basic reproduction number of the epidemic model. Moreover,

Theorem 2.3 (Theorem 2, [28])**.** *The model is locally asymptotically stable at DFE if $\mathscr{R} < 1$ and it is unstable if $\mathscr{R} > 1$, where locally asymptotically stable means that solutions that start close enough to the equilibrium remain close and also eventually converges to the disease free equilibrium.*

In the following section we consider on the basic compartmental model of Kermack and McKendrick SIR and we find the formula of the basic reproduction number for this model.

2.7 SIR model

One of the simplest and most effective models that has become the basic form for many other models is the SIR model. As mentioned earlier, the authors of this model are Kermack and McKendrick [2] who described the relationship between compartments by using the system of ordinary differential equations.

Many epidemiological models are based on the division of a population into compartments. The SIR model consists of three compartments: S for the number

of susceptible, that is, not infected at a given time, I for the number of infectious, infected who can transmit the infection, and R for the number of those who have been recovered from the disease and are unable to become infected again. The SIR model was constructed according to the basic assumptions that there is a homogeneous mixing of the infected and susceptible populations and that the total number of population does not change over time. Lets denote susceptible, infectious and recovery as S, I and R respectively. The number of people in each compartment at a particular time-t_0 can be found from the equations $S(t_0)$, $I(t_0)$ and $R(t_0)$. The SIR model is dynamical, since all variables can fluctuate over time.

Each member of the population usually progress from susceptible to infectious to recovery. Let, show it in transmission flow diagram of SIR model 2.1.

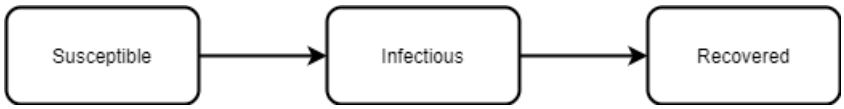


Figure 2.1: SIR

For a complete model specification, arrows must be labeled with compartment conversion factors. Between S and I, the speed of the transition is βIS as shown in Figure 2.2, let's explain this transition. Each day, infectious individuals have a fixed number of contacts, denoted as β. But not all of these contacts are with susceptible people. Based on the combination of these factors and on the assumption that there is homogeneous mixing of population, then, on average, each infectious individual produces βS new infectious cases every day.

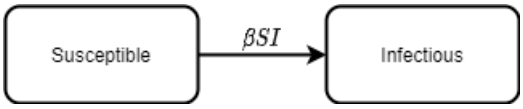


Figure 2.2: SI

The rate of transition from I to R is equal to γI, where γ is the rate of complete recovery of an infected individual. Figure 2.3 provides the transmission flow diagram of this transmission. The value of the γ coefficient is inversely proportional to the recovery period, that is, if the recovery period is designated as H, then the γ=$\frac{1}{H}$. For example, the recovery period for COVID-19 is about 14 days, and it turns out that $\gamma = \frac{1}{14} = 0.071428$

Finally, we obtain the system of nonlinear differential equations 2.1:

$$\begin{cases} \dot{S} = -\dfrac{\beta SI}{N}, \\ \dot{I} = \dfrac{\beta SI}{N} - \gamma I, \\ \dot{R} = \gamma I. \end{cases} \tag{2.1}$$

where β, $\gamma > 0$.

We should note that this model does not include the dynamics of life, that is, it does not take into account the dynamics of birth and mortality.

Since β is the transition coefficient from susceptible to infected, then for $\dot{S}$ it will be negative, because people are no longer receptive. For $\dot{I}$ we add people from the susceptible and subtract cured. Accordingly $\dot{R}$ shows the number of recovered.

Notice that, the sum of this three compartments is:

$$\dot{S} + \dot{I} + \dot{R} = -\frac{\beta SI}{N} + \frac{\beta SI}{N} - \gamma I + \gamma I = 0$$

This 0 means that the number of population is constant. While in real life, we know that this cannot be. While in modeling the constant population is permissible, assuming that the epidemics take place in a short time span.

What we are going to do is we are going to analyze this model. First of all, we should find steady state solution of SIR model. The obvious steady state is $(S, I, R) = (N, 0, 0)$.

So, why this point should be a steady state? The answer is if there is no virus to begin with, then you are never going to see anyone getting sick. Such points are called disease free equilibrium (DFE) and if the model does not have that property, we have the wrong model.

What are the conditions for an epidemic? An epidemic occurs if the number of infected individuals increases.

$$\frac{dI}{dt} > 0 \iff \beta SI - \gamma I > 0$$

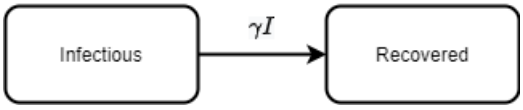


Figure 2.3: IR

or

$$\frac{dI}{dt} > 0 \iff (\beta S - \gamma)I > 0$$

We know that $I > 0$, so

$$\beta S - \gamma > 0 \Rightarrow \beta S > \gamma$$

At the DFE:

$$\beta N > \gamma \Rightarrow \frac{\beta N}{\gamma} > 1$$

So, from this we can find basic reproduction number for the SIR model, namely $\mathscr{R}_0 = \frac{\beta N}{\gamma}$.

This calculations shows us if $\mathscr{R}_0 > 1$, then it can causing an epidemic, whereas if $\mathscr{R}_0 < 1$, then the number of infectious individuals decreases monotonically to 0 and the disease disappears.

3. Mathematical Analysys of the SEI_rI_uRD model

In this chapter we prove Theorem 1.3. To this end, we estimate the basic reproduction number in two different methods.

3.1 Proof of Theorem 1.3 by using the Linearization Method

In this section we prove our first result using Hartman-Grobman theorem aka linearisation method.

Proof of Theorem 1.3. Since the system of differential equations are not linear, we can not find the analytical solution. As we know, according to the Hartman-Grobman theorem [29], the behaviour of a dynamical system in a domain near a hyperbolic equilibrium point is qualitatively the same as the behaviour of its linearisation near this equilibrium point, where hyperbolicity means that no eigenvalue of the linearisation has real part equal to zero. So let us to linearize the system at disease free equilibrium point, by using the *Jacobian*. We consider only to the first four compartment S, E, I_r and I_u from the system, since other two compartments R and D does not influence on the overall solution of the system, so we excluded them.

Initially, lets, find the *disease free equilibrium* (DFE) solution, which means the solution of the system when there is no disease. We find it from the system of ODE, by equalizing all E, I_r and I_u compartments to zero and equalizing the $\dot{S}$ to zero and because of there in no disease, it follows that exposed and both

infectious compartments equal to zero so we obtain the DFE solution:

$$S^* = \frac{\Lambda}{\nu+\theta}, E^* = 0, I_r^* = 0, I_u^* = 0$$

The *Jacobian* J of the system of the first four ODE is defined by:

$$J = \begin{pmatrix} \frac{\partial}{\partial S}(\frac{dS}{dt}) & \frac{\partial}{\partial E}(\frac{dS}{dt}) & \frac{\partial}{\partial I_r}(\frac{dS}{dt}) & \frac{\partial}{\partial I_u}(\frac{dS}{dt}) \\ \frac{\partial}{\partial S}(\frac{dE}{dt}) & \frac{\partial}{\partial E}(\frac{dE}{dt}) & \frac{\partial}{\partial I_r}(\frac{dE}{dt}) & \frac{\partial}{\partial I_u}(\frac{dI_r}{dt}) \\ \frac{\partial}{\partial S}(\frac{dI_r}{dt}) & \frac{\partial}{\partial E}(\frac{dI_r}{dt}) & \frac{\partial}{\partial I_r}(\frac{dI_r}{dt}) & \frac{\partial}{\partial I_u}(\frac{dI_r}{dt}) \\ \frac{\partial}{\partial S}(\frac{dI_u}{dt}) & \frac{\partial}{\partial E}(\frac{dI_u}{dt}) & \frac{\partial}{\partial I_r}(\frac{dI_u}{dt}) & \frac{\partial}{\partial I_u}(\frac{dI_u}{dt}) \end{pmatrix}$$

Lets, compute the *Jacobian* for our epidemic model:

$$J(S;E;I_r;I_u) =$$
$$= \begin{pmatrix} \frac{-\beta}{N}(I_r+\alpha I_u) - (\nu+\theta) & 0 & \frac{-\beta S}{N} & \frac{-\alpha\beta S}{N} \\ \frac{\beta}{N}(I_r+\alpha I_u) & -(\lambda+\nu+\theta) & \frac{\beta S}{N} & \frac{\alpha\beta S}{N} \\ 0 & \epsilon\lambda & -(\gamma+\nu+\mu) & 0 \\ 0 & (1-\epsilon)\lambda & 0 & -(\gamma+\nu+\mu) \end{pmatrix}$$

Lets, evaluate the *Jacobian* at the DFE, we obtain

$$J(S^*;E^*;I_r^*;I_u^*) = J(\frac{\Lambda}{\nu+\theta};0;0;0) =$$
$$= \begin{pmatrix} -(\nu+\theta) & 0 & \frac{-\beta\Lambda}{N(\nu+\theta)} & \frac{-\alpha\beta\Lambda}{N(\nu+\theta)} \\ 0 & -(\lambda+\nu+\theta) & \frac{\beta\Lambda}{N(\nu+\theta)} & \frac{\alpha\beta\Lambda}{N(\nu+\theta)} \\ 0 & \epsilon\lambda & -(\gamma+\nu+\mu) & 0 \\ 0 & (1-\epsilon)\lambda & 0 & -(\gamma+\nu+\mu) \end{pmatrix}$$

The *characteristic polynomial* $\chi(x)$ of the 4×4 above *Jacobian* matrix is

$$\chi(x) = \det(J - xI) = 0.$$

Implementing cofactor expansion along the first column yields

$$\chi(x) = -(\nu+\theta+x)\begin{vmatrix} -(\lambda+\nu+\theta)-x & \frac{\beta\Lambda}{N(\nu+\theta)} & \frac{\alpha\beta\Lambda}{N(\nu+\theta)} \\ \epsilon\lambda & -(\gamma+\nu+\mu)-x & 0 \\ (1-\epsilon)\lambda & 0 & -(\gamma+\nu+\mu)-x \end{vmatrix}.$$

Now considering the determinant of 3×3 matrix we get

$$\begin{aligned}
\chi(x) &= -(\nu+\theta+x)[-(\lambda+\nu+\theta+x)(\gamma+\nu+\mu+x)(\gamma+\nu+\mu+x) \\
&\quad + \frac{\alpha\beta\Lambda\lambda(1-\epsilon)}{N(\nu+\theta)}(\gamma+\nu+\mu+x) + \frac{\beta\epsilon\lambda\Lambda}{N(\nu+\theta)}(\gamma+\nu+\mu+x)] \\
&= -(\nu+\theta+x)(\gamma+\nu+\mu+x)[-(\lambda+\nu+\theta+x)(\gamma+\nu+\mu+x) \\
&\quad + \frac{\alpha\beta\Lambda\lambda(1-\epsilon)}{N(\nu+\theta)} + \frac{\beta\epsilon\lambda\Lambda}{N(\nu+\theta)}] \\
&= (\nu+\theta+x)(\gamma+\nu+\mu+x)[x^2 + x(\lambda+2\nu+\theta+\gamma+\mu) \\
&\quad + [(\lambda+\nu+\theta)(\gamma+\mu+\nu) - \frac{(\alpha(1-\epsilon)+\epsilon)\lambda\beta\Lambda}{N(\nu+\theta)}]].
\end{aligned}$$

Lemma 3.1. *For the mentioned quadratic equation $x^2 + px + q = 0$; if $p>0$ and $q>0$, then the real parts of the solutions are negative.*

Proof. Let, $x_1 = a + bi$ and $x_2 = a - bi$ are complex conjugate solutions of the given mentioned quadratic equation. Then, according to Vieta's theorem: $-p = x_1 + x_2 = a + bi + a - bi = 2a$ and $q = x_1x_2 = (a + bi)(a - bi) = a^2 + b^2$. Therefore, if $p > 0$, then $a < 0$ □

Two *eigenvalues* are obvious $x_1 = -\nu - \theta$ and $x_2 = -\gamma - \nu - \mu$, another two *eigenvalues* we will not find (it is complicated), but we want the real parts of all eigenvalues should be negative. Since all parameters are positive, so $(\lambda + 2\nu + \theta + \gamma + \mu) > 0$. Thus, if $[(\lambda+\nu+\theta)(\gamma+\mu+\nu) - \frac{(\alpha(1-\epsilon)+\epsilon)\lambda\beta\Lambda}{N(\nu+\theta)}] > 0$, it means if $\frac{\beta\lambda\Lambda(\epsilon+\alpha(1-\epsilon))}{(\lambda+\nu+\theta)(\gamma+\nu+\mu)(\nu+\theta)N} < 1$ then the real parts of all eigenvalues are negative, according to *lemma.*

Therefore, the *basic reproduction number* is

$$\mathscr{R}_0 = \frac{\beta\lambda\Lambda(\epsilon+\alpha(1-\epsilon))}{(\lambda+\nu+\theta)(\gamma+\nu+\mu)(\nu+\theta)N}$$

□

3.2 Proof of Theorem 1.3 by using the Next Generation Matrix Method

In this section we use the second approach to prove the formula of the basic reproduction number, which is called Next Generation Matrix Method

Proof. According to the paper work of P. van den Driessche and James Watmough [28]. We consider only the infected individuals E, I_r and I_u. From our proposed model (1.1) the rate of new infections in each compartment $\mathscr{F}$ and the rate of other transitions between compartments $\mathscr{V}$ can be rewritten as:

$$\mathscr{F} = \begin{pmatrix} \frac{\beta S I_r}{N} + \frac{\alpha\beta S I_u}{N} \\ 0 \\ 0 \end{pmatrix} \text{ and } \mathscr{V} = \begin{pmatrix} E(\lambda+\nu+\theta) \\ -\epsilon\lambda E + I_r(\gamma+\mu+\nu) \\ -(1-\epsilon)\lambda E + I_u(\gamma+\mu+\nu) \end{pmatrix}$$

Thus, computing their Jacobian we arrive at

$$F = \begin{pmatrix} 0 & \frac{\beta S}{N} & \frac{\alpha\beta S}{N} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} \lambda+\nu+\theta & 0 & 0 \\ -\epsilon\lambda & \gamma+\mu+\nu & 0 \\ -(1-\epsilon)\lambda & 0 & \gamma+\mu+\nu \end{pmatrix}$$

To find the inverse matrix of V, we need the determinant of V and the matrix of cofactors where elements are minors of the matrix V. So we get the inverse matrix:

$$V^{-1} = \begin{pmatrix} \frac{1}{\lambda+\nu+\theta} & 0 & 0 \\ \frac{\epsilon\lambda}{(\nu+\gamma+\mu)(\lambda+\nu+\theta)} & \frac{1}{\gamma+\mu+\nu} & 0 \\ \frac{(1-\epsilon)\lambda}{(\lambda+\nu+\theta)(\gamma+\mu+\nu)} & 0 & \frac{1}{\gamma+\mu+\nu} \end{pmatrix}$$

Therefore the next generation matrix is

$$FV^{-1} = \begin{pmatrix} \frac{\beta\lambda\Lambda(\epsilon+\alpha(1-\epsilon))}{(\lambda+\nu+\theta)(\gamma+\nu+\mu)(\nu+\theta)N} & \frac{\beta\Lambda}{N(\nu+\theta)(\gamma+\mu+\nu)} & \frac{\alpha\beta\Lambda}{N(\nu+\theta)(\gamma+\mu+\nu)} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

Since the next generation matrix is an upper triangular matrix so its eigenvalues are diagonal entries. Therefore, two eigenvalues equal to zero, while the third one is equal to $\frac{\beta\lambda\Lambda(\epsilon+\alpha(1-\epsilon))}{(\lambda+\nu+\theta)(\gamma+\nu+\mu)(\nu+\theta)N}$. Since all parameters are positive, then

this eigenvalue is also positive $\frac{\beta\lambda\Lambda(\epsilon+\alpha(1-\epsilon))}{(\lambda+\nu+\theta)(\gamma+\nu+\mu)(\nu+\theta)N} > 0$. As discussion in § 2.6 the largest eigenvalue or spectral radius of FV^{-1} is the basic reproduction number.

$$\mathscr{R}_0 = \rho(FV^{-1})$$

Finally, the *basic reproduction number* of the proposed epidemic model 1.1 is:

$$\mathscr{R}_0 = \frac{\beta\lambda\Lambda(\epsilon + \alpha(1-\epsilon))}{(\lambda+\nu+\theta)(\gamma+\nu+\mu)(\nu+\theta)N}$$

□

4. Parameter estimation

4.1 Goverment cost function

At the present time, during the pandemic, various events are happening all over the world, some countries are going bankrupt due to a lack of workers, some countries are rising in the economic mainstream due to the fact that they were prepared for such a situation. Different countries produce different treatments, including a vaccine, with the opinion that the situation will fall into place, as before. In our country,there are several types of vaccines, including our domestic QazCovid.

For analysis with the available data, calculating certain things, predicting the situation of the pandemic, we chose one vaccine, produced by the country of Russia, under called Sputnik-V. In cases of vaccination of the population, what will happen if the state pays for the vaccine to the population, in which cases the state kazyna will be replenished, this is the most important question for the state, and we have calculated all this thanks to this function.

This function contains all the points in the case of vaccination. The tax paid to the state from the salary, in the amount of 10 percent. Treatment that is paid by the state for the sick, in the amount of 500 thousand tenge for two weeks and the vaccine itself.

In our case Government cost is a linear function that has a minimum and maximum vaccination rate. We take 0.01 as the maximum value, and 0.0001 as the minimum. In mathematical optimization, the loss function, a function to be minimized.

4.1.1 Dependence of vaccination rate θ to the discount

Dependencies between parameters are present, since these are all variables that depend on each other. Vaccination rate if you look at the profit side, attracting marketing to increase vaccination, there are different ways.

The simplest and most understandable is to reduce the price of vaccination, after which the number of vaccinated will increase significantly. The dependencies can be viewed from the function, in our case, the vaccination function directly depends on the discount, as in the usual cubic function, where the function y depends on x.

Below are examples of the dependency, and then the function itself. Where we look that the function is linear and has a maximum and minimum value.

We take the maximum value as 0.01, and the minimum value as 0.0001.Where did these numbers come from and how to understand them, we assume that if the vaccination reaches the maximum value of 0.01, if you translate this into days, you get 100 days. If you explain it in ordinary words, the entire population is vaccinated in a few days, also for the minimum value.

To model θ in terms of government discount we assume:

- people are more likely to get vaccinated with discounted price
- linear dependence.

$$\theta(discount) = \theta_0 + (discount/20000) \times (\theta_1 - \theta_0),$$

$$\theta_0 = 0.0001, \theta_1 = 0.01$$

Now I will go through the points of the function. To find the government expenses we need to find the daily cost, this is our Treatment+Vaccination Price-Tax.

- Daily cost = -Tax+Treatment+Vaccination Price

Let's go through each of them the first is our tax,we assume that half of the entire population works, and we have a tax of 10 percent of the salary. In a day, the average salary is 3.41 US dollar, and we have a working time of 8 hours, multiply them and get the average daily wage.

- Tax=$\frac{1}{2}$ (average daily wage)(tax rate)

Treatment we have is equal to the number of cases multiplied by the cost of daily treatment, and we have it according to the Internet for two weeks 500 thousand, divide it by 14.

- Treatment=(Number of patients)(Daily treatment cost)

The cost of vaccination is equal to the level of vaccination multiplied by the amount of infected and clean, and still multiply by how much to pay the state. All this is considered in three years apart.

- Vaccination price=$\theta(E+S)$(vaccination cost to government),
- Total cost= $\sum_{t=0}^{1000} dailycost_t(x)\exp^{-\sigma t}$

$$\text{Total cost} = \sum_{i=0}^{1000}((e^{-\sigma i}) \times (N_i \times \text{tax rate} \times \text{average daily wage} +$$

$$IR_i \times \text{Daily treatment cost} + \theta \times (E_i + S_i) \times \text{vaccination cost to government}))$$

4.2 Python simulation

4.2.1 SEI_rI_uRD model

The technical part consists of several stages, the first of which is writing the model to a function. The model is the same one that we chose SEI_rI_uRD. Opening the function, we give all the parameters that are present in the model. Next, we also write down the entire differential equation, for these stages we do not use any libraries yet, but everything is still ahead.

```
def SE(I_R)(I_U)RD_model(y, t, beta, gamma, alfa, new, lambdaa, epsilon, mu,
    tau, teta):
    S, E, IR, IU, R, D = y

    dS_dt = tau -((beta*S*IR)/N0) - ((alfa*beta*S*IU)/N0) - S*(new + teta)
    dE_dt = ((beta*S*IR)/N0) + ((alfa*beta*S*IU)/N0) - E*(lambdaa + new +
   teta)
```

```
    dIR_dt = epsilon*lambdaa*E - ((gamma+mu+new)*IR)
    dIU_dt = ((1-epsilon)*lambdaa*E) - ((gamma+mu+new)*IU)
    dR_dt = gamma*(IR+IU) - (new*R) + teta*(S + E)
    dD_dt = mu*(IR+IU) + new*(S+E+IU+IR+R)

    return([dS_dt, dE_dt, dIR_dt, dIU_dt, dR_dt, dD_dt])
```

Listing 4.1: SEI_rI_uRD model

4.2.2 Model parameters

The next step is related to the parameters that we took from official sources "https://www.worldometers.info". Where are the required initial digits for each individual parameter.

If you are wondering how we have identified unreported individuals, we take the cases by a percentage of 60 to 40. We assume that 60 percent are reported individuals, and the remaining 40 percent are unreported individuals.

Λ–daily birth, β–transmission rate, α–infection effect, ϵ–proportion of reported Infectious, ν–death rate due to disease, μ–natural death rate, γ–1/recovered period, λ–1/incubation period, θ–vaccination rate.

```
#Kazakhstan
N0 = 18907256 # population
S0 = N0
IR0 = 16321 # reported
IU0 = 6528 # unreported
E0 = (IR0 + IU0)*5
R0 = 167914 # recovered
D0 = 2476 # dead
beta = 0.4 # tranmission rate
gamma = 1/14 # 1/recovery period
lambdaa = 1/5 # 1/incubattion period
epsilon = 0.6
mu = 2476/(R0) # due to covid
new = 165556/(365*N0) # natural death rate
teta = 0 # vaccination
alfa = 0.21 # infection effect
tau = 419582/365 # daily birth
```

Listing 4.2: Parameters

4.2.3 Solving equation

Scipy library

The technical part of our thesis, all our calculations and analysis were carried out in the python platform. If we talk about python, it is a high-level general-purpose programming language with dynamic strict typing and automatic memory management, focused on improving developer productivity, code readability and quality, as well as ensuring the portability of programs written in it.

Python has ready-made libraries for solving problems in the field of mathematics, including our problem with an ordinary differential equation. To do this, we used a library called SciPy, SciPy is an open source library for the Python programming language designed to perform scientific and engineering calculations. The features of this library are very versatile, for example:

- search for minima and maxima of functions;
- calculation of function integrals;
- support for special functions;
- signal processing;
- image processing;
- working with genetic algorithms;
- solution of ordinary differential equations;
- etc.

The target audience is users of MATLAB and Scilab products.

To visualize the results of calculations, the Matplotlib library is often used, which is an analog of the MATLAB graphics output tools.

The SciPy library is distributed under the terms of the BSD license. The developers are funded by the company "Enthought". The main data structure in SciPy is a multidimensional array implemented by the NumPy module (older versions of SciPy used the Numeric module).

How to use the library in our task, let's explain in the section what and how. First of all, we need to write our model to a function, then we use the integrate.odeint function in the libraries and give it the model itself, after the initial values for all parameters and most importantly in what time interval. After the model, we divide the list according to the available parameters.

Differential equation solve

```
import scipy
from scipy.integrate import odeint
for x in range(0,20001,100):
    teta = teta_0 + (x/20000)*(teta_1-teta_0)
    vaccdiscount = (20000-x)
    solution = scipy.integrate.odeint(SEIRD_model, [S0, E0, IR0,IU0, R0, D0
   ], t, args=(beta, gamma, alfa, new, lambdaa, epsilon, mu, tau, teta))
    solution = np.array(solution)
    S = solution[:, 0]
    E = solution[:, 1]
    IR = solution[:, 2]
    IU = solution[:, 3]
    R = solution[:, 4]
    D = solution[:, 5]

    N = S + E + IR + IU + R
```

Listing 4.3: Solving equation

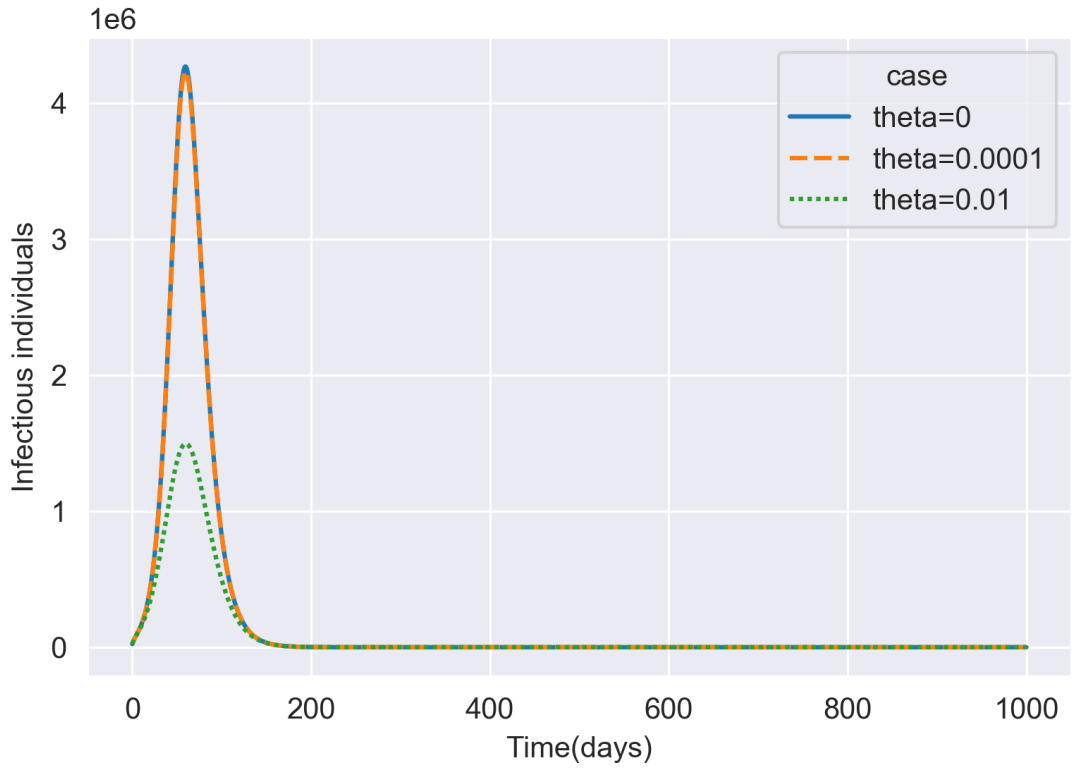
Dynamics of $I(t)$

In the first graph:4.1, we drew the number of cases, in three cases, when theta is zero, maximum and minimum. We see that in the first half of the year there will be a lot of cases, and that if people are vaccinated, the number of cases will be less by 250 thousand.

The dynamics of the total number infectious individuals in the first three years is represented in following line graph 4.1, where the Ox axis is the days, while the Oy axis is the number of infected individuals. According to the diagram, we can observe that even if the health care organization will vaccinate the citizens, the peak of infectious individuals will be in first half of the year. Although, the vaccination is significantly improves the situation in the number of infectious cases, we can observe that the vaccination with the maximum capacity makes it better in

approximately three times from the 4.25 million cases (without vaccination) to 1.5 million cases. Another important thing, that worth to mention is following: the vaccination with the minimum capacity does not change the situation absolutely, but with any vaccination rate, after the first half of the year the situation will be stabilized and the number of infectious individuals will approach to zero. It means, in the long term period there is no difference in making or not making the vaccination, but the total number of death due disease is considerably different, how we can observe in the next graph. Now, let consider on the dynamic of death in the following line graph.

Figure 4.1: Dynamics of $I(t)$



Dynamics of $D(t)$

The line graph below:4.2 illustrates death of individuals in the three different cases of vaccination of the population in the prospects for more than two years.

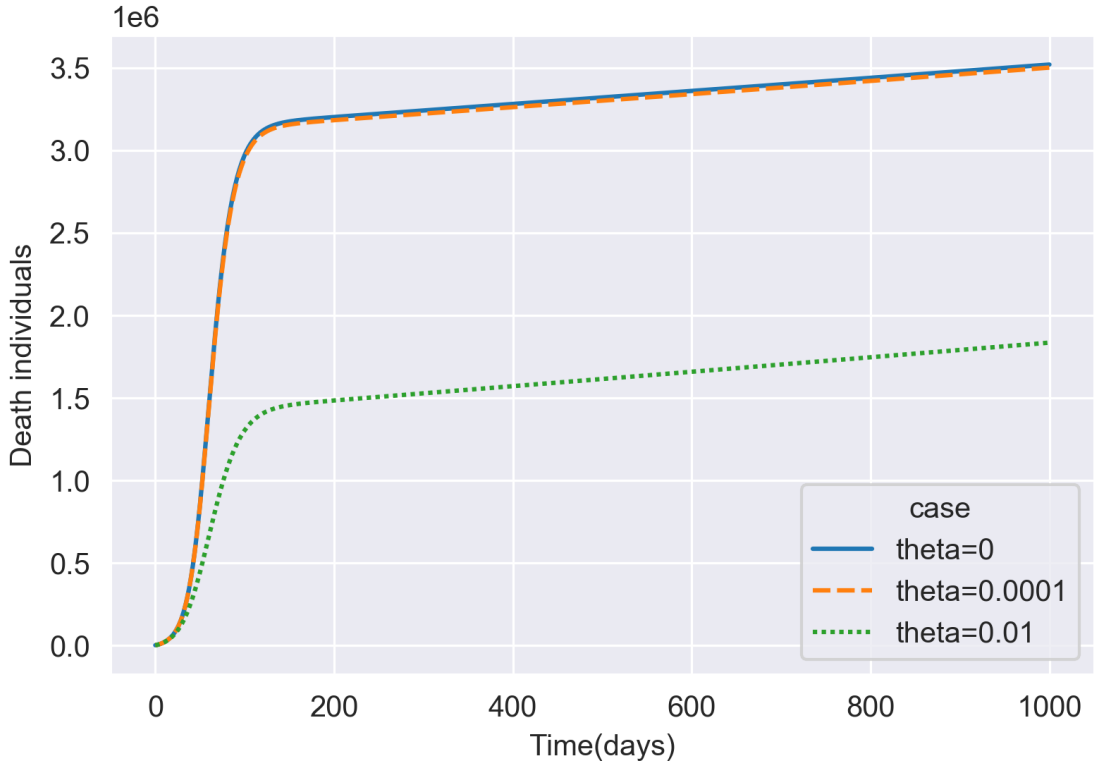
Overall after vaccination of population, the death effect begins after about 20 days. The death of vaccination cases rises rapidly, the reason for that is as it was mentioned before, that this is directly related to the number of infected people,

and after six months it begins to increase slightly. If the number of infected people increases, respectively, the mortality rate also grows.

Unvaccinated and minimally vaccinated cases don't make much difference, which is about 50 people.

Up to 20 days, the total mortality was single. Further, the vaccinated people began to die sharply, reaching a point of about 1.4 thousand people. While, with the same period of time, the unvaccinated and the minimum vaccinated number of citizens died quickly, reaching 3.2 and 3.25 thousand people, respectively. After half a year, the mortality rate began to go up slowly. The number of deaths in vaccinated people has reached 1.7 thousand in 1000 days, whereas in unvaccinated and minimally vaccinated people, the death rate reaches 3.5 and 3.55 thousand.

Figure 4.2: Dynamics of $D(t)$



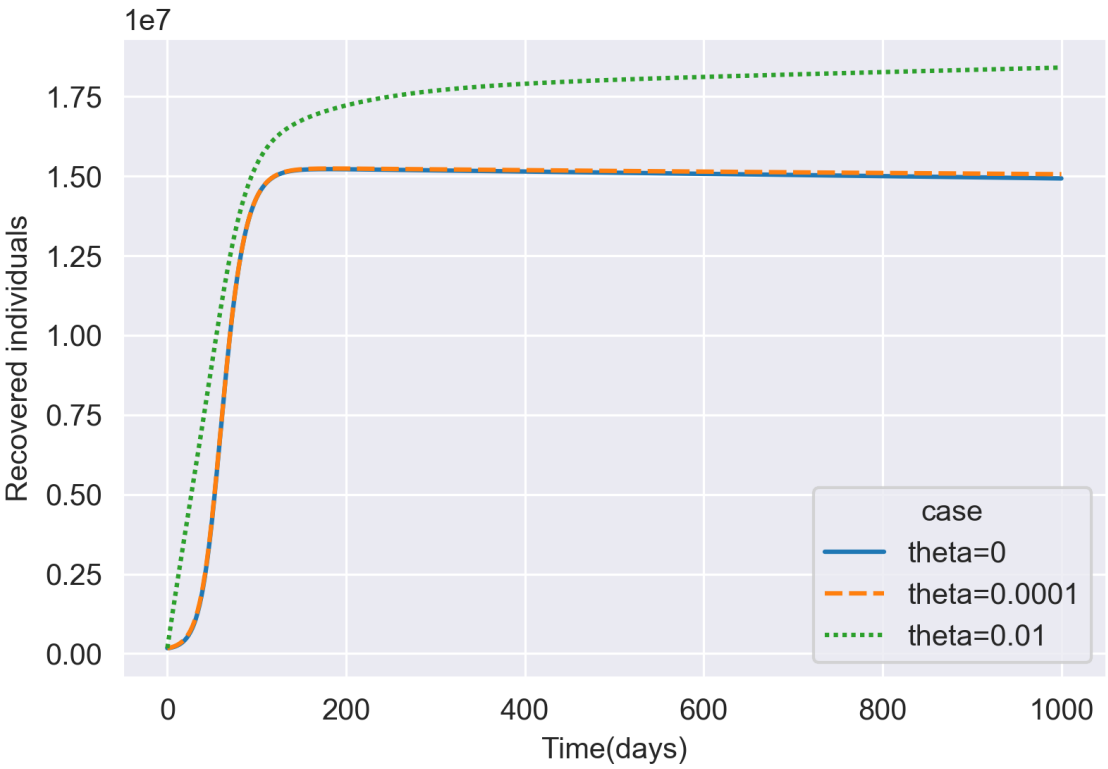
Dynamics of $R(t)$

The line graph below :4.3 illustrates recovered individuals in the three different cases of vaccination of the population in the time of 1000 days.

Unvaccinated and minimally vaccinated cases don't make much difference.

Vaccinated case of recovered individuals shows steeply soar up to six months reaching 16.3 thousand people. Then it can be noticed a tendency for a gradual increase to 18.5 thousand people in 1000 days. Recovered people who were not vaccinated or minimally vaccinated before 20 days, the indicator was minimal, because the immune system began to work and it took a certain time. After 20 days began to feel good dramatically and the number of people was about 15.0 thousand. Further, value remains stable up to 1000 days.

Figure 4.3: Dynamics of $R(t)$



Dynamics of $S(t)$ and $R(t)$

The line graph below:4.4 illustrates recovered and sustainable individuals in the three different cases of vaccination of the population in the time of 1000 days.

Unvaccinated and minimally vaccinated cases don't make much difference in both options. The graph shows two variations in order to compare.

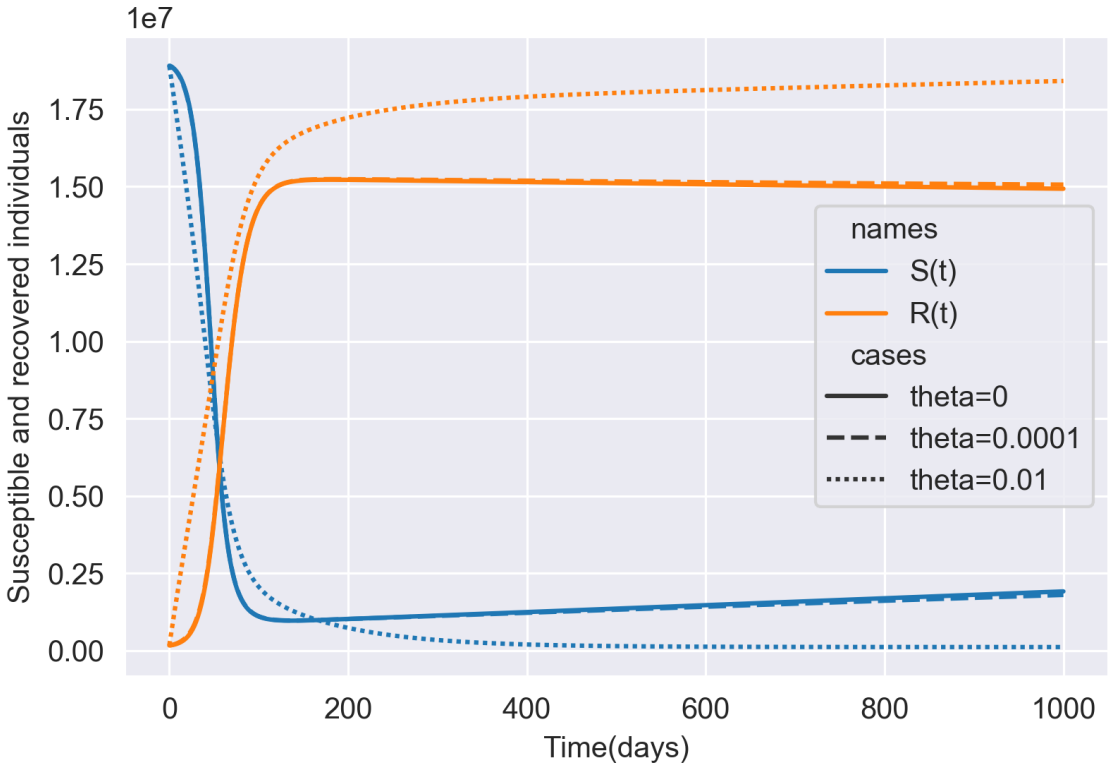
For example, sustainable option contains own three cases of vaccination, and recovered option also contains the same own cases. Sustainable unvaccinated and minimally vaccinated option rapidly go down from 18.0 thousand to 6.0 thousand of people in 80 days, and at this point intersect with the recovered unvaccinated

and minimally vaccinated option which steeply climb from 0. Sustainable unvaccinated and minimally vaccinated option further rapidly go down reaching thousand people in 100 days, and slightly increase to two thousand people in 1000 days. While, recovered unvaccinated and minimally vaccinated option further steeply climb up 15 thousand individuals at 120 days. Further, value remains stable up to 1000 days.

Sustainable vaccinated option sharply declines from 18.0 thousand to 8.5 thousands individuals and intersects with recovered vaccinated option at this point in 70 days, also sustainable vaccinated option intersects with sustainable unvaccinated and minimally vaccinated and recovered unvaccinated and minimally vaccinated options in 80 days reaching 6 thousand individuals. Further, both of them continue their trajectory, sustainable vaccinated option in 100 days drop slightly from 2 thousand to 0 up to 1000 days, while recovered vaccinated option in 100 days slowly rise up from 17 thousand to 18 thousand up to 1000 days.

To sum up, it can be observed that the number of sustainable people declines, the rate of recovered individuals will rise accordingly. Both values are dependent on each other and this is illustrated on one graph.

Figure 4.4: Dynamics of $S(t)$ and $R(t)$



Optimization government cost

The most recent and main graph: 4.5, shows the profit of the state at a percentage of the paid/unpaid vaccine. The vertical Oy axis illustrates government cost, while the horizontal Ox axis demonstrates discount rate percentage. Even if the values on the vertical axis are negative, this means a profit for the state in billions of money. 0 percent means that the vaccine was unpaid for the population, whereas 100 percent means that the vaccine was free for people.

In the graph, there can be seen one curve that is directed downward. So, starting from zero, the vaccine that was not paid brings in profits to the state in the amount of 50 billion, then until it reaches 20 percent, the curve grows slightly, and then there is a considerably plummet. For instance, 40 percent of paid vaccine government cost achieves 53 billion. 80 percent shows value of 66 billion, and with 100 percent of free vaccine, graph shows 76.5 billion of government cost.

To sum up, it can be observed that with full payment for the vaccine, it is beneficial to both the state and the population. The population will not pay by themselves for the vaccine, and the state will receive the maximum benefit of 76.5 billion.

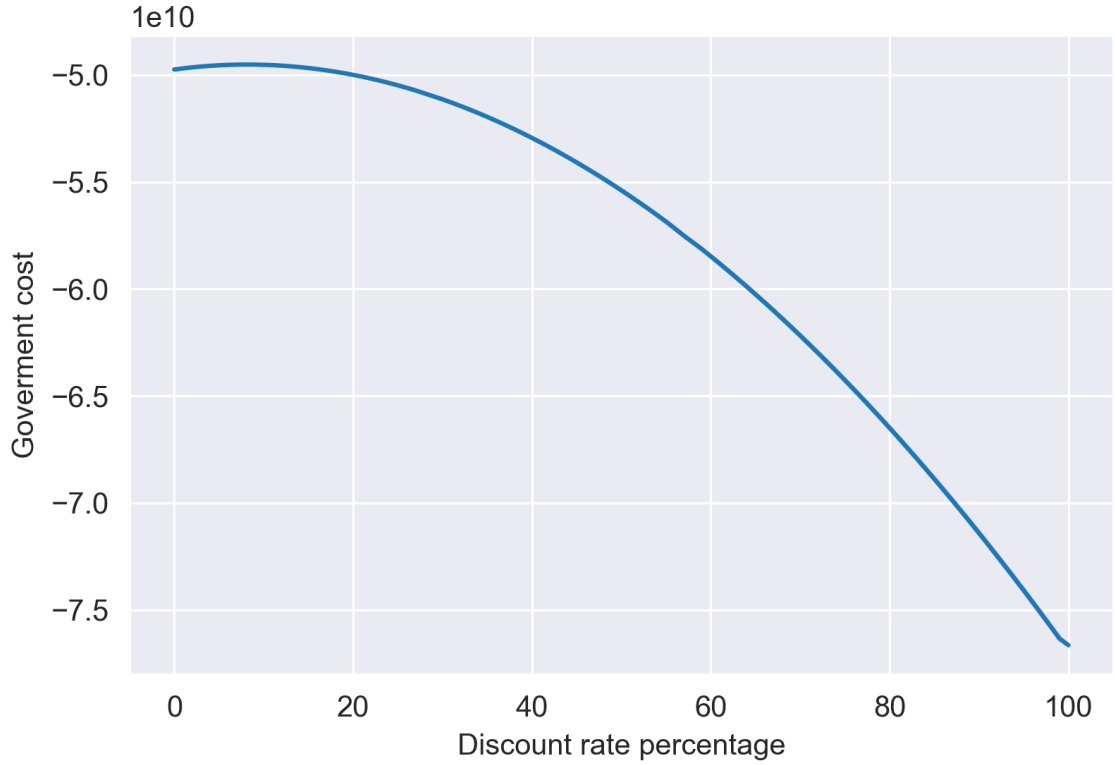
```
for i in range(0,1000):
  cost = cost + np.exp(-delta*i)*(-tax*dailyavewage*N[i]/2 + treatment*IR[i]
    + vaccdiscount*teta*(S[i]+E[i]))
gcost.append(cost)
cost = 0
```

Reflections for 1000 days since February 2021

We saw several variants of graphs with different parameters. Now, to accurately determine the figures for the main parameters, it was possible to build a table with a discount. We chose the parameters that are the most important, they are the number of death individuals, the government cost, number of reproductions. What is the reproduction number, this parameter describes the contagion of the epidemic.

Now we look at the figures for the government cost, we see that at 0 and 20 percent of the discount, the difference is not very large about 200 million tenge, and between 20 and 40 percent of the discount, the difference is already 3 billion tenge, the further the difference grows. At 40 and 60 percent of the discount, the difference is already 4.5 billion tenge, and at 60 and 80 percent of the discount,

Figure 4.5: Dynamics of government cost function



the difference is 8 billion tenge. At the very last interval, the difference is already rounding out 10 billion.

Then moving on to the second column, we see the number of death individuals, also at these intervals. If you count the difference between the intervals, there is no very large jump or drop, the difference lies between 290-350 thousand people.

The most recent column is the reproduction number in the range from 0 to 100 percent discount. The biggest decline is in the first interval between 0 and 20 percent of the discount, the reproduction number drops from 1.5 to 0.09, then it moves steadily in one interval.

Reflections for 1000 days since February 2021			
Discount Rate Percentage	Government cost	Total death	R_0
0%	-49 776 480 958	3 501 265	1.55545
20%	-49 965 090 003	3 137 293	0.09076
40%	-52 851 488 449	2 783 307	0.04631
60%	-58 326 088 595	2 443 722	0.03088
80%	-66 289 629 640	2 125 084	0.02306
100%	-76 652 225 146	1 835 327	0.01833

5. Conclusion

To sum up our diploma project, the goals which we pursued, such us to find the formula of the *basic reproduction number* 1.3 and to optimize the government costs 1.6 were successfully achieved. Our work contains four chapters.

The actuality of the problem and the development of our SEI_rI_uRD epidemic 1.2 model with the main results 1.3 were presented in the introduction chapter.

In the background chapter we get acquainted with the topics which were related to our study, also we introduced the history of the epidemiology development and its applications. For better understanding of the compartmental epidemic models theory we introduced in details the construction and analysis of the SIR epidemic model 2.7. To analyse the compartmental epidemic models, we presented two approaches such us the Linearization (Hartman-Grobman) method 2.5 and the Next-Generation matrix method 2.6, which have been used to find the formula of the basic reproduction number 1.1, which is the most important parameter in the epidemiology.

In the following section we prove our formula of the basic reproduction number by using two different methods.

The main optimization results and numerical solution were presented in the chapter four. The optimization of the government cost give us the following result: the government cost is minimized with making vaccination fully free of charge.

In our work, we offer one of the possible solution for the government how to optimize the government costs during the financial crises due to COVID-19. Moreover, we find the formula of the basic reproduction number, so by taking empirical data it is possible to find the value of the basic reproduction number for further analysis. Although, we have done the local stability analysis, there is still open questions regarding the global stability of the epidemic model or the sensitivity analysis of the basic reproduction number formula.

A. Appendix code

Here is the photon code which we used to solve the model and optimize the government cost.

```
def SE(I_R)(I_U)RD_model(y, t, beta, gamma, alfa, new, lambdaa, epsilon, mu,
    tau, teta):
    S, E, IR, IU, R, D = y

    dS_dt = tau -((beta*S*IR)/N0) - ((alfa*beta*S*IU)/N0) - S*(new + teta)
    dE_dt = ((beta*S*IR)/N0) + ((alfa*beta*S*IU)/N0) - E*(lambdaa + new +
   teta)
    dIR_dt = epsilon*lambdaa*E - ((gamma+mu+new)*IR)
    dIU_dt = ((1-epsilon)*lambdaa*E) - ((gamma+mu+new)*IU)
    dR_dt = gamma*(IR+IU) - (new*R) + teta*(S + E)
    dD_dt = mu*(IR+IU) + new*(S+E+IU+IR+R)

    return([dS_dt, dE_dt, dIR_dt, dIU_dt, dR_dt, dD_dt])
```

Listing A.1: SEI_rI_uRD model

```
#Kazakhstan
N0 = 18907256 # population
S0 = N0
IR0 = 16321 # reported
IU0 = 6528 # unreported
E0 = (IR0 + IU0)*5
R0 = 167914 # recovered
D0 = 2476 # dead
beta = 0.4 # tranmission rate
gamma = 1/14 # 1/recovery period
lambdaa = 1/5 # 1/incubattion period
epsilon = 0.6
mu = 2476/(R0) # due to covid
new = 165556/(365*N0) # natural death rate
teta = 0 # vaccination
alfa = 0.21 # infection effect
tau = 419582/365 # daily birth
```

Listing A.2: Parameters

```
import scipy
from scipy.integrate import odeint
for x in range(0,20001,100):
    teta = teta_0 + (x/20000)*(teta_1-teta_0)
    vaccdiscount = (20000-x)
    solution = scipy.integrate.odeint(SEIRD_model, [S0, E0, IR0,IU0, R0, D0
   ], t, args=(beta, gamma, alfa, new, lambdaa, epsilon, mu, tau, teta))
    solution = np.array(solution)
    S = solution[:, 0]
    E = solution[:, 1]
    IR = solution[:, 2]
    IU = solution[:, 3]
    R = solution[:, 4]
    D = solution[:, 5]

    N = S + E + IR + IU + R
```

Listing A.3: Solving equation

```
plt.figure(figsize=[8, 6])
plt.plot(t, R, label="theta is equal 0",color='red')
plt.plot(t, R1, label="theta is minimum",color='green')
plt.plot(t, R2, label="theta is maximum",color='blue')
plt.grid()
plt.legend()
plt.xlabel("Time(days)")
plt.ylabel("Population")
# plt.title("SEIRD model")
plt.savefig('R.png',dpi=300)
plt.show()
```

Listing A.4: Draw graph

```
RepNum = (beta*lambdaa*tau*(epsilon+alfa*(1-epsilon)))/((lambdaa+gamma+teta)
   *(gamma+new+mu)*(new+teta)*N0)
print('Reproduction number with get parameters:',RepNum)
```

Listing A.5: Calculate reproduction number

```
c = []
for x in range(0,20001,20):
    c.append((x/20000)*100)
plt.figure(figsize=[8, 6])
plt.plot(c, IR+IU, label="I(t)",color='red')
plt.plot(c, R, label="R(t)",color='green')
plt.plot(c, D, label="D(t)",color='yellow')
plt.grid()
plt.legend()
plt.xlabel("Discount rate percentage")
plt.ylabel("Parameters")
```

```
# plt.title("SEIRD model")
plt.savefig('Table.png',dpi=300)
plt.show()
```

Listing A.6: Draw second graph

```
plt.figure(figsize=[8, 6])
plt.plot(t, IR+IU,'1', label="theta is equal 0",color='red')
plt.plot(t, IR1+IU1,'H', label="theta is minimum",color='green')
plt.plot(t, IR2+IU2,'o', label="theta is maximum",color='blue')
plt.grid()
plt.legend()
plt.xlabel("Time(days)")
plt.ylabel("Population")
# plt.title("SEIRD model")
# plt.savefig('I.png',dpi=300)
plt.show()
```

Listing A.7: Draw third graph

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