NEZİHAL GÖKBULUT

MATHEMATICAL AND STATISTICAL MODELLING OF COVID-19

2020 NEU

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A THESIS SUBMITTED TO THE GRADUATE SCHOOL OF APPLIED SCIENCES

OF

NEAR EAST UNIVERSITY

By

NEZİHAL GÖKBULUT

In Partial Fulfillment of the Requirements for the Degree of Master of Science in Applied Mathematics

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Approval of Director of Graduate School of Applied Sciences

Prof.Dr.Nadire ÇAVUŞ

We certify this thesis is satisfactory for the award of the degree of Masters of Science in Mathematics

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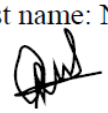
Signature:  .

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To my parents…

ABSTRACT

In this thesis, some of the popular ideas about controlling the spread of the infectious disease Covid-19, which became a pandemic, are analyzed.

At first, herd immunity idea is discussed since at the beginning of the pandemic, it was one of the frequent asked questions. By using the data of cases in North Cyprus, basic reproduction number and effective reproduction number, i.e., herd immunity threshold, are constructed and calculated for this country in order to analyze the idea of herd immunity. Then, the number of reported cases of the countries Sweden, Norway, Finland, and Denmark are compared with the consideration of same regions with same economic, cultural, and health conditions should have similar results. Here, Sweden is the only country in these countries that supports herd immunity idea and so this comparison showed the effect of herd immunity.

Finally, the answer of the most popular question 'Can we control the spread of Covid-19 by using death rates?' is investigated by using statistical modelling with statistical distributions. For this purpose, reported death cases are used. In order to achieve an accurate result, gamma distribution is used for the delay of reported deaths with the expectation of decrease in error. For the assumption of deaths, prior distribution is chosen as binomial distribution. With this prior distribution, posterior distribution is applied for finding death ratio.

Keywords: Covid-19; effective reproduction number; basic reproduction number; statistical modelling; gamma distribution; delay; binomial distribution

ÖZET

Tezde, günümüzde dünya çapında salgın haline gelen Covid-19 hastalığının yayılımını kontrol edebilmek için popüler olan görüşlerden bazıları analiz edilmiştir.

İlk olarak, salgının başlangıcından beri tartışılan sürü bağışıklığı fikri incelenmiştir. Kıbrıs'ın kuzeyindeki günlük vaka sayıları kullanılarak, bu ülke için sürü bağışıklığı fikrini analiz etmek amacıyla, hastalığın temel üreme oranı ve etkin üreme oranı, diğer adıyla sürü bağışıklığı eşiği, oluşturulmuş ve hesaplanmıştır. Daha sonra, aynı bölgede yer alan ve aynı ekonomik, kültürel ve sağlık koşullarına sahip olan İsveç, Norveç, Finladiya ve Danimarka ülkeleri, bu nedenlerden dolayı benzer sonuçlar vermeleri gerektiği düşünülerek, ülkelerin rapor edilen vaka sayıları karşılaştırılmıştır. Ülkeler arasında sürü bağışıklığı fikrini savunan tek ülke İsveç olduğundan, yapılan karşılaştırma bu fikrin hastalık üzerindeki etkisini göstermiştir.

Son olarak, güncelliğini koruyan 'Covid-19 hastalığının yayılımı ölüm oranlarıyla kontrol edilebilir mi?' sorusu istatistiksel modelleme ve dağılımlarla araştırılmıştır. Bu amaçla, rapor edilen ölüm oranları kullanılmıştır. Kesin sonuç elde edebilmek için rapor edilen ölümlerdeki gecikme süresi gamma dağılımı ile hesaplanmıştır. Buradaki beklenti gama dağılımının, gecikme süresini, dolayısıyla hesaplamalardaki hatayı en aza indirgemesidir. Ölümlerin varsayımında önsel dağılım olarak binom dağılımı kullanılmıştır. Bu önsel dağılım ile ölüm oranını bulmak için sonsal dağılım uygulanmıştır.

Anahtar Kelimeler: Covid-19; etkin çoğalma oranı; temel çoğalma oranı; istatistiksel modelleme; gama dağılımı; gecikme; binom dağılımı

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INTRODUCTION

1.1 Mathematical and Statistical Modelling

Epidemiology is defined as the science of epidemics. In other words, it is a field of study that aims investigating the factors responsible from the formation and spread of infectious diseases. Mathematicians make respectable contributions to epidemics that humanity face with during the centuries by constructing mathematical models (Cetin, Kiremitci, & Yurt, 2009). Mathematical models are very useful to understand the transmission and infectiousness of epidemics. These models use occurred cases or deaths to forecast the future of an epidemic. The earliest study of mathematical modelling in infectious diseases was made by Daniel Bernoulli in 1760. He constructed a mathematical (deterministic) model to show the positive effect of vaccination on smallpox (Bacaer, 2011; White & Enright, 2010).

In mathematical modelling, finding the basic reproduction number of any infectious disease is the most common way for the control of the spread. Basic reproduction number, denoted by R_0, is the average number of secondary infections occurred by each primary infection in a fully susceptible population (Guerra, et al., 2017).

Next Generation Matrix (NGM) method is one of the most popular methods for calculating R_0 of any infectious disease. This method was first introduced in 1990, by Diekmann and Hesterbeek. In order to use NGM method, firstly, population should be divided into compartments. Then, system of Ordinary Differential Equations should be constructed with the compartments of population for the disease. By using this system, two matrices are

constructed as the ones that are new infected in the population, denoted by F, and the rest of the population, denoted by V. Then, the spectral radius of the matrix multiplication $F.V^{-1}$ gives the basic reproduction number, R_0 (Diekmann, Heesterbeek, & Roberts, 2010; Roberts & Heesterbeek, 2012).

A statistical model is a type of mathematical model that approximates the truth and by using these approximations we can make predictions about the future of a disease. In order to construct a model, we need random and non-random variables to define a relationship between them. These models help us to understand the evolution of an epidemic in time, individual level process of transmission in a population, and prevalence of an infectious disease (Grassly & Fraser, 2008). In this modelling, statistical methods are used to analyze the collected data and forecast the future of an epidemic. The validity of inferences depends on the quality and accuracy of collected data. So, the most important thing is to have a real data.

Techniques like SIR and SIS models in mathematical modelling are typically deterministic that neglect randomness and variability. Usually, they calculate a single estimation for new infections at each time point and in that estimation, they do not count any uncertainty. However, methods in statistical modelling can give evidence about whether an infection is spreading or under control, decisions made by the government are enough or not, public health interventions are efficient or not, or whether an infection can affected by demographic factors or not. We can collect evidences about these questions in terms of probability (Brown & Ozanne, 2019).

One of the valuable works in statistical modelling was made by Enko in 1889. He published a notable probabilistic model to describe the measles epidemic in discrete time. By using the model, he estimated the number of contacts between susceptible and infected individuals in

the population. The model of Enko pioneers the well-known Reed-Frost chain binomial model, which is the basis of contemporary stochastic epidemic modelling. The other successful statistical model belongs to John Snow. He collected spatiotemporal data and constructed a map by using collected data for the cholera epidemic happened in London, in 1854. His statistics helped to annihilate the disease (Siettos & Russo, 2013).

As we can see, statistical modelling is very effective while fighting with a pandemic. Hence, the governments can use the results of models while making decisions about the future of their countries during pandemics.

1.2 History of Covid-19

A pandemic can be defined as an infectious disease that affects a large number of countries or even the whole world. The formal definition does not include the population's immunity, severity of a disease or virology. Infectious diseases can cross boundaries of countries (Kelly, 2011).

From the beginning, our world has seen so many pandemics affecting people's lives, economic situations, and education of public. Black plague, HIV/AIDS, influenza pandemics, smallpox, and measles are some of the pandemics that our world faced with before or continue to struggle. On 14th century, 75-200 million people died because of black plague (Wikipedia, Black Death, 2020). Until 2019, HIV/AIDS claim the lives of approximately 33 million people all around the world (WHO, HIV/AIDS, 2020). Between 1918-1919, the pandemic influenza virus killed almost 40 million people in America, Europe, Asia, and Africa. In the following decades, in 1957 and 1963, influenza pandemics took two and ten million lives, respectively. Smallpox caused the death of almost 300 million people only in the 20th century (Lee, et al., 2007). The ones that recovered from smallpox scarred terribly (Flight, 2011). Measles, caused by the measles virus, is the most infectious disease known. Before the discover of vaccine in 1963, it took approximately 2,6 million lives per year (WHO, Measles, 2019).

Nowadays, the whole world is fighting with a new disease which became a pandemic, called Covid-19. This disease came into our lives on December 2019. As we know, it has started in Wuhan, a city of China, and spread all around the world. People can catch Covid-19 when they infected by the virus named as SARS-CoV-2 (Chakraborty & Maity, 2020). This virus is a member of coronavirus family which has been discovered by the Chinese Center for Disease

Control and Prevention (CDC) from a swab sample of an infected person. The name Covid-19 was given by World Health Organization (WHO) (Chen, et al., 2020).

People can catch Covid-19 from an infected person when he/she coughs, speaks or sneezes, through small droplets. Until 30th November of 2020, approximately 65 million people infected and more than 1,4 million people died according to WHO (COVID-19 Explorer, 2020). People can be sure whether they carry the disease or not by applying PCR tests.

Since the disease began to spread, it took so many lives and infected millions of people. However, when we check the researches that examined the infectiousness of Covid-19, we see that other pandemics like measles, smallpox and other members of coronavirus family like MERS-CoV and SARS-CoV are more infectious than SARS-CoV-2 (Hincal, Kaymakamzade, & Gokbulut, 2020).

It has been stated that SARS is the most severe one in coronavirus infections, which caused by the virus SARS-CoV. It was detected in November 2002 first in China and spread more than 30 countries. It caused 774 deaths with more than 8000 cases. It was the first time that CDC suggested travel restrictions. MERS, which occurred as a result of MERS-CoV virus, started in April 2012 in Jordan. Between 2012 and 2019, it affected 27 countries with 2494 cases and 858 deaths (Tesini, 2020; Wikipedia, Middle East respiratory syndrome–related coronavirus, 2020).

Although all symptoms of Covid-19 are not known for sure, known common symptoms include high fever, dry cough, aches and pains, and tiredness (WHO, Coronavirus, 2020). On the other hand, most of the infected people don’t show any symptoms. This explains the rapid

spread of the disease because without any symptoms, people don't consult hospitals or PCR tests. For these patients, we use the term 'asymptomatic' (Long, et al., 2020). So, in order to control the spread of this disease, more random tests should be done by governments.

Many governments took some serious restrictions between March and May 2020. These restrictions include closure of airports, bazaars, schools, and workplaces. Spain, Italy, Denmark, and Iran are some of the countries that were on lockdown in that time. However, as the economy and education began to suffer, restrictions began to be lifted after the disease was brought under control (Kaplan, Frias, & McFall-Johnsen, 2020). Although the disease continues to spread and take lives, researches show that the death rate has dropped considerably. There are many opinions for this drop. Some scientists claim that this is because of the mutation of the virus; while some of them claim that the spread of disease is now more in younger people than in March 2020 and younger people has lower fatality rate than older people (Expert reaction to comments made by Paul Tambyah (president-elect of the International Society of Infectious Diseases) about the SARS-CoV-2 virus, suggesting the D614G mutation may explain a reduced death rate from COVID-19 in some parts of the world, 2020).

There are many views about how we can control the fatality rate and spread of Covid-19 in the world. These are; herd immunity, vaccination, mutation of the virus, and control by using occurred death rates. Countries that supported the herd immunity idea have not been successful. But the reason of this is still unknown; it may be because there are no enough immune people in world (by the word enough we mean, without a vaccine, at least 70% of the world population) (Orlowski & Goldsmith, 2020).

In this study, two most popular of these views, herd immunity idea and control of spread by using occurred deaths, are examined and were tried to determine which idea is more effective for Covid-19.

1.3 Guide to Thesis

In Chapter 2, herd immunity and the importance of effective reproduction number are defined. Then, by using NGM method, basic reproduction number is calculated for North Cyprus. With basic reproduction number, effective reproduction number is calculated to see the extent of the outbreak and to analyze the herd immunity idea by using daily cases in North Cyprus.

In Chapter 3, descriptions of the statistical distributions that are used in the model are given. Future deaths are estimated by using these distributions and occurred deaths of the selected countries. Then, estimations compared with the real data.

In Chapter 4, conclusions are given.

CHAPTER 2

EFFECTIVE REPRODUCTION NUMBER

2.1 Herd Immunity

Herd immunity provides an indirect protection from infection for susceptible individuals. It occurs when enough people in a population become resistant to the cause of any disease, such as bacteria or virus. In order to gain herd immunity in a population, herd immunity threshold should be reached. When the needed threshold for transmission stays above the proportion of susceptible individuals, population reaches the herd immunity threshold (Randolph & Barreiro, 2020). The herd immunity threshold is calculated by the formula

$$1 - \frac{1}{R_0}, \tag{2.1}$$

where R_0 is the basic reproduction number. For gaining herd immunity in a population, there are two options: infection to develop immunity and vaccine (Gajewski, 2020). In order to reach the threshold for herd immunity, at least 70% of the population should be infected (Orlowski & Goldsmith, 2020).

2.2 Effective Reproduction Number for Covid-19 in TRNC

Effective reproduction number, denoted by R_t, is the average number of infections of secondary cases by primary cases per time. In contrast to basic reproduction number R_0, R_t does not assume the whole population as susceptible; it counts immune people also (Randolph & Barreiro, 2020). When R_t value is above 1, it means that disease continues to spread so, in order to say that the spread of any infectious disease has stopped, R_t value should be below 1. For this, herd immunity threshold should be reached because R_t value for herd immunity is calculated by using the Formula (2.1). In order to find R_t values for any disease, R_0 values should be known according to the Formula (2.1). As in R_t, it can be said that any disease is under control if R_0 values are less than 1.

In this section, herd immunity idea was examined for Covid-19 in TRNC. The first Covid-19 case in the country was seen on 10^{th} of March. After that day, the government took some serious precautions including closure of schools, workplaces, and airport. Daily cases that are used in this work are taken from the TRNC Ministry of Health (KUZEY KIBRIS COVID-19 GÜNLÜK TABLO, 2020).

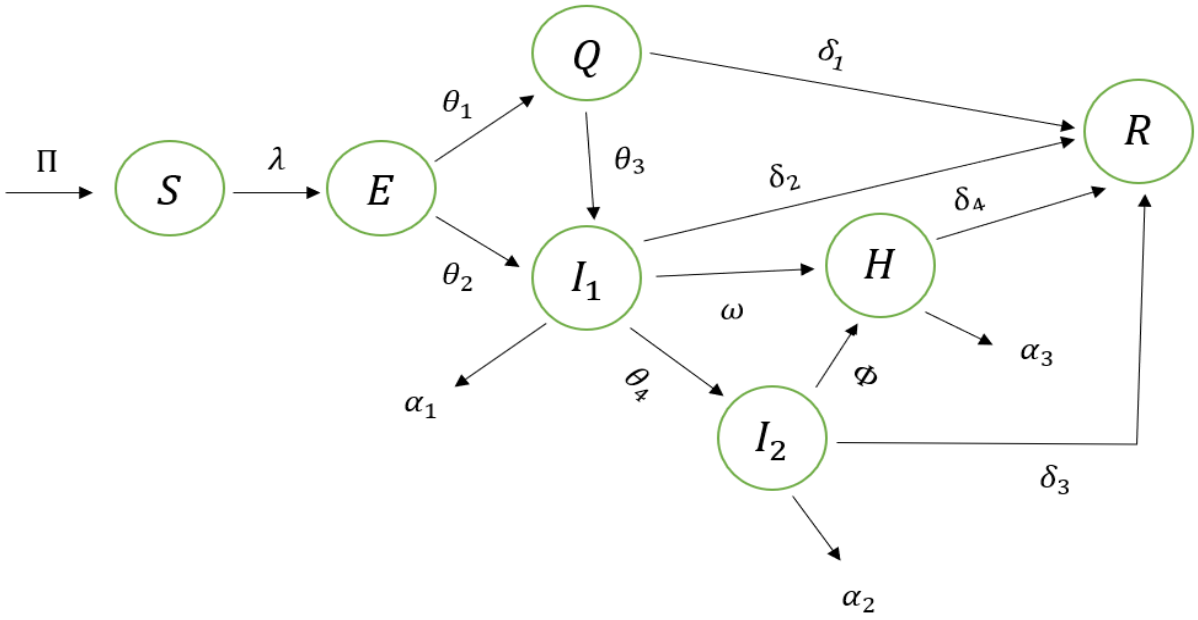

Figure 2.1: Diagram of the model that is used to calculate R_0 values.

Firstly, by using the diagram given in Figure 2.1, a system of ODE is constructed. Here, N represents the whole population and S_0 is the disease-free population. Details of the system can be seen in (Hincal, Kaymakamzade, & Gokbulut, 2020). In the model, new infected individuals are in the compartment E. So, following matrices can be constructed with new infections as f and the rest of the population as v.

$$f = \begin{bmatrix} \frac{\beta(\tau_1 I_1 + \tau_2 I_2 + \tau_3 Q + \tau_4 H)}{N} S_0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \qquad v = \begin{bmatrix} (\theta_1 + \theta_2)E \\ -\theta_1 E + (\delta_1 + \theta_3)Q \\ -\theta_2 E - \theta_3 Q + (\delta_2 + \omega + \theta_4 + \alpha_1)I_1 \\ -\theta_4 I_1 + (\Phi + \alpha_2 + \delta_3)I_2 \\ -\omega I_1 - \Phi I_2 + (\delta_4 + \alpha_3)H \end{bmatrix}. \tag{2.2}$$

By differentiating the matrices in (2.2) with respect to each compartment, the following matrices are obtained.

$$F = \begin{bmatrix} 0 & \beta\tau_1 & \beta\tau_2 & \beta\tau_3 & \beta\tau_4 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}, \qquad V = \begin{bmatrix} k_1 & 0 & 0 & 0 & 0 \\ -\theta_1 & k_2 & 0 & 0 & 0 \\ -\theta_2 & -\theta_3 & b_1 & 0 & 0 \\ 0 & 0 & -\theta_4 & b_2 & 0 \\ 0 & 0 & -\omega & -\Phi & k_3 \end{bmatrix}.$$

Then,

$$V^{-1} = \begin{bmatrix} k_1^{-1} & 0 & 0 & 0 & 0 \\ \dfrac{\theta_1}{k_2 k_1} & k_2^{-1} & 0 & 0 & 0 \\ \dfrac{(\theta_2 k_2 + \theta_3\theta_1)}{b_1 k_1 k_2} & \dfrac{\theta_3}{b_1 k_2} & b_1^{-1} & 0 & 0 \\ \dfrac{\theta_4(\theta_2 k_2 + \theta_3\theta_1)}{b_1 b_2 k_1 k_2} & \dfrac{\theta_3\theta_4}{b_1 b_2 k_2} & \dfrac{\theta_4}{b_1 b_2} & b_2^{-1} & 0 \\ \dfrac{(\theta_2 k_2 + \theta_3\theta_1)(\omega b_2 + \Phi\theta_4)}{b_1 b_2 k_1 k_2 k_3} & \dfrac{\theta_3(\omega b_2 + \Phi\theta_4)}{b_1 b_2 k_2 k_3} & \dfrac{\omega b_2 + \Phi\theta_4}{b_1 b_2 k_3} & \dfrac{\Phi}{\mathrm{b}_2 k_3} & k_3^{-1} \end{bmatrix}.$$

Hence, the basic reproduction number will be the dominant eigenvalue of the matrix multiplication $F.V^{-1}$, that is,

$$R_0 = \frac{\left((b_1\beta\tau_1+\beta\tau_2\theta_3)\theta_1+\beta\tau_2k_2\theta_2)k_3+\omega\beta\tau_4(\theta_2k_2+\theta_3\theta_1)\right)b_2+\theta_4(\beta\tau_4\Phi+\beta\tau_3k_3)(\theta_2k_2+\theta_3\theta_1)}{k_1k_2k_3b_1b_2},$$

(2.3)

where $S_0 = N,$ $k_1 = \theta_1 + \theta_2, k_2 = \delta_1 + \theta_3, k_3 = \delta_4 + \alpha_3, b_1 = \delta_2 + \omega + \theta_4 + \alpha_1,$ and $b_2 = \Phi + \alpha_2 + \delta_3.$

Also, λ is the force of infection with the formula

$$\lambda = \frac{\beta(\tau_1 I_1 + \tau_2 I_2 + \tau_3 Q + \tau_4 H)}{N}.$$

The definitions of variables and parameters are given in Table 2.1 and Table 2.2.

Table 2.1: Descriptions of variables that were used in the model.

Variables	**Descriptions**
N	Total population
S	Susceptible individuals
E	Exposed individuals
I_1	Moderate infected individuals
I_2	Severe infected individuals
Q	Quarantined individuals
H	Hospitalized individuals
R	Recovered individuals

Table 2.2: Descriptions of parameters that were used in the model.

Parameters	**Descriptions**
Π	Recruitment rate
β	Transmission rate
τ_i $(i = 1, 2, 3, 4)$	Parameters for the increase or decrease of infectiousness in humans
θ_i $(i = 1, 2, 3, 4)$	Progression rates
ω	Hospitalization rate from the compartment I_1
Φ	Hospitalization rate from the compartment I_2
α_i $(i = 1, 2, 3, 4)$	Disease induced death rates
δ_i	Recovery rates

Then, with the Formula (2.3), R_0 values were calculated for each day which can be seen in Figure 2.2. After this, with the Formula (2.1) and daily R_0 values, R_t values were calculated day by day. R_0 and R_t values cover the dates from 11^{th} of March to 30^{th} of November.

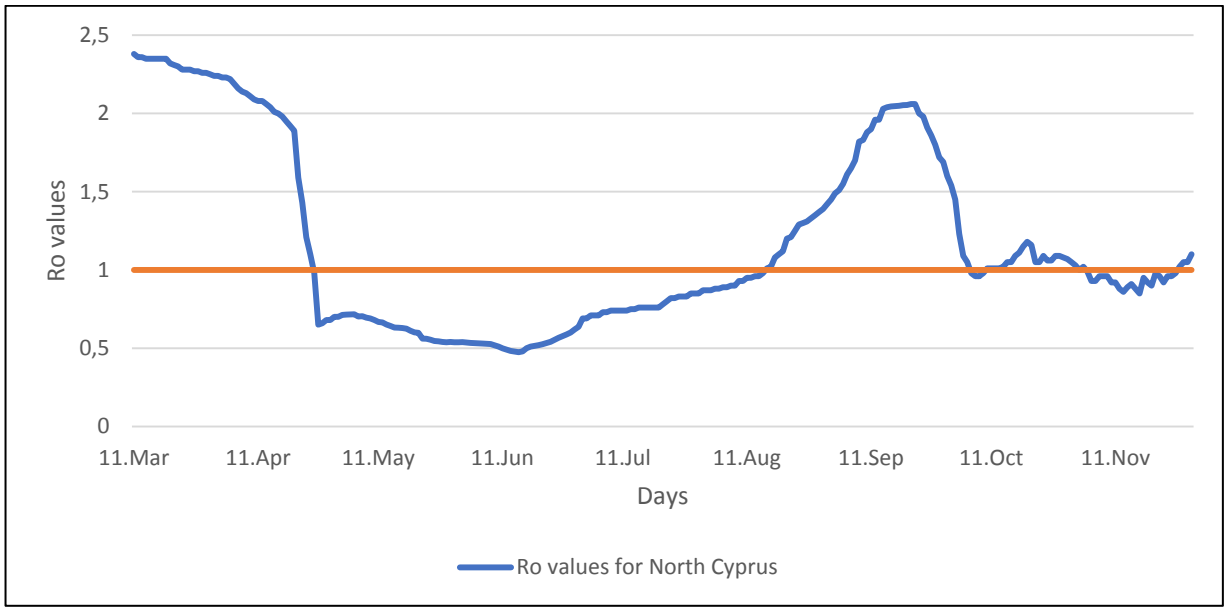

Figure 2.2: R_0 values of North Cyprus from 11^{th} March to 30^{th} November 2020.

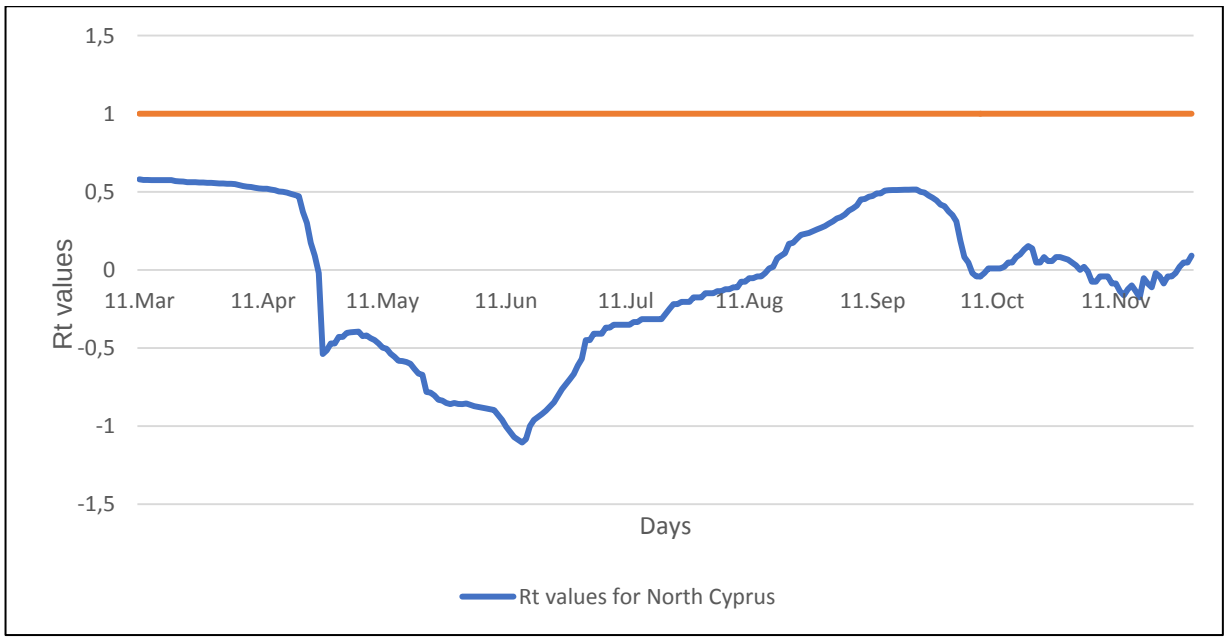

Figure 2.3: R_t values of TRNC from 11^{th} March to 30^{th} November 2020.

As can be seen from the Figure 2.3, R_t values are always below 1. From the definition of herd immunity threshold, it can be interpreted as the population in North Cyprus reached the threshold since it is always below 1. However, disease continues to spread in North Cyprus. This oppositeness tells us that herd immunity is not an option for fighting with Covid-19 in North Cyprus (Kaymakamzade, Hincal, Mustapha, & Gokbulut, 2020).

In Figure 2.2, R_0 values are above 1 until some point. This means that the disease was an epidemic at first, but after some point, under the precautions of those days, the epidemic was brought under control until the end of August. Hence, when Figure 2.2 and Figure 2.3 are compared, it can be easily observed that tackling R_0 values are more sensible than tackling R_t values for North Cyprus for the control of the spread.

In Figures 2.4, 2.5, and 2.6, I_1 denotes the mild infected individuals while I_2 denotes the severe infected individuals. Figure 2.4 shows what is expected to happen without lockdown and with high mobility in North Cyprus when the disease started at first. Since the disease was unknown and its infectiousness was very high at that time, i.e., in March for North Cyprus, there would be approximately 1,800 cases in 3 months. As can be seen from Figure 2.5, there was an increase in the beginning of the disease but after applied precautions and decrease in mobility, spread of the disease was taken under control, until July. According to the Figure 2.5, the total number of infected individuals stayed under 150 which is consistent with the reality. In Figure 2.6, it is presented that an increase was happened in cases with decrease in precautions and increase in mobility, which represents the time after July. However, decrease in severe infected individuals shows that the effect of virus is decreasing. These figures are consistent with R_0 values and hence they support the idea that the disease can be controlled with R_0 in North Cyprus.

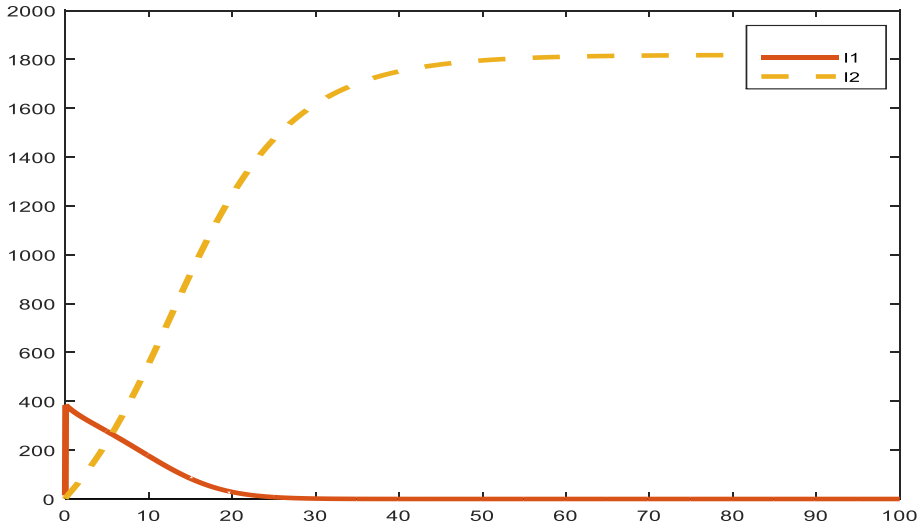

Figure 2.4: Expected cases in North Cyprus without lockdown at the beginning of the epidemic, in March.

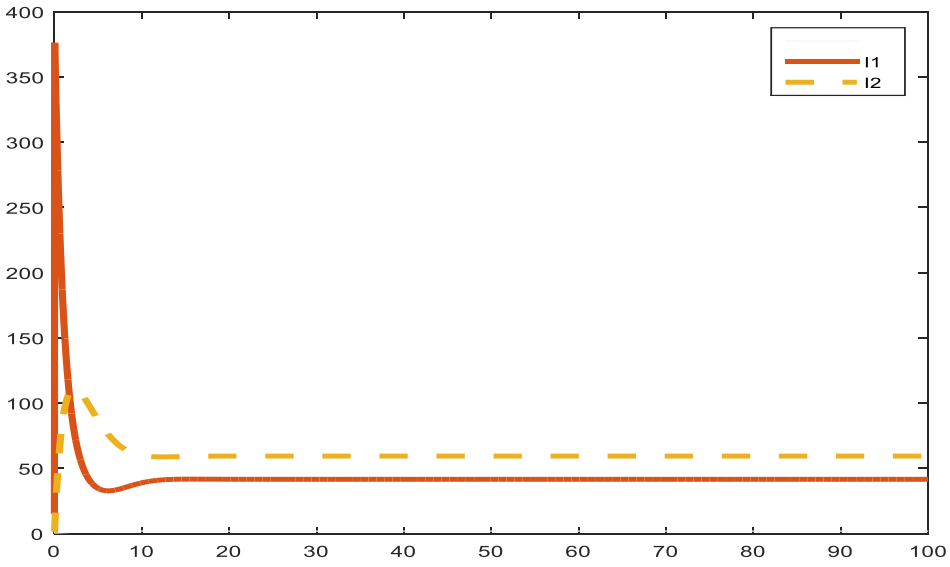

Figure 2.5: Occurred cases in North Cyprus with lockdown until July.

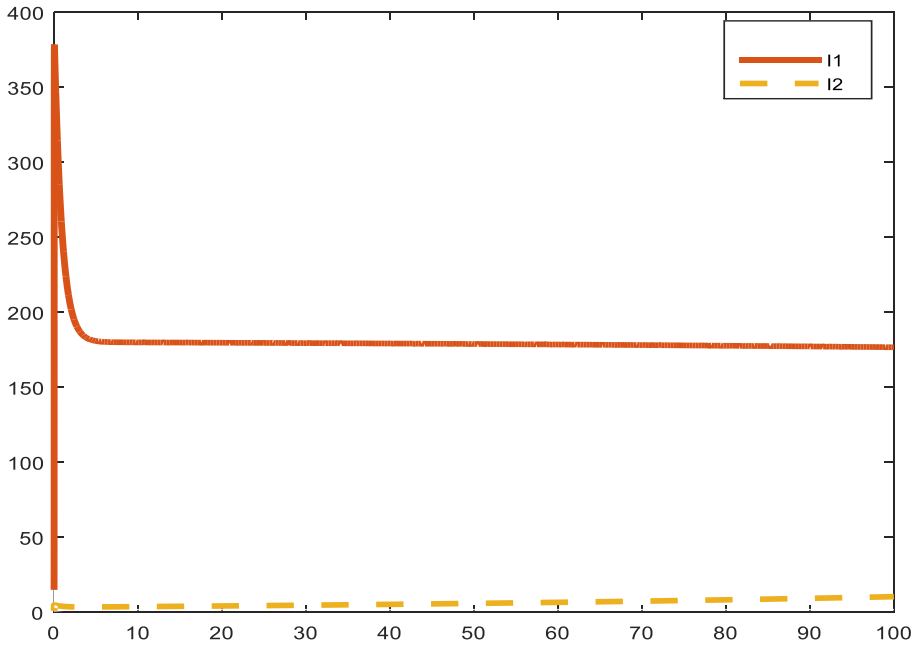

Figure 2.6: Occurred cases in North Cyprus after July.

There are many countries that supported herd immunity idea, refused to take precautions and as a result they failed. These countries include Sweden, England, and Netherlands. Sweden comes first among the countries that advocate this idea.

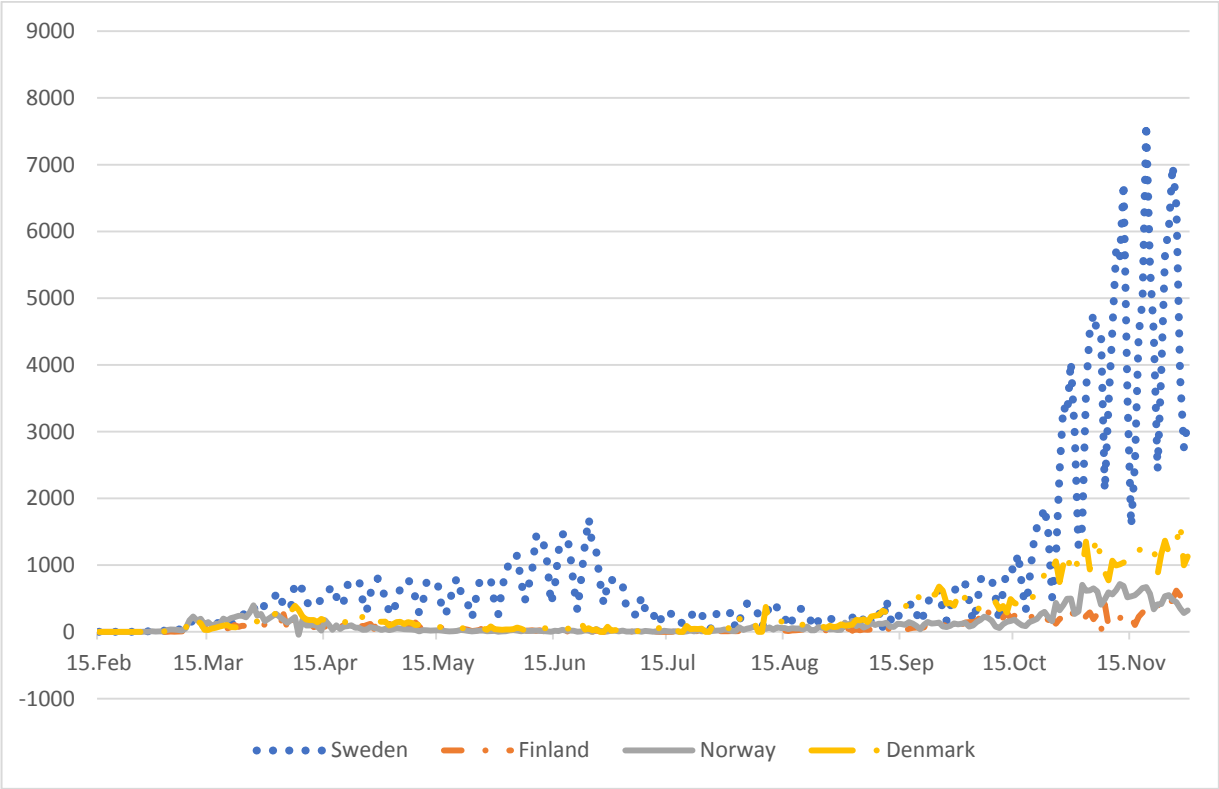

Figure 2.7: Daily cases for the countries Sweden, Finland, Norway, and Denmark from 15^{th} February to 30^{th} November 2020.

In Figure 2.7, comparison of daily cases for the countries that are in the same region are given. Here the data were taken from WHO (COVID-19 Explorer, 2020). These countries have similarities in the way of economy, politics, culture, and demography. So, it makes sense to expect alike effects of virus in these regions. However, they followed different strategies for the control of the spread of Covid-19. Hence, the purpose of the figure is to show the incidence rate of the disease in the same region with different strategies, to see the importance of decisions through an epidemic.

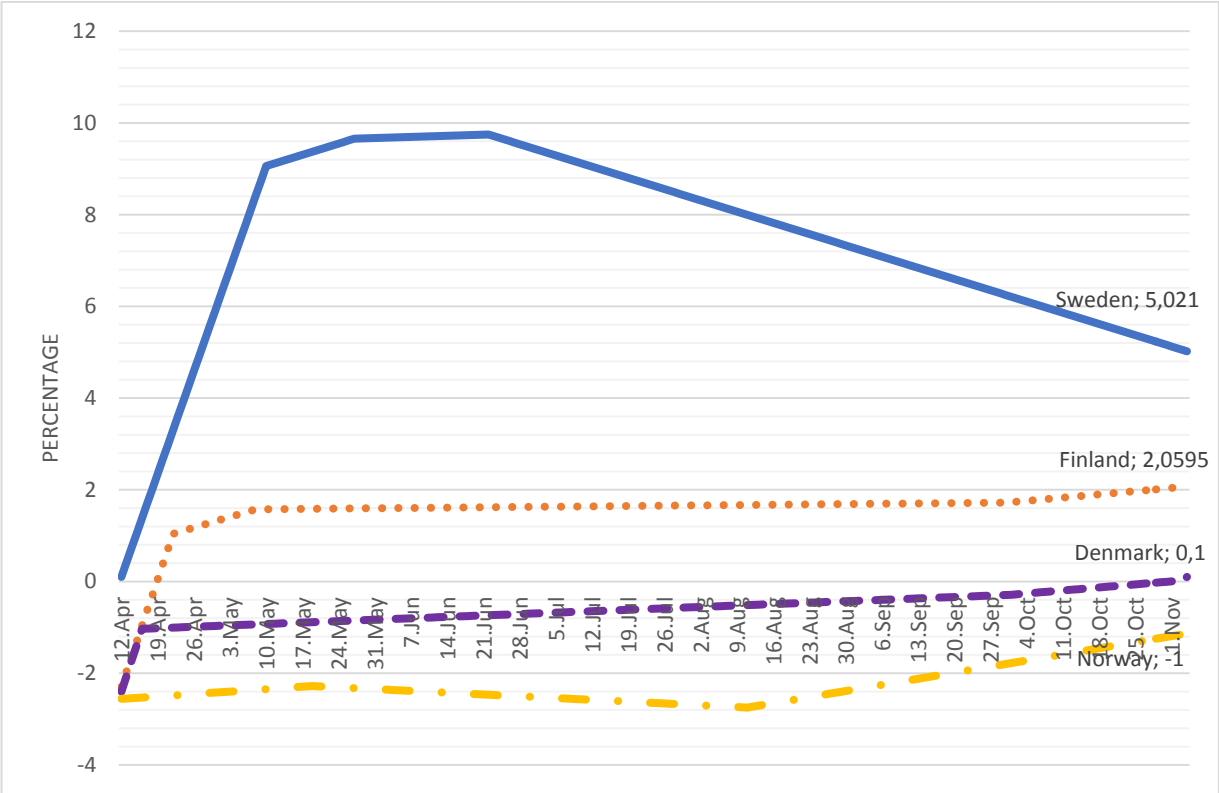

Figure 2.8: Excess mortality rate for the countries Sweden, Finland, Norway, and Denmark from 11^{th} April to 9^{th} November 2020.

In Figure 2.8, excess mortality rates of the same regions are shown. From the Figure 2.8, it can be easily seen that, in 2020, Sweden has the highest excess mortality rate between the countries that are mentioned and are in the same region with Sweden. Especially, during summer, mortality rate in Sweden is very high and even it has a peak point. Since Covid-19 started to spread in months March and April, it is easy to say that the reason for the huge increase in the mortality rate of Sweden can be explained by the pandemic. Because, the countries that are in the same region and are expected to have close mortality rates with Sweden, have less mortality rates than previous years, specifically in Norway. Beside this, the steady decrease in mortality rates for Sweden can be discussed as the fatality rate of the virus is decreasing day by day with the mutation of the virus.

Actually, Sweden is the one which took a different route than Finland, Norway, and Denmark. Prohibition of crowded meetings, closure of schools and businesses, and lockdown are some of the important precautions that Norway and Denmark applied (Tiirinki, et al., 2020). In addition, Norway has introduced quarantine for those coming from abroad. However, Sweden took less and later precautions like prohibition of home visits and closure of universities and high schools. As a result, when the Figure 2.7 and Figure 2.8 are examined, it can be easily seen that Sweden has many peak points with higher daily cases and death rates than other countries. Also, it is known that Sweden is the one with the highest number of infected people in intensive care units in these countries (Næss-Schmidt, Jensen, Virtanen, & Nielsen, 2020). This proves that the herd immunity idea that is interiorized by Sweden is a wrong route to take for Covid-19.

CHAPTER 3

ESTIMATING DEATH RATES BY USING BINOMIAL MODEL

3.1 Statistical Methods

In this model, gamma distribution, binomial distribution, negative binomial distribution, and posterior distribution are used in order to control the spread of Covid-19 by using death rates.

Gamma function is defined by the integral

$$\Gamma(\alpha) = \int_0^\infty e^{-x} x^{\alpha-1}\, dx. \qquad (3.1)$$

Also, factorial definition of gamma function is given as

$$\Gamma(\alpha) = (\alpha - 1)!. \qquad (3.2)$$

In the following proposition, it is shown that from Equation 3.1, Equation 3.2 can be obtained.

Proposition: A continuous function, for $x > 0$ and $\alpha \geq 1$,

$$f(x) = \frac{\lambda^{\alpha} x^{\alpha-1} e^{-\lambda x}}{\int_0^{\infty} e^{-x} x^{\alpha-1}\, dx} \tag{3.3}$$

is the probability density function (pdf) of a continuous random variable. That is,

$$\int_0^{\infty} e^{-x} x^{\alpha-1}\, dx = (\alpha - 1)!. \tag{3.4}$$

Proof: Let the Equation (3.3) be a continuous function. In order to say that it is a pdf of any continuous random variable,

$$\int_0^{\infty} e^{-x} x^{\alpha-1}\, dx = (\alpha - 1)!$$

should be satisfied and in that way, it can be shown that gamma distribution can be used. For this proof, mathematical induction will be used.

For $\alpha = 1$, we have

$$\int_0^{\infty} e^{-x} x^{\alpha-1}\, dx = \int_0^{\infty} e^{-x} x^{1-1}\, dx = \int_0^{\infty} e^{-x}\, dx = \lim_{b\to\infty} \int_0^{b} e^{-x}\, dx = \lim_{b\to\infty} \left(-e^{-x}|_0^b\right)$$
$$= \lim_{b\to\infty} (-e^{-b} + e^{0}) = 1 = (1-1)!$$

Assume that the Equation (3.4) is true for $\alpha = k - 1$, i.e.,

$$\int_0^\infty e^{-x} x^{k-2}\, dx = (k-2)!$$

Let $\alpha = k$, then the Equation (3.4) will be

$$\int_0^\infty e^{-x} x^{k-1}\, dx. \qquad (3.5)$$

By letting $x^{k-1} = u$, $(k-1)x^{k-2}dx = du$, $e^{-x}dx = dv$, and $-e^{-x} = v$ in Equation (3.5),

$$\int_0^\infty e^{-x} x^{k-1}\, dx = \lim_{b\to\infty}\left[\left(-e^{-x}x^{k-1}|_0^b\right) + (k-1)\int_0^b e^{-x}\, x^{k-2}dx\right]$$

$$= (k-1)\lim_{b\to\infty}\int_0^b e^{-x}x^{k-2}dx = (k-1)\int_0^\infty e^{-x}x^{k-2}dx$$

$$= (k-1)(k-2)!\text{ , from the Equation (3.5)}$$

$$= (k-1)!$$

Thus,

$$\int_0^\infty e^{-x}x^{\alpha-1}\,dx = (\alpha-1)!.$$

■

In order to study gamma distribution, gamma function should be used. Gamma function was first introduced by the mathematician Leonhard Euler. As mentioned above, this function is a generalization of the factorial $n!$ and it is defined as

$$\Gamma(\alpha) = \int_0^\infty x^{\alpha-1}e^{-x}dx, \qquad \alpha \in (0,\infty).$$

The gamma distribution of a continuous random variable X is denoted by $X \sim \Gamma(\alpha,\lambda)$ for the positive parameters α and λ. This notation can be read as 'a random variable X is gamma-distributed with shape α and rate λ'. The probability density function of X should be given as follows

$$f_X(x) = \begin{cases} \dfrac{\lambda^\alpha x^{\alpha-1}e^{-\lambda x}}{\Gamma(\alpha)}, & x > 0 \\ 0, & otherwise \end{cases}$$

to use gamma distribution for X (Gamma function, 2017).

The difference between gamma and exponential distribution is that exponential distribution is used to predict the incidence rate for the 'very first' event. However, gamma distribution predicts the incidence rate after the 'k^{th}' event occurs. So, especially in infectious diseases, it is more sensible to use gamma distribution to see the actual attack rate of the disease (Kim, 2019).

The binomial distribution is deduced from the process called Bernoulli trial. When a trial, which can be a random experiment or process, can conclude with exactly two possible outcomes (e.g., failure or success, sick or well, alive or dead), this trial is called a Bernoulli trial (Daniel, 2005). Bernoulli distribution symbolizes the number of success or failure for a single Bernoulli trial. On the other hand, to decide the number of successes or failures of n independent Bernoulli trials, Binomial Distribution is used, where $n \in \mathbb{Z}^+$. $X \sim Bin(n, p)$ is the notation of binomial distribution of a random variable X. Here, p is the probability of the success of the trial.

Negative Binomial Distribution can be used when a specific success is required. That is, if X is a random variable which represents the trial for the r^{th} success that will be occurred, then formula for Negative Binomial Distribution of X is given as follows (Freund, 1992):

$$P(X = x|r, p) = \binom{x-1}{r-1} p^r (1-p)^{x-r}, \quad x = r, r+1, \ldots$$

Bayesian statistics accepts that unknown parameters of population are measurable random variables such that probability distributions (like Binomial distribution) can be used in order to describe them. In this kind of statistics, conditional probabilities are modified. With the collected data, prior distribution is constructed to obtain a posterior distribution. Bayes' Theorem is the base of Bayesian statistics. For events $A_1, A_2, \ldots, A_n$, and B, the theorem is given as

$$P(A_i|B) = \frac{P(B|A_i)P(A_i)}{\sum_{j=1}^{n} P(B|A_j)P(A_j)},$$

where $i = 1, \dots, n$. In this formula, $P(A_i)$ and $P(B)$ denotes the probabilities of occurrence of A_i and B, respectively. $P(A_i|B)$ is conditional probability which can be read as when the event B is true, what the occurring likelihood of A_i is. In the same way, for $P(B|A_i)$ means when the event A_i is true, what the occurring likelihood of B is.

As mentioned before, posterior distribution is an extension of this theorem. An evidence about the events is needed in order to use posterior distribution (Puga, Krzywinski, & Altman, 2015; Daniel, 2005).

3.2 Estimating Covid-19 Deaths by using Statistical Distributions

In this section, by using the distributions mentioned in Section 3.1, death rates of 59 countries are forecasted. Data that are used in this model are taken from WHO (COVID-19 Explorer, 2020) with the assumption that quality of data is the most accurate. This study captures the dates between 1^{st} of July and 30^{th} of November. Aim of this study is to see the whether the applied restrictions by governments are enough or should be increased.

Let $D_{i,t}$ be the number of deaths and $I_{i,t}^{r}$ be the number of reported cases in country i at time t. Firstly, it is assumed that delay in death reporting, δ, is gamma distributed with mean μ and standard deviation σ, i.e.,

$$\delta \sim \Gamma(\mu, \sigma).$$

At the beginning, Covid-19 was an unknown disease that is people didn't know the symptoms, the way of protection or the infectiousness of the disease. So, at first a huge increase in death rates were seen in the whole world. Because of this reason, gamma distribution is used in the delay of reported deaths since it counts the incidence rates of death after the disease become on the track. Thus, the idea is that it should decrease the error in reported death delay.

$r_{i,t}$ denotes the ratio of deaths to reported cases for the country i at time t. Then, Binomial distribution is used for the assumption of deaths. Hence,

$$D_{i,t} \sim Binom\left(\int_{0}^{\infty} \Gamma(x|\mu,\sigma) I_{i,t-x}^{r} dx, r_{i,\mu}\right).$$

With this binomial formula, since an evidence was obtained as a prior distribution, a posterior distribution is found for $r_{i,t}$.

Posterior distribution for $r_{i,t}$ defined as

$$P(r_{i,t}|D_{i,t}) = \frac{P(D_{i,t}|r_{i,t})}{P(D_{i,t})} P(r_{i,t}). \quad (3.6)$$

As can be seen from the Equation 3.6, posterior probability is proportional to

likelihood of event × prior probability.

Error value for cases is defined by

$$\rho_{i,t} = \frac{FR}{r_{i,t}}. \quad (3.7)$$

In the Equation (3.7), FR denotes the future records of deaths. By using the posterior distributions that are obtained for $r_{i,t}$ and FR, a posterior distribution for $\rho_{i,t}$ could be found.

In order to obtain $I_{i,t}^{appropriate}$, posterior distribution of FR is used for the time interval over which data taken on deaths, up to time $t - \mu$. $I_{i,t}^{appropriate}$ is the number of appropriate cases in a country i at time t. It is the total number of cases that didn't die. In this case, the number of appropriate cases is approximately

$$I_{i,t}^{appropriate} \sim D_{i,t-\mu} + NBin\left(D_{i,t-\mu}, FR\right).$$

In above formula, $NBin(n,p)$ is a negative binomial distribution where n denotes the number of failures, i.e., deaths and the probability of observing this failure is p. The success of negative binomial distribution is thought as taking the spread of the virus under control and preventing the death of infected individuals.

For the time interval that no information was known, that is after the time $t-\mu$, posterior distribution is used for case ascertainment. As a result,

$$I_{i,t}^{appropriate} \sim I_{i,t}^{r} + NBin\left(I_{i,t}^{r}, \rho_{i,t}\right)$$

is obtained.

In order to find the estimated number of deaths, with the assumption of taken data are real,

$$\int_{0}^{\infty} \Gamma(x|\mu,\sigma) I_{i,t-x}^{r} dx$$

is used.

The recorded cases in the following week might die within the same week. So, for $x \in \{0, 7\}$ we have $\Gamma(x|\mu, \sigma) > 0$. That is, incubation period of the virus is taken into account. For the prediction of new registered cases in the upcoming week, a gamma distribution is used. The sample, that is taken for the gamma distribution with mean and standard deviation, is the prediction of the number of occurred cases in the last week. Since this situation does not assume any increase or decrease in the upcoming week, it can be controlled by the assumption. This assumption is a null hypothesis scenario because with the assumption, contribution to death rates, due to those, is very small (i.e., less than 1.5%) and results of the study can not be affected.

After that, the estimated death numbers accomplished as

$$D_{i,t} \sim Binom\left(\int_0^{\infty} \Gamma(x|\mu, \sigma) I_{i,t-x}^{r} dx, r_{i,\mu}\right),$$

where $r_{i,\mu}$ is the estimation of the ratio of deaths to reported cases for the data of last week.

Here the terms

$$\int_0^{\infty} \Gamma(x|\mu, \sigma) I_{i,t-x}^{r} dx, r_{i,\mu}$$

depend on detected reported cases until the last day with accessible and estimated reported cases which are described above.

In this model, 59 countries that has the highest death and case rates are taken into account. For the number of cases and deaths, data is taken from WHO (COVID-19 Explorer, 2020), with the assumption that data is the most accurate (Kaymakamzade, Hincal, Suren, & Gokbulut, 2020). In the Table 3.1, 5 of the countries with expected death rates and announced death rates are given. Rest of the table that contains the data of other countries are given in Appendix 3.

Table 3.1: Comparison of expected and announced death rates of 10 of the countries that are used in this study.

Countries	**Occurred Cases**	**D(50%)**	**E(50%)**
Argentina	1,432,570	0.051	0.269
Austria	289,461	0.035	0.395
Brazil	6,436,650	0.096	0.143
France	2,244,635	0.136	0.101
Iran	989,572	0.038	0.364
Italy	1,641,610	0.129	0.107
Sweden	266,158	0.081	0.171
Turkey	700,880	0.018	0.749
United Kingdom	1,659,256	0.077	0.179
United States of America	14,258,331	0.051	0.27

In the Table 3.1 D(50%) denotes death rates of the countries with 50 percent and E(50%) denotes the expected death rates of the countries with 50 percent. From this table, it is easy to see that there is an enormous difference between announced death rates and expected death rates. Since, the error minimized in death rates by gamma distribution in the model, it can be concluded that the record of deaths cannot be controlled and this results in uncontrolled spread of the Covid-19. As a result, it can be said that this model can be used for determining the size of the pandemic and asymptomatic patients which contains mostly unrecorded patients.

CHAPTER 4

CONCLUSION

In this thesis, two of the most popular ideas for the spread of Covid-19 examined. For the herd immunity idea, firstly North side of the Cyprus considered by using daily cases, basic reproduction number, R_0, and effective reproduction number, R_t. At the end of Chapter 2, it is concluded that effective reproduction number, which is the herd immunity threshold, is not an option for controlling the spread of the disease in North Cyprus. Then, the leading country as the supporter of herd immunity, Sweden, compared with the other countries that are in the same region with it (in Figure 2.7 and Figure 2.8). Especially, Figure 2.8 showed that Covid-19 has a great effect in deaths for Sweden in a negative way. With this data, it was seen that herd immunity is not an option in general. Afterwards, in Chapter 3, to control the spread of Covid-19, death rates of the countries are calculated by constructing a statistical model with distributions (Gamma distribution, Binomial distribution, and Posterior distribution). With this model, it is seen that gamma distribution is a very useful way to use for the delay of reported deaths of Covid-19 and for the control of the pandemic. Because, in the model, error in delay of reported deaths is minimized by using gamma distribution with the aim of finding actual death rates of countries. Results showed that between the expected and announced death rates there is a huge difference. Hence, statistical modelling is a very efficient way to control the spread of any infectious disease so that governments can use while taking precautions for their countries.

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APPENDICES

APPENDIX 1

ETHICAL APROVAL DOCUMENT

Date: 22/12/2020

To the **Graduate School of Applied Sciences**

The research project titled "**Mathematical and Statistical Modelling of Covid-19**" has been evaluated. Since the researcher(s) will not collect primary data from humans, animals, plants or earth, this project does not need to go through the ethics committee.

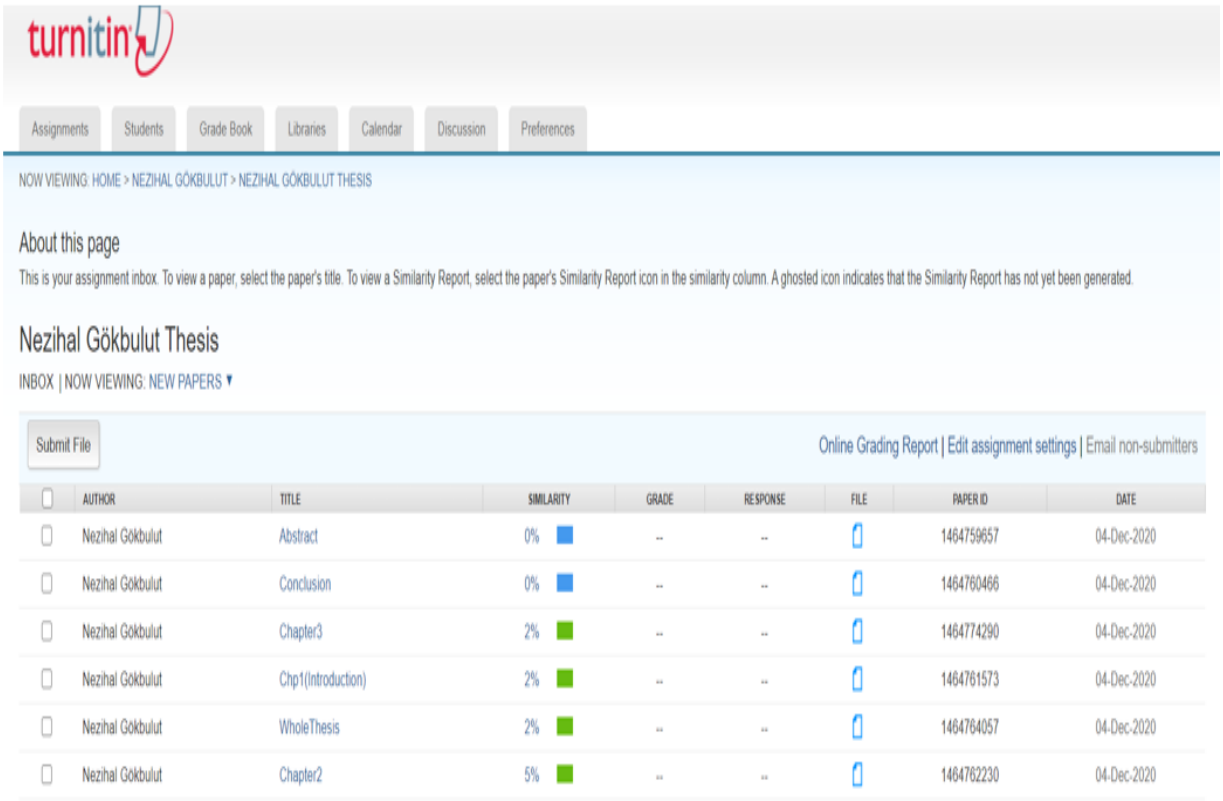
Title: Prof.Dr.

Name Surname: Evren Hınçal

Signature:

Role in the Research Project: Supervisor

APPENDIX 2



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Prof.Dr.Evren HINÇAL

APPENDIX 3

TABLE OF COMPARISON OF EXPECTED AND ANNOUNCED DEATH RATES OF 59 OF THE COUNTRIES THAT ARE USED IN THE STUDY IN CHAPTER 3.

Countries	Occurred Cases	D(50%)	E(50%)
Afghanistan	47,258	0.025	0.555
Algeria	85,084	0.04	0.343
Argentina	1,432,570	0.051	0.269
Austria	289,461	0.035	0.395
Bangladesh	471,739	0.022	0.616
Belarus	141,609	0.005	1
Belgium	582,252	0.078	0.176
Bolivia	144,994	0.061	0.225
Bosnia and Herzegovina	91,539	0.06	0.228
Brazil	6,436,650	0.096	0.143
Bulgaria	151,913	0.062	0.222
Cameroon	24,487	0.03	0.459
Canada	393,081	0.076	0.18
Chile	555,406	0.022	0.625
Colombia	1,334,089	0.037	0.375
Czechia	535,760	0.056	0.248
Denmark	85,140	0.026	0.531
Dominican Republic	146,009	0.015	0.934
Ecuador	194,876	0.085	0.162
Egypt	116,724	0.043	0.317
Finland	26,422	0.017	0.8
France	2,244,635	0.136	0.101
Germany	1,118,001	0.055	0.248

Greece	111,537	0.091	0.151
Honduras	109,144	0.048	0.288
Hungary	231,844	0.144	0.095
India	9,556,881	0.039	0.351
Indonesia	557,877	0.087	0.159
Iran	989,572	0.038	0.364
Iraq	558,767	0.058	0.24
Ireland	73,228	0.053	0.26
Israel	340,867	0.051	0.269
Italy	1,641,610	0.129	0.107
Japan	152,827	0.116	0.118
Kuwait	143,574	0.008	1
Mexico	1,133,613	0.169	0.081
Moldova	112,307	0.039	0.354
Netherlands	538,050	0.078	0.177
Nigeria	67,960	0.026	0.522
Pakistan	406,810	0.023	0.595
Panama	169,339	0.025	0.562
Peru	967,075	0.039	0.355
Philippines	435,413	0.029	0.483
Poland	1,028,610	0.031	0.437
Portugal	307,618	0.054	0.253
Romania	492,211	0.048	0.288
Russia	2,375,546	0.011	1
Saudi Arabia	358,102	0.006	1
Serbia	199,158	0.019	0.742
South Africa	796,472	0.035	0.391
Spain	1,693,591	0.066	0.209

Sudan	18,254	0.062	0.221
Sweden	266,158	0.081	0.171
Switzerland	340,115	0.114	0.121
Turkey	700,880	0.018	0.749
Ukraine	772,760	0.033	0.411
United Arab Emirates	172,751	0.007	1
United Kingdom	1,659,256	0.077	0.179
United States of America	14,258,331	0.051	0.27