

USING THE SIR EPIDEMIC MODEL TO INFER THE SARS OUTBREAK IN
BEIJING, 2003

by

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(Under the Direction of Liang Liu)

ABSTRACT

The purpose of this study is to use a compartmental model, Susceptible-Infectious-Recovered (SIR) model, to study the outbreak of Severe Acute Respiratory Syndrome (SARS) in Beijing in 2003. The disease originated from south China, hit Beijing severely, afterwards spread to the world. In this study, we developed a least square method to estimate parameters of the SIR model using SARS infection data released by the Beijing Center for Disease Control and Prevention during April 20th to June 24th. Then we used the least square estimates of the model parameters to simulate SARS infection data suggested. The simulation suggested that the SARS outbreak would occur in 30 days from the first day of the government's report, which was consistent with the SARS outbreak occurred in Beijing in 2003. Under this outbreak timeline, we can predict the future SARS outbreaks and establish an effective monitoring system and epidemic prevention mechanism.

INDEX WORDS: Severe acute respiratory syndrome, Epidemic model, Beijing,
Parameter estimation

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CHAPTER 1

INTRODUCTION

Severe acute respiratory syndrome (SARS), also called *Fei Dian* in China, is an acute respiratory disease caused by the SARS virus, coronavirus. The main symptoms of SARS include fever, headache, muscle pain, and respiratory failure. The first SARS case can be traced back to November 16th, 2002 in Foshan, Guangdong Province of China (Smith, 2006). It soon spread to most parts of Mainland of China. In March 2003, SARS began to affect the whole world. The outbreaks in totality led to the infection of 8422 people and the deaths of 916 people across the world, according to the World Health Organization (WHO) report on summary of SARS cases by country in 2003 (WHO, 2003a).

China was one of the countries that were most severely affected. The total number of SARS cases in China was 5327, with 343 deaths (Zhou & Ma, 2003). The assessment team at the WHO even announced that “If SARS is not brought under control in China, there will be no chance of controlling the global threat of SARS” (WHO, 2003b). The rapid transmission of SARS in China began in April and continued to increase until early May. During that period, more than 100 new cases were reported daily (Zhou & Ma, 2003).

Beijing is the capital city of China, an important population distribution center. Its first case was reported on March 6th, 2003, afterwards it spread quickly. In the late April, it was confirmed that there were over 300 cases reported in Beijing, the government

decided to close all primary and secondary schools and entertainment venues in order to prevent the transmission (Khan & William, 2016). The city then began to release the number of new SARS cases to the public every day. In the late April and May, Beijing became the city most severely hit by SARS (Wang & Ruan, 2004). It quarantined more than 30,000 individuals at the peak of the outbreak (Wang & Ruan, 2004). The disease was not under control until early June. On June 24th, the WHO finally removed the name of Beijing from its list of local transmission areas and changed the city's travel recommendation that people should postpone the travel to Beijing (WHO, 2003c).

Although it is well known that SARS is a viral respiratory illness caused by coronavirus, no effective drugs or vaccines were available to treat coronavirus infection during the Beijing outbreak. There were two alternative treatments to control the SARS infection: early detection of SARS infection and effective isolation of asymptomatic contacts. Although no sustained transmission of SARS has occurred since 2003, the probability of the disease's re-emergence remains high.

Based on the points mentioned above, the main purpose of this paper is to use one of the commonly used mathematical models for epidemics, i.e., SIR model, to simulate the outbreak of SARS in Beijing in 2003 with the released data from Beijing Center for Disease Control and Prevention from April 20 to June 23.

The thesis consists 5 chapters:

Chapter 1 introduces the background of the study, its objectives and the structure of the thesis.

Chapter 2 reviews some previous studies about SARS, the timeline of the outbreak in Beijing and in other regions, as well as concepts of the SIR model.

Chapter 3 presents the disease data collected in Beijing, explains the model and the method used in the study.

Chapter 4 shows the results obtained by simulating Beijing SARS outbreak data in 2003, using the designed parameters and the model inferred.

Chapter 5 gives overall conclusions.

CHAPTER 2

LITERATURE REVIEW

2.1 A general introduction to SARS

In 2006, scientists stated that based on the studies of Chinese Centre for Disease Control, there was a genetic link of the SARS coronavirus to civets and in humans. This confirmed that the virus spread across species from the beginning. It was then transmitted from person to person mainly through droplets, both direct and indirect contact (Zhou & Ma, 2003). Cross-regional travel also facilitated its dissemination. That is why SARS can spread so quickly in the world in such a short time. According to the WHO report, the case fatality rate of SARS varied from 0% to 50% depending on people's age. Its estimated total mortality rate is around 14% to 15% (WHO, 2003d.).

The rapidity and severity of SARS alarmed the Chinese government and people. Since April 20, 2003, the government decided to start reporting the number of SARS infection cases to the public every day. Because of those warnings, people began to try everything to protect themselves from being infected. Various disease control and information campaigns were launched, too. For example, many different media channels started to publicize SARS prevention knowledge to the public. Many public places were sprayed with disinfectant. People who had been in direct or indirect contact with suspected SARS cases were all isolated (Zhou & Ma, 2003). Many schools and entertainment venues were closed. Travelers needed to take a body temperature check. Every big city in China had at least one hospital specialized in SARS treatment. In

Beijing, for example, the place that received most patients was the emergency quarantine center of Xiaotangshan Hospital which was built in eight days (Zhou & Ma, 2003).

In the late April and early May, there were a large number of new confirmed cases every day until the decline began after mid-May. During this period, the number of new probable cases reported daily in mainland China dropped sharply from early May (166 cases on average) to the end of that month (16 cases on average) (Zhou & Ma, 2003). By the time of early June, the outbreak was under its control.

2.2 The epidemics of SARS in Beijing

Of all the cities in China, Beijing was attacked most severely by SARS. It started on March 6, when a business woman with SARS symptoms returned to Beijing from Guangdong Province, the cradle of SARS. The disease soon transferred to ten healthcare workers in the hospital that the woman went to and eight of her relatives. As people did not realize the significance of the problem at the beginning, no personal protective equipment was used for healthcare workers when taking care of the patient. Soon after, SARS began to spread rapidly in Beijing and became difficult to control. By the end of June 2003, 2521 individuals were infected. Among them, 193 people died (Chen et al., 2005). The number of cases in Beijing represented about 30% of the global total number (Cao et al., 2010).

Some prior studies have summarized some characteristics of SARS cases in Beijing (Lau et al., 2010; Liang et al., 2004; Chen et al., 2005). From their results, the average age of Beijing's patients was 34.7 years old. Individuals aged between 20 to 39 years old accounted for half of all cases. Healthcare worker was probably the most

vulnerable occupation, accounting for 16.2% of all patients, while retired workers had the highest death rate (24.54%) among all occupations, followed by soldiers (11.11%). More people were infected in the urban areas (67.55%) than in the suburbs (32.45%), while the case fatality rate is higher in suburbs than in urban areas. Neither the infection case number nor the case fatality rate have any significant differences for gender. The total case fatality rate for Beijing is around 7.66%, higher than the rate of the whole mainland of China (6.55%). Beijing ranked the third highest in death rate among all areas in China (The first two are Inner Mongolia and Tianjin). For Beijing, the case fatality rate was higher at the beginning of the outbreak than later, dropping from 16.98% in March to 5.55% after late May (Chen et al., 2005), though the highest number of deaths occurred during the peak stage.

2.3 The epidemics of SARS in other areas

Besides Beijing, the SARS disease in other regions of China such as Guangdong and Inner Mongolia were also studied (Ng et al., 2003; Wu et al., 2003; Chen et al., 2003). These studies mainly focus on making comparison of characteristics with other places or to verify the effectiveness of some new epidemic inference models. Countries such as Singapore, Japan, Vietnam, and Canada had some detailed analysis about their disease characteristics, too (Shi, 2003; Liu et al., 2004; Lipsitch et al., 2003; Chowell, 2003; Choi & Pak, 2003; Nishiura et al., 2004; Zhou & Yan, 2003; Meyers et al., 2005; Wallinga & Teunis, 2004; Gumel et al., 2004). Among all of them, Hong Kong, China had most of the studies.

The SARS disease occurred in Hong Kong on February 21th, 2003. Similar to Beijing, the officials in Hong Kong began to provide daily case reports one month later on March 21th. Also in late March, the city started to close all schools and entertainment venues. The epidemic occurred mainly from late March to Mid-April (Lau et al., 2010). The last reported case was in early June. The overall SARS timeline of Hong Kong was about a month earlier than that of Beijing, probably because it was much closer to the cradle of disease, Guangdong, than Beijing. The case fatality rate in Hong Kong was very high, around 10% of all confirmed cases (Mkhatshwa & Mummert, 2010). However, its rate of onset and progression was roughly the same as in Beijing.

Related researches in Hong Kong included using compartmental (SIR) model to infer the SARS transmission with factors such as quarantine and isolation (Lipsitch et al., 2003), classified susceptibility levels (Chowell et al., 2003), virus strains (Ng et al., 2003), super-spreading events (Mkhatshwa & Mummert, 2010), and other kinds of models such as logistic model (Zhou & Yan, 2003) and contact network model (Masuda et al., 2004).

There were many similarities between Hong Kong and Beijing on aspects of SARS transmission. Since not as much relevant research exists for Beijing as for Hong Kong, we will use relevant literature and research methods in Hong Kong for reference.

2.4 The SIR model

The main model used in this study is a compartmental model, the SIR model. This model was first introduced by Kermack and McKendrick in 1927 (Martcheva, 2015), then developed by Ronald Ross, William Hamer in the early twentieth century (Weiss,

2013). They assumed that when a disease spreads in a fixed population of N , the number of individuals can be classified into three compartments according to the disease status:

- Susceptible (S): The number of individuals who are healthy but can contact the disease and become infected.
- Infectious (I): The number of individuals who have been infected with the disease. They are also infectious.
- Immune/Recovered (R): The number of individuals who have recovered from the disease and will be no longer infected.

The process for the basic model without vital dynamics (birth rate/death rate of population N) is shown below:

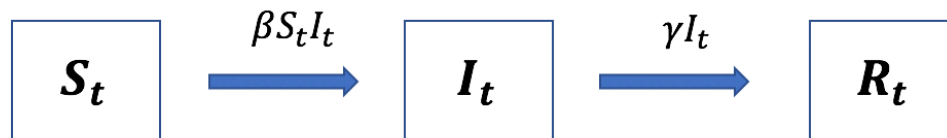


Figure 1. The process of disease transmission in the SIR model

$$\frac{dS_t}{dt} = -\beta S_t I_t$$

$$\frac{dI_t}{dt} = \beta S_t I_t - \gamma I_t$$

$$\frac{dR_t}{dt} = \gamma I_t$$

Basic reproductive number: $A_0 = \frac{\beta S_0}{\gamma}$

A few assumptions are made based on this model. They are:

- The population size N is constant over time;
- For the three compartments, $S_{t=0} > 0$, $I_{t=0} > 0$, $R_{t=0} \geq 0$;
- At any time t , the equation of these compartments is: $N = S_t + I_t + R_t$;
- β and γ are constant, no intervention to prevent the transmission of the disease,

the treatments remain consistent over time;

- The population is homogeneously mixed; every case has the same infectious rate;
- The infection is short (an outbreak) compared with the lifetime of an individual, so births and natural deaths will not affect the size of the three classes;
- Individuals recovered from the disease will have full immunity and cannot be infected again.

There are two parameters in this model; β is the infectious rate, which means the probability of getting the disease when a susceptible individual is in contact with an infectious individual. γ is recover rate, which means the probability of recovering or dying for an infectious individual. When a susceptible individual comes into contact with an infectious individual, the susceptible one may be infected with a certain probability and transfers from the susceptible group to the infectious group. So, at this fixed time, the number of susceptible individuals decreases by the number of individuals who become infected, and the number of infectious individuals will increase by the same number of newly infected ones. At the same time, individuals who recover will move out from the infectious group and go into the recover group. The number now added to the recovered group is the same as the ones deducted from the infectious group. Therefore, the two

parameters β and γ in the model help explain the whole process of disease transmission. This process can also be seen in Figure 1.

The basic reproduction number A_0 is considered to be the average number of secondary cases that one infectious individual generates from the susceptible group during its infectious period. In the basic SIR model, it equals to $\frac{\beta S_0}{\gamma}$. This value can be gained from the initial ordinary differential equation in the SIR model. If we change the type of the second equation $\frac{dI_t}{dt} = \beta S_t I_t - \gamma I_t$ into $\frac{dI_t}{dt} = (\beta \frac{S_t}{\gamma} - 1)\gamma I_t$, we can see that part of the equation on the right hand side is the basic reproduction number. Since we assumed that γ is constant and I_t is the number of infectious at time t , the increase or decrease of this equation depends on $\beta \frac{S_t}{\gamma} - 1$. Therefore, A_0 is an important threshold value for a disease because if $A_0 \leq 1$, then I_t will gradually decrease to zero as $t \rightarrow \infty$, which means the infection will die out soon. But if $A_0 > 1$, then I_t will start to increase first, reach its maximum, then decrease to zero as $t \rightarrow \infty$. This means the disease will become an epidemic. In general, the larger the value of A_0 is, the harder to control the disease. And as the equation shows, this number is determined by the number of susceptible individuals, infection rate, and recovery rate.

There are many studies using compartmental model to infer the SARS outbreak. Besides the ones mentioned above on Hong Kong, related SARS studies on Beijing also used this model and considered different factors, such as the model with 2 viral strains (Ng et al., 2003), the model with exposed, quarantined individuals (Wang & Ruan, 2004), the model with quarantined and isolated individuals (Gumel et al., 2004), the model with time series and Bayes analysis (Fang et al., 2003), the model with “anti-epidemic factor”

(Shi, Xu & Shui, 2004), the model with time and spatial factors (Wang et al., 2005), the model focusing on the group of healthcare workers (Cai et al., 2005), and the model focusing on the effectiveness of the so-called “screening for fever” action (Zeng et al., 2005).

Based on the studies mentioned above, our study focused on Beijing’s SARS outbreak from April to June in 2003. Related data, methods, and the designed model explanation were presented in Chapter 3.

CHAPTER 3

DATA AND METHODS

3.1 2003 SARS data in Beijing

Since Beijing started to release the case data on April 20, our study used the infectious and recovered data from Beijing Centers for Disease Control and Prevention during April 20 to June 23. This period was just right the main period of the SARS outbreak in Beijing. The general timeline which indicates the overall trend of the outbreak related to main event is shown in Figure 2.

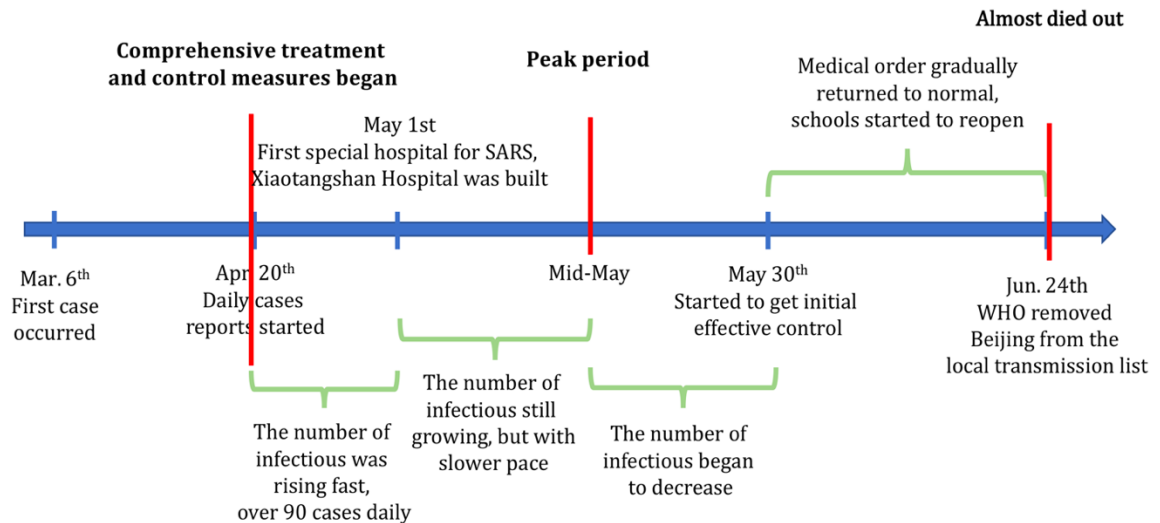


Figure 2. The timeline of SARS outbreak in Beijing during 3/6 to 6/24, 2003

Figure 3 and Figure 4 show the cumulative number of infectious individuals and recovered individuals every day from April 20th to June 23th (totally 65 days). For the

number of infectious individuals, it was calculated by the daily cumulated infection number minus the daily cumulated recovery number. And we can see that this number started from 306 on April 20th, increased dramatically during the first 10 to 15 days, slowly reached its maximum, 2132 cases, around middle May, then began to decrease till the cut-off time of the data. On the other hand, the cumulative number of recovered individuals (includes both the number of recovered and the number of death) is very low at the beginning as only 33 people were recovered on April 20th. It seems that its growth trend is also very slow before late May. But afterwards the number began to increase rapidly and reached the highest value, 2277, till the cut-off time of the data.

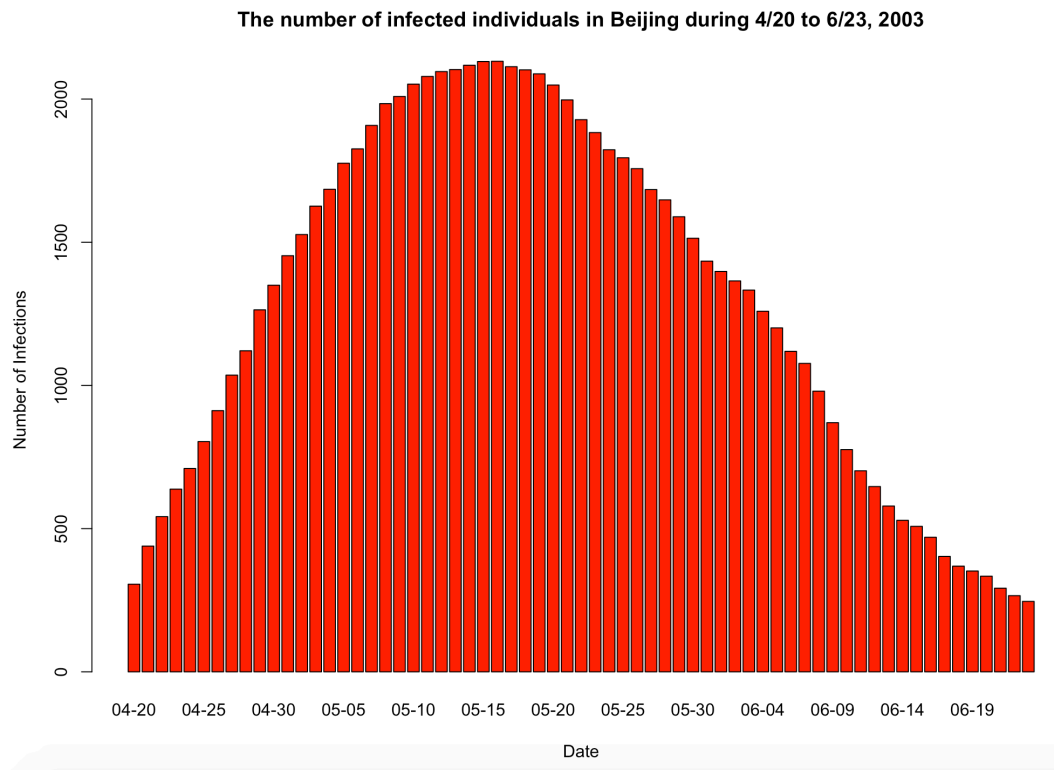


Figure 3. The number of infected individuals in Beijing during 4/20 to 6/23, 2003

The number of recovered individuals in Beijing during 4/20 to 6/23, 2003

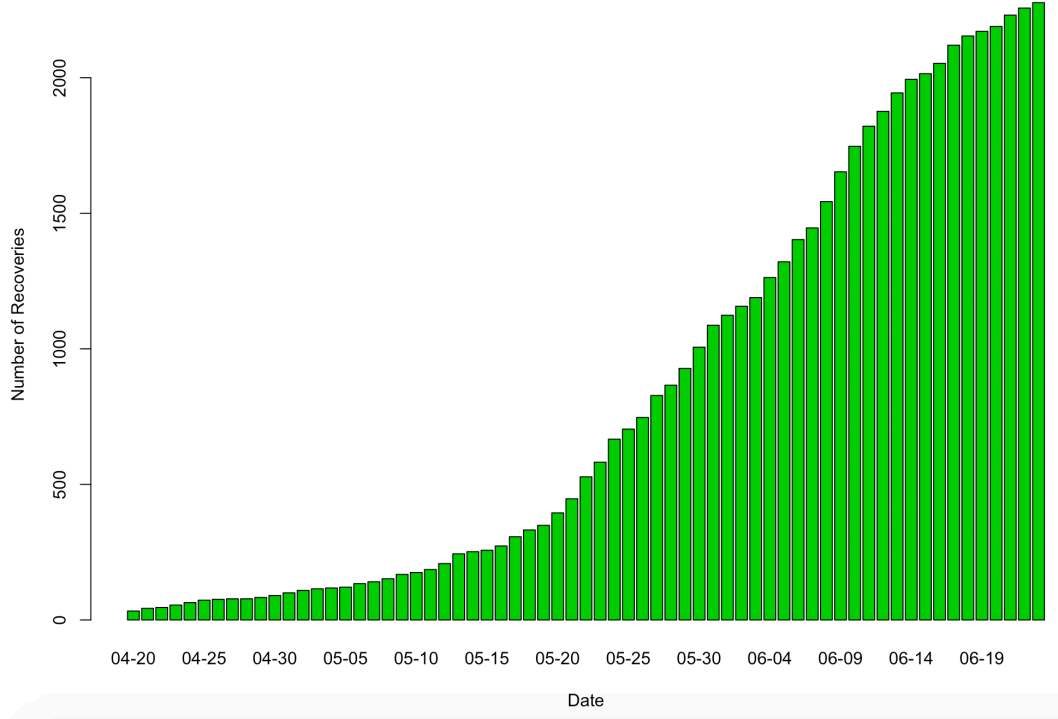


Figure 4. The number of recovered individuals in Beijing during 4/20 to 6/23, 2003

One important issue is try to fix the population size, or the number of susceptible. In 2003, the total population of Beijing is around 14.56 million according to the census of National Bureau of Statistics of China. This number is very large. If we treat it as the initial susceptible population, a small change of parameters, especially for parameter β , will result in significant influence on the value of A_0 . Besides, some people may have very low probability to be infected by SARS. Therefore, the sensitivity of parameters may lead to some unacceptable errors in our prediction for the model and cause problems. But this sensitivity can be reduced if we try to fit the data with a smaller acceptable population. Katriel and Stone (2010) proposed a related formula in their H1N1 pandemic

research in order to calculate the number of susceptible individuals from the total population. The formula calculates a so-called effective reproduction number, which is:

$$\frac{A_e}{S_e} = \frac{A_0}{S_0}$$

Here, A_e is the effective reproduction number; A_0 is the basic reproduction number; S_e is the assumed population; S_0 is the total population. In order to calculate A_e , we need to first assume the value of recovery rate γ , the value of basic reproduction number A_0 , and the duration (number of days) of the epidemic D . Fortunately, a study made by Lau et al. (2010) has estimated that the mean SARS incubation period for Beijing is 5.7 days with 9.7 days standard deviation, and the recovery rate = $\frac{1}{\text{incubation period}}$. In this case, it is $\frac{1}{5.7} = 0.1754$. Also, a study made by Wu et al. (2003) determined the A_0 for Beijing SARS outbreak as 3.5. Therefore, we will use these two assumed values to continue our calculation. On the other hand, the duration of the epidemic $D = t_1 - t_2$, in which $I(t_1) = I(t_2)$, and the period D can cover 90% of the total cases. By calculation, this period is around 66 days. According to the criteria made by Katriel and Stone, A_e should be around 1.5. Thus, we assume the initial susceptible number to be 6.2 million and we treat this number of people as a closed population, so N is a constant. By deducting the number infectious and the number of recovered, the trend of Susceptible number is shown in Figure 5.

The number of susceptible individuals in Beijing during 4/20 to 6/23, 2003

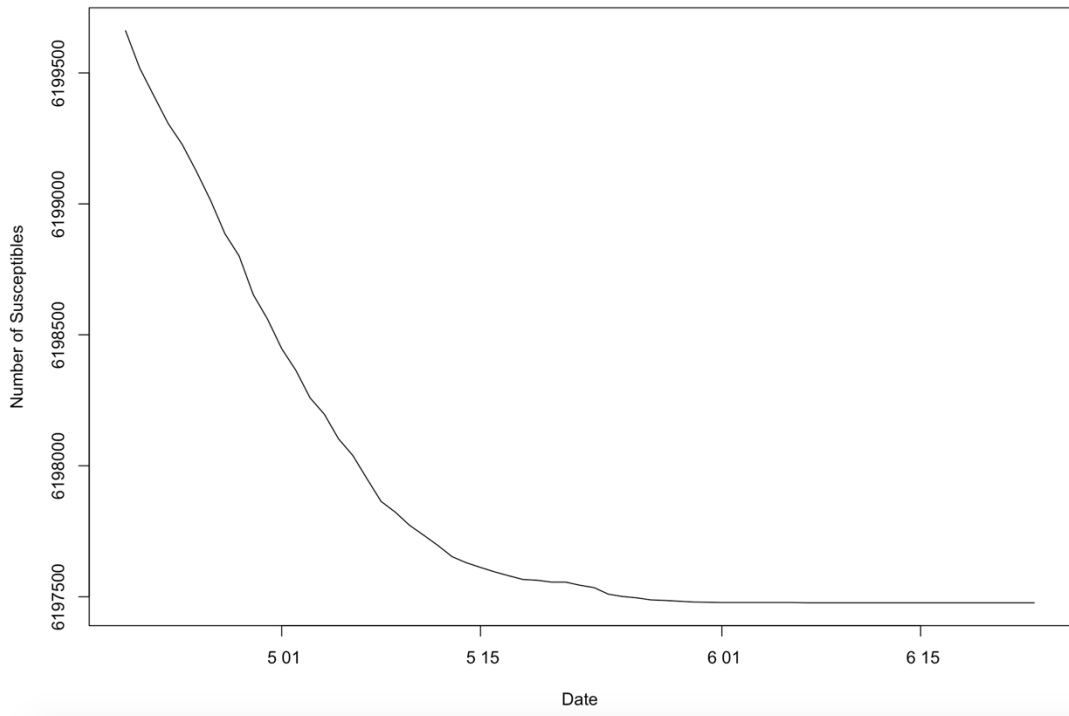


Figure 5. The number of susceptible individuals in Beijing during 4/20 to 6/23, 2003

3.2 Parameters estimation with the least square method

The main model that we used in this study was the basic SIR model with parameters β and γ . We assume that once infectious individuals are fully recovered, they will never be infected again. Therefore, there is no immunity loss in this study. The vital dynamics parameters “natural birth rate” and “death rate” are not applicable here because the duration of SARS is much shorter than an average human life. On the other hand, no effective vaccine was developed during the SARS outbreak, so vaccination rate will not be considered either.

The SIR model is a non-linear system of ODE’s. Unlike linear equations, compartmental models should be solved with algorithms such as Euler’s method. In order

to estimate the value of parameters β and γ , we used the Least Square method to quantify the goodness-of-fit. By using this method, we try to find the minimum sum of squared point-by-point distance between the model expected values and the observed values. The equation is:

$$LS = \sum_{t=1}^{65} (I_t - \hat{I}_t)^2$$

In our case, I_t are the observed values for the number of infections reported by the Beijing CDC. \hat{I}_t are the expected values calculated from the SIR model with parameters β and γ , and we assume that it follows a normal distribution with the mean equal to the solution of the differential equations. We have 65 days data, so the range of t is (1, 65). Since the model is a nonlinear model, it cannot be solved by hand. Therefore, we used an ode function in package `deSolve` in R in order to get the expected values. To find the minimum sum of squared errors, we need to try various β and γ value combinations within an acceptable range of. For β , the range is (1e-10, 1e-06). For γ , the range is (0, 1). Within each parameter's range, we randomly selected 800 values and did various combinations of all possible values and made repeated calculations. Then we will try to calculate their minimum sum of squared errors (SSE) value.

CHAPTER 4

RESULTS

By using the Least Square method to estimate the value of parameters β and γ , we randomly selected 800 values of γ within its estimated range (0, 1), and 800 values of β within its estimated range (1e-10, 1e-06). Then we did various combinations of all possible values for these two parameters and made repeated calculations. By comparing their calculated sum of squared errors (SSE) value, we got a distribution of the SSE value. The result is shown in Figure 6. In this case, probably the model would fit best when γ equals 0.72727, and β equals 1.213e-07, with the sum of squared error being 4311908. Therefore, we will use these two parameters to determine the final model. Figure 7 shows the fitted line with 95% confidence interval and the observed data. The difference between them is not very big, though it seems that during the rising period of the disease, the estimated value lags slightly behind the actual value. Their general peak stage, decreasing stage, and terminating stage are very close. The peak point occurred on day 27 according to the real data, while this occurred on day 29 from our expected data.

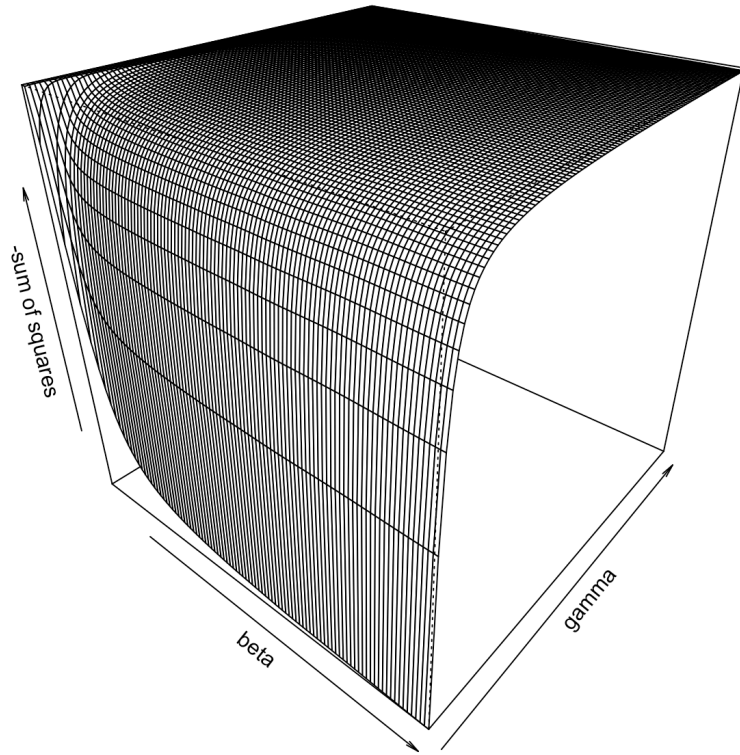


Figure 6. The distribution of SSE value for different values of β and γ

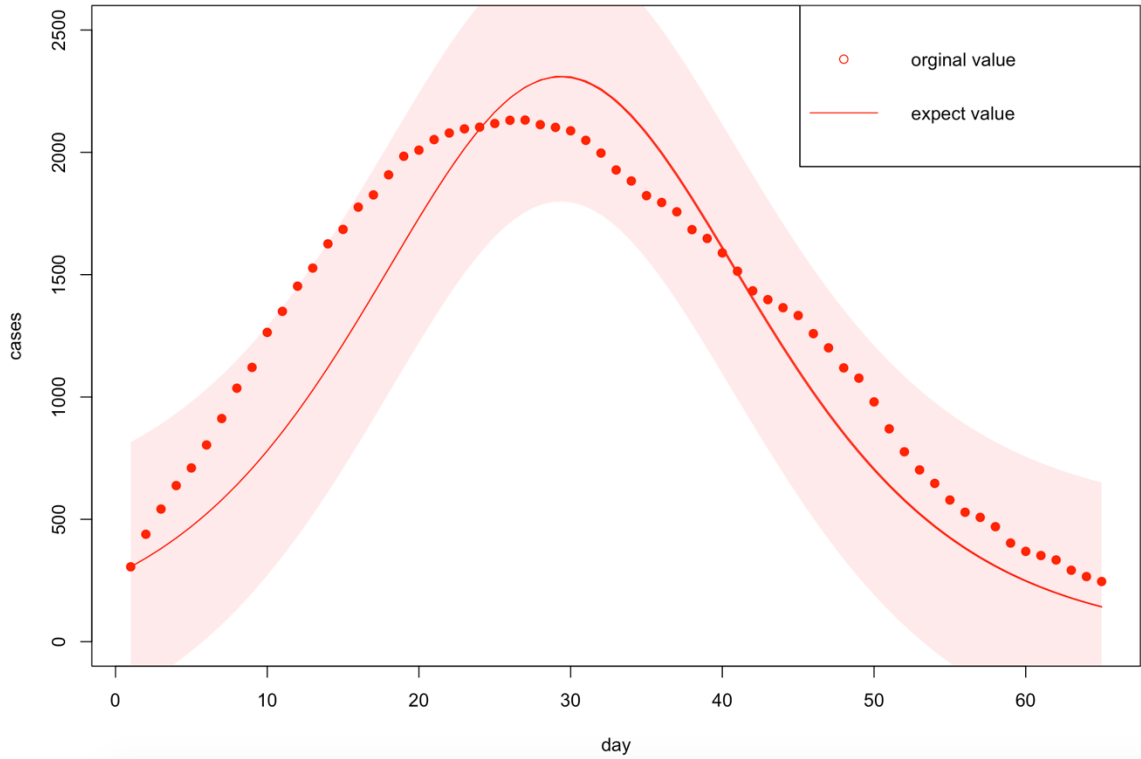


Figure 7. The estimated and observed numbers of infected individuals in Beijing during 4/20 to 6/23, 2003

In order to see the performance of our estimated parameters and model, we made a simulation for the infectious outbreak by using the expected results and adding a standard normal distribution error. Part of these results are presented in Table 1. The MSE value compared to the original data is 66311.57.

Then we tried to use these data to estimate a new pair of parameters β and γ with the same method we used before. According to the results of SSE, the model was the best when γ equals 0.72536, β equals 1.332e-07, which was very close to the one we estimated before. Therefore, our estimation worked well.

Day	Original I	Predicted I	Predicted I with errors
1	306	306	306.3720
7	912	675.3734	675.7461
14	1626	1305.7818	1305.1518
21	2052	1904.0489	1904.4209
25	2118	2136.0234	2136.3954
26	2131	2174.5516	2174.9236
27	2132	2185.1826	2185.5546
28	2113	2194.7741	2194.1461
29	2102	2209.5230	2209.8949
30	2088	2190.0088	2190.3807
35	1823	1981.5081	1981.8801
42	1434	1426.6012	1426.9732
49	1077	899.1041	899.4761
56	529	401.0387	401.4107
63	292	249.0331	249.4051
65	246	168.4115	168.7835

Table 1. Part of the number of infected individuals for observed, predicted, and simulated data

CHAPTER 5

CONCLUSION

In this study, we focused on inferring the outbreak timeline of SARS in Beijing, 2003. As one of the four biggest outbreaks in the world since the beginning of this century, SARS brought severe damage to the whole world, especially to rich urban areas (WHO, 2003f.). Since we do not know whether a SARS outbreak will occur again in the future, it is better that we could be able to forecast the SARS outbreak, so that various prevention and treatment measures can be taken to help delay or shorten the outbreak.

In our study, the fundamental epidemiological model, the Susceptible-Infected-Removed (SIR) epidemic model was used to predict the trend of SARS spread in Beijing. Though the first case occurred in early March in Beijing, the released data provided by the governments only started from April 20th. Therefore, the estimation was based on the SARS cases during April 20th to June 24th. The number of susceptible individuals for SARS was estimated according to the method proposed by Katriel and Stone based on the effective reproduction number. Parameters of infectious rate and recover rate were estimated by least square method. We then used these estimated parameters to predict the trend of SARS outbreak in Beijing and illustrated the performance of the model based on the simulated data.

The results show that the outbreak would occur within 30 days if we treated April 20th as the first day of SARS. The predicted outcome provided us the basic

characteristics of the outbreak, including its timeline for spreading stage, peak stage, decreasing stage, and terminating stage.

However, there are some limitations to this study. First, we did not do any analysis for the disease's imported stage, that is, the first one and a half month after the first case occurred on March 6. This limitation attributed to the lack of valid data for this period. During this period, government and people paid little attention to SARS. Therefore, few precautions were taken about SARS too. It can be imaged that the dynamics of the disease transmission in the first month would be quite different from the one we studied.

In our study, we simply treated April 20th as the initial date of the epidemic. We assumed that there is no intervention to prevent the transmission of the disease because we need the two parameters β and γ to be constant. However, it seems that the infection during the imported stage is much closer to this assumption. If there were any available data for the first month to help us study the initial transmission pattern of the disease, our study would be more meaningful for the future prevention and treatment efforts due to that we could obtain more useful information by comparing the initial transmission pattern with the following period transmission pattern in which government and people's precautions played an important role. In the future study the effects of this difference on model performance should be considered.

On the other hand, the SIR model is just a fundamental compartmental model for epidemiology study. It only considers the two major parameters of disease transmission, infection rate and recovery rate. However, in fact there are probably more factors that need to be considered, such as vaccination rate and super-spreading events. More relevant

parameters will make the model estimation more accurate, but this only happens when the accuracy of the related data is undisputed. If the data of these parameters have high uncertainty, adding them to the model may cause greater deviation between the predicted values and the real values.

The model we made here provides a useful methodology to the future research. If we want to further study this problem with a more complicated model, the first thing we need to do might be how to control many possible causes of epidemics and find a solution for estimating the related parameters.

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