A mathematical study of basic reproduction R_0 and its significance in controlling of corona-virus (COVID-19) disease transmission

Krishna pada Das[†]
[†]Department of Mathematics
Mahadevananda Mahavidyalaya
Monirampore, P.O.-Barrackpore
Kolkata 700120, India
krishnaisi@yahoo.co.in

Abstract

The basic reproduction number of an infectious agent is the average number of infections one case can generate over the course of the infectious period, in a naive, uninfected population. This primer article focuses on the basic reproduction number, R0, for infectious diseases, and other reproduction numbers related to R_0 that are useful in guiding control strategies. Beginning with a simple population model, the concept is developed for a threshold value of R0 determining whether or not the disease dies out. The next generation matrix method of calculating R0 in a compartmental model is described and illustrated. To address control strategies reproduction numbers are defined and these theoretical ideas are then applied to models that are formulated for different SI, SI with incubation delay, SIR, SEIR and SEQIR the novel coronavirus (2019-nCoV) infection model , the reproduction number has been found to vary, reflecting the dynamics of transmission of the coronavirus outbreak as well as the case reporting rate. If $R_0 > 1$, then the number of latently infected individuals exponentially grows. However, if $R_0 < 1$ (e.g. due to quarantine measures and contact restrictions imposed by public authorities), then the number of infected decays exponentially. We then consider the available data on the disease development in different countries to show

that there are three possible patterns: growth dynamics, growth- decays dynamics, and patchy dynamics. During this period of time, the growth rate of the total number of infected was gradually decreasing.

1   Introduction

Coronaviruses are a group of enveloped viruses with a positive-sense, single-stranded RNA and viral particles resembling a crown e from which the name derives. They belong to the order of Nidovirales, family of Coronaviridae, and subfamily of Orthocoronavirinae [1](Carlos, Dela Cruz, Cao, Pasnick, & Jamil, 2020). They can affect mammals, including humans, causing generally mild infectious disorders, sporadically leading to severe outbreaks clusters, such as those generated by the Severe Acute Respiratory Syndrome (SARS) virus in 2003 in mainland China, and by the Middle East Respiratory Syndrome (MERS) virus in 2012 in the Kingdom of Saudi Arabia and in 2015 in South Korea [2](Gralinski & Menachery, 2020). Currently, there exist no vaccines or anti-viral treatments officially approved for the prevention or management of the disease. Anti-retroviral drugs belonging to the class of protease inhibitors, including Lopinavir and Ritonavir, usually utilized for the treatment of HIV/AIDS patients, seem to exert anti-viral effects against coronaviruses. GS-734 (Remdesivir), a nucleotide analogue pro-drug, originally developed against the Ebola and the Marburg viruses, has been recently suggested to be effective also against coronaviruses. Other potential pharmaceuticals include nucleoside analogues, neuraminidase inhibitors, and RNA synthesis inhibitors. Also, Umifenovir (Abidol), used for treating severe influenza cases, anti-inflammatory drugs and EK1 peptide have been proposed as possible drugs against coronaviruses [3](Lu, 2020).

The outbreak of COVID-19 originated from the four admitted patients with pneumonia who had been working in Wuhan Huanan seafood wholesale market, doing business in live poultry, aquatic products, and some wild animals. The now closed market being a common factor in infections encouraged the belief that the infection may be linked with certain animals. The species that harbored the SARS-CoV-2 was probably bat, containing 96 % identical

---

[0]*Corresponding author* E-mail:krishnaisi@yahoo.co.in

at the whole genome level [4]. The COVID-19 may include signs of fever, cough, shortness of breath and general breathing difficulties, organ failures or even death, posing a severe threat to the whole society. The WHO declared the coronavirus outbreak a global health emergency on 30 January 2020 [5]. The global epidemic seemed to be spreading at an alarming rate, causing 79 824 accumulative laboratory-confirmed infections with 2870 deaths as of 29 February 2020 in China[6] and 6009 outside China [7], so it deserved priority attention and intensive research. Chinese health authorities stated that it was likely to transmit from person to person even before any actual signs appeared, which made it especially difficult to prevent and control [8].

Mathematical modelling can play an important role in helping to quantify possible disease control strategies by focusing on the important aspects of a disease, determining threshold quantities for disease survival, and evaluating the effect of particular control strategies. A very important threshold quantity is the basic reproduction number, sometimes called the basic reproductive number or basic reproductive ratio [9], which is usually denoted by R0. The epidemiological definition of R_0 is the average number of secondary cases produced by one infected individual introduced into a population of susceptible individuals, where an infected individual has acquired the disease, and susceptible individuals are healthy but can acquire the disease. The interaction between medical and theoretical epidemiology of infectious diseases is probably not as strong as it should. Many results in the respective fields fail to migrate to the other. There are of course exceptions. Perhaps the most important are the ideas of epidemic thresholds and the parameter R0the basic reproduction numberas a key predictor of the epidemiological severity of a disease [9, 10]. R_0 is defined as the expected number of other individuals that an infected individual will infect if he or she enters a population entirely composed of susceptible individuals. It is thus a combined property of the process of contagion and the contact patterns of the population. In classic mathematical models of infectious disease spreading, $R_0 = 1$ marks an epidemic threshold. If $R_0 < 1$, the expected fraction of infected people in an outbreak, denoted by Ω, will not depend on the total population size . If $R_0 > 1$, the expected value of Ω is proportional to population. In other words, in the limit of large populations, a finite fraction of the population can be infected. The focus on R_0 in the literature has sometimes been so strong that researchers rather calculate R_0 than quantities directly related to the outbreak, such as prevalence, incidence, and time to the peak prevalence. The aim of this review is to elaborate on mathematical ways of finding R_0

3

for ODE disease models in a population, bearing in mind the epidemiological meaning of R_0, and to demonstrate how this and other reproduction numbers can be used to guide control strategies. In this study we have used the basic reproduction number as a essential controling parameter for spreading and controlling of COVID-19 disease. In this endemic situation in China Indian Govt. will be careful to protect such type disease transmission in local as well as community and they follow the guide line and instruction by WHO.

2   basic reproduction number:

2.1   Derivation of R_0 from SI model:

We consider susceptible-infected (SI) model without demographic issue i.e. natural birth and death of the individuals. The model we use is called an SI model.

The simple SI model

$$
\begin{aligned}
\frac{dS}{dt} &= -\beta SI \\
\frac{dI}{dt} &= \beta SI - \gamma I
\end{aligned}
\tag{1}
$$

Here β is theinfection rate and γ is the diseas induced mortality rate of the infected population.

If infection is very low level, $S >> I$. We consider $S \cong S_0$. Since the coronavirus epidemics is admittedly still in its early stage, let us only determine the condition of the disease progression at its beginning, i.e. when the number of infected/recovered/dead is much less than the number of susceptible, and hence S in the model above can be considered as constant, $S \cong S_0$.

Let $I = I_0 e^{mt}$ be solution of the equation

$$
\frac{dI}{dt} = \beta SI - \gamma I
\tag{2}
$$

.

Then we get

$$
I = I_0 e^{(\beta S_0 - \gamma)t}.
$$

Therefore $I \to 0$ iff $\beta S_0 - \gamma < 0$ i.e. $\frac{\beta S_0}{\gamma} = R_0 < 1$.

Therefore if $R_0 < 1$, $I \to 0$ i.e. system will be disease free. But if $R_0 > 1$, then infected population will grows exponentially and as a result system will be endemic.

This R_0 is called basic reproduction number. Here βS_0 is the new born infected population and $\frac{1}{\gamma}$ is the life span of infected individual. Therefore basic reproduction number can be described as total number of new born infected individuals by a infected individual in its life span. A model that allows for the incubation period will be considered in the next subsection.

2.2 Derivation of R_0 from SI model with incubation delay:

If we take assumption that coronavirus disease spread among community to take some time which is called incubation delay, the system (1) can be written as

$$\frac{dS}{dt} = -\beta S I$$
$$\frac{dI}{dt} = \beta S(t - \tau)I(t - \tau) - \gamma I$$

where τ is incubation period of infected individual.

Here as $t >> \tau$ we consider $S \cong S_0$ and $I = I_0 e^{mt}$ be solution of the equation of the equation

$$\frac{dI}{dt} = \beta S(t - \tau)I(t - \tau) - \gamma I.$$

From above equation we get

$$I_0 m e^{mt} = \beta S_0 I_0 e^{m(t-\tau)} - \gamma I_0 e^{mt}$$
$$m = \beta S_0 e^{-m\tau} - \gamma$$
$$m = \gamma(R_0 e^{-m\tau} - 1)$$

$$m = \gamma(R_0 e^{-m\tau} - 1)$$

5

This equation has solution $m = 0$ for all values of parameters. Besides this solution, it can have a positive or a negative solution m. The function $f(m) = \beta S_0 e^{-m\tau} - \gamma$ is an decreasing function with the asymptotic limit βS_0 at infinity. The sign of the solution is determined by the derivative $f'(0)$. If $f'(0) > 1$, then there is a positive solution, if $f'(0) < 1$, the solution is negative. In terms of the basic reproduction number $R_0 = \beta S_0 e^{-\tau}$, the condition is similar as for the SI model. However, the meaning of this parameter is different. It characterizes the total infection rate during the incubation period and not its ratio with the rates of recover and death.

2.3   Derivation of R_0 from SIR model:

Now we considered susceptible-infected-recovered (SIR) model in case of coronavirus (COVID-19) disease. If we will consider recovery rate σ for infected population the system (1) can be written as

$$
\begin{aligned}
\frac{dS}{dt} &= -\beta SI \\
\frac{dI}{dt} &= \beta SI - \gamma I - \sigma I \\
\frac{dR}{dt} &= \gamma I
\end{aligned}
\tag{3}
$$

It is assumed here that recovered individuals do not return to susceptible class, that is, recovered individuals have immunity against the COVID-19 disease; they cannot become infected again and cannot infect susceptibles either.

What are the conditions for an epidemic? An epidemic occurs if the number of infected individuals increase i.e. $\frac{dI}{dt} > 0$.

At the outset of COVID-19 epidemic, early every susceptible population is very large than infected ones. So we can say that $S \cong S_0$. Substituting $S = S_0$, we arrive at the following inequality

$$
\begin{aligned}
\beta S_0 I - \gamma I - \sigma I &> 0 \\
\beta S_0 I &> (\gamma + \sigma)I \\
\frac{\beta S_0}{(\gamma + \sigma)} &> 1
\end{aligned}
$$

6

$\frac{\beta S_0}{(\gamma+\sigma)} = R_0$ is called the basic reproduction number. If $R_0 > 1$, then the number of infected will grow, if $R_0 < 1$ it will decay. Thus, R_0 plays the key role in the covid -19 epidemics development. In particular, one can change the course of the disease dynamics by changing R_0. For instance, if measures are introduced that push the value of R_0 below one (e.g. by making β to decrease), the exponential growth changes to exponential decay. Interestingly, this is exactly what has happened in China after restrictions on daily life were introduced.

The classical SIR model therefore determines the condition of the disease development from the comparison of the disease transmission rate with the sum of the recover and death rates. In the other words, we compare the rates of adding and removal of infected. The model does not account for the incubation period of the disease that was shown to be important in the case of coronavirus spread: individuals can become infective before showing any symptoms.

2.4 Derivation of R_0 from next generation matrix:

2.4.1 Basic concept on next generation matrix:

If R_0 is the number of secondary infections produced by a single typical infection in a rarefied population, how do we define it when there are multiple types of infected individuals. For example, what is a typical infection in a vector-borne disease like malaria? What about a sexually transmitted infection where there are large asymmetries in transmissibility (like HIV)? Or what about a multi-host pathogen like influenza ? It turns out that there is a straightforward extension of the theory for structured epidemic models. The mathematics behind this theory is not especially difficult, but it does involve scary German terms that are not familiar to the non-engineers in our midst. The key concept is that we now need to average the expected number of new infections over all possible infected types. Assume that we have a system in which there are multiple discrete types of infected individuals (e.g., mosquitoes and humans; women and men; or humans, dogs, and chickens). We define the next generation matrix as the square matrix G in which the ijth element of G, g_{ij} , is the expected number of secondary infections of type i caused by a single infected individual of type j, again assuming that the population of type i is entirely susceptible. That is, each element of the matrix G is a reproduction number, but one where who infects whom is

accounted for. Once we have G, we are one step away from R_0. The basic reproduction number is given by the spectral radius of G. The spectral radius is the also known as the dominant eigenvalue of G. The next generation matrix has a number of desirable properties from a mathematical standpoint. In particular, it is a non-negative matrix and, as such, it is guaranteed that there will be a single, unique eigenvalue which is positive, real, and strictly greater than all the others. This is R_0.

For illustrative purposes, we will limit our discussion to the case where there are two classes of infected individual. The next generation matrix is thus 22. Define

$$G = \begin{bmatrix} a & b \\ c & d \end{bmatrix}$$

The eigenvalues of G are:

$$\lambda = \frac{T}{2} \sqrt{(\frac{T}{2})^2 - D}$$

where $T = a + d$ is the trace and $D = ad - bc$ is the determinant of matrix G.

For example, you have a sexually transmitted disease in a completely heterosexual population. Define f as the expected number of infected women and m as the expected number of infected men given contact with a single infected member of the opposite sex in a completely susceptible population. The next generation matrix is

$$G = \begin{bmatrix} 0 & f \\ m & 0 \end{bmatrix}$$

R_0 is thus $\sqrt{mf}$. It is worth noting that this is the geometric mean of the expected number of female and male secondary cases.

2.4.2 Derivation of R_0

Hefferman et al. (2005) provides a nice readable introduction for calculating R_0 in structured population models. Consider the next generation matrix G. It is comprised of two parts: F and V^{-1}, where

$$F = \frac{\partial F_i(x_0)}{\partial x_j} \tag{4}$$

and

$$V = \frac{\partial V_i(x_0)}{\partial x_j} \tag{5}$$

The F_i are the new infections, while the V_i transfers of infections from one compartment to another. x_0 is the disease-free equilibrium state. R_0 is the dominant eigenvalue of the matrix $G = FV^{-1}$.

Consider a Susceptible-Exposed-Infected-Removed (SEIR) Epidemic. This is an appropriate model for a disease where there is a considerable post-infection incubation period in which the exposed person is not yet infectious.

The simple SEIR model consists of a set of four differential equations:

$$
\begin{aligned}
\frac{dS}{dt} &= A - \beta SI - \mu S \\
\frac{dE}{dt} &= \beta SI - (\mu + k)E \\
\frac{dI}{dt} &= E - (\gamma + k)I \\
\frac{dR}{dt} &= \gamma I - \mu R
\end{aligned}
\tag{6}
$$

where β is the effective contact rate, A is the birth rate of susceptibles, μ is the mortality rate, k is the progression rate from exposed (latent) to infected, γ is the removal rate.

To calculate the next generation matrix for the SEIR model, we need to enumerate the number of ways that (1) new infections can arise and (2) the number of ways that individuals can move between compartments. There are two disease states but only one way to create new infections:

$$F = \begin{bmatrix} \frac{\beta A}{\mu} & 0 \\ 0 & 0 \end{bmatrix}.$$

In contrast, there are various ways to move between the states:

$$V = \begin{bmatrix} 0 & k + \mu \\ \gamma + \mu & -k \end{bmatrix}.$$

R_0 is the leading eigenvalue of the matrix FV^{-1}. This is reasonably straightforward to calculate since FV^{-1} is simply a 2 2 matrix.

9

$$R_0 = \frac{k\beta A}{\mu(k+\mu)(\gamma+\mu)}.$$

It is interesting to note that R_0 is also the product of the rate of production of (1) new exposures and (2) new infections, as it should be. It can be shown easily from Jacobian matrix around the disease free equilibrium point that if $R_0 < 1$, the disease free equilibrium point will stable. This implies disease can be wiped out from the system. If $R_0 > 1$, the disease free equilibrium point will be unstable and disease will be endemic in the system. Since R_0 is the increasing function of two important parameters β and A. If the effective contact rate β is increased the unknown disease such as COVID-19 will be spread in the community. If the birth rate A of the susceptible individuals is increased the value of R_0 will be increased and which implies COVID-19 disease transmits among the community rapidly. So we can conclude R_0 is the controlling parameter for spearing COVID-19 disease transmission.

2.5   Quarantine COVID-19 model:

A compartmental differential equation model for COVID is formulated. We adopt a variant that reflects some key epidemiological properties of COVID-19. The model monitors the dynamics of five sub-populations, namely susceptible $(S(t))$, exposed $(E(t))$, quarantined $(Q(t))$, infected $(I(t))$, and recovered $(R(t))$ individuals. The total population size is $N(t) = S(t) + E(t) + Q(t) + I(t) + R(t)$. In this model, quarantine refers to the separation of COVID infected individuals from the general population when the population are infected but not infectious, whereas isolation describes the separation of COVID infected individuals when the population become symptomatic infectious. Our model incorporates some demographic effects by assuming a proportional natural death rate $\mu > 0$ in each of the five sub-populations of the model. In addition, our model includes a net inflow of susceptible individuals into the region at a rate A per unit time. This parameter includes new births, immigration and emigration. By recruiting individuals into the region, the susceptible population is increased and reduced by natural death. Also the susceptible population decreases after infection, acquired through interaction between a susceptible individual and an infected person who may be quarantined, infected. For these two groups of infected individuals, the transmission coefficients are β, $r_Q\beta$, respectively. We consider the β as a

transmission rate along with the modification factors for quarantined r_Q. The interaction between infected individuals (quarantined, infected) and susceptible is modelled in the form of total population without quarantined using mass action incidence incidence. Population who are exposed are infected individuals but not infectious for the community. The exposed population decreases with quarantine at a rate of γ_1, and become infected at a rate k_1 and σ_1 is the recovery rate of quarantine individuals natural death at a rate μ. The infected individuals are produced by a proportion of k_1 of exposed class after the exposer of clinical symptoms of COVID-19 by exposed individuals. σ_2 is the recovery rate and natural death at a rate μ. Quarantined, infected individuals recover from the disease at rates σ_1, σ_2 respectively, and this population is reduced by a natural death rate μ.

Under these assumptions, we consider the quarantine COVID-19 model:

$$
\begin{aligned}
\frac{dS}{dt} &= A - \beta SI - r_Q \beta QS - \mu S \\
\frac{dE}{dt} &= \beta SI + r_Q \beta QS - (\gamma_1 + k_1 + \mu)E \\
\frac{dQ}{dt} &= \gamma_1 E - (\sigma_1 + \mu)Q \\
\frac{dI}{dt} &= k_1 E - (\sigma_2 + \mu)I \\
\frac{dR}{dt} &= \sigma_1 Q + \sigma_2 I - \mu R
\end{aligned}
$$

The diseases-free equilibrium can be obtained for the system (7) by putting $E = 0$, $Q = 0$, $I = 0$, which is denoted by $L_0 = (S^0, \ 0, \ 0, \ 0, R^0)$, where $S^0 = \frac{A}{\mu}$, $R^0 = 0$.

The basic reproduction number, a central concept in the study of the spread of communicable diseases, is the number of secondary infections caused by a single infective in a population consisting essentially only of susceptibles with the control measures in place (quarantined and isolated class)[11]. This dimensionless number is calculated at the DFE by next generation operator method [12] and it is denoted by R_0. For this, we assemble the compartments which are infected from the system (7) and decomposing the right hand side as $\Gamma - \Lambda$, where Γ is the transmission part, expressing the the production of new infection, and the transition part is Λ, which describe the change in state.

$$\Gamma = \begin{bmatrix} \beta SI + r_Q \beta SQ \\ 0 \\ 0 \end{bmatrix}.$$

$$\Lambda = \begin{bmatrix} (\gamma_1 + k_1 + \mu)E \\ -\gamma_1 E + (\sigma_1 + \mu)Q \\ k_1 E + (\sigma_2 + \mu)I \end{bmatrix}.$$

Now we calculate the Jacobian of F and V at DFE L_0

$$F = \frac{\partial \Gamma}{\partial X} = \begin{bmatrix} 0 & r_Q \beta & \beta \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

and

$$V = \frac{\partial \Lambda}{\partial X} = \begin{bmatrix} \gamma_1 + k_1 + \mu & 0 & 0 \\ -\gamma_1 & \sigma_1 + \mu & 0 \\ k_1 & 0 & \sigma_2 + \mu \end{bmatrix}.$$

From next generation matrix $R_0 = \rho(FV^{-1})$, where ρ is the spectral radius of the next-generation matrix (FV^{-1}). Thus, from the model (7), we have the following expression for R_0 and $R_0 = \frac{r_Q \beta \gamma_1}{(\gamma_1 + k_1 + \mu)(\sigma_1 + \mu)} + \frac{\beta k_1}{(\gamma_1 + k_1 + \mu)(\sigma_2 + \mu)}$

We have observed the impact of quarantine which is measured qualitatively on the disease transmission dynamics. A threshold study of the parameter correlated with the quarantine of exposed individuals γ_1 is performed by measuring the partial derivatives of the basic reproduction number R_0 with respect to the parameter.

We have observed that

$$\frac{dR_0}{d\gamma_1} = \frac{r_Q \beta (k_1 + \mu)}{(\gamma_1 + k_1 + \mu)^2 (\sigma_1 + \mu)} - \frac{\beta k_1}{(\gamma_1 + k_1 + \mu)^2 (\sigma_2 + \mu)}$$

so that $\frac{dR_0}{d\gamma_1} < 0 (> 0)$ iff $r_Q < r_{\gamma_1}$ $(r_Q > r_{\gamma_1})$ where $0 < r_{\gamma_1} = \frac{k_1(\sigma_1 + \mu)}{(k_1 + \mu)(\sigma_2 + \mu)}$.

From the above analysis it is obvious that if the relative infectiousness of quarantine individuals r_Q will not cross the threshold value r_{γ_1}, then quarantining of exposed individ- uals results in reduction of the basic reproduction number R_0 and therefore reduction of the disease burden. On the other side, if $r_Q > r_{\gamma_1}$, then the basic reproduction number R_0 would rise due to the increase in infectiousness of the quarantine rate and thus the disease burden

will also rise. So if the disease infectiousness into the quarantine population increases, the use of quarantine in this scenario is harmful.

3 Will An Epidemic Infect Everyone?

Will an epidemic, once it has taken off in a population, eventually infect everyone ? In order to answer this question, we want to know how i changes with respect to the fuel for the epidemic, S. We thus get from system (1)

$$\frac{dI}{dS} = -1 - \frac{\gamma}{\beta S}.$$

We solve this equation and get

$$log(S_\infty) = R_0(S_\infty - 1). \tag{7}$$

This is an implicit equation for S_∞, the number of susceptible at the end of the epidemic. When $R_0 > 1$, this equation has exactly two roots, only one of which lies in the interval $(0, 1)$. Subtract $log(S_\infty)$ from both sides and we get $R_0(S_\infty - 1) - log(S_\infty) = 0$. Call the whole left-hand side y. y will have different values for different values of $log(S_\infty)$. Only a couple of those will satisfy equation (7). $log(S_\infty) = 1$ will always satisfy the requirement of $y = 0$ (plug it in and see!). When $R_0 > 1$, the other solution to $y = 0$ is the actual value of the final size. This is the one we really care about. If $R_0 < 1$, the only value that satisfies equation (7) is $log(S_\infty) = 1$. In words, at the end of the epidemic, everyone will still be susceptible (i.e., no one gets infected). Figure 3 shows the solutions of equation (7) for various values of $R_0 > 1$ in black. The point where the curve crosses the horizontal axis is the value for S_∞, the total fraction of the population infected at the end of the epidemic. As R_0 gets larger, the final size of the epidemic gets larger as well. Figure(1) also shows the solution when $R_0 < 1$ in the red. The curve never crosses the horizontal axis, meaning that essentially none of the total population becomes infected when an infection is sub-critical. The conclusion we can draw from all this analysis is that, in general, a fraction of the population will escape infection. That is, $S_\infty < 1$. This is one of the fundamental insights of mathematical theory of epidemics.
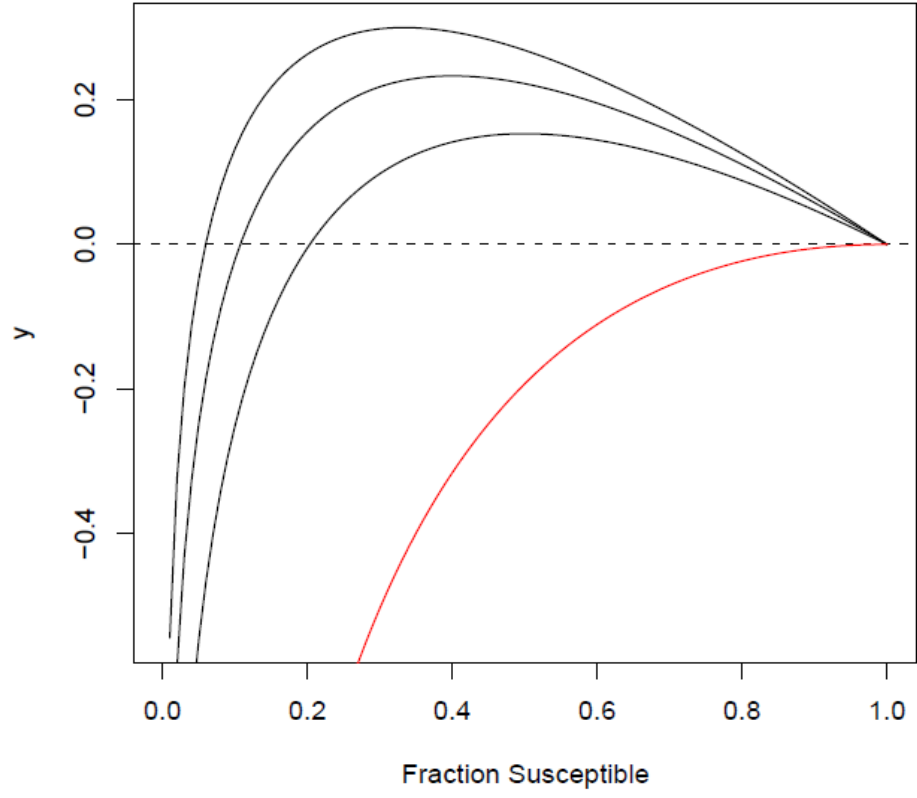
Figure 1: Solutions of equation (7) for various values of $R_0 > 1$. The solution of equation (7) when $R_0 < 1$ is plotted in red. 15

4   Optimal Virulence:

Here we consider a SI epidemic model:

$$\frac{dS}{dt} = -\beta SI - \mu S \tag{8}$$
$$\frac{dI}{dt} = \beta SI - (\mu + \delta)I$$

Here β is disease transmission rate, μ is natural death rate and δ is the disease-induced mortality rate.

The basic reproduction number of above system is

$$R_0 = \frac{\beta}{\mu + \delta}.$$

The parameter μ is independent of the epidemic, but the parameters, μ and δ can conceivably be functions of virulence, which we denote by x. An Evolutionary Stable Strategy (ESS) is a phenotype that can not be invaded by a rare mutant. Loosely speaking, it represents the optimal phenotype. The ESS virulence occurs where $\frac{dR_0}{dx} = 0$.

Now

$$\frac{dR_0}{dx} = \frac{\beta'(\mu + \delta) - \gamma'\beta}{(\mu + \delta)^2} = 0.$$

Rearranging and evaluating $\beta(x)$ and $\delta(x)$ and the ESS values of x (denoted x^*), we have

$$\frac{d\beta(x)}{d\delta(x^*)} = \frac{\beta(x^*)}{\mu + \delta(x^*)}. \tag{9}$$

This result has a nice geometric interpretation. The ESS virulence occurs where a line rooted at the origin is tangent to the curve that relates β to δ. This result is known as the Marginal Value Theorem and has applications in economics and ecology as well as epidemiology. The MVT model for optimal virulence is plotted in figure(2). In the lower curve, the tangent line hits further out on the horizontal axis and mortality is higher.
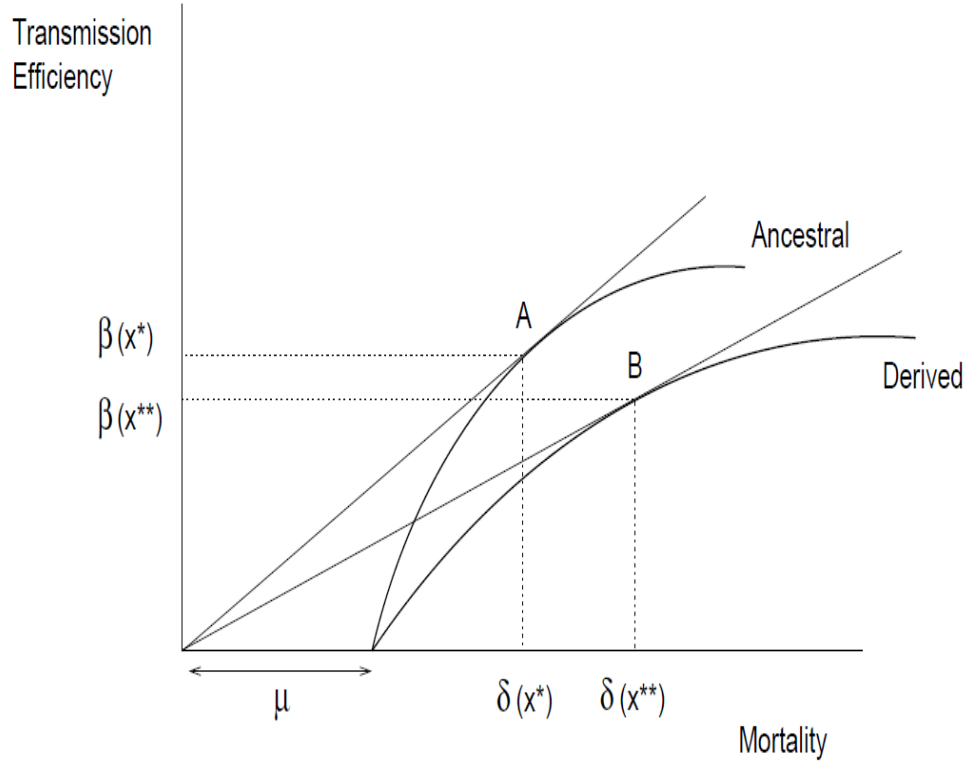
Figure 2: Marginal value theorem for optimal virulence. The ESS virulence occurs where a line rooted at the origin is tangent to the curve that relates β to δ. Two curves are depicted. The first curve shows a pathogen in which transmissibility increases relatively rapidly with mortality. Point A indicates the optimal balance between $\beta(x)$ and $\delta(x)$ under this case, and the optimal virulence is indicated x^*. For the second curve, relative transmission is less efficient. Therefore, the tangent line from the origin to the curve hits further out (B) along the mortality axis and the optimal virulence is higher (x^{**}).
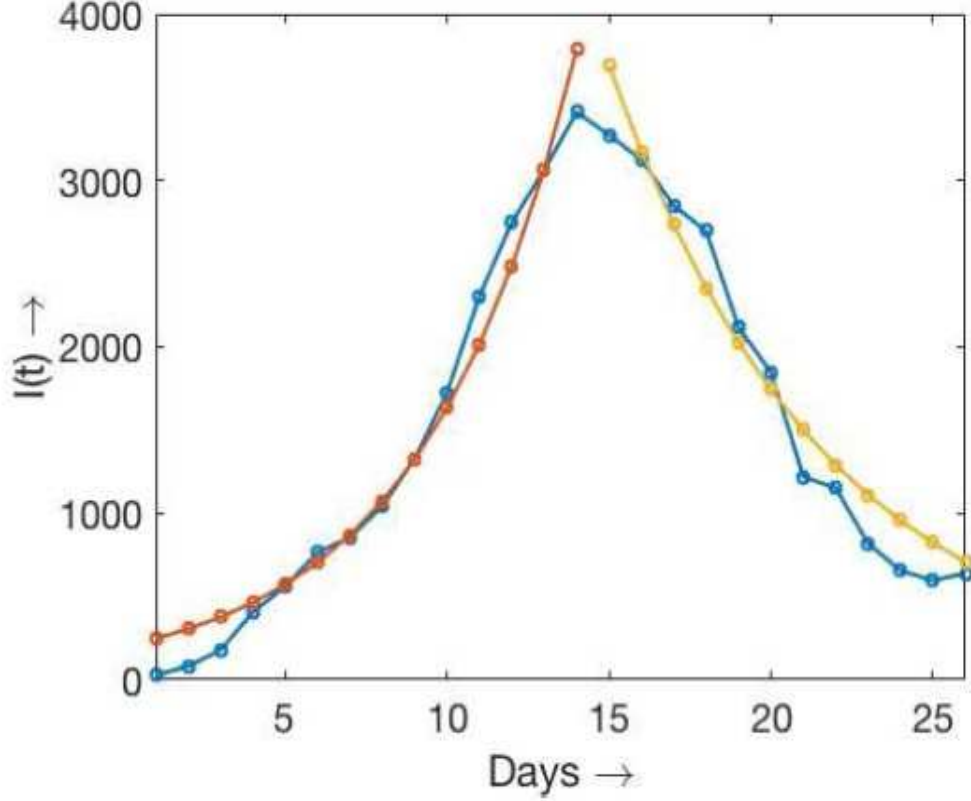
Figure 3: The pattern of infected individuals obtained as a sum of daily cases during the quartine period of 5 days data in South Korea, the growing branch is approximated by the exponential, decaying .

5 Data

We used the data from [4] showing the total number of infected individuals and daily cases in different countries and worldwide. Across the world, daily cases clearly show two-mode dynamics such as in China (growth-decay) and Europe (growth). There are periods of exponential growth, decay and re-growth. The origin of the outbreak on February 12 (in China) is not clear yet. It may be related to the method of data collection. Daily reported cases curves in China and South Korea correspond to the growth-decay dynamics.

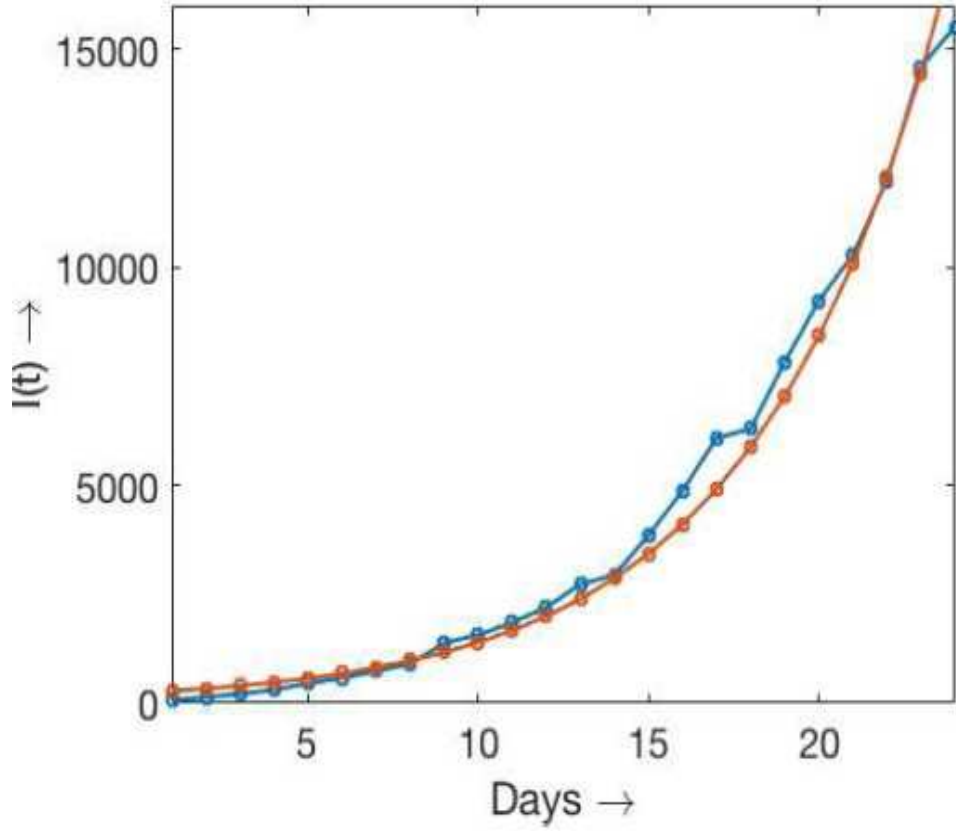The daily new cases curves for France, Germany, Italy, Spain, USA cor-

Figure 4: The pattern of infected population during the 5 days quarantine period in Italy.

respond to the growth mode. Note that the data on daily reported cases do not exactly correspond to the variable I(t). The latter represents a sum of daily cases during the quarantine period. Taking into consideration that the quarantine period to be of 5 days, we therefore obtain the graphs for the infected individuals. We observe growth-decay dynamics for South Korea (Figure(3)) and growth dynamics in Italy (Figure(4)). Fitting the data allows us to determine the growth of infected population from equation (7).

6 Conclusion:

In the present study we have studied different model in respect of coronavirus diease outbreak in Chaina, South Korea and Italy. We have different technique to derive the basic reproduction number which has important role to predic the disease will be endemic or not endemic. It has been shown that if $R_0 < 1$, system will be disease free. But if $R_0 > 1$, disease will be endemic for any SI, SEI and SEIR models. From the above analysis it is obvious that if the relative infectiousness of quarantine individuals r_Q will not cross the threshold value r_{γ_1} , then quarantining of exposed individuals results in reduction of the basic reproduction number R_0 and therefore reduction of the disease burden. On the other side, if $r_Q > r_{\gamma_1}$, then the basic reproduction number R_0 would rise due to the increase in infectiousness of the quarantine rate and thus the disease burden will also rise. So if the disease infectiousness into the quarantine population increases, the use of quarantine in this scenario is harmful. Our model confirms the efficiency of the approach to stop the disease spread by the limiting the number of contacts between the individuals through quarantine of infected individuals. This is quite obvious in theory, with the help of the simplest model formulation, but difficult in practice. Success of the strategy also depends upon the appropriate time of implementa- tion. Experience of China and South Korea shows that the peak of infection (maximum of newly reported cases on daily basis) is reached about 10 days after adopting serious restric- tive measures. The number of infection increased during this time in 10-20 times. In Italy 10 days after the universities and schools were closed (March 4) the peak of infection does not seem to be reached, and exponential growth continues. Moreover, the exponential growth rate of the total number of infected in China and in South Korea observed before the adopted measures (January 25 and February 22, respec- tively) rapidly changed to a slower growth rate afterward . Similar situation is observed in Iran though the information about adopted measures is not fully available yet. However, in Italy the exponential growth rate does not change up to March 4. This can be an indication that the introduced measures are not sufficient or that they are not respected by local people. Our updated findings suggest that the best measure is persistent and strict self-isolation. The epidemics will continue to grow, and can peak soon with the peak time depending highly on the public health interventions practically implemented. Exceptional measures adopted for the coronavirus infection suggest to introduce another model of infection development. We

consider the sub-population of latently infected individuals who are already infected but do not show any symptom during the incubation period. When the incubation period is over, the disease manifests itself with its symptoms, and the individual is isolated in the quarantine where he/she cannot infect the others.

References

[1] Carlos, W. G., Dela Cruz, C. S., Cao, B., Pasnick, S., & Jamil, S. (2020). Novel Wuhan (2019-nCoV) coronavirus. American Journal of Respiratory and Critical Care Medicine. https://doi.org/10.1164/rccm.2014P7.

[2] Gralinski, L. E., & Menachery, V. D. (2020). Return of the coronavirus: 2019-nCoV. Viruses, 12(2).

[3] Lu, H. (2020). Drug treatment options for the 2019-new coronavirus (2019-nCoV). Bioscience Trends. https://doi.org/10.5582/bst.2020.01020. Majumder, M., & Mandl, K. D. (2020). Early transmissibility assessment of a novel coronavirus inWuhan, China. Social Science Research Network. $https://doi.org/10.2139/ssrn.3524675.$

[4] Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020. $https://doi.org/10.1038/s41586 - 020 - 2012 - 7.$

[5] World Health Organization. Statement on the Second Meeting of the International Health Regulations. $https : //www.who.int/news - room/detail/$ 30-01-2020-statement-on-the-second-meeting-of-the-internationalhealth-regulations-(2005)-emergency-committee-regarding-the-outbreak of-novel-coronavirus-(2019-ncov). Accessed February 4, 2020.

[6] National Health Commission of the People's Republic of China. The updates of COVID-19 as of 29 February, 2020. $http : //www.nhc.gov.cn/xcs/yqtb/202003/9d462194284840ad96ce75eb8e4c8039.shtml.AccessedMar$

[7] World Health Organization. Coronavirus disease 2019 (COVID-19) situation report (40). $https : //www.who.int/docs/default -$

$source/coronaviruse/situation-reports/20200229-sitrep-40-covid-19.sfvrsn = 849d0665_2.AccessedMarch1, 2020.$

[8] Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan,China, of novel coronavirus-infected pneumonia. [published online ahead of print January 29, 2020]. N Engl J Med. $https : //doi.org/10.1056/NEJMoa2001316$

[9] Heffernan, J. M., Smith, R. J., & Wahl, L. M. (2005). Perspectives on the basic reproductive ratio. Journal of the Royal Society Interface, 2(4), 281e293.

[10] Diekmann O, Heesterbeek H. Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation. New York: Wiley; 2000. doi: 10.1016/j.mbs.2008.02.005 PMID: 18405926

[11] P Van den Driessche and James Watmough. Further notes on the basic reproduction number. In Mathematical epidemiology, pages 159178. Springer, 2008.

[12] Pauline Van den Driessche and James Watmough. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Mathematical biosciences, 180(1-2):2948, 2002.