Int. J. Nonlinear Anal. Appl. 13 (2022) No. 1, 185-195
ISSN: 2008-6822 (electronic)
http://dx.doi.org/10.22075/ijnaa.2022.5470

Mathematical optimization modeling for estimating the incidence of clinical diseases

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(Communicated by Madjid Eshaghi Gordji)

Abstract

The notion that infectious disease transmission and dissemination are governed by rules that may be expressed mathematically is not new. In fact, the nonlinear dynamics of infectious illness transmission were only fully recognized in the twentieth century. However, with the Coronavirus outbreak, there is a lot of discussion and study regarding the origin of the epidemic and how it spreads before all vulnerable people are infected, as well as ideas about how the disease virulence changes during the epidemic. In this paper, we provide some critical mathematical models which are SIR and SIS and their differences in approach for the interpretation and transmission of viruses and other epidemics as well as formulate the optimal control problem with vaccinations.

Keywords: Mathematical Modeling, SIR Model, SIS Model, Epidemiology's threshold theorem, the optimal control problem with vaccinations.

1. Introduction

Since the spread of the Corona (Covid 19) pandemic around the world, we have been following how mathematics has had a daily impact on our entire lives through the decisions that countries have taken to limit the spread of the virus. Such as nationwide closures, and then the imposition of social distancing and mandatory wearing of masks [6, 10]. This is based on some mathematical models designed by scientists from different countries to help understand how the virus spreads, monitor it and thus control it [2, 5]. This pandemic has brought health experts, academic experts and mathematical modeling experts to work together, forming several research teams around the world to win the battle against the virus. Mathematical models have a prominent role in the study of epidemiology and its

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Received: March 2021 *Accepted:* May 2021

conclusions, to obtain quantitative information that contributes to the processes of understanding and managing the outbreak of the epidemic, and to suggest strategies to combat it. It is believed that the first to use mathematical modeling to study the spread of epidemics was the mathematician Daniel Bernoulli, during his study of smallpox in 1760 AD [9, 15]. Mathematical modeling is the application of mathematics to a real-world problem such as how does a population grow? How do viruses and epidemics spread? Or how do we detect diabetes in the blood? Or how long should a traffic light stay yellow? Or what is the waiting time at the intersection of traffic lights and other problems [8, 13]. These problems are solved by turning them into a mathematical problem consisting of a set of mathematical equations with a certain number of variables, which simulate the reality of the problem, and then solving it and testing the results of the solution before generalizing it to verify the mathematical model, and then predicting what can happen in reality [7, 9]. Sometimes the model is improved and modified several times, until the solutions to the math equations match what we already know about the problem. The results of the pandemic simulation for reality depend on the criteria of the model used, some of these criteria are biological and related to the disease, and others are related to demographics. In the case of the Corona pandemic model, the available information about the spread of the Corona virus, for example: the number of infections, the number of cases of recovery, or the confirmed number of deaths due to infection, was used to infer how the virus will spread in the future [6, 9]. Another model focused on flight data to predict which airports are most likely to contribute to the spread of the virus around the world.

Another model was used to find out how social distancing affects the transmission of the virus. One result of the mathematical models is the predicted epidemiological curve, which represents the number of infections that the virus will cause over time. There is no single mathematical model that can answer everything, sometimes we need to develop the model in proportion to the data, and sometimes we need several models to answer the various questions resulting from the problem to be solved, as is the case with the Corona pandemic [9, 10]. It is worth noting that the 40th (General) UNESCO Conference, which was held in November 2019, announced the adoption of March 14 as the International Day of Mathematics, due to the great role it plays in the various aspects of our lives, including meteorology, aviation, medicine and monetary transactions, among others.

2. Mathematical Modeling Fundamentals

In recent years, there has been an increase in the number of articles that use mathematical models, both in high-profile journals and more broadly (Figure 1). This is linked to a better grasp of what models can provide in terms of prediction and insight. A model is a conceptual tool that describes how an item (or a set of things) will behave [2, 6, 9]. A mathematical model use mathematical terminology to create a more detailed and exact representation of the system. In epidemiology, models allow us to extrapolate from one set of circumstances to another or translate between behaviors at multiple scales [7]. Transmission models, as opposed to statistical models, are based on a mechanistic description of infection transmission between two people. This mechanistic explanation allows for the mathematical description of the temporal evolution of an epidemic, connecting the individual level mechanism of transmission with a population level description of infectious disease incidence and prevalence [4, 6]. The precise mathematical formulation of these relationships necessitates a thorough examination of all dynamic mechanisms that contribute to disease transmission. As a result, creating a mathematical model aids in focusing thoughts on the critical processes involved in defining the epidemiology of an infectious illness, as well as revealing the most significant and controllable elements. Mathematical modeling is also integrative in that it brings together information from many

fields such as microbiology, social sciences, and clinical sciences [10, 12].

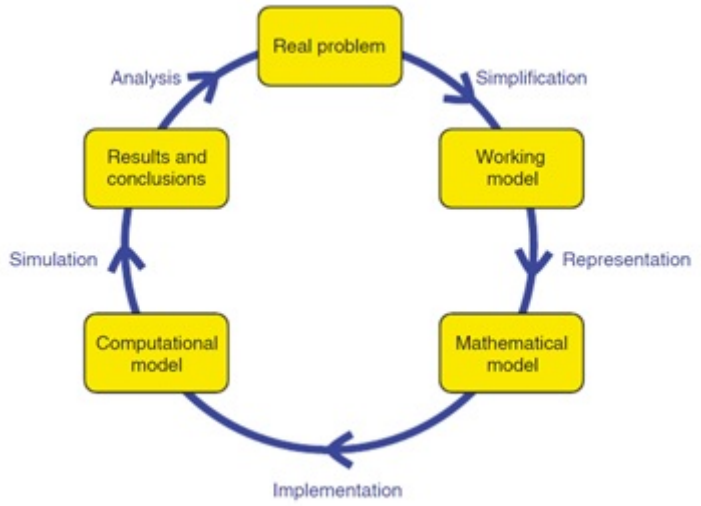

Figure 1: The mathematical modeling method is depicted in a simple diagram.

2.1. What is the point of mathematical modeling in steps?

(i) Infection-related factors have a nonlinear relationship.

9ii A better understanding of the variables that influence the transmission of infectious pathogens.

(iii) It is provide theories that can be tested.

(iv) Extrapolation to different circumstances or periods of time.

3. SIR Model

The SIR model was used in the early 1980s, after the HIV/AIDS outbreak. In fact, its basic idea is simple: There are three groups of people: those who are healthy and susceptible to this disease (S), infected people (I), and people who have recovered (R), (there are Many other models used in epidemiology to model the spread of a particular epidemic are an extension of SIR. Form Including: SEIR and Expanded SEIR, the SEIR model differs from the SIR model in adding the incubation period E [6, 10, 15]. To model the movement of disease spread according to the SIR model, we need three differential equations. As for the parameters: beta, gamma, and new, they are as follows:

$$\begin{aligned}\frac{dS}{dt} &= -\beta\frac{SI}{N} - \sigma S\\ \frac{dI}{dt} &= \beta\frac{\mathrm{SI}}{N} - \gamma I\\ \frac{dR}{dt} &= \gamma I - \sigma S\\ N &= S + I + R\end{aligned}$$

β: represents the rate of transmission of the disease through contact between susceptible individuals, Gama represents the recovery rate from an injury and sigma represents Vaccination rate for those exposed to the disease.

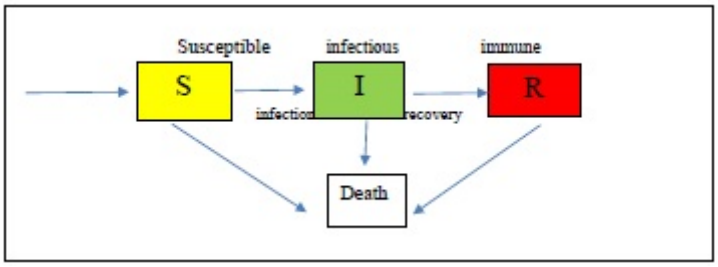

Figure 2: The SIR model in a diagram.

3.1. SIR Model Assumptions

Under the following conditions, this model is appropriate for use:

(i) The number of people is constant.

(ii) When an infection infects a particular group of society, they are the only ones who can leave the group. Furthermore, the only way a person might leave an infected group is if they recover from the disease, at which point they will have gained complete immunity. The risk is not affected by age, gender, marital status, or race.

(iii) There is no such thing as hereditary immunity.

(iv) Any person in the population has the same interaction with everyone else and to the same degree.

Finally, it is the rates of change that characterize our infectious illness model. We can see the SIR curve if we specify the variables and start iterating over Day 1, Day 2, and Day 3 [6, 10, 13].

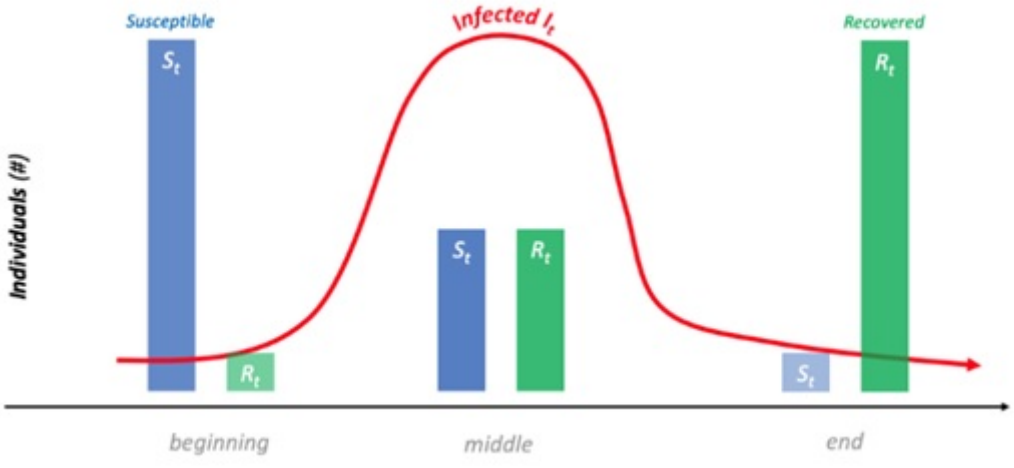

Figure 3: SIR curve if we specify the variables in certain days.

3.2. $\mathbf{R_0}$ *is the infection's basic reproductive rate*

The basic reproductive rate, also known as the basic reproductive number or the basic reproductive ratio, is often indicated as R0. In a fully "susceptible" population, it is the predicted (average) number of secondary cases produced by a typical original instance. R_0 is the mathematical expression for the infection's reproduction rate as follows [3**?** , 5, 6].

$$R_0 = \frac{S_0}{\varepsilon}$$

which leads to

$$R_0 = \frac{\beta S_0}{\alpha}$$

The reproduction rate R_0 is critical for predicting whether or not an epidemic will occur [5, 13].

Theorem 3.1 (Epidemiology's Threshold Theorem). *If* $S_0 \leq \frac{\alpha}{\beta}$*, then I (t) decreases monotonically. If* $S_0 > \frac{\alpha}{\beta}$*, an epidemic begins, in which the number of "infected" rises to a peak before falling to zero over time.*

The following concepts explain to us what this theory implies:

(i) There is no pandemic if $S_0 \leq \varepsilon$, which gives us $R_0 \leq 1$.

(ii) there will be epidemic if $S_0 > \varepsilon$ that is $R_0 > 1$

As a result, ending an epidemic is generally associated with lowering R_0 below 1.

4. SIS Model

SIR models have been introduced. , in which the transitions are from susceptible to infective to eliminate. In fact, there are two cases either by means of complete immunity or diseases -related death [1, 3, 5]. An SIS model, in which infectives revert to the susceptible class after recovery since the illness provides no immunity against reinfection, is another sort of model [6, 8, 15].
Most diseases transmitted by bacterial or helminth agents, as well as most sexually transmitted diseases, may be modelled using these methods as gonorrhea, but not like the diseases that have no cure like AIDS. One significant difference between SIS and SIR models is that the former has a steady stream of fresh victims for recovered infectives . Kermack and McKendrick (1932) created the most basic SIS model as follows:

$$\acute{S} = -\beta SI + \gamma I$$
$$\acute{I} = \beta SI - \gamma I$$

The only difference between this and the SIR model is that instead of passing to the class R, the class S at a rate of I is the situation that happens to the recovered members. Since $(S + I) = 0$, the entire population $S + I$ is a constant. This is known as the constant N; in other cases, population size is measured in K units, resulting in a total population size of one. By substituting N-I for S, we may simplify a single differential equation for the model [9, 13].

$$\acute{I} = \beta I(N - I) - \gamma I = (\beta N - \gamma)I - \beta I^2 = (\beta N - I)I(1 - \frac{I}{N - \frac{\gamma}{\beta}})$$

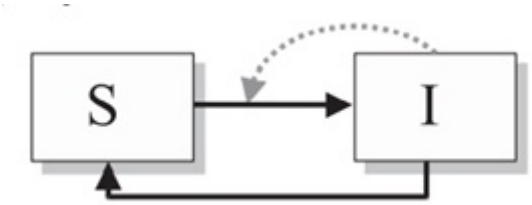

Figure 4: The SIS model in a simple diagram.

Simply put, a pair of coupled ordinary differential equations explain these SIS models:

$$\frac{\mathrm{dS}}{\mathrm{dt}} = \gamma I - \beta IS,$$
$$\frac{\mathrm{dS}}{\mathrm{dt}} = \beta IS - \gamma I.$$

Demography (births and deaths) has been disregarded in this simple example. Despite the dearth of susceptible newborns, the illness can still spread since infectious individuals recover and the vulnerable pool is replenished. As a result, we may simplify above equation by substituting $S = 1 - I$ and simplify to get

$$\frac{dI}{dt} = (\beta - \beta I - \gamma)\, I = \beta I \left(\left(1 - \frac{1}{R_0} \right) - I \right),$$

$R_0 = \frac{\beta}{\gamma}$, as is customary. The logistic equation, which is used to describe density-dependent population increase in ecology, is identical to this equation (Murray 1989). Setting above equation to zero and solving for I^* yields the population's equilibrium number of infectives. As a result,

$$I^* = (1 - \frac{1}{R_0}), \quad \text{and}$$
$$S^* = \frac{1}{R_0},$$

As long as $R_0 > 1$, the equilibrium will stay stable. On the other hand, this type of model has a monotonic convergence to equilibrium and no fluctuating activity. Finally, for an infectious illness that does not provide long-term immunity, loss of immunity will ensure the infection's long-term survival as long as the virus is able to infect the population.

5. Mathematical Modeling in Special Case

We have provided the general framework for a mathematical modeling approach to modeling (SIR, SIS). We shall endeavor to trace the path they both take and the relationship between them according to the aspects of births and deaths and the difference between the two approaches to calculating estimates for this objective.

- The endemic equilibrium in the Births and deaths are included in the SIR model as defined by the proportion of susceptible in the population being the inverse of R_0.
- The endemic equilibrium is stable in the SIR model with births and deaths if $\mathrm{R}_0 > 1$, otherwise the disease-free equilibrium state is stable.

According to the above, susceptible individuals (S) become infected and enter the infected class (I), whereas infected individuals who recover enter the recovered, or immune class (R). Assuming that the birth rate (B) is equal to the death rate (σ), the following results are obtained [13, 15].

$$\frac{\mathrm{dS}}{\mathrm{dt}} = \sigma N - \beta SI - \sigma S$$
$$\frac{\mathrm{dI}}{\mathrm{dt}} = \beta SI - \gamma I - \sigma I$$
$$\frac{\mathrm{dI}}{\mathrm{dt}} = \gamma I - \sigma R$$

Let's say the unit of time we're working with is days.
σN : indicates the number of births per day into the population, assuming that everyone is born susceptible.
βSI : indicates the number of susceptible people who become infected each day.
σS : is the daily number of susceptible (or infected/ immune) people that die.
γI : is the daily number of afflicted people who recover.
We may build a flow diagram illustrating the direction of passage of persons across these compartments using above equations:

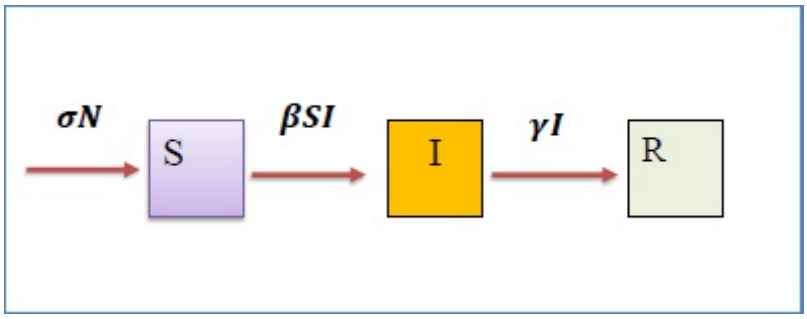

Figure 5: Individuals' passage through these compartments is depicted.

We must solve these equations using numerical integration methods to determine the number of susceptible, infected, and recovered people over time. The important aspect is that we include the vaccination, for that we must change the equations above so that a percentage, say k, of new births entering the population is vaccinated (and thus immune to infection). Those who have been vaccinated will skip the susceptible class and proceed directly to the recovered class, while those who have not been vaccinated will remain in the susceptible class. On the assumption that if K is the proportion of people who have been vaccinated, $(1 - k)$ is the proportion of people who have not been vaccinated. As a result, the number of vaccinated new births (per unit time) is σNk, whereas the number of unvaccinated new births is $\sigma N(1 - k)$. As a result, our equations become:

$$\frac{\mathrm{dS}}{\mathrm{dt}} = \sigma N(1 - k) - \beta SI - \sigma S$$
$$\frac{\mathrm{dI}}{\mathrm{dt}} = \beta SI - \gamma I - \sigma I$$
$$\frac{\mathrm{dI}}{\mathrm{dt}} = \gamma I - \sigma R + \sigma Nk$$

We may change the above model by eliminating the equation for R and transferring the variable αI representing the rate of recovery from infection to the equation for S, as in the SIR model, to

describe a disease in which infective recover with immunity against reinfection and includes births and deaths.. Accordingly, this technique gives this new model

$$\begin{aligned} \acute{S} &= \beta SI + \sigma (H - S) + \alpha I \\ \acute{I} &= \beta SI - \alpha I - \sigma I - \gamma I \end{aligned} \tag{5.1}$$

Assume a population in which the number of births remains constant H per unit time, nm a proportional death rate in each category, infective people who die as a result of infection, and (α) a portion of those who recover without immunity to reinfection. However, if $y > 0$, the overall population fluctuates, with H in this model maximum feasible population size. The model's analysis (6.4) is fairly similar to the SIR model's, with the exception that there is no equation to be eliminated for R. The only change is that in the equation for S, there is an extra component called αI, and none of the qualitative outcomes are affected. We have a fundamental reproduction number, much like in the SIR model.

$$R_0 = \frac{\beta H}{\sigma + \gamma + \alpha} = \frac{H}{S_\infty}$$

If R_0 is less than one, the disease-free equilibrium $S = H, I = 0$ is asymptotically stable, but if R_0 is more than one, an endemic equilibrium (S_∞, I_∞) with $\beta S_\infty = \sigma + \gamma + \alpha$ and I_∞ is asymptotically stable. There are, however, differences that the qualitative analysis does not reveal. We found that when the epidemiological and demographic time scales are significantly dissimilar, the SIR model performs well. The process of approaching endemic equilibrium is similar to a quick and severe epidemic. In the SIS model, something similar happens, especially when there are a lot of disease-related deaths. As a result of the above, we can write a relationship between the two equations for the two models (SIR, SIS)

$$\grave{I} = I [\beta S - (\sigma + \alpha + \gamma)] = \beta I [S - S_\infty]$$

That is epidemic-like behavior is conceivable. If $R_0 < 1$ and S < H, then I is 0, and so $\acute{I} < 0$ is declining. As a result, if $R_0 < 1$, I cannot increase, there will be no pandemic.

6. Formulate The Optimal Control Problem with vaccinations

The parameters calculated using the suggested inverse problem are utilized to formulate both OCPs. In order to find the best vaccine administration control method, a new variable W, which represents the quantity of vaccinations utilized, is introduced, according to previous studies in 2010 and 2014 by (Neilan and Lenhart) and (Biswas et al) respectively. The total number of vaccinations accessible during the whole time period is proportionate to uS for this purpose. Physically, u denotes the proportion of vaccine-eligible people who are immunized per unit of time. It crucial to note that u serves as the system's control variable. However, if $u = zero$, there is no vaccination, and if u equals one, all vulnerable populations have been vaccinated. Figure 2 depicts a schematic representation of illness transmission across people in the SIR model with immunization. The SIR model in the presence of control is stated mathematically as:

$$\frac{\mathrm{dS}}{\mathrm{dt}} = -\beta \frac{\mathrm{SI}}{N} - uS, S(0) = S_0 \tag{6.1}$$

$$\frac{\mathrm{dI}}{\mathrm{dt}} = \beta \frac{\mathrm{SI}}{N} - \gamma I, I(0) = I_0 \tag{6.2}$$

$$\frac{\mathrm{dR}}{\mathrm{dt}} = \gamma I, R(0) = R_0 \tag{6.3}$$

$$\frac{\mathrm{dW}}{\mathrm{dt}} = uS, W(0) = W_0 \tag{6.4}$$

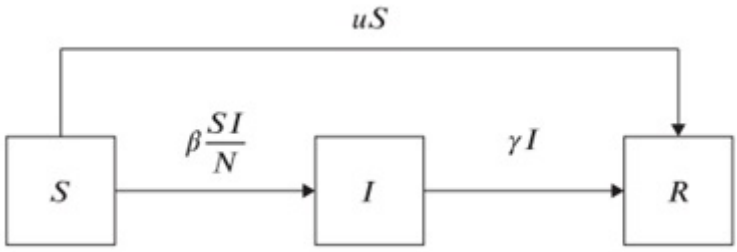

Figure 6: Vaccination compartments in the SIR model.

W_0 is the starting point for the all number of vaccinations. It's crucial to note that the population size (N) after incorporating this additional variable W over time t is expresses as

$$N(t) = S(t) + I(t) + R(t) + W(t)$$

The first formulation tries to find the best vaccine administration (u) to reduce the number of sick people, which is represented by μ_1. As a result, let us

$$\pi_1 \equiv \int_{t_0}^{t_f} \mathrm{I}\ \mathrm{dt} \tag{6.5}$$

The OCP is defined as the following:
Subject to Eqs. (6.1) to (6.4) and $u_{\min} \leq u \leq u_{\max}$, where t_0 and t_f are the start and final times, respectively, and $u_{\min}$ and $u_{\max}$ are the control variable's lower and upper limits, respectively. The second formulation takes into account two goals: determining the best vaccine delivery in order to reduce the number of sick people while also reducing the quantity of vaccinations required [4, 5, 13, 14]. The total number of vaccinations may be calculated using the following formula:

$$\pi_2 \equiv \int_{t_0}^{t_f} \mathrm{u}\ \mathrm{dt} \tag{6.6}$$

Eq.(6.5) gives the number of affected persons. As a result, the multi-objective optimization problem is written as follows:

$$\arg\min(\pi_1, \pi_2) \tag{6.7}$$

Subject to Eqs. (6.1) to (6.4) and $u_{\min} \leq u \leq u_{\max}$. The control variable u must be discretized in both problems. In this instance, transform the original OCP into a nonlinear optimization problem, according to the proposed method. We consider the bang-bang control, which consists of a binary feedback control that turns either "on" or "off" (in our case, when $u = u_{\max} = 1$) or (when $u = u_{\min} = 0$) at various time points defined by system input in order to develop a vaccine delivery control technique that may be employed in medical practice. Because the control variable at the start and finish times is known, and the control technique u is constant by parts, the suggested optimal control problem has N_{elem}-2 unknown parameters in this case. Finally, DE is used to address the nonlinear optimization problems that occur for the mono-objective problem given by Eq. (6.5) and MODE for the multi-objective problem stated by Eq (6.7). As shown in Figures (5,6,7) the difference appears clear that the dynamic general situation of the population in each case, which is according to (susceptible population, infected population and recovered population) respectively with different aspects of control [5, 11, 14].

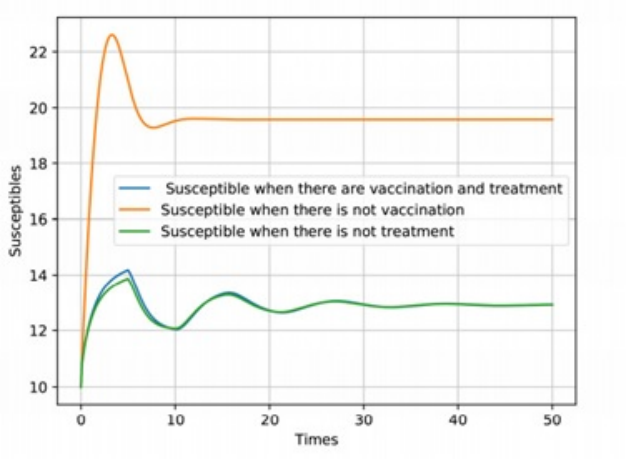

Figure 7: The susceptible population dynamic with many aspects of control.

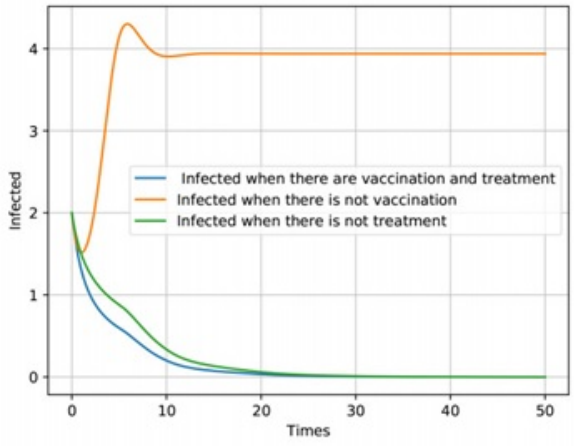

Figure 8: The Infected population dynamic with many aspects of control..

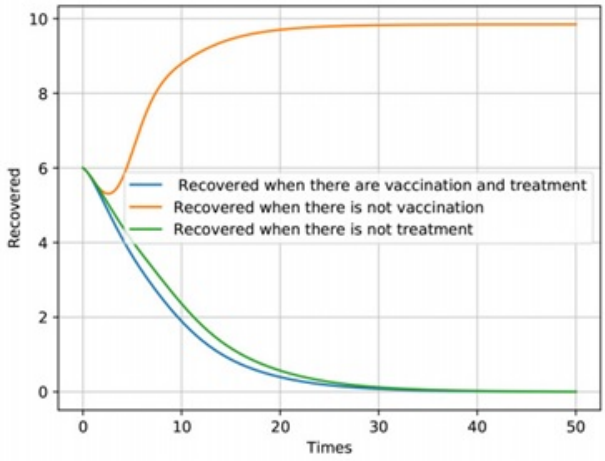

Figure 9: The recovered population dynamic with many aspects of control.

7. Conclusion

The important mathematical models, namely SIR and SIS, and the differences between them in the approach to interpretation and transmission of viruses and other epidemics, were presented. In fact, a bridge has also been established between the two methods and another approach that will enhance the reduction of expected injuries, increase recovery rates and reduce mortality. Finally, formulate the optimal control problem with vaccinations has been described, and a proposal is made for a future study of this approach to improved and tested in order to obtain potentially better and more effective results.

8. Future work

The final model of our work can be optimization according to the ABCs of optimal solution. First of all, we can achieve the best control method in the epidemiological SIR model with a time delay in the condition and control variables. Second, by using a vaccination program to reduce the number of the weak and sick while increasing the number of people who recover. Further, the optimal control and system solution are described by using a discretionary approach based on approximating the difference forward and backward. Finally, we base the result by a numerical simulation that relies on collecting data from a specific population infected with (coronavirus).

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