Modeling and Optimal Control Analysis of COVID-19: Case Studies from Italy and Spain

Akhil Kumar Srivastav* Mini Ghosh †

Division of Mathematics, School of Advanced Sciences

Vellore Institute of Technology, Chennai, India

Xue-Zhi Li‡

College of Mathematics and Information Sciences

Henan Normal University, Xinxiang 453007, China

Liming Cai§

Department of Mathematics

Xinyang Normal University, Xinyang 464000, China

Abstract

Coronavirus disease 2019 (COVID-2019) is a viral disease which is declared as a pandemic by WHO. This disease is posing a global threat, and almost every country in the world is now affected by this disease. Currently, there is no vaccine for this disease and because of this containing COVID-19 is not an easy task. It is noticed that elderly people got severely affected by this disease specially in Europe. In the present paper, we propose and analyze a mathematical model for COVID-19 virus transmission by dividing whole population in old and young groups. We find disease-free equilibrium and the basic reproduction number (R_0). We estimate the parameter corresponding to rate of transmission and rate of detection of COVID-19 using real data from Italy and Spain by least square method. We also perform sensitivity analysis to identify the key parameters which influence the basic reproduction number and hence regulate

*E-mail: akhilkumar.srivastav2016@vitstudent.ac.in
†Corresponding author's E-mail: minighosh@vit.ac.in
‡E-mail: xzli66@126.com
§E-mail: limingcai@amss.ac.cn

the transmission dynamics of COVID-19. Finally, we extend our proposed model to optimal control problem to explore the best cost-effective and time-dependent control strategies that can reduce the number of infectives in a specified interval of time.

Keywords: COVID-19 Model; Basic reproduction number; Sensitivity Analysis; Parameter estimation; optimal control.

1 Introduction

A novel coronavirus (COVID-19) originated from Wuhan, China. Now it has spread to 213 countries worldwide. Up to May 15, 2020, the total number of confirmed cases were 4,525,420 with a death toll of 303,372. Italy and Spain are in the list of top five countries which are severely affected by this disease [1]. The transmission of COVID-19 virus is primarily through droplets of saliva or discharge from the nose of an infected individual while coughing or sneezing. At present there is no vaccines or specific treatments for COVID-19. Trials of vaccines are in progress in different part of the world and it may take few months for a approved vaccine to come into the market. In this situation the best way to prevent and retard the transmission of this disease is to be well informed about the COVID-19 virus, the disease it causes and models of its transmission. The protective measures as per WHO guidelines involve washing hands or using an alcohol based rub frequently and not touching face [2]. As there are large number of asymptomatic cases, maintaining a safe distance while roaming out i.e. physical distancing is another effective measure to reduce the chance of getting infected by this virus.

There are several studies on COVID-19 based on real data [3, 4, 5]. A simple SEIR type mathematical model for the transmission of COVID-19 is proposed and analyzed in [6] where authors estimated the basic reproduction number based on the data from Wuhan, China. A stochastic model combined with data on number of COVID-19 cases in Wuhan, China is studied by Kucharski et al. [7]. Here authors concluded that the there was more than 50% decline in the basic reproduction number (R_0) after the introduction travel control measures. In [8, 9], authors discussed the impact of different scenario of lock-down to study the transmission dynamics of COVID-19 in India. As the correct estimation of asymptomatic cases are not easy, so the predictions did not go well with the current situation of COVID-19 spread in India. As India is comparatively young country so the number of deaths in India is much less compared to many developed nations. Italy and Spain are among the top five worst affected countries in the World. It is observed that most of the deaths took place among elderly people and those who had other existing health issues.

In this paper, we have constructed mathematical model for COVID-2019 taking simple mass action type incidence. Here we formulate our model by keeping in mind that COVID-19 behaves differently with elderly compared to young people. The remaining of this paper is organized as follows: Section 2 describes the model; Section 3 deals with the existence of equilibrium and basic reproduction number; Section 4 deals with data scenario and parameter estimation; Section 5 describes optimal control problem and the simulation results of the optimal control model and finally Section 6 concludes the paper.

2 The Model

The main route of transmission of COVID-19 is human to human [10]. Here we formulate our mathematical model for COVID-19 by divide the total human population $N(t)$ into two groups namely, group of elderly individuals and group of young individuals keeping in mind that major death reported in elderly people. Again we divide these groups into different compartments, namely, Susceptible individuals who are young $S_1(t)$, Exposed individuals who are young $E_1(t)$, Infected individuals who are young $I_1(t)$, Susceptible individuals who are old $S_2(t)$, Exposed individuals who are old $E_2(t)$, Infected individuals who are old $I_2(t)$, Home isolated/hospitalized individuals of both groups who are identified as COVID-positive and under medical supervision $H(t)$, and Recovered individuals $R(t)$. Here we assume that I_1 and I_2 are undetected infectives and rate of transmission due to individuals in these two groups is very high. Here individuals in $H(t)$ are also infectious but as they are under medical supervision so transmission due to individuals in H class is very low. It is assumed that the rates of transmission, rates of reinfection, rates of screening/detection, rates of movement of exposed individuals to infected compartment and disease related deaths in groups of elderly people and young people are different. As elderly people can have some existing health issues, so it is assumed that the rate of transmission in elderly individuals will be more compared to rate of transmission in young individuals. Here the compartments $H(t)$ and $R(t)$ contain both young and elderly individuals. The schematic diagram of our proposed model is shown in Figure 1 and the mathematical model is given as

Table 1: Description of parameters

Parameter		Description
β_1	:	Transmission rate from I_1 or I_2 to S_1,
β_2	:	Transmission rate from I_1 or I_2 to S_2,
β_3	:	Transmission rate from H to S_1,
β_4	:	Transmission rate from H to S_2
δ_1	:	Disease related death rate in I_1 compartment,
δ_2	:	Disease related death rate in I_2 compartment,
δ_3	:	Disease related death rate in H compartment,
ν_1	:	Rate of detection/isolation in I_1 compartment,
ν_2	:	Rate of detection/isolation in I_2 compartment,
η_1	:	Rate of progression of individuals from E_1 to I_1,
η_2	:	Rate of progression of individuals from E_1 to I_1,
γ_1	:	Rate of reinfection in E_1 compartment,
γ_2	:	Rate of reinfection in E_2 compartment,
α	:	Recovery rate of home isolated/hospitalized people.

follows:

$$
\begin{aligned}
\frac{dS_1}{dt} &= -\beta_1 S_1(I_1+I_2) - \beta_3 S_1 H \\
\frac{dE_1}{dt} &= \beta_1 S_1(I_1+I_2) + \beta_3 S_1 H - \gamma_1 E_1(I_1+I_2) - \eta_1 E_1 \\
\frac{dI_1}{dt} &= \eta_1 E_1 + \gamma_1 E_1(I_1+I_2) - \nu_1 I_1 - \delta_1 I_1 \\
\frac{dS_2}{dt} &= -\beta_2 S_2(I_1+I_2) - \beta_4 S_2 H \\
\frac{dE_2}{dt} &= \beta_2 S_2(I_1+I_2) + \beta_4 S_2 H - \gamma_2 E_2(I_1+I_2) - \eta_2 E_2 \\
\frac{dI_2}{dt} &= \eta_2 E_2 + \gamma_2 E_2(I_1+I_2) - \delta_2 I_2 - \nu_2 I_2. \\
\frac{dH}{dt} &= \nu_1 I_1 + \nu_2 I_2 - \delta_3 H - \alpha H. \\
\frac{dR}{dt} &= \alpha H.
\end{aligned} \tag{1}
$$

where $\beta_2 > \beta_1$. Here β_3 and β_4 can be taken equal as these correspond to transmission of COVID-19 from patients under medical supervision. Additionally, we assume that $\nu_2 > \nu_1$ as the rate of detection in elderly people will be more as they will fall sick faster than younger individuals. Here all the parameters are considered positive and its description are given in Table 1.

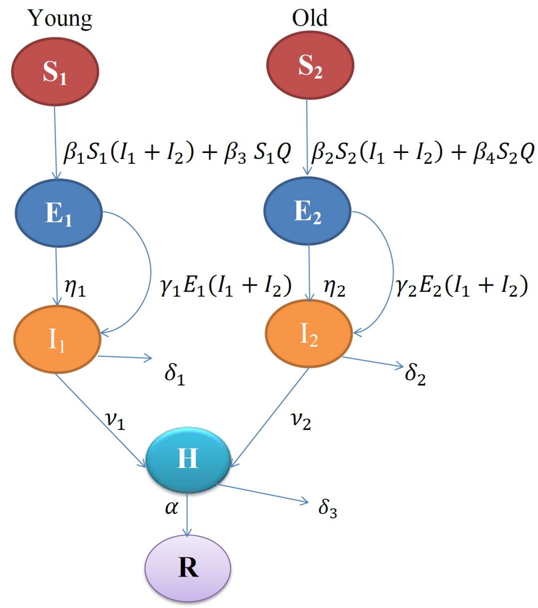


Figure 1: Schematic diagram of the model.

3 Analysis of the model

We consider the system (1) and find the disease-free equilibrium. For our model we have disease-free equilibrium as

$$E_0 = ({S_1}^0, {E_1}^0, {I_1}^0, {S_2}^0, {E_2}^0, {I_1}^0, H^0, R^0) = (N_1^0, 0, 0, N_2^0, 0, 0, 0, 0)$$

.

We find the basic reproduction number R_0 by following the next generation matrix method described in [16]. Following the same notations as in [16], we find the vector $\mathcal{F}$ and $\mathcal{V}$ as follows:

$$\mathcal{F} = \begin{pmatrix} \beta_1 S_1(I_1 + I_2) + \beta_3 S_1 H \\ \beta_2 S_2(I_1 + I_2) + \beta_4 S_2 H \\ 0 \\ 0 \end{pmatrix} \text{ and } \mathcal{V} = \begin{pmatrix} \gamma_1 E_1(I_1 + I_2) + \eta_1 E_1 \\ \gamma_2 E_2(I_1 + I_2) + \eta_2 E_2 \\ -\eta_1 E_1 - \gamma_1 E_1(I_1 + I_2) + \nu_1 I_1 + \delta_1 I_1 \\ -\eta_2 E_2 - \gamma_2 E_2(I_1 + I_2) + \delta_2 I_2 + \nu_2 I_2 \\ -\nu_1 I_1 - \nu_2 I_2 + (\delta_3 + \alpha) H \end{pmatrix},$$

$$\text{F= Jacobian of } \mathcal{F} \text{ at } E_0 = \begin{pmatrix} 0 & 0 & \beta_1 S_1^0 & \beta_1 S_1^0 & \beta_3 S_1^0 \\ 0 & 0 & \beta_2 S_2^0 & \beta_2 S_2^0 & \beta_4 S_2^0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

$$\text{and V=Jacobian of } \mathcal{V} \text{ at } E_0 = \begin{pmatrix} \eta_1 & 0 & 0 & 0 & 0 \\ 0 & \eta_2 & 0 & 0 & 0 \\ -\eta_1 & 0 & (\nu_1+\delta_1) & 0 & 0 \\ 0 & -\eta_2 & 0 & (\nu_2+\delta_2) & 0 \\ 0 & 0 & -\nu_1 & -\nu_2 & (\delta_3+\alpha) \end{pmatrix}$$

and it follows that

$$FV^{-1} = \begin{pmatrix} a_{11} & a_{12} & a_{13} & a_{14} & a_{15} \\ a_{21} & a_{22} & a_{23} & a_{24} & a_{25} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

where

$$a_{11} = \frac{\beta_1 S_1^0}{\nu_1+\delta_1} + \frac{\beta_3 \nu_1 S_1^0}{(\delta_3+\alpha)(\nu_1+\delta_1)}, \quad a_{12} = \frac{\beta_1 S_1^0}{\nu_2+\delta_2} + \frac{\beta_3 \nu_2 S_1^0}{(\delta_3+\alpha)(\nu_2+\delta_2)},$$

$$a_{13} = \frac{\beta_1 S_1^0}{\nu_1+\delta_1} + \frac{\beta_3 \nu_1 S_1^0}{(\delta_3+\alpha)(\nu_1+\delta_1)}, \quad a_{14} = \frac{\beta_1 S_1^0}{\nu_2+\delta_2} + \frac{\beta_3 \nu_2 S_1^0}{(\delta_3+\alpha)(\nu_2+\delta_2)}, \quad a_{15} = \frac{\beta_3 S_1^0}{\alpha+\delta_3},$$

$$a_{21} = \frac{\beta_2 S_2^0}{\nu_1+\delta_1} + \frac{\beta_4 \nu_1 S_2^0}{(\delta_3+\alpha)(\nu_1+\delta_1)}, \quad a_{22} = \frac{\beta_2 S_2^0}{\nu_2+\delta_2} + \frac{\beta_4 \nu_2 S_2^0}{(\delta_3+\alpha)(\nu_2+\delta_2)},$$

$$a_{23} = \frac{\beta_2 S_2^0}{\nu_1+\delta_1} + \frac{\beta_4 \nu_1 S_2^0}{(\delta_3+\alpha)(\nu_1+\delta_1)}, \quad a_{24} = \frac{\beta_2 S_2^0}{\nu_2+\delta_2} + \frac{\beta_4 \nu_2 S_2^0}{(\delta_3+\alpha)(\nu_2+\delta_2)}, \quad a_{25} = \frac{\beta_4 S_2^0}{\alpha+\delta_3}.$$

Three eigenvalues of the above matrix are zero and remaining two are the roots of the following quadratic equation:

$$\lambda^2 - (a_{11}+a_{22})\lambda + a_{11}a_{22} - a_{12}a_{21} = 0,$$

and $a_{11}a_{22} - a_{12}a_{21} = \dfrac{S_1^0 S_2^0}{(\delta_3+\alpha)(\nu_1+\delta_1)(\nu_2+\delta_2)}[(\nu_1-\nu_2)(\beta_2\beta_3-\beta_1\beta_4)]$.

The basic reproduction number (R_0) is the largest positive root of the above quadratic and is computed as follows:

$$R_0 = \frac{R_{01} + \sqrt{R_{01}^2 + 4R_{02}^2}}{2},$$

where

$$R_{01} = \frac{\beta_1 S_1^0}{\nu_1+\delta_1} + \frac{\beta_3 \nu_1 S_1^0}{(\delta_3+\alpha)(\nu_1+\delta_1)} + \frac{\beta_2 S_2^0}{\nu_2+\delta_2} + \frac{\beta_4 S_2^0 \nu_2}{(\delta_3+\alpha)(\nu_2+\delta_2)},$$

$$R_{02} = \sqrt{\frac{S_1^0 S_2^0}{(\delta_3+\alpha)(\nu_1+\delta_1)(\nu_2+\delta_2)}[(\nu_2-\nu_1)(\beta_2\beta_3-\beta_1\beta_4)]}.$$

4 Data Scenario and Parameter Estimation

The total number of cases recorded in Italy as on May 10, 2020 was 219070 and total deaths was 30560. In Spain too the number of cases is increasing day by day.The total number of cases recorded in Spain as on May 10, 2020 was 264663 and total deaths was 26621. The High rate of death from COVID-19 in Italy and Spain may be explained by the country's relatively high proportion of elderly people. Here we assume that 60% of total population is of young age and 40% of total population is elderly. Research has shown that the death rate is very high in elderly [21]. At the beginning of 2020, Italy had an estimated population of 60.3 million and at the end of the first decade of the 21st century, one in five Italians was over 65 years old [17]. And the estimated population of Spain was 46.75 million in 2020 [18]. Keeping in view of these data, we did parameter estimation by least square method using R software [19]. We calibrated our 2019-nCoV model (1) to the active COVID cases for both Italy and Spain. Daily active COVID cases are collected for the period

$$15th February, 2020 - 10th May, 2020$$

from the $https://www.worldometers.info/coronavirus/country/italy/$.[1]. For the Spain daily active COVID cases are collected for the period

$$23rd February, 2020 - 10th May, 2020$$

from the $https://www.worldometers.info/coronavirus/country/spain/$[20].
We fit the model (1) to active cases of COVID in the Italy. We estimate the diseases transmission rates β_1, β_2, and rate of detection of infected individuals ν_1 and ν_2. The other parameter values and the estimated values are listed in Table 2-3 respectively.

The observed active cases and fitted one for Italy and Spain can be seen in Figure 2 and Figure 3 respectively. We also perform sensitivity analysis for the parameters involved in Reproduction number (R_0), which reflects that increase or decrease in these parameter causes increase or decrease in (R_0). The sensitivity of R_0 to different parameters is shown in Figure 4. It is used to discover the parameters that have a high impact on R_0 and should be targeted by intervention strategies. Sensitivity indicess allows to measure the relative change in a variable when parameter changes. For that we use the forward sensitivity index of a variable, with respect to a given parameter, which is defined as the ratio of the relative change in the variable to the relative change

Table 2: Values of parameters

Parameter		value	
β_3	:	0.000513	assumed
β_4	:	0.000672	assumed
γ_1	:	0.14	assumed
η_1	:	0.08	(1-14 days)[11]
η_2	:	0.1	(1-14 days) [11]
γ_2	:	0.2	assumed
δ_1	:	0.013	assumed
δ_2	:	0.014	assumed
δ_3	:	0.015	0.001-0.1 [12]
α	:	0.071	(14-28 days)[13, 14]

Table 3: Values of parameters

Country	Estimated Values	Value of R_0
Italy	$\beta_1 = 0.0028$ $\beta_2 = 0.0086$ $\nu_1 = 0.031$ $\nu_2 = 0.058$	2.644
Spain	$\beta_1 = 0.0024$ $\beta_2 = 0.0085$ $\nu_1 = 0.043$ $\nu_2 = 0.053$	2.137

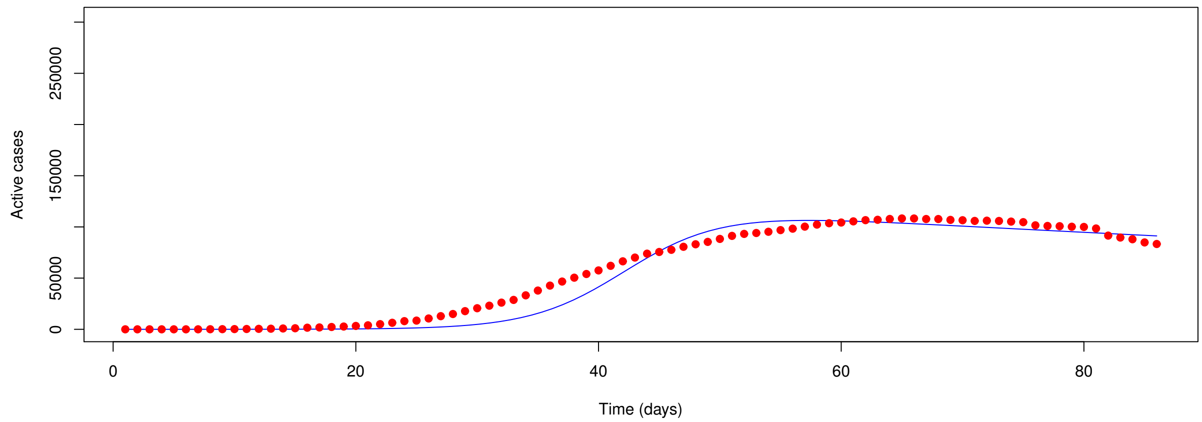


Figure 2: Plots of the output of the fitted model (1) and the observed Corona active cases for Italy. Dotted line shows data points and line showed model solution

in the parameter. If such variable is differentiable with respect to the parameter, then the sensitivity index is defined using partial derivatives, [15]. The normalized forward sensitivity index of R_0, which is differentiable with respect to a given parameter ϵ, is defined by

$$\gamma_{\epsilon}^{R_0} = \frac{\partial R_0}{\partial \epsilon} \frac{\epsilon}{R_0}$$

The above formula can be used to compute the analytical expression for the sensitivity of R_0 to each parameter that it includes. From Figure 4, we can conclude that β_i and ν_i for $i = 1, 2$ are very sensitive parameters as small variation in these parameters can cause large variation in the value of R_0. So correct estimation of these parameters is very important to predict transmission of this disease.

5 The Optimal Control Model

Here the mathematical model (1) is extended to formulate optimal control problem. Generally, control policies depend upon the severity of the epidemic in the area under investigation. It is clear from the sensitivity analysis of our proposed model that the parameters related to transmission of disease i.e. $\beta's$ and screening/detection i.e. $\nu's$ are very important and it can have great impact in reducing the infection prevalence. Keeping this in view, we incorporate optimal control in our proposed model by considering two types of control parameters, namely, $u_1(t)$ and $u_2(t)$. Here the control variable $u_1(t)$ represents the reduction in the transmission between human to human via social distancing, awareness of transmission of disease and sanitization.

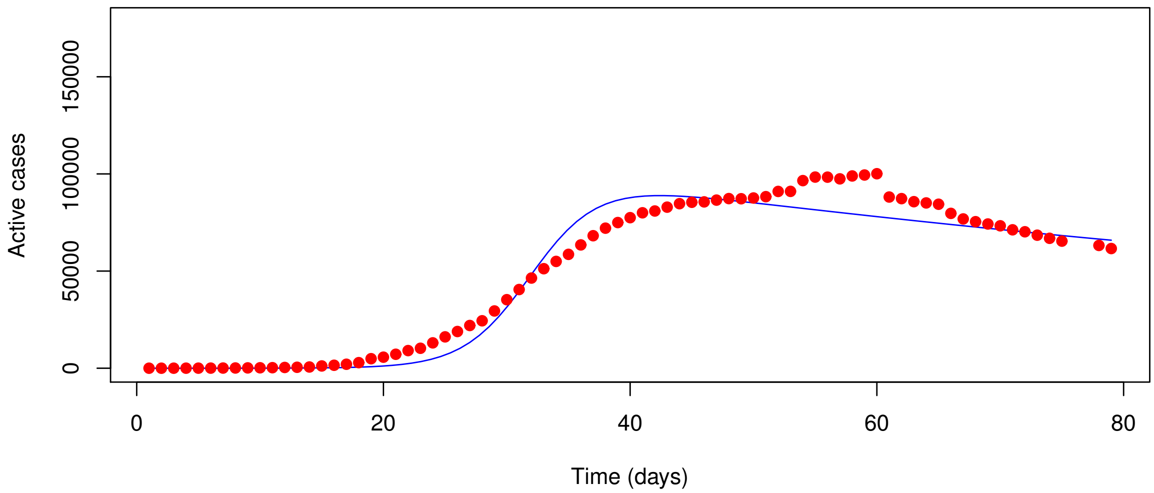


Figure 3: Plots of the output of the fitted model (1) and the observed Corona active cases for Spain. Dotted line shows data points and line showed model solution

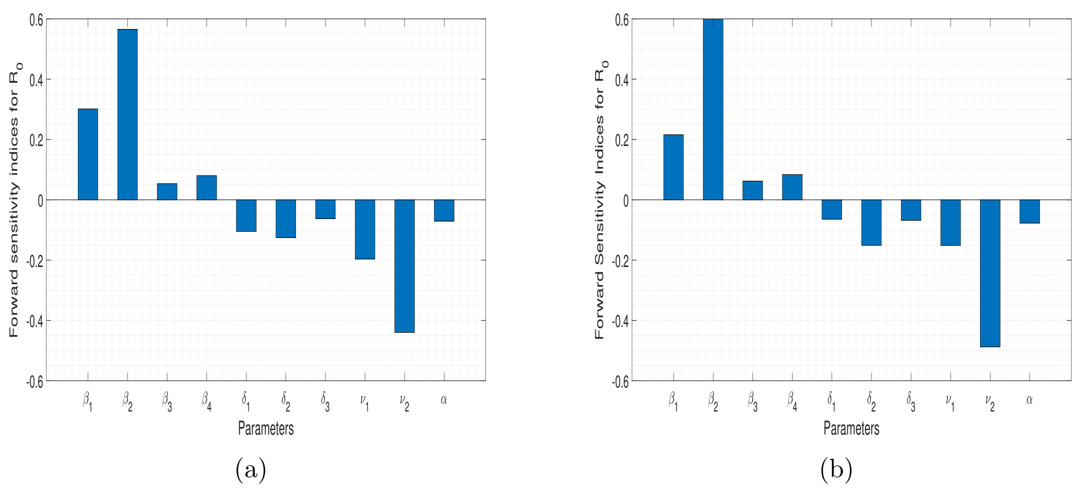


Figure 4: Forward Sensitivity analysis of the parameters on R_0 (a)Italy (b)Spain

The control variable $u_2(t)$ corresponds to the increase in testing facility which can lead to fast detection of Covid-positive cases and we add additional time dependent parameter $a_c u_2(t)$ in rate of detection ν_i for $i = 1, 2$. Keeping in view of the above assumptions, the optimal control model is formulated as follows:

$$\begin{aligned}
\frac{dS_1}{dt} &= -(1-u_1)\beta_1 S_1(I_1+I_2) - \beta_3 S_1 H \\
\frac{dE_1}{dt} &= (1-u_1)\beta_1 S_1(I_1+I_2) + \beta_3 S_1 H - \gamma_1 E_1(I_1+I_2) - \eta_1 E_1 \\
\frac{dI_1}{dt} &= \eta_1 E_1 + \gamma_1 E_1(I_1+I_2) - (\nu_1 + a_c u_2) I_1 - \delta_1 I_1 \\
\frac{dS_2}{dt} &= -(1-u_1)\beta_2 S_2(I_1+I_2) - \beta_4 S_2 H \\
\frac{dE_2}{dt} &= (1-u_1)\beta_2 S_2(I_1+I_2) + \beta_4 S_2 H - \gamma_2 E_2(I_1+I_2) - \eta_2 E_2 \\
\frac{dI_2}{dt} &= \eta_2 E_2 + \gamma_2 E_2(I_1+I_2) - \delta_2 I_2 - (\nu_2 + a_c u_2) I_2. \\
\frac{dH}{dt} &= (\nu_1 + a_c u_2) + (\nu_2 + a_c u_2) I_2 - \delta_3 H - \alpha H. \\
\frac{dR}{dt} &= \alpha H.
\end{aligned} \tag{2}$$

5.1 The Optimal Control Problem

In this section, we study the behavior of the proposed model by using optimal control theory. The objective functional for fixed time t_f is given by:

$$J = \int_0^{t_f} (C_1 I_1 + C_2 I_2 + \frac{1}{2} C_3 {u_1}^2 + \frac{1}{2} C_4 {u_2}^2). \tag{3}$$

Here the parameter $C_1 \geq 0$, $C_2 \geq 0$, $C_3 \geq 0$, $C_4 \geq 0$ and they represent the weight constants. Our objective is to find the control ${u_1}^*$ and ${u_2}^*$, such that

$$J({u_1}^*, {u_2}^*) = \min_{u_1, u_2 \in \Omega} J(u_1, u_2), \tag{4}$$

where Ω is the control set and is defined as
$\Omega = \{u_1, u_2 : \text{measurable and } 0 \leq u_1, u_2 \leq 1\}$ and $t \in [0, t_f]$.
The Lagrangian of this problem is defined as :
$L(I_1, I_2, I_v, u_1, u_2) = C_1 I_1 + C_2 I_2 + \frac{1}{2} C_3 {u_1}^2 + \frac{1}{2} C_4 {u_2}^2$
For our problem, the associated Hamiltonian $\mathcal{H}$ given by :
$\mathcal{H} = L(I_1, I_2, I_v, u_1, u_2) + \lambda_1 \frac{dS_1}{dt} + \lambda_2 \frac{dE_1}{dt} + \lambda_3 \frac{dI_1}{dt} + \lambda_4 \frac{dS_2}{dt} + \lambda_5 \frac{dE_2}{dt} + \lambda_6 \frac{dI_2}{dt} + \lambda_7 \frac{dH}{dt} + \lambda_8 \frac{dR}{dt}$,

where λ_i for $i = 1 \dots 8$ are the adjoint variables. Now adjoint variables in the form of differential equation can be written as follows:

$$\begin{aligned}
\frac{d\lambda_1}{dt} = -\frac{\partial \mathcal{H}}{\partial S_1} &= ((1-u_1)\beta 1(I_1+I_2)+\beta_3 H)(\lambda_1-\lambda_2) \\
\frac{d\lambda_2}{dt} = -\frac{\partial \mathcal{H}}{\partial E_1} &= (\gamma_1)(I_1+I_2)+\eta_1)(\lambda_2-\lambda_3) \\
\frac{d\lambda_3}{dt} = -\frac{\partial \mathcal{H}}{\partial I_1} &= -C_1+(1-u_1)\beta 1 S_1(\lambda_1-\lambda_2)+(1-u_1)\beta 2 S_2(\lambda_4-\lambda_5)+\gamma_1 E_1(\lambda_2-\lambda_3) \\
&\quad +(\nu_1+a_c u_2)(\lambda_3-\lambda_7)+\delta_1\lambda_3 \\
\frac{d\lambda_4}{dt} = -\frac{\partial \mathcal{H}}{\partial S_2} &= ((1-u_1)\beta_2(I_1+I_2)+\beta_4 H)(\lambda_6-\lambda_7) \\
\frac{d\lambda_5}{dt} = -\frac{\partial \mathcal{H}}{\partial E_2} &= (\gamma_2)(I_1+I_2)+\eta_2)(\lambda_5-\lambda_6) \\
\frac{d\lambda_6}{dt} = -\frac{\partial \mathcal{H}}{\partial I_2} &= -C_2+(1-u_1)\beta_1 1 S_1(\lambda_1-\lambda_2)+(1-u_1)\beta_2 S_2(\lambda_4-\lambda_5)+\gamma_1 E_1(\lambda_2-\lambda_3) \\
&\quad +(\nu_1+a_c u_2)(\lambda_6-\lambda_7)+\delta_2\lambda_6 \\
\frac{d\lambda_7}{dt} = -\frac{\partial H}{\partial \mathcal{H}} &= \delta_3\lambda_7+\alpha(\lambda_7-\lambda_8) \\
\frac{d\lambda_8}{dt} = -\frac{\partial \mathcal{H}}{\partial R} &= 0
\end{aligned}$$

Let $\widetilde{S}$, $\widetilde{I}_2$ $\widetilde{R}$, $\widetilde{S_v}$, $\widetilde{I}_v$, be the optimum values of S, I, R, S_v, I_v respectively, and $\widetilde{\lambda}_1$, $\widetilde{\lambda}_2$, $\widetilde{\lambda}_3$, $\widetilde{\lambda}_4$, $\widetilde{\lambda}_5$ be the solution of the above system of differential equations.
By using [22, 23], we state and prove the following theorem:

Theorem 5.1. *There exist optimal controls $u_1{}^*, u_2{}^* \in \Omega$ such that $J(u_1{}^*, u_2{}^*) = \min J(u_1, u_2)$ subject to system (2).*

Proof : To prove this theorem we use [23]. Here all the state variables and the controls are taken as positive. For this minimizing problem, the necessary convexity of the objective functional in (u_1, u_2) is satisfied. The control variable set $u_1, u_2 \in \Omega$ is also convex and closed by the definition. The integrand of the functional
$D_1 I + D_2(S_v + I_v) + \frac{1}{2} D_3 u_1{}^2 + \frac{1}{2} D_4 u_2{}^2$ is convex on the control set Ω and the state variables are bounded.

Since there exist optimal controls for minimizing the functional subject to equations (4), we use Pontryagin's maximum principle to derive the necessary conditions to find the optimal solutions as follows:

If (x, u) is an optimal solution of an optimal control problem, then there exist a non-trivial vector function $\lambda = \lambda_1, \lambda_2, \lambda_3, \ldots\ldots., \lambda_n$ satisfying the following equalities.

$$\frac{dx}{dt} = \frac{\partial \mathcal{H}(t,x,u,\lambda)}{\partial \lambda}$$
$$0 = \frac{\partial \mathcal{H}(t,x,u,\lambda)}{\partial u}$$
$$\frac{d\lambda}{dt} = -\frac{\partial \mathcal{H}(t,x,u,\lambda)}{\partial x}$$

With the help of Pontryagin's maximum principle [23] and theorem (5.1), we proved the following theorem:

Theorem 5.2. *The optimal controls* $({u_1}^*, {u_2}^*)$ *which minimizes* J *over the region* Ω *given by*

$${u_1}^* = min\{1, max(0, \widetilde{u_1})\}$$
$${u_2}^* = min\{1, max(0, \widetilde{u_2})\},$$

where

$$\widetilde{u_1} = \frac{(I_1 + I_2)[\beta_1 S_1(\lambda_2 - \lambda_1) + \beta_2 S_2(\lambda_5 - \lambda_4)]}{C_3}$$
$$\widetilde{u_2} = \frac{a_c I_1(\lambda_3 - \lambda_7) + a_c I_2(\lambda_6 - \lambda_7)}{C_4}$$

Proof: Using optimally condition :

$$\frac{\partial \mathcal{H}}{\partial u_1} = 0, \qquad \frac{\partial \mathcal{H}}{\partial u_2} = 0,$$

we get,

$$\frac{\partial \mathcal{H}}{\partial u_1} = C_3 u_1 + \beta_1 S_1 (I_1 + I_2)(\lambda_1 - \lambda_2) + \beta_2 S_2(\lambda_4 - \lambda_5) = 0.$$

This implies

$$u_1 = \frac{(I_1 + I_2)[\beta_1 S_1(\lambda_2 - \lambda_1) + \beta_2 S_2(\lambda_5 - \lambda_4)]}{C_3} = \widetilde{u_1}$$

And,

$$\frac{\partial \mathcal{H}}{\partial u_2} = u_2 C_4 + a_c I_1(\lambda_7 - \lambda_3) + a_c I_2(\lambda_7 - \lambda_6) = 0$$

gives

$$u_2 = \frac{a_c I_1(\lambda_3 - \lambda_7) + a_c I_2(\lambda_6 - \lambda_7)}{C_4} = \widetilde{u_2}$$

Again upper and lower bounds for these control are 0 and 1 respectively. i.e. $u_1 = u_2 = 0$ if $u_1 < 0$ and $u_2 < 0$, and $u_1 = u_2 = 1$ if $\widetilde{u_1} > 1$ and $\widetilde{u_2} > 1$, otherwise $u_1 = \widetilde{u_1}$ and $u_2 = \widetilde{u_2}$. Hence for these controls ${u_1}^*, {u_2}^*$ we get optimum value of the function J.

6 Numerical Simulation

Here we use MATLAB to simulate our optimal control. All the parameter values are kept same as described in Tables 2-3. The weight constants for the optimal control problem are taken as $C_1 = 1, C_2 = 1, C_3 = 40, C_4 = 60$. We solve the optimality system by iterative method by using forward and backward difference approximations [22]. We consider the final time as 120 days i.e. the time interval as [0,120]. First we solve the state equations by using forward difference approximation method then we solve the adjoint equation by using the backward difference approximation method. We explore different types of control strategies to visualize the impact of optimal control in the total number of infected human.

Strategy I: When only one type of control is used at a time
Here we try to find which type of optimal control is more effective in reducing the infective population. So we apply each type of control one by one. We simulate our model first for Italy and then for Spain.
Italy: In Fig. 5 and 7, the control profiles of different types of optimal control when they are applied alone are shown and corresponding effects on total number of infectives $(I_1 + I_2)$ and home isolated/hospitlized people (H) are shown in Fig. 6(a),8(a) and 6(b),8(b) respectively.
Spain: In Fig. 11 and 13, the control profiles of different types of optimal control when they are applied alone are shown and corresponding effects on total number of infectives $(I_1 + I_2)$ and home isolated/hospitlized people (H) are shown in Fig. 12(a),14(a) and 12(b),14(b) respectively.
From these figures it is clear that the optimal control $u_1(t)$ is little more effective compared to other type of controls but we need to maintain it to 1 for a longer duration which is not easy to achieve. This is the control through social distancing, awareness of transmission of disease and sanitization.

Strategy II: When both controls are used
Here all the control mechanism (u_1, u_2) are used to optimize the objective function J .
Italy: The variation of total infected human and home isolated/hospitlized people (H) with time is shown in Fig 10(a) and 10(b). Here it is observed that there is a reasonable decrease in the total number of infectives when both controls are used simultaneously. Fig. 9(a)(b), show the control profiles of u_1 and u_2 respectively.
Spain: The variation of total infected human and isolated/hospitlized people (H) with time is shown in Fig 16(a) and 16(b). Here it is easy to observe that there is a reasonable decrease in the total number of infectives when both controls are used simultaneously. Fig. 15(a)(b), show the control profiles of u_1 and u_2 respectively.
The simulation result demonstrates the effectiveness of optimal control strategies in reducing the number of infectives. It is observed that combined controls are more useful in reducing the number of infected cases significantly.

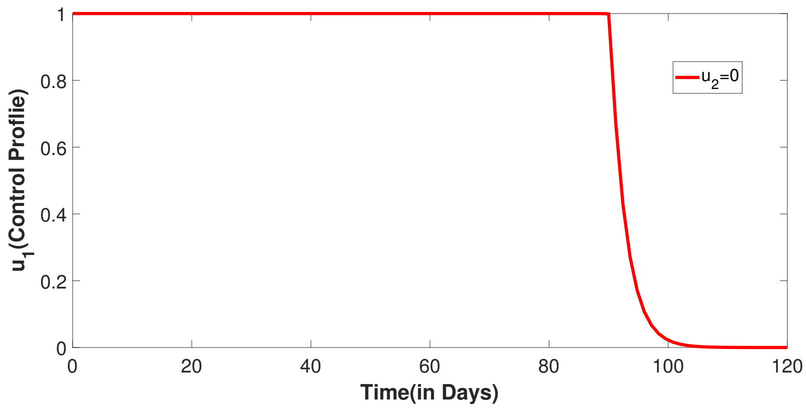
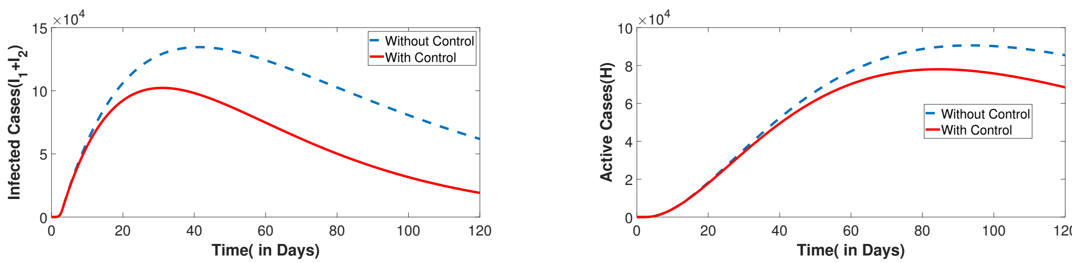


Figure 5: Control Profile (u_1) when $u_2 = 0$



(a) (b)

Figure 6: (a) Plot of $(I_1 + I_2)$ verses time with and without control (b)Plot of H verses time with and without control

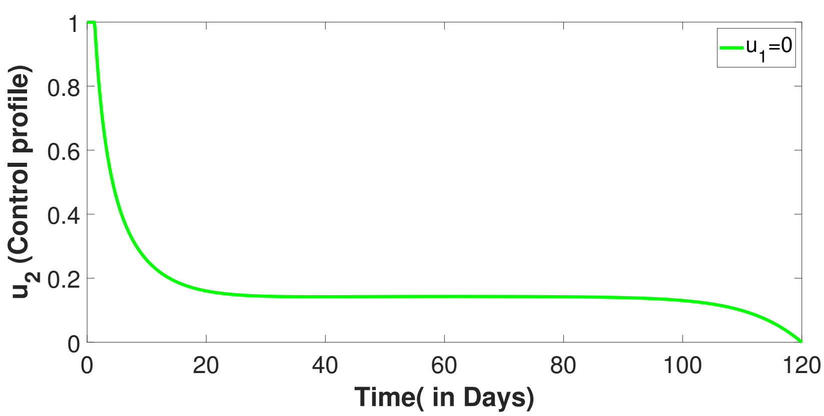
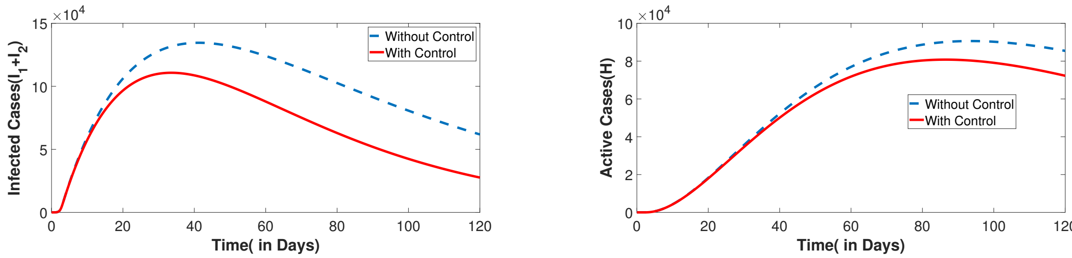
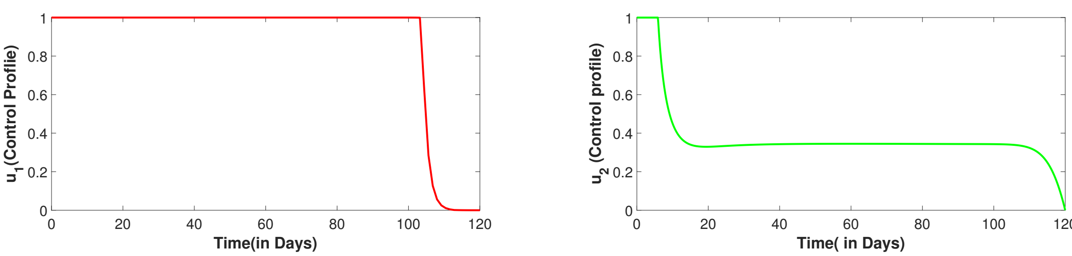


Figure 7: Control Profile (u_2) when $u_1 = 0$



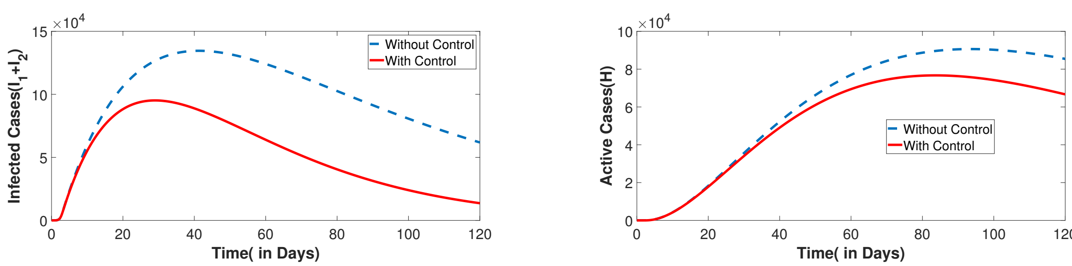
(a) (b)

Figure 8: (a) Plot of (I_1+I_2) verses time with and without control (b) Plot of H verses time with and without control



(a) (b)

Figure 9: (a) Control Profile (u_1) (b) Control Profile (u_2)



(a) (b)

Figure 10: (a) Plot of $(I_1 + I_2)$ verses time with and without control (b) Plot of H verses time with and without control

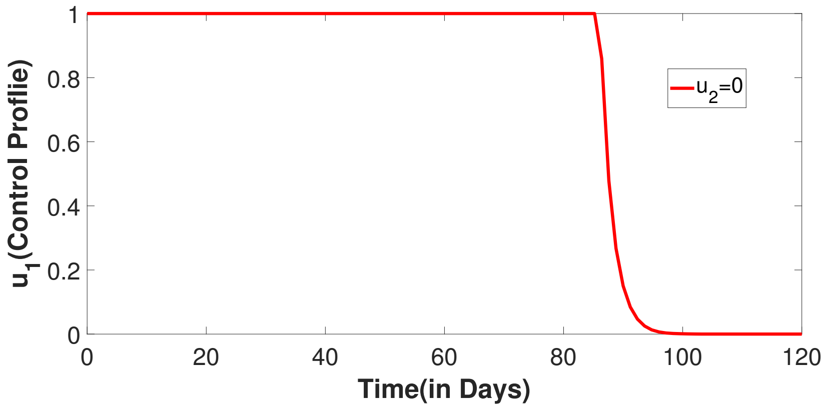
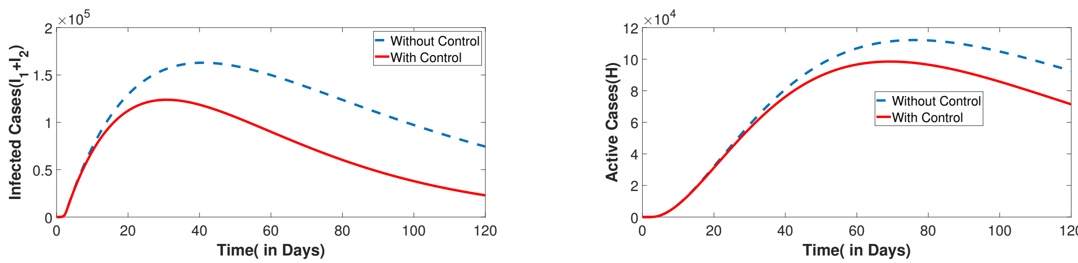


Figure 11: Control Profile (u_1) when $u_2 = 0$



(a)

(b)

Figure 12: (a) Plot of $(I_1 + I_2)$ verses time with and without control (b) Plot of H verses time with and without control

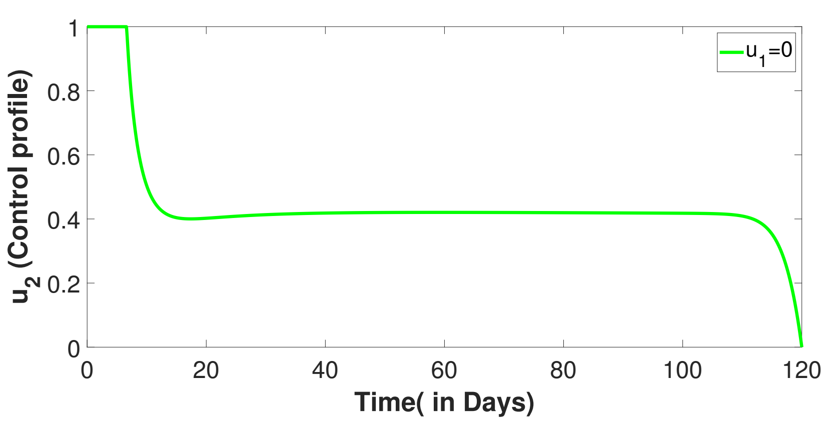
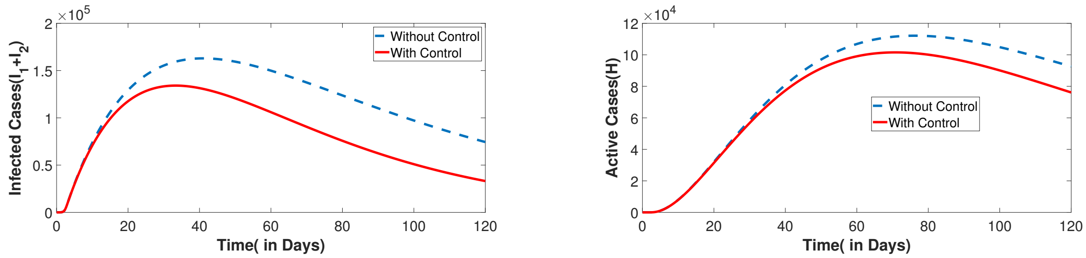
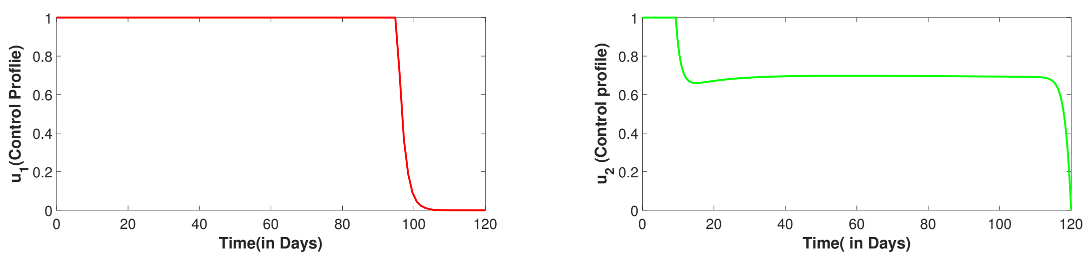


Figure 13: Control Profile (u_2) when $u_1 = 0$



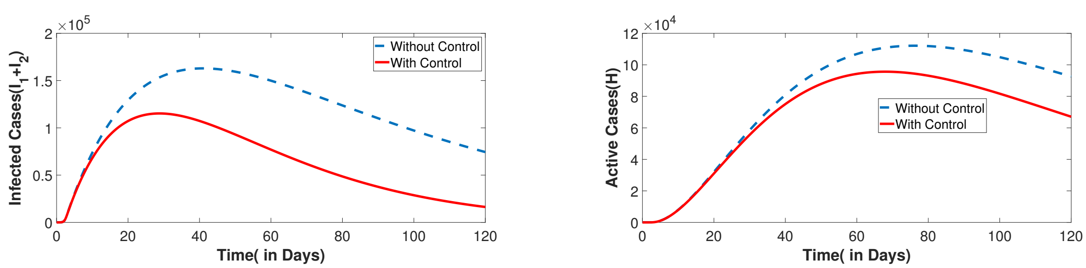
(a) (b)

Figure 14: (a) Plot of $(I_1 + I_2)$ verses time with and without control (b) Plot of H verses time with and without control



(a) (b)

Figure 15: (a) Control Profile (u_1) (b) Control Profile (u_2)



(a) (b)

Figure 16: (a) Plot of $(I_1 + I_2)$ verses time with and without control (b) Plot of H verses time with and without control

7 Conclusion

Here a mathematical model for COVID-19 virus disease is formulated and analyzed.We computed disease-free equilibrium and basic reproduction number R_0. We estimated the key parameters using least square estimation method using real life data fitted with mathematical model for Italy and Spain. Sensitivity analysis is performed to find the key parameters that are very sensitive to basic reproduction number R_0. Further, the proposed model is extended to optimal control problem by incorporating two types of controls. Then Pontryagins maximum principle is used to analyze the optimal control problem. The numerical simulation is explored by considering different combinations of optimal controls. Simulation results indicate that optimal control strategy is in fact effective in reducing the total number of infectives if both the controls are applied simultaneously.

Acknowledgments Mini Ghosh was supported by the research grants of DST, Govt. of India, via a sponsored research project: File No. MSC/2020/000051. Xue-Zhi Li was supported by National Science Foundation, China (Grant No. 11771017).

References

[1] Worldmeters, https://www.worldometers.info/coronavirus/country/italy/

[2] WHO https://www.who.int/health-topics/coronavirus

[3] Hellewell J, Abbott S, Gimma A, Bosse NI, Jarvis CI, Russell TW, Munday JD, Kucharski AJ, Edmunds WJ, Funk S, Eggo RM, Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts,Lancet Glob Health 2020; 8: e48896.

[4] Benvenuto D, Giovanetti M, Vassallo L, Angeletti S, Ciccozzi M, Application of the ARIMA model on the COVID-2019 epidemic dataset,Data in brief,2020; 105340.

[5] Zhanga S, Diaob M-Y, Yuc w, Peic L, Lind Z, Chena D, Estimation of the reproductive number of novel coronavirus (COVID-19) and the probable outbreak size on the Diamond Princess cruise ship: A data-driven analysis, International Journal of Infectious Diseases.2020; 201204.

[6] Lina Q, Zhaob S, Gaod D, Loue Y, Yangf S, Musae SS, Wangb MH, Caig Y, Wangg W, Yangh L, Hee D,A conceptual model for the coronavirus disease 2019 (COVID-19) outbreak in Wuhan, China with individual reaction and governmental action,International Journal of Infectious Diseases. 2020; 211-216.

[7] Kucharski AJ, Russell TW, Diamond C, Liu Y, Edmunds J, Funk S, Eggo RM, Early dynamics of transmission and control of COVID-19: a mathematical modelling study, Lancet Infect Dis. 2020;5(20),553-558;DOI:https://doi.org/10.1016/S1473-3099(20)30144-4

[8] Singh R, Adhikari R, Age-structured impact of social distancing on the COVID-19 epidemic in India, arXiv preprint arXiv:2003.12055, 2020.

[9] Sardar T, Nadim Sk-S, Chattopadhyay J, Assessment of 21 Days Lockdown Ect in Some States and Overall India: A Predictive Mathematical Study on COVID-19 Outbreak, arXiv preprint arXiv: 2004.03487, 2020.

[10] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao y, Gao H,Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B, Clinical features of patients infected with 2019 novel coronavirus in Wuhan,China.Lancet2020; Available from:https://doi.org/10.1016/S0140-6736(20)30183-5. [Accessed 24 January 2020].

[11] https://www.who.int/news-room/q-a-detail/q-a-coronaviruses

[12] Ferguson NM, Laydon D, Gilani GN, Imai N,Ainslie K, Baguelin M, Bhatia S, Boonyasiri a, Cucunub Z, Dannenburg GC, Dighe A, Dorigatti I, Fu H, Gaythorpe K, Green W, Hamlet A, Hinsley W, Okell LC, Elsland SV, Thompson H, Verity R, Volz E, Wang H, Wang Y, Walker P-GT, Walters C, Winskill P, Whittaker C, Donnelly CA, Riley s, Ghani AC. .Report 9: Impact of non-pharmaceutical interventions (NPIs) to reduce COVID19 mortality and healthcare demand.2020

[13] Tang B, Bragazzi NL, Li Q, Tang S, Xiao Y, Wu J, An updated estimation of the risk of transmission of the novel coronavirus (2019-nCov). Infectious Disease Modelling,2020; 5, 248255.

[14] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, Cao B. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study, The Lancet;2020; 395(10229).

[15] Chitnis N, Hyman JM, Cushing JM, Determining important parameters in the spread of malaria through the sensitivity analysis of a mathematical model. Bull. Math. Biol.,2008; 70(5):12721296.

[16] Driessche PV, Watmough J. Reproduction numbers and subthreshold endemic equilibria for compartmental models of disease transmission, Math Biosci,2002; 180:2948

[17] EUROSTAT. "Ageing characterises the demographic perspectives of the European societies - Issue number 72/2008" (PDF). Archived from the original (PDF) on 2 January 2009. Retrieved 28 April 2009.

[18] World Population Review, https://worldpopulationreview.com/countries/spain-population/

[19] White LF, Pagano M, A likelihoodbased method for realtime estimation of the serial interval and reproductive number of an epidemic. Stat. Med. 2008, 27, 29993016.

[20] https://www.worldometers.info/coronavirus/country/spain/

[21] https://www.worldometers.info/coronavirus/coronavirus-age-sex-demographics/

[22] Lenhart S, Workman JT, Optimal Control Applied to Biological Models, CRC Press, 2007.

[23] Pontryagin LS, Boltyanskii VG, Gamkrelidze RV, Mishchenko EF, The Mathematical Theory of Optimal Processes, Interscience Publishers, 1962.