Hindawi Computational and Mathematical Methods Volume 2022, Article ID 5780719, 16 pages https://doi.org/10.1155/2022/5780719



Research Article

Deterministic and Stochastic Dynamics of COVID-19: The Case Study of Italy and Spain

Akhil Kumar Srivastav , Nico Stollenwerk, and Maíra Aguiar , and Maíra Aguiar

Correspondence should be addressed to Akhil Kumar Srivastav; asrivastav@bcamath.org

Received 15 September 2021; Accepted 5 December 2021; Published 13 February 2022

Academic Editor: Kuo Shou Chiu

Copyright © 2022 Akhil Kumar Srivastav et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

In December 2019, a severe respiratory syndrome (COVID-19) caused by a new coronavirus (SARS-CoV-2) was identified in China and spread rapidly around the globe. COVID-19 was declared a pandemic by the World Health Organization (WHO) in March 2020. With eventually substantial global underestimation, more than 225 million cases were confirmed by the end of August 2021, counting more than 4.5 million deaths. COVID-19 symptoms range from mild (or no symptoms) to severe illness, with disease severity and death occurring according to a hierarchy of risks, with age and preexisting health conditions enhancing the risks of disease severity manifestation. In this paper, a mathematical model for COVID-19 transmission is proposed and analyzed. The model stratifies the studied population into two groups, older and younger. Applied to the COVID-19 outbreaks in Spain and in Italy, we find the disease-free equilibrium and the basic reproduction number for each case study. A sensitivity analysis to identify the key parameters which influence the basic reproduction number, and hence regulate the transmission dynamics of COVID-19, is also performed. Finally, the model is extended to its stochastic counterpart to encapsulate the variation or uncertainty found in the transmissibility of the disease. We observe the variability of the infectious population finding its distribution at a given time, demonstrating that for small populations, stochasticity will play an important role.

1. Introduction

The coronavirus pandemic and its emerging variants are currently a major global public health threat. Globalisation has speeded up the spread of infections over a short period of time. This has an impact on the public healthcare system and is also detrimental to the economic development of many countries. Since the outbreaks began, more than 215 million cases were confirmed by mid of August 2021, with more than 4 million deaths [1].

COVID-19 symptoms can range from mild (or no symptoms) to severe illness, with disease severity and death occurring according to a hierarchy of risks, with age and pre-existing health conditions enhancing risks of disease severity [2]. Vaccines against COVID-19 have been developed in record time and are now globally distributed [3–8]. The

analysis of the impact of different vaccine administration is ongoing, mostly using previous research experiences applied to other infectious diseases [9–17] and will be discussed in detail in our forthcoming publications [18, 19].

As an example of the impact of the pandemic in Europe, Spain has reported, up to date, more than 4.7 million cases with around 83 thousand deaths [20], while in Italy, although the total number of cases are similar, 4.5 million, a higher mortality rate was reported, counting more than 128 thousand deaths [21]. It is important to notice that mortality is higher in older than younger individuals in all populations [22, 23].

As the COVID-19 pandemic progressed, research on mathematical modeling became imperative and very influential to understand the epidemiological dynamics of disease spreading. Task forces were created to assist public health

¹Basque Center for Applied Mathematics, BCAM, Bilbao, Spain

²Dipartimento di Matematica, Universita degli Studi di Trento, Italy

³Ikerbasque, Basque Foundation for Science, Bilbao, Spain

managers and governments, with many research papers being recently published. Applied to the outbreaks in the Basque Country, Spain, a flexible framework was developed within the so-called COVID-19 Basque Modeling Task Force (BMTF). As an extension of the basic SHAR (Susceptible-Hospitalized-Asymptomatic-Recovered) model, the SHARUCD models were parameterized and validated with epidemiological data continuously collected and provided by the Basque Health Department and the Basque Health Service (Osakidetza) and have been used (up until now) to monitor COVID-19 spreading and control over the course of the pandemic [18, 19, 24–28]. Modeling refinements and results on the evolution of the epidemic in the Basque Country are regularly updated and publicly available on the "SHARUCD Dashboard" [29].

Over the course of the pandemic, a broad spectrum of research has been produced, e.g., statistical work using two common approaches, the SIR model and a log-linear model, analyzing the available empirical data and estimating the reproduction values for Spain and Italy countries [30]. Deterministic and stochastic models were developed [31, 32] to study the effects of facial masks and hospitalization of symptomatic people and asymptomatic quarantine of people on the prevalence of the coronavirus outbreak in India [31] and the transmission dynamics of the COVID-19 in Wuhan, China [32]. And still, many questions remain to be investigated.

In this paper, we present a mathematical model to describe COVID-19 dynamics in Spain and Italy. The population is divided into two groups, young and old. Considering simple mass action type incidence, the model is formulated by assuming that the course COVID-19 infection leads to a different outcome for the elderly population as compared to the younger population. This paper is organized as follows. Section 2 describes the model formulation, followed by the model analysis in Section 3, showing the existence of equilibrium and basic reproduction number. Section 4 presents the results for the sensitivity analysis for the parameters involved in reproduction number. Section 5 describes impact of different parameter on COVID-19 prevalence. Section 6 presents the stochastic modeling approach, and in Section 7, the simulation results are shown. Finally, in Section 8, we conclude this work, with a discussion on both modeling approaches.

2. The Model

This model is a refinement of the model proposed by Srivastav et al. [33]. A new parameter ε is introduced to differentiate the infectivity of young infected individuals (I_1) with respect to the baseline infectivity of elderly individuals $I_2(t)$ in a population of N individuals.

The value of ε can be tuned to reflect different situations: a value of $\varepsilon > 1$ reflects the fact that young individuals, which are likely to develop mild disease and higher mobility, have larger infectivity, than elderly individuals, which are at higher risk of developing severe disease and are more likely to be detected and isolated [24]. On the other hand, $\varepsilon < 1$ indicates that young individuals have smaller infectivity than

elderly individuals, and that could be justified due to lower or higher viral load during the infection, which is correlated with disease symptoms. Here, the assumption relies on the epidemiological observation of young population developing mild or no symptoms with lower viral load, affecting disease transmissibility, versus severe disease and higher viral load, mostly observed in older ages.

The total human population N(t) is divided into eight compartments, stratified into two age classes, namely, young and old: susceptible $S_1(t)$ and $S_2(t)$, exposed $E_1(t)$ and $E_2(t)$, and infected $I_1(t)$ and $I_2(t)$ for the young and for the old, respectively. Two extra classes to accommodate individuals from both age groups are also considered: quarantined/hospitalized H(t) for those identified as COVID-19-positive case with symptoms and needing medical assistance and finally the recovered individual class R(t).

We assume that the transitions/movements, from one disease related class to another, are different between the elderly and the young individuals. However, the H(t) class includes both groups. For the mathematical modeling framework development, we make the following assumptions:

- (1) Total population N is constant
- (2) The susceptible young individuals S_1 become exposed to the infection and join the young exposed class E_1 on effective contacts with infectious human population I_1, I_2 and H at rates β_1 and β_3 , respectively, with $\beta_3 < \beta_1$
- (3) Exposed people E_1 will move to I_1 with rate of η_1 . If young exposed people E_1 will get contact with I_1, I_2 unknowingly, then exposed people E_1 will move fast into I_1 class with rate γ_1
- (4) The susceptible old individuals S_2 become exposed to the infection and join the old exposed class E_2 on effective contacts with infectious human population I_1, I_2 and (H) at the rates β_2 and β_4 , respectively, with $\beta_4 < \beta_2$
- (5) Exposed people E_2 will move to I_2 with rate of η_2 ; if old exposed people E_2 will get contact with I_1, I_2 unknowingly, then exposed people E_2 will move fast in I_2 with rate γ_2
- (6) Infected, young I_1 and old I_2 , will move to hospitalized class (H) with rates v_1 and v_2 , respectively
- (7) Hospitalized people (H) will get recovered from COVID-19 and join recovered class (R) with rate α

The schematic diagram of our proposed model is shown in Figure 1, and the mathematical model is given as follows:

$$\frac{dS_1}{dt} = -\beta_1 S_1 (\varepsilon I_1 + I_2) - \beta_3 S_1 H,\tag{1}$$

$$\frac{dE_1}{dt} = \beta_1 S_1(\varepsilon I_1 + I_2) + \beta_3 S_1 H - \gamma_1 E_1(\varepsilon I_1 + I_2) - \eta_1 E_1, \quad (2)$$

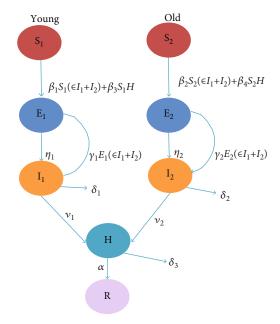


FIGURE 1: Schematic diagram of the model.

$$\frac{dI_1}{dt} = \eta_1 E_1 + \gamma_1 E_1 (\varepsilon I_1 + I_2) - \nu_1 I_1 - \delta_1 I_1, \tag{3}$$

$$\frac{dS_2}{dt} = -\beta_2 S_2 (\varepsilon I_1 + I_2) - \beta_4 S_2 H, \tag{4}$$

$$\frac{dE_{2}}{dt} = \beta_{2}S_{2}(\varepsilon I_{1} + I_{2}) + \beta_{4}S_{2}H - \gamma_{2}E_{2}(\varepsilon I_{1} + I_{2}) - \eta_{2}E_{2}, \quad (5)$$

$$\frac{dI_2}{dt} = \eta_2 E_2 + \gamma_2 E_2 (\varepsilon I_1 + I_2) - \delta_2 I_2 - \nu_2 I_2, \tag{6}$$

$$\frac{dH}{dt} = v_1 I_1 + v_2 I_2 - \delta_3 H - \alpha H,\tag{7}$$

$$\frac{dR}{dt} = \alpha H. \tag{8}$$

Here, all the parameters are positive and the description of these parameters is given in Table 1. Parameter values given in Tables 2 and 3 are already defined in [33].

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

$$E_{0} = \left(S_{1}^{\ 0}, E_{1}^{\ 0}, I_{1}^{\ 0}, S_{2}^{\ 0}, E_{2}^{\ 0}, I_{1}^{\ 0}, H^{0}, R^{0}\right) = \left(N_{1}^{0}, 0, 0, N_{2}^{0}, 0, 0, 0, 0\right). \tag{9}$$

We find the basic reproduction number R_0 by following the next-generation matrix method described in [38]. Following the same notations as in [38], we find the vector \mathscr{F}

Table 1: Description of parameters.

Parameter	Description
β_1	Transmission rate from I_1 or I_2 to S_1
eta_2	Transmission rate from I_1 or I_2 to S_2
eta_3	Transmission rate from H to S_1
eta_4	Transmission rate from H to S_2
ε	Modification parameter
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/quarantine in \mathcal{I}_1 compartment
ν_2	Rate of detection/quarantine in \mathcal{I}_2 compartment
η_1	Rate of progression of individuals from ${\cal E}_1$ to ${\cal I}_1$
η_2	Rate of progression of individuals from ${\cal E}_1$ to ${\cal I}_1$
γ_1	Rate of reinfection in E_1 compartment
γ_2	Rate of reinfection in E_2 compartment
α	Recovery rate of quarantine/hospitalized people

and $\mathcal V$ as follows:

$$\mathcal{F} = \begin{pmatrix} \beta_{1}S_{1}(\varepsilon I_{1} + I_{2}) + \beta_{3}S_{1}H \\ \beta_{2}S_{2}(\varepsilon I_{1} + I_{2}) + \beta_{4}S_{2}H \\ 0 \\ 0 \\ 0 \end{pmatrix},$$

$$(10)$$

$$\mathcal{V} = \begin{pmatrix} \gamma_{1}E_{1}(\varepsilon I_{1} + I_{2}) + \eta_{1}E_{1} \\ \gamma_{2}E_{2}(\varepsilon I_{1} + I_{2}) + \eta_{2}E_{2} \\ -\eta_{1}E_{1} - \gamma_{1}E_{1}(\varepsilon I_{1} + I_{2}) + \nu_{1}I_{1} + \delta_{1}I_{1} \\ -\eta_{2}E_{2} - \gamma_{2}E_{2}(\varepsilon I_{1} + I_{2}) + \delta_{2}I_{2} + \nu_{2}I_{2} \\ -\nu_{1}I_{1} - \nu_{2}I_{2} + (\delta_{3} + \alpha)Q \end{pmatrix}.$$

F =Jacobian of \mathcal{F} at

Table 2: Values of parameters.

Parameter	Value	
β_3	0.000513 assumed	
eta_4	0.000672 assumed	
γ_1	0.14 assumed	
η_1	0.08 (1-14 days) [34]	
η_2	0.1 (1-14 days) [34]	
γ_2	0.2 assumed	
δ_1	0.013 assumed	
δ_2	0.014 assumed	
δ_3	0.015 0.001-0.1 [35]	
α	0.071 (14-28 days) [36, 37]	

Table 3: Values of parameters.

Country	Estimated values	Value of R_0	
	$\beta_1 = 0.0028$		
T. 1	$\beta_2 = 0.0086$	2 6 4 4	
Italy	$v_1 = 0.031$	2.644	
	$v_2 = 0.058$		
	$\beta_1 = 0.0024$		
Consider	$\beta_2 = 0.0085$	2.137	
Spain	$v_1 = 0.043$		
	$v_2 = 0.053$		

and $V = \text{Jacobian of } \mathcal{V}$ at

$$E_{0} = \begin{pmatrix} \eta_{1} & 0 & 0 & 0 & 0 \\ 0 & \eta_{2} & 0 & 0 & 0 \\ -\eta_{1} & 0 & (\nu_{1} + \delta_{1}) & 0 & 0 \\ 0 & -\eta_{2} & 0 & (\nu_{2} + \delta_{2}) & 0 \\ 0 & 0 & -\nu_{1} & -\nu_{2} & (\delta_{3} + \alpha) \end{pmatrix}.$$
(12)

And it follows that

where

$$a_{11} = \frac{\beta_{1} \varepsilon S_{1}^{0}}{\nu_{1} + \delta_{1}} + \frac{\beta_{3} \nu_{1} S_{1}^{0}}{(\delta_{3} + \alpha)(\nu_{1} + \delta_{1})},$$

$$a_{12} = \frac{\beta_{1} S_{1}^{0}}{\nu_{2} + \delta_{2}} + \frac{\beta_{3} \nu_{2} S_{1}^{0}}{(\delta_{3} + \alpha)(\nu_{2} + \delta_{2})},$$

$$a_{13} = \frac{\beta_{1} \varepsilon S_{1}^{0}}{\nu_{1} + \delta_{1}} + \frac{\beta_{3} \nu_{1} S_{1}^{0}}{(\delta_{3} + \alpha)(\nu_{1} + \delta_{1})},$$

$$a_{14} = \frac{\beta_{1} S_{1}^{0}}{\nu_{2} + \delta_{2}} + \frac{\beta_{3} \nu_{2} S_{1}^{0}}{(\delta_{3} + \alpha)(\nu_{2} + \delta_{2})},$$

$$a_{15} = \frac{\beta_{3} S_{1}^{0}}{\alpha + \delta_{3}},$$

$$a_{21} = \frac{\beta_{2} \varepsilon S_{2}^{0}}{\nu_{1} + \delta_{1}} + \frac{\beta_{4} \nu_{1} S_{2}^{0}}{(\delta_{3} + \alpha)(\nu_{1} + \delta_{1})},$$

$$a_{22} = \frac{\beta_{2} \varepsilon S_{2}^{0}}{\nu_{2} + \delta_{2}} + \frac{\beta_{4} \nu_{2} S_{2}^{0}}{(\delta_{3} + \alpha)(\nu_{1} + \delta_{1})},$$

$$a_{23} = \frac{\beta_{2} \varepsilon S_{2}^{0}}{\nu_{1} + \delta_{1}} + \frac{\beta_{4} \nu_{1} S_{2}^{0}}{(\delta_{3} + \alpha)(\nu_{1} + \delta_{1})},$$

$$a_{24} = \frac{\beta_{2} S_{2}^{0}}{\nu_{2} + \delta_{2}} + \frac{\beta_{4} \nu_{2} S_{2}^{0}}{(\delta_{3} + \alpha)(\nu_{2} + \delta_{2})},$$

$$a_{25} = \frac{\beta_{4} S_{2}^{0}}{\alpha + \delta_{3}}.$$

Three eigenvalues of the above matrix are zero and the remaining two are the roots of the following quadratic equa-

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

$$a_{11}a_{22} - a_{12}a_{21} = \frac{S_{1}^{0}S_{2}^{0}}{(\delta_{3} + \alpha)(\nu_{1} + \delta_{1})(\nu_{2} + \delta_{2})} [(\varepsilon\nu_{2} - \nu_{1})(\beta_{1}\beta_{4} - \beta_{2}\beta_{3})].$$
(15)

So the basic reproduction number (R_0) is the positive root of the above quadratic and is given by

$$R_0 = \frac{R_{01} + \sqrt{R_{01}^2 + 4R_{02}^2}}{2},\tag{16}$$

where

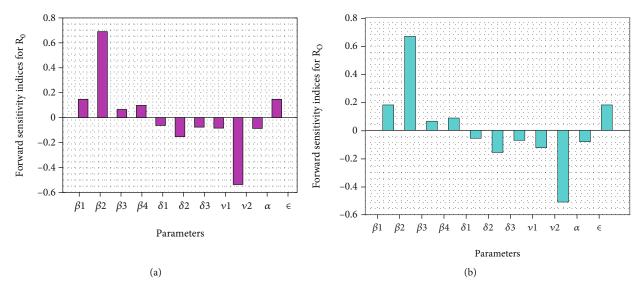


Figure 2: Forward sensitivity analysis of the parameters on R_0 in (a) Italy and in (b) Spain.

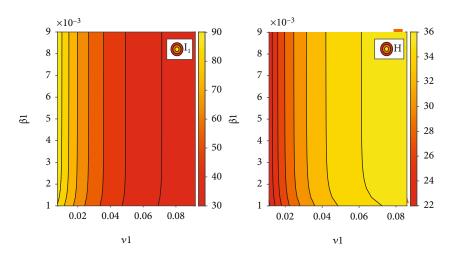


FIGURE 3: Contour plots representing the effects of v_1 and β_1 on I_1 (first column) and H (second column) for Italy.

4. Sensitivity Analysis

We also perform a sensitivity analysis for the parameters involved in reproduction number (R_0) , which reflects that the increase or decrease in these parameter values will lead to the increase or decrease of (R_0) . The sensitivity of R_0 to different parameters is shown in Figure 2. This analysis is performed to evaluate which parameters have the highest impact on R_0 and hence being targeted as the most effective intervention measures for each case study. The sensitivity indices allow 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 in the parameter. If the variable is varying with respect to a parameter, then the sensitivity index is defined using partial derivatives [39]. The normalized forward sensitivity index of R_0 , which is differentiable with respect to a given parameter p, is defined by

$$\gamma_p^{R_0} = \frac{\partial R_0}{\partial p} \frac{p}{R_0}.$$
 (18)

The above formula can be used to compute the analytical expression for the sensitivity of R_0 to each parameter included in the system. From Figure 2, we can conclude that β_i , ν_i for i=1,2 and p, for both case study, Italy and Spain, are very sensitive parameters, with small changes in these parameters leading to a significant change in the value of R_0 .

5. Impact of Different Parameters on Prevalence of COVID-19

From Figures 3 and 4, we observe that the increase of transmission rate β_1 , from infected young and old individuals to

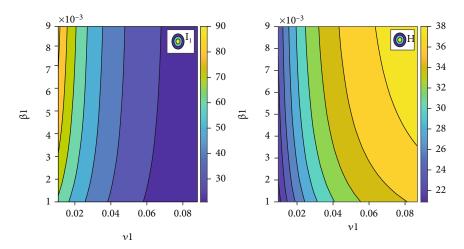


Figure 4: Contour plots representing the effects of v_1 and β_1 on I_1 (first column) and H (second column) for Spain.

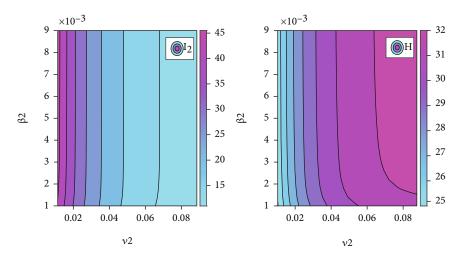


Figure 5: Contour plots representing the effects of v_1 and β_1 on I_1 (first column) and H (second column) for Italy.

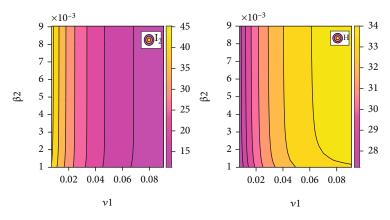


FIGURE 6: Contour plots representing the effects of v_1 and β_1 on I_1 (first column) and H (second column) for Spain.

susceptible young individuals, leads to an increment of the infected young individuals in Italy and in Spain. However, the increase of ν_1 , the detection rate of infected young indi-

viduals, will decrease the number of infections in the young human population class, but increasing the number of hospitalizations overall. Similarly as described above, Figures 5

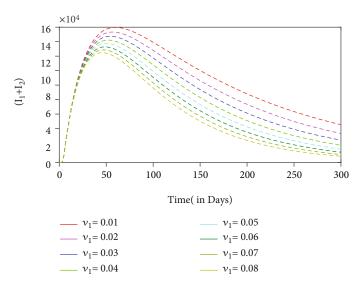


Figure 7: Variation of $(I_1 + I_2)$ with time for different values of v_1 .

and 6 show that the infections in old populations I_2 will increase as β_2 , the transmission rate from infected young and old individuals to susceptible old individuals, increases. Nevertheless, the increase of ν_2 , the detection rate of infected old individuals, will decrease the number of infections in the old population, but also increasing the overall hospitalizations.

From these figures, we can conclude that controlling the transmission between human to human and increasing the detection rates, providing better treatment for the infected hospitalized people, will be of a major importance to control the epidemics in Italy and in Spain, with a significant decrease of number of infections in the population.

Finally, Figure 7 shows the effect of the variation of the parameter v_1 on the number of infections. As v_1 increases, the overall infected population decreases. Note that variations of the parameter v_2 show similar effects on the number of overall infections.

6. Stochastic Model

As all natural systems are prone to stochastic perturbations, we extended our deterministic model, equation system (1), to the corresponding stochastic model. The derivation of the stochastic model and its analysis are important when populations are small and hence with the dynamics being severely affected by small changes in the parameter values. Thus, for the initial phase of the disease outbreak, such as COVID-19, the stochastic model setup is the most appropriate modeling approach to be used for a local epidemiological evaluation.

The derivation of a stochastic differential equation (SDE) model is a diffusion approximation from the underlying state discrete Markov process [26, 40–44]. Let $X(t) = (X_1(t), X_2(t), X_3(t), X_4(t), X_5(t), X_6(t), X_7(t), X_8(t))^T$ be a continuous random variable for $(S_1(t), E_1(t), I_1(t), S_2(t), E_2(t), I_2(t), H(t), R(t))^T$, where T denotes the transpose of the matrix. Further, let $\Delta X = X(t + t)$

 Δt) – $X(t) = (\Delta X_1, \Delta X_2, \Delta X_3, \Delta X_4, \Delta X_5(t), \Delta X_6(t), \Delta X_7(t), \Delta X_8(t))^T$ denote the random vector for the change in the random variables during time interval Δt . Here, we will write the transition maps which define all possible changes between states in the SDE model. Based on our deterministic model, see equation system (1), we see that there exist 19 possible changes between states in a small time interval Δt (see Table 4). Here, it is emphasized that the one and only possible change is in the time Δt . For example, let us consider the case when one uninfected individual becomes infected by coronavirus. This will be given by the state change ΔX , denoted by $\Delta X = (-1, 1, 0, 0, 0, 0, 0, 0)$, and the change in its probability is given by

$$\begin{split} &\operatorname{prob}(\Delta X_{1}, \Delta X_{2}, \Delta X_{3}, \Delta X_{4}, \Delta X_{5}, \Delta X_{6}, \Delta X_{7}, \Delta X_{8}(t)) \\ &= (-1, 1, 0, 0, 0, 0, 0, 0) | (X_{1}, X_{2}, X_{3}, X_{4}, X_{5}, X_{6}, X_{7}, X_{8}) \\ &= P_{1} = \beta X_{1} X_{2} \Delta t + O(t). \end{split} \tag{19}$$

One can easily determine the expectation change $E(\Delta X)$ and its covariance matrix $V(\Delta X)$ associated with ΔX by neglecting the higher order terms $O(\Delta t)$. The expectation of ΔX is given by

$$E(\Delta X) = \sum_{i=1}^{20} P_i(\Delta X)_i \Delta t = \begin{pmatrix} -\beta_1 X_1(\varepsilon X_3 + X_6) - \beta_3 X_1 X_7 \\ \beta_1 X_1(\varepsilon X_3 + X_6) + \beta_3 X_1 X_7 - \gamma_1 X_1(\varepsilon X_3 + I_6) - \eta_1 X_2 \\ \eta_1 X_2 + \gamma_1 X_1(\varepsilon X_3 + I_6) - (\nu_1 + \delta_1) X_3 \\ -\beta_2 X_4(\varepsilon X_3 + X_6) - \beta_4 X_4 X_7 \\ \beta_2 X_4(\varepsilon X_3 + X_6) + \beta_4 X_1 X_7 - \gamma_2 X_5(\varepsilon X_3 + X_6) - \eta_2 X_5 \\ \eta_2 X_5 + \gamma_2 X_5(\varepsilon X_3 + X_6) - (\nu_2 + \delta_2) X_6 \\ \nu_1 X_3 + \nu_2 X_6 - \delta_3 X_7 - \alpha X_7 \\ \alpha X_7 \end{pmatrix} \Delta t$$

$$= f(X_1, X_2, X_3, X_4, X_5, X_6, X_7, X_8) \Delta t. \tag{20}$$

Table 4: Possible changes of states and their probabilities.

Possible state change	Probability of state change
$\overline{\left(\Delta X\right)_{1} = \left(-1, 1, 0, 0, 0, 0, 0, 0\right)^{T}}$	$P_1 = \beta_1 \varepsilon X_1 X_3 \Delta t + O(\Delta t)$
Change when people meet young infective $\left(I_{1}\right)$ and then population becomes exposed	$F_1 = p_1 \varepsilon X_1 X_3 \Delta \iota + O(\Delta \iota)$
$(\Delta X)_2 = (-1, 1, 0, 0, 0, 0, 0, 0)^T$	$P_2 = \beta_1 X_1 X_6 \Delta t + O(\Delta t)$
Change when people meet old infective $\left(I_{2}\right)$ and then population becomes exposed	$F_2 = p_1 \Lambda_1 \Lambda_6 \Delta t + O(\Delta t)$
$(\Delta X)_2 = (-1, 1, 0, 0, 0, 0, 0, 0, 0)^T$	$P_3 = \beta_3 X_1 X_7 \Delta t + O(\Delta t)$
Change when people meet hospitalized (H) and then population becomes exposed	$I_3 - p_3 x_1 x_7 \Delta t + O(\Delta t)$
$(\Delta X)_4 = (0, -1, 1, 0, 0, 0, 0, 0)^T$	
Change when young exposed with mild symptoms meet young infective (I_1) and then population becomes infected	$P_4 = \gamma_1 \varepsilon X_2 X_3 \Delta t + O(\Delta t)$
$(\Delta X)_5 = (0, -1, 1, 0, 0, 0, 0, 0)^T$	$P_5 = \gamma_1 X_2 X_6 \Delta t + O(\Delta t)$
Change when young exposed with mild symptoms meet old infective (I_2) and then population becomes infected	75 7111211621 (21)
$(\Delta X)_6 = (0, -1, 1, 0, 0, 0, 0, 0)^T$	$P_6 = \eta_1 X_2 \Delta t + O(\Delta t)$
Change when young exposed people move to young infected class $\left(I_{1}\right)$	16 7/12/20 (20)
$(\Delta X)_7 = (0, 0, -1, 0, 0, 0, 0, 1, 0)^T$	$P_7 = v_1 X_3 \Delta t + O(\Delta t)$
Change when young infective join hospitalized class	1) 111321 (21)
$(\Delta X)_8 = (0, 0, -1, 0, 0, 0, 0, 0)^T$	$P_8 = \delta_1 X_3 \Delta t + O(\Delta t)$
Disease-related death rate of young infected population (I_1)	
$(\Delta X)_9 = (0, 0, 0, -1, 1, 0, 0, 0)^T$	$P_9 = \beta_2 \varepsilon X_4 X_3 \Delta t + O(\Delta t)$
Change when old people meet young infective $\left(I_{1}\right)$ and then population becomes exposed	$\Gamma_9 - \rho_2 \epsilon \Lambda_4 \Lambda_3 \Delta \iota + O(\Delta \iota)$
$(\Delta X)_{10} = (0, 0, 0, -1, 1, 0, 0, 0)^T$	$P_{10} = \beta_2 X_4 X_6 \Delta t + O(\Delta t)$
Change when old people meet old infective $\left(I_{2}\right)$ and then population becomes exposed	
$(\Delta X)_{11} = (0, 0, 0, -1, 1, 0, 0, 0)^T$	$P_{11} = \beta_4 X_4 X_7 \Delta t + O(\Delta t)$
Change when old susceptible meet hospitalized (H) and then population becomes exposed	
$(\Delta X)_{12} = (0, 0, 0, 0, -1, 1, 0, 0)^T$	$P_{12} = \gamma_2 \varepsilon X_5 X_3 \Delta t + O(\Delta t)$
Change when old exposed with mild symptoms meet young infective (I_1) and then population becomes infected	12 72 5 5 (. /
$(\Delta X)_{13} = (0, 0, 0, 0, -1, 1, 0, 0)^T$	$P_{13} = \gamma_1 X_5 X_6 \Delta t + O(\Delta t)$
Change when old exposed with mild symptoms meet old infective $\left(I_{2}\right)$ and then population becomes infected	13 11 3 6
$(\Delta X)_{14} = (0, 0, 0, 0, -1, 1, 0, 0)^T$	$P_{14} = \eta_2 X_2 \Delta t + O(\Delta t)$
Change when young exposed people move to young infected class (I_1)	14 1/2 2
$(\Delta X)_{15} = (0, 0, 0, 0, 0, -1, 0, 0)^T$	$P_{15} = \delta_2 X_3 \Delta t + O(\Delta t)$
Disease-related death rate of young infected population (I_2)	115 0211321 (21)
$(\Delta X)_{16} = (0, 0, 0, 0, 0, 0, -1, 1, 0)^T$	$P_{16} = v_2 X_6 \Delta t + O(\Delta t)$
Change when old infective join hospitalized class (H)	$r_{16} = v_2 n_6 \Delta t + O(\Delta t)$
$(\Delta X)_{17} = (0, 0, 0, 0, 0, 0, -1, 1)^T$	$P_{17} = \alpha X_7 \Delta t + O(\Delta t)$
Change when hospitalized people (H) join recover class	
$(\Delta X)_{18} = (0, 0, 0, 0, 0, -1, 0)^T$	$D = \hat{X} Y \Lambda_{t} + O(\Lambda_{t})$
Disease-related death rate of hospitalized population $\left(I_{2}\right)$	$P_{18} = \delta_3 X_3 \Delta t + O(\Delta t)$
$(\Delta X)_{19} = (0, 0, 0, 0, 0, 0, 0, 0, 0)^T$	$P_{19} = 1 - \sum_{i=1}^{18} \Delta t + O(\Delta t)$
No change	<u>i=1</u>

Note that the expectation vector and the function f are in the same form as those in deterministic system (1). With the covariance matrix $V(\Delta X) = E((\Delta X)(\Delta X)^T) - E(\Delta X)E((\Delta X)^T)$ and $E(\Delta X)E((\Delta X)^T) = f(X)(f(X)^T)$, it can be approximated by $\Omega \times \Delta t$ by neglecting the term of $(\Delta t)^2$ such that

$$\begin{split} E\Big((\Delta X)(\Delta X)^T\Big) &= \sum_{i=1}^{19} P_i\Big((\Delta X)_i(\Delta X)_i^T\Big) \Delta t \\ &= \begin{pmatrix} V_{11} & V_{12} & 0 & 0 & 0 & 0 & 0 & 0 \\ V_{21} & V_{22} & V_{23} & 0 & 0 & 0 & 0 & 0 \\ 0 & V_{32} & V_{33} & 0 & 0 & 0 & V_{37} & 0 \\ 0 & 0 & 0 & V_{44} & V_{45} & 0 & 0 & 0 \\ 0 & 0 & 0 & V_{54} & V_{55} & V_{56} & 0 & 0 \\ 0 & 0 & 0 & 0 & V_{65} & V_{66} & V_{67} & 0 \\ 0 & 0 & V_{73} & 0 & 0 & V_{76} & V_{77} & V_{78} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & V_{87} & V_{88} \end{pmatrix} \cdot \Delta t \\ &= \Omega \cdot \Delta t, \end{split}$$

where

$$\begin{split} V_{11} &= P_1 + P_2 + P_3 = \beta_1(\varepsilon X_1 X_3 + X_1 X_6) + \beta_3 X_1 X_7, \\ V_{12} &= V_{21} = -P_1 - P_2 - P_3 = -\beta_1(\varepsilon X_1 X_3 + X_1 X_6) - \beta_3 X_1 X_7, \\ V_{22} &= P_1 + P_2 + P_3 + P_4 + P_5 + P_6 \\ &= \beta_1(\varepsilon X_1 X_3 + X_1 X_6) + \beta_3 X_1 X_7 + \gamma_1(\varepsilon X_1 X_3 + X_1 X_6) + \eta_1 X_2, \\ V_{23} &= V_{32} = -P_4 - P_5 - P_6 = -\gamma_1(\varepsilon X_1 X_3 + X_1 X_6) - \eta_1 X_2, \\ V_{33} &= P_4 + P_5 + P_6 + P_7 + P_8 = \gamma_1(\varepsilon X_1 X_3 + X_1 X_6) + \eta_1 X_2 + \nu_1 X_3 + \delta_1 X_3, \\ V_{37} &= V_{73} = -P_7 = -\nu_1 X_3, \\ V_{44} &= P_{10} + P_{11} + P_9 = \beta_2 X_4 X_6 + \beta_4 X_4 X_7 + \beta_2 \varepsilon X_4 X_7, \\ V_{45} &= V_{54} = -P_{10} - P_{11} - P_9 = -\beta_2 X_4 X_6 - \beta_4 X_4 X_7 - \beta_2 \varepsilon X_4 X_7, \\ V_{55} &= P_{10} + P_{11} + P_{13} + P_{12} + P_{14} = \beta_2 X_4 X_6 + \beta_4 X_4 X_7 + \gamma_1 X_5 X_6 + \gamma_1 \varepsilon X_5 X_3 + \eta_2 X_2, \\ V_{56} &= V_{65} = -P_{12} - P_{13} - P_{14} = -\gamma_1 \varepsilon X_5 X_3 - \gamma_1 X_5 X_6 - \eta_2 X_2, \\ V_{66} &= P_{12} + P_{13} + P_{14} + P_{15} + P_{16} = \gamma_1 \varepsilon X_5 X_3 + \gamma_1 X_5 X_6 + \eta_2 X_2 + \delta_2 X_3 + \nu_2 X_6, \\ V_{67} &= V_{76} = -P_{16} = -\nu_2 X_6, \\ V_{77} &= P_{16} + P_{17} + P_{18} + P_7 = \nu_2 X_6 + \alpha X_7 + \delta_3 X_3 + \nu_1 X_3, \\ V_{78} &= V_{87} = -P_{17} = \alpha X_7, V_{88} = P_{17} = \alpha X_7. \end{split}$$

The diffusion matrix Ω is symmetric and positive definite.

Using the approach of [26, 41, 44], we construct a matrix M such that $\Omega = MM^T$, where M is an 8×10 matrix given as

where

$$\begin{split} M_1^1 &= \sqrt{P_1 + P_2 + P_3}, \\ M_2^1 &= -\sqrt{P_1 + P_2 + P_3}, \\ M_2^2 &= \sqrt{P_4 + P_5 + P_6}, \\ M_2^3 &= -\sqrt{P_4 + P_5 + P_6}, \\ M_3^3 &= \sqrt{P_7}, \\ M_3^4 &= \sqrt{P_8}, \\ M_4^5 &= \sqrt{P_9 + P_{10} + P_{11}}, \\ M_5^5 &= -\sqrt{P_9 + P_{10} + P_{11}}, \\ M_5^6 &= \sqrt{P_{12} + P_{13} + P_{14}}, \\ M_6^6 &= -\sqrt{P_{12} + P_{13} + P_{14}}, \\ M_6^7 &= \sqrt{P_{15}}, \\ M_7^7 &= -\sqrt{P_7}, \\ M_7^7 &= -\sqrt{P_{16}}, \\ M_7^9 &= -\sqrt{P_{16}}, \\ M_7^9 &= -\sqrt{P_{17}}, \\ M_8^{10} &= -\sqrt{P_{17}}. \\ M_8^{10} &= -\sqrt{P_{17}}. \end{split}$$

Then, the $It\widehat{o}$ stochastic differential equation system has the form

$$d(X(t)) = f(X_1, X_2, X_3, X_4, X_5, X_6, X_7)dt + M \cdot dW(t),$$
(25)

with initial condition

$$X(0) = (X_1(0), X_2(0), X_3(0), X_4(0), X_5(0), X_6(0), X_7(0))^T,$$
(26)

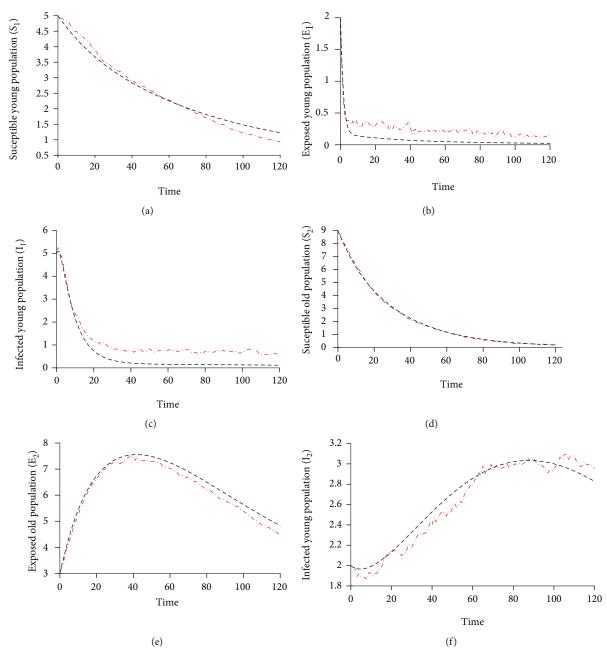


FIGURE 8: Continued.

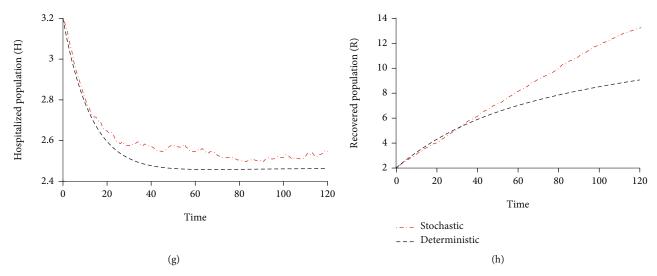


FIGURE 8: Time evolution of (a) S_1 , (b) E_1 , (c) I_1 , (d) S_2 , (e) E_2 , (f) I_2 , (g) H, and (h) R for deterministic and stochastic systems (Italy).

and a Wiener process

$$W(t) = (W_1(t), W_2(t), W_3(t), W_4(t), W_5(t), W_6(t), W_7(t), W_8(t), W_9(t), W_{10}(t))^T.$$

$$(27)$$

In view of the above facts, we construct the stochastic differential equation model as

$$dS_{1} = (-\beta_{1}S_{1}(\varepsilon I_{1} + I_{2}) - \beta_{3}S_{1}H)dt + \sqrt{\beta_{1}S_{1}(\varepsilon I_{1} + I_{2}) + \beta_{3}S_{1}H}dW_{1},$$
(28)

$$\begin{split} dE_1 &= [\beta_1 S_1(\varepsilon I_1 + I_2) + \beta_3 S_1 H - \gamma_1 E_1(\varepsilon I_1 + I_2) - \eta_1 E_1] dt \\ &- \sqrt{\beta_1 S_1(\varepsilon I_1 + I_2) + \beta_3 S_1 H} dW_1 + \sqrt{\gamma_1 E_1(\varepsilon I_1 + I_2) + \eta_1 E_1} dW_2, \end{split}$$
 (29)

$$\begin{split} dI_1 &= \left[\eta_1 E_1 + \gamma_1 E_1 (\varepsilon I_1 + I_2) - \nu_1 I_1 - \delta_1 I_1 \right] dt \\ &- \sqrt{\gamma_1 E_1 (\varepsilon I_1 + I_2)} + \eta_1 E_1 dW_2 + \sqrt{\nu_1 I_1} dW_3 + \sqrt{\delta_1 I_1} dW_4, \end{split} \tag{30}$$

$$dS_{2} = (-\beta_{2}S_{2}(\varepsilon I_{1} + I_{2}) - \beta_{4}S_{2}H)dt + \sqrt{\beta_{2}S_{2}(\varepsilon I_{1} + I_{2}) + \beta_{4}S_{2}H}dW_{5},$$
(31)

$$\begin{split} dE_2 &= \left[\beta_2 S_2(\varepsilon I_1 + I_2) + \beta_4 S_2 H - \gamma_2 E_2(\varepsilon I_1 + I_2) - \eta_2 E_2\right] dt \\ &- \sqrt{\beta_2 S_2(\varepsilon I_1 + I_2)} + \beta_4 S_2 H dW_5 + \sqrt{\gamma_2 E_2(\varepsilon I_1 + I_2) + \eta_2 E_2} dW_6, \end{split} \tag{32}$$

$$\begin{split} dI_2 &= \left[\eta_2 E_2 + \gamma_2 E_2 (\varepsilon I_1 + I_2) - \nu_2 I_2 - \delta_2 I_2 \right] dt \\ &- \sqrt{\gamma_2 E_2 (\varepsilon I_1 + I_2) + \eta_2 E_2} dW_6 + \sqrt{\nu_2 I_2} dW_7 + \sqrt{\delta_2 I_2} dW_8, \end{split} \tag{33}$$

$$dH = [v_1 I_1 + v_2 I_2 - \alpha H - \delta_3 H] dt - \sqrt{v_1 I_1} dW_3 - \sqrt{v_2 I_2} dW_7 + \sqrt{\alpha H} dW_{10} + \sqrt{\delta_3 H} dW_9,$$
(34)

$$dR = [\alpha H]dt - \sqrt{\alpha H}dW_{10}.$$
 (35)

7. Stochastic Simulation Results

To emphasize the impact of stochasticity in the system, we simulate the stochastic model shown in system (28) by using Euler-Maruyama method [45]. For this purpose, we use the following set of parameter values given in Tables 2 and 3. We perform simulations of system (28) for 120 days and 100 simulation runs. First, we compare the mean of 100 runs of stochastic model simulation with the results of corresponding deterministic model and plot the time series of all the variables; see Figure 8 for Italy and Figure 9 for Spain. From these figures, we observe that the mean of 100 runs of stochastic simulation is very close to the simulation results of the deterministic model for the susceptible population (S_1) and (S_2), whereas for the other populations a small deviation between stochastic and deterministic simulations results is observed.

In order to understand these results better, we also plot the distributions of the infected young (I_1) and old (I_2) populations at the 50th, 80th, and 120th days. These can be seen in Figures 10 and 11 for Italy and Spain, respectively. One can easily see the change in distribution of the population as time progresses.

8. Results and Discussion

With an unprecedented global health burden, the COVID-19 pandemic has changed the behavior of societies around the globe which were significantly affected by the extreme measures implemented to control disease transmission.

In this paper, a mathematical model for COVID-19 transmission is formulated and analyzed. We computed the disease-free equilibrium and the basic reproduction number R_0 . Sensitivity analysis was performed to find the key parameters that are most sensitive to basic reproduction number R_0 . The deterministic model was extended to its

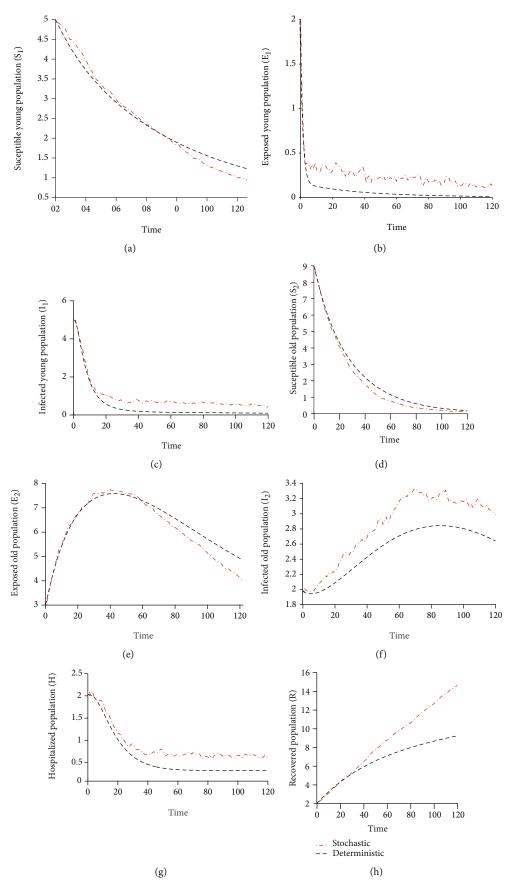


FIGURE 9: Time evolution of (a) S_1 , (b) E_1 , (c) I_1 , (d) S_2 , (e) E_2 , (f) I_2 , (g) H, and (h) R for deterministic and stochastic systems (Spain).

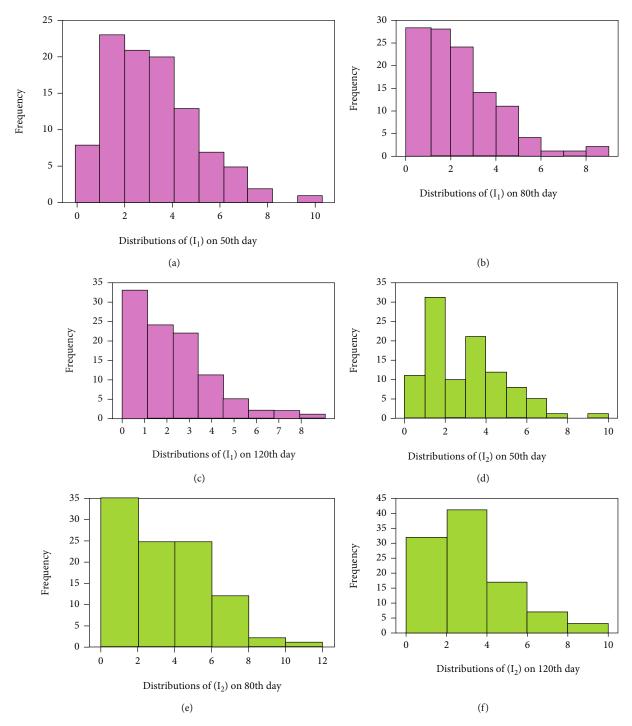


Figure 10: Distributions of symptomatic infected population I_1 and I_2 on days 50, 80, and 120 (Italy).

stochastic counterpart. Using numerical simulations, the distributions of young infected and old infected populations have shown the behaviors of trajectories when the model is affected by stochastic perturbations.

In this work, we have introduced a new parameter ε that plays a very important role to reduce the infectivity of the young population. While $\varepsilon > 1$ represents higher infectivity of young population than the infectivity of older population, the assumption of $\varepsilon < 1$ represents a lower infectivity of

young population than the infectivity of older population. A detailed analysis of this specific parameter is ongoing.

Results presented here support the reduction of the transmission rate between human to human, by the proper use of nonpharmaceutical intervention and vaccination, to affect the most the dynamics of the pandemic. Moreover, a fast detection of the infected individuals would lead to a better treatment, decreasing the disease mortality rate in the population. We would like to emphasize that this is an

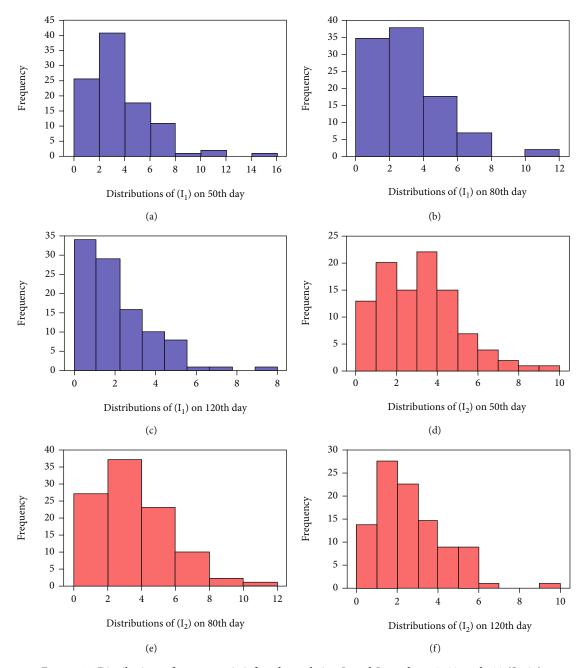


Figure 11: Distributions of symptomatic infected population I_1 and I_2 on days 50, 80, and 120 (Spain).

ongoing work and models will be refined and extended, using the present model as a baseline for future research. As an example, applied to the Basque Country, Spain, scenario, the incorporation of asymptomatic classes for both young and old groups is proposed to evaluate its impact on the control measures implemented over the pandemic time.

Abbreviations

ANA: Antinuclear antibodies APC: Antigen-presenting cells IRF: Interferon regulatory factor.

Data Availability

Previously reported data on COVID-19 cases for Italy and Spain were used to support this study and are available at doi:10.1002/mma.7344. These prior studies (and datasets) are cited at relevant places within the text as references [20, 21].

Conflicts of Interest

The authors declare no potential conflict of interests.

Authors' Contributions

M.A. supervised the development of this study. A.K.S. conceived and performed the numerical simulations. All authors contributed to the development of the modeling framework, analysis of the results, and the writing of the manuscript.

Acknowledgments

This research is supported by the Basque Government through the "Mathematical Modeling Applied to Health" Project, BERC 2018-2021 program, and by the Spanish Ministry of Sciences, Innovation and Universities: BCAM Severo Ochoa accreditation SEV-2017-0718.

References

- [1] World Health Organization, "Coronavirus disease (COVID-19)," June 2021, https://www.who.int/health-topics/coronavirustab=tab1.
- [2] M. Aguiar and N. Stollenwerk, "Condition-specific mortality risk can explain differences in COVID-19 case fatality ratios around the globe," *Public Health*, vol. 188, pp. 18–20, 2020.
- [3] M. Voysey, S. A. C. Clemens, S. A. Madhi et al., "Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS- CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK," *The Lancet*, vol. 397, no. 10269, pp. 99–111, 2021.
- [4] F. P. Polack, S. J. Thomas, N. Kitchin et al., "Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine," *New England Journal of Medicine*, vol. 383, no. 27, pp. 2603–2615, 2020.
- [5] L. R. Baden, H. M. el Sahly, B. Essink et al., "Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine," *New England Journal of Medicine*, vol. 384, no. 5, pp. 403–416, 2021.
- [6] J. Sadoff, G. Gray, A. Vandebosch et al., "Safety and efficacy of single-dose Ad26.COV2.S vaccine against Covid-19," New England Journal of Medicine, vol. 384, no. 23, pp. 2187–2201, 2021
- [7] N. Dagan, N. Barda, E. Kepten et al., "BNT162b2 mRNA Covid-19 vaccine in a nationwide mass vaccination setting," *New England Journal of Medicine*, vol. 384, no. 15, pp. 1412– 1423, 2021.
- [8] V. J. Hall, S. Foulkes, A. Saei et al., "COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study," *The Lancet*, vol. 397, no. 10286, pp. 1725–1735, 2021.
- [9] M. A. Luís Mateus and N. Stollenwerk, "Bayesian estimation of vaccine efficacy," in *Proceedings of the 15th International Con*ference on Mathematical Methods in Science and Engineering, pp. 794–802, Cadiz, Spain, 2015.
- [10] M. Aguiar, N. Stollenwerk, and S. B. Halstead, "The impact of the newly licensed dengue vaccine in endemic countries," *PLOS Neglected Tropical Diseases*, vol. 10, no. 12, article e0005179, 2016.
- [11] M. Aguiar, N. Stollenwerk, and S. B. Halstead, "The risks behind Dengvaxia recommendation," *The Lancet Infectious Diseases*, vol. 16, no. 8, pp. 882-883, 2016.
- [12] M. Aguiar, S. B. Halstead, and N. Stollenwerk, "Consider stopping Dengvaxia administration without immunological

- screening," Expert Review of Vaccines, vol. 16, no. 4, pp. 301-302, 2016.
- [13] M. Aguiar and N. Stollenwerk, "Dengvaxia efficacy dependency on serostatus: a closer look at more recent data," *Clinical Infectious Diseases*, vol. 66, no. 4, pp. 641-642, 2017.
- [14] M. Aguiar and N. Stollenwerk, "Dengvaxia: age as surrogate for serostatus," *The Lancet Infectious Diseases*, vol. 18, no. 3, p. 245, 2018.
- [15] M. Aguiar, "Dengue vaccination: a more ethical approach is needed," *The Lancet*, vol. 391, no. 10132, pp. 1769-1770, 2018.
- [16] S. B. Halstead, L. C. Katzelnick, P. K. Russell et al., "Ethics of a partially effective dengue vaccine: lessons from the Philippines," *Vaccine*, vol. 38, no. 35, pp. 5572–5576, 2020.
- [17] M. Aguiar and N. Stollenwerk, "The impact of serotype cross-protection on vaccine trials: DENVax as a case study," *Vaccine*, vol. 8, no. 4, p. 12, 2020.
- [18] N. Stollenwerk, J. Mar, J. Bidaurrazaga Van-Dierdonck, O. Ibarrondo, C. Estadilla, and M. Aguiar, Modeling COVID-19 Vaccine Efficacy and Coverage towards Herd-Immunity in the Basque Country, medRxiv, Spain, 2021.
- [19] M. Aguiar, J. B. Van-Dierdonck, J. Mar, and N. Stollenwerk, "The role of mild and asymptomatic infections on COVID-19 vaccines performance: a modeling study," *Journal of Advanced Research*, 2021.
- [20] November 2021, https://www.worldometers.info/coronavirus/ country/spain/.
- [21] November 2021, https://www.worldometers.info/coronavirus/country/italy/.
- [22] "The statistics portal, Statista," February 2018, https://www.statista.com/statistics/1105596/covid-19-mortality-rate-by-age-group-in-spain-march/.
- [23] "The statistics portal, Statista," February 2018, https://www.statista.com/statistics/1105061/coronavirus-deaths-by-region-in-italy/.
- [24] M. Aguiar and N. Stollenwerk, "SHAR and effective SIR models: from dengue fever toy models to a COVID-19 fully parametrized SHARUCD framework," *Communication in Biomathematical Sciences*, vol. 3, no. 1, pp. 60–89, 2020.
- [25] M. Aguiar, G. Dosi, D. Knopoff, and M. E. Virgillito, "A multi-scale network-based model of contagion dynamics: heterogeneity, spatial distancing and vaccination," *Mathematical Models and Methods in Applied Sciences*, pp. 1–30, 2021.
- [26] M. Aguiar, E. Millán Ortuondo, J. Bidaurrazaga Van-Dierdonck, J. Mar, and N. Stollenwek, "Modelling COVID 19 in the Basque Country from introduction to control measure response," *Scientific Reports*, vol. 10, p. 17306, 2020.
- [27] M. Aguiar, J. Bidaurrazaga Van-Dierdonck, J. Mar et al., "Critical fluctuations in epidemic models explain COVID-19 post-lockdown dynamics," *Scientific Reports*, vol. 11, p. 13839, 2021.
- [28] M. Aguiar, J. Bidaurrazaga Van-Dierdonck, and N. Stollenwerk, "Reproduction ratio and growth rates: measures for an unfolding pandemic," *PLoS One*, vol. 15, article e0236620, 2020.
- [29] "The epidemiological SHARUCD model dashboard," July 2021, https://wp.bcamath.org/news/en/epidemiological-sharucd-model/introduction.
- [30] J. Chu, "A statistical analysis of the novel coronavirus (COVID-19) in Italy and Spain," *PLoS One*, vol. 16, no. 3, article e0249037, 2021.
- [31] A. K. Srivastav, P. K. Tiwari, P. K. Srivastava, M. Ghosh, and Y. Kang, "A mathematical model for the impacts of face mask,

- hospitalization and quarantine on the dynamics of COVID-19 in India: deterministic vs. stochastic," *Mathematical Biosciences and Engineering*, vol. 18, no. 1, pp. 182–213, 2021.
- [32] D. Olabode, J. Culp, A. Fisher, A. Tower, D. Hull-Nye, and X. Wang, "Deterministic and stochastic models for the epidemic dynamics of COVID-19 in Wuhan," *China. Mathematical Biosciences and Engineering*, vol. 18, no. 1, pp. 950–967, 2021.
- [33] A. K. Srivastav, M. Ghosh, X.-Z. Li, and L. Cai, "Modeling and optimal control analysis of COVID-19: case studies from Italy and Spain," *Mathematical Methods in the Applied Sciences*, vol. 44, no. 11, pp. 9210–9223, 2021.
- [34] "Coronavirus disease (COVID-19)," https://www.who.int/news-room/q-a-detail/q-a-coronaviruses.
- [35] N. M. Ferguson, D. Laydon, G. Nedjati-Gilani et al., Impact of non-pharmaceutical interventions (NPIs) to reduce COVID19 mortality and healthcare demand, Imperial College London, 2020
- [36] B. Tang, N. L. Bragazzi, Q. Li, S. Tang, Y. Xiao, and J. Wu, "An updated estimation of the risk of transmission of the novel coronavirus (2019-nCov)," *Infectious Disease Modelling*, vol. 5, pp. 248–255, 2020.
- [37] F. Zhou, T. Yu, R. du et al., "Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study," *The Lancet*, vol. 395, no. 10229, pp. 1054–1062, 2020.
- [38] P. V. Driessche and J. Watmough, "Reproduction numbers and subthreshold endemic equilibria for compartmental models of disease transmission," *Mathematical Biosciences*, vol. 180, no. 1, pp. 29–48, 2008.
- [39] N. Chitnis, J. M. Hyman, and J. M. Cushing, "Determining important pa- rameters in the spread of malaria through the sensitivity analysis of a mathematical model," *Bulletin of Mathematical Biology*, vol. 70, no. 5, pp. 1272–1296, 2008.
- [40] N. Stollenwerk and V. Jansen, Population Biology and Criticality: From Critical Birth–Death Processes to Self-Organized Criticality in Mutation Pathogen Systems, World Scientific, London, 2011.
- [41] E. J. Allen, L. J. S. Allen, A. Arciniega, and P. Greenwood, "Construction of equivalent stochastic differential equation models," *Stochastic Analysis and Application*, vol. 26, pp. 274–297, 2008.
- [42] N. G. van Kampen, Stochastic Processes in Physics and Chemistry, North-Holland, Amsterdam, 1992.
- [43] C. W. Gardiner, Handbook of Stochastic Methods, Springer, New York, 1985.
- [44] Y. Yuan and L. J. S. Allen, "Stochastic models for virus and immune system dynamics," *Mathematical Biosciences*, vol. 234, no. 2, pp. 84–94, 2011.
- [45] P. E. Kloeden and E. Platen, *Numerical Solution of Stochastic Differential Equations*, Springer, Berlin, 1992.