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An Epidemic Model with Time-Distributed Recovery and Death Rates

Samiran Ghosh¹ · Vitaly Volpert^{2,3} · Malay Banerjee¹ 

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Abstract

A compartmental epidemiological model with distributed recovery and death rates is proposed. In some particular cases, the model can be reduced to the conventional SIR model. However, in general, the dynamics of epidemic progression in this model is different. Distributed recovery and death rates are evaluated from COVID-19 data. The model is validated by the epidemiological data for different countries, and it shows better agreement with the data than the SIR model. The time-dependent disease transmission rate is estimated.

Keywords Epidemic model · Variable recovery rate · SIR model · Effective infection rate

1 Introduction

The world population undergoes successive epidemics of viral infections with important health, social and economical consequences. During the last decades these were SARS epidemic in 2002 – 2003 (Anderson et al. 2004; Lam et al. 2003), H5N1 influenza in 2005 (Chen et al. 2006; Kilpatrick et al. 2006), H1N1 influenza in 2009

✉ Malay Banerjee
malayb@iitk.ac.in

Samiran Ghosh
samiran@iitk.ac.in

Vitaly Volpert
volpert@math.univ-lyon1.fr

¹ Department of Mathematics and Statistics, Indian Institute of Technology Kanpur, Kanpur 208016, Uttar Pradesh, India

² Institut Camille Jordan, UMR 5208 CNRS, University Lyon 1, 69622 Villeurbanne, France

³ Peoples Friendship University of Russia (RUDN University), 6 Mikulkho-Maklaya St, Moscow 117198, Russian Federation

(Girard et al. 2010; Jain et al. 2009), Ebola in 2014 (Frieden et al. 2014; WHO Ebola Response Team 2014), and currently, COVID-19 pandemic which continues already two years and further evolution of which remains unpredictable.

Nowadays, importance of mathematical modeling in epidemiology is generally accepted, but the outcome of this modeling is controversial. On one hand, classical compartmental models allow the evaluation of the main tendencies of epidemic progression. There are various developments of the epidemic models to multicompartments models (see, e.g., Brauer 2008; Giordano et al. 2020; Sharma et al. 2020), models with time varying or nonlinear disease transmission rate (d'Onofrio et al. 2020; Sun et al. 2008). Multipatch models (Bichara and Iggidr 2018; Lahodny and Allen 2013; McCormack and Allen 2007), multigroup models (Elbasha and Gumel 2021), spatiotemporal models (Ahmed et al. 2019; Filipe and Maule 2004) have been formulated and studied to understand various aspects of epidemic growth (see the monographs (Brauer et al. 2019; Martcheva 2015) and review articles (Hethcote 2000; Hurd and Kaneene 1993) for further details). However, the main questions about the prediction of epidemic outbreaks and their efficient managing remain unsolved. This can be partially explained by the unpredictable emergence of new viruses or virus variants, but the lack of understanding of epidemic progression and its economical consequences in a complex multiconnected modern society leads to an empirical try and error method clearly illustrated during COVID-19 pandemic (Supino et al. 2020).

Ongoing pandemic stimulated important modeling efforts directed to the application of the existing models and to their critical rethinking. Compartmental epidemiological models, like the classical SIR model, are based on the assumptions that newly infected individuals at time t appear with the rate proportional to the product of the numbers of susceptible individuals $S(t)$ and infected individuals $I(t)$ and that the recovery and death rates are proportional to the number of infected individuals. The first assumption is justified for homogeneous populations, but the second assumption has a limited applicability. Indeed, assuming that an average disease duration is τ , we conclude that the recovery and death rates at time t are determined by the number of infected individuals at time $I(t - \tau)$ (disease onset), which can be very different from $I(t)$, unless the epidemic progression is slow (basic reproduction number is close to 1). In a more detailed description, we do not consider a fixed disease duration but take into account that the recovery and death rates depend on the disease status of infected individuals, that is, on time passed after the disease onset.

The recovery and death rates can significantly vary depending on the individual disease progression (Github 2022). These factors are rarely taken into account in mathematical models (Feng et al. 2007; Hethcote and Tudor 1980), and further studies are needed to enlighten the significance of immunological factors to capture the incubation period (Culshaw et al. 2003; Leclerc et al. 2014; Vargas-De-León 2012), time-dependent immunity (Kyrychko and Blyuss 2005; Taylor and Carr 2009; Yuan and Bélair, 2014) and other factors. Continuous dependence of the disease transmission rate on immunological parameters (e.g., instantaneous viral load) is also incorporated and studied using continuous time delay models (Gilchrist and Sasaki 2002).

In this work, we continue to study the influence of the disease time course on the epidemic progression. We propose a compartmental model based on integro-differential equations where we take into account that recovery and death rates at time t depend

on the time interval $t - \eta$ from the disease onset for the individuals infected at time η . We determine the main features of epidemic progression and show that they are different in comparison with conventional compartmental models. Further, we illustrate the application of this modeling approach to the COVID-19 data.

The contents of the paper are as follows. In Sect. 2, we introduce the model and study the positiveness of solutions. Next, we show how it can be reduced to the conventional SIR model in some particular cases. In order to apply this model to the investigation of COVID-19 epidemic, we determine time-dependent recovery and death rates from the available data (Sect. 3). We compare the characteristics of epidemic progression in the data and in different models in Sects. 4 and 5. Time-dependent disease transmission rate is estimated in Sect. 6.

2 Model with Distributed Recovery and Death Rates

Recovery and death rates of infected individuals depend on time after the disease onset. In this section, we will derive a model based on the number of newly infected individuals and their recovery and death rates depending on time after infection. We will study some properties of this model and will show that conventional SIR model can be obtained from it under some particular assumptions.

2.1 Model Formulation

We propose an integro-differential equation model where the recovery and death rates depend on the time-since-infection of the infected individuals. Let $J(t)$ be the number of newly infected individuals at time t , while $S(t)$, $I(t)$, $R(t)$ and $D(t)$ denote the total numbers of susceptible, infected, recovered and dead individuals at time t . The total number of infected at time t is given by the following expression:

$$I(t) = \int_0^t J(\eta) d\eta - R(t) - D(t). \quad (1)$$

We assume that the total population size remains constant, $S(t) + I(t) + R(t) + D(t) = N$, that is, natural natality and mortality rates are assumed to be equal to each other. Using the equality $I(t) + R(t) + D(t) = N - S(t)$ and differentiating equality (1), we obtain: $\frac{dS}{dt} = -J(t)$. On the other hand, the rate of change of the susceptible population is given by the equation

$$\frac{dS}{dt} = -\beta \frac{S}{N} I \quad (= -J(t)),$$

where β is the disease transmission rate.

Let $r(t - \eta)$ and $d(t - \eta)$ be the recovery and death rates depending on the time-since-infection $t - \eta$. Then the number of infected individuals who will recover at time t is given by the expression:

$$\int_0^t r(t - \eta)J(\eta)d\eta.$$

Similarly, we determine the number of infected individuals who will die at time t :

$$\int_0^t d(t - \eta)J(\eta)d\eta.$$

Thus, the rate of change of the infected compartment $I(t)$ is given by the following equation:

$$\frac{dI}{dt} = \beta \frac{S}{N} I - \int_0^t r(t - \eta)J(\eta)d\eta - \int_0^t d(t - \eta)J(\eta)d\eta.$$

The rates of change of the recovered $R(t)$ and the death compartment $D(t)$ are given, respectively, by the equations:

$$\frac{dR}{dt} = \int_0^t r(t - \eta)J(\eta)d\eta, \quad \frac{dD}{dt} = \int_0^t d(t - \eta)J(\eta)d\eta.$$

Hence, we obtain the following model:

$$\frac{dS}{dt} = -\beta \frac{S}{N} I, \tag{2a}$$

$$\frac{dI}{dt} = \beta \frac{S}{N} I - \int_0^t r(t - \eta)J(\eta)d\eta - \int_0^t d(t - \eta)J(\eta)d\eta, \tag{2b}$$

$$\frac{dR}{dt} = \int_0^t r(t - \eta)J(\eta)d\eta, \tag{2c}$$

$$\frac{dD}{dt} = \int_0^t d(t - \eta)J(\eta)d\eta, \tag{2d}$$

where $J(t) = \beta S(t)I(t)/N$. This system of equations should be completed by the initial condition $S(0) = N, I(0) = I_0 > 0, R(0) = 0, D(0) = 0$ and $J(t) = 0$ for $t \leq 0$. We will study below some properties of this model and will apply it to assess the epidemic progression.

The proposed model is capable of capturing the features of multicompartment models consisting of symptomatic and asymptomatic compartments implicitly. Their explicit consideration assumes that the individuals belonging to two compartments have different strength of infectivity and difference in time required to recovery. We explain below that $r(t)$ and $d(t)$ follow gamma distribution. Without any loss of generality, we can assume that asymptomatic individuals can recover much earlier than symptomatic individuals. The distributed recovery rate takes care of the time difference between the recovery of individuals belonging to two different compartments. Multicompartment epidemic models for COVID-19 also include exposed compartments and they are less infectious than the infected individuals. This aspect is taken into account by calculating the rate of infectivity from the time series of daily infected.

125 Available data for COVID-19 infection do not differentiate between exposed, symp-
 126 tomatic and asymptomatic infected individuals; hence, we can consider them as a
 127 single compartment (Ghosh et al. 2022).

128 **2.2 Positiveness of Solutions**

129 Since Eq. (2b) contains negative integral terms, we should verify that the solution of
 130 system (2a)–(2d) remains positive. From (2a), we observe that, if $S(t_*) = 0$ at some
 131 time t_* then $\frac{dS}{dt}|_{t=t_*} = 0$. This shows that $S(t) \geq 0$ for all $t > 0$. From (2c), (2d)
 132 we get that $R(t)$, $D(t)$ are increasing functions. Hence, $R(t)$ and $D(t)$ also remain
 133 positive for all t . Next, we prove that $I(t) > 0$. Take some $t_0 > 0$. Then from (1) we
 134 have

$$135 \quad I(t_0) = \int_0^{t_0} J(\eta)d\eta - R(t_0) - D(t_0). \tag{3}$$

136 Integrating (2c), (2d) from 0 to t_0 with $R(0) = D(0) = 0$ and taking their sum, we
 137 get the equality

$$138 \quad R(t_0) + D(t_0) = \int_0^{t_0} \left(\int_0^t (r(t - \eta) + d(t - \eta))J(\eta)d\eta \right) dt.$$

139 Changing the order of integration, we obtain

$$140 \quad R(t_0) + D(t_0) = \int_0^{t_0} \left(\int_\eta^{t_0} (r(t - \eta) + d(t - \eta))dt \right) J(\eta)d\eta. \tag{4}$$

141 Since the integral $\int_\eta^{t_0} (r(t - \eta) + d(t - \eta))dt$ gives the proportion of recovered and
 142 dead individuals from time η to t_0 among those infected at time η , it follows that it is
 143 less than 1. Consequently,

$$144 \quad R(t_0) + D(t_0) < \int_0^{t_0} J(\eta)d\eta.$$

145 Together with (3), this inequality gives that $I(t_0) > 0$. Therefore, $I(t)$ remains positive
 146 for all t . This conclusion completes the proof of positiveness of solution of system
 147 (2a)–(2d).

148 **2.3 Reduction to the SIR Model**

149 In this section, we show that model (2a)–(2d) can be reduced to conventional SIR
 150 model under some assumptions. Consider the recovery and death rates in the form

$$151 \quad r(t - \eta) = \begin{cases} r_0, & t - \tau < \eta \leq t \\ 0, & \eta < t - \tau \end{cases}, \quad d(t - \eta) = \begin{cases} d_0, & t - \tau < \eta \leq t \\ 0, & \eta < t - \tau \end{cases}, \tag{5}$$

152 where $\tau > 0$ is disease duration and r_0 and d_0 are some constants. Substituting these
 153 functions in (2c) and (2d), we get

$$154 \quad \frac{dR}{dt} = r_0 \int_{t-\tau}^t J(\eta)d\eta, \quad \frac{dD}{dt} = d_0 \int_{t-\tau}^t J(\eta)d\eta. \quad (6)$$

155 Integrating these equalities from $t - \tau$ to t , we obtain

$$156 \quad R(t) - R(t - \tau) = r_0 \int_{t-\tau}^t \left(\int_{s-\tau}^s J(\eta)d\eta \right) ds,$$

$$157 \quad D(t) - D(t - \tau) = d_0 \int_{t-\tau}^t \left(\int_{s-\tau}^s J(\eta)d\eta \right) ds.$$

158 Since we assume that the disease duration is τ , then (1) can be written as follows:

$$159 \quad I(t) = \int_{t-\tau}^t J(\eta)d\eta - (R(t) - R(t - \tau)) - (D(t) - D(t - \tau)), \quad (7)$$

160 where $(R(t) - R(t - \tau))$ and $(D(t) - D(t - \tau))$ represent the number of recovered
 161 and dead during the time interval $(t - \tau, t)$, respectively. Hence, from (7), we have

$$162 \quad I(t) = \int_{t-\tau}^t J(\eta)d\eta - (r_0 + d_0) \int_{t-\tau}^t \left(\int_{s-\tau}^s J(\eta)d\eta \right) ds. \quad (8)$$

163 Now, from (2b) and (8),

$$164 \quad \frac{dI}{dt} = \beta \frac{S}{N} I - (r_0 + d_0) \int_{t-\tau}^t J(\eta)d\eta$$

$$165 \quad = \beta \frac{S}{N} I - (r_0 + d_0) \left[I(t) + (r_0 + d_0) \int_{t-\tau}^t \left(\int_{s-\tau}^s J(\eta)d\eta \right) ds \right].$$

166 Assuming that $(r_0 + d_0)$ is small enough, we neglect the term involving $(r_0 + d_0)^2$.
 167 Hence, we obtain

$$168 \quad \frac{dI}{dt} \approx \beta \frac{S}{N} I - (r_0 + d_0)I. \quad (9)$$

169 In this case, system (2a)–(2d) is reduced to conventional SIR model

$$170 \quad \frac{dS}{dt} = -\beta \frac{S}{N} I, \quad (10a)$$

$$171 \quad \frac{dI}{dt} = \beta \frac{S}{N} I - (r_0 + d_0)I, \quad (10b)$$

$$172 \quad \frac{dR}{dt} = r_0 I, \quad \frac{dD}{dt} = d_0 I. \quad (10c)$$

173 Thus, assuming uniform distribution of recovery and death rates (5) and that they are
 174 small enough, we can reduce model (2a)–(2d) to the classical SIR model. However, in
 175 general, these assumptions do not hold, and we need to take into account more realistic
 176 recovery and death rate distributions.

177 3 Estimation of Recovery and Death Rate Functions

178 3.1 Gamma Distribution

179 In this section, we estimate the recovery $r(t)$ and death $d(t)$ rate functions in the case
 180 of COVID-19 epidemic. The data for 120 recovered patients and 31 dead individuals
 181 from Ref. (Github 2022; Verity et al. 2019) were used to fit a gamma distribution.
 182 Note that there are no recovery or death during the first two days after infection. The
 183 maximums of these distributions are reached between 13 and 18 days for recovery and
 184 10–15 days for death (Fig. 2). For some individuals, the recovery time is quite long.
 185 These distribution functions for recovery and death take into account asymptomatic,
 186 symptomatic and hospitalized compartments. Individuals recovered within 7 to 10
 187 days from infection can be considered as asymptomatic either due to less viral load or
 188 due to strong immune response. On the other hand, death after significant time period
 189 from the day of infection can be assumed to be contribution from the hospitalized
 190 compartments. Further, in the literature on epidemic modeling, the choice of gamma
 191 function to model distributed recovery period is well known (Bailey 1954; Chowell
 192 et al. 2009; Lloyd 2001).

193 We estimate the mean time from the disease onset to recovery as 17.85 days and the
 194 mean time to death as 13.19 days. The best-fitted gamma distribution corresponding
 195 to recovery, which is shown by the red curve in Fig. 1a is given by the expression

$$196 \quad f_1(t) = \frac{1}{b_1^{a_1} \Gamma(a_1)} t^{a_1-1} e^{-\frac{t}{b_1}}$$

197 with the estimated parameter values $a_1 = 8.06275$ and $b_1 = 2.21407$. Similarly,
 198 the best-fitted gamma distribution corresponding to death shown by the red curve in
 199 Fig. 1b is given by:

$$200 \quad f_2(t) = \frac{1}{b_2^{a_2} \Gamma(a_2)} t^{a_2-1} e^{-\frac{t}{b_2}},$$

201 where $a_2 = 6.00014$ and $b_2 = 2.19887$.

202 These functions are normalized in such a way that the total probability of recovery
 203 and death equals 1. We set $r(t) = p_0 f_1(t)$, $d(t) = (1 - p_0) f_2(t)$, where p_0 is the
 204 survival probability. Its value is estimated from the data as $p_0 = 0.97$ (Paul and Lorin
 205 2021).

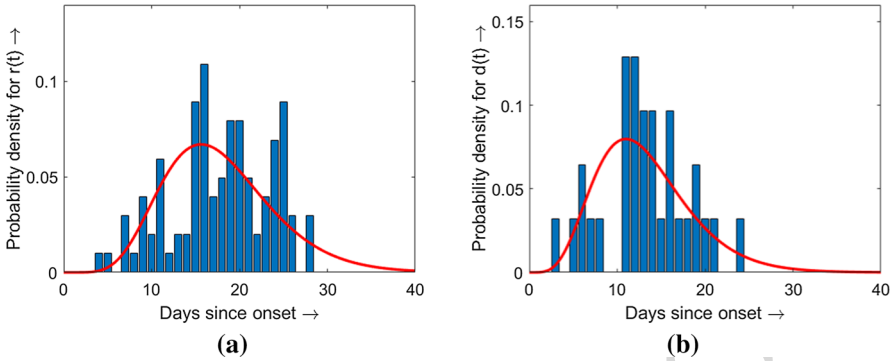


Fig. 1 Probability distribution of recovery **a** and death **b** as a function of time (in days) after the onset of infection. The red curves show the best fit gamma distributions (the values of parameters are given in the text) (Color figure online)

206 **3.2 Bimodal Gamma Distribution**

207 Instead of the gamma distribution, some other distribution functions can be used to
 208 describe the recovery and death rates. It is observed that in some cases there are two
 209 groups of recovered (dead) individuals, where one group has a shorter time interval
 210 to recovery (death) and another group a longer time period. In such cases, to obtain
 211 a better parametrization of the recovery and death rate functions, we can consider
 212 a bimodal gamma distribution, that is, a linear combination of two different gamma
 213 distributions. In (Paul and Lorin 2021), the distribution of recovery and death as
 214 functions of onset-to-recovery and onset-to-death are estimated using the COVID-19
 215 data in Canada. The corresponding data are shown in Fig. 2 by the blue bars. We have
 216 fitted these data by bimodal gamma distributions \mathcal{F}_1 and \mathcal{F}_2 (red curves in Fig. 2)

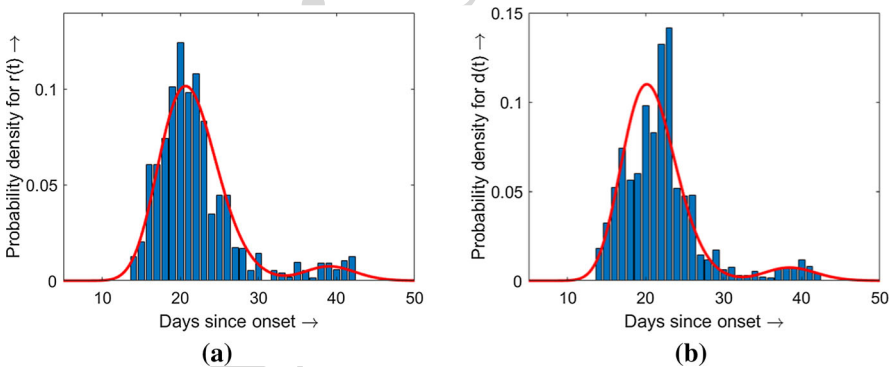


Fig. 2 Probability distribution of recovery **a** and death **b** as a function of time (in days) after the onset of infection. The red curves show the best fit (the values of parameters are given in the text) (Color figure online)

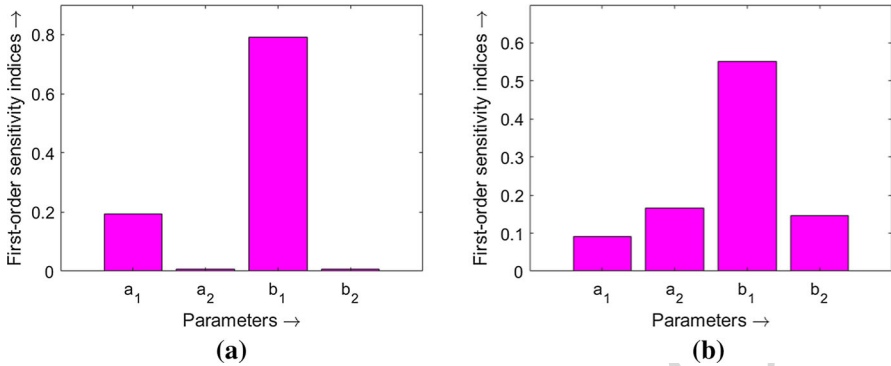


Fig. 3 The left panel shows the first-order sensitivity indices corresponding to the model outcome I_m and the right panel to t_m in the case of gamma distribution (Color figure online)

217 corresponding to recovery and death rate functions, respectively:

$$\begin{aligned}
 \mathcal{F}_1(t) &= \frac{0.91}{b_1^{a_1} \Gamma(a_1)} t^{a_1-1} e^{-\frac{t}{b_1}} + \frac{0.09}{d_1^{c_1} \Gamma(c_1)} t^{c_1-1} e^{-\frac{t}{d_1}}, \\
 \mathcal{F}_2(t) &= \frac{0.94}{b_2^{a_2} \Gamma(a_2)} t^{a_2-1} e^{-\frac{t}{b_2}} + \frac{0.06}{d_2^{c_2} \Gamma(c_2)} t^{c_2-1} e^{-\frac{t}{d_2}},
 \end{aligned}$$

220 where the best-fitted parameter values are as follows: $a_1 = 32.52447$, $b_1 = 0.65547$,
 221 $c_1 = 150.40545$, $d_1 = 0.26171$ and $a_2 = 36.02855$, $b_2 = 0.57511$, $c_2 = 140.11379$,
 222 $d_2 = 0.27636$.

223 3.3 Sensitivity Analysis

224 Parameters in the recovery and death distributions presented above are estimated from
 225 the individual data which can vary depending on country, time period, and on the virus
 226 variant. We will estimate the sensitivity of the model outcomes (maximal number of
 227 infected I_m and time to the maximal number of infected t_m) to the shape and scale
 228 parameters a_1, a_2, b_1, b_2 . For this purpose, we use variance-based sensitivity analysis
 229 with the Monte Carlo numerical procedure described in (Saltelli et al. 2008) for computing
 230 the full set of first-order sensitivity indices S_j for $j = 1, 2, 3, 4$ corresponding
 231 to the parameters a_1, a_2, b_1 and b_2 , respectively. We have estimated the parameters a_1 ,
 232 a_2, b_1 and b_2 from the individual level data given in (Github 2022). Then we use a set
 233 of sample points obtained by using Latin hyper-cube sampling in the neighborhood
 234 of these estimated parameter values and perform numerical simulation as described in
 235 in (Saltelli et al. 2008).

236 The first-order sensitivity indices are shown in Fig. 3 and summarized in Table 1.
 237 This sensitivity analysis shows that the model outcomes I_m (maximal number of
 238 infected) and t_m (time to the maximal number of infected) are most sensitive to the
 239 scale parameter b_1 in the gamma distribution for the recovery rate.

Table 1 First-order sensitivity indices \mathcal{S}_i (gamma distribution)

Parameters	a_1	a_2	b_1	b_2
Sensitivity of I_m	0.1940	0.0068	0.7905	0.0059
Sensitivity of t_m	0.0922	0.1312	0.4971	0.2208

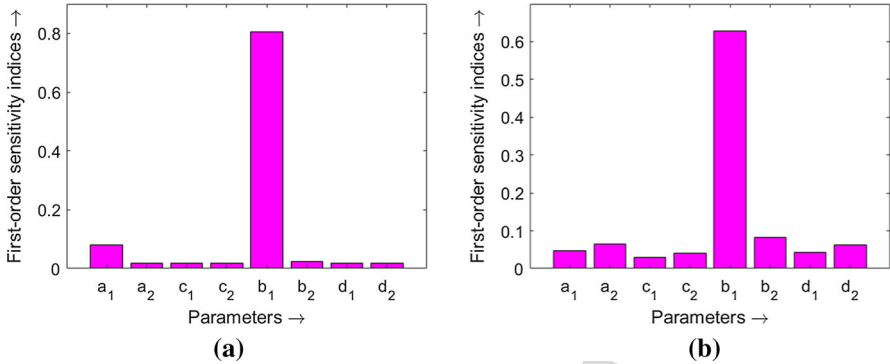


Fig. 4 The left panel shows the first-order sensitivity indices corresponding to the model outcome I_m and the right panel to t_m in the case of bimodal gamma distribution (Color figure online)

Table 2 First-order sensitivity indices \mathcal{S}_i (bimodal gamma distribution)

Parameters	a_1	a_2	c_1	c_2	b_1	b_2	d_1	d_2
Sensitivity of I_m	0.0807	0.0188	0.0195	0.0191	0.8051	0.0244	0.0193	0.0194
Sensitivity of t_m	0.0480	0.0646	0.0304	0.0413	0.6291	0.0816	0.0435	0.0625

A similar method is used to perform the sensitivity analysis for the parameters $a_1, a_2, c_1, c_2, b_1, b_2, d_1$ and d_2 involved in the bimodal gamma distribution. The corresponding first-order sensitivity indices are shown in Fig. 4 and summarized in Table 2. We can observe that b_1 is the most sensitive parameter to I_m and t_m as compared to other parameters.

4 Comparison with the SIR Model

We showed in Sect. 2 that classical SIR model can be obtained as a particular case of distributed model (2a)–(2d). We will compare dynamics of epidemic progression in the two models using the estimated recovery and death rates.

Since the estimated average time to recovery is 17.85 days and to death 13.19 days, we take average disease duration as 16 days. The corresponding value in SIR model is $r_0 + d_0 \approx 1/16$. We set $p_0 = 0.97$, that is, out of 100 infected individuals, 97 infected will recover. This estimate matches with most of the COVID-19 epidemic data from various countries (Worldometer 2022; Paul and Lorin 2021).

Though the parameters of the two models correspond to each other, system (2a)–(2d) and SIR model (10a)–(10c) give different dynamics of epidemic progression (Fig.

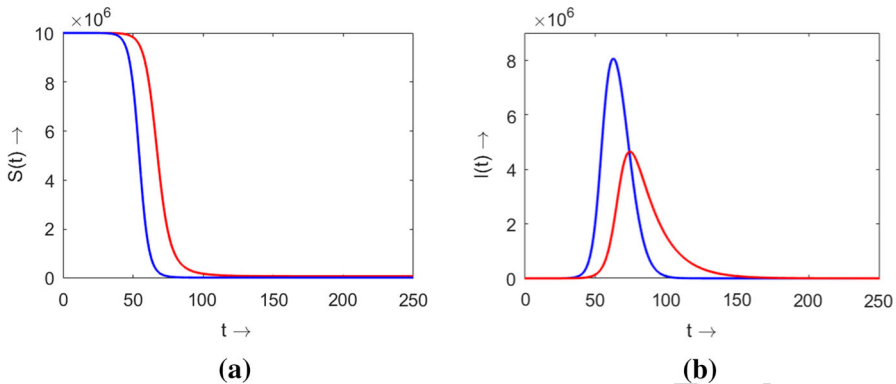


Fig. 5 Comparison between the solutions of the system (2a)–(2d) (blue curves) and SIR model (red curves): **a** the number of susceptible individuals $S(t)$, **b** the number of infected individuals $I(t)$. In both models $N = 10^7$. The values of other parameters for the SIR model: $\beta = 0.3$, $r_0 + d_0 = 1/16$, $I(0) = 1$; and for model (2a)–(2d): $\beta = 0.3$, $a_1 = 8.06275$, $b_1 = 2.21407$, $a_2 = 6.00014$, $b_2 = 2.19887$, $p_0 = 0.97$, $S(0) = N - 1$, $I(0) = 1$ (Color figure online)

5). We notice that the maximal number of infected individuals $I(t)$ is much higher for system (2a)–(2d) as compared to the SIR model (10a)–(10c), while time to the maximal number of infected t_m is less.

Comparison of the final size of epidemic S_f , maximal number of infected I_m and the time to the maximal number of infected t_m between system (2a)–(2d) with gamma distribution and the SIR model are shown in Fig. 6 for different values of parameters. As before, the maximal number of infected individuals I_m in model (2a)–(2d) is much higher than for the SIR model (10a)–(10c), time t_m and the final size S_f are less for the distributed model. This difference can be explained by the fact that the recovery and death rates are uniformly distributed during the disease duration for the SIR model (Sect. 2), contrary to the gamma distribution in (2a)–(2d). Therefore, there is a shift to earlier recovery and death for the SIR model.

Similarly, we compare system (2a)–(2d) with bimodal gamma distribution with the conventional SIR model. In this case, the estimated mean time from onset-to-recovery is 22.63 and the mean time from onset-to-death is 21.80. Hence, the average disease duration is taken approximately 22.2 days, and $r_0 + d_0 \approx 1/22.2$. All other parameters are kept the same as above. The properties of the final size of epidemic, maximal number of infected individuals, time to maximum are similar to the previous case and not shown here.

5 Model Validation with Epidemiological Data

In order to validate the model with distributed recovery and death rates, we compare the results of modeling with the epidemiological data. Distributed recovery $r(t - \eta)$ and death $d(t - \eta)$ rates are estimated in Sect. 3.1 from the data in China in February 2020 (Github 2022; Verity et al. 2019). Once these functions are determined, we take the number $J(t)$ of daily infected individuals from the epidemiological data and find

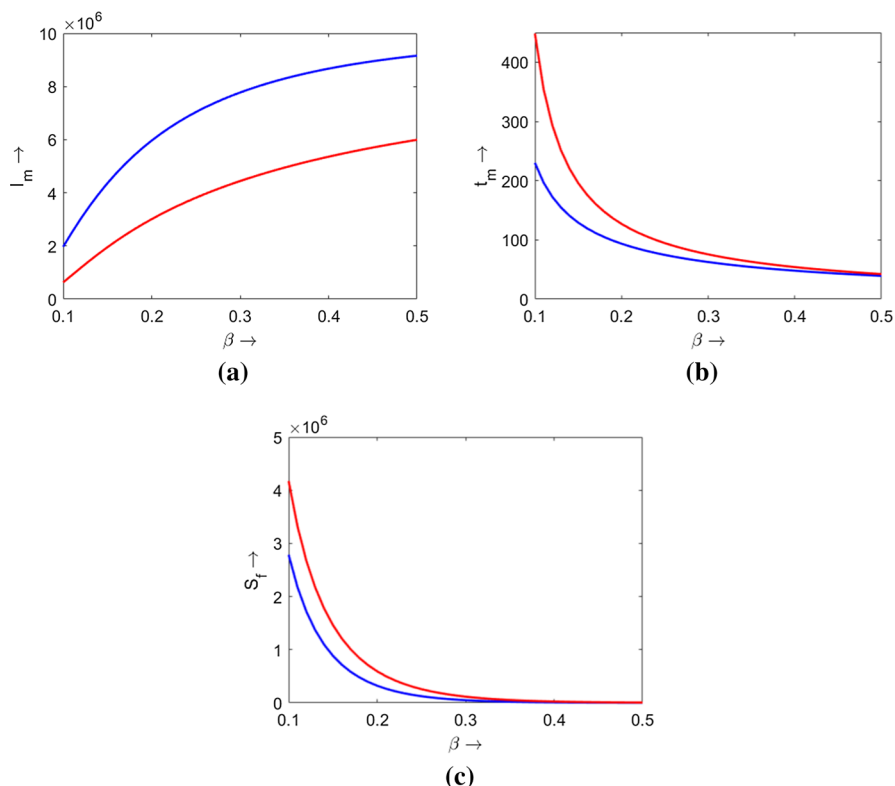


Fig. 6 Comparison of the maximal number of infected individuals I_m **a**, time to reach the maximal number t_m **b** and the final size of epidemic S_f **c** between the system (2a)–(2d) (blue curves) and the SIR model (red curves) for different values of β . The values of parameters: $N = 10^7$, $I_0 = 1$, for the SIR model $r_0 + d_0 = 1/16$; and for the system (2a)–(2d): $a_1 = 8,06275$, $b_1 = 2.21407$, $a_2 = 6.00014$, $b_2 = 2.19887$, $p_0 = 0.97$ (Color figure online)

281 the sum of daily recoveries and deaths from the expression

$$282 \quad \Sigma(t) = \int_0^t r(t - \eta)J(\eta)d\eta + \int_0^t d(t - \eta)J(\eta)d\eta. \quad (11)$$

283 These results are compared with the sum of recoveries and deaths in the data. Figure 7
 284 shows the result of such comparison for China from January 23, 2020, to April 15,
 285 2020, with the data from (Worldometer 2022) (7-day moving average).

286 Recoveries and deaths can also be determined as a proportion of active cases $\sigma(t) =$
 287 $(r_0 + d_0)I(t)$ as it is done in the SIR model. Here $I(t)$ is taken from the data and
 288 $r_0 + d_0 = 1/16$. In agreement with the results of the previous section, SIR model
 289 overestimates the sum of recovered and dead.

290 A similar comparison is done for other countries (Fig. 8). It is important to mention
 291 here that we used the same gamma distribution as determined before from the data for
 292 China (Sect. 3.1).

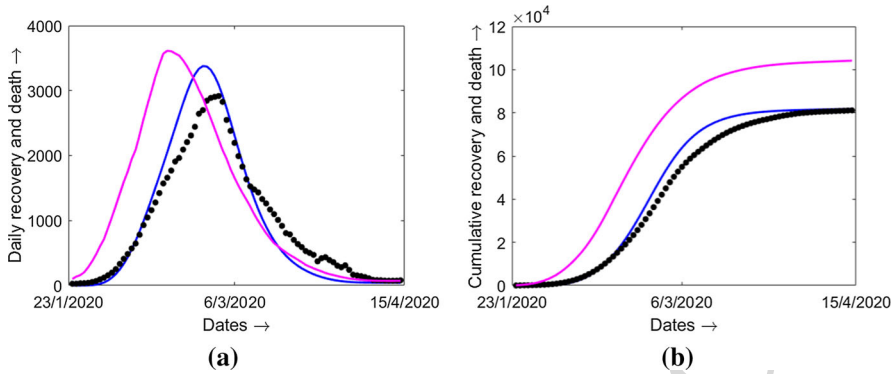


Fig. 7 In the left panel, the blue curve shows the number $\Sigma(t)$ of recovered and dead in the distributed model, the magenta curve corresponds to $\sigma(t)$ in the SIR model, and the black dots correspond to the 7-days moving average of daily recoveries and death in China. The right panel shows the corresponding cumulative recovery and death (Color figure online)

293 Next, we consider the bimodal gamma distribution determined above (Sect. 3.2)
 294 and calculate $\Sigma(t)$ for a longer period of time from March 10, 2020, to June 16, 2020
 295 (Fig. 9), than used for the determination of the distribution parameters. As before, we
 296 compare the results with the SIR model and observe that it overestimates the total
 297 recovery and death.

298 Thus, the model with gamma distribution gives a good description of the recovery
 299 and death in different countries compared with the epidemiological data, while the
 300 SIR model overestimates it.

301 **6 Estimation of the Time-Dependent Disease Transmission Rate $\beta(t)$**

302 In this section, we will consider time-dependent transmission rate, $\beta(t)$ and will esti-
 303 mate it from the COVID-19 epidemiological data. Dynamics of the transmission rate
 304 can help in the understanding of epidemic progression (Mummert 2013).

305 **Theorem 1** For the model (2a)–(2d), the time-dependent transmission function $\beta(t)$
 306 is given by the following expression:

$$307 \quad \beta(t) = \frac{NJ(t)}{I(t) \left(N - \int_0^t J(\eta) d\eta \right)}. \tag{12}$$

308 **Proof** We have

$$309 \quad \beta(t) \frac{S(t)}{N} I(t) = J(t) \Rightarrow \beta(t) = \frac{NJ(t)}{I(t)S(t)}. \tag{13}$$

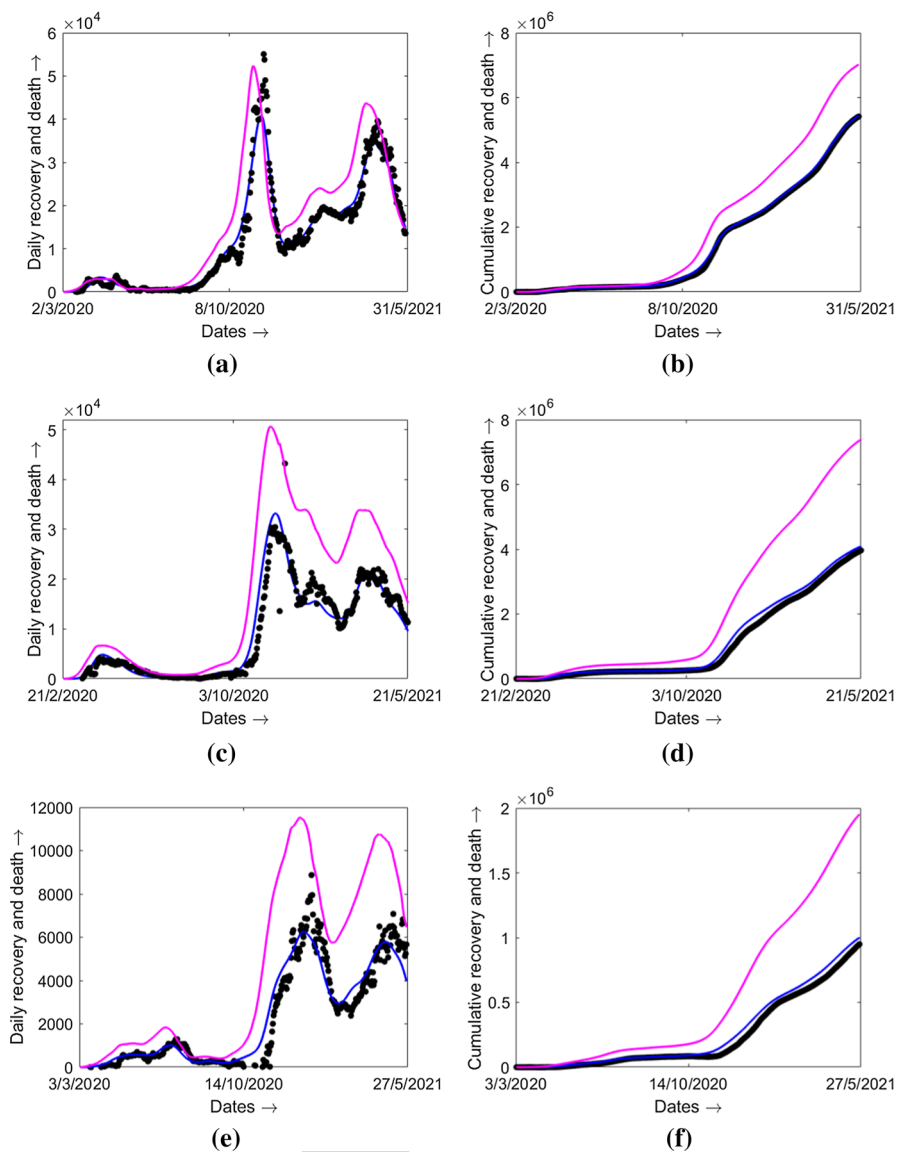


Fig. 8 $\Sigma(t)$, $\sigma(t)$ are plotted for different countries, using the gamma distributions for recovery and death rates as estimated in Sect. 3.1. In the left panel, the blue curves correspond to $\Sigma(t)$, the magenta curves correspond to $\sigma(t)$ and the black dots correspond to the 7-day moving average of daily recovery and death in different countries. The right panel shows the corresponding cumulative recovery and death. **a, b:** France; **c, d:** Italy; **e, f:** Sweden (Color figure online)

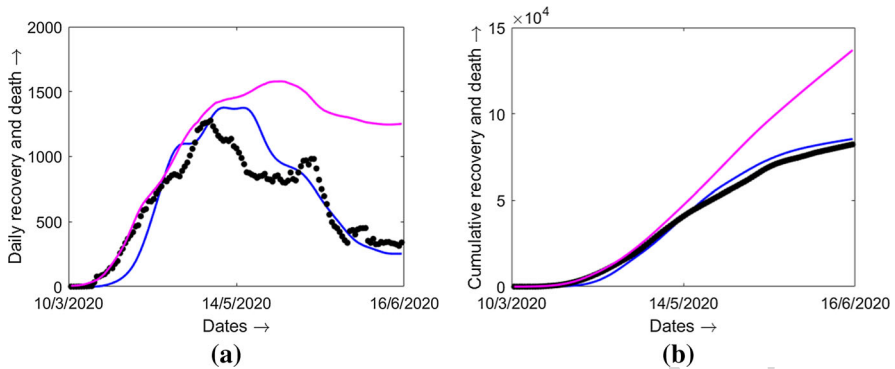


Fig. 9 In the left panel, the blue curve corresponds to $\Sigma(t)$, the magenta curve corresponds to $\sigma(t)$ and the black dots correspond to the 7-day moving average of daily recovery and death in Canada. The right panel shows the corresponding cumulative recovery and death (Color figure online)

310 Now, we also know that

$$311 \quad I(t) = \int_0^t J(\eta)d\eta - (R(t) + D(t)).$$

312 Using $S(t) = N - (I(t) + R(t) + D(t))$ in the previous equation, we get

$$313 \quad S(t) = N - \int_0^t J(\eta)d\eta.$$

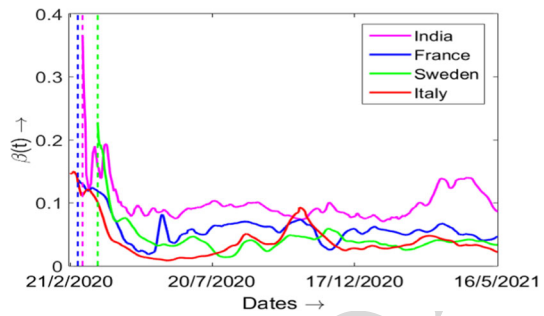
314 Substituting this expression into (13), we obtain (12). □

315 As an illustration of this theorem, we consider the COVID-19 data taken from
 316 (Worldometer 2022) for new daily cases and total active cases. In order to decrease
 317 the irregularity of data, we take the 7-day moving average of $J(t)$ and $I(t)$. Note
 318 that $\int_0^t J(\eta)d\eta$ represents the cumulative number of infected. Consequently, we can
 319 determine the function $\beta(t)$ using formula (12).

320 We consider the COVID-19 infection data for a span of approximately 450 days.
 321 We use the data for India from March 7, 2020, for France from March 2, 2020, for
 322 Italy from February 21, 2020, and for Sweden from March 23, 2020, and up to May
 323 20, 2021, for all the four countries (Worldometer 2022). Then we plot $\beta(t)$ for four
 324 countries with the help of (12) and plot in Fig. 10. The initial date corresponds to the first
 325 reported case in a given country (marked with vertical dashed lines). Initial transient
 326 observed in case of India may be related to the inaccuracy of the reporting strategy.
 327 Growth and decline in $\beta(t)$ at different time correspond to various social restrictions
 328 as well as onset of a new outbreak. It is interesting to note that the declining pattern for
 329 two neighboring European countries, France and Italy, are similar in the beginning.
 330 However, an increasing peak for $\beta(t)$ may indicate that the relaxation of lockdown
 331 restriction in France was more rapid compared to other countries.

332 We can note from the presented results that $\beta(t)$ oscillates according to increasing
 333 or decreasing epidemic waves. Furthermore, average value of this function is different

Fig. 10 Time varying β for COVID-19 in France, India, Italy, Sweden calculated by formula (12) for the model with gamma distribution and the parameter values: $a_1 = 8.06275$, $b_1 = 2.21407$, $a_2 = 6.00014$, $b_2 = 2.19887$, $p_0 = 0.97$ (Color figure online)



334 in different countries. As such, it is about 0.1 in India and about 0.05 in France. In
 335 order to interpret dynamics of time-dependent transmission rate $\beta(t)$, we simplify
 336 expression (12) assuming that $\int_0^t J(\eta)d\eta \ll N$. This assumption is justified since the
 337 total number of infected remains in most countries much less than the total population.
 338 Then $\beta(t) \approx J(t)/I(t)$. The same expression for $\beta(t)$ can be obtained from the SIR
 339 model if $S \approx N$.

340 In order to give further estimates of $\beta(t)$, suppose that disease duration is τ . Then
 341 $I(t) = \int_{t-\tau}^t J(\eta)d\eta$, that is, the individuals infected at time $t - \tau$ recover or die at
 342 time t but not before. Hence, we obtain approximate formula

343
$$\beta(t) = \frac{J(t)}{\int_{t-\tau}^t J(\eta)d\eta} .$$

344 Set $J(t) = J(\tau)e^{\lambda(t-\tau)}$ and then substituting in above equation, we find $\beta(t) =$
 345 $\lambda/(1 - \exp(-\lambda\tau))$. If $\lambda = 0$, then $\beta(t) = 1/\tau$, that is, the disease transmission rate is
 346 inversely proportional to the disease duration. This estimate is in agreement with an
 347 average disease duration 16 days determined in Sect. 2. For $\lambda > 0$, β characterizes
 348 the rate of growth of newly infected individuals, and for negative λ , the rate of decay.

349 **7 Discussion**

350 Ongoing COVID-19 pandemic has stimulated scientific research in various disciplines
 351 ranging from economy to education (Volpert et al. 2020). A wide variety of modeling
 352 approaches are considered in the recent literature (see, e.g., Rahimi et al. 2021; Sharma
 353 et al. 2020 for more detail). However, validation of these models is complicated by
 354 the uncertainty of the data, especially for asymptomatic cases.

355 Another shortcoming of conventional epidemiological model is that they consider
 356 recovery and death rate as a given proportion of active infected cases at the same
 357 moment of time. Clearly, this is a strong assumption which can lead to a large error in
 358 the evaluation of epidemic progression. In order to overcome this issue, we propose
 359 in this work a new type of immunoepidemiological models based on the daily number
 360 of infected individuals and their time-distributed recovery and death rates. Distributed
 361 recovery and death rates are evaluated from the data from China and Canada. They give

362 a reliable description of data for different countries and time periods. We note that the
363 parameters of gamma distribution can depend on the virus variant. This question can
364 be addressed in the future studies when the time-dependent recovery rate is available
365 in particular for the Omicron variant.

366 We compare this approach with the SIR model with appropriate recovery and death
367 rates. It is clearly seen that the SIR model overestimates the daily recoveries and
368 deaths which, in turn, underestimates the daily number of infected, maximal and total
369 numbers of infected individuals. The recovery and death rate functions are estimated
370 with the limited real data from China and Canada on the number of days spent since
371 infection before recovery and death (Github 2022; Paul and Lorin 2021). These data
372 sets are used to estimate the parameters involved with two different parametrization of
373 the recovery and death rate functions. Time-since-infection-based recovery and death
374 rates implicitly take into account mild and severe infection which can be considered as
375 symptomatic and asymptomatic compartments. Numerical validation of the proposed
376 model with the COVID-19 epidemic data from five different countries indicates that the
377 parametrization of recovery and death rates with gamma function effectively captures
378 the daily and cumulative recoveries and deaths, although the real data show large
379 irregularity.

380 It is important to mention here that the proposed modeling approach can be used
381 to predict the disease progression accurately if we have specific data for the first days
382 in order to estimate the parameters involved in the recovery and death rate functions.
383 Availability of such kind of data is a challenging issue in the beginning of epidemic.
384 However, we should highlight that the estimates of $r(t)$ and $d(t)$ with the data from
385 China during the onset of COVID-19 epidemic works well to study the disease progres-
386 sion in France, Italy and Sweden. Having these information, the proposed modeling
387 approach can be used to predict the maximal number of infected and the time to
388 maximal number of infected. This predictions can be used to estimate the required
389 number of hospital beds and readiness of medical facilities based upon the appropriate
390 information about the rate of hospitalization and severity of the viral strain.

391 We have also described a method to calculate time-dependent infectivity rate based
392 upon the daily incidence data. It clearly indicates that the rate of transmission of
393 infection from one individual to another not only depends upon the fixed transmission
394 rate, but rather it is solely related with the time period over which one individual
395 remain infected. The next challenging issue will be to estimate the rate of infection
396 transmission depending on time-dependent viral load for different virus variants.

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400 **Data availability** All data generated or analyzed during this study are included in this article and mentioned
401 in the reference section.

402 **Declarations**

403 **Conflict of interest** The authors declare that they have no conflict of interest.

References

- 404
- 405 Ahmed N, Wei Z, Baleanu D, Rafiq M, Rehman MA (2019) Spatio-temporal numerical modeling of reaction-
406 diffusion measles epidemic system. *Chaos* 29:103101
- 407 Anderson RM, Fraser C, Ghani AC, Donnelly CA, Riley S, Ferguson NM, Leung GM, Lam TH, Hedley
408 AJ (2004) Epidemiology, transmission dynamics and control of SARS: the 2002–2003 epidemic. *Phil*
409 *Trans R Soc Lond B* 359:1091–1105
- 410 Bailey NTJ (1954) A statistical method of estimating the periods of incubation and infection of an infectious
411 disease. *Nature* 174: 139–140
- 412 Bichara D, Iggidr A (2018) Multi-patch and multi-group epidemic models: a new framework. *J Math Biol*
413 77:107–134
- 414 Brauer F (2008) Compartmental models in epidemiology. In: Brauer F, Driessche PVD, Wu J *Mathematical*
415 *epidemiology*, Springer, New York, pp 19–79
- 416 Brauer F, Castillo-Chavez C, Feng Z (2019) *Mathematical models in epidemiology*. vol 32, Springer, New
417 York
- 418 Chen H, Smith GJD, Li KS, Wang J, Fan XH, Rayner JM, Vijaykrishna D, Zhang JX, Zhang LJ, Guo CT,
419 et al. (2006) Establishment of multiple sublineages of H5N1 influenza virus in Asia: implications for
420 pandemic control. *Proc Natl Acad Sci U S A* 103:2845–2850
- 421 Chowell G, Hyman JM, Bettencourt LMA, Castillo-Chavez C, Nishiura H (2009) *Mathematical and statisti-*
422 *cal estimation approaches in epidemiology*. Springer, New York
- 423 Culshaw RV, Ruan S, Webb G (2003) A mathematical model of cell-to-cell spread of HIV-1 that includes
424 a time delay. *J Math Biol* 46:425–444
- 425 d’Onofrio A, Banerjee M, Manfredi P (2020) Spatial behavioural responses to the spread of an infectious
426 disease can suppress Turing and Turing-Hopf patterning of the disease. *Phys A: Stat Mech Appl*
427 545:123773
- 428 Elbasha EH, Gumel AB (2021) Vaccination and herd immunity thresholds in heterogeneous populations. *J*
429 *Math Biol* 83:1–23
- 430 Feng Z, Xu D, Zhao H (2007) Epidemiological models with non-exponentially distributed disease stages
431 and applications to disease control. *Bull Math Biol* 69:1511–1536
- 432 Filipe JAN, Maule MM (2004) Effects of dispersal mechanisms on spatio-temporal development of epi-
433 demics. *J Theor Biol* 226:125–141
- 434 Frieden TR, Damon I, Bell BP, Kenyon T, Nichol S (2014) Ebola 2014-new challenges, new global response
435 and responsibility. *N Engl J Med* 371:1177–1180
- 436 Ghosh S, Banerjee M, Volpert V (2022) Immuno-epidemiological model-based prediction of further
437 COVID-19 epidemic outbreaks due to immunity waning. *Math Model Nat Phenom* 7:9
- 438 Gilchrist MA, Sasaki A (2002) Modeling host-parasite coevolution: a nested approach based on mechanistic
439 models. *J Theor Biol* 218:289–308
- 440 Giordano G, Blanchini F, Bruno R, Colaneri P, Filippo AD, Matteo AD, Colaneri M (2020) Modelling the
441 COVID-19 epidemic and implementation of population-wide interventions in Italy. *Nat Med* 26:855–
442 860
- 443 Girard MP, Tam JS, Assossou OM, Kieny MP (2010) The 2009 A (H1N1) influenza virus pandemic: A
444 review. *Vaccine* 28:4895–4902
- 445 Github (2022) https://github.com/mrc-ide/COVID19_CFR_submission
- 446 Hethcote HW (2000) The mathematics of infectious diseases. *SIAM Rev* 42:599–653
- 447 Hethcote HW, Tudor DW (1980) Integral equation models for endemic infectious diseases. *J Math Biol*
448 9:37–47
- 449 Hurd HS, Kaneene JB (1993) The application of simulation models and systems analysis in epidemiology:
450 a review. *Prev Vet Med* 15:81–99
- 451 Jain S, Kamimoto L, Bramley AM, Schmitz AM, Benoit SR, Louie J, Sugerman DE, Druckenmiller JK,
452 Ritger KA, Chugh R, et al. (2009) Hospitalized patients with 2009 H1N1 influenza in the United
453 States, April–June 2009. *N Engl J Med* 361:1935–1944
- 454 Kilpatrick AM, Chmura AA, Gibbons DW, Fleischer RC, Marra PP, Daszak P (2006) Predicting the global
455 spread of H5N1 avian influenza. *Proc Natl Acad Sci U S A* 103:19368–19373
- 456 Kyrychko YN, Blyuss KB (2005) Global properties of a delayed SIR model with temporary immunity and
457 nonlinear incidence rate. *Nonlinear Anal Real World Appl* 6:495–507
- 458 Lahodny GE, Allen LJS (2013) Probability of a disease outbreak in stochastic multipatch epidemic models.
459 *Bull Math Biol* 75:1157–1180

- 460 Lam WK, Zhong NS, Tan WC (2003) Overview on SARS in Asia and the world. *Respirology* 8:S2–S5
- 461 Leclerc M, Doré T, Gilligan CA, Lucas P, Filipe JAN (2014) Estimating the delay between host infection
462 and disease (incubation period) and assessing its significance to the epidemiology of plant diseases.
463 *PLoS One* 9:e86568
- 464 Lloyd AL (2001) Realistic distributions of infectious periods in epidemic models: changing patterns of
465 persistence and dynamics. *Theor Pop Biol* 60:59–71
- 466 Martcheva M (2015) *An introduction to mathematical epidemiology*. Springer, New York
- 467 McCormack RK, Allen LJS (2007) Multi-patch deterministic and stochastic models for wildlife diseases.
468 *J Biol Dyn* 1:63–85
- 469 Mummert A (2013) Studying the recovery procedure for the time-dependent transmission rate (s) in epidemic
470 models. *J Math Biol* 67:483–507
- 471 Paul S, Lorin E (2021) Estimation of COVID-19 recovery and decrease periods in Canada using delay model.
472 *Sci Rep* 11:1–15
- 473 Rahimi I, Chen F, Gandomi AH (2021) A review on COVID-19 forecasting models. *Neural Comput Appl*
474 1–11
- 475 Saltelli A, Ratto M, Andres T, Campolongo F, Cariboni J, Gatelli D, Saisana M, Tarantola S (2008) *Global
476 sensitivity analysis: the primer*. John Wiley & Sons
- 477 Sharma S, Volpert V, Banerjee M (2020) Extended SEIQR type model for COVID-19 epidemic and data
478 analysis. *Math Biosci Eng* 17:7562–7604
- 479 Sun GQ, Jin Z, Liu QX, Li L (2008) Chaos induced by breakup of waves in a spatial epidemic model with
480 nonlinear incidence rate. *J Stat Mech: Theory Exp* 2008:P08011
- 481 Supino M, d’Onofrio A, Luongo F, Occhipinti G, Co AD (2020) The effects of containment measures in
482 the Italian outbreak of COVID-19. *BMC Public Health* 20(1), 1–8
- 483 Taylor ML, Carr TW (2009) An SIR epidemic model with partial temporary immunity modeled with delay.
484 *J Math Biol* 59:841–880
- 485 Vargas-De-León C (2012) Global analysis of a delayed vector-bias model for malaria transmission with
486 incubation period in mosquitoes. *Math Biosci Eng* 9:165
- 487 Verity R, Okell LC, Dorigatti I, Winskill P, Whittaker C, Imai N, Cuomo-Dannenburg G, Thompson H,
488 Walker PGT, Fu H, et al. (2019) Estimates of the severity of coronavirus disease 2019: a model-based
489 analysis. *Lancet Infect Dis* 20:669–677
- 490 Volpert V, Banerjee M, D’Onofrio A, Lipniacki T, Petrovskii S, Tran VC (2020) Coronavirus-scientific
491 insights and societal aspects. *Math Model Nat Phenom* 15 E2
- 492 WHO Ebola Response Team (2014) Ebola virus disease in West Africa—the first 9 months of the epidemic
493 and forward projections. *N Engl J Med* 371:1481–1495
- 494 Worldometer (2022) <https://www.worldometers.info/coronavirus/>
- 495 Yuan Y, (2014) Threshold dynamics in an SEIRS model with latency and temporary immunity. *J Math Biol*
496 69(4), 875–904

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