MATHEMATICAL BIOSCIENCES
AND ENGINEERING
Volume **4**, Number **4**, October **2007**

http://www.mbejournal.org/

pp. **675–686**

FINAL AND PEAK EPIDEMIC SIZES FOR *SEIR* MODELS WITH QUARANTINE AND ISOLATION

Zhilan Feng

Department of Mathematics
Purdue University, West Lafayette, IN 47907

(Communicated by: Yang Kuang)

Abstract. Two *SEIR* models with quarantine and isolation are considered, in which the latent and infectious periods are assumed to have an exponential and gamma distribution, respectively. Previous studies have suggested (based on numerical observations) that a gamma distribution model (GDM) tends to predict a larger epidemic peak value and shorter duration than an exponential distribution model (EDM). By deriving analytic formulas for the maximum and final epidemic sizes of the two models, we demonstrate that either GDM or EDM may predict a larger epidemic peak or final epidemic size, depending on control measures. These formulas are helpful not only for understanding how model assumptions may affect the predictions, but also for confirming that it is important to assume realistic distributions of latent and infectious periods when the model is used for public health policy making.

1. **Introduction.** Quarantine (of exposed individuals) and isolation (of infectious individuals) are two of the most commonly implemented control measures for infectious diseases, especially in the case of SARS. Mathematical models such as the *SEIR* type of epidemiological models have been used to assess the effectiveness of various control strategies (see, for example, [2], [6], [9]). Some of the models are made mathematically simpler by assuming exponentially distributed latent and infectious periods, while others are made more complicated (and more realistic) by replacing the exponential distribution with gamma distributions (see [4], [10]). The gamma distribution assumption (GDA) is considered to be more realistic than the exponential distribution assumption (EDA) as the gamma distribution can fit epidemiological data much better in most cases. It has been shown that models under GDA and EDA may generate different disease dynamics (see [5], [7]).

When a mathematical model is used to study disease control, it is common to consider certain quantities (derived from the model) that can provide information about the effect of control measures on disease prevalence. These quantities include the (control) reproductive number, final epidemic size, maximum (peak) value of an epidemic, etc. Although formulas for the maximum and final epidemic sizes have been derived previously for some *SIR* or *SEIR* types of epidemic models (see [1], [3], [8]), formulas for models with quarantine, isolation, or both or with GDA have not been available. In this article, we derive these formulas for two such models,

2000 *Mathematics Subject Classification.* 92D25, 92D30, 34C60.

Key words and phrases. mathematical model, infectious diseases, final epidemic size, peak epidemic size, disease control.

the EDM (2) and the GDM (3), and employ these formulas to compare model predictions regarding the effectiveness of disease control strategies.

Based on numerical observations, Wearing et al. [10] concluded that, in comparison to a gamma-distributed model, the epidemic given by the exponentially distributed model (i) takes off at a dramatically slower rate, (ii) predicts a significantly smaller peak number of cases, and (iii) lasts much longer. We demonstrate using the formulas derived in this paper that either the EDM or GMD may predict a larger epidemic peak, a larger final epidemic size, or both. For example, we show analytically that the EDM may predict a larger peak number of cases when the quarantine rate is low, whereas the GDM may predict a larger peak number of cases when the isolation rate is low. We also use the formulas to show that the two models may provide substantially different assessments, some of which are even contradictory to each other, when comparing the effect of control strategies.

2. **The models and formulas for maximum and final sizes.**

The two models we will consider in this paper are extensions of the standard $SEIR$ model (without vital dynamics):

$$\begin{aligned} S' &= -\beta SI, \\ E' &= \beta SI - \alpha E, \\ I' &= \alpha E - \delta I, \\ R' &= \delta I, \end{aligned} \tag{1}$$

with initial conditions $S(0) = S_0,\ E(0) = E_0,\ I(0) = I_0$, and $R(0) = R_0$. Here, $S(t)$, $E(t)$, $I(t)$, and $R(t)$ denote the fractions of susceptible, latent (exposed but not infectious), infectious, and removed individuals at time t, and $S(t) + E(t) + I(t) + R(t) = 1$. β is the transmission rate, α is the rate at which an exposed individual becomes infectious, and δ is the recover rate.

Model (1) implicitly assumes that the latent and infectious stages are exponentially distributed with $1/\alpha$ and $1/\delta$ being the mean latent and infectious periods, respectively. It is known that for many infectious diseases, these stage distributions are more reasonably approximated by gamma distributions [10]. It is particularly important to assume a gamma distribution when (imperfect) quarantine and/or isolation are considered. In [4], Feng et al. developed a general model by assuming arbitrarily distributed latent and infectious periods with the inclusion of a quarantined class (Q) and an isolated (hospitalized) class (H). It also allows for the possibility of imperfect isolation with $\rho \in [0, 1]$ representing the isolation effectiveness, in which case the force of infection is $\beta\big(I + (1-\rho)H\big)$. The general model is an integral equations model, which is shown to reduce to simpler ODE models under specific assumptions on the disease stages. For example, when the distributions of latent and infectious periods are exponential given by

$$p_E(s) = e^{-\alpha s} \quad \text{and} \quad p_I(s) = e^{-\delta s}$$

with $T_E = 1/\alpha$ and $T_I = 1/\delta$ being the mean latent and infectious periods respectively, the general model reduces to the following model, which we refer to as the

EDM:

$$\begin{aligned} S' &= -\beta S\Big(I + (1-\rho)H\Big), \\ E' &= \beta S\Big(I + (1-\rho)H\Big) - (\chi+\alpha)E, \\ Q' &= \chi E - \alpha Q, \\ I' &= \alpha E - (\phi+\delta)I, \\ H' &= \alpha Q + \phi I - \delta H, \\ R' &= \delta I + \delta H. \end{aligned} \tag{2}$$

The quarantine and isolation rates are χ and ϕ, respectively.

When the two disease stages are assumed to have gamma distributions given by

$$p_m(s,\alpha) = \sum_{k=0}^{m-1} \frac{(m\delta s)^k\ e^{-m\alpha s}}{k!}, \qquad p_n(s,\delta) = \sum_{k=0}^{n-1} \frac{(n\delta s)^k\ e^{-n\delta s}}{k!}, \qquad m,\ n \geq 1$$

with latent and infectious periods equal to $T_E = 1/\alpha$ and $T_I = 1/\delta$ respectively, the general model reduces to the following model, which we refer to as the GDM:

$$\begin{aligned} &S' = -\beta S\Big(I + (1-\rho)H\Big), \\ &E_1' = \beta S\Big(I + (1-\rho)H\Big) - (m\alpha+\chi)E_1, \qquad E_i' = m\alpha E_{i-1} - (m\alpha+\chi)E_i, \\ &Q_1' = \chi E_1 - m\alpha Q_1, \qquad Q_i' = m\alpha Q_{i-1} + \chi E_i - m\alpha Q_i, \\ &I_1' = m\alpha E_m - (n\delta+\phi)I_1, \qquad I_j' = n\delta I_{j-1} - (n\delta+\phi)I_j, \\ &H_1' = \phi I_1 + m\alpha Q_m - n\delta H_1, \qquad H_j' = \phi I_j + n\delta H_{j-1} - n\delta H_j, \\ &R' = n\delta I_n, \qquad i = 2,3,\cdots,m,\ j = 2,3,\cdots,n, \\ &\text{with } I = \textstyle\sum_{j=1}^n I_j,\ H = \sum_{j=1}^n H_j. \end{aligned} \tag{3}$$

Here, χ, ϕ, and ρ have the same meaning as in (2). The values of m and n are determined by the disease; for example, $m = 2$ and $n = 3$ for SARS, and $m = 40$ and $n = 4$ for smallpox (see [10]). Clearly, the EDM (2) is a special case of the GDM (3) when $m = n = 1$. It is easy to verify that solutions of the EDM and GDM will remain positive for all $t > 0$ for appropriate initial conditions.

2.1. **Final and peak epidemic sizes for the EDM and GDM.** In the EDM (2), variables representing infected individuals include E, Q, I, and H. Obviously, these disease variables should be involved in the quantity that can be used to measure the epidemic size at time t. However, this quantity needs not to be the sum of these variables, $E + Q + I + H$, as the main use of the model is to assess disease control programs by comparing them. Here, we define this quantity for the EDM to be the following weighted sum (see Appendix for the derivation):

$$Y_e(t) = E(t) + b(Q(t) + H(t)) + cI(t) \tag{4}$$

(e for exponential), where

$$b = \frac{1}{B}, \quad c = \frac{1}{B}\Big(1 + \frac{\rho}{1-\rho}\ \frac{\delta}{\delta+\phi}\Big), \quad B = 1 + \frac{\rho}{1-\rho}\ \frac{\alpha}{\alpha+\chi}\ \frac{\delta}{\delta+\phi}. \tag{5}$$

Then we can show that Y_e satisfies the differential equation:

$$Y_e' = \beta\Big(S - \frac{1}{\mathcal{R}_e}\Big)\Big(I + (1-\rho)H\Big), \tag{6}$$

where $\mathcal{R}_e$ is the control reproductive number for the EDM and is given by

$$\mathcal{R}_e = \frac{\beta}{\delta}\Big[1 - \rho\Big(1 - \frac{\alpha}{\alpha+\chi}\,\frac{\delta}{\delta+\phi}\Big)\Big]. \tag{7}$$

Here, we have used the relation $(1-\rho)B\beta/\delta = 1/\mathcal{R}_e$ to obtain (6). From the S equation in (2) and the Y_e equation (6),

$$\frac{dY_e}{dS} = -1 + \frac{1}{\mathcal{R}_e S}. \tag{8}$$

It follows that the solution of the EDM satisfies the equation:

$$S(t) + Y_e(t) - \frac{1}{\mathcal{R}_e}\ln S(t) = S_0 + Y_{e0} - \frac{1}{\mathcal{R}_e}\ln S_0 \qquad \text{for all } t > 0, \tag{9}$$

where S_0 and $Y_{e0} = E_0 + b(Q_0 + H_0) + cI_0$ are determined by the initial conditions of the EDM. Hence, the system has a preserved quantity (i.e., it does not change with time t) given by $S(t) + Y_e(t) - \frac{1}{\mathcal{R}_e}\ln S(t)$.

To determine the peak value of $Y_e(t)$, we discuss two possibilities. The first one occurs when $\mathcal{R}_e < 1$, in which case $Y_e'(t) \le 0$ for all $t > 0$ (see (6) and recall that $S \le 1$) and the maximum value occurs at $t = 0$. The second case arises when $\mathcal{R}_e > 1$, in which case there exists a $t = t_m > 0$ such that $Y_e'(t_m) = 0$. From equation (6) we know that $S(t_m) = 1/\mathcal{R}_e$. Using equation (9) for $t = t_m$ we obtain the maximum value $Y_{emax} = Y_e(t_m)$:

$$Y_{emax} = S_0 + Y_{e0} - \frac{1}{\mathcal{R}_e}\Big[1 + \ln(\mathcal{R}_e S_0)\Big]. \tag{10}$$

To verify that the variable Y_e provides a reasonable quantity for assessing control programs, we illustrate in Figures 1(a) and (b) that Y_e provides the same qualitative information as the direct sum of all disease variables, $E + Q + I + H$, concerning the effect of various control measures for model (2). In Figure 1, (c) illustrates both the time plot of the solution of (2) and the value Y_{emax} (marked with a diamond) computed using the formula (10). The figure shows that the value Y_{emax} indeed matches the peak value of $Y_e(t)$.

We now derive an equation for the final epidemic size defined by $C = S_0 - S(\infty)$, where $S(\infty) = \lim_{t\to\infty} S(t)$. We observe that $S'(t) < 0$ for all $t > 0$ and hence $S(\infty)$ exists. Then $S(t) < 1/\mathcal{R}_e$ for all $t > t_m$ as $S(t_m) = 1/\mathcal{R}_e$. Hence, from (6) we know that $Y_e'(t) < 0$ for all $t > t_m$, and hence, $\lim_{t\to\infty} Y_e(t)$ exists. Choose a sequence $t_k \to \infty$ such that $Y_e'(t_k) \to 0$ as $k \to \infty$. Then using (6) we have $I(t_k) \to 0$ and $H(t_k) \to 0$ as $k \to \infty$ (for $S(t_k) < 1/\mathcal{R}_e$). Thus, $I_\infty = \liminf_{t\to\infty} I(t) = 0$ and $H_\infty = 0$. Using the fact that we can choose a sequence $s_k \to \infty$ such that $I'(s_k) \to 0$ and $I(s_k) \to I_\infty$ as $k \to \infty$, from the I equation in (2) and $I_\infty = 0$ we have $E(s_k) \to 0$, and hence $E_\infty = 0$. Similarly we can use the H equation in (2) to show that $Q_\infty = 0$. It follows from (4) that $Y_{e\infty} = 0$ and hence $Y_e(\infty) = 0$.

Taking the limit $t \to \infty$ in (9), we get

$$S(\infty) + Y_e(\infty) - \frac{1}{\mathcal{R}_e}\ln S(\infty) = S_0 + Y_{e0} - \frac{1}{\mathcal{R}_e}\ln S_0.$$

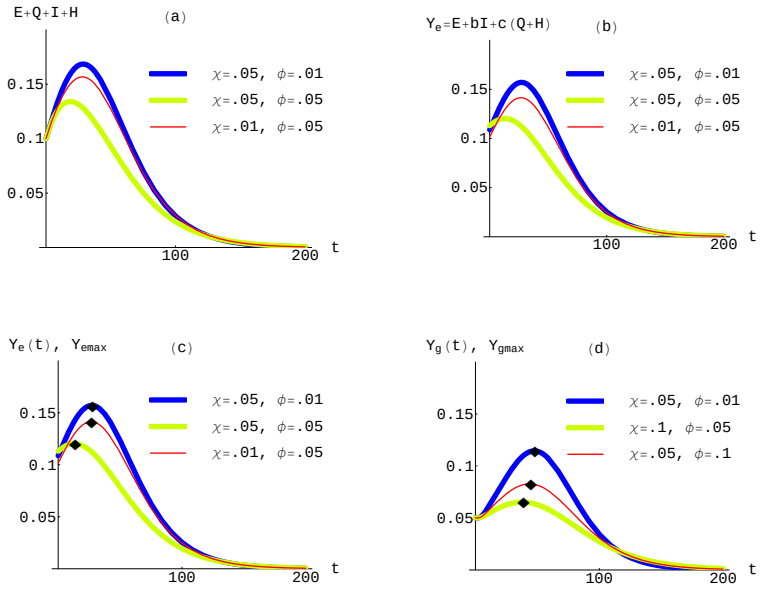

FIGURE 1. In (a) and (b), time plots of the usual sum $E+Q+I+H$ and the weighted sum Y_e are shown for various values of control parameters χ and ϕ. It shows that the two quantities provide qualitatively the same prediction. Figure 1(c) plots solution curves of $Y_e(t)$ and the corresponding values of Y_{emax} (diamonds) of the EDM (2) for the same sets of χ and ϕ as in (b). Figure 1(d) is similar to (c) but is for the GDM (3). They show that values calculated from the formulas in (10) and (18) for Y_{imax} match exactly the maximum values of $Y_i(t)$ $(i = e, g)$. Parameter values used are: $\alpha = 1/10$, $\delta = 1/10$, $\beta = 0.2$, $\rho = 0.6$, $S_0 = 0.9$, $E_0 = I_0 = 0.05$, and $Q(0) = H(0) = R(0) = 0$.

From $S(\infty) = S_0 - C$ and $Y_e(\infty) = 0$, we have $-\mathcal{R}_e(C + Y_{e0}) = \ln \frac{S_0 - C}{S_0}$, which yields the following equation for C:

$$C = S_0[1 - e^{-\mathcal{R}_e(C+Y_{e0})}]. \tag{11}$$

Next, we derive corresponding formulas for the GDM. In this case, we define the following quantity $Y_g(t)$ (g for gamma) as a measure for the epidemic size, which is a weighted average of all disease variables (see Appendix for the derivation):

$$Y_g(t) = \sum_{i=1}^{m} \Big(\tilde{a}_i E_i(t) + \tilde{b}_i Q_i(t)\Big) + \sum_{j=1}^{n} \Big(\tilde{c}_j I_j(t) + \tilde{d}_j H_j(t)\Big), \tag{12}$$

where

$$\tilde{a}_i = \frac{a_i}{a_1}, \quad \tilde{b}_i = \frac{b_i}{a_1}, \quad \tilde{c}_j = \frac{c_j}{a_1}, \quad \tilde{d}_j = \frac{d_j}{a_1}$$

with

$$\begin{aligned} a_i &= 1+\frac{1}{n}\Big(\frac{\rho}{1-\rho}\Big)\Big(\frac{m\alpha}{m\alpha+\chi}\Big)^{m-i+1}\sum_{k=1}^{n}\Big(\frac{n\delta}{n\delta+\phi}\Big)^{k},\\ b_i &= 1,\\ c_j &= \frac{n-j+1}{n}+\frac{1}{n}\Big(\frac{\rho}{1-\rho}\Big)\sum_{i=1}^{n-j+1}\Big(\frac{n\delta}{n\delta+\phi}\Big)^{i},\\ d_j &= \frac{n-j+1}{n}, \end{aligned} \tag{13}$$

for $i = 1, 2, \cdots, m$, $j = 1, 2, \cdots, n$. Then, Y_g satisfies the differential equation:

$$Y_g' = \beta\Big(S-\frac{1}{\mathcal{R}_g}\Big)\Big(I+(1-\rho)H\Big), \tag{14}$$

where $\mathcal{R}_g$ is the reproductive number for the GDM and is given by

$$\mathcal{R}_g = \frac{\beta}{\delta}\Big\{1-\rho\Big[1-\frac{1}{n}\Big(\frac{m\alpha}{m\alpha+\chi}\Big)^{m}\sum_{j=1}^{n}\Big(\frac{n\delta}{n\delta+\phi}\Big)^{j}\ \Big]\Big\}. \tag{15}$$

Using the S equation in (3) and the Y_g equation (14), we know that the solution of the GDM (3) satisfies the equation

$$S(t)+Y(t)-\frac{1}{\mathcal{R}_g}\ln S(t) = S_0+Y_{g0}-\frac{1}{\mathcal{R}_g}\ln S_0, \quad \text{for all} \quad t>0, \tag{16}$$

where S_0 and $Y_{g0} = \sum_{i=1}^{m}\Big(\tilde{a}_i E_{i0}+\tilde{b}_i Q_{i0}\Big)+\sum_{j=1}^{n}\Big(\tilde{c}_j I_{j0}+\tilde{d}_j H_{j0}\Big)$ are the initial values of the system (3). Hence, the preserved quantity for the GDM is $S(t)+Y_g(t)-\frac{1}{\mathcal{R}_g}\ln S(t)$. Using (16) and $Y_g(\infty)=0$, we can show that the final epidemic size $C = S_0 - S(\infty)$ satisfies the equation

$$C = S_0[1-e^{-\mathcal{R}_g(C+Y_{g0})}]. \tag{17}$$

In the case of $\mathcal{R}_g > 1$, the maximum value of $Y_g(t)$ occurs at some $t_m > 0$ and is given by

$$Y_{gmax} = S_0+Y_{g0}-\frac{1}{\mathcal{R}_g}\Big[1+\ln(\mathcal{R}_g S_0)\Big]. \tag{18}$$

As in the case of Y_e, we can show that Y_g provides the same qualitative information as the direct sum, $\sum_{i=1}^{m}(E_i+Q_i)+\sum_{j=1}^{n}(I_j+H_j)$, concerning the effect of various control measures for the model (3). Also, the value Y_{gmax} computed using the formula (18) is indeed the peak value of $Y_g(t)$ (see Figure 1(d)).

We remark that for the EDM and GDM, the final epidemic size formulas have the same structure (see (11) and (17)) and the maximum epidemic size formulas have the same structure (see (10) and (18)). In fact, if the initial values are identical, then the only difference in these formulas between the two models is in the reproductive number, $\mathcal{R}_e$ or $\mathcal{R}_g$. Since $\mathcal{R}_e$ and $\mathcal{R}_g$ depend on the control parameters χ and ϕ in different ways (see (7) and (15)), it is likely that the effect of χ and ϕ on the final or peak epidemic size for the two models will be different, as will be shown in the next section. Another important remark is that the peak size formula for the GDM may not have the form as shown in (18) if a different variable (other than the Y_g defined in (12)) is used.

3. **Comparison of model outcomes of the EDM and GDM.** In this section, we apply the formulas for the final and maximum epidemic sizes (see (10), (11), (17) and (18)) to investigate the differences in the assessment of disease control by the EDM and GDM. We use two examples to demonstrate this. One is to look at the influence of quarantine (χ) and isolation (ϕ) on the peak values of an epidemic (Y_{emax} and Y_{gmax}) predicted by the EDM and the GDM, and the other is to examine the effect of various combinations of control (χ and ϕ) on the reduction of the final epidemic size (C). We remark that, in the special case when $m = n = 1$, $Y_g(t) = Y_e(t)$ and $Y_{gmax} = Y_{emax}$.

Previous studies have suggested that the GDM tends to predict a larger $\mathcal{R}$ and a higher epidemic peak, while the EDM tends to predict a longer duration of an epidemic (e.g., see [10]). Our results, both numerical and analytic, show that this may not always be the case. Numerically, as illustrated in Figure 2, it is more likely to have $Y_{gmax} > Y_{emax}$ when χ is small (see (a) and (b)), whereas it is more likely to have $Y_{gmax} < Y_{emax}$ when ϕ is small (see (d) and (e)). We also observe that, although in (c) it seems true that the GDM predicts a higher peak and shorter duration then the EDM, the opposite is true in (f).

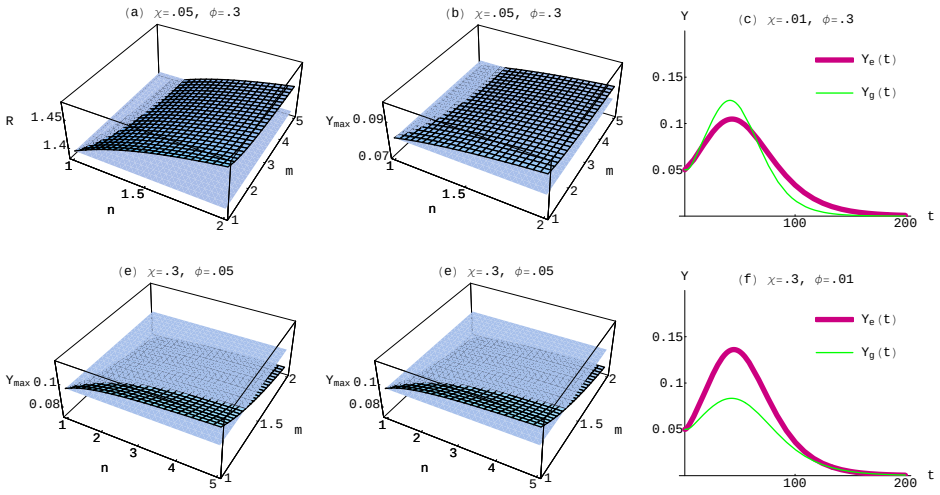

FIGURE 2. In (a),(b),(d),(e), the values of $\mathcal{R}_e$ and Y_{emax} (planes) are plotted for two sets of χ and ϕ, and the values of $\mathcal{R}_g$ and Y_{gmax} are plotted as functions of m and n (surfaces) for the same sets of χ and ϕ. We observe that, for most values of m and n, $Y_{gmax} > Y_{emax}$ when χ is small (see (a) and (b)), whereas $Y_{gmax} < Y_{emax}$ when ϕ is small (see (d) and (e)). Graphs (c) and (f) are time plots of $Y_e(t)$ and $Y_g(t)$ for $m = n = 3$ for the corresponding two sets of χ and ϕ, and $\alpha = 1/7$, $\delta = 1/10$, $\beta = 0.4$, and $\rho = 0.8$. We observe that, although in (c) it seems true that the GDM predicts a higher peak and shorter duration then the EDM, it is not the case in (f).

To examine analytically the observations illustrated in Figure 2, we consider the case in which the EDM and GDM have the same initial value $S_0 > 0$ and $Y_{e0} = Y_{g0} > 0$ with other initial values equal to zero. Then, from (10) and (18) we

have

$$Y_{gmax} - Y_{emax} = \frac{1}{\mathcal{R}_e}\Big[1 + \ln(\mathcal{R}_e S_0)\Big] - \frac{1}{\mathcal{R}_g}\Big[1 + \ln(\mathcal{R}_g S_0)\Big]. \tag{19}$$

Let

$$f(\mathcal{R}) = \frac{1}{\mathcal{R}}\Big[1 + \ln(\mathcal{R} S_0)\Big],$$

then (19) can be written as

$$Y_{gmax} - Y_{emax} = f(\mathcal{R}_e) - f(\mathcal{R}_g). \tag{20}$$

Recall that Y_{imax} occurs at some $t > 0$ only if $\mathcal{R}_i > 1$ $(i = e, g)$. This implies that, if $S_0 \approx 1$ (i.e., the initial fraction of infected is very small), then $\mathcal{R}_i S_0 > 1$. Thus,

$$f'(\mathcal{R}) = -\frac{\ln(\mathcal{R} S_0)}{\mathcal{R}^2} < 0,$$

and $f(\mathcal{R})$ decreases monotonically with $\mathcal{R}$. Then, from (20) we know that the sign of $Y_{gmax} - Y_{emax}$ is the same as the sign of $\mathcal{R}_g - \mathcal{R}_e$. Hence, it suffices to investigate how the parameters χ, ϕ, m, and n may affect the sign of $\mathcal{R}_g - \mathcal{R}_e$.

Let

$$F(m, \chi) = \Big(\frac{m\alpha}{m\alpha + \chi}\Big)^m, \quad G(n, \phi) = \frac{1}{n}\sum_{j=1}^{n}\Big(\frac{n\delta}{n\delta + \phi}\Big)^j.$$

Then $\mathcal{R}_g$ (see (15)) can be rewritten as

$$\mathcal{R}_g = \frac{(1-\rho)\beta}{\delta} + \frac{\rho\beta}{\delta} F(m, \chi) G(n, \phi).$$

Rewrite $F(m, \chi)$ as

$$F = \left(\frac{1}{\big(1 + \frac{1}{x}\big)^x}\right)^{\frac{x}{\alpha}}, \quad \text{with } \; x = \frac{m\alpha}{\chi}.$$

Then, it is easy to see that F is a decreasing function of $m \geq 1$ for all χ, as $\big(1 + \frac{1}{x}\big)^x$ is an increasing function of $x > 0$. Notice that G can be rewritten as

$$G(n, \phi) = \frac{\delta}{\phi}\left[1 - \Big(\frac{n\delta}{n\delta + \phi}\Big)^n\right],$$

and that $\big(\frac{n\delta}{n\delta+\phi}\big)^n$ is a decreasing function of n for all δ and ϕ (similar to F). Thus, G is an increasing function of n for all ϕ. Thus, $\mathcal{R}_g$ decreases with m and increases with n.

Recall that $\mathcal{R}_g = \mathcal{R}_e$ when $m = n = 1$. Also notice that the change of $\mathcal{R}_g$ with m is negligible if χ is small (i.e., $m\alpha/(m\alpha + \chi) \approx 1$), and that the change of $\mathcal{R}_g$ with n is negligible if ϕ is small (i.e., $n\delta/(n\delta + \phi) \approx 1$). Therefore, when χ is small, $\mathcal{R}_g$ is an increasing function of n and does not change much with m, which leads to $\mathcal{R}_e < \mathcal{R}_g$ for most m and n. When ϕ is small, $\mathcal{R}_g$ is a decreasing function of m and does not change much with n, which leads to $\mathcal{R}_e > \mathcal{R}_g$ for most m and n. Consequently, $Y_{gmax} > Y_{emax}$ when χ is small, and $Y_{gmax} < Y_{emax}$ when ϕ is small.

Next, we examine the discrepancies between the EDM and GDM by looking at the final epidemic size C. Notice that both (11) and (17) can be written in the form

$$C = S_0[1 - e^{-\mathcal{R}(C + Y_0)}] \tag{21}$$

with $\mathcal{R} = \mathcal{R}_e$, $Y_0 = Y_{e0}$ for the EDM and $\mathcal{R} = \mathcal{R}_g$, $Y_0 = Y_{g0}$ for the GDM. Equation (21) defines implicitly a curve of C as a function of $\mathcal{R}$. Since $\mathcal{R}_e$ and $\mathcal{R}_g$ depend on χ and ϕ in very different ways, the impact of χ and ϕ on C for the two models will also be different. This can be seen clearly in Figure 3.

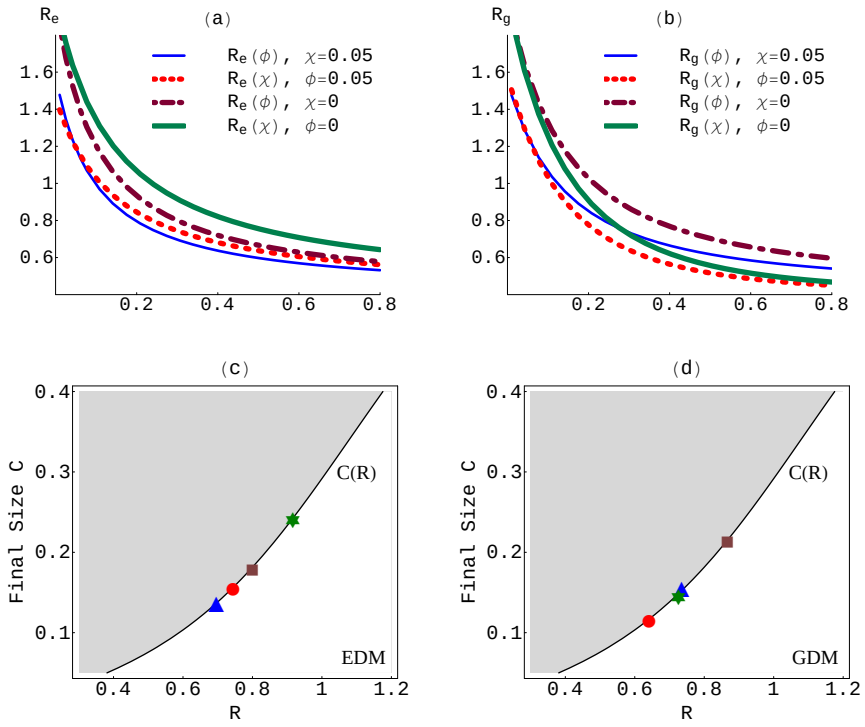

FIGURE 3. In (a) and (b), $\mathcal{R}_e$ and $\mathcal{R}_g$ are plotted either as a function of χ for a fixed value of $\phi = 0.05$ (thin line) or as a function of ϕ for a fixed value of $\chi = 0.05$ (thick line); (c) and (d) are contour plots of the equation $C - S_0\left[1 - e^{-\mathcal{R}(C+Y_0)}\right] = 0$ which determines a curve $C = C(\mathcal{R})$ for the final size. Here, $Y_0 = Y_{e0} = Y_{g0}$. Figure 3(c) is for the EDM and (d) is for the GDM with $m = n = 3$. We observe in (a) and (b) that the curves show different orders for $\mathcal{R}_e$ and $\mathcal{R}_g$, representing the different effect of a given control strategy on reducing the reproductive number predicted by the EDM and the GDM, respectively. In (c) and (d), the symbols on the curve mark the final sizes of C for four values of $\mathcal{R}$ determined by four sets of χ and ϕ: (i) $\chi = 0.05$, $\phi = 0.3$ (triangle), (ii) $\chi = 0.3$, $\phi = 0.05$ (circle), (iii) $\chi = 0$, $\delta = 0.3$ (square), and (iv) $\chi = 0.3$, $\phi = 0$ (star). Also, $\alpha = 1/7$, $\delta = 1/10$, $\beta = 0.2$, $\rho = 0.8$. The EDM predicts that the square strategy is more effective in reducing C, while the GDM predicts the opposite. Similarly, while the EDM predicts that the triangle strategy is much more effective than the star strategy, the GDM predicts that the effect of the two strategies are not very different. These observations suggest that the two models may provide dramatically different assessments of control programs.

In Figure 3, if we look at the two control programs represented by the square and the star, the EDM predicts that the square strategy is more effective in reducing the final epidemic size, while the GDM predicts the opposite. The same

problem is observed with the circle and the triangle. Also, if we look at the two strategies represented by the triangle and the star, then while the GDM predicts that the effect of the two strategies are not very different, the EDM predicts that the triangle strategy is much more effective than the star strategy. These observations suggest that the two models may provide dramatically different assessments of control programs.

4. **Conclusion.** This article focuses on two issues concerning the uses of mathematical models for assessing disease control programs. The first issue relates to the derivation (from the models) of quantities or measurements that can be used to evaluate control programs, and the second issue concerns the appropriateness of simple models for evaluating control programs. Two models, the EDM (2) and GDM (3), are considered to illustrate our approach. These two models are of $SEIR$ type with the inclusion of quarantine and isolation, and the EDM assumes an exponential distribution for the latent and infectious periods, whereas the GDM assumes a gamma distribution.

The concepts of final epidemic size and peak epidemic value have been widely used to describe the severity of an epidemic. However, analytic formulas of final and peak epidemic sizes for models with quarantine and isolation have not been available, and numerical observations often lead to biased or misleading predictions. In this paper, we derive these formulas and use them to examine the qualitative and quantitative differences between the EDM and GDM in model predictions on effectiveness of control measures.

We identified quantities (Y_e and Y_g) for the EDM and GDM that can be used to measure the peak epidemic size and in the description of final epidemic size. These quantities are the weighted sum of all disease variables (i.e., variables representing exposed and infectious individuals) and provide the same information as the sum of the disease variables. (It is not clear whether it is possible to derive similar formulas using the usual sum.) The formulas for the peak or maximum epidemic size (Y_{emax} and Y_{gmax}) allow us to examine analytically how the epidemics may be affected by various control programs described by the quarantine rate χ and isolation rate ϕ. We showed that either $Y_{emax} > Y_{gmax}$ or $Y_{emax} < Y_{gmax}$ is possible; that is, either the EDM or the GDM may predict a higher peak epidemic value. This contrasts with the previous finding that an exponentially distributed model tends to predict a smaller peak number of cases (see [10]).

We compared model predictions by the EDM and GDM using the formula for final epidemic size, which show substantial discrepancies between the two models regarding the effectiveness of disease control programs. For example, we considered several sets of quarantine and isolation strategies specified by values of χ and ϕ, and we found that, while the EDM predicts one strategy will be more effective than another one in reducing the final epidemic size, the GMD predicts the opposite outcome. This confirms our earlier finding that the simple model with exponentially distributed latent and infectious periods may not be appropriate to use in assessing disease control [4].

5. **Appendix.** In this appendix we present how to choose the variable that can be used as a measure for the epidemic intensity (for example, Y_e in the EDM or Y_g in the GDM).

Consider the system

$$\begin{aligned} S' &= -\beta \mathbf{b}\mathbf{x} S, \\ \mathbf{x}' &= \Pi \beta \mathbf{b}\mathbf{x} S - V\mathbf{x}, \\ R' &= \mathbf{w}\mathbf{x}. \end{aligned} \tag{22}$$

Some of the notations are adopted from [1]. Here, S denotes the fraction of susceptibles, $\mathbf{x} \in \mathbf{R}^n$ is a column vector whose components are fractions of infected individuals, and R denotes the fraction of recovered individuals. The background rate of disease transmission β is a constant, and $\mathbf{b} \in \mathbf{R}^n$ is a row vector whose components represent the relative transmission ability of the disease variables in $\mathbf{x}$. V is an $n \times n$ matrix describing the transition between infected classes as well as removals from infected classes; $\Pi \in \mathbf{R}^n$ is a row vector with the components representing the fractions of susceptibles going into the corresponding infected compartments on becoming infected; and $\mathbf{w} \in \mathbf{R}^n$ is a row vector whose components represent the rates at which infected individuals become recovered.

In the system (22), the force of infection $\lambda(\mathbf{x})$ and the reproductive number $\mathcal{R}$ are respectively

$$\lambda(\mathbf{x}) = \beta \mathbf{b}\mathbf{x} \qquad \text{and} \qquad \mathcal{R} = \beta \mathbf{b} V^{-1} \Pi. \tag{23}$$

Note that the components of the row vector $\beta \mathbf{b} V^{-1}$ describe the contribution of individuals in the disease classes (that are represented by components of $\mathbf{x}$) to the magnitude of $\mathcal{R}$. We use these components (scaled by $\mathcal{R}$) to define a new variable Y as:

$$Y = \frac{1}{\mathcal{R}} \beta \mathbf{b} V^{-1} \mathbf{x}. \tag{24}$$

That is, Y is a weighted sum of the disease variables, and the weight of each disease variable is determined by its contribution to $\mathcal{R}$. Therefore, it is reasonable to use Y as a measure for the epidemic intensity. It is easy to verify that Y satisfies the following differential equation:

$$Y' = \lambda(\mathbf{x}) \big(S - \frac{1}{\mathcal{R}} \big). \tag{25}$$

Example. In the EDM (2), we have $\mathbf{b} = (0, 0, 1, 1-\rho) \in \mathbf{R}^4$ (here $n = 4$),

$$\mathbf{x} = \begin{pmatrix} E \\ Q \\ I \\ H \end{pmatrix}, \ \Pi = \begin{pmatrix} 1 \\ 0 \\ 0 \\ 0 \end{pmatrix}, \ V = \begin{pmatrix} \chi + \alpha & 0 & 0 & 0 \\ -\chi & \alpha & 0 & 0 \\ -\alpha & 0 & \phi + \delta & 0 \\ 0 & -\alpha & -\phi & \delta \end{pmatrix}.$$

In this case, from (23), the force of infection is $\lambda(\mathbf{x}) = \beta \big(I + (1-\rho) H \big)$ and the reproductive number is the same as $\mathcal{R}_e$ given in (7). The variable defined in (24) with $\mathcal{R}$ replaced by $\mathcal{R}_e$ is exactly the variable Y_e given in (4), and the equation (25) yields the same differential equation for Y_e given in (6).

Acknowledgments This research is supported in part by the NSF and by the James S McDonnell Foundation.

REFERENCES

[1] J. Arino, F. Brauer, P. van den Driessche, J. Watmough, J. Wu, The basic reproduction number and a final size relation for general epidemic models, MBE. 4 (2), 159-175 (2007).
[2] G. Chowell, P. Fenimorea, M. Castillo-Garsowc, C. Castillo-Chavez. SARS outbreaks in Ontario, Hong Kong and Singapore: The role of diagnosis and isolation as a control mechanism. J. Theo. Bio. 224, 1-8 (2003).
[3] O. Diekmann, J. A. P. Heesterbeek. Mathematical epidemiology of infectious diseases: Model building, analysis and interpretation (Wiley Series in Mathematical and Computational Biology, 2000).
[4] Z. Feng, Z., D. Xu, H. Zhao. Epidemiological models with non-exponentially distributed disease stages and applications to disease control. Bull. Math. Biol. 69, 1511-1536 (2007).
[5] H. Hethcote, D. Tudor. Integral equation models for endemic infectious diseases. J. Math. Biol. 9, 37-47 (1980).
[6] M. Lipsitch, T. Cohen, B. Copper, et al, Transmission dynamics and control of severe acute respiratory syndrome. Science. 300, 1966-70 (2003).
[7] A. Lloyd. Realistic distributions of infectious periods in epidemic models. Theor. Pop. Biol. 60, 59-71 (2001).
[8] J. Ma, D. J. D. Earn. Generality of the final size formula for an epidemic of a newly invading infectious disease. Bull. Math. Biol. 68, 679-702 (2006).
[9] S. Riley, C. Fraser, C. A. Donnelly, A. C. Ghani, et al. Transmission dynamics of the etiological agent of SARS in Hong Kong-impact of public health interventions. Science. 300, 1961-1966 (2003).
[10] H. J. Wearing, P. Rohani, M. J. Keeling. Appropriate models for the management of infectious diseases. PLoS Medicine 2 (7) e174, 621-627 (2005).

Received on July 24, 2007. Accepted on August 5, 2007.

E-mail address: zfeng@math.purdue.edu