LETTERS IN BIOMATHEMATICS
An International Journal

Intercollegiate Biomathematics Alliance

RESEARCH ARTICLE

OPEN ACCESS

The Influence of Quarantine Before Obtaining a Partially Effective Preventive Measure

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ABSTRACT

We study an epidemic model for a generic infectious disease with an ongoing spread in a closed community. The disease is assumed to not cause additional mortality and without providing immunity. We also assume the availability of a preventive measure that is both scarce and only partially effective in reducing the infection risk. We analyze the model focusing on the effect of a class of susceptibles that chooses to quarantine itself from the epidemic while waiting for the preventive measure to be available. Of particular interest is the case when the model exhibits bi-stability between the disease-free equilibrium and an endemic state which indicates that the disease may persist even if the epidemic reproductive number is less than one. We investigate the conditions whereby increasing the quarantine rate eliminates the bi-stability scenario thereby improving the predictive value of the model when assessing whether the disease evolves toward an endemic state or not.

ARTICLE HISTORY
Received November 9, 2021
Accepted July 20, 2022

KEYWORDS
quarantine, partially effective, preventive measure, vaccination, bi-stability

1 Introduction

The ongoing SARS-CoV-2 pandemic intensified the research on respiratory infectious diseases and the related multitude of measures to counteract it (both medical and of social policy nature). In particular, diseases such as the common cold (caused by more than 200 strains of viruses according to the Center for Disease Control and Prevention) and the flu are of special importance because there is a possibility that SARS-CoV-2 will evolve to behave like one of these viruses: more benign but endemic with ongoing infection and re-infection (see Lavine et al., 2011, and references within). In such a scenario, a significant portion of the population (for example young people) will not have dangerous symptoms yet the disease may remain serious enough to motivate the desire to avoid it via medical or behavioral means. Various medically administered preventive measures exist for these diseases and new ones are continuously proposed such as vaccines or prophylactic treatments. Some of these measures have limited or unproven efficacy (see Smit et al., 2021, and references within). In general, one can expect partial effectiveness and limited duration of efficacy which, sometimes, varies from year to year. The flu vaccine is notorious in this regard as its efficacy can be quite low in a given epidemic season.

Preventive measures may have limited availability for the general public especially if they are new and prescription based only. The rapid creation and distribution of the vaccines against SARS-CoV-2 provide a convenient recent example. Initial limited quantity, logistic issues, and other problems made prioritization of these vaccines a necessity. There were many strategies designed to address the allocation of these resources. High priority groups included the medical and the emergency personnel, those working in high-density communities, people with certain underlying health conditions, older age groups, etc. These policies vary by country or, as is the case in the U.S.A., by state (Jain et al., 2021). Kiem et al. (2021) provide a comparative analysis of the impact of different prioritization strategies, vaccine effectiveness and how these can direct the policy of relaxation of restriction measures against transmission.

There are many models that, among other things, include vaccination as a feature (see Hethcote, 1998, 2000). These models are often used to assess intervention strategies for controlling an epidemic. A well-known quantity of interest in these models is the *epidemic reproductive number*, typically denoted by $\mathcal{R}_0$. This quantity is an estimation of the number of secondary infections caused by an infectious person in a susceptible population. If a vaccine or preventive measure is available, it will have the effect of reducing the value of this number. Usually, if $\mathcal{R}_0 < 1$, the model will predict that the epidemic will eventually end. Otherwise, if

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$\mathcal{R}_0 > 1$, one will expect a persistent endemic state in the long run. On the other hand, this dichotomy may not hold if the vaccine is only partially effective. In such a case, it is shown that, under certain parameter conditions, the epidemic may still evolve toward an endemic state even though $\mathcal{R}_0 < 1$. Mathematically this occurs in the form of two locally asymptotically stable equilibria (a disease-free state and an endemic state). This possibility has been observed in various models for both human and animal diseases (see Kribs-Zaleta and Martcheva, 2002; Kribs-Zaleta and Velasco-Hernandez, 2000; Dushoff et al., 1998; Greenhalgh et al., 2000; Huang et al., 1992; Arino et al., 2003, and references within). This bi-stability situation indicates that one needs to reduce the epidemic reproductive number below a threshold that is less than 1 to ensure a disease-free state. Therefore, we can view bi-stability as a situation that makes it difficult to predict the success of an intervention based on vaccination or any other form of preventive measure. From this point of view, it may be important to identify the conditions in the population that make this situation less likely.

The availability of a preventive measure with some level of scarcity brings an incentive for susceptible individuals to take drastic measures to avoid the infection while waiting their turn. This is because the waiting time may be short enough making the self-imposed restrictions demanded by quarantine both *possible and worthwhile*. How much of this behavior is present in the population is difficult to measure because it also depends on both subjective and objective factors such as: the fear perception of the disease symptoms, the possibility of working from home, living in very low population density areas, the waiting time until obtaining the preventive measure, etc. Several studies on behavioral changes that individuals undertake in response to the epidemic factors are provided by Poletti et al. (2009, 2012).

The purpose of this paper is to build a model that includes this class of individuals that are able to quarantine themselves from infection *before* obtaining the preventive measure. The main goal is to analyze the potential for this class to have a beneficial influence on the evolution of the epidemic. To this end, we first establish the conditions for the existence and stability of biologically feasible equilibria and the bi-stability between the disease-free equilibrium and an endemic state. Then we analyze the conditions on quarantine that can eliminate the bi-stability so that we can quantify the beneficial effect of this *quarantine until vaccine or prophylaxis* scenario. The model is for a generic (i.e., not pathogen specific) disease that is transmitted in a closed community over a relatively short period such that demographic factors (birth or natural death) can be neglected. We also assume that the disease does not provide immunity after recovery and does not cause additional mortality. An example of such a community could be a residential university campus. We assume that a partially effective preventive measure is available. In this paper, we understand this as any prophylactic drug therapy or vaccine given to a susceptible individual that has some effect in reducing the probability of infection.

The paper is structured as follows. In the following section, we introduce our model and show that the disease evolves toward a disease-free state, an endemic state, or a bi-stability scenario where the outcome is either a disease-free state or an endemic state depending on the initial conditions. In Section 3 we present several examples and identify the minimum level of quarantine that guarantees the elimination of the bi-stability scenario and discuss why this could be a desired objective. We conclude the paper with our thoughts on the implications and limitations of these results and ideas for further research.

2 The Model

We consider an epidemic model with the population split into four categories: susceptibles (S), individuals taking a preventive measure (V), the infected (I), and the susceptibles who quarantine themselves before taking the preventive measure (Q). We denote by λ the standard incidence infection rate. The effectiveness of the preventive measure is modeled by ξ with $0 < \xi < 1$ which acts as a reduction factor of the infection rate. The meaning of the remaining parameters is as follows: q is the rate of quarantine of the susceptibles before taking the preventive measure, v is the rate of susceptibles taking the preventive measure, α is the rate of quarantined individuals taking the preventive measure, δ is the rate at which the preventive measure is stopped or loses its effectiveness, and r is the natural recovery rate from the disease.

$$\begin{cases} S' = -\lambda \dfrac{SI}{S+I+V} - qS - vS + rI + \delta V, \\ V' = vS + \alpha Q - \lambda\xi \dfrac{VI}{S+I+V} - \delta V, \\ I' = \lambda \dfrac{SI}{S+I+V} + \lambda\xi \dfrac{VI}{S+I+V} - rI, \\ Q' = qS - \alpha Q. \end{cases} \tag{1}$$

In order to simplify, to an extent, the mathematical exposition, we will not analyze System (1) directly. Instead, we will use an equivalent system that has fewer variables and simpler equations.

2.1 The equivalent simplified model

First, notice that the total population remains constant as we can see from adding the equations of System (1): $S' + V' + I' + Q' = 0$. Denoting the total population by $K := S + V + I + Q$, one can reduce (1) to a system in three equations by replacing one of the state variables with the difference between K and the sum of the other three. This, however, still maintains the fractional terms that appear in the model. Instead, we will construct an equivalent system with three equations by using the following variable changes:

$$x := \frac{S}{S+I+V}, \qquad y := \frac{I}{S+I+V}, \qquad z := \frac{Q}{S+I+V}.$$

We prefer this approach since the resulting system contains only linear and quadratic terms. Notice that the fraction of the vaccinated individuals in the exposed (i.e., not quarantined) population becomes $\frac{V}{S+I+V} = 1 - x - y$. The relationship between the old and the new variables is given below:

$$S = \frac{Kx}{1+z}, \qquad I = \frac{Ky}{1+z}, \qquad Q = \frac{Kz}{1+z}, \qquad V = \frac{K(1-x-y)}{1+z}.$$

The equivalent system in x, y and z becomes

$$\begin{cases} x' = -\lambda xy - qx - vx + ry + \delta(1-x-y) - x(\alpha z - qx), \\ y' = \lambda xy + \lambda\xi y(1-x-y) - ry - y(\alpha z - qx), \\ z' = (qx - \alpha z)(1+z). \end{cases} \tag{2}$$

2.2 The reproductive number, the stability of the disease-free equilibrium, and the existence of endemic equilibria

We establish first the biological conditions that must be satisfied by the state variables of System (2). The invariant biologically feasible domain for this system is

$$\Omega := \left\{ (x,y,z) \,\middle|\, x \geq 0,\ y \geq 0,\ z \geq 0,\ x + y \leq 1 \right\}.$$

The last condition is due to the fact that x and y are fractions of the population outside quarantine (i.e., $x + y = \frac{S+I}{S+I+V} \leq 1$). The reduced model (2) always has a disease-free equilibrium (DFE) given by

$$\bar{x} = \frac{\delta}{\delta + q + v}, \qquad \bar{y} = 0, \qquad \bar{z} = \frac{\delta q}{\alpha(\delta + q + v)}.$$

Any possible endemic state can be written in a more compact form as

$$x^* = \frac{A}{\lambda}, \qquad y^* = \frac{A(1-\xi) + \lambda\xi - r}{\lambda\xi}, \qquad z^* = \frac{qA}{\lambda\alpha},$$

where A is any feasible root of

$$h(A) := (1-\xi)A^2 + \left[\xi(\lambda + q + r + v) + \delta - 2r\right]A - r(\delta + \lambda\xi - r).$$

The necessary conditions on the roots of $h(A)$ are those that will cause x^*, y^* and z^* to be in the feasible domain Ω. These conditions require $A > 0$ and $\frac{r-\lambda\xi}{1-\xi} < A < r$. The last inequality also requires $r < \lambda$. Altogether, the feasibility condition on the value of A corresponding to any possible endemic equilibrium (EE) is

$$A > 0 \qquad \text{and} \qquad \frac{r - \lambda\xi}{1-\xi} < A < r < \lambda. \tag{3}$$

We now proceed to analyze the existence and the local stability of equilibria of System (2). For the latter we will use the Routh-Hurwitz theorem (Gradshteyn and Ryzhik, 2007). Among the results presented below, we will show that the epidemic reproductive number is

$$\mathcal{R}_0 := \frac{\lambda\left[\delta + \xi(q+v)\right]}{r(\delta + q + v)}.$$

It is more convenient to formulate the first theorem and its proof as a classification by thresholds of the recovery rate r and the infection rate λ. To this end, in order to simplify the exposition, we define first the following quantities:

$$T_1 := \lambda\xi + \delta,$$

$$T_2 := \frac{\delta + \xi(\lambda + q + v)}{2 - \xi}, \qquad \lambda^* := \frac{(q + v + \delta)\left[\xi(q + v) + \delta\right]}{\xi(1 - \xi)(q + v)},$$

$$T_3 := \frac{\lambda\left[\xi(q + v) + \delta\right]}{q + v + \delta}, \qquad r_1 := \frac{\lambda\xi + \delta + (2 - \xi)(q + v) - 2\sqrt{(1 - \xi)(q + v)(\lambda\xi + \delta + q + v)}}{\xi},$$

$$T_4 := \frac{\xi(\lambda - q - v) - \delta}{\xi}, \qquad r_2 := \frac{\lambda\xi + \delta + (2 - \xi)(q + v) + 2\sqrt{(1 - \xi)(q + v)(\lambda\xi + \delta + q + v)}}{\xi}.$$

Notice also that $\mathcal{R}_0 = \frac{T_3}{r}$ and we also define $\mathcal{R}_0{}^* := \frac{T_3}{r_1}$. This will allow us to re-state and discuss our results in a more biologically meaningful form.

Theorem 2.1. *The biologically feasible equilibria for System (2) occur according to the following conditions:*

- *If $r < T_3$, then the DFE is unstable and there exists a unique EE.*
- *If $\lambda > \lambda^*$ and $T_3 < r < r_1$, then the DFE is locally asymptotically stable and there are two EE.*
- *In all other cases the DFE is stable and there are no EE. That is, when either $T_3 < r < r_1$ and $\lambda < \lambda^*$ or $r_1 < r$.*

Proof. We begin with establishing the stability condition of the disease-free equilibrium, which is straightforward, followed by the analysis of the existence of endemic equilibria satisfying condition (3).

The disease-free equilibrium

The Jacobian of System (2) evaluated at the DFE is

$$\begin{bmatrix} -\dfrac{q\left[1 - \bar{x}(1 - \bar{x})\right] + v}{1 - \bar{x}} & r - \lambda\bar{x} - \dfrac{\bar{x}(q + v)}{1 - \bar{x}} & -\dfrac{q\bar{x}^2}{\bar{z}} \\ 0 & \lambda\left[\bar{x} + \xi(1 - \bar{x})\right] - r & 0 \\ q(1 + \bar{z}) & 0 & -\dfrac{q\bar{x}(1 + \bar{z})}{\bar{z}} \end{bmatrix}.$$

This is obtained substituting α and δ from the identities

$$\alpha = \frac{q\bar{x}}{\bar{z}}, \qquad \delta = \frac{\bar{x}(q + v)}{1 - \bar{x}}.$$

The second row of the matrix has only one non-zero entry positioned on the main diagonal. Hence, it is an eigenvalue denoted by

$$e_1 := \lambda\bar{x} + \lambda\xi(1 - \bar{x}) - r.$$

The other two eigenvalues are given by a 2×2 sub-matrix obtained from eliminating the second row and the second column of the Jacobian. The trace and the determinant of this sub-matrix are

$$\text{trace} = -\frac{\left[\bar{z} + \bar{x}(1 - \bar{x})\right] + v\bar{z}}{\bar{z}(1 - \bar{x})} < 0,$$

$$\det = \frac{q\bar{x}(1 + \bar{z})(q + v)}{\bar{z}(1 - \bar{x})} > 0.$$

These two inequalities show that the eigenvalues of the sub-matrix have negative real part. Hence the DFE is locally asymptotically stable whenever the first eigenvalue is negative, i.e., $e_1 < 0$. This is equivalent to $\frac{\lambda[\delta + \xi(q+v)]}{r(\delta + q + v)} < 1$. Since the left side of this inequality is $\mathcal{R}_0$, as expected, the local stability condition of the DFE can be written as $\mathcal{R}_0 < 1$.

The endemic equilibria

Consider the quadratic $h(A)$ whose roots identify the possible endemic equilibria. These are

$$\begin{aligned} A_1 &:= \frac{1}{2(1-\xi)}\left[-\xi(\lambda+q+r+v)+2r-\delta-\sqrt{f(r)}\right], \\ A_2 &:= \frac{1}{2(1-\xi)}\left[-\xi(\lambda+q+r+v)+2r-\delta+\sqrt{f(r)}\right]. \end{aligned} \tag{4}$$

where

$$f(r) := \xi^2 r^2 - 2\xi\left[\lambda\xi+\delta+(2-\xi)(q+v)\right]r + \left[\delta+\xi(\lambda+q+v)\right]^2.$$

In what follows we establish the existence conditions of the roots of $h(A)$ satisfying the feasibility condition (3). This entails two aspects: ensuring that the roots are real and comparing them with the bounds shown in this condition. To this end, we take advantage of the predictable shapes of the graphs of $h(A)$ and $f(r)$ which are both quadratic functions. For example, the sign of the first derivative of these functions can localize various points on either the decreasing or the increasing branch of these parabolas. We will also use Vieta's formulas for the roots of a quadratic which state that if A_1 and A_2 are the roots of $mA^2+nA+p=0$ with $m\neq 0$ then

$$A_1+A_2=-n/m, \qquad \text{and} \qquad A_1A_2=p/m.$$

First, notice that $h(A)$ is a parabola opened upward since the leading coefficient $1-\xi$ is positive. We have two general cases depending on the sign of the constant term $h(0)$.

Case 1: $r < T_1$

This implies that $h(0)<0$ and the graph of $h(A)$ intersects the horizontal axis at a positive and a negative coordinate. Therefore $h(A)$ has two real roots with $A_1A_2<0$. From (4) we see that $A_1<A_2$ which means $h(A)$ has a unique positive real root equal to A_2. We now establish the conditions on A_2 that satisfy the feasibility criteria (3). Notice that

$$h(r)=r\xi(q+v)>0$$

which implies $A_2<r$ because $h(A)<0$ on the interval $(0,A_2)$. The left bound on A_2 is trivially satisfied if $r<\lambda\xi$ which also implies $r<\lambda$. Otherwise, if $\lambda\xi<r$, the left bound condition on A_2 is equivalent to

$$h\left(\frac{r-\lambda\xi}{1-\xi}\right)=\left(\frac{\xi}{1-\xi}\right)\left\{r(q+v+\delta)-\lambda\left[\xi(q+v)+\delta\right]\right\}<0,$$

which is true if and only if $r<T_3$. Notice also that $r<T_3$ is equivalent to $\mathcal{R}_0>1$ which implies that the Disease Free Equilibrium is unstable. It is also easy to see that $T_3<\lambda$ always. Hence if $r<\lambda\xi$ or $\lambda\xi<r<T_1$ and $r<T_3$ we have the situation where the DFE is unstable and there exists a unique endemic state. On the other hand,

$$T_3-\lambda\xi=\frac{\lambda\delta(1-\xi)}{q+v+\delta}>0$$

so $\lambda\xi<T_3$ always. Therefore this case can be summarized as follows:

- If $r<T_1$ and $r<T_3$ there is a unique endemic equilibrium and the DFE is unstable.
- If $r<T_1$ and $r>T_3$ there is no feasible endemic equilibrium and the DFE is locally asymptotically stable.

Case 2: $r > T_1$

In this case $h(0)>0$ and $A_1A_2>0$. Hence $h(A)$ either has no real roots (if its discriminant is negative) or it has two real roots both positive or both negative. We shall establish under what conditions the positive real roots exist and also satisfy the feasibility condition (3). The discriminant of $h(A)$, seen as a function in r, has two positive real roots r_1 and r_2 as defined earlier. $f(r)$ is also a parabola in r opened upward since its leading coefficient ξ^2 is positive. Hence $f(r)>0$ and, therefore $h(A)$ has real roots, provided that

$$0<r<r_1 \qquad \text{or} \qquad r_2<r. \tag{5}$$

Furthermore, $A_1+A_2>0$ provided that $r>T_2$. Together with $A_1A_2>0$, it follows that the roots of $h(A)$ are positive if $r>T_2$. Turning to the feasibility condition (3), recall that it requires $\lambda>r$. This implies that $h'(r)=(\lambda+q-r+v)\xi+\delta>0$ and, together with $h(r)=r\xi(q+v)>0$, if follows that r is the horizontal coordinate of a point on the positive and increasing branch of $h(A)$. This implies $A_1<A_2<r$. This satisfies the right-hand side bound of the feasibility condition (3). For the left-hand side bound we distinguish two sub-cases:

Case 2.1: $h\left(\frac{r-\lambda\xi}{1-\xi}\right) < 0$

This is equivalent to $r < T_3$ and it places this bound between the roots of of $h(A)$, i.e. $A_1 < \frac{r-\lambda\xi}{1-\xi} < A_2$. This leads to, again, a unique feasible endemic state with $A = A_2$. However, we need to verify the other feasibility conditions (5) for r that ensure the existence of real roots for $h(A)$. First notice that $T_3 > T_1$ is equivalent to $\lambda > \frac{q+v+\delta}{1-\xi}$. This implies $T_3 > T_2$ because this is equivalent to

$$\lambda > \frac{(q+v+\delta)\big[\xi(q+v)+\delta\big]}{(1-\xi)\big[\xi(q+v)+2\delta\big]} \qquad \frac{(q+v+\delta)\big[\xi(q+v)+\delta\big]}{(1-\xi)\big[\xi(q+v)+2\delta\big]} < \frac{q+v+\delta}{1-\xi}.$$

$T_3 > T_1$ also implies $T_1 > T_2$ since it is equivalent to

$$\lambda > \frac{q+v+\delta}{1-\xi} - \frac{\delta}{\xi(1-\xi)}.$$

Another computation shows that $f(T_1) > 0$ and $f(T_3) > 0$ since

$$f(T_1) = \big[\lambda\xi^2 + (\delta+q+v-\lambda)\xi - \delta\big]^2,$$
$$f(T_3) = \frac{\big[\lambda(q+v)\xi^2 - (q+v)(\lambda-q-v-\delta)\xi + \delta(q+v+\delta)\big]^2}{(q+v+\delta)^2}.$$

Furthermore, $f'(T_1) < 0$ and $f'(T_3) < 0$ since

$$f'(T_1) = -2\xi\big[(1-\xi)(\lambda\xi+\delta) + (2-\xi)(q+v)\big],$$
$$f'(T_3) = -\frac{2\xi^2(1-\xi)(q+v)}{q+v+\delta}\left[\lambda - \frac{q+v+\delta}{1-\xi}\right] - 2\xi\big[\delta + 2(q+v)\big].$$

This shows, due to the geometry of the graph of $f(r)$, that $T_2 < T_1 < T_3 < r_1$. This case can be summarized as: if $T_1 < r < T_3$ and $\lambda > \frac{q+v+\delta}{1-\xi}$ then $A = A_2$ corresponds to a unique feasible endemic state and the DFE is unstable. So *Case 1* and *Case 2.1* combine as follows: if $r < T_3$ then the DFE is unstable and there exists a unique positive endemic state. This proves the first part of the theorem.

Case 2.2: $h\left(\frac{r-\lambda\xi}{1-\xi}\right) > 0$

This implies $r > T_3$ and either $A_1 < A_2 < 0$ or $0 < A_1 < A_2$. In other words, we have no endemic state in the feasible interval or we may have two of them. We analyze the conditions when we can have two endemic states. This also requires $h'\left(\frac{r-\lambda\xi}{1-\xi}\right) < 0$ which implies $r < T_4$. This is because the left bound of condition (3) must be on the decreasing branch of $h(A)$. Furthermore $T_4 > T_3$ implies

$$\lambda > \lambda^* = \frac{(q+v+\delta)\big[\xi(q+v)+\delta\big]}{\xi(1-\xi)(q+v)}$$

which, in turn, implies $f(T_4) < 0$. It also implies $f'(T_3) < 0$ because this is equivalent to

$$\lambda > \frac{(q+v+\delta)\big[\xi(q+v)+\delta\big]}{\xi(1-\xi)(q+v)} - \frac{2(q+v+\delta)}{\xi(1-\xi)(q+v)}.$$

Hence the interval of existence for two positive endemic states is

$$T_3 < r < r_1.$$

Notice also that $\lambda^* > \frac{q+v+\delta}{1-\xi}$ which means $T_1 < T_3$. Also, in this interval, the DFE is locally asymptotically stable which suggests bi-stability between DFE and an endemic state. This proves the remaining part of the theorem. □

2.3 The stability of the endemic equilibria

The stability of an endemic steady state is difficult to establish in general. However, we conjecture that the unique EE is locally asymptotically stable whenever it exists and, when two EE exist, the one with $A = A_1$ is unstable and the one with $A = A_2$ is locally asymptotically stable leading to bi-stability between the DFE and EE. In what follows we establish this result subject to some additional sufficient conditions. Checking all Routh-Hurwitz conditions for the Jacobian is unfeasible. Instead, we will use an indirect method by using an additional matrix whose eigenvalues are related to the eigenvalues of the Jacobian. We summarize these results in the following:

Theorem 2.2. *The endemic state with $A = A_1$ is unstable whenever it exists. If $\delta > r$ or $\lambda > \frac{(r-\delta)(\delta+q+v)}{\delta}$ the endemic state with $A = A_2$ is locally asymptotically stable whenever it exists.*

Proof. Replacing the x^*, y^*, and z^* with their corresponding values in terms of A we obtain the following Jacobian matrix denoted by $J(A)$:

$$J(A) = \begin{bmatrix} -\frac{q}{\lambda}(\lambda - A) - \frac{1-\xi}{\xi}\left(A - \frac{r-\lambda\xi}{1-\xi}\right) - (\delta + v) & -A + r - \delta & -\frac{A\alpha}{\lambda} \\ \frac{1-\xi}{\lambda\xi}\left(A - \frac{r-\lambda\xi}{1-\xi}\right)[q + \lambda(1-\xi)] & -(1-\xi)\left(A - \frac{r-\lambda\xi}{1-\xi}\right) & -\frac{\alpha(1-\xi)}{\lambda\xi}\left(A - \frac{r-\lambda\xi}{1-\xi}\right) \\ q\left(1 + \frac{qA}{\lambda\alpha}\right) & 0 & -\frac{\alpha\lambda+qA}{\lambda} \end{bmatrix}.$$

It is easy to see that the trace of $J(A)$ is negative since each of its entries is negative following from the feasibility condition (3). The determinant is

$$\det(J(A)) = -\frac{1-\xi}{\lambda\xi}(Aq + \lambda\alpha)\left(A - \frac{r-\lambda\xi}{1-\xi}\right)\left[2(1-\xi)A + \xi(\lambda + q + r + v) + \delta - 2r\right].$$

It follows that the determinant is negative provided that

$$A > \frac{2r - \delta - \xi(\lambda + q + r + v)}{2(1-\xi)}.$$

However the right hand side of the above inequality is the horizontal coordinate of the minimum of $h(A)$ since

$$h'\left(\frac{2r - \delta - \xi(\lambda + q + r + v)}{2(1-\xi)}\right) = 0.$$

Therefore this expression is between the two roots A_1 and A_2. Hence we always have a negative determinant in the case $A = A_2$ and a positive one if $A = A_1$. This proves the endemic equilibrium with $A = A_1$ is unstable whenever it exists. Denote now by e_1, e_2, and e_3 the eigenvalues of $J(A_2)$ and let's assume, without loss of generality, that $R(e_1) \le R(e_2) \le R(e_3)$ where $R(e_i)$ denotes the real part of e_i. Since all possible eigenvalues come in conjugate pairs, it follows that at least one eigenvalue must be real. We established, from the signs of the trace and the determinant of $J(A_2)$, that

$$e_1 + e_2 + e_3 < 0 \qquad \text{and} \qquad e_1e_2e_3 < 0.$$

The second inequality implies that there must be at least one eigenvalue that is real with a negative real part. If all three have a negative real part then the endemic equilibrium with $A = A_2$ is stable and the proof is done. Otherwise, let's assume that there is at least one eigenvalue with a positive real part. Taking into account the ordering assumption above it follows that e_1 must be real and $R(e_1) < 0$ and the other two have both positive or both negative real parts. Since we already assumed a positive one then they are both positive. Then, $R(e_2 + e_3) > 0$ and, from $e_1 + e_2 + e_3 < 0$, we also have

$$R(e_1 + e_2) \le -R(e_3) < 0 \qquad \text{and} \qquad R(e_1 + e_3) \le -R(e_2) < 0.$$

Li and Wang (1998) provide a criterion for the stability of matrices using their second compound additive version. Specifically, given the square matrix

$$\begin{bmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ a_{31} & a_{32} & a_{33} \end{bmatrix}$$

with eigenvalues e_1 , e_2, e_3, its second additive compound is

$$\begin{bmatrix} a_{11} + a_{22} & a_{23} & -a_{13} \\ a_{32} & a_{11} + a_{33} & a_{12} \\ -a_{31} & a_{21} & a_{22} + a_{33} \end{bmatrix}$$

with eigenvalues $e_1+e_2, e_1+e_3, e_2+e_3$. In our case, the second additive compound of the Jacobian denoted by $F(A)$ is

$$\begin{bmatrix} -\frac{q}{\lambda}(\lambda-A)-(\delta+v)-\frac{1-\xi^2}{\xi}\left(A-\frac{r-\lambda\xi}{1-\xi}\right) & -\frac{\alpha(1-\xi)}{\lambda\xi}\left(A-\frac{r-\lambda\xi}{1-\xi}\right) & \frac{A\alpha}{\lambda} \\ 0 & -\frac{1-\xi}{\xi}\left(A-\frac{r-\lambda\xi}{1-\xi}\right)-(q+v+\alpha+\delta) & -A-\delta+r \\ -q\left(1+\frac{qA}{\lambda\alpha}\right) & \frac{1-\xi}{\lambda\xi}\left(A-\frac{r-\lambda\xi}{1-\xi}\right)\left[\lambda(1-\xi)+q\right] & -(1-\xi)\left(A-\frac{r-\lambda\xi}{1-\xi}\right)-\left(\frac{Aq}{\lambda}+\alpha\right) \end{bmatrix}.$$

Notice that, since e_1 is real and e_2 and e_3 are either real or complex conjugates, then e_2+e_3 must be real. Furthermore

$$(e_1+e_2)(e_1+e_3)(e_2+e_3) = \det\big(F(A_2)\big).$$

If the determinant of $F(A_2)$ is negative, then $R(e_2+e_3) < 0$ which contradicts our assumption. Therefore all eigenvalues of $J(A_2)$ will have negative real part and this equilibrium is locally asymptotically stable. Looking at the sign of the entries of $F(A_2)$ we see that its determinant is negative whenever $-A_2-\delta+r<0$. This is trivially satisfied if $\delta > r$. Otherwise, assuming $\delta < r$, another sufficient condition for stability is $h(r-\delta) < 0$ which implies $A_1 < r-\delta < A_2$. This condition is equivalent to $\lambda > \frac{(r-\delta)(\delta+q+v)}{\delta}$ which, together with $\lambda > \lambda^*$, implies a level of infection rate above a certain threshold. □

The condition $\delta > r$ may or may not be realistic depending on the type of preventive measure used. The condition can be written as $\frac{1}{\delta} < \frac{1}{r}$. This translates into the assumption that the duration of taking the preventive measure (or the duration of effectiveness in the case of vaccines) is less than the duration of the disease itself. For actual vaccines, this is unrealistic. For example, the flu vaccine is effective up to a year while the disease takes about 2-3 weeks. If, however, we apply the model to prophylactic measures that are taken for several days the protection of such a measure may be short lived. Theorem 2.1 can be restated in a more biologically meaningful form using the notation $\mathcal{R}_0{}^* = \frac{T_3}{r_1}$ and recalling that the epidemic reproductive number is $\mathcal{R}_0 = \frac{T_3}{r}$:

Theorem 2.3. *The biologically feasible equilibria for System (2) occur according to the following conditions:*

- *If $\mathcal{R}_0 > 1$, then the DFE is unstable and there exists a unique EE.*
- *If $\lambda > \lambda^*$ and $\mathcal{R}_0{}^* < \mathcal{R}_0 < 1$, then the DFE is locally asymptotically stable and there are two EE.*
- *In all other cases the DFE is stable and there is no EE. That is, when either $\mathcal{R}_0 < 1$ but with $\lambda < \lambda^*$ or $\mathcal{R}_0 < \mathcal{R}_0{}^*$.*

As mentioned earlier, the reproductive number $\mathcal{R}_0$ represents the expected number of secondary cases of infection caused by a typical infected person in a susceptible population. Similarly, we can view $\mathcal{R}_0{}^*$ as a lower bound on $\mathcal{R}_0$ above which the bi-stability between the two endemic states happens. In other words, if the number of secondary cases of infection is less than 1 but exceeds R_0^* an endemic state is still possible even though the disease-free state is locally asymptotically stable.

3 The Effect of Increasing the Quarantine in a Bi-Stability Environment

In the evolution of the epidemic, the existence of bi-stability between the disease-free state and an endemic state can be detrimental. This is due to multiple reasons. First of all, the bi-stability implies that the disease may be endemic despite the epidemic reproductive number being less than one. Often the reduction of the reproduction number is the most immediate way of trying to control the infection spread since it is a quantity easy to compute in most models. Secondly, the long-term evolution of the disease depends on the initial conditions (i.e., the population size in each category) and it is not clear which population size combinations lead the evolution of the epidemic toward an endemic state. Thus, in addition to ensuring that the reproductive number is less than one (or, alternatively, $r > T_3$), an additional goal could be the reduction or the elimination of the bi-stability interval for the recovery rate r. We will analyze in this section to what extent the quarantine of susceptibles before taking the preventive measure can achieve this goal.

Suppose the parameter values satisfy the bi-stability case, that is $T_3 < r < r_1$ and $\lambda > \lambda^*$. We want to analyze the monotonicity of these thresholds with respect to the quarantine rate q. First notice that

$$\frac{dT_3}{dq} = -\frac{\lambda\delta(1-\xi)}{(q+v+\delta)^2} < 0 \qquad \text{for all } q > 0.$$

Furthermore

$$\frac{d\lambda^*}{dq} = \frac{\xi(q+v)^2-\delta^2}{\xi(1-\xi)(q+v)^2}.$$

Table 1: Impact of varying the rate of quarantine (q) and the effectiveness of a preventive measure (ξ) corresponding to a short course (10 days) of Tamiflu ($\delta = 1/10$), some scarcity of the preventive measure ($v = 0.03$), and a relatively high infection rate ($\lambda = 6$). The shaded values indicate $q = q^*$.

ξ	q	T_3	r_1	$\mathcal{R}_0{}^*$	λ^*	Interpretation
	0.50	1.46	1.75	0.834	2.02	For high effectiveness of the
0.1	2.00	0.85	0.90	0.944	3.53	preventive measure, high quarantine
	4.25	0.723		1	6.00	is needed to eliminate the bi-stability.
	0.50	3.48	3.87	0.899	1.74	
0.5	1.00	3.27	3.46	0.945	2.70	—
	2.66	3.11		1	5.99	
	0.05	5.733	5.739	0.9989	4.30	For low effectiveness of the
0.9	0.2	5.582	5.585	0.9993	4.89	preventive measure, low quarantine is
	0.33	5.53		1	6.02	needed to eliminate the bi-stability.

This shows that $\lambda^*(q)$ is decreasing for $q < q_1 := \frac{\delta}{\sqrt{\xi}} - v$ and increasing for $q > q_1$. Finally

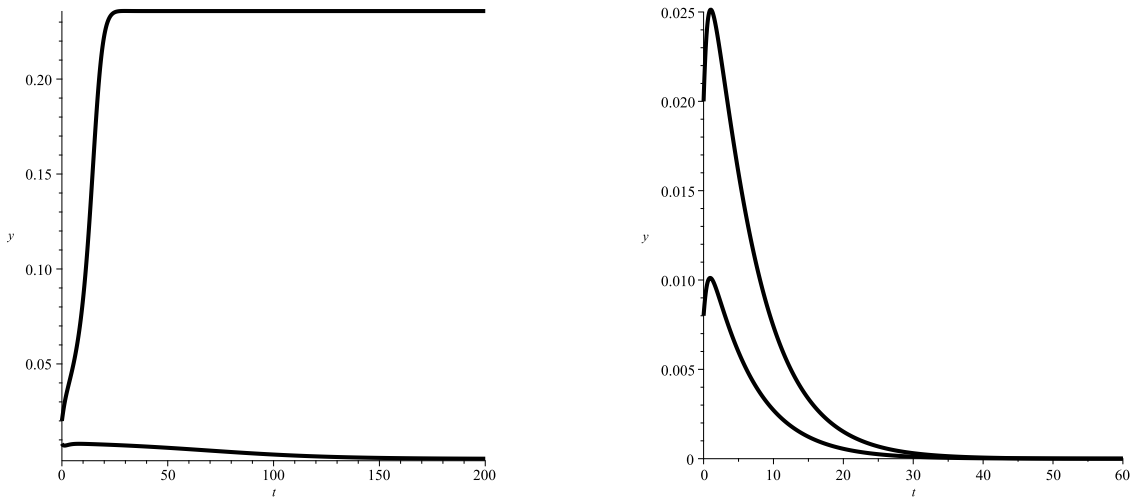
$$\frac{dr_1}{dq} = \frac{2-\xi}{\xi} - \frac{1-\xi}{\xi}\frac{\lambda\xi + \delta + 2q + 2v}{\sqrt{(1-\xi)(q+v)(\lambda\xi+\delta+q+v)}}.$$

One can then show, after some computation that we omit here, that r_1 is decreasing for $0 < q < q_2 := \frac{(1-\xi)(\lambda\xi+\delta)}{\xi} - v$ and increasing for $q > q_2$. From these inequalities, we can see that it is not immediately obvious whether increasing the quarantine rate q is beneficial in the sense defined above (that of reducing the size of the bi-stability interval for r). More generally, it is also not clear whether increasing q "moves" against the bi-stability condition. For example, the fact that r_1 increases for $q > q_2$ suggests that the bi-stability interval would actually increase with higher rates of quarantine. Such an unexpected and counter-intuitive effect can happen under other circumstances such as when risk-taking behavior in response to treatment and/or vaccination is taken into account (see Sega et al., 2015; Maxin et al., 2016). However, this is not the case for the model we analyze here. Below we show that, by the time r_1 will increase with q, the other necessary condition of bi-stability, $\lambda > \lambda^*$ will no longer hold. To see this, first, notice that $q_1 < q_2$ in the bi-stability regimen. The opposite inequality would conflict with $\lambda > \lambda^*$. Furthermore,

$$\lambda^*|_{q=q_2} - \lambda = \frac{2\delta\left[\lambda\xi(1-\xi) + \delta(1-\xi/2)\right]}{\xi(1-\xi)^2(\lambda\xi+\delta)} > 0.$$

Thus, increasing the quarantine rate q will make the bi-stability between the disease-free state and the endemic state less likely. Moreover, in some situations, for certain values of q, the bi-stability interval range for r will reduce to zero (i.e., $r_1 = T_3$). This means that, if quarantine reaches a certain level, then the bi-stability scenario will no longer happen for any level of recovery/treatment r and the condition $r > T_3$ will be sufficient to reach a disease-free state. Let us also denote by q^* the level of quarantine of susceptibles for which $T_3 = r_1$ (i.e., $\mathcal{R}_0{}^* = 1$). It is the level of quarantine for which the lower bound $\mathcal{R}_0{}^*$ on the reproductive number is equal to 1, making impossible a bi-stability scenario with $\mathcal{R}_0 < 1$. Even more generally, q^* is the quarantine threshold that causes this model to behave like a classical one whereby the epidemic evolves toward only two outcomes: either a disease-free state when $\mathcal{R}_0 < 1$ or an endemic state when $\mathcal{R}_0 > 1$.

For the remainder of this section, we will consider several examples where increasing the quarantine rate q can eliminate the bi-stability between the DFE and an endemic state. We start with a case somewhat related to influenza where the preventive measure is the drug Tamiflu. This medicine can be used both as treatment or as prophylactic (source `www.fda.gov`). Treatment is usually given for 5 days and it can be incorporated in the model as an augmenting factor of the recovery rate r. When given as a prophylactic, it can be administered from as little as 10 days which can be increased up to 6 weeks. The protection holds for the duration of taking it. For our first set of numerical examples let us consider a short course of Tamiflu of 10 days (i.e., $\delta = \frac{1}{10}$). We will choose a relatively low value for $v = 0.03$ to indicate some scarcity of the preventive measure. This corresponds to an expected time of one month in the susceptible class until being able to take the preventive measure. In the case of vaccination against SARS-CoV-2, this figure varied widely across countries and states in the U.S.A. Let's also consider, first, a relatively high infection rate $\lambda = 6$. In Table 1 we show the values of the r bi-stability thresholds for various levels of preventive measure effectiveness and levels of quarantine. To see how increasing the quarantine rate q may eliminate the bi-stability let's consider the example in the fifth row of Table 1 with $\xi = 0.5$ and $q = 1$ and let's choose $r = 3.3$ which falls in the bi-stability range for this case. As we can see in Figure 1a, the ratio of infected $y(t)$ either goes to zero or approaches an endemic state (depending on initial conditions). Increasing the quarantine rate to $q = 2$, the recovery rate $r = 3.3$ falls out of the bi-stability range and we



(a) (b)

Figure 1: Model simulations with parameter values $\lambda = 6$, $\upsilon = 0.03$, $\xi = 0.5$, $r = 3.3$, $\delta = 1/10$, $\alpha = 0.4$ where (a) bi-stability between the disease-free and the endemic state occurs with $q = 1$, and (b) the DFE is locally asymptotically stable with no bi-stability with $q = 2$.

Table 2: Impact of varying the rate of quarantine (q) and the effectiveness of a preventive measure (ξ) corresponding to a long course (42 days) of Tamiflu ($\delta = 1/42$), some scarcity of the preventive measure ($\upsilon = 0.03$), and a relatively high infection rate ($\lambda = 6$). The shaded values indicate $q = q^*$.

ξ	q	T_3	r_1	$\mathcal{R}_0{}^*$	λ^*	Interpretation
	0.50	3.13	3.76	0.833	1.21	For high effectiveness of the
0.5	2.00	3.03	3.08	0.986	4.20	preventive measure, high quarantine
	2.90	3.024		1	6.00	is needed to eliminate the bi-stability.
	0.1	5.49	5.59	0.983	1.85	For low effectiveness of the
0.9	0.3	5.44	5.46	0.996	3.82	preventive measure, low quarantine is
	0.52	5.425		1	6.01	needed to eliminate the bi-stability.

have a locally asymptotically stable DFE and no bi-stability as seen in Figure 1b. On the other hand, the real-life conditions for this result are unlikely since the bi-stability range will happen at unrealistically high values of the recovery rate r.

In the second set of examples provided in Table 2 we consider a long term course of Tamiflu of 42 days ($\delta = \frac{1}{42}$) with the same values for the infection and the prevention measure taking rate $\lambda = 6$ and $\upsilon = 0.03$. This case is similar to the previous one but with limited practicality due to the very high ranges for r in the bi-stability case.

Next, in Table 3, we consider two more cases with $\delta = \frac{1}{42}$ but a low infection rate $\lambda = 0.5$ and $\upsilon = 0.03$. These cases show more realistic values for both q and r in the bi-stability case. The typical flu takes 7 days, or $r = \frac{1}{7} = 0.14$ which may fall in the bi-stability range depending on the effectiveness of the prevention measure and the level of quarantine. Furthermore, the level of quarantine needed to eliminate the bi-stability is low as well. From a predictive standpoint we can infer that, in the context of a disease that does not spread too rapidly (i.e., low λ), the ability to quarantine before receiving the vaccine or prophylaxis treatment has the most impact on eliminating the bi-stability.

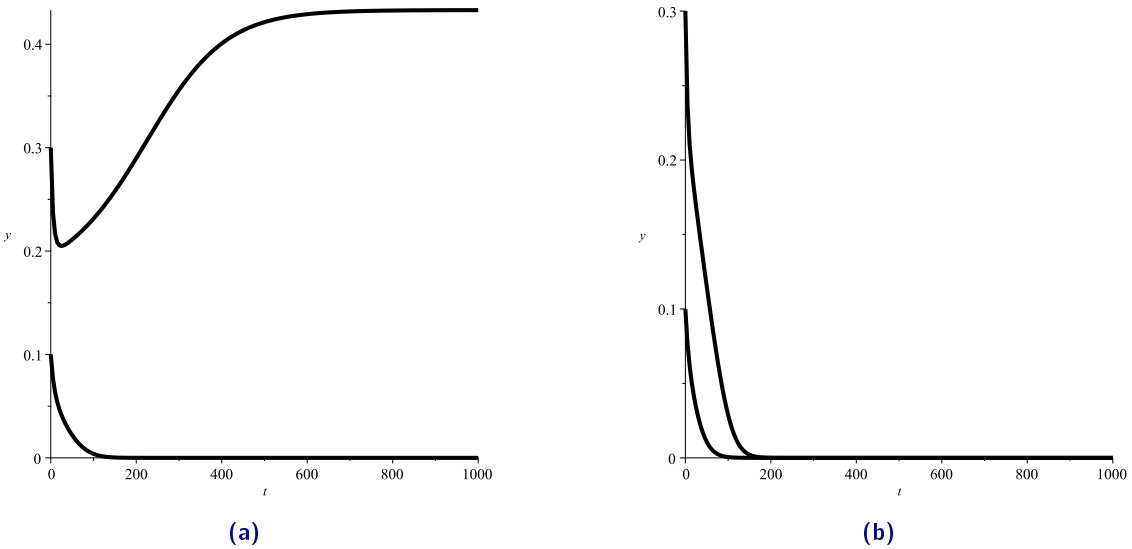
We include one more situation in Table 4 that considers an actual vaccine with an effectiveness for 360 days ($\delta = \frac{1}{360}$) and all other parameters as in the previous case: $\lambda = 0.5$, $\upsilon = 0.03$, $\xi = 0.1$ and $r = \frac{1}{7} = 0.14$. In this case $q^* = 0.39$ which corresponds to $T_3 = r_1 = 0.053$. We see that even a very small increase in quarantine q will render the recovery rate $r = 0.14$ outside the bi-stability range which suggests that this is the type of framework for which this behavior is most significant. We illustrate this case in the following figures. In Figure 2a we show the bi-stability case in the absence of quarantine ($q = 0$). In Figure 2b we show how the bi-stability is eliminated in the presence of quarantine ($q = 0.02$).

Table 3: Impact of varying the rate of quarantine (q) and the effectiveness of a preventive measure (ξ) corresponding to a long course (42 days) of Tamiflu ($\delta = 1/42$), some scarcity of the preventive measure ($v = 0.03$), and a relatively low infection rate ($\lambda = 0.5$). The shaded values indicate $q = q^*$.

ξ	q	T_3	r_1	$\mathcal{R}_0{}^*$	λ^*	Interpretation
	0.02	0.19516	0.19526	0.99952	0.47	For low infection rate, a low quarantine is
0.1	0.06	0.14414	0.14431	0.9988	0.46	needed to eliminate the bi-stability regardless
	0.12	0.11		1	0.5	of preventive measure effectiveness.
	0.001	0.387	0.391	0.9897	0.31	
0.6	0.05	0.346	0.347	0.996	0.388	—
	0.1	0.33		1	0.5	

Table 4: Impact of varying the rate of quarantine (q) and the effectiveness of a preventive measure (ξ) corresponding to a vaccine that wanes after 360 days ($\delta = 1/360$), some scarcity of the preventive measure ($v = 0.03$), and a relatively low infection rate ($\lambda = 0.5$). The shaded values indicate $q = q^*$.

ξ	q	T_3	r_1	$\mathcal{R}_0{}^*$	λ^*	Interpretation
	0.001	0.087	0.15	0.581	0.071	For a highly effective annual vaccine
0.1	0.009	0.08	0.134	0.598	0.079	and a low infection rate, a very small
	0.02	0.07	0.12	0.63	0.091	increase in quarantine may be needed
	0.39	0.053		1	0.5	to eliminate the bi-stability.



(a) (b)

Figure 2: Model simulations with parameter values $\lambda = 0.5$, $v = 0.03$, $\xi = 0.1$, $r = 1/7$, $\delta = 1/360$, $\alpha = 0.4$ where (a) bi-stability between the disease-free and the endemic state occurs with $q = 0$, and (b) the DFE is locally asymptotically stable with no bi-stability with $q = 0.02$.

4 Conclusions

We analyzed a model of an infectious disease that is driven by infection and re-infection subject to a scarcely available preventive measure whereby a certain portion of the susceptibles quarantine themselves until such measure is available for them. We showed that, in addition to the usually expected disease-free state and the endemic state, under some conditions, the disease can also evolve toward either disease clearance or an endemic state depending on the initial population sizes (i.e., the bi-stability scenario). Then, we ran several examples that illustrate under what conditions (preventive measure effectiveness and level of infection) the quarantine before taking the preventive measure can have a meaningful impact. The more interesting cases involve a relatively low infection rate and a longer duration of preventive measure effectiveness because. In these situations, even a relatively small level of quarantine may be sufficient to eliminate the bi-stability.

These types of results can help in deciding whether a certain public policy intervention is worthwhile to pursue or not since its success in implementation depends on a multitude of factors. Can a typical susceptible be able to quarantine? In the context of a student campus, this can translate, for example, into the ability to take online classes. Is the level of quarantine expected to happen sufficient to make a dent in how the disease evolves? Is the level of protection from the preventive measure sufficient? Of important note is that this last question may have a different answer as time goes by. Obviously, no model (including this one) is completely accurate, however, the values of the thresholds q^*, T_3, and r_1 (and their relation to $\mathcal{R}_0$ and $\mathcal{R}_0{}^*$) should provide an approximate picture of the disease dynamics when trying to answer these questions.

The epidemic reproductive number $\mathcal{R}_0$, albeit an imperfect quantity, is widely used both in the specialized literature and in the common news. It may justify public policy. The model we analyzed here provides another similar quantity, $\mathcal{R}_0{}^*$, that adds some nuance to the idea that if $\mathcal{R}_0 < 1$ then things are moving in the right direction. If the number of secondary cases of infection is less than 1 but still too large (i.e., exceeding $\mathcal{R}_0{}^*$) the disease may still become endemic. Finally, the threshold q^* which corresponds to $\mathcal{R}_0{}^* = 1$, if it can be measured, indicates how much quarantine is needed to eliminate this effect and to have more confidence that the epidemic evolves to a disease-free state if $\mathcal{R}_0 < 1$.

There are several limitations of this model and its results. The gap in the proof of the stability of the endemic equilibria needs to be addressed whenever the parameter values do not satisfy the sufficiency condition in Theorem 2.2. More generally, various diseases and the population affected by them may not be covered by our model assumptions: demographic factors, natural immunity, disease-induced mortality, etc. Another important consideration is how these results are different or similar if a different infection transmission term is used such as homogeneous mixing or asymptotic incidence. We plan to address these questions in the near future.

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