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On considering the influence of recovered individuals in disease propagations

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ABSTRACT

Consider diseases transmitted through personal contacts, for which recovery usually confers complete and long-lasting immunity, like some of the common viral infections of childhood. Here, an epidemic model based on differential equations is proposed to evaluate the influence of the recovered (immune) individuals on the spread of such diseases. Indeed, immune individuals can affect the infection rate of susceptible individuals and the recovery rate of sick individuals. The predictive ability of the proposed model is assessed from records concerning the incidence of varicella in three European countries, in a pre-vaccination era.

1. Introduction

Consider infectious diseases that propagate through social contacts. Specifically, think about typical viral infections of childhood, like varicella (chickenpox). Recovery from this disease commonly confers full and sustained immunity [5,8,27].

Epidemic models on varicella do not usually include the influence of the recovered (immune) individuals on the spread of this disease [4,7,12,16,20,21]. Such an influence, however, should be taken into account. Habitually, immune individuals take care of sick children, reducing the convalescence period. Immune individuals also act as catalysts by facilitating the interaction among susceptible and infective children in clubs, parks, schools. In fact, children generally go out their homes only accompanied by immune adults. Thus, recovered individuals can increase the contagion rate, which is harmful to the host population; but they can also increase the recovery rate, which is beneficial.

Here, these opposite effects are taken into consideration in an epidemic SIR model written in terms of ordinary differential equations. We did not find in the literature any epidemic model about any contagious disease with this feature. The model proposed in this work allows the existence of multiple stable equilibria. The predictions of this model are evaluated by comparing them to real data related to the annual incidence rate of varicella in Belgium [22], Germany [25], and Italy [6], prior to varicella vaccination [15].

This manuscript on the influence of recovered individuals in infection propagation is organized as follows: in Section 2, the proposed model is analyzed; in Section 3, numerical simulations performed with hypothetical and real parameter values are presented; in Section 4, the main results are discussed.

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2. Model and analytical results

SIR models have been successfully employed in epidemiological studies [1,3,9–11]. This work is based on the following SIR model:

$$\frac{dS(t)}{dt} = f_1 = -aS(t)I(t)[1 + q_1R(t)] + cI(t) + eR(t) \tag{1}$$

$$\frac{dI(t)}{dt} = f_2 = aS(t)I(t)[1 + q_1R(t)] - bI(t)(1 + q_2R(t)) - cI(t) \tag{2}$$

$$\frac{dR(t)}{dt} = f_3 = bI(t)(1 + q_2R(t)) - eR(t). \tag{3}$$

The variables $S(t)$, $I(t)$, and $R(t)$ denote the numbers of susceptible, infective, and recovered individuals at the time t, respectively. It is supposed that these three kinds of individuals are homogeneously distributed over the space [1,23].

The six parameters a, b, c, e, q_1, and q_2 are positive numbers: a is the infection rate constant, b is the recovery rate constant, c is the rate constant of death of I-individuals, e is the rate constant of death of R-individuals, q_1 is the constant expressing the impact of R-individuals on the contagion of S-individuals, q_2 is the constant denoting the influence of R-individuals on the cure of I-individuals. The analytical form of the terms containing q_1 and q_2 shows a linear variation with $R(t)$, because this is the simplest way of representing the effects of recovered people on a disease spreading. Thus, it becomes the natural choice for such terms in this early investigation.

In this model, it is assumed that deaths of I and R-individuals are balanced by births of S-individuals; that is, when I and R-individuals die, S-individuals replace them. Hence, $dS(t)/dt + dI(t)/dt + dR(t)/dt = 0$; consequently, $S(t) + I(t) + R(t) \equiv N$, in which N is the total number of individuals. Therefore, the size of the population remains constant and equal to N. Note that the terms involving the parameters c and e in Eq. (1) represent the birth rate. Note also that $R(t) = N - S(t) - I(t)$; therefore, this model is a second-order autonomous dynamical system. Hence, the attractors can be either steady states or limit cycles [2,14].

A steady state is a stationary solution. It corresponds to an equilibrium point (S^*, I^*) in the state space $S \times I$, in which S^* and I^* are constants satisfying $f_1(S^*, I^*) = 0$ and $f_2(S^*, I^*) = 0$ for any time t (obviously, $R^* = N - S^* - I^*$). The local stability of an equilibrium point (S^*, I^*) can be inferred from the eigenvalues of the Jacobian matrix obtained from the system of Eqs. (1) and (2) linearized around such a point [2,14]. Hartman–Grobman theorem states that (S^*, I^*) is locally asymptotically stable if both eigenvalues have negative real parts [2,14]. For this second-order system, the eigenvalues $\lambda_{1,2}$ are the roots of the polynomial $\lambda^2 - T\lambda + \Delta = 0$, in which $T = [\partial f_1/\partial S + \partial f_2/\partial I]_{(S,I)=(S^*,I^*)}$ is the trace and $\Delta = [(\partial f_1/\partial S)(\partial f_2/\partial I) - (\partial f_1/\partial I)(\partial f_2/\partial S)]_{(S,I)=(S^*,I^*)}$ is the determinant of the Jacobian matrix computed at (S^*, I^*). The eigenvalues $\lambda_{1,2}$ have negative real parts if $T < 0$ and $\Delta > 0$.

A limit cycle is a periodic solution. It is represented by a closed and isolated trajectory in the state space $S \times I$. By varying the parameter values, a limit cycle enclosing an equilibrium point can appear via Hopf bifurcation [2,14]. If $T = 0$ and $\Delta > 0$ for an equilibrium point, then a Hopf bifurcation can occur, and a limit cycle with stability opposite to this equilibrium point emerges in the state space.

For the proposed model, the stationary solution given by $(S^*_{free}, I^*_{free}) = (N, 0)$ corresponds to the disease-free steady-state (that is, the steady state without infective individuals). It exists for any values of q_1 and q_2. For this solution, $T = (R_0 - 1)/(b + c) - e$ and $\Delta = e(1 - R_0)/(b + c)$, with $R_0 \equiv aN/(b + c)$. Therefore, the disease-free steady-state is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$. The (bifurcation) parameter R_0 is usually known as basic reproduction number [1,18].

The existence and the stability of endemic steady-states (S^*_{ende}, I^*_{ende}) (that is, steady states with infective individuals) depend on q_1 and q_2. The scenario with $q_1 = 0$ and $q_2 = 0$ was already analyzed by Schimit and Monteiro [19]. In this case, there is only one endemic steady-state given by:

$$(S^*_{ende}, I^*_{ende}) = \left(\frac{N}{R_0}, \frac{eN}{e + b}\left(1 - \frac{1}{R_0}\right)\right) \tag{4}$$

which is locally asymptotically stable if $R_0 > 1$ and unstable if $R_0 < 1$. Observe that the system experiences a transcritical bifurcation in $R_0 = 1$, because the steady states (S^*_{free}, I^*_{free}) and (S^*_{ende}, I^*_{ende}) of opposite stabilities exchange their stabilities when R_0 is varied around 1 [19].

Here, the case $q_1 > 0$ and $q_2 = 0$ is first investigated; then, it is taken $q_1 = 0$ and $q_2 > 0$; and, finally, it is considered $q_1 > 0$ and $q_2 > 0$.

Case 1: $q_1 > 0$ and $q_2 = 0$ (that is, R-individuals only affect the propagation rate). Endemic steady-states are obtained from:

$$a_0(I^*_{ende})^2 + a_1 I^*_{ende} + a_2 = 0 \tag{5}$$

with $a_0 = q_1 b(b + e)/e^2$, $a_1 = 1 + b(1 - q_1 N)/e$, $a_2 = N(1 - R_0)/R_0$, and:

$$S^*_{ende} = N - \left(1 + \frac{b}{e}\right) I^*_{ende}. \tag{6}$$

The roots of Eq. (5) are $I^*_{ende,1} = (-a_1 + \rho)/(2a_0)$ and $I^*_{ende,2} = (-a_1 - \rho)/(2a_0)$, with $\rho = \sqrt{a_1^2 - 4a_0a_2}$. Only positive and real roots are biologically meaningful. Observe that $a_0 > 0$. If $a_2 < 0$ (that is, $R_0 > 1$), then the only positive root is $I^*_{ende,1}$; if $a_2 > 0$,

then $I^*_{ende,1}$ and $I^*_{ende,2}$ are positive and real numbers only if $q_1 > q_1^c$, in which the critical value q_1^c is derived from $a_1 < 0$ and $a_1^2 > 4a_0a_2$.

For $(S^*_{ende,1}, I^*_{ende,1})$, $T = -(b+c)I^*_{ende,1}/S^*_{ende,1} - e < 0$ and $\Delta = ae\rho I^*_{ende,1} > 0$; for $(S^*_{ende,2}, I^*_{ende,2})$, $T = -(b+c)I^*_{ende,2}/S^*_{ende,2} - e < 0$ and $\Delta = -ae\rho I^*_{ende,2} < 0$. Hence, $(S^*_{ende,1}, I^*_{ende,1})$ is locally asymptotically stable and $(S^*_{ende,2}, I^*_{ende,2})$ is unstable (because $\Delta < 0$). By varying R_0, a transcritical bifurcation involving (S^*_{free}, I^*_{free}) and $(S^*_{ende,1}, I^*_{ende,1})$ takes place at $R_0 = 1$, as in the case with $q_1 = q_2 = 0$. By varying q_1 with $R_0 < 1$, then a saddle-node bifurcation occurs at $q_1 = q_1^c$. This bifurcation corresponds to the creation or destruction of two equilibrium points of opposite stability due to the variation of a parameter value [2,14]. A similar bifurcation scenario was found in a SIS model [24].

If $q_1 \gg 1$, then the attractor is $(S^*_{ende,1}, I^*_{ende,1}) = (0, eN/(b+e))$.

Note that T cannot be null for the endemic equilibrium points; thus, a limit cycle enclosing these points cannot be created via Hopf bifurcation.

In short: for $q_1 > 0$ and $q_2 = 0$, if $R_0 > 1$, then the global attractor is $(S^*_{ende,1}, I^*_{ende,1})$; if $R_0 < 1$, then the solution converges either to (S^*_{free}, I^*_{free}) or to $(S^*_{ende,1}, I^*_{ende,1})$, depending on the initial condition and on the parameter values. In fact, for $R_0 < 1$, there can be two locally asymptotically stable equilibria. For $q_1 \gg 1$, the susceptible individuals tend to disappear of the host population.

Case 2: $q_1 = 0$ and $q_2 > 0$ (that is, R-individuals only affect the recovery rate). Endemic equilibrium points are determined from:

$$a_3(I^*_{ende})^2 + a_4 I^*_{ende} + a_5 = 0 \tag{7}$$

with $a_3 = bq_2$, $a_4 = -b - e - bq_2N + bcq_2/a$, $a_5 = eN(R_0 - 1)/R_0$, and:

$$S^*_{ende} = N - I^*_{ende} - \frac{bI^*_{ende}}{e - bq_2 I^*_{ende}}. \tag{8}$$

The roots of Eq. (7) are $I^*_{ende,3} = (-a_4 + \sigma)/(2a_3)$ and $I^*_{ende,4} = (-a_4 - \sigma)/(2a_3)$ with $\sigma = \sqrt{a_4^2 - 4a_3a_5}$. Note that $a_3 > 0$. If $a_5 < 0$ (that is, $R_0 < 1$), then the only positive root is $I^*_{ende,3}$; however, this solution is unstable because $\Delta = -a(a_3(I^*_{ende,3})^2 + |a_5|) < 0$ for any value of a_4. If $a_5 > 0$, then $I^*_{ende,3}$ and $I^*_{ende,4}$ are positive and real numbers only if $a_4 < 0$ and $a_4^2 > 4a_3a_5$. The locally asymptotically stable equilibrium point is $I^*_{ende,4}$, because $T = -(aI^*_{ende,4} + bI^*_{ende,4}/R^*_{ende,4}) < 0$ and $\Delta = a\sigma(|a_4| - \sigma)/(2a_3) > 0$.

For $q_2 \gg 1$, the attractor is $(S^*_{ende,4}, I^*_{ende,4}) = (N, 0)$.

As in the Case 1, self-sustained oscillations cannot arise via Hopf bifurcation of the endemic steady-states, because T is always a negative number. Thus, when an equilibrium point is locally asymptotically stable, it is, indeed, globally asymptotically stable.

In short: for $q_1 = 0$ and $q_2 > 0$, the global attractor is (S^*_{free}, I^*_{free}) if $R_0 < 1$; the global attractor is $(S^*_{ende,4}, I^*_{ende,4})$ if $R_0 > 1$, and a transcritical bifurcation takes place at $R_0 = 1$ as for $q_1 \geq 0$ and $q_2 = 0$. If $q_2 \gg 1$, the host population tends to be composed only by susceptible individuals.

Case 3: $q_1 > 0$ and $q_2 > 0$ (that is, both influences of R-individuals on disease propagation are taken into account). The endemic solutions are obtained from:

$$\begin{aligned}&(e - bq_2I^*_{ende})^2(aN - aI^*_{ende} - c) + \\ &(e - bq_2I^*_{ende})(-abq_1I^*_{ende} - abI^*_{ende} + abNq_1I^*_{ende} - be) - ab^2q_1(I^*_{ende})^2 = 0.\end{aligned} \tag{9}$$

For $q_2 = 0$, this expression becomes Eq. (5); for $q_1 = 0$, it becomes Eq. (7). Such an expression can be rewritten as:

$$a_6(I^*_{ende})^3 + a_7(I^*_{ende})^2 + a_8 I^*_{ende} + a_9 = 0 \tag{10}$$

with $a_6 = b^2q_2(q_1 - q_2)$, $a_7 = bq_2(2e + bNq_2 + b - bNq_1 - bcq_2/a) - bq_1(b+e)$, $a_8 = eb(Nq_1 - 2Nq_2 - 1 + bq_2/a + 2cq_2/a - e/b)$, $a_9 = e^2N(R_0 - 1)/R_0$. In addition:

$$S^*_{ende} = \frac{c + eb/(e - bq_2I^*_{ende})}{a[1 + bq_1I^*_{ende}/(e - bq_2I^*_{ende})]}. \tag{11}$$

No conclusion about the existence of stationary solutions can be easily inferred from Eq. (10), because the signs of the coefficients a_6, a_7, a_8, and a_9 are undetermined. However, by rewriting Eq. (10) in terms of $R^*_{ende} = N - S^*_{ende} - I^*_{ende}$, then:

$$a_{10}(R^*_{ende})^3 + a_{11}(R^*_{ende})^2 + a_{12}R^*_{ende} + a_{13} = 0 \tag{12}$$

with $a_{10} = q_1q_2$, $a_{11} = q_2(1 + bq_2/a) + q_1(1 + e/b) - Nq_1q_2$, $a_{12} = 2bq_2/a + cq_2/a + e/b + 1 - N(q_1 + q_2)$, and $a_{13} = N(1 - R_0)/R_0$. Observe that $a_{10} > 0$ and $a_{13} < 0$ if $R_0 > 1$. Thus, if $R_0 > 1$, there exists at least one positive real root of Eq. (12), thanks to the Descartes' rule of sign [13]. Therefore, if $R_0 > 1$, there is at least one endemic equilibrium point with biological meaning. For such a point, the trace T and the determinant Δ derived from the Jacobian matrix are given by:

$$T = -\left[aI^*_{ende}(1 + q_1R^*_{ende}) + \frac{bI^*_{ende}}{R^*_{ende}}\right] \tag{13}$$

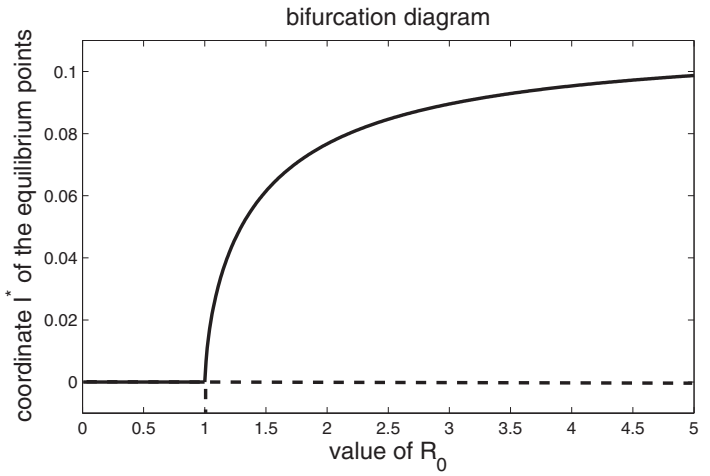

Fig. 1. Bifurcation diagram showing I^* in function of R_0 for $b = 0.8$, $c = 0.2$, $e = 0.1$, $q_1 = 1$, $q_2 = 0$, and $N = 1$. Solid line represents asymptotically stable equilibrium point; dashed line, unstable equilibrium point. In this diagram, $I^*_{ende,1}$ and I^*_{free} switch their stabilities in $R_0 = 1$, corresponding to a transcritical bifurcation.

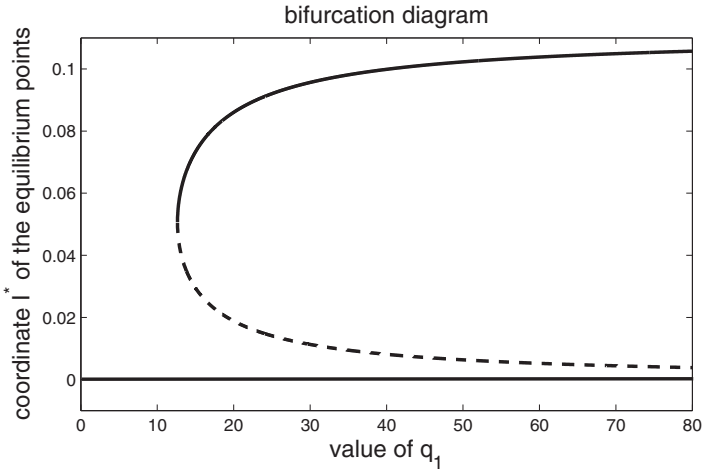

Fig. 2. Bifurcation diagram presenting I^* in function of q_1 for $R_0 < 1$ (that is, $a_2 > 1$), $a_1 < 0$, $a_1^2 > 4a_0a_2$, and $q_2 = 0$. Solid line stands for asymptotically stable equilibrium point; dashed line, unstable equilibrium point. For $a = 0.3$, $b = 0.8$, $c = 0.2$, $e = 0.1$, and $N = 1$ (thus, $R_0 = 0.3$), the endemic solutions $I^*_{ende,1}$ and $I^*_{ende,2}$ are real and positive numbers if $q_1 > 12.65$. Note that $I^*_{ende,1}$ and I^*_{free} are asymptotically stable and $I^*_{ende,2}$ is unstable. This diagram exhibits a saddle-node bifurcation, because above the critical value $q_1^c = 12.65$, two (endemic) steady states ($I^*_{ende,1}$ and $I^*_{ende,2}$) with opposite stability are created. For $q_1 \geq 12.65$, the disease either can persist or can be naturally eradicated from the host population, depending on the initial condition.

$$\Delta = aI^*_{ende}(1 + q_1R^*_{ende})\left[\frac{bI^*_{ende}}{R^*_{ende}} + b(1 + q_2R^*_{ende})\right] + bI^*_{ende}(1 + q_2R^*_{ende})(bq_2 - aq_1S^*_{ende}). \tag{14}$$

Note that $T < 0$ and, as in the Cases 1 and 2, Hopf bifurcation cannot occur. The value of Δ can be numerically calculated, in order to determine its sign and, consequently, the stability of the endemic steady-state.

In the next section, these analytical results are illustrated by numerical simulations performed with hypothetical and real parameter values.

3. Numerical results

Here, $N = 1$; thus, $S(t)$, $I(t)$, and $R(t)$ are the percentages at the instant t of S-individuals, I-individuals, and R-individuals, respectively. Usually, it is more convenient to deal with normalized variables when comparisons about the incidence of a disease in distinct regions (with distinct population sizes) are made.

Figs. 1 and 2 illustrate the bifurcations found in the proposed model. Fig. 1 presents a transcritical bifurcation; Fig. 2, a saddle-node bifurcation. Solid line indicates asymptotically stable steady-state; dashed line, unstable steady-state. In Fig. 1, the asymptotically stable steady-states are global attractors; in Fig. 2, they are local attractors for $q_1 \geq q_1^c$.

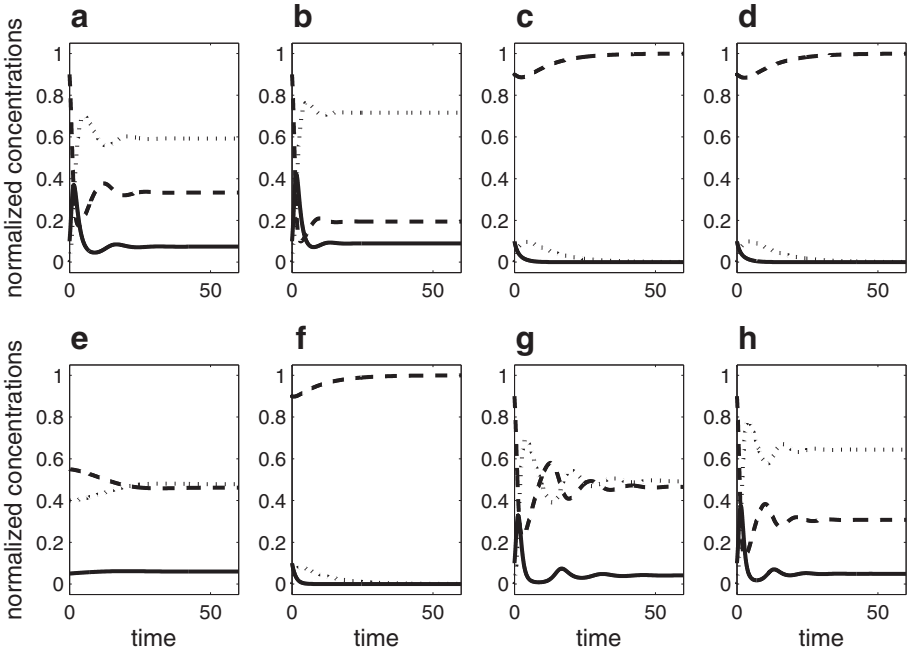

Fig. 3. Temporal evolutions of $S(t)$ (dashed line), $I(t)$ (solid line), and $R(t)$ (dotted line) by numerically integrating Eqs. (1)–(3) with $N = 1$. Thus, these variables represent normalized concentrations. In all cases, $b = 0.8$, $c = 0.2$, and $e = 0.1$. In all cases, the initial condition is $S(0) = 0.9$, $I(0) = 0.1$, $R(0) = 0$; with the exception of (e), in which $S(0) = 0.55$, $I(0) = 0.05$, $R(0) = 0.40$. In (a), $a = 3$, $q_1 = 0$, $q_2 = 0$; in (b), $a = 3$, $q_1 = 1$, $q_2 = 0$; in (c), $a = 0.3$, $q_1 = 12$, $q_2 = 0$; in (d) and (e), $a = 0.3$, $q_1 = 13$, $q_2 = 0$; in (f), $a = 0.3$, $q_1 = 0$, $q_2 = 1$; in (g), $a = 3$, $q_1 = 0$, $q_2 = 1$; and in (h), $a = 3$, $q_1 = 1$, $q_2 = 1$. In (c), (d), and (f), the system converges to the disease-free solution; in the other cases, to an endemic solution.

Fig. 3 exhibits temporal evolutions of $S(t)$ (in dashed line), $I(t)$ (in solid line), and $R(t)$ (in dotted line), obtained by numerically integrating Eqs. (1)–(3). The aim of these simulations is to show how the parameters a, q_1, and q_2 affect the disease spread. In this figure, the parameters b, c, and e, related to cure and death, are kept fixed. Arbitrarily chosen values are $b = 0.8$, $c = 0.2$, and $e = 0.1$.

The values of b, c, and e are not easily modified in practice, because such modifications require investments in researches on new medications, improvements in the public health system and in the access to food and water of satisfactory quality and quantity, and so on. The values of a, q_1, and q_2 can be more easily altered. For instance, they can be altered by isolating infected persons, restricting long-range population movements, staying at home to take care of a sick child, stimulating social interactions, and so on.

In all cases of Fig. 3, the initial condition is $S(0) = 0.9$, $I(0) = 0.1$, $R(0) = 0$; with the exception of the case (e), in which $S(0) = 0.55$, $I(0) = 0.05$, $R(0) = 0.40$. In (a), $a = 3$, $q_1 = 0$, $q_2 = 0$; in (b), $a = 3$, $q_1 = 1$, $q_2 = 0$; in (c), $a = 0.3$, $q_1 = 12$, $q_2 = 0$; in (d) and (e), $a = 0.3$, $q_1 = 13$, $q_2 = 0$; in (f), $a = 0.3$, $q_1 = 0$, $q_2 = 1$; in (g), $a = 3$, $q_1 = 0$, $q_2 = 1$; and in (h), $a = 3$, $q_1 = 1$, $q_2 = 1$.

In (a), $q_1 = 0$, $q_2 = 0$, and $R_0 = 3 > 1$; thus, the disease remains present in the host population. The corresponding endemic steady-state is given by $(S^*, I^*) = (0.333, 0.074)$, which is in agreement with the numbers calculated from Eq. (4). This simulation was accomplished just for reference in order to be compared to the cases with $q_1 > 0$ and/or $q_2 > 0$.

First, the simulations for $q_1 > 0$ and $q_2 = 0$ (the Case 1 of the last section). In (b), $q_1 = 1$ and $R_0 = 3 > 1$; hence, an endemic steady-state is reached. It is given by $(S^*, I^*) = (0.194, 0.090)$, corresponding to $(S^*_{ende,1}, I^*_{ende,1})$. By comparing (b) to (a), note that increasing q_1 increases I^* and reduces S^*.

In (c)–(e), $R_0 = 0.3 < 1$ and $q_1^c = 12.65$ (recall that q_1^c is computed from $a_1 < 0$ and $a_1^2 > 4a_0a_2$). In (c), $q_1 = 12 < q_1^c$; in (d), $q_1 = 13 > q_1^c$. In both these cases, the population converges to the disease-free steady-state. In (e), for $q_1 = 13$, the disease becomes endemic. The difference between (d) and (e) is the initial condition. Observe that two asymptotically stable equilibria coexist when $R_0 < 1$ and $q_1 > q_1^c$, as theoretically predicted.

Now, the simulations for $q_1 = 0$ and $q_2 > 0$ (the Case 2). In (f), $R_0 = 0.3 < 1$ and the disease dies out; in (g), $R_0 = 3 > 1$ and the disease persists as the time passes; thus, the value of R_0 is enough to determine the fate of the pathogenic agent in the host population. In (g), $(S^*, I^*) = (0.465, 0.041)$ corresponds to $(S^*_{ende,4}, I^*_{ende,4})$. By comparing (g) to (a), note that increasing q_2 reduces I^* and increases S^*.

Finally, in (h), $q_1 = 1$ and $q_2 = 1$ (the Case 3). In this scenario, $R_0 = 3$ and $(S^*, I^*) = (0.307, 0.049)$, which is in agreement with Eqs. (10) and (11). By comparing (g) to (h), increasing q_1 with $q_2 \neq 0$ increases I^* and reduces S^*; by comparing (b) to (h), increasing q_2 with $q_1 \neq 0$ reduces I^* and increases S^*.

The Case 3 is further explored by using data related to the varicella incidence in Belgium, Germany, and Italy, when vaccination programmes had not yet been implemented. Let the time t be measured in days. Recall that the parameters of the model are:

a, b, c, e, q_1, and q_2. The value of a can be obtained from R_0 (the basic reproduction number), which corresponds to the average number of secondary infections caused by a single infectious individual introduced into a completely susceptible population [1,18]. The values of b, c, and e are the inverse of the mean lifetimes related, respectively, to the transitions $I \to R$ (recovery), $I \to S$ (death of a sick individual), $R \to S$ (death of an immune individual). The values of q_1 and q_2 are determined from the simulations. Actually, the purpose is to find out the values of q_1 and q_2 yielding S^* and I^* observed in the "real world". If the correct numbers of S^* and I^* are obtained with $q_1 \simeq 0$ and $q_2 \simeq 0$, then this means that the influence of immune individuals on the spread of the considered disease may be neglected.

Varicella is a highly contagious illness, transmitted from person to person usually either by direct contact or inhalation of airborne respiratory droplets [5,8,27]. Its infectious period is about one week. For immunocompetent individuals, it is generally a mild-to-moderate illness. Its mortality rate can be considered "low": about 3 per 100, 000 cases [5,8,27]. Thus, in the model, $b = 1/7$ day^{-1} and $c = e$ (that is, I and R-individuals have equal mortality rates).

Below, the subscript "model" denotes the results obtained from the analytical expressions derived in the last section, and the subscript "data" denotes the records found in demographic and epidemiologic statistics. The optimal values of q_1 and q_2 were numerically found by performing an exhaustive search in the intervals $q_1 \in [1, 30]$ and $q_2 \in [0.1, 10]$, by varying q_1 with step of 1 and q_2 with step of 0.1. Thus, 300 simulations were carried out for each country.

In 1999, the average life expectancy in Germany was 78 years [29]; hence, $c = 1/(78 \times 365)$ day^{-1}. In that year, the basic reproduction number concerning varicella was estimated to be $R_0 = 5.5 > 1$ [15]. With these values and taking $N = 1$, the asymptotically stable stationary solution for $R_0 > 1$ and $q_1 = q_2 = 0$ is $(S^{*(q_1=0,q_2=0)}_{model}, I^{*(q_1=0,q_2=0)}_{model}) = (0.18, 0.00020)$, obtained from Eq. (4). In that year, the total German population was about 83 million people [28]. Thus, the model predicts an annual incidence of $A^{q_1=0,q_2=0}_{model} = 2.0 \times 10^{-4} \times 8.3 \times 10^7 \times 365/7 = 870,000$ cases. According to the public health records, $A_{data} = 760,000$ were infected by varicella in 1999 [25], which corresponds to $I^*_{data} = 7.6 \times 10^5 \times 7/(8.3 \times 10^7 \times 365) = 0.00018$. In addition, in that year, approximately 96% of children under 15 years of age had already acquired immunity, and 98% were immune above this age [15]. Children under 15 corresponds to 16% of the total population [28]. Thus, $S^*_{data} = 1 - (0.00018 + 0.96 \times 0.16 + 0.98 \times 0.84) = 0.023$. Therefore, $S^{*(q_1=0,q_2=0)}_{model} \simeq 8S^*_{data}$ and $I^{*(q_1=0,q_2=0)}_{model} \simeq I^*_{data}$. Thus, $q_1 = 0$ and $q_2 = 0$ are not the best choices. More suitable choices are $q_1 = 10$ and $q_2 = 0.4$, because they yield $(S^{*(q_1=10,q_2=0.4)}_{model}, I^{*(q_1=10,q_2=0.4)}_{model}) = (0.023, 0.00017)$ as attractor of the epidemic model, which are numbers closer to the official data. This equilibrium point, determined from Eq. (10), is asymptotically stable because, from Eqs. (13) and (14), $T < 0$ and $\Delta = 2.9 \times 10^{-4} > 0$.

In Italy, in 1996, $c = 1/(80 \times 365)$ day^{-1} [29] and $R_0 = 3.3$ [15]; consequently, from Eq. (4), $(S^{*(q_1=0,q_2=0)}_{model}, I^{*(q_1=0,q_2=0)}_{model}) = (0.30, 0.00017)$. Therefore, the annual incidence rate should be about $A^{q_1=0,q_2=0}_{model} = 500,000$, since the population living in Italy in that year was 57 million people [28]. According to the epidemiologic statistics, the annual rate was $A_{data} = 97,000$ cases [6]. Also, 82% under 15 had already been infected and 91% above this age [15]. The fraction under 15 was 15% of the whole population [28]. Hence, $I^*_{data} = 0.000033$ and $S^*_{data} = 0.10$. Note that $S^{*(q_1=0,q_2=0)}_{model} \simeq 3S^*_{data}$ and $I^{*(q_1=0,q_2=0)} \simeq 5I^*_{data}$. The model gives a better prediction by taking $q_1 = 20$ and $q_2 = 6$, because with these choices the endemic attractor is $(S^{*(q_1=20,q_2=6)}_{model}, I^{*(q_1=20,q_2=6)}_{model}) = (0.10, 0.000034)$, with $\Delta = 2.7 \times 10^{-4} > 0$.

In Belgium, in 2002, $c = 1/(78 \times 365)$ day^{-1} [29] and $R_0 = 6.5$ [15]; thus, $(S^{*(q_1=0,q_2=0)}_{model}, I^{*(q_1=0,q_2=0)}_{model}) = (0.15, 0.00021)$. For a population of 10 million people [28], the annual incidence rate predicted by the model is $A^{q_1=0,q_2=0}_{model} = 110,000$. From the epidemiologic records, the annual rate was $A_{data} = 113,000$ [22]. The immune portion was composed of 94% under 15 years of age, corresponding to 15% of the total population, and 97% above 15; thus, the immune portion was equal to $0.94 \times 0.15 + 0.97 \times 0.85 = 96.5\%$ [15,28]. Therefore, $I^*_{data} = 0.00022$ and $S^*_{data} = 0.035$. In short, $S^{*(q_1=0,q_2=0)}_{model} \simeq 4S^*_{data}$ and $I^{*(q_1=0,q_2=0)} \simeq I^*_{data}$. Perfect match between model and data is obtained by taking $q_1 = 4$ and $q_2 = 0.1$.

In conclusion, for Germany, $q_1 = 10$ and $q_2 = 0.4$; for Italy, $q_1 = 20$ and $q_2 = 6$; for Belgium, $q_1 = 4$ and $q_2 = 0.1$. Therefore, considering the effects of the R-population in varicella spread can be relevant in these three countries, because the best predictions are obtained with $q_1 \neq 0$ and $q_2 \neq 0$.

4. Discussion

Some results derived from the proposed model are not surprising: when a contagious disease chronically persists, increasing q_1 increases I^*; increasing q_2 decreases I^*. Other results are not so obvious: the model supports the coexistence of disease-free and endemic attractors, and it reveals that the processes of contagion and recovery can be mediated by immune individuals, at least for varicella incidence in three European countries in a pre-vaccination era.

The cases of varicella are usually under-reported to the public health departments, even in countries where it is a notifiable disease [15,17,26]. This compromises the accuracy of the statistics and the predictions of the models. Besides, the estimations of the parameters b and R_0 for childhood viral infections already indirectly take into account the influence of the immune population (because children usually do not live alone, do not prepare your food, do not buy your medication). These biased estimations obviously affect the predictions of this and other models. Hence, we cannot assure that the different values of q_1 and q_2, found for Belgium, Germany, and Italy, reflect differences on cultural aspects, on patterns of social behaviors, and on the topologies of the underlying contact networks concerning the people living in these countries. However, these can be possible explanations.

The next steps of this study are to evaluate the model predictions to other countries and/or other contagious diseases, and to include the effect of vaccine (if available) against the corresponding pathogen. Vaccination causes the transition $S \rightarrow R$, which is also affected by the R-population in childhood infections, since (immune) parents decide about the vaccination of their (susceptible) children.

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References

[1] Anderson RM, May RM. Infectious diseases of humans: dynamics and control. Oxford: Oxford University Press; 1991.
[2] Argyris J, Faust G, Haase M. An exploration of chaos. Amsterdam: North-Holland; 1994.
[3] Brauer F, van den DP, Wu J. Mathematical epidemiology. editors. New York: Springer; 2008.
[4] Brisson M, Edmunds WJ, Gay NJ, Law B, De Serres G. Modelling the impact of immunization on the epidemiology of varicella zoster virus. Epidemiol Infect 2000;125(3):651–69.
[5] Centers for Disease Control and Prevention. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR2007;56(RR-4):1–40.
[6] Gabutti G, Penna C, Rossi M, Salmaso S, Rota MC, Bella A, et al. Serological study group. the seroepidemiology of varicella in Italy. Epidemiol Infect 2001;126(3):433–40.
[7] Garnett GP, Grenfell BT. The epidemiology of varicella-zoster virus infections: a mathematical model. Epidemiol Infect 1992;108(3):495–511.
[8] Heininger U, Seward JF. Varicella. Lancet 2006;368(9544):1365–76.
[9] Hethcote HW. The mathematics of infectious diseases. SIAM Rev 2000;42(4):599–653.
[10] Keeling MJ, Rohani P. Modeling infectious diseases in humans and animals. Princeton: Princeton University Press; 2008.
[11] Kermack WO, McKendrick A. A contribution to the mathematical theory of epidemics. Proc R Soc Lond A 1927;115(772):700–21.
[12] Jackson C, Mangtani P, Fine P, Vynnycky E. The effects of school holidays on transmission of varicella zoster virus, England and Wales, 1967–2008. PLoS One 2014;9(6):e99762.
[13] Larson R, Hostetler RP. Precalculus: a concise course. Boston: Houghton Mifflin; 2007.
[14] Monteiro LH. Overview of dynamical systems and chaos. In: Eisencraft M, Attux R, Suyama R, editors. Chaotic signals in digital communications. Boca Raton: FL: CRC Press; 2014. p. 83–109.
[15] Nardone A, de Ory F, Carton M, Cohen D, van Damme P, Davidkin I, et al. The comparative sero-epidemiology of varicella zoster virus in 11 countries in the European region. Vaccine 2007;25(45):7866–72.
[16] Ospina Giraldo J, Hincapié Palacio D. Deterministic SIR (Susceptible–Infected–Removed) models applied to varicella outbreaks. Epidemiol Infect 2008;136(5):679–87.
[17] Papaloukas O, Giannouli G, Papaevangelou V. Successes and challenges in varicella vaccine. Ther Adv Vaccines 2014;2(2):39–55.
[18] Schimit PHT, Monteiro LHA. On estimating the basic reproduction number in distinct stages of a contagious disease spreading. Ecol Model 2012;240(10):156–60.
[19] Schimit PHT, Monteiro LHA. On the basic reproduction number and the topological properties of the contact network: an epidemiological study in mainly locally connected cellular automata. Ecol Model 2009;220(7):1034–42.
[20] Schuette MC. A qualitative analysis of a model for the transmission of varicella-zoster virus. Math Biosci 2003;182(2):113–26.
[21] Silhol R, Boëlle PY. Modelling the effects of population structure on childhood disease: the case of varicella. PLoS Comput Biol 2011;7(7):e1002105.
[22] Thiry N, Beutels P, Shkedy Z, Vranckx R, Vandermeulen C, Wielen MV, et al. The seroepidemiology of primary varicella-zoster virus infection in flanders (Belgium). Eur J Pediatr 2002;161(11):588–93.
[23] Turnes Jr PP. Monteiro LHA. an epidemic model to evaluate the homogeneous mixing assumption. Commun Nonlinear Sci Numer Simul 2014;19(11):4042–7.
[24] van den DP, Watmough J. A simple SIS epidemic model with a backward bifurcation. J Math Biol 2000;40(6):525–40.
[25] Wagenpfeil S, Neiss A, Banz K, Wutzler P. Empirical data on the varicella situation in germany for vaccination decisions. Clin Microbiol Infect 2004;10(5):425–30.
[26] Weller TH. Varicella and herpes zoster: a perspective and overview. J Infect Dis 1992;166:S1–6.
[27] World Health Organization. Varicella and herpes zoster vaccines: WHO position paper. Wkly Epidemiol Rec 2014;89(25):265–88.
[28] World Health Organization. Population: data by country (all years). Available at: http://apps.who.int/gho/data/view.main.POP2040?lang=en [accessed 18.05.15].
[29] World Health Organization. Life expectancy: data by country (data by WHO region). Available at: http://apps.who.int/gho/data/view.main.680?lang=en [accessed 18.05.15].