The reinfection threshold

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Abstract

Thresholds in transmission are responsible for critical changes in infectious disease epidemiology. The epidemic threshold indicates whether infection invades a totally susceptible population. The reinfection threshold indicates whether self-sustained transmission occurs in a population that has developed a degree of partial immunity to the pathogen (by previous infection or vaccination). In models that combine susceptible and partially immune individuals, the reinfection threshold is technically not a bifurcation of equilibria as correctly pointed out by Breban and Blower. However, we show that a branch of equilibria to a reinfection submodel bifurcates from the disease-free equilibrium as transmission crosses this threshold. Consequently, the full model indicates that levels of infection increase by two orders of magnitude and the effect of mass vaccination becomes negligible as transmission increases across the reinfection threshold.

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Breban and Blower (2005) challenge our use of the word "threshold" to name the "Reinfection Threshold" (Gomes et al., 2004a) on the basis that this is not a bifurcation point. Assuming that a misnomer of the concept would invalidate its implications, they deduce that our results have no epidemiological consequences. Here we explain the terminology but, more importantly, we emphasize that the choice of name does not affect the implications of the concept. We assert that the epidemiological behaviour associated with $R_0 = 1/\sigma$ remains unchanged.

The recognition that partial immunity divides the transmissibility axis into two distinct modes of transmission emerged almost simultaneously from two studies: a systematic analysis of microparasite transmission under suboptimal immunity (Gomes et al., 2004a); and a representation of the transmission dynamics of tuberculosis leading to a hypothesis for the widely debated

variable efficacy of the bacille Calmette-Guérin (BCG) vaccine (Gomes et al., 2004b). The two studies overlap through a modified *SIR* model

$$\frac{\mathrm{d}S}{\mathrm{d}t} = (1-v)e - R_0 IS - eS,$$
$$\frac{\mathrm{d}I}{\mathrm{d}t} = R_0 I(S + \sigma R) - I, \qquad (1)$$

where S and I are the proportions of fully susceptible and infected individuals, respectively, and $R = 1 - S - I$ is the proportion recovered with partial immunity.

In units of average duration of infection, births and deaths occur at a rate e, and a proportion v of the population is vaccinated at birth to enter compartment R. Individuals in S are infected at a rate, $R_0 I$, and individuals in R are infected at a reduced rate, $\sigma R_0 I$, where $0 \leqslant \sigma \leqslant 1$. The existence of these two distinct rates of infection is the key to our findings.

The endemic equilibria of model (1) are represented in Fig. 1 as a function of the basic reproduction number, R_0. The proportion of infectious individuals is represented in linear (a) and logarithmic (b) scales, and the
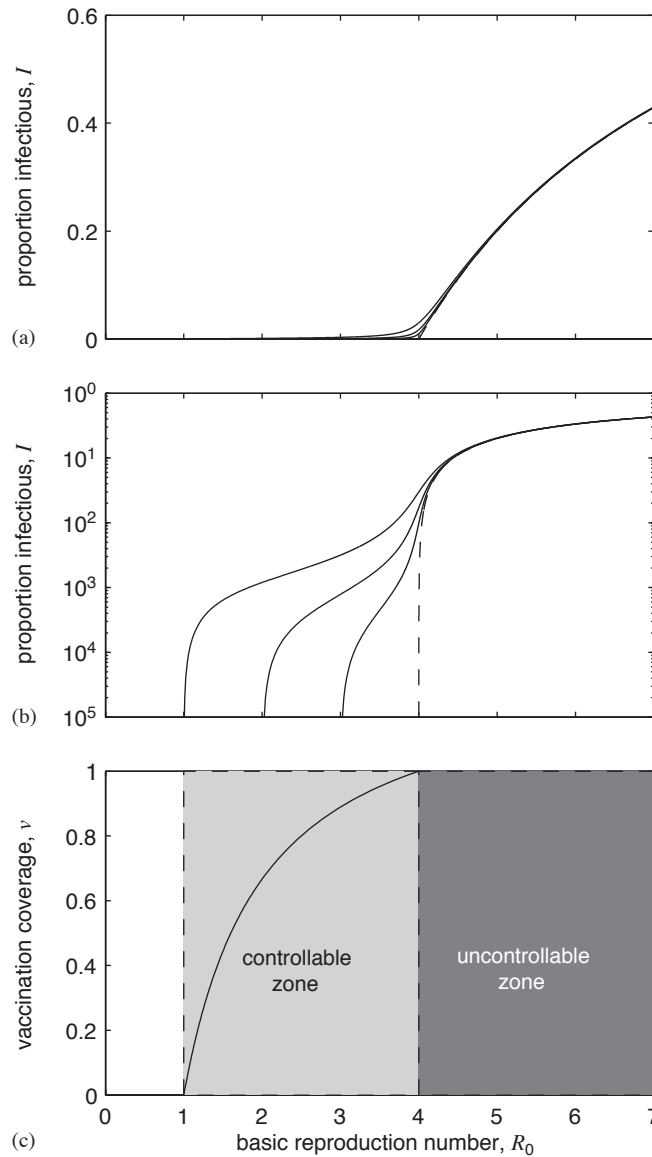
Fig. 1. Endemic equilibria, and potential impact of vaccination as a function of transmissibility illustrated for $\sigma = 0.25$. (a, b) proportion infectious in linear and logarithmic scale, respectively, under four levels of vaccination coverage: $v = 0, 0.67, 0.89, 1$, from left to right. The non-vaccination line marks the epidemic threshold ($R_0 = 1$), and the full-vaccination line (dashed) marks the reinfection threshold ($R_0 = 1/\sigma$). (c) vaccination coverage required to eliminate infection in the controllable (light) zone. Mass vaccination is generally ineffective in the uncontrollable (dark) zone.

four curves correspond to different vaccination coverage: $v = 0, 0.67, 0.89, 1$, from left to right. For the purpose of illustration we chose $\sigma = 0.25$, but the conclusions remain valid for any value between 0 and 1. We set $e = 0.0012$, which is attained under a life expectancy of 70 years and an average duration of infection of 1 month. Shorter infectious periods would enhance the effects that follow.

Breban and Blower (2005) carry out a bifurcation analysis of the $v = 0$ model, and correctly conclude that the only bifurcation point is the epidemic threshold, $R_0 = 1$ (Kermack and McKendrick, 1927). However, we note that all curves show a marked increase in the

prevalence of infection as R_0 increases across $R_0 = 1/\sigma$. In Fig. 1(a) this effect is more evident, and in Fig. 1(b) we observe that vaccination can eliminate infection for $1 < R_0 < 1/\sigma$, while this is ineffective for $R_0 > 1/\sigma$. Fig. 1(c) shows the vaccination coverage required to eliminate infection in the controllable (light) zone ($1 < R_0 < 1/\sigma$) while this is impossible in the uncontrollable (dark) zone ($R_0 > 1/\sigma$). We attribute this behaviour to a bifurcation in the reinfection submodel that takes place at $R_0 = 1/\sigma$. The reinfection submodel is obtained by setting $v = 1$, and the associated equilibria are thus represented by the dashed curve in Fig. 1(b). Consequently, we term $R_0 = 1/\sigma$ as the "reinfection thresh-

old''. When $v < 1$, the reinfection threshold is no longer a bifurcation point, but remains as a useful value to interpret levels of infection and to determine the potential impact of vaccination programmes.

The reinfection threshold is determined by the degree of protection conferred by a previous infection or vaccine, whichever is more protective. Therefore, its position can be manipulated by more potent vaccines widening the controllable zone. The reinfection threshold sets the targets for vaccine development and use, and its quantitative characterization cannot be overemphasized. This is perhaps the most important message for public health.

Final remarks

Our final remarks refer to the last paragraph of Breban and Blower (2005). Their final sentence is misleading.[1] The authors restate that no epidemiological consequences can be assigned to the reinfection threshold because $R_0 = 1/\sigma$ is not a bifurcation point. They claim that our findings concerning reinfection reduce to a nonlinear increase in the prevalence of infection as R_0 increases, as previously reported by Blower et al. (1998) and Feng et al. (2000). This is not the case. As described above we have analysed the form of the nonlinear increase and the variability in the effectiveness of vaccination. We have detected a bifurcation in the reinfection submodel at $R_0 = 1/\sigma$, we have shown that levels of infection of the full epidemic model increase by two orders of magnitude as R_0 increases across a vicinity of $1/\sigma$, we have demonstrated that the same vaccine can eliminate infection if $R_0 < 1/\sigma$ and appears impotent if $R_0 > 1/\sigma$. We named this critical value the reinfection threshold and discussed its implications for vaccine development and public health policy.

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[1]Breban and Blower (2005) refer to tuberculosis and quote from a previous article: ''the higher the susceptibility to reinfection the easier it will be to achieve eradication'' (Blower et al., 1998). The full sentence in the original article is: ''For any particular (endemic equilibrium) incidence rate, the higher the susceptibility to reinfection the easier it will be to achieve eradication'' (Blower et al., 1998). The two statements have different meanings. The first could imply that increasing susceptibility to reinfection with *M. tuberculosis* (e.g. by spreading AIDS) would bring us closer to eradicating tuberculosis. This does not make sense. The second applies solely to the interpretation of a given endemic equilibrium: the higher the reinfection, the lower the R_0 required for a given endemic equilibrium and, in principle, lower R_0 implies easier eradication.