Wildlife disease elimination and density dependence

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Abstract

Disease control by managers is a crucial response to emerging wildlife epidemics, yet the means of control may be limited by the method of disease transmission. In particular, it is widely held that population reduction, while effective for controlling diseases that are subject to density-dependent transmission, is ineffective for controlling diseases that are subject to frequency-dependent transmission. We investigate control for horizontally transmitted diseases with frequency-dependent transmission where the control is via culling or harvest that is nonselective with respect to infection and the population can compensate through density-dependent recruitment or survival. Using a mathematical model, we show that culling or harvesting can eradicate the disease, even when transmission dynamics are frequency-dependent. Eradication can be achieved under frequency-dependent transmission when density-dependent birth or recruitment induces compensatory growth of new, healthy individuals, which has the net effect of reducing disease prevalence by dilution. We also show that if harvest is used simultaneously with vaccination, and there is high enough transmission coefficient, application of both controls may be less efficient than vaccination alone. We illustrate the effects of these control approaches on disease prevalence for chronic wasting disease in deer where the disease is transmitted directly among deer and through the environment.

Key words: disease modeling, disease management, chronic wasting disease, frequency-dependent transmission

Introduction

Control of any disease is related to thresholds, either in parameters or in population size. For example, a disease may be unable to spread if the population is below some critical size or the proportion of immune individuals is greater than a certain level. Such thresholds can be characterized by the basic reproduction number R_0 [1-3]: if $R_0>1$ the disease can spread. For wildlife diseases a manager's set of possible control actions is limited: reduction in population density, removal of infected individuals, or a vaccination of susceptibles. In the case of population reduction, a threshold must exist with respect to the population size at which the disease will die out. Population thresholds depend upon the disease transmission mechanism [4]. Typical mechanisms involve either density-dependent (DD) or frequency-dependent (FD) transmission [5,6]. In the former, the number of per capita contacts grows with population size due to increased contact rates with infected individuals. In FD case the number of per capita contacts is constrained to be independent of population size, such as when contacts occur in social groups, and group size is independent from the overall population size [5]. In the case of DD, population reduction can eliminate disease spread by reducing the population below a critical population threshold. In contrast, a population threshold is not exhibited in the case of FD, so population reduction, by itself, is not considered to be appropriate for disease management, see e.g. [7]. Disease transmission mechanisms other than DD or FD are possible [5-9], but FD and DD mechanisms are the most commonly assumed in disease modeling.

In this paper we present a Susceptible-Infected-Vaccinated (SIV) model for the infection dynamics of a disease that has FD transmission mechanisms that occur through direct and environmental contact and is coupled to DD population birth and survival rates and no recovery from the disease. We describe the model in terms of population size n and disease prevalence i. We show that for the model there exists a population threshold in spite of FD disease transmission. It arises due to DD birth that allows populations to 1) withstand culling/harvesting at levels sufficient to remove diseased individuals before they, on average, infect new susceptibles, and 2) effectively dilute disease prevalence

with new, uninfected individuals. On the other hand, in populations exhibiting DD mortality non-selective harvest may not increase removal of diseased individuals, just fewer of them die from natural causes. For this reason, DD birth or recruitment appears to be critical for harvest control of a disease that has FD transmission.

We illustrate these effects by modeling chronic wasting disease (CWD) in deer [10]. CWD is a prion disease, and, to date, it is not known how to control the disease. Our previous modeling work [11] showed evidence that CWD transmission may result primarily from FD mechanisms related to deer social organization for both direct and environmental transmission [12]. In case when the disease prevalence grows significantly slower than the rate at which prions decay or become inaccessible to deer [13], both mechanisms can be described within the framework of SI-type model without explicit environmental compartment. Here environmental prion content is approximately proportional to the current number of infected individuals due to the difference in the rates (see Supplementary Materials for the details of this approach). Deer also show DD recruitment of new adults to the population [14]. Assuming FD transmission, we investigate disease dynamics, and whether culling/harvesting results in disease extinction via a parameter-based threshold. Finally, we consider the possibility of vaccination as an alternative strategy that can be coupled to control via culling/harvesting to control disease and estimate levels needed to control the disease.

The model

We use a simple population model, deriving conditions for disease eradication, in a manner that makes analysis transparent and shows the role of culling/harvesting and DD deer recruitment and survival in disease management. We consider three adult disease classes: susceptible S, infected I, and immune after vaccination V with the total population size being $n=S+I+V$. The per capita recruitment of young into the populations, $b(n)$, is assumed to be a nonincreasing function of n, and the per capita natural mortality, $m(n)$, is assumed to be a nondecreasing function of n. In other words,

both may be DD, but with no Allee effects present [15] . The increase in mortality rate due to infection is denoted by μ, and hence the mortality rate for diseased individuals is $m(n)+\mu$. Here $(m(n)+\mu)^{-1}$ is the average duration of infection prior to death. The disease transmission function is of a general form $\beta(n)(I/n)S$, where $\beta(n)=\beta_{DD}n$ for DD transmission and $\beta(n)=\beta_0$ for FD transmission. Susceptible individuals become immune at per capita rate γ, which accounts both for vaccination intensity and vaccine efficiency. Finally, susceptibles, immune and infected individuals are culled or harvested at the same rate h, i.e., animals are non-selectively removed from the population.

The model takes the form:

$$\frac{dS}{dt} = b(n)(S+I+V) - m(n)S - \beta(n)(I/n)S - \gamma S - hS \tag{1}$$

$$\frac{dI}{dt} = \beta(n)(I/n)S - (m(n)+\mu)I - hI\,, \tag{2}$$

$$\frac{dV}{dt} = \gamma S - m(n)V - hV\,, \tag{3}$$

For the subsequent analysis it is convenient to rewrite the system in terms of population size n, disease prevalence $i=I/n$ and immune fraction $v=V/n$. (see e.g. [16,17]). Then $S=(1-i-v)n$, $I=in$ and $V=vn$, and, after some transformations,

$$\frac{dn}{dt} = [b(n) - m(n) - \mu i - h]n \tag{4}$$

$$\frac{di}{dt} = iF(n,v,i), \qquad F = \beta(n)(1-v-i) - \mu(1-i) - b(n) \tag{5}$$

$$\frac{dv}{dt} = \gamma(1-v-i) - (b(n) - \mu i)v \tag{6}$$

(Supplementary Material). This new form yields interesting insights: (a) culling or harvesting does not directly influence disease prevalence i — culling/harvesting intensity h does not enter into (5) because nonselective harvest takes an equal proportion out of all classes (see similar conclusion in [17]); and (b) culling/harvesting drives down the population size n and affects the disease prevalence indirectly by modifying the DD

contact rate $\beta(n)$ and birth rate $b(n)$. In turn, DD contact rate and birth rate can play a major role in determining the disease prevalence *i* in (5).

The basic reproduction number R_0 for this system can be obtained by standard methods at disease free equilibrium $n = n_0, i = 0, v = v_0$ (see Supplementary Material), and the condition for the disease persistence is

$$R_0 = \frac{\beta(n_0)(1-v_0)}{\mu + m(n_0) + h} > 1. \qquad (7)$$

We interpret this as the rate of production of new infectives $\beta(n_0)(1-v_0)$ times the average life span of infective individuals $\tau_I = (\mu + m(n_0) + h)^{-1}$. Vaccination increases v_0 and hence decreases the rate of new infections; selective harvest increases μ and decreases τ_I. Both of these methods, when available, work regardless of the details of the disease and population dynamics. However, when there is no vaccine and infected individuals are hard to find or to distinguish from healthy ones, the only practical measure is nonselective population harvest *h*. As we will show, nonselective harvesting can influence n_0, v_0 and τ_I, and its effect depends on the details of disease transmission and population self-regulation.

First we analyze the case when v_0 is fixed. Though potentially such control policy could be implemented, we consider it as a simplification allowing us to avoid interaction of several factors. Then changes in R_0 may be only due to $\beta(n_0)$ and τ_I. Harvest decreases n_0, and in case of DD transmission $\beta(n) = \beta_{DD} n$ it reduces the rate of new infections as well. In case of FD transmission $\beta(n) = \beta_0$ harvest does not change the rate of new infections, which for some models implies no disease control [4].

The dependence of τ_I on *h* is determined by the population self-regulation mechanism. There are two extreme cases (e.g. [18]):

a) density-dependent birth (DB) and density independent mortality: *m* is independent from *n*, and *b*(*n*) is a decreasing function of *n*;

b) density-independent birth and density dependent mortality (DM): b is independent from n and $m(n)$ is an increasing function of n.

At disease-free equilibrium ($i = 0$) the following equality always holds,

$$b(n_0) = m(n_0) + h, \tag{8}$$

see (4). Therefore in case (a) we have $b(n_0) = m + h$; that is an increase in h is compensated by an increase in births of new healthy individuals. Total mortality $m + h$ increases, which causes decrease of τ_I and decrease of R_0. Therefore, there exists population threshold below which the disease cannot persist provided the population survives harvest of the required intensity.

In case (b) we have $b = m(n_0) + h$; that is an increase in harvest reduces the equilibrium population size n_0 and natural mortality $m(n_0)$, but does not change total mortality. This means more individuals die of harvest, but fewer die of natural causes. The average life span of infective individuals τ_I also remains unchanged.

Therefore we have four combinations of disease transmission and population self-regulation: DD+DB, DD+DM, FD+DB, FD+DM. Only in the latter case there is no population threshold due to nonselective harvest because both the rate of new infection and average life span of infective individuals are independent from population size n_0.

Taking in account (8), we can rewrite (7) as

$$R_0 = \frac{\beta(n_0)(1 - v_0)}{\mu + b(n_0)} > 1, \tag{9}$$

which makes the above statements more obvious. Note that the same condition for disease persistence $\beta(n)(1 - v) > \mu + b(n)$ can be obtained from (5) as a requirement of positive prevalence growth rate $F(n,v,i)$ at i=0, but (5) does not require the system to be at equilibrium, and hence (9) is valid even when the population is in a transient regime after some perturbations. In particular, it shows that local culling events that lower population size enough to decrease $\beta(n_0)$ or increase $b(n_0)$ can temporarily slow down the disease progression.

From now on we consider only the case of DD birth (DB) for population regulation with *m* being constant. One of the forms of DB dependence has been used in [18],

$$b(n) = b_0\left(1-(n/n_c)^{\theta}\right), \qquad m = \text{const}, \tag{10}$$

where θ takes values between 1 and 7, depending on species (note that n_c is greater than carrying capacity). In case $\theta = 1$ it is possible to obtain analytical estimates for population thresholds n_{0T} corresponding to R_0=1 (9) or $\beta(n_{0T})(1-v_0) = \mu + b_0(1-n_{0T}/n_c)$ in DD and FD cases:

DD transmission: $\beta(n) = \beta_{DD} n$ and $n_{0T} = (\mu + b_0)/(\beta_{DD}(1-v_0) + b_0/n_c)$.

FD transmission: $\beta(n) = \beta_0$ and $n_{0T} = n_c(\mu + b_0 - \beta_0(1-v_0))/b_0$.

In both cases the threshold is a decreasing function of transmission coefficient. However, in DD case the threshold always exists, while in FD case it exists only in case of a moderate transmission coefficient or a large enough b_0, i.e., maximum population growth potential. Below we analyze conditions for b_0 in more detail. We also point out that in the case of DD, dependence of *b* on *n* decreases the threshold, which agrees with [19].

Disease management: harvest and vaccination

The above analysis has been done under the assumption that v_0 is fixed. A more realistic assumption is that the vaccination rate γ is fixed and simultaneous use of both vaccination and harvest causes their interaction. On the one hand, nonselective harvest may hinder the disease spread, but on the other hand it removes a part of vaccinated individuals and hence may facilitate the disease. At the disease-free equilibrium proportion of immune individuals is $v_0 = \gamma/(\gamma + m + h)$. We characterize competition of harvest and vaccination by the value of vaccination rate $\gamma_{er}(h)$ needed to make R_0=1 and eradicate the disease at the given intensity of harvest *h*. In the case of FD transmission, there is a critical value of the transmission coefficient $\hat{\beta}_0 = (m+\mu)^2/\mu$, such that for $\beta_0 < \hat{\beta}_0$ $\gamma_{er}(h)$ is strictly decreasing, and an increase in harvest means that vaccination efforts can be reduced (Fig.

1). However, for $\beta_0 > \hat{\beta}_0$ $\gamma_{er}(h)$ is increasing for small h, reaches its peak value at $h = \sqrt{\mu\beta_0} - m - \mu$, and only then it starts to decrease. We conclude that there are parameter regions where combinations of two control measures may be less effective than vaccination alone. In the case of DD transmission the qualitative behaviour of $\gamma_{er}(h)$ is similar to FD transmission, although expressions become more complicated.

In case of FD transmission and intensive vaccination, harvest can increase the endemic disease prevalence of (4)-(6) $i_* = 1 - \frac{(\mu + m + h)(\gamma + m + h)}{\beta_0 (m + h)}$. For $\gamma > (m+h)^2 / \mu$ $di_*/dh > 0$, that is i_* increases with h. Similar counterintuitive behaviour of prevalence has been observed in [20] for a disease with an immune recovered class. The reason for the effect, as in our case, is the removal of immune individuals due to harvest and replacing them by new susceptibles due to DB population regulation (see Supplementary Materials for mathematical details).

If harvest is the only available measure, assuming no vaccination (γ=0, v=0), it can be applied as a control measure only if the population were not to go extinct due to harvesting. The ability of the population to survive harvest of the given intensity h depends on its maximum possible growth rate b_0 (10). We estimate the maximum possible effect of harvest in case of frequency-dependent disease transmission $\beta(n) = \beta_0$ and identify conditions for population collapse, disease control, and disease eradication in terms of b_0. Our analysis does not require an exact form of DD recruitment; we focus only on some of the qualitative properties of the effect. We assume that $b(n)$ is qualitatively similar to (10), i.e., it has a maximum b_0 at n=0 and decreases monotonically until it equals zero at $n=n_c$, in particular θ can take any positive value. This is sufficient to apply phase plane analysis to the system represented by Eqs. (4), (5) (Supplementary Material). The results can be presented as a bifurcation diagram that plots the equilibrium disease prevalence i_* as a function of the maximum recruitment rate b_0 and the culling/harvesting rate h (Fig. 2). Three qualitative outcomes pertain. Low maximum recruitment rates $b_0 < b_{0coll}$, $b_{0coll} = (\beta_0 - \mu)(m + \mu)/\beta_0$, results in population

collapse even without harvest. Intermediate recruitment rates $b_{0\text{coll}} < b_0 < b_{0\text{elim}}$, $b_{0\text{elim}} = \beta_0 - \mu$, allow for reduction of disease prevalence via culling/harvesting. Prevalence can be maintained between $i_{*\max} = 1-(m+\mu)/\beta_0$ and $i_{*\min} = 1-b_0/(\beta_0-\mu)$, further harvest increase above $h_{max} = b_0\beta_0/(\beta_0-\mu)-m-\mu$ causes population collapse. Finally, if $b_0 > b_{0\text{elim}}$, recruitment allows for complete disease eradication via culling/harvesting at harvest intensity $h_e = \beta_0 - m - \mu$.

The expression for h_e has a simple interpretation. In the beginning of the epidemics, when $i << 1, v = 0, b(n) = m + h$, (5) can be rewritten as

$$di/dt \approx i(\beta_0 - \mu - m - h). \quad (11)$$

This has the solution $i(t) \sim \exp(\lambda t)$ where $\lambda = \beta_0 - \mu - m - h = h_e - h$. The exponent of the prevalence growth λ can be experimentally determined from prevalence data. This gives a simple management rule: to eradicate the disease it is necessary to increase harvest rate by the value of λ. Assuming FD transmission and DB regulation, (11) allows one to estimate R_0 in terms of λ as well, provided mortality and harvest rates are known: $R_0 = 1 + \lambda/(\mu + m + h)$.

Application: Chronic Wasting Disease

To show how these theoretical results can be applied to a specific disease of great concern, we consider CWD in white-tailed deer. In the case of CWD, we use a SI-type model for a prion disease that can spread among individuals or through the environment. We assume a rate of decay in prion availability obtained in [13] is faster than the rate of CWD prevalence growth, and hence the amount of prion in the environment is proportional to the current number of infected individuals deposition. Details of this approach are given in the Supplementary Materials. The deer population is primarily regulated by DD juvenile mortality, i.e. DD recruitment of new adults [14]. There is no current vaccination for CWD but one is anticipated to be available in the future.

Transmission coefficients for this species in Wisconsin have been estimated by Wassenberg et al. [21]. For purposes here, if we assume that CWD transmission is FD and using the estimate $\beta_0 \approx 1.64$ infections/year from [21], and the estimate of $\mu \approx 0.57\,\text{year}^{-1}$ as measured in captive mule deer [13], we obtain the condition of disease persistence (9) for a completely susceptible population as

$$1.64 > 0.57 + b(n) \quad \text{or} \quad b(n) < 1.07\,\text{year}^{-1}$$

(assuming there is no difference in CWD duration between species). Because CWD is mostly evident in adult deer [22], we can interpret *b* as recruitment of new adults, which accounts for both birth rate and survival of juveniles during their first year. White-tailed deer have high fertility and, on average, adult females bear close to 2 or more fawns each year. Assuming buck:doe ratio as approximately 1:3, 2 fawns per year per adult female results in 2 fawns per 4/3 adults or 1.5 fawns/adult. However, typically only about 40% of the fawns survive until adulthood [23], which gives $b(n) \approx 0.6$ year^{-1} < 1.07 year^{-1}. From the equilibrium condition $b(n) = m + h$ and typical values for $h \sim 0.1$–0.3 year^{-1} and $m \sim 0.1$ year^{-1}, the estimate is even lower, $b(n) \sim 0.2$–0.4 year^{-1}. Therefore, our analysis shows that, according to condition (9), CWD prevalence should increase among free-ranging white-tailed deer under these conditions, assuming no or moderate harvest.

Using the values of β_0 and μ used in [21] we obtain $b_{0\text{elim}} = 1.07\,\text{year}^{-1}$. To estimate the collapse threshold we need the deer natural mortality rate *m*. In [21] the estimate of survival is 0.97 (per half a year), which corresponds to $m = 0.06\,\text{year}^{-1}$, and gives $b_{0\text{coll}} = 0.41\,\text{year}^{-1}$. With this information it is possible to determine the effect of harvest on CWD prevalence, once the maximum recruitment rate b_0 is known (Fig. 2). At present there are limited data on b_0 for white-tailed deer. However, there is evidence that juvenile survival can increase by $0.16\,\text{year}^{-1}$ in population with reduced density [24], which would increase the above estimate for $b(n)$ to $0.76\,\text{year}^{-1}$, so we may assume this value as a low estimate of b_0. An upper estimate of b_0 should correspond to the highest possible survival of fawns. For mule deer the highest registered fawn survival rate is close to 0.8 [25], so we can assume that $b_0 < 1.20\,\text{year}^{-1}$. Therefore most probably $b_0 > b_{0\text{coll}}$, and the

deer would not die out due to CWD. An assumption $b_0 > b_{0\text{elim}}$ does not seem unrealistic, but practical use of this inequality would require an increase of juvenile survival to about 0.72 via release from density-dependence. Such high survival is unlikely to occur except in very productive environments where deer densities are kept far below food-based carrying capacity by harvest and in years of mild environmental conditions. The most plausible assumption is that $b_{0\text{coll}} < b_0 < b_{0\text{elim}}$, and we conclude that under these conditions the modelled deer population is in the middle domain in Fig. 2 where harvest can reduce the disease prevalence, but it cannot eradicate the disease. Therefore, disease eradication would require vaccination as well as harvest.

In the absence of vaccination (v=0) and low harvest, we obtained a value of basic reproduction number at disease-free equilibrium for CWD $R_0 = \beta_0 / (\mu + b(n)) \approx 1.4 - 2.1$ (9), which agrees with the values reported by Miller et al. [13] for mule deer. Thus an effective immunity level of $v_0 \approx 0.3 - 0.6$ yields a basic reproduction number of $R_0 \approx 1$. Hence immunity of about a half of adult population would be necessary to stop CWD spread under the assumption of FD transmission with negligible vertical transmission, and for the assumed parameter values above. An estimate of the critical value of FD transmission coefficient in Fig. 1 is $\hat{\beta}_0 \approx 0.70$. Thus harvest may increase the required vaccination efforts for disease eradication.

The parameter estimates we are using are only preliminary and require additional and better data on deer and CWD [26] before they can be used to guide management, particularly with respect to prion dynamics in the environment and their accessibility over time. To show that predicted outcomes of our modeling depend crucially upon parameter estimates, we considered a set of alternative parameters that may apply to white-tailed deer populations like in Wisconsin. If we use exponential fit to CWD prevalence and deer harvest data from [27], then (11) gives a different estimate of transmission coefficient $\beta_0 \approx 1.08\,\text{year}^{-1}$ (Supplementary Materials), which corresponds to $b_{0\text{coll}} \approx 0.30\,\text{year}^{-1}$ and $b_{0\text{elim}} \approx 0.51\,\text{year}^{-1}$. These values are well below the estimated recruitment rate for white tailed deer $b(n)$=0.76, and this, in turn, is below the value b_0.

For this scenario eradication via harvesting could be a possibility. Deer mortality also may contribute to uncertainty in results: e.g. the estimate of survival rate for deer in North-eastern Minnesota [28] is m=0.21 year^{-1}, and in [29] there is the estimate of decrease in lifespan due to CWD as 0.63, which corresponds to $\mu \approx 0.43\,\mathrm{year}^{-1}$. Hence, detailed information on parameters related to deer population dynamics and disease dynamics is required for determining efficient control measures for region-specific CWD management.

Discussion and conclusions

In this paper we have studied a model of fatal disease with frequency-dependent transmission. We have shown that non-selective population harvest (i.e., removal of infected and uninfected animals at equal rate) may still be a useful disease management tool even under FD transmission, when population self-regulates through DD birth or recruitment, but it may not be possible when population self-regulates through DD adult mortality. Under the former conditions, the most important population characteristic for applicability of the harvest control is its maximum recruitment rate at low population density. Harvest may both facilitate and impede disease management by vaccination, depending on the disease transmission coefficient, so the optimal management policy depends on the disease. To the best of our knowledge, the harvest control of diseases with FD transmission has not been considered in detail previously, perhaps because it potentially can be applied only to species having the corresponding population regulation mechanism and high recruitment potential.

For a disease with FD transmission harvest alone may be insufficient for disease eradication, or an intensive harvest may be socially unacceptable. Then harvest must be combined with vaccination, which may lead to counterintuitive synergistic effect: when vaccination has to be intensive, or, in other words, a big enough proportion of population should be vaccinated, harvest may enhance disease spread and increase the disease prevalence due to removal of immune individuals; see [20] and Supplemental Material as well. When immunity is only temporary, a large proportion of immune individuals may

cause big disease outbreaks in the future [30]. Another harvest effect may arise in structured population models with DD juvenile survival: the increase in juveniles due to release of density-dependence may exceed the removal of adults, and harvest may actually temporarily increase the total population size. In the case of DD transmission this may increase $\beta(n)$ and enhance the disease transmission (see also modeling results in [19]). Thus efficient management of a disease with DD transmission may even reqiure fertility reduction [31]. Ecological data also show possibility of complicated population response to harvest, i.e., increased litter size, or change in animal spatial movement [32,33]. While possible, no such factors have yet been identified for deer and CWD.

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Figure Legends

Fig. 1. Examples of vaccination rate necessary to eradicate the disease $\gamma_{er}(h)$ as a function of harvest rate *h* under frequency-dependent disease transmission and density-dependent recruitment. For the values of transmission coefficient $\beta_0 > \hat{\beta}_0 = (m+\mu)^2/\mu$ there is an interval of *h* values where joint use of two controls is worse than vaccination alone.

Fig. 2. Minimum equilibrium disease prevalence $i_{*\min}(b_0)$ that can be achieved by population harvest as a function of maximum population fecundity or recruitment b_0 (dotted line), and the required harvest rate *h* (dashed line) to achieve it for the case of FD transmission. For too small b_0 population collapses after disease introduction; at medium b_0 values population harvest can only reduce the prevalence, and too intensive harvest also causes population collapse; at high b_0 values harvest allows to eradicate the disease at $h = h_e$.

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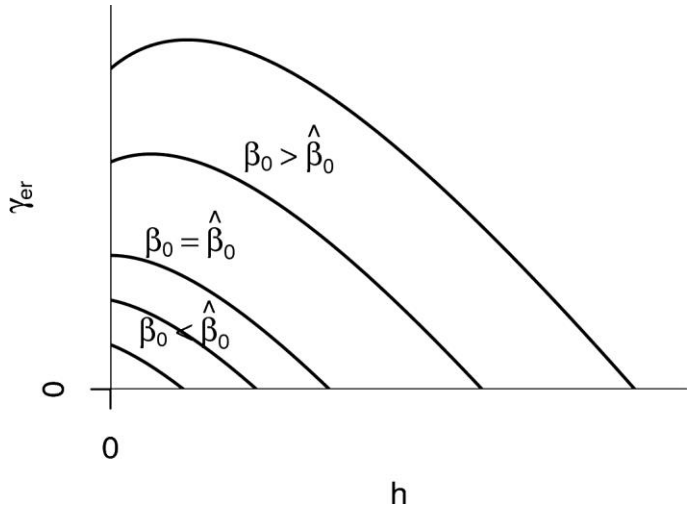
γer
β0 > β̂0
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Fig. 1

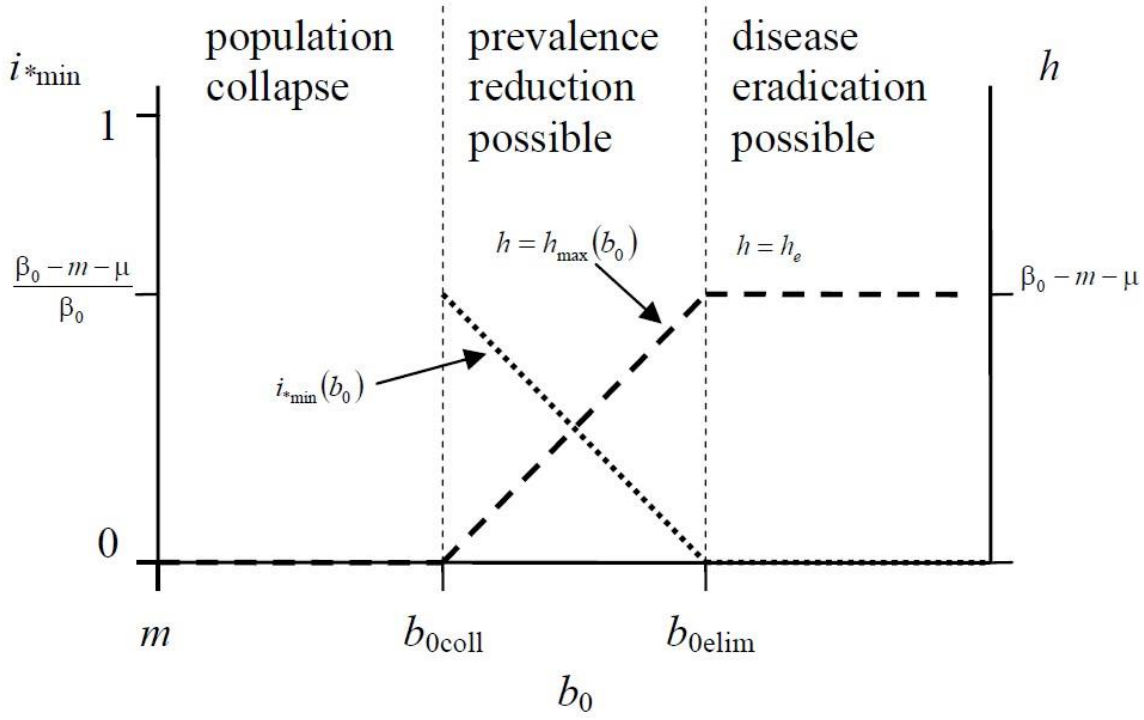
i*min
population collapse
prevalence reduction possible
disease eradication possible
h
1
(β0 − m − μ)/β0
h = hmax(b0)
h = he
β0 − m − μ
i*min(b0)
0
m
b0coll
b0elim
b0

Fig. 2.