

Should we expect population thresholds for wildlife disease?

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Abstract

Host population thresholds for invasion or persistence of infectious disease are core concepts of disease ecology, and underlie on-going and controversial disease control policies based on culling and vaccination. Empirical evidence for these thresholds in wildlife populations has been sparse, however, though recent studies have narrowed this gap. Here we review the theoretical bases for population thresholds for disease, revealing why they are difficult to measure and sometimes are not even expected, and identifying important facets of wildlife ecology left out of current theories. We discuss strengths and weaknesses of selected empirical studies that have reported disease thresholds for wildlife, identify recurring obstacles, and discuss implications of our imperfect understanding of wildlife thresholds for disease control policy.

Introduction

Ideas about threshold levels of host abundance for invasion or persistence of infectious diseases are central to the theory and practice of disease ecology [1-3], but have their roots in human epidemiology. The notion of a THRESHOLD POPULATION FOR INVASION (N_T) is a founding principle of epidemiological theory [4-6], and the CRITICAL COMMUNITY SIZE (CCS) required for disease persistence dates back to Bartlett's seminal analyses of measles data [7]. Evidence of population thresholds in wildlife disease systems has been described as "rare" [8] and "weak" [9], yet these concepts underpin all efforts to eradicate wildlife diseases by reducing numbers of susceptible hosts through controversial methods such as culling, sterilisation, or vaccination (e.g. [10-12]). Recent empirical studies have sought to identify invasion and persistence thresholds in wildlife, with mixed success [8, 9, 12-15]. Here we consider these findings in the context of theoretical models of disease spread, which reveal that sharp population thresholds are not

expected for many disease-host systems. Moreover, even when thresholds are expected DEMOGRAPHIC STOCHASTICITY makes them difficult to measure under field conditions. We discuss how conventional theories underlying population thresholds neglect many factors relevant to natural populations, such as seasonal births or compensatory reproduction, raising doubts about the general applicability of standard threshold concepts in wildlife disease systems. These findings call into question the wisdom of centering control policies on threshold targets, and open important avenues for future research.

Setting the stage

Numbers, densities, and transmission models

Populations can be quantified in terms of numbers or densities of individuals. The choice has implications for how standard models of disease transmission are interpreted, and proper usage and terminology are a topic under active debate among disease modellers [16-19]. For our general discussion of population thresholds, the critical issue is whether transmission rates increase with population abundance N —however it is measured—or remain constant (reflecting some behavioral limit to contact rates [2, 20]). We will contrast two classical models of disease transmission, in which the hazard rate of infection for each susceptible individual scales linearly with the number or density of infectious individuals (yielding density-dependent transmission) or with the proportion of infectious individuals in the population (yielding frequency-dependent transmission). In reality, many diseases are likely to exhibit density-dependent and frequency-dependent transmission characteristics at low and high population sizes, respectively [2, 16, 19].

Reproductive numbers and disease spread

The BASIC REPRODUCTIVE NUMBER (R_0) of a disease is the expected number of secondary cases caused by a typical infectious individual in a wholly susceptible population [4, 21, 22]. If $R_0 < 1$, then each case does not replace itself on average and the disease will die out. If $R_0 > 1$, then the invasion can succeed. When only a fraction s of the population is susceptible (e.g. if some hosts are immune due to previous infection or vaccination), disease spread is described by the EFFECTIVE REPRODUCTIVE NUMBER $R_{\text{eff}} = sR_0$. Again $R_{\text{eff}} < 1$ implies the disease will decrease in prevalence and eventually die out. The value of R_0 (and R_{eff}) depends on all factors influencing transmission, including the rate of contacts among hosts, mixing patterns, factors affecting infectiousness and susceptibility, and the length of the infectious period (Box 1) [4, 21, 22].

Population thresholds for disease invasion*Deterministic foundations*

Invasion thresholds are conceptually straightforward: if R_0 is an increasing function of N , as in density-dependent transmission, then the invasion threshold N_T is that population size for which $R_0 = 1$ (Box 1). In DETERMINISTIC MODELS, populations with $N > N_T$ can sustain major disease invasions ($R_0 > 1$), while those with $N < N_T$ cannot. If R_0 is independent of N , as in frequency-dependent transmission, then no threshold population size for invasion exists (though if some individuals are immune there can be a threshold proportion of susceptibles, $s_T = 1/R_0$; this is the principle underlying HERD IMMUNITY [23]). The simple epidemic models in Box 1 can be elaborated endlessly, potentially yielding N -dependence in R_0 (and hence an invasion threshold N_T) via any processes affected by competition for resources or complex social interactions.

Stochastic complications

When the number of individuals carrying the disease is small, such as during the early phases of disease invasion or when total population size is small, chance events can play a significant role. STOCHASTIC MODELS reveal that an invasion can fail by chance even when $R_0 > 1$ [22, 24]. Observing failed invasions therefore does not necessarily imply a population below the invasion threshold (Fig 1). In the simplest models, where individuals leave the infectious state at a fixed *per capita* rate, the probability of a failed invasion when $R_0 > 1$ is $(1/R_0)^{I_0}$, where I_0 is the initial number of infected individuals [22]. Thus a disease with $R_0 = 3$, introduced by a single infected case, has 33% chance of dying out. In more realistic models incorporating non-random mixing or heterogeneous infectiousness, this complication is heightened because stochastic extinction can become much more likely for a given R_0 [25, 26].

Random variation in outbreak size (i.e. the number of individuals infected) can blur the distinction between successful and failed invasions. In relatively large populations or when $R_0 \gg 1$, the distribution of outbreak sizes is bimodal with distinct peaks corresponding to successful and failed invasions (Fig 1). As population size decreases, or as R_0 approaches 1, this clear distinction is lost and classifying any given outbreak as a success or failure becomes difficult. Even if many outbreaks are observed it can be difficult to discern when the invasion threshold has been crossed—there is little difference between outbreak size distributions for $R_0 = 0.9$ versus 1.1 (or even $R_0 = 1.5$ in small populations). One proposed solution to this problem is to define the threshold as the point where the distribution changes from monotonically decreasing to bimodal [27], but in practice it will be near-impossible to obtain enough replicate outbreaks to characterize borderline cases.

Stochastic fadeout and thresholds for disease persistence

After a disease has successfully invaded a population, it can still go extinct or “fade out” by chance. ENDEMIC FADEOUT refers to extinction of a disease from a relatively stable endemic state, due to random fluctuations in the number of infected individuals (Fig 2a) [21]. EPIDEMIC FADEOUT describes extinction occurring after a major outbreak depletes the available pool of susceptibles, reducing the potential for on-going transmission until the number of susceptibles is replenished (Fig 2b) [21]. The notion of a critical community size (CCS), above which disease can persist, arose from studies of measles that suggested high probabilities of fadeout between biennial epidemics in communities smaller than about 250,000 people, but likely persistence in larger communities [7, 28]. Further study of measles has reinforced the CCS paradigm [21, 29-31], encouraging researchers to look for persistence thresholds in other systems (Table 1)—but reviewing the basic theory shows that sharp thresholds should not be expected.

Endemic fadeout is less likely when equilibrium abundance of infectious individuals (I^*) is higher, and deterministic models show that I^* increases with population size (Box 1). Stochastic models reveal that disease persistence in finite populations is inherently temporary because fluctuations always cause extinction over very long timescales [32]. Analysis of endemic fadeout therefore focuses on the expected time to extinction, T_E , beginning from the QUASISTATIONARY DISTRIBUTION of I (i.e. the distribution of I conditional on non-extinction), which is approximately normal for diseases with $R_0 > 1$ in large populations [32, 33]. The time to extinction from quasi-stationarity is distributed exponentially, with mean T_E increasing nonlinearly with N (Fig 2c) [32-34]. Thus we expect longer persistence in larger populations—with stochastic fadeout a very remote possibility for sufficiently large N —but no sharp threshold value of N that distinguishes populations where disease can or cannot persist. Further, T_E

depends strongly on the relative timescales of disease and demographic processes (Fig 2c), as summarised by the ratio ρ of mean host lifespan to mean infectious period (Box 1) [35]. For given values of R_0 and N , faster demographic turnover (smaller ρ) favours longer disease persistence; ρ also affects the range of N for which T_E becomes very large. These timescale effects occur partly because I^* increases as ρ decreases (Box 1), but the influence of relative timescales on fluctuations in I needs clarification.

Epidemic fadeout is more complicated than endemic fadeout, involving stochastic fluctuations in I superimposed on a changing epidemic curve (Fig 2b). As a major epidemic declines, R_{eff} drops below 1 due to depletion of susceptibles, and transmission will slow or stop. S grows back via birth, immigration, or loss of protective immunity, and if the disease can persist until R_{eff} again exceeds 1 then another epidemic can result. This cycle repeats, generating a series of periodic epidemics (with diminishing intensity in simple models, but see [21]) for as long as the disease persists. Persistence through the “troughs” between epidemics depends on the duration of the waning tail of the initial outbreak, the number of individuals that escaped without infection, and the rate of replenishment of the susceptible pool. The variable N interacts with these factors in complex ways—particularly in wildlife populations (Box 2)—but even the simplest models exhibit no sharp threshold in population size (Fig 2d). Instead, epidemic fadeout depends fundamentally on timescales, because rapid demographic turnover (small ρ) speeds replenishment of S and aids persistence (Fig 2d) [22, 36], and on the intensity of the initial epidemic (governed by ρ and the infectiousness of the disease), because more individuals escaping infection leaves a greater pool of susceptibles [7, 24]. The detectable CCS for measles, with its short infectious period and extraordinary transmissibility, may be more the exception than the rule. In general, fadeout rates are determined by relationships among N and the

timescales of demography and transmission [22, 33, 36], yielding gradual dependence on N but often no sharp threshold effects.

Detecting thresholds in natural populations: observations and challenges

Several recent studies have explicitly tested for population thresholds in wildlife disease systems (Table 1). These studies represent major investments in field research and analysis, but their ability to draw definitive conclusions has often been limited by the inherent challenges described above and additional complexities of real disease-host interactions (Box 3). Here we review their substantial contributions and identify recurring obstacles.

The most obvious challenge is a low level of replication in wildlife studies compared with human datasets, which limits the ability of field workers to detect a threshold when one does exist (Fig. 1). Combined with sampling error and stochastic extinctions, it also raises the possibility of spurious claims of thresholds. A related limitation is that documentation of failed invasion or persistence is frequently lacking. For rabies in red foxes *Vulpes vulpes*, a frequently-cited dataset suggests a threshold in rabies prevalence associated with the number of foxes killed in a region (itself a controversial metric of relative density) [37]. However, because there were no observed densities (infected or not) below the putative threshold of 0.4 foxes killed/km², the threshold's validity is ambiguous. Another oft-cited example of wildlife disease thresholds suggested that brucellosis could not invade or persist in bison *Bison bison* herds of less than 200 individuals, but of the 18 herds studied only one herd had 200 bison (with seroprevalence near zero) and none were smaller than this [12]. In contrast, in the case of phocine distemper in harbour seals *Phoca vitulina*, analysis illustrates that if a CCS exists it is well above the estimated population size [14]. To demonstrate disease thresholds requires documenting not

only successful invasion or persistence at high host populations, but also failure of the disease to invade or persist in populations with N below the putative threshold. Failed invasions by their nature are difficult to observe, compounding the difficulty of identifying these thresholds.

The confounding effects of environmental reservoirs or multiple host species arise in several studies (Table 1). An invasion threshold was suggested for both parvovirus and calicivirus in lions *Panthera leo*, based upon a susceptible pool assumed to equal the number of animals born between one outbreak and the next (thus neglecting immigration or animals that escaped previous infection) [15]. The authors acknowledge, though, that a critical determinant of outbreak timing—and thus of any threshold estimated from cumulative births—is introduction of the pathogen, so the patterns they observe could arise from disease dynamics within the unknown reservoir. The spectre of unknown alternative host species looms over many wildlife disease studies, though some recent research has inferred the role of reservoirs from disease dynamics in their focal species [38, 39]. Definitive documentation of thresholds for a multi-host disease requires measuring the abundances of all important host species and their intra- and interspecific transmission rates (e.g. [40, 41]).

Even the most exhaustive studies demonstrating thresholds are beset by these fundamental problems. Analysis of a 30-year time series convincingly showed a threshold density of great gerbils *Rhombomys opimus* below which plague (*Yersinia pestis* infection) was not present [9]. However, the authors could not distinguish between invasion and persistence thresholds, and the cause of an observed 2-year lag between gerbil abundance and plague outbreak is unclear. On-going and extensive research of cowpox dynamics in a two-species rodent metapopulation [8, 41, 42] recently reported evidence of separate invasion and persistence thresholds for one host species, but only when abundances were measured in numbers, not as

densities [8]. While quite compelling, these data are confounded somewhat by inter-species transmission (including an unstudied third host species [41]) and by possible differences in movement and mixing between island and mainland populations.

Finally, we note an independent line of relevant research: a number of recent studies demonstrate that disease transmission or prevalence increases with population size [43-45]. This indicates that R_0 increases with N , a necessary but not sufficient condition for disease thresholds (Box 1).

Thresholds in disease control: applications and evidence

A longstanding approach to managing wildlife diseases is reduction of the susceptible population through culling, sterilisation or vaccination [3, 43, 46-53]. These control measures represent both the most important practical application of threshold concepts and the best potential source of large-scale experimental data testing those concepts.

When links to theory are stated explicitly, most vaccination and population reduction targets seem to be aimed at reducing R_{eff} below 1, rather than on the more ambiguous CCS [46, 53, 54]. Seeking eradication through herd immunity by vaccinating a threshold proportion of the population is sound in principle, provided the population is well-mixed; otherwise targeted vaccination policies may be required, focusing on regions [48, 55] or pursuing thresholds calculated for specific groups [56]. Disease control by culling is theoretically more effective under some circumstances [46], but is less reliable due to its basic assumption that R_0 increases with N (Box 1) and its vulnerability to unpredictable effects of population change, such as compensating reproduction (Box 2) or social perturbation [10]. Some wildlife control programs have achieved the ultimate success of regional eradication [47, 53], notably fox rabies in Europe

[52], while others have reduced disease incidence [52, 53] and a few have increased disease spread [10]. We believe an important lesson of our review is that population thresholds for disease are not sharp in natural systems—there are no “magic numbers”—so the often escalating cost of final, incremental steps toward a supposed threshold may not be justified.

Control programs that manipulate the abundance of susceptible hosts provide a unique source of information on the validity of population threshold concepts in wildlife disease. Unfortunately, studies of these programs suffer from the same methodological issues as the field studies described above. Individual studies rarely include replication or a range of control effort and thus do not allow proper estimation of thresholds. For example, a New Zealand trial eradicated bovine tuberculosis *Mycobacterium bovis* regionally by culling brushtail possum *Trichosurus vulpecula* densities to 22% of pre-control levels for 10 years [47]. This outcome is consistent with a model-predicted threshold at 40% of pre-control levels [54], but yields no further information regarding a precise threshold level. Efforts to pool results from multiple control programs can be frustrated by inconsistent reporting practices, and by lack of comparability between different control methods. For decades fox rabies control (by culling and more recently vaccination) has been extensive throughout Europe, but programs rarely give results from a range of fox densities and frequently do not report densities at all [52]; local eradications have been achieved, but programs failing to eradicate rabies (essential to determining thresholds) are probably under-reported.

Conclusions and the way forward

The concept of population thresholds for wildlife disease has potential to guide or mislead us, and should be applied with caution in research and control efforts. The clearest

thresholds occur when the disease's reproductive number increases with population size—these can apply to either invasion or persistence, but resist precise determination in ecological datasets due to stochastic effects and complex population structures. For endemic or epidemic fadeout, no threshold exists in the sense of a sharp boundary between regimes. Instead persistence increases gradually with population size, and can depend as strongly on timescales of demographic and transmission processes as it can on N . Many questions remain regarding the influences of population and community ecology on threshold theory (Boxes 2, 3), and further investigation is badly needed.

Empirical studies seeking disease thresholds in wildlife systems are challenged by the indistinct nature of their target, as well as by issues of sample size versus stochasticity and confounding ecological factors. Future empirical research can follow two parallel paths. Top-down studies seeking to identify invasion or persistence thresholds for wildlife must address the recurring methodological issues listed above, compiling well-replicated disease datasets over a range of host abundances—and for persistence, also tracking mortality, recruitment and migration of hosts and identifying possible reservoirs. These are lofty standards, and will be met only under rare circumstances. Bottom-up mechanistic studies, meanwhile, can investigate the basic processes underlying thresholds (e.g. birth, death, immigration, and transmission), particularly the density dependence common in wildlife systems. We believe that these complementary approaches, linked by new theory appropriate to wildlife disease, represent the surest path to well-grounded empirical evidence of disease thresholds.

Our review emphasises that control policies predicated on reducing susceptible populations can reduce prevalence or eradicate disease, but perverse outcomes are possible and “magic number” thresholds, while alluring to policy-makers, are not supported by evidence.

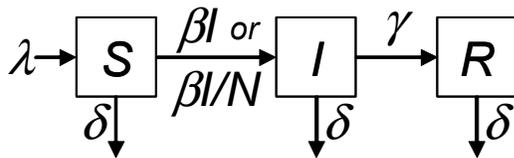
Regardless of outcome, all control programs should monitor and publish their results, because they represent a critical opportunity to better our understanding of population thresholds and density dependence of wildlife disease.

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Box 1. Insights from simple deterministic models

Basic principles of disease spread are illustrated clearly by deterministic models, which divide a population into compartments based on disease status and depict disease transitions as predictable flows among groups. Here we consider a non-fatal disease, without a significant latent period, from which individuals recover to a state of permanent immunity—we therefore use a so-called SIR model, named after the three disease compartments. Due to the critical role of the transmission process in determining population thresholds, we analyse the model for both density-dependent and frequency-dependent transmission. Because inflow of new susceptibles is essential to the long-term persistence of such a disease, we include a simple treatment of demographic dynamics. The models are as follows:



S, I, R = densities of Susceptible, Infectious, and Recovered hosts ($N = S + I + R$)

λ = input of new susceptibles

δ = death rate not associated with disease

γ = recovery rate of infecteds

β = transmission coefficient

Transmission:
Model equations:

Density-Dependent (βI)

$$\frac{dS}{dt} = \lambda - \delta S - \beta IS$$

$$\frac{dI}{dt} = \beta IS - (\gamma + \delta)I$$

$$\frac{dR}{dt} = \gamma I - \delta R$$

Basic reproductive number:

$$R_0 = \frac{\beta N}{\gamma + \delta}$$

Endemic equilibrium:

$$S^* = \frac{\gamma + \delta}{\beta}, I^* = \frac{\beta \lambda - \delta(\gamma + \delta)}{\beta(\gamma + \delta)}$$

Frequency-Dependent ($\beta I/N$)

$$\frac{dS}{dt} = \lambda - \delta S - \frac{\beta I}{N} S$$

$$\frac{dI}{dt} = \frac{\beta I}{N} S - (\gamma + \delta)I$$

$$\frac{dR}{dt} = \gamma I - \delta R$$

$$R_0 = \frac{\beta}{\gamma + \delta}$$

$$S^* = \frac{\lambda(\gamma + \delta)}{\delta \beta}, I^* = \frac{\lambda[\beta - (\gamma + \delta)]}{\beta(\gamma + \delta)}$$

For both models, the total population size has a stable equilibrium at $N^* = \lambda/\delta$.

We immediately gain several insights from these simple models. Because R_0 increases with N in the model with density-dependent transmission, we predict a population threshold for invasion $N_T = \frac{\gamma + \delta}{\beta}$. Conversely, in the frequency-dependent model R_0 depends only on rate parameters, so there is no population threshold for invasion [16, 57].

With regard to persistence, we first ask whether an endemic equilibrium is possible at all. For both simple models, non-zero values of I^* exist whenever $R_0 > 1$ —if a disease is able to invade, then it will reach endemic steady state in the deterministic model [21]. Therefore, for density-dependent transmission the existence of an endemic equilibrium depends on population density, whereas for frequency-dependent transmission it does not. Another important question is how far the endemic equilibrium is from $I=0$. While deterministic models do not include random fluctuations, in real populations there is greater danger of stochastic fadeout when I is small (just as for population fluctuations of severely endangered species). All else being equal, the disease will persist longer for larger values of I^* . Note that the endemic equilibria for both models can be written $S^* = \frac{N^*}{R_0}$ and $I^* = \frac{N^*}{1 + \rho} \left(1 - \frac{1}{R_0} \right)$, where $\rho = \gamma/\delta$ is the ratio of mean host lifespan to mean infectious period [35]. For a given value of $R_0 > 1$, therefore, we expect I^* to increase with N^* in both models, and hence we expect persistence times to increase gradually with N^* . Note that I^* also decreases as ρ increases, so transient diseases are predicted to be more vulnerable to stochastic fadeout.

Box 2. Density dependence and the critical community size

A core assumption underlying the CCS is that the rate of susceptible replenishment (usually due to birth and/or immigration) increases with population size [7, 28, 30]. In human systems, the population growth rate generally satisfies this assumption (Fig 1a). In wildlife systems, however, density-dependent effects can dominate recruitment, such that the replenishment rate of new susceptibles may actually decrease as N increases (Fig 1b). Many different curves—some highly non-linear—can describe the relationship between population size and recruitment rates, and often death rates also exhibit density dependence [58]. Immigration and emigration can vary similarly, as animals distribute themselves via density-dependent habitat selection [59].

These ecological complexities contribute uncertainty to the already fuzzy CCS, casting doubt on its general applicability in wildlife disease systems. They also introduce potential for perverse outcomes of control efforts: culling programs may increase birth rates (through compensating recruitment) or immigration (as conspecifics re-colonize a cleared habitat via the “vacuum effect” [46]), thus increasing the chance of disease persistence [36, 46]. Finally, disease-induced mortality of a host species may itself interact with density-dependent effects, generating complex dynamics and possible feedback cycles with unpredictable effects on disease persistence.

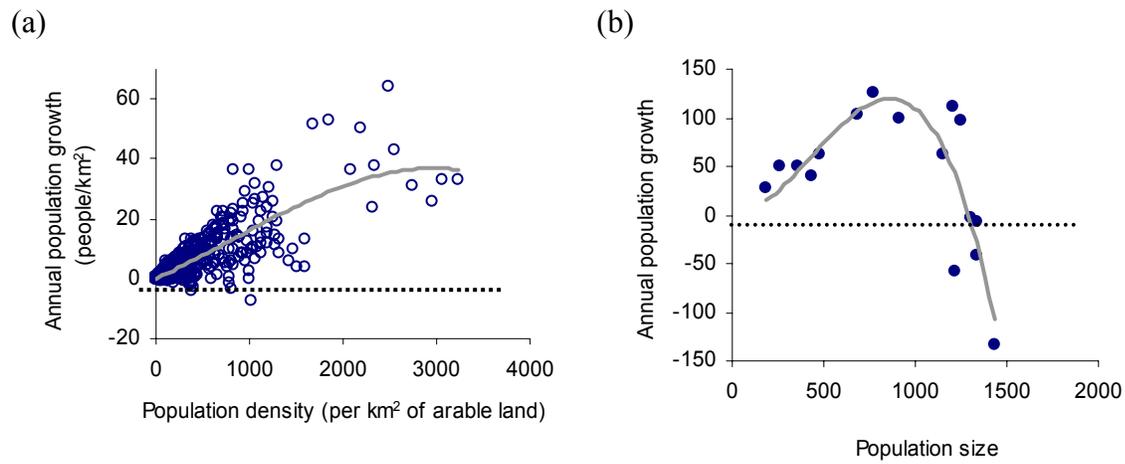


Figure I. Annual population growth for (a) humans from 187 countries from 1960 to 2000 and (b) wildebeest in the Serengeti. Data redrawn from [60]. Human population density was calculated using the amount of arable land available in 1960. Third-order polynomials were fit to the data with the y-intercept set to zero.

Box 3. Simple theories, complex realities

The theoretical results presented in the text apply to well-mixed host populations in constant environments, with single directly-transmitted pathogens and no alternative host species. The insights obtained are valuable, but real disease systems exist under much more complex conditions. The following complexities are found in many real systems, both human and wildlife:

- Spatial or social structure in a population can impede disease invasion [25], and can help or hinder persistence depending on the strength of coupling between subgroups [14, 35, 61]. The relevant scale to measure N can be unclear, and will depend on the relative frequency of between-group movements [62]. Group-level heterogeneities further obscure threshold determination, e.g. a disease may invade and persist in a high-risk core group but not in the general population [21].
- Disease-host systems involving additional complexities, including macroparasitic and vector-borne diseases, or those with environmental reservoirs, may exhibit altered or additional thresholds [2, 36].
- Transmission rates vary seasonally due to environmental or social changes, potentially coupling with natural timescales of the disease-host interaction to produce dramatic effects on invasion or persistence [30, 31, 63, 64].
- Host-pathogen coevolution influences long-term persistence of endemic diseases [65] through immune escape mechanisms [66] and evolution of virulence [67], and can influence invasion of novel pathogens via adaptation to the new host [68].
- In wildlife, density-dependent effects in recruitment, death and movement alter population responses to changes in N [46]—see Box 2.

- Strong seasonality in wildlife births will increase fadeout due to irregular supply of new susceptibles, and variation in per capita birth rates can be an order of magnitude higher than in humans [60]. Wildlife populations also fluctuate due to trophic interactions and environmental stochasticity, again favouring fadeout during periods when N is low.
- Alternative host species can change the basic dynamics of transmission, particularly if they act as endemic reservoirs for a disease [69]. In evaluating persistence, it is critical to distinguish true single-host persistence from repeated failed invasions from a reservoir or sustained interspecific transmission [39, 41, 70].

Table 1. Selected empirical studies testing for population thresholds for wildlife disease

Ref	Host	Pathogen(s)	Sampling unit (number of individuals per unit)	Duration of study	Type of evidence and conclusion	Observations
[9]	Great gerbils (<i>Rhombomys opimus</i>)	Plague (<i>Yersinia pestis</i>)	2 populations	40 yr	<ul style="list-style-type: none"> • Prevalence over time • Statistical model <p>Periods of plague absence suggest a population threshold for invasion and persistence</p>	Strong data, but model did not distinguish between invasion and persistence; Possible effects of vector; 2-year lag between host abundance and disease
[8]	Bank voles (<i>Clethrionomys glareolus</i>) and wood mice (<i>Apodemus sylvaticus</i>)	Cowpox	15 populations (5-140)	2 yr	<ul style="list-style-type: none"> • Prevalence as a function of host densities and numbers • Estimates of movement <p>Evidence for “fuzzy”</p>	Limited replication relative to the large effects of stochasticity in small populations; Possible alternative hosts; Unknown effect of background

					invasion and persistence thresholds in one host species, in population number (but not density)	populations in single mainland patch
[13]	Semi-feral dogs (<i>Canis familiaris</i>)	Rabies	3 populations	3-5 yr	<ul style="list-style-type: none"> Rabies presence or absence as a function of host density and number <p>Evidence for CCS in population density (but not number)</p>	Limited replication; Possible alternative reservoirs; No temporal replication
[14]	Harbour seals (<i>Phoca vitulina</i>)	Phocine distemper virus	Pooled datasets for 25 sub-populations	1-2 yr	<ul style="list-style-type: none"> Observed fade-outs Mathematical modelling <p>If CCS exists, it is much larger than the entire population</p>	Only mathematical support of CCS; Possible alternative hosts
[12]	American bison (<i>Bison</i>)	<i>Brucella abortus</i>	Pooled datasets for	Datasets cover	<ul style="list-style-type: none"> Prevalence as a function of host 	No data below putative threshold;

	<i>bison</i>)		18 herds (200-3200)	45+ yr	density Brucella fails to invade herds of less than 200 individuals	Only one herd without brucellosis; Possible alternative hosts
[15]	African lion (<i>Panthera leo</i>)	Six feline viruses	2 populations (40-260)	20-25 yr	<ul style="list-style-type: none"> Outbreaks over time as a function of the number of susceptibles Certain viruses invade only after buildup of susceptibles	Possible alternative hosts—source of diseases unknown; Sparse sampling in one of two populations
[30, 31]	Humans ^a	Measles	60 cities (10,000 – 30,000)	22 yr	<ul style="list-style-type: none"> # of cases over time Mathematical modelling Disease does not persist in isolated populations of less than 250,000 individuals	Strongest example of CCS to date

^a This classic example is included for comparison to human disease systems.

Figure 1

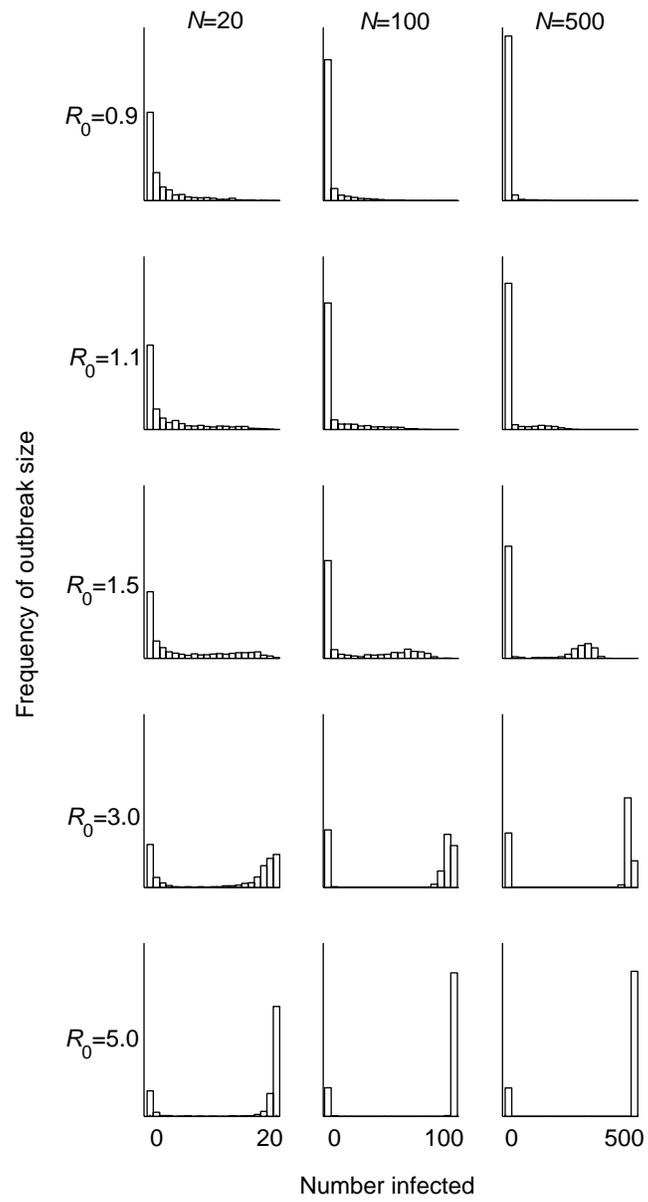
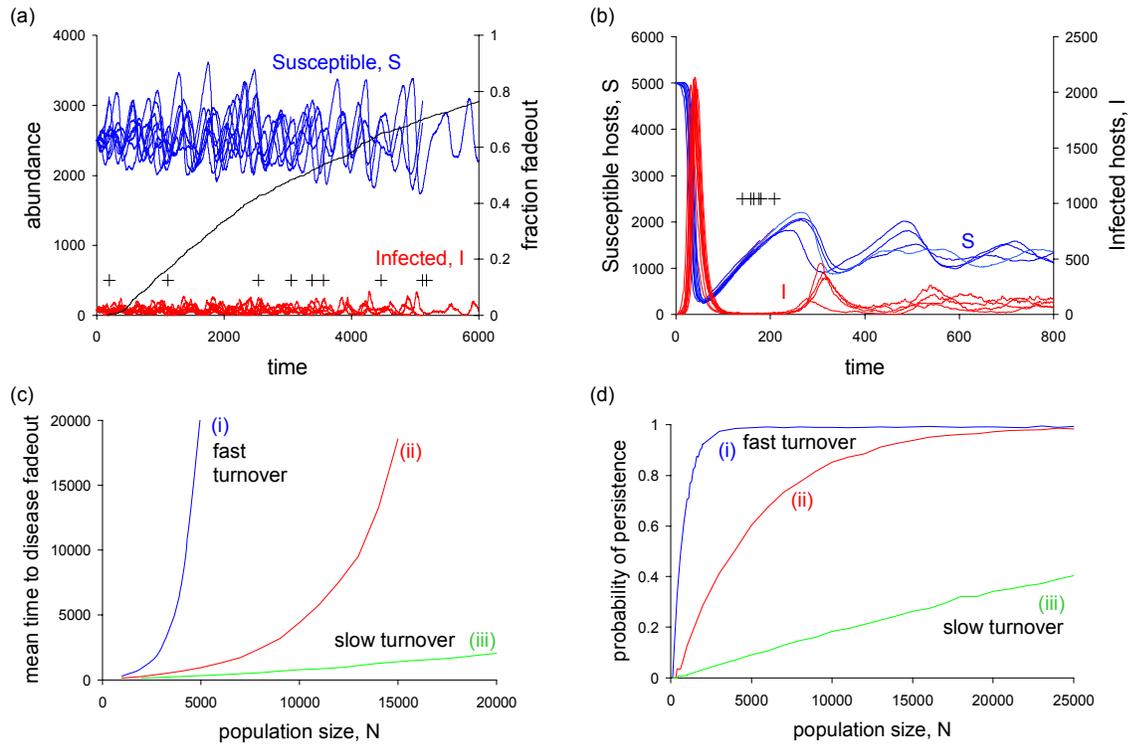


Figure 2



Glossary

Basic reproductive number (R_0): The expected number of secondary cases caused by the first infectious individual in a wholly susceptible population. This acts as a threshold criterion because disease invasion can succeed only if $R_0 > 1$.

Critical community size (CCS): The population size above which stochastic fadeout of a disease is less likely. Because disease dynamics do not change sharply with population size, the CCS is traditionally set by subjective assessment or arbitrarily chosen criteria. Originally defined in the context of epidemic fadeout, the CCS is now often used as a general term for any population threshold for disease persistence.

Demographic stochasticity: The variation evident in dynamics of small populations due to the probabilistic nature of individual processes such as birth, death or transmission.

Deterministic model: A mathematical or simulation model in which chance plays no role, so the results are determined entirely by model structure, parameter values, and initial conditions.

Effective reproductive number (R_{eff}): The expected number of secondary cases caused by each infectious individual in a partially immune population. In well-mixed populations this will equal $R_{\text{eff}} = sR_0$ where s is the fraction of the population that is susceptible.

Endemic fadeout: Extinction of the disease from a stable endemic state due to random fluctuations in the number of infected individuals (represented by the quasi-stationary distribution of I).

Epidemic fadeout: Extinction of the disease during the period following an epidemic when the pool of susceptibles is depleted. This can be result from random fluctuations in the number of infected individuals or from a protracted period with $R_{\text{eff}} < 1$.

Herd immunity: A phenomenon whereby disease can be excluded from a population despite the presence of some susceptibles, because the proportion of individuals that are immune is sufficient to ensure that $R_{\text{eff}} < 1$.

Quasistationary distribution: The stationary distribution of a quantity (here, the number of infected individuals, I) conditional on not having gone extinct yet. This concept is used to describe “equilibrium” behaviour in stochastic models where extinction is assured as time goes to infinity.

Stochastic model: A mathematical or simulation model incorporating chance events, particularly important when small numbers of individuals play an important role (as in invasions) or when fluctuations around mean behaviour are important.

Threshold population for invasion (N_T): The minimum population size required for a disease to be able to successfully invade a host population.

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Figure legends

Figure 1. Distribution of outbreak sizes for diseases with different R_0 values and host population sizes. Histograms show the total number of individuals infected in each of 1000 simulated SIR outbreaks. Each outbreak began with one infectious individual and N susceptibles. Simulations were based on the discrete-time analogue of the frequency-dependent model in Box 1, but for simplicity we depict the per-timestep probabilities of recovery and death using the continuous-time rates γ and δ (a slight approximation, because the exact probabilities have the form $1 - e^{-\gamma}$). In these simulations, the demographic rates $\lambda = \delta = 0$, and $\gamma = 0.1$. For each susceptible, the infection probability per timestep was $1 - \exp(-\beta I/N)$, with $\beta = \gamma R_0$. Because N was fixed, this is precisely equivalent to density-dependent transmission with infection probability $1 - \exp(-\beta I)$ and $\beta = \gamma R_0/N$.

Figure 2. Endemic and epidemic fadeout

(a) Endemic fadeout: 10 stochastic simulations of endemic disease dynamics, begun from endemic equilibrium conditions (+ signs show instances of endemic fadeout, when I fluctuated to zero). Black line shows cumulative fraction of runs with disease fadeout, out of 1000 stochastic simulations. $N^* = \lambda/\delta = 10000$, $\delta = 0.001$, $\rho = \gamma\delta = 100$.

(b) Epidemic fadeout: 10 stochastic simulations of epidemic disease dynamics, begun with $S=4999$, $I=1$, $R=0$ (+ signs show instances of epidemic fadeout during the trough in I following the first epidemic peak). $N^* = \lambda/\delta = 5000$, $\delta = 0.003$, $\rho = \gamma\delta = 33.3$.

(c) Average time (out of 1000 runs started at the endemic equilibrium) to endemic fadeout as a function of N and the relative rate of demographic turnover. Along each curve, equilibrium population size, $N^* = \lambda/\delta$, was varied by changing the input of new susceptibles, λ , while

keeping δ constant. Different rates of demographic turnover (i.e. different curves at a given population size) were achieved by simultaneously varying λ and δ , while keeping the ratio $N^* = \lambda/\delta$ constant. Thus δ varies between curves, which alters $\rho = \gamma\delta$. For curve (i) $\delta = 0.002$, $\rho = \gamma\delta = 50$; for (ii) $\delta = 0.001$, $\rho = \gamma\delta = 100$; and for (iii) $\delta = 0.0005$, $\rho = \gamma\delta = 200$.

(d) Probability of persisting through the first inter-epidemic trough as a function of N and the relative rate of demographic turnover, estimated from the fraction of 10,000 runs that persisted (starting with $S=N^*-1$, $I = 1$, and $R = 0$, conditional on successful invasion of the disease).

Equilibrium population size, and demographic turnover rates were varied as in (c). For curve (i)

$\delta = 0.005$, $\rho = \gamma\delta = 20$; for (ii) $\delta = 0.003$, $\rho = \gamma\delta = 33.3$; and for (iii) $\delta = 0.002$, $\rho = \gamma\delta = 50$.

With $\delta = 0.001$, $\rho = \gamma\delta = 100$ no runs persisted through the first trough.

In all panels, simulations were based on the same model as in Figure 1, with $\beta = (\gamma + \delta)R_0$, $R_0 = 4$, and $\gamma = 0.1$.