Ecological Applications, 15(4), 2005, pp. 1402–1414

EXPOSING EXTINCTION RISK ANALYSIS TO PATHOGENS: IS DISEASE JUST ANOTHER FORM OF DENSITY DEPENDENCE?

LEAH R. GERBER,[1,5] HAMISH MCCALLUM,[2] KEVIN D. LAFFERTY,[3] JOHN L. SABO,[1] AND ANDY DOBSON[4]

[1]*School of Life Sciences, Arizona State University, Box 871501, Tempe, Arizona 85287-1501 USA*
[2]*Department of Zoology and Entomology, University of Queensland, Brisbane 4072, Australia*
[3]*USGS, University of California, Marine Science Institute, Santa Barbara, California 93106 USA*
[4]*Ecology and Evolutionary Biology, Princeton University, Princeton, New Jersey 08544 USA*

Abstract. In the United States and several other countries, the development of population viability analyses (PVA) is a legal requirement of any species survival plan developed for threatened and endangered species. Despite the importance of pathogens in natural populations, little attention has been given to host–pathogen dynamics in PVA. To study the effect of infectious pathogens on extinction risk estimates generated from PVA, we review and synthesize the relevance of host–pathogen dynamics in analyses of extinction risk. We then develop a stochastic, density-dependent host–parasite model to investigate the effects of disease on the persistence of endangered populations. We show that this model converges on a Ricker model of density dependence under a suite of limiting assumptions, including a high probability that epidemics will arrive and occur. Using this modeling framework, we then quantify: (1) dynamic differences between time series generated by disease and Ricker processes with the same parameters; (2) observed probabilities of quasi-extinction for populations exposed to disease or self-limitation; and (3) bias in probabilities of quasi-extinction estimated by density-independent PVAs when populations experience either form of density dependence. Our results suggest two generalities about the relationships among disease, PVA, and the management of endangered species. First, disease more strongly increases variability in host abundance and, thus, the probability of quasi-extinction, than does self-limitation. This result stems from the fact that the effects and the probability of occurrence of disease are both density dependent. Second, estimates of quasi-extinction are more often overly optimistic for populations experiencing disease than for those subject to self-limitation. Thus, although the results of density-independent PVAs may be relatively robust to some particular assumptions about density dependence, they are less robust when endangered populations are known to be susceptible to disease. If potential management actions involve manipulating pathogens, then it may be useful to model disease explicitly.

Key words: density dependence; diffusion approximation; disease; epidemic; epidemiology; extinction risk; host–pathogen interactions; parasite; pathogen; population viability analysis; PVA; reservoir host.

INTRODUCTION

Disease and host–pathogen interactions play a central role in determining the dynamics and persistence of populations (Dobson and Foufopoulos 2001). However, disease has traditionally received much less attention than other community interactions (e.g., predation and competition) in the ecological literature (Gulland 1995). There are several well-known case studies bearing on the effects of disease on the fate of endangered populations, and there is increasing attention on how the ecological theory of diseases (e.g., Anderson and May 1991) may bear on conservation issues (Lafferty and Gerber 2002).

Manuscript received 25 May 2004; revised 8 November 2004; accepted 15 November 2004. Corresponding Editor: R. S. Ostfeld.

[5] E-mail: leah.gerber@asu.edu

Population viability analysis (PVA) is one of the quintessential tools in conservation biology for quantifying extinction risk. Very generally, there are two forms of single-population PVA (Morris and Doak 2002): (1) time series models and (2) matrix population models. Here we focus on the efficacy of time series PVAs faced with forecasting the future persistence of populations exposed to disease. The simplest and most commonly used time series PVAs (e.g., Lande and Orzack 1988, Dennis et al. 1991, Holmes 2001, Morris and Doak 2002) assume, among other things, that population growth is density *independent* and that species interactions such as disease can be ignored or treated as density-independent mortality.

The impact of a pathogen often depends on host density (Anderson and May 1979, May and Anderson 1979). Thus, in traditional host–pathogen models, both the probability of occurrence *and* severity of an epidemic (in terms of mortality) are strongly tied to host

density. This suggests two important points about the blind application of density-independent PVAs to populations exposed to disease. First, density dependence brought on by disease may reduce the precision of density-independent PVA models at forecasting risk (e.g., Sabo et al. 2004). More specifically, time series PVAs that assume density-independent (''linear'' on a log scale) population growth are often robust to density dependence when density effects are not strong and when populations are near their maximum abundance level, but generate biased estimates of risk for populations that grow quickly (Sabo et al. 2004). Thus, if disease dynamics mirror those of density dependence, then we should expect density-independent PVAs, when applied to populations subject to disease, to perform well in the same sorts of situations (for declining, slowly recovering, or strongly fluctuating populations).

Second, because the probability of an epidemic occurring is also related to the host density, the ''process'' of disease adds a second source of stochasticity to host population dynamics. This additional stochasticity could further bias estimates of growth parameters and risk made by density-independent PVA models. This key distinction between a disease and more traditional density-dependent processes (e.g., Volterra 1928, Ricker 1954) suggests that the performance of density-independent PVAs may be qualitatively different for populations experiencing epidemics and self-limitation. One of the main reasons for using PVA models is not to estimate the probability of persistence of a given population as it currently exists, but as a decision analysis tool to compare the consequences for population persistence of alternative management actions (Morris et al. 1999, Possingham et al. 2001). This approach requires modeling the processes that determine population size and the effects of management actions upon them, and not simply projecting a stochastic time series into the future. Consequently, treating an epidemic infectious disease as simply variation in catastrophic stochasticity may not be an adequate approach. If potential management actions involve manipulating pathogens, then it may be necessary to model disease explicitly.

One key challenge in improving the application of PVA in conservation settings is developing a clear link between plausible biological factors driving population dynamics, such as pathogens, and species population biology. Although several theoretical approaches to improve the accuracy of PVA predictions have recently been put forth in the literature (e.g., Dennis et al. 2001, Holmes 2001, DeValpine and Hastings 2002), few published PVAs explicitly include disease (Haydon et al. [2002] is an exception). This problem is, at least in part, attributable to deficiencies in the theoretical framework for examining disease in analyses of extinction risk (Lafferty and Gerber 2003) and a lack of data to parameterize density-dependent models (Sabo et al. 2004). PVA models that explicitly include disease dynamics may allow scientists to test the sensitivity of a species' persistence to changes in life history parameters influenced by disease outbreaks. This may help to identify causes of population declines for fluctuating populations.

In this paper, we ask two questions about disease, density dependence, and the performance of time series PVA models that assume density-independent population growth. (1) Do endangered populations exposed to disease exhibit population dynamics identical to those of more traditional forms of self-limitation (e.g., Ricker 1954)? (2) Do disease and density dependence alter probabilities of extinction for endangered populations in a qualitatively similar fashion? In summary, we evaluate the need for explicit incorporation of disease in population viability analyses.

Relevant Principles of Epidemiology

The density of a population is an important parameter for both PVA and host–pathogen theory. A fundamental principle of epidemiology is that the spread of an infectious disease through a population is a function of the density of both susceptible and infectious hosts. If infectious agents are supportable by the host species of conservation interest, the impact of a pathogen on a declining population is likely to decrease as the host population declines. A pathogen will spread when, on average, it is able to transmit to a susceptible host before an infected host dies or eliminates the infection (Kermack and McKendrick 1927, Anderson and May 1991). If the parasite affects the reproduction or mortality of its host, or the host is able to mount an immune response, the parasite population may eventually reduce the density of susceptible hosts to a level at which the rate of parasite increase is no longer positive. Most epidemiological models indicate that there is a host threshold density (or local population size) below which a parasite cannot invade, suggesting that rare or depleted species should be less subject to host-specific disease. This has implications for small, yet increasing, populations. For example, although endangered species at low density may be less susceptible to a disease outbreak, recovery to higher densities places them at increasing risk of future disease-related decline (e.g., southern sea otters; Gerber et al. 2004).

In the absence of stochastic factors (such as those modeled in PVA), and given the usual assumption of disease models that the chance that a susceptible host will become infected is proportional to the density of infected hosts (the mass action assumption) a host-specific pathogen cannot drive its host to extinction (McCallum and Dobson 1995). Extinction in the absence of stochasticity is possible if alternate hosts (sometimes called reservoir hosts) relax the extent to which transmission depends on the density of the endangered host species. Similarly, if transmission occurs at a rate proportional to the frequency of infected hosts relative to uninfected hosts (see McCallum et al. 2001), endangered hosts at low density may still face the threat

of extinction by disease. These possibilities suggest that the complexities characteristic of many real host–pathogen systems may have very direct implications for the recovery of rare endangered species.

Diseases affecting wildlife can be broadly divided into *endemic* infections, which are present continuously in a particular population, at a more or less constant level, and *epidemic* infections, which occur sporadically, pass through the population, and then disappear. Endemic infections might potentially be handled within the framework of a density-independent PVA model. If the disease is present continuously, then mortality and fecundity rates measured in the field will include components due to the influence of the parasite. To estimate the impact that removal of an endemic parasite has on population viability, it would be possible, in principle, to manipulate parasite levels in some hosts, to estimate the resulting vital rates in both infected and parasite-free hosts (e.g., Gulland 1992, Hudson et al. 1992), and then use a conventional PVA model to compare the viability of populations with and without parasite infection. Such an approach does not, however, model the density-dependent nature of parasite population dynamics.

Epidemic infections are likely to require more fundamental changes to the PVA process. Their inclusion requires consideration of four questions in developing PVAs:

1) What is the likelihood of pathogen arrival into the population under consideration?

2) Given that infection has arrived, what is the likelihood that an epidemic will become established in the population?

3) Once it has become established, what will be the impact of the pathogen on the host population?

4) How long will the pathogen persist in the population, once it has become established?

The answers to each of these questions will depend on the biology of the pathogen and host. For example, it is important to consider the host range (is it restricted to the species for which the PVA is being developed?), the mode of pathogen transmission (is there a vector, intermediate host, or long-lived infective stage?) and the effect of the pathogen on the host.

One approach to capturing the dynamics of an epidemic in a PVA framework is to incorporate this type of disease as catastrophic mortality (e.g., Gerber and Hilborn 2001). To do this, one assumes that it is possible to estimate the probability that the pathogen will arrive in the population and become established, and that it is possible to estimate the proportion of individuals that will die, or fail to reproduce, as a consequence. This approach further assumes that neither of these probabilities depends strongly on host population size or density, and that the infection persists for one time step only. Empirical studies of epidemics (Gulland 1992, Heide-Jorgensen and Harkonen 1992, Dobson and Meagher 1996) show that these model assumptions are clearly inadequate for understanding the true effects of this type of disease on the viability of a recovering species. Thus, a more sophisticated PVA that explicitly incorporates density dependence in transmission may be warranted.

In addition to density, environmental factors (such as pollution that increases host susceptibility) or genetic population structure (which may make certain host–parasite genotypes more compatible from the parasite's perspective), may influence the efficiency of transmission to new hosts. The vital demographic rates of both the pathogen and the host are also of importance in determining a parasite's success. Factors (such as medication and immune response) that alter the birth and death rates of parasitic and free-living stages of the parasite might substantially affect disease spread and persistence. Many parasites require passage through several host species to complete life cycles. These complex life cycles may increase the conditions that must be met for the disease to spread. Although the death of a host often results in the death of its parasites, resulting in selection for reduced virulence (although not necessarily avirulence; May and Anderson 1990), this will not be the case where death of the intermediate host through predation is a necessary part of the parasite's life cycle.

Finally, the basic reproductive rate (R_0) of pathogens is the key epidemiological quantity necessary to parameterize a PVA, in addition to the usual host demographic parameters. R_0 is the basic reproductive number, or the number of secondary infections per primary infection in a completely susceptible host population. However, the way in which this value scales with host density will have a major influence on disease dynamics, particularly if R_0 estimated from one population is applied to another. In some cases, there may be sufficient information to empirically estimate the relationship between R_0 and host density. Failing this, the conventional assumption of most host–pathogen models is that R_0 is directly proportional to host density (density dependence), but vector- or sexually transmitted pathogens often follow frequency-dependent transmission, in which R_0 is independent of density (McCallum et al. 2001).

PVA: A Role for Infectious Pathogens?

There are two quite different approaches that can be used to predict the range of possible trajectories of a population affected by stochastic factors. First, Dennis et al. (1991) proposed a method that uses time series abundance data to estimate the rate of increase of the population, together with its variance. These two parameters can then be used to generate a frequency distribution of potential population size at any given time. This approach involves the estimation of two parameters, the population growth rate (μ) and the variability in that rate (σ^2), although a later variation provides a method for estimating density-dependent growth pa-

rameters as well (Dennis and Taper 1994, Foley 1994). These time series methods provide estimates of parameters by analyzing the pattern of abundance over time, but make no attempt to model the processes generating the observed pattern directly. Alternatively, the major packaged PVA computer models are process based. They attempt to generate the trajectory of the population via an age- or stage-structured stochastic model. This means that they require the estimation of a large number of demographic parameters, minimally survivorship and fecundity, together with their variances, for each of the age or sex classes that are modeled. Because processes are modeled, it would be possible, in principle, to include parasite or pathogen effects in these models explicitly, and to evaluate the effectiveness of various control actions.

In the next section, we develop a simple model that includes key features of the effects of epidemic pathogens on stochastic host populations. Our model is designed to examine two questions. *First, how well does modeling epidemics as density-independent catastrophes capture the effect of epidemics on population viability? Second, how do pathogen epidemics differ from other forms of density dependence in their impact on host population viability?*

Our model assumes that the density of the host species being modeled drives the dynamics of the epidemic. It is therefore not directly applicable to situations in which the dynamics of the pathogen are driven by its interaction with a much more common reservoir species, and infection of the endangered host occurs primarily by cross-infection from the reservoir. Although it is certainly the case that many pathogen threats to endangered species involve a reservoir host (McCallum and Dobson 1995, Gog et al. 2002, Lafferty and Gerber 2002), there are numerous examples of pathogens causing endangerment in which the disease propagates primarily within the species of conservation interest. For example, Haydon et al. (2002) estimated that transmission of both rabies and canine distemper virus occurred at much higher rates within and between Ethiopian wolf packs than it did between reservoir dog populations and wolves. In African lions in the Serengeti, epidemics of several viruses (including canine distemper virus) are associated with minimum threshold densities of susceptible hosts (Packer et al. 1999), indicating that host density drives the dynamics of these pathogens. Stress due to droughts or the presence of other pathogens that weaken host immunity may lower establishment thresholds (Lafferty and Holt 2003). Koalas (*Phascolarctos cinereus*) suffer high rates of mortality from lymphomas and leukemia (up to 80% of all mortalities of captive koalas in some colonies), and a host-specific retrovirus may be responsible (Hanger et al. 2000).

Modeling Effects of Epidemic Pathogens on Stochastic Host Populations

Our general approach was to use commonly used methods of PVA (e.g., Dennis et al. 1991, Morris et al. 1999, Holmes 2001) to examine: (1) quantitative differences in the dynamics of populations exposed to disease and a more traditional form of single-species density dependence expressed in the Ricker model; (2) how disease and density dependence influence probabilities of an 80% decline, a common risk metric used in management decisions (e.g., IUCN Red List; Mace and Lande 1991); and (3) how density-independent PVAs perform when the underlying population processes include disease or density dependence. Our overarching hypothesis is that although the density-dependent effects of disease (e.g., on host mortality) are similar to other forms of density dependence *when* an epidemic occurs, the variable effects of disease with host density and the probabilistic nature of epidemics occurring may lead to distinctly different population dynamics than simple density dependence. As a result, we predict that density-dependent PVAs will be less robust to data influenced by disease than by simple density dependence.

To do this we first simulated time series for replicate populations with disease *or* with simple density dependence for a variety of parameters describing the growth rate of the population (μ) and the intensity of density dependence. Previous cross-validation studies have used these parameters to identify case studies in which the performance of density-independent PVA models is robust despite density dependence (Sabo et al. 2004). Our objective was to compare the effects of disease and density dependence on population viability. Here we used the probability of an 80% decline in abundance, P_{80}, as an extinction risk metric because it is easy to compute (numerically) and is applied by conservation organizations worldwide as one of several listing criteria.

To assess the impact of disease on predictions made by density-independent PVA protocols (e.g., Dennis et al. 1991), we used a diffusion approximation (DA) model to estimate growth parameters for populations affected by either infectious disease or density dependence in the time series just generated (Dennis et al. 1991). These growth parameters were then used to numerically estimate P_{80} values for comparison with observed values for this risk metric from the simulated disease- and density-dependent processes. We used the DA model because it has been widely used to estimate extinction risks for species of conservation interest (e.g., Dennis et al. 1991, Nicholls et al. 1996, Gerber et al. 1999, Morris et al. 1999, Holmes 2001).

The basic PVA model was the stochastic difference equation, as described by Dennis (1991):

$$N_{t+1} = N_t \exp(\mu_t). \quad (1)$$

Here N_t and N_{t+1} are the population size in generations t and $t + 1$, respectively, and μ_t is a stochastic parameter drawn from a normal distribution with a mean and variance determined by the parameters μ_0 and σ^2, respectively. In the absence of pathogen infection, μ_t was

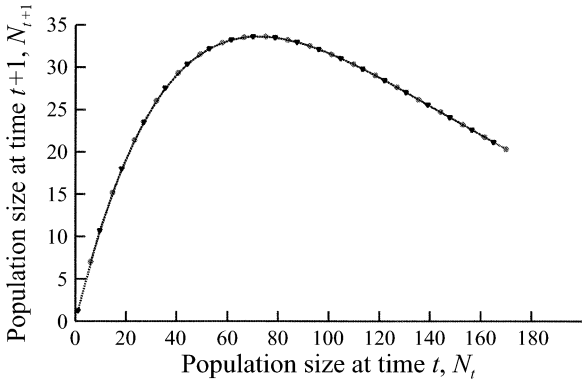

FIG. 1. The deterministic skeletons for population dynamics generated by disease (Eq. 3) and self-limitation as described by the Ricker model (Eq. 5) for $\beta/\alpha = 0.01$, $\mu_0 = 0.1$. Axes are population size at time t (N_t, abscissa) and at time $t + 1$ (N_{t+1}, ordinate). Dynamics of these two models converge when $R_0 > 1$ (with these parameters, when $N_t > 100$), given that an epidemic occurs. Note that the dynamics are quite different when $R_0 < 1$, because the disease model has no density dependence when $R_0 < 1$, whereas it is always present in the Ricker model.

drawn at random from a normal distribution with mean μ_0 and a specified density-independent deviation. In practice, estimates of μ_0 and its variance can be obtained from a time series of population size (see Dennis et al. 1991, McCallum 2000).

To simulate populations exposed to disease, we adjusted N_t at each time step to mimic the effects of an epidemic of a virulent pathogen in which all hosts were initially susceptible and in which the disease was fatal. There were two sequential aspects to each epidemic, both of which were density dependent. The first was the probability of an epidemic occurring. This was the probability a of an infected individual entering a population times the probability b that this infected individual would cause an epidemic. In the model results reported here, we assumed that $a = 1$. Epidemiological theory shows that a pathogen will not invade a host population if $R_0 < 1$, but is not inevitable even if $R_0 > 1$ (Anderson and May 1986). Using a result obtained by Dietz (1993), we assumed that b, the probability of an epidemic occurring, given that $R_0 > 1$, was

$$b = 1 - \frac{1}{R_0}. \quad (2)$$

We further made the conventional assumption that transmission was density dependent (see McCallum et al. 2001). When transmission is density dependent, $R_0 = N\beta/(\gamma + \alpha)$, where β is the transmission rate of the disease, γ is the recovery rate, and α is the instantaneous death rate of infected hosts. Because our model concerns a fatal disease with no recovery, we can simplify such that $R_0 = N\beta/\alpha$. To calculate the impact of the disease if the disease were to invade the host population, we estimated the uninfected fraction (f) of the initially susceptible hosts remaining after an epidemic as $f = \exp(-R_0)$. This estimate is only accurate if $R_0 > 3$ (Swinton 1998). At lower values of R_0, $f = \exp(-R_0(1 - f))$, which does not have a closed-form solution. We found solutions for f *numerically*, and solved for the numerical relationship between f and R_0, which resulted in the approximate relationship $f = \exp(1.24 - 1.39R_0)$ when $R_0 < 3$. This approximation allows estimation of f to within 0.05, unless R_0 is less than 1.15, when it underestimates f. Using these estimates for f, we modified Eq. 1 to include the effect of a virulent pathogen as $N_{t+1} = fN_t\exp(\mu t)$. Thus, disease dynamics follow the form in Eq. 1 when $R_0 < 1$. With $R_0 > 1$, and given that an epidemic occurs with probability b (see Eq. 2), we then express the effects of disease on host density as

$$N_{t+1} = N_t\exp(1.24 - 1.39R_0)\exp(\mu_t) \quad \text{for } 1 < R_0 < 3 \quad (3)$$

$$N_{t+1} = N_t\exp(-R_0)\exp(\mu_t) \quad \text{for } R_0 > 3. \quad (4)$$

The dynamics in Eq. 3 can be represented in the form of one of the more traditional expressions of self-limitation, the Ricker model:

$$N_{t+1} = N_t\exp\left[r\left(1 - \frac{N_t}{K}\right)\right] \quad (5)$$

where the carrying capacity, K, and the density-independent growth rate, r, are described in terms of disease parameters as

$$K = \frac{(1.24 + \mu)}{R_0} \quad (6)$$

$$r = \mu_t + 1.24. \quad (7)$$

Ignoring stochasticity ($\mu_t = \mu$), and assuming a low growth rate, the dynamics of disease and simple density dependence are identical (Fig. 1). The key distinction between a density-dependent model following the form in Eq. 5 and host dynamics subject to a density-dependent epidemic (Eqs. 1–4) is that in the latter, the onset of density dependence is probabilistic, and both this probability and the effects of the epidemic are determined by the host density (see Eq. 2). In simple density-dependent population growth, dynamics follow Eq. 5 in *every* time step. This is not true for a disease model. Thus, our goals were to quantify differences between the processes of disease and simple density dependence and then to evaluate how differences in the processes may corrupt risk estimates from density-independent PVA models in qualitatively different ways.

To accomplish these goals, we first simulated time series for populations exposed to disease or experiencing density dependence in which the parameters used (i.e., values for μ_0 and σ^2) were identical for both. We ran Monte Carlo simulations (40 years, 1000 iterations each) for four scenarios for each type of population process: (1) steady but variable populations

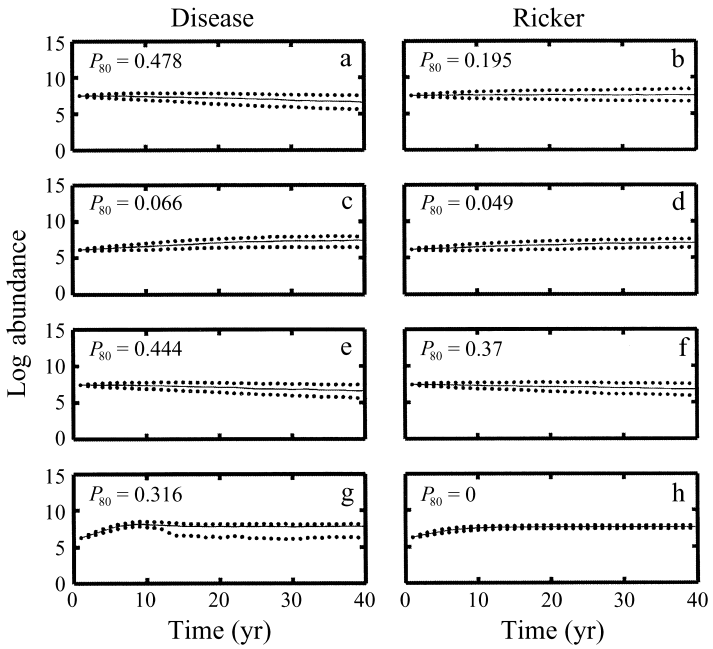

FIG. 2. Disease and Ricker dynamics with low environmental stochasticity for four conservation case studies. Median (solid) and upper and lower quartile (dotted) log-transformed abundance levels are shown for populations exposed to disease (left-hand panels) or driven by a Ricker process (right-hand panels). Here we show four case studies relevant to conservation (top to bottom): (a, b) steady but variable populations ($N_0 = K$, $\mu_0 = 0$); (c, d) slowly recovering populations ($N_0 = 0.1K$, $\mu_0 = 0.05$); (e, f) slowly declining populations ($N_0 = K$, $\mu_0 = -0.05$); and (g, h) rapidly recovering populations ($N_0 = 0.1K$, $\mu_0 = 0.3$). Probabilities of quasi-extinction (probability of an 80% decline in 40 years, P_{80}) are given in the upper left corner of each panel. All other parameters were as follows: $\alpha = 0.2$, $\beta = 0.0001$, and σ^2 (variance in μ_t) = 0.05, roughly the median of 22 empirical estimates of this parameter (Sabo et al. 2004).

hovering near their carrying capacity; (2) slowly declining populations; (3) slowly recovering populations; and (4) rapidly recovering populations. These situations correspond to case studies in which linear PVA models perform well (cases 1–3) or poorly (case 4) despite density dependence (Sabo et al. 2004). This was repeated for populations experiencing low and moderate levels of stochasticity ($\sigma^2 = 0.05$ or 0.134, respectively). The Ricker model generates damped oscillations, cycles, and chaos at successively higher values for μ (Figs. 2–6). We investigated the effects of these sources of deterministic variation on population persistence in a second series of Monte Carlo simulations. Finally, we examined the effects of disease and density dependence on the efficacy of density-independent PVA models by comparing observed risk (P_{80}) estimated empirically across 1000 replicate 40-year time series and a risk estimate from a linear PVA. Estimated P_{80} values were calculated in two steps. First, we estimated the parameters μ and σ^2 from each (1000) time series following (Dennis et al. 1991) and extracted the median value for each. Second, we used these median values to project 1000 replicate populations according to an exponential process (Eq. 1) and calculated the P_{80} numerically from these time series. This was done for disease and density dependence, and using a wide range of values for the parameters α/β and μ to generate the original disease- and density-dependent time series.

MODEL RESULTS

Dynamics of disease and simple density-dependent processes for endangered populations

Over a wide range of parameter values, disease dynamics differed significantly from those generated by a Ricker process. When growth rates were low (Figs. 2–3), median realizations were often similar for disease and Ricker processes. Despite this qualitative similarity, however, variability in abundance (e.g., 25th and 75th percentile abundance levels for a given year) and associated probabilities of decline to the quasi-extinction threshold (P_{80}) were typically higher for populations experiencing disease than simple self-limitation. Probabilities of quasi-extinction were higher for disease under a regime of low environmental stochasticity when populations were near their carrying capacity (Fig. 2 a, b) or recovering rapidly toward this threshold abundance level (Fig. 2 g, h). Observed values for P_{80} were 2.35 times higher for populations exposed to disease than those experiencing self-limitation when intrinsic growth rates were negligible ($\mu_0 = 0$) but variable ($\sigma^2 = 0.05$). Moreover, P_{80} increased with μ_0 for population exposed to disease, but decreased with μ_0 for populations experiencing self-limitation (compare Fig. 2c, d and g, h). By contrast, variability and probabilities of quasi-extinction were more similar between disease and Ricker processes when populations increased slowly toward K (Figs. 2c, d and 3c, d) or had negative intrinsic growth rates (Figs. 2e, f and 3e, f). Finally, disease dynamics diverged even further from self-limitation under a regime of higher levels of environmental stochasticity ($\sigma^2 = 0.134$; compare panels in Figs. 2 and 3).

Population dynamics were most different between models driven by disease and Ricker processes when populations experienced higher intrinsic growth rates ($\mu_0 = 0.51$, 1.01, 1.51, and 2.01). Median and upper and lower quartile realizations were highly variable for populations experiencing disease, but extremely con-

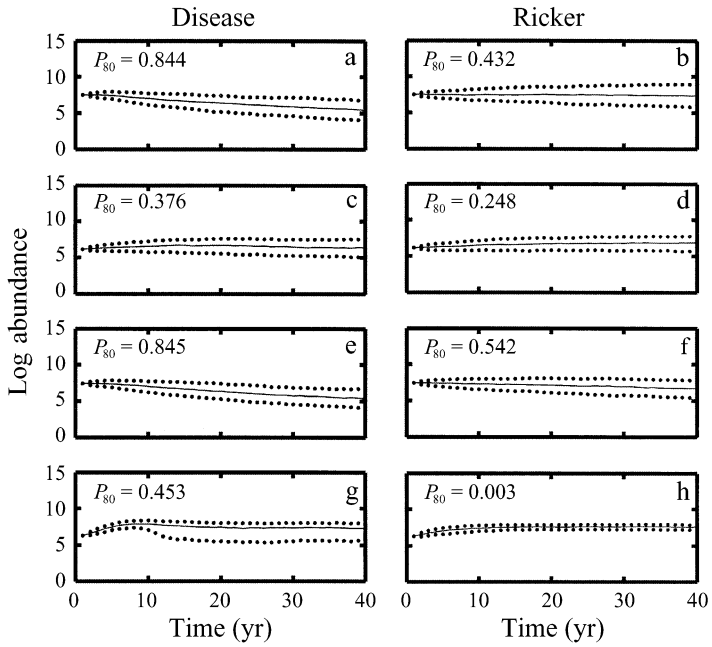

FIG. 3. Disease and Ricker dynamics with moderate levels of environmental stochasticity for four conservation case studies. Median (solid) and upper and lower quartile (dotted) abundance levels are shown for populations exposed to disease (left-hand panels) or driven by a Ricker process (right-hand panels). Here we show four case studies relevant to conservation: (a, b) steady but variable populations ($N_0 = K$, $\mu_0 = 0$); (c, d) slowly recovering populations ($N_0 = 0.1K$, $\mu_0 = 0.05$); (e, f) slowly declining populations ($N_0 = K$, $\mu_0 = -0.05$); and (g, h) rapidly recovering populations ($N_0 = 0.1K$, $\mu_0 = 0.3$). Probabilities of quasi-extinction (probability of an 80% decline in 40 years, P_{80}) are given in the upper left corner of each panel. All other parameters were as follows: $\alpha = 0.2$, $\beta = 0.0001$, and σ^2 (variance in μ_t) = 0.134, roughly the mean of 22 empirical estimates of this parameter (Sabo et al. 2004).

sistent for populations growing according to a simple Ricker process (Fig. 4). Similarly, observed values of P_{80} were consistently much higher for populations exposed to disease than self-limitation for both low and moderate levels of environmental stochasticity (Figs. 4 and 5, respectively). In fact, populations experiencing density dependence as a Ricker process and growing rapidly declined to our a priori risk level of 20% N_0 only when growth rates were extremely high ($\mu_0 > 2$) and environmental stochasticity was high ($\sigma^2 = 0.134$). These results illustrate the additional stochasticity introduced by the disease process (via *b*, the probability of the epidemic occurring once it arrives to a population). Although this stochasticity causes little deviation in the median trend of population trajectories, variance about this trend is changed significantly by the form of the disease model used in our analysis (Eqs. 1–3).

In contrast to disease dynamics, when populations *always* grow according to a Ricker process (as in self-limitation) and growth rates are high, the process greatly diminishes the effect of environmental stochasticity

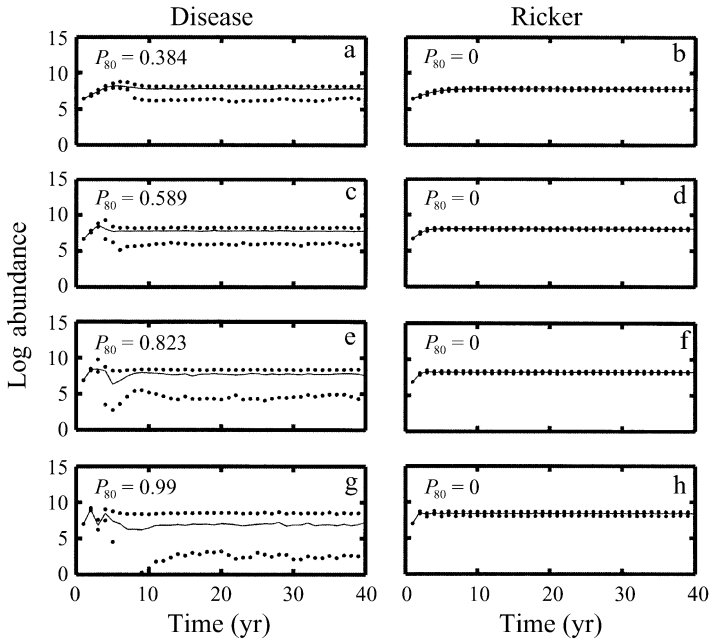

FIG. 4. Disease and Ricker dynamics with low environmental stochasticity when threatened populations have high intrinsic growth rates. Median (solid) and upper and lower quartile (dotted) abundance levels are shown for populations exposed to disease (left-hand panels) or driven by a Ricker process (right-hand panels). Here we show results for four levels of the intrinsic growth rate: (a, b) $\mu_0 = 0.51$; (c, d) $\mu_0 = 1.01$; (e, f), $\mu_0 = 1.51$; and (g, h) $\mu_0 = 2.01$. Probabilities of quasi-extinction (probability of an 80% decline in 40 years, P_{80}) are given in the upper left corner of each panel. All other parameters were as follows: $\alpha = 0.2$, $\beta = 0.0001$, $N_0 = K$, and σ^2 (variance in μ_t) = 0.05, roughly the median of 22 empirical estimates of this parameter (Sabo et al. 2004).

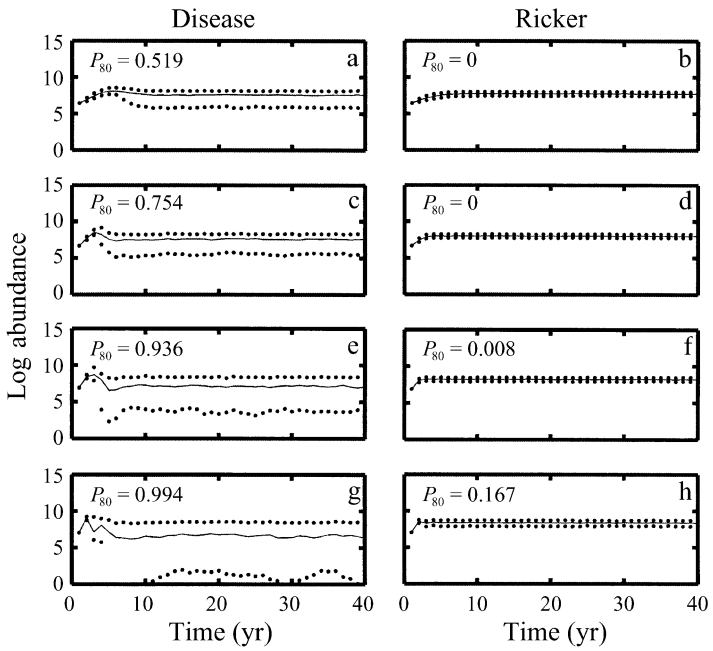

FIG. 5. Disease and Ricker dynamics with moderate levels of environmental stochasticity when threatened populations have high intrinsic growth rates. Median (solid) and upper and lower quartile (dotted) abundance levels are shown for populations exposed to disease (left-hand panels) or driven by a Ricker process (right-hand panels). Here we show results for four levels of the intrinsic growth rate: (a, b) $\mu_0 = 0.51$; (c, d) $\mu_0 = 1.01$; (e, f), $\mu_0 = 1.51$; and (g, h) $\mu_0 = 2.01$. Probabilities of quasi-extinction (probability of an 80% decline in 40 years, P_{80}) are given in the upper left corner of each panel. All other parameters were as follows: $\alpha = 0.2$, $\beta = 0.0001$, $N_0 = K$, and σ^2 (variance in μ_t) = 0.134, roughly the mean of 22 empirical estimates of this parameter (Sabo et al. 2004).

(e.g., in μ_t). In a pure Ricker processes, strong signals (e.g., high growth rates) greatly overshadow noise (low background variation in the mean growth rate). In summary, disease dynamics become increasingly stochastic and Ricker dynamics increasingly deterministic for high values of intrinsic population growth. In a disease process, density dependence does not consistently occur for populations that overshoot the threshold abundance level captured in R_0. Thus, populations exposed to disease can overshoot this threshold during several consecutive years, leading to even stronger overcompensation when the disease finally occurs. Time-delayed density dependence appears to strongly enhance the probability of extinction in populations exposed to disease.

Effects of disease and self-limitation on extinction risk estimates

Observed probabilities of quasi-extinction (P_{80}) were similar for populations with negative intrinsic growth rates (μ_0), but much different for almost all nonnegative values of this parameter (Fig. 6). Observed P_{80} values were higher for populations exposed to disease for nearly all positive values of μ_0, irrespective of the threshold for density dependence (β/α). Differences in observed P_{80} values between disease and Ricker processes exceeded 0.8 when growth rates were high. Predicted P_{80} values were frequently lower than observed values (i.e., underestimated) for disease, and were higher than observed values (i.e., overestimated) for a Ricker process. For example, for populations exposed to disease, predicted values for moderate growth rates ($\mu_0 = 0.1$–0.3) are underestimated by as much as 20% (Fig. 7). At the same growth rate, populations experiencing self-limitation experience essentially no risk of quasi-extinction ($P_{80} = 0$), whereas predicted levels are somewhat higher (0–0.2). P_{80} is only rarely underestimated for populations growing according to a Ricker process (e.g., at very high growth rates where limit cycles prevail). In practice, these results suggest that risk estimates more often will be overly optimistic for modestly recovering populations exposed to disease than for similar populations limited by a more traditional density-dependent process. Errors are much smaller, and in many cases conservative, for more rapidly growing populations infected by disease (Fig. 7). Thus, error in estimating the probability of large declines in abundance is similar for populations exposed to disease and more traditional forms of density dependence when intrinsic growth rates are high.

DISCUSSION

Prospects for including disease in PVA

Our results suggest three practical consequences of incorporating disease dynamics into population viability analysis. First, in addition to reducing population growth rates, disease can increase the variance in population abundance over time. This is an important observation because increased variance in abundance is negatively correlated with persistence time (Dennis et al. 1991, Morris et al. 1999), and increased nonrandom variation in population dynamics may influence the success of density-independent PVAs at estimating risk. Second, patterns of quasi-extinction (e.g., P_{80}) are qualitatively different for disease dynamics than for more traditional forms of density-dependent self-limitation. Disease typically increases the observed prob-

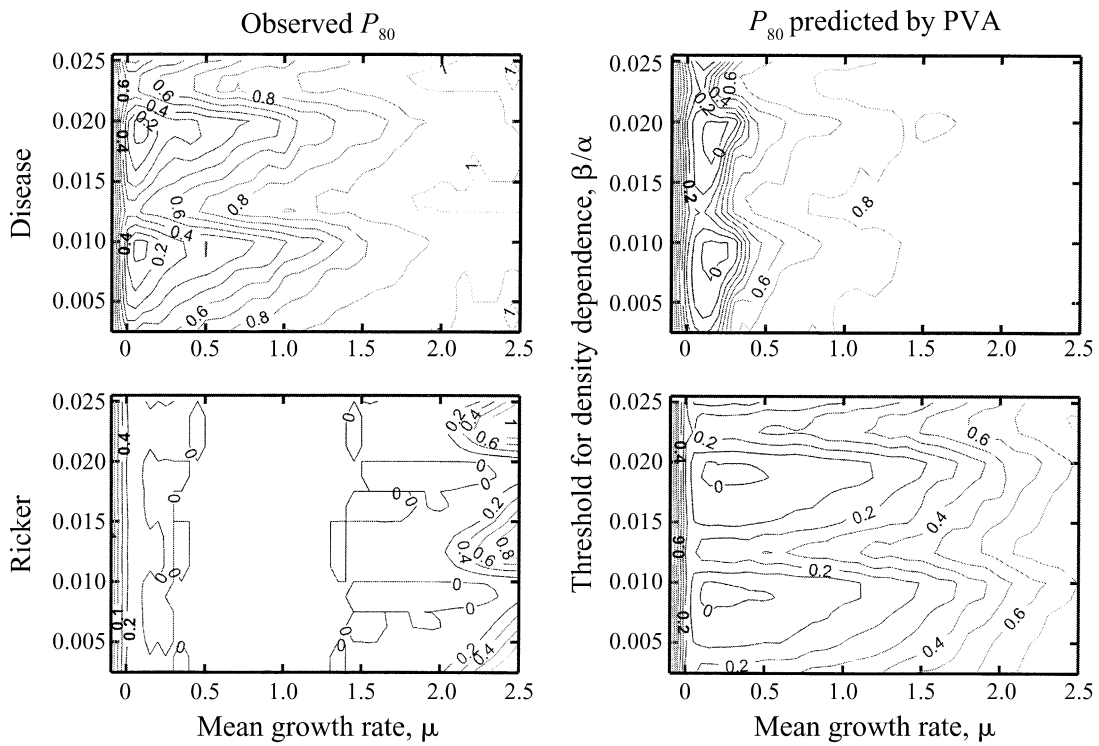

FIG. 6. Effect of the intrinsic growth rate (μ_0) and the ''density threshold,'' β/α, which controls the density at which density-dependent effects occur in disease and Ricker processes, on observed probabilities of 80% declines (left-hand panels) and estimated values for the same declines from PVA (right-hand panels). Results are shown for time series generated by a disease model (top row) and a Ricker model (bottom row). Contours are probabilities of decline (P_{80}). All other parameters were as follows: $N_0 = K$ and σ^2 (variance in μ_t) = 0.05, roughly the median of 22 empirical estimates of this parameter (Sabo et al. 2004).

ability of quasi-extinction more strongly than does simple density dependence, especially when intrinsic population growth rates (μ_0) are high. This suggests that the strongly overcompensatory characteristics of our disease model may alter viability in a way characteristically different from that of more traditional forms of density dependence. Finally, DA estimates of quasi-extinction from a time series of a population with a history of epidemic disease are more likely to be overly optimistic than those from populations affected by Ricker type density dependence. For populations with moderately high intrinsic growth rates (μ_0 = 0.1–0.3), DA methods almost always underestimate risk for infected populations. As a consequence, populations with seemingly rosy prospects for recovery are both more susceptible to disease than declining populations and, at the same time, most likely to produce overly optimistic estimates of risk using density-independent PVA models.

Disease has only recently been incorporated into user-friendly PVA packages. For example, a beta version of a program called ''OUTBREAK'' that aims to investigate disease impacts has recently appeared on the VORTEX web site. Although the details of disease are not transparent in this program, it is one of the first to offer disease as an explicit factor in viability analysis. Few of the other common packages for PVA models (RAMAS, VORTEX, NEMESIS, ALEX; respective sources are: Ferson et al. [1988], Lacy et al. [1995], Gilpin [1993], Possingham et al. [1992]) permit moving beyond treating epidemic disease as ''catastrophic stochasticity,'' because none explicitly includes parameter fields for disease. In principle, standard epidemiological models (Anderson and May 1991) could be added to the framework of PVA models such as VORTEX. However, these epidemiological models are based on differential equations, whereas the usual PVA models are structured as difference equations, usually with a time step of one year. The difference in the characteristic time scale at which parasites and pathogen populations change compared to that on which host populations change means that simply combining the two classes of model will not be successful. One solution is to develop a much more elaborate individual-based model along the lines used by Haydon et al. (2002). However, fully parameterizing any host–parasite model is likely to be particularly difficult for a pathogen affecting an endangered species. A possible solution to these problems is to use the difference in the time scale of the two systems to make some approximations that may enable the system to be handled without a full-scale epidemic model of the Anderson

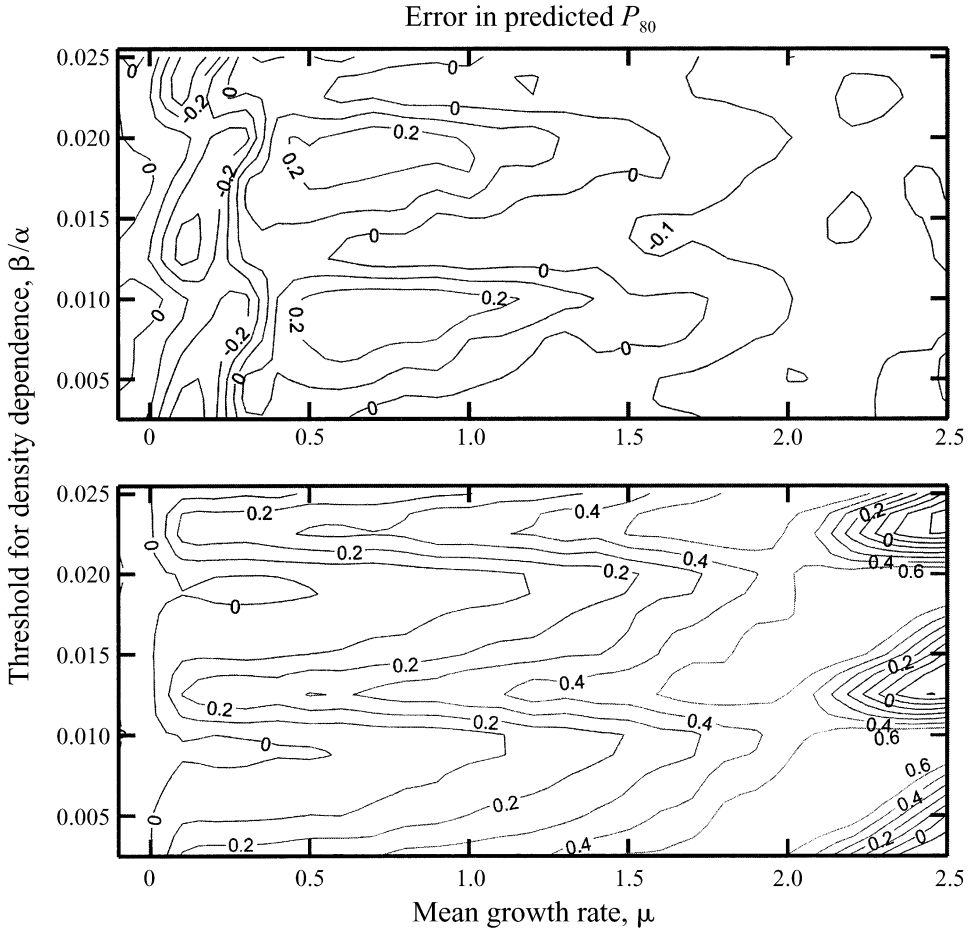

FIG. 7. Raw error in predicted probabilities of an 80% decline (P_{80}) for populations exposed to disease (top) or experiencing self-limitation via a pure Ricker process (bottom). Raw error is defined as the difference between predicted and observed P_{80} such that overly optimistic error has negative values and conservative error has positive values.

and May format. Our model, which assumes that epidemics run to completion within a single time step, is an example of such an approach. More appropriately, stochastic single-population models should explicitly incorporate uncertainty in processes that may occur when populations become small or large (e.g., Ginzburg et al. 1990, Mangel and Tier 1994), such as Allee effects or increased disease transmission.

Embracing the complexity of disease in the context of PVA

Although our analysis helps to elucidate the questions identified as essential in any PVA for which disease dynamics are relevant, the disease transmission model that we employed is admittedly a simplified, first-cut approach at incorporating disease, which is often more complicated in the real world. Returning to the four questions that disease poses for the application of PVA to real populations (see *Relevant principles of epidemiology*), our results shed light on two of these issues (2 and 3). Specifically, our results suggest that disease introduces biases that are qualitatively different from those of simple density dependence, as a result of the probabilistic nature of disease occurring (i.e., Eq. 2). Thus, when applying PVA to real populations experiencing disease, the likelihood that an epidemic will become established in the population once it has arrived (question 2) is more important than the strength of the impact of the pathogen on the host population once it has become established (question 3). In other words, the additional stochastic element of disease (Eq. 2) produces population realizations that are inherently more likely to yield overly optimistic forecasts than accurate or conservative ones. This result is in contrast to most of the parameter space explored by Sabo et al. (2004) for three types of simple density dependence. However, more empirical and theoretical work should be conducted to address issues (1) and (4) raised above in *Relevant principles of epidemiology*.

In practice, there will be several quantities that need to be estimated to determine the effect of an epidemic on the persistence of a small population. It is important to note that our model assumes that epidemics occur in one time step. Although this may be appropriate for

some situations (e.g., seal morbillivirus, plague in prarie dogs, canine distemper in black footed ferrets; McCallum and Dobson 1995), it will be necessary to incorporate more long-term effects for chronic diseases (for example, *Chlamydia* in koalas [Augustine 1998] or nematodes in grouse [Hudson et al. 1992]). Second, our model also assumes that all infected individuals die, rather than recover. In nature, a fraction of infected individuals survive following infection from most pathogens, although mortality rates may be very close to 100% when a naïve host population is exposed to a novel pathogen. For example, Australian rabbits experienced >99% mortality when first exposed to the myxoma virus (Fenner and Ratcliffe 1965), Hawaiian birds experienced 100% mortality when exposed to avian pox (Warner 1968), and some amphibian species experienced 100% mortality when exposed to the chytrid fungus (Daszak et al. 1999). Thus, the results from our simple model represent a worst-case scenario with regard to risk of extinction. Finally, although our approach captures the stochastic nature of the probability of an epidemic occurring when the population is above the threshold, there is likely to be further stochasticity, depending on variation in the number of infected individuals migrating into the population. This would lead to a further divergence between populations subject to disease and self-limiting populations. Incorporating these more realistic, often complex, dynamics is an important next step in understanding the role of disease in population viability.

How are the effects of disease on extinction risk likely to vary with host properties?

In the situation in which the pathogen is the dominant regulatory factor in a population, it is likely that populations of species with high birth and death rates will be relatively more vulnerable to extinction than species with slow demographic rates. This effect occurs primarily because species with rapid population growth rates can achieve much higher population densities in years when a disease outbreak fails to occur. This increases both the probability and magnitude of a subsequent epidemic. In contrast, larger bodied species with slow demographic rates will tend to experience frequent low-level disease outbreaks when close to the threshold at which the pathogen can establish; these will only reduce the host population by relatively small increments. These predictions are supported by limited field data on epidemics. Species that have experienced local extinction in disease outbreaks have been relatively small species with small body sizes, for example black-footed ferrets (Thorne and Williams 1988) and prairie dogs (Lechleitner et al. 1968). Where outbreaks have occurred in larger bodied species with slower dynamics, the epidemic has been followed by recovery (e.g., lions [Roelke-Parker et al. 1996]; gray seals [Harwood and Hall 1990, Heide-Jorgensen and Hankonen 1992]; wildebeest and buffalo [Sinclair et al. 2000]).

The future of disease in PVA

Conservation biologists have embraced PVA as a tool for comparing the relative risk associated with various management options. We have shown that PVA also holds promise in evaluating the efficacy of alternative treatment options for minimizing the effects of infectious disease on imperiled populations. To explicitly assess the role of disease in analyses of extinction risk for particular species of conservation concern, information on host density dependence, pathogen R_0, and probability of pathogen arrival will need to be included in conventional PVA models. Inclusion of disease dynamics should be considered in analyses of extinction risk when pathogens or parasites are a likely source of variability in either mortality or fecundity. This is especially true for recovering species, because most epidemics are density dependent, as is the intensity of infection for endemic diseases. As emerging infectious disease becomes increasingly recognized among conservation biologists as a threat to biodiversity, the need for tools to consider this threat will follow. Future management actions for endangered species may involve manipulating pathogens to reduce the threat of extinction of these species. For such situations, a PVA that incorporates disease explicitly will be essential to forecast how much manipulation is necessary to increase population persistence.

Acknowledgments

This paper was initiated at the NCEAS Working Group on ''Disease and Conservation Biology.'' We are grateful for contributions made by all members of the Working Group, and to NCEAS Staff, University of California Santa Barbara, and NSF for support. An anonymous reviewer of an earlier version of this paper provided the insight on which Fig. 1 is based.

Literature Cited

Anderson, R. M., and R. M. May. 1979. Population biology of infectious diseases. Part I. Nature **280**:361–367.

Anderson, R. M., and R. M. May. 1986. The invasion, persistence and spread of infectious dieases within animal and plant communities. Philosophical Transactions of the Royal Society of London Series B **314**:533–570.

Anderson, R. M., and R. M. May. 1991. Infectious diseases of humans. Oxford University Press, Oxford, UK.

Augustine, D. J. 1998. Modelling *Chlamydia*–koala interactions: coexistence, population dynamics and conservation implications. Journal of Applied Ecology **35**:261–272.

Daszak, P., L. Berger, A. A. Cunningham, A. D. Hyatt, D. E. Green, and R. Speare. 1999. Emerging infectious diseases and amphibian population declines. Emerging Infectious Diseases **5**:735–748.

Dennis, B., R. A. Desharnais, J. M. Cushing, S. M. Henson, and R. F. Costantino. 2001. Estimating chaos and complex dynamics in an insect population. Ecological Monographs **71**:277–303.

Dennis, B., P. L. Munholland, and J. M. Scott. 1991. Estimation of growth and extinction parameters for endangered species. Ecological Monographs **61**:115–143.

Dennis, B., and M. L. Taper. 1994. Density dependence in time series observations of natural populations: estimation and testing. Ecological Monographs **64**:205–224.

De Valpine, P., and A. Hastings. 2002. Fitting population models incorporating process noise and observation error. Ecological Monographs **72**:57–76.

Dietz, K. 1993. The estimation of the basic reproductive number for infectious diseases. Statistical Methods in Medical Research **2**:23–41.

Dobson, A. P., and J. Foufopoulos. 2001. Emerging infectious pathogens in wildlife. Philosophical Transactions of the Royal Society of London **1411**:1001–1012.

Dobson, A. P., and M. Meagher. 1996. The population dynamics of brucellosis in the Yellowstone National Park. Ecology **77**:1026–1036.

Fenner, F., and F. N. Ratcliffe. 1965. Myxomatosis. Cambridge University Press, Cambridge, UK.

Ferson, S., F. J. Rohlf, L. R. Ginzburg, and G. Jacquez. 1988. RAMAS/a user manual: modeling fluctuations in age-structured populations. Exeter Publishing, Setauket, New York, USA.

Foley, P. 1994. Predicting extinction times from environmental stochasticity and carrying capacity. Conservation Biology **8**:124–137.

Gerber, L. R., D. P. DeMaster, and P. M. Kareiva. 1999. Gray whales illustrate the value of monitoring data in implementing the Endangered Species Act. Conservation Biology **13**:1215–1219.

Gerber, L. R., and R. Hilborn. 2001. Estimating the frequency of catastrophic events and recovery from low densities: examples from populations of otariids. Mammal Review **31**(2):131–150.

Gerber, L. R., M. T. Tinker, D. Doak, and J. Estes. 2004. Mortality sensitivity in life-stage simulation analysis: a case study of southern sea otters. Ecological Applications **14**:1554–1565.

Gilpin, M. 1993. NEMESIS. Version 1.0 users guide. Conservation biology simulations: process simulations of dynamics at the level of genes, individuals, populations and metapopulations. © Michael Gilpin, 419 W. Harrison, Bozeman, Montana 59715 USA.

Ginzburg, L. R., S. Ferson, and H. R. Akçakaya. 1990. Reconstructability of density dependence and the conservative assessment of extinction risks. Conservation Biology **4**:63–70.

Gog, J., R. Woodroffe, and J. Swinton. 2002. Disease in endangered metapopulations: the importance of alternative hosts. Proceedings of the Royal Society of London, Series B **269**:671–676.

Gulland, F. M. 1992. The role of nematode parasites in Soay sheep (*Ovis aries* L.) mortality during a population crash. Parasitology **105**:493–503.

Gulland, F. M. 1995. The impact of infectious diseases on wild animal populations. Pages 20–51 *in* B. T. Grenfell and A. P. Dobson, editors. Ecology of infectious diseases in natural populations. Cambridge University Press, Cambridge, UK.

Hanger, J. J., L. D. Bromham, J. J. McKee, T. M. O'Brien, and W. F. Robinson. 2000. The nucleotide sequence of koala (*Phascolarctos cinereus*) retrovirus: a novel type C endogenous virus related to gibbon ape leukemia virus. Journal of Virology **74**:4264–4272.

Harwood, J., and A. Hall. 1990. Mass mortality in marine mammals: its implications for population dynamics and genetics. Trends in Ecology and Evolution **5**:254–257.

Haydon, D. T., M. K. Laurenson, and C. Sillero-Zubiri. 2002. Integrating epidemiology into population viability analysis: managing the risk posed by rabies and canine distemper to the Ethiopian wolf. Conservation Biology **16**:1372–1385.

Heide-Jorgensen, M. P., and T. Harkonen. 1992. Epizootiology of the seal disease in the eastern North Sea. Journal of Applied Ecology **29**:99–107.

Holmes, E. E. 2001. Estimating risks in declining populations with poor data. Proceedings of the National Academy of Sciences (USA) **98**:5072–5077.

Hudson, P. J., D. Newborn, and A. P. Dobson. 1992. Regulation and stability of a free-living host–parasite system: *Trichostrongylus tenuis* in red grouse. I. Monitoring and parasite reduction experiments. Journal of Animal Ecology **61**:477–486.

Kermack, W. O., and A. G. McKendrick. 1927. A contribution to the mathematical theory of epidemics. Proceedings of the Royal Society of London, Series B **115**:700–721.

Lacy, R. C., K. A. Hughes, and P. S. Miller. 1995. VORTEX: a stochastic simulation of the extinction process. Version 7 user's manual. IUCN/SSC [International Union for the Conservation of Nature/Species Survival Commission] Conservation Breeding Specialist Group, Apple Valley, Minnesota, USA.

Lafferty, K., and L. R. Gerber. 2002. Good medicine for conservation biology: the intersection of epidemiology and conservation theory. Conservation Biology **16**:1–12.

Lafferty, K., and R. D. Holt. 2003. How should environmental stress affect the population dynamics of disease? Ecology Letters **6**:654–664.

Lande, R., and S. H. Orzack. 1988. Extinction dynamics of age-structured populations in a fluctuating environment. Proceedings of the National Academy of Sciences (USA) **85**:7418–7421.

Lechleitner, R. R., L. Kartman, M. I. Goldenbe, and B. W. Hudson. 1968. An epizootic of plague in Gunnison's prairie dogs (*Cynomys gunnisoni*) in south-central Colorado. Ecology **49**:734–743.

Mace, G. M., and R. Lande. 1991. Assessing extinction threats: toward re-evaluation of IUCN threatened species categories. Conservation Biology **5**:148–157.

Mangel, M., and C. Tier. 1994. Four facts every conservation biologist should know about persistence. Ecology **75**:607–614.

May, R. M., and R. M. Anderson. 1979. Population biology of infectious diseases. Part II. Nature **280**:455–461.

May, R. M., and R. M. Anderson. 1990. Parasite–host coevolution. Parasitology **100**:S89–S101.

McCallum, H. 2000. Population parameters: estimation for ecological models. Blackwell Science, Oxford, UK.

McCallum, H., N. D. Barlow, and J. Hone. 2001. How should transmission be modelled? Trends in Ecology and Evolution **16**:295–300.

McCallum, H. I., and A. P. Dobson. 1995. Detecting disease and parasite threats to endangered species and ecosystems. Trends in Ecology and Evolution **10**:190–194.

Morris, W. F., and D. F. Doak. 2002. Quantitative conservation biology: theory and practice of population viability analysis. Sinauer, Sunderland, Massachusetts, USA.

Morris, W., D. Doak, M. Groom, P. Kareiva, J. Fieberg, L. Gerber, P. Murphy, and D. Thomson. 1999. A practical handbook for population viability analysis. The Nature Conservancy, Washington, D.C., USA.

Nicholls, A. O., P. C. Viljoen, M. H. Knight, and A. S. vanJaarsveld. 1996. Evaluating population persistence of censused and unmanaged herbivore populations from the Kruger National Park, South Africa. Biological Conservation **76**:57–67.

Packer, C., S. Altizer, M. Appel, E. Brown, J. Martenson, S. J. O'Brien, M. E. Roelke-Parker, R. Hofmann-Lehmann, and H. Lutz. 1999. Viruses of the Serengeti: patterns of infection and mortality in African lions. Journal of Animal Ecology **68**:1161–1178.

Possingham, H., I. A. Davies, and I. Noble. 1992. ALEX 2.2 operation manual. Department of Applied Mathematics, University of Adelaide, Adelaide, South Australia 5005 Australia.

Possingham, H. P., D. B. Lindemayer, and M. A. McCarthy.

2001. Population viability analysis. Pages 831–843 *in* S. A. Levin, editor. Encyclopedia of biodiversity. Academic Press, San Diego, California, USA.

Ricker, W. T. 1954. Stock and recruitment. Journal of the Fisheries Research Board of Canada **11**:559–623.

Roelke-Parker, M. E., et al. 1996. A canine distemper virus epidemic in Serengeti lions (*Panthera leo*). Nature **379**: 441–445.

Sabo, J. L., E. E. Holmes, and P. Kareiva. 2004. Efficacy of simple viability models in ecological risk assessment: Does density dependence matter? Ecology **85**:328–341.

Sinclair, A. R. E., S. A. R. Mduma, and P. Arcese. 2000. What determines phenology and synchrony of ungulate breeding in Serengeti? Ecology **81**:2100–2111.

Swinton, J. 1998. Extinction times and phase transitions for spatially structured closed epidemics. Bulletin of Mathematical Biology **60**:215–230.

Thorne, E. T., and E. S. Williams. 1988. Disease and endangered species: the black-footed ferret as a recent example. Conservation Biology **2**:66–74.

Volterra, V. 1928. Variations and fluctuations of the number of individuals in animal species living together. Journal du Conseil International pour l'Exploration de la Mer **3**:3–51. [Reprinted in 1931 *in* R. N. Chapman, editor. Animal ecology. McGraw-Hill, New York, New York, USA.]

Warner, R. E. 1968. The role of introduced diseases in the extinction of the endemic Hawaiian avifauna. Condor **70**: 101–120.