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Independent and Competing Disease Risks: Implications for Host Populations in Variable Environments

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ABSTRACT: Disease models usually assume disease to act independently of other mortality- and morbidity-causing factors. Alternatively, disease may function as a competing risk factor, for example, killing already moribund hosts. Using tuberculosis (TB) in African buffalo as a model system, we explore consequences of competing or independent disease effects for host population dynamics. We include scenarios with density-dependent and density-independent effects of environmental variation, exemplified by variable food availability (driven by rainfall) and catastrophic droughts, respectively. Independent disease effects reduce population size linearly with prevalence, irrespective of the nature of environmental variation. Competing disease risks alter population size only if density-independent variation is present; then, disease reduces population size nonlinearly. Field data indicate that the net effect of TB on buffalo likely falls between the extremes of total independence and competition with other risk factors: TB increases mortality and decreases fecundity in some prime-aged buffalo, suggesting independent disease risks in these individuals, while similar disease effects in senescent buffalo may act as competing risks. Moreover, increased survival and fecundity of TB-negative buffalo may compensate for some disease-related losses. Model assumptions on independent or competing disease risks and environmental variability should be considered explicitly when assessing disease effects on wildlife populations.

Keywords: disease, competing or independent risk, compensation, environmental variability, African buffalo, bovine tuberculosis.

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Pathogens and parasites can have drastic effects on their hosts (Harvell et al. 1999; Daszak et al. 2000; Altizer et al. 2003) and are often cited as important drivers of population and community dynamics (Anderson and May 1992; Dobson and Crawley 1994; McCallum and Dobson 1995; Hudson and Greenman 1998; Kiesecker and Blaustein 1999; Kohler and Hoiland 2001; MacNeil et al. 2003). In biological conservation, infectious diseases are increasingly recognized as a threat to imperiled populations across the gamut of taxa, geographic locations, and habitats (review in de Castro and Bolker 2005). Studies measuring reductions in individual survival and fecundity due to disease are beginning to accumulate (reviews in Gulland 1995 and Tompkins and Begon 1999; Albon et al. 2002). However, predicting population-level implications of these effects remains challenging (Tompkins et al. 2002), given the difficulty of understanding the dynamics of natural populations. When translating vital rate reductions to population dynamic effects, assumptions must be made concerning the way in which disease and other mortality/morbidity factors interact and patterns of environmental variability affecting the host population (Huffaker et al. 1984; Case 2000).

First, specifically, disease-related reductions in host survival and fecundity may act independently of other risk factors. In this case, disease effects are additive. Alternatively, disease and other risk factors may act interchangeably, for example, if disease simply removes already moribund animals. In this case, disease and other mortality/morbidity factors act as competing risks, and removing disease makes no difference to host vital rates. Finally, the effects of disease may be synergistic, if disease and other risk factors interact to cause higher mortality than the sum of both factors in isolation. For example, loss of condition due to disease may increase vulnerability to predation, so that removing disease eliminates mortalities due to predation as well as disease. These different scenarios were identified more than 2 decades ago (Hassell et al. 1982), and evidence at the time suggested that independent disease risks may typify many invertebrate hosts, while diseases of vertebrates may more often act as competing risk factors (Holmes 1982). Since then, a number of laboratory

studies (e.g., Anderson and Crombie 1984; Scott 1987) and one field study of gastrointestinal worm infections in grouse (Dobson and Hudson 1992; Hudson et al. 1992*b*, 1998) have shown that vertebrate populations can also be regulated by parasites, suggesting independent disease effects. On the other hand, several field studies have found interactions between disease and predation (Hudson et al. 1992*a*; Murray et al. 1997; Joly and Messier 2004*a*) or among diseases (Joly and Messier 2004*b*), indicating synergistic effects. Given the limited number of studies on disease effects in natural populations and their mixed results, it is still far from clear whether disease effects are typically independent, competing, or synergistic or whether such a generalization can legitimately be made at all. A large medical statistical literature is dedicated to analyzing independent and competing disease risks retrospectively in human cohort studies (e.g., Fusaro et al. 1996; Gilbert 2000; Yan et al. 2000; Yip et al. 2005), but the implications of interactions between disease and other risk factors for host population dynamics have not been explored. Disease dynamic models to date generally carry an implicit assumption of independent disease effects on population growth rate (Anderson and May 1992; Heesterbeek and Roberts 1995; Roberts et al. 1995; Tompkins et al. 2002).

Second, in conservation and wildlife management applications, it is usually the potential effects of disease on population size and variability, rather than population growth rate, that are of primary concern. These will depend on the nature and amount of environmental variability to which the host population is subject. Understanding the relationship between disease impacts and environmental variability is particularly relevant in the context of global climate change (Colwell 1996; Anderson et al. 2004; Harvell et al. 2002). Some recent studies examine the influence of environmental variability on disease dynamics through its effects on host contact patterns or susceptibility and, therefore, disease transmission rates (Pascual et al. 2000; Hay et al. 2002; Koelle and Pascual 2004). Studies on ungulate population dynamics, too, have emphasized the importance of environmental variability (reviews in Saether 1997 and Gaillard et al. 2000; Ogutu and Owen-Smith 2003). In savanna ecosystems, variable rainfall drives ungulate population dynamics through its effect on food availability (Owen-Smith 1990; Mduma et al. 1999; Illius and O'Connor 2000; Davis et al. 2002; Georgiadis et al. 2003) and carrying capacity (Coe et al. 1976; Sinclair 1977; Fritz and Duncan 1994). However, the response to disease of host populations in variable environments has rarely been explored (but see Cattadori et al. 2005).

This study focuses on two questions. First, how does the assumption of disease as an independent risk factor or as a competing risk factor affect disease impacts on population size and variability? Second, how are disease impacts on host population dynamics affected by patterns of density-dependent and density-independent environmental variability to which the population is subject? We present African buffalo (*Syncerus caffer*) and bovine tuberculosis (TB; caused by *Mycobacterium bovis*) as a model system to illustrate the combined effects of disease and temporal environmental variability on population size and variability. We examine field data from our study system for evidence of TB as an independent or competing mortality factor, and we analyze long-term rainfall records to characterize annual variation in rainfall and the frequency of major droughts. We formulate a simple population model to investigate the ramifications of independent or competing disease risks for population-level disease impacts. We subsume the synergistic case under independent effects for two reasons. First, the scenario where disease increases host vulnerability to some other risk factor x is formally indistinguishable from the scenario where factor x is absent but the disease imposes more severe direct impacts. Second, the two scenarios are difficult to distinguish from field data. Demonstrating synergistic risks requires experimental manipulation of both factors in a factorial design (e.g., Krebs et al. 1995) or measuring the effects of risk factor x on infected and uninfected individuals (e.g., Hudson et al. 1992*a*). We have not had the opportunity to use either approach to examine interactions of disease and other putative risk factors, such as predation or starvation, in our system. In our models, we use rainfall variability as the basis for density-dependent effects of environmental variability, while severe droughts exemplify density-independent disturbances.

Methods

Study System

Mycobacterium bovis causes chronic infection in a wide range of mammalian hosts (Bengis 1999). The pathogen is exotic to sub-Saharan Africa, and bovine TB is emerging as a wildlife disease in southern Africa (de Lisle et al. 2002; Michel et al. 2006). In African savanna ecosystems, buffalo appear to be the primary maintenance host of the disease (de Vos et al. 2001), though several other species have been diagnosed with *M. bovis* infection (Keet et al. 1996). Tuberculosis-infected buffalo may suffer declines in body condition (Caron et al. 2003) and reduced adult survival and fecundity (Jolles et al. 2005). Tuberculosis can infect buffalo of all age groups, including prime-aged adults. Disease-related mortality is not limited to calves and senescent buffalo, which are most vulnerable to other risk factors, such as starvation or predation. One would there-

fore expect to see some additive disease effects. However, disease effects may vary across study populations (cf. Rodwell et al. 2001). Our research was conducted at HluhluweiMfolozi Park (HIP), South Africa (28°S, 31°–32°E), where TB was first diagnosed in 1986 in a buffalo. The park currently has a buffalo population of about 3,000 individuals, with TB infection distributed patchily across different areas (Jolles 2004).

Weather Variation and Its Effects at HIP

Monthly rainfall data were obtained from KwaZulu-Natal Wildlife, the organization administering the parks and reserves of the KwaZulu-Natal Province (KZN). Rainfall data for HIP have been collected by KZN Wildlife since 1934 at up to seven rainfall stations across the park. We used wavelet analysis to characterize the long-term rainfall fluctuations at HIP. We used annual data averaged across all stations in the park for this analysis and monthly data from the station with the longest continual record (Egodeni). Wavelet analysis identifies the frequency of periodic oscillations as well as their trends over time (Torrence and Compo 1998). It is useful for the analysis of ecological time series, particularly under conditions of global change, when the emphasis is on detecting alterations in the periodicity of time series (applications; e.g., Grenfell et al. 2001; Koelle and Pascual 2004). We evaluated temporal change in rainfall variability by regressing the SD of annual rainfall in 3–5-year periods over time. We avoided potential problems due to autocorrelation between data points by evaluating nonoverlapping time intervals (e.g., SD of rainfall in years 1–3, 4–6, etc.).

Buffalo Disease Survey

Buffalo capture and TB testing were conducted by KZN Wildlife and the KZN State Veterinary Service. A detailed description of the capture and testing protocols can be found in Jolles et al. (2005). Briefly, buffalo are captured by the herd, or parts of herds, into large corrals set up within the park. All captured animals are marked with brands to allow identification of recaptured animals in subsequent years. Buffalo are tested for TB using an intradermal skin test. Tuberculosis-positive buffalo are slaughtered, and negatives are released back into the park. Culled animals are examined postmortem, and disease severity is measured on a scale of 0 (no macroscopic evidence of TB infection found) to 4 (animal would have likely died of TB within a year) on the basis of the number, size, and distribution across organs of TB lesions. The TB testing program has been in operation since 1999, targeting different areas within the park each year and processing 250–900 animals annually. We estimated age in animals up to 5 years old from tooth emergence patterns, body size, and horn development (Grimsdell 1973; Sinclair 1977). In adult buffalo, we used tooth wear as an indicator of age by measuring the height of incisor 1, which declines by approximately 1 mm/year in this population (A. E. Jolles, unpublished data). Pregnancy tests of 918 females older than 4 years of age were performed rectally by the park veterinarian, and we manually checked 895 females of the same age group for lactation (presence/absence of milk). We examined our buffalo disease data focusing on the following questions.

Is there evidence for mortality due to TB acting as a competing risk factor? Many mortality risks (e.g., predation, starvation during the dry season) tend to affect juvenile and senescent ungulates disproportionately. In the absence of TB, mortality rates in juvenile and senescent buffalo are indeed higher than in prime-aged adults (Jolles et al. 2005). We predict that if TB-related mortality acts as a competing risk factor, deaths due to TB will be concentrated in the more vulnerable age groups (juveniles, senescents).

We know from previous work that TB increases mortality in adult buffalo and decreases fecundity in most age groups of females (Jolles et al. 2005). Such vital rate impairments might suggest additive disease effects. However, at the herd level, TB-negative animals may compensate for these losses through increased survival and fecundity. In this case, it would be erroneous to model disease effects as additive based on vital rate impairments in infected animals. We therefore ask:

Is there evidence for compensatory survival in TB-negative buffalo? If so, we predict that TB-negative adult buffalo from high-prevalence herds are older, on average, than TB-negative adult buffalo from low-prevalence herds.

Is there evidence for compensatory fecundity in TB-negative females? If so, we predict that TB-negative females from high-prevalence herds have higher pregnancy and/or lactation rates than TB-negative females from low-prevalence herds.

We used χ^2 tests to compare disease prevalence among different age groups, Kruskal-Wallace ANOVA by ranks to compare TB severity among age groups, Mann-Whitney *U*-tests to compare disease severity in young/old versus prime-aged buffalo and to compare adult age between buffalo from herds with low and high prevalence, and linear regression to explore the effect of TB prevalence on lactation and pregnancy rates across buffalo herds. Buffalo removals for disease control might cause biases in age and fecundity patterns observed in subsequent years, but it is not clear, a priori, which direction these biases might take. In addition to analyses including all animals and herds, we therefore present analyses including only herds that

had not been handled before when investigating compensatory survival and fecundity.

Population Models

We modeled buffalo population dynamics based on the discrete-time logistic model:

$$N_{t+1} = N_t\left[1 + R\left(1 - \frac{N_t}{K}\right)\right],$$

where N_t is the population size at time t, R is the per capita growth rate for a population unconstrained by density dependence, and K is the carrying capacity determined by rainfall. Model time steps are annual. Jolles (2004) used buffalo census data from 1956–1985 to estimate growth rate and carrying capacity for the HIP population. Since the first case of TB in the park was detected only in 1986, we assume that TB prevalence over the census period was low and had little impact on population dynamics. Buffalo population growth was thus estimated at $R = 0.113$ and carrying capacity K at 5,300 (Jolles 2004), using the above model with an annual removal term that explicitly takes into account buffalo culling and live sales. We do not include a removal term here, because it is not our aim to examine the effect of the disease control program on buffalo or disease dynamics. Instead, we are interested in the interactions of disease effects and density dependence, and we are merely using the buffalo-TB system to illustrate much more general points.

We added independent disease effects to the basic model by assuming that losses due to TB and density dependence are additive; thus,

$$N_{t+1} = N_t\left[1 + R\left(1 - \frac{N_t}{K}\right) - L(P)\right],$$

where $L(P)$ are the per capita losses to fecundity and survival due to disease (fig. 1*a*).

In the competing risks version of the model, we assume that the animals killed by disease or that fail to reproduce because of disease are the same individuals that would have been thus affected by density dependence:

$$N_{t+1} = N_t\left[1 + R(P)\left(1 - \frac{N_t}{K}\right)\right],$$

$$R(P) = R(0) - L(P),$$

where $R(0)$ is the disease-free per capita growth rate and $R(P)$ denotes population growth rate as a function of disease prevalence P (fig. 1*b*). These two forms of the logistic model are discussed in Gabriel et al. (2005). We calculated $L(P)$ using age-specific estimates of TB effects on buffalo vital rates (Jolles et al. 2005). While the fecundity of young adults is not affected by disease, infected subadults, older adults, and senescent individuals have lower fecundities. Infected juveniles have unchanged survival probabilities because it takes time for the disease to have an effect; but infected subadults, adults, and senescents suffer from reduced survival probabilities. Though the effects of disease on population age distribution are subtle, we calibrated per capita disease losses across all age groups according to expected population age distributions for different values of P using Jolles et al.'s (2005) buffalo population matrix model. Table A1 in the online edition of the *American Naturalist* lists values of $L(P)$ for the relevant range of TB prevalences.

We examined density-dependent environmental effects by adding rainfall variability to the model, which affects buffalo population growth through its influence on resource availability. A random value was picked from a lognormal rainfall distribution with mean = 6.58254, as observed at HIP, for each modeled time step. The carrying capacity, K, was then determined according to $K = (0.0161 \times \text{rain} - 4.1) \times \text{area}$. This linear relationship between annual rainfall and carrying capacity for buffalo was described by Sinclair (1977); we modified the intercept to fit buffalo densities observed at HIP. To assess the effects of rainfall variability on the buffalo population, we varied the SD of the rain distribution between 0 and the distribution's mean. We restricted the linear relationship between rainfall and carrying capacity to an interval $[K_{\min}, K_{\max}]$; outside this interval, we assumed no effect of rainfall on K. The minimum carrying capacity represents the number of buffalo that can survive on standing dead grass supplemented with green forage surrounding permanent rivers and wetlands. (Major water courses running dry would represent drought events outside the normal weather variability of the region). At the other extreme, increasing rainfall will result only in improved food resources for buffalo within the growth capacity of the local grass sward. No field estimates of minimum and maximum carrying capacity for the park are available, so we evaluated model output for a range of values of $K_{\min}$ and $K_{\max}$. Model predictions for population size and variability are insensitive to choice of $K_{\max}$ (fig. A1*a* in the online edition of the *American Naturalist*). They are somewhat more sensitive to choice of $K_{\min}$, but population size still varies by only a few hundred animals over a reasonable range (e.g., 1,000–2,500 animals) of $K_{\min}$ (fig. A1*b*). Values for $K_{\min}$ and $K_{\max}$ were subsequently set at 1,000 and 12,275 buffalo, respectively, to incorporate most of the rainfall variation observed in the park, only clipping outliers differing from the average by more than 2 SDs.

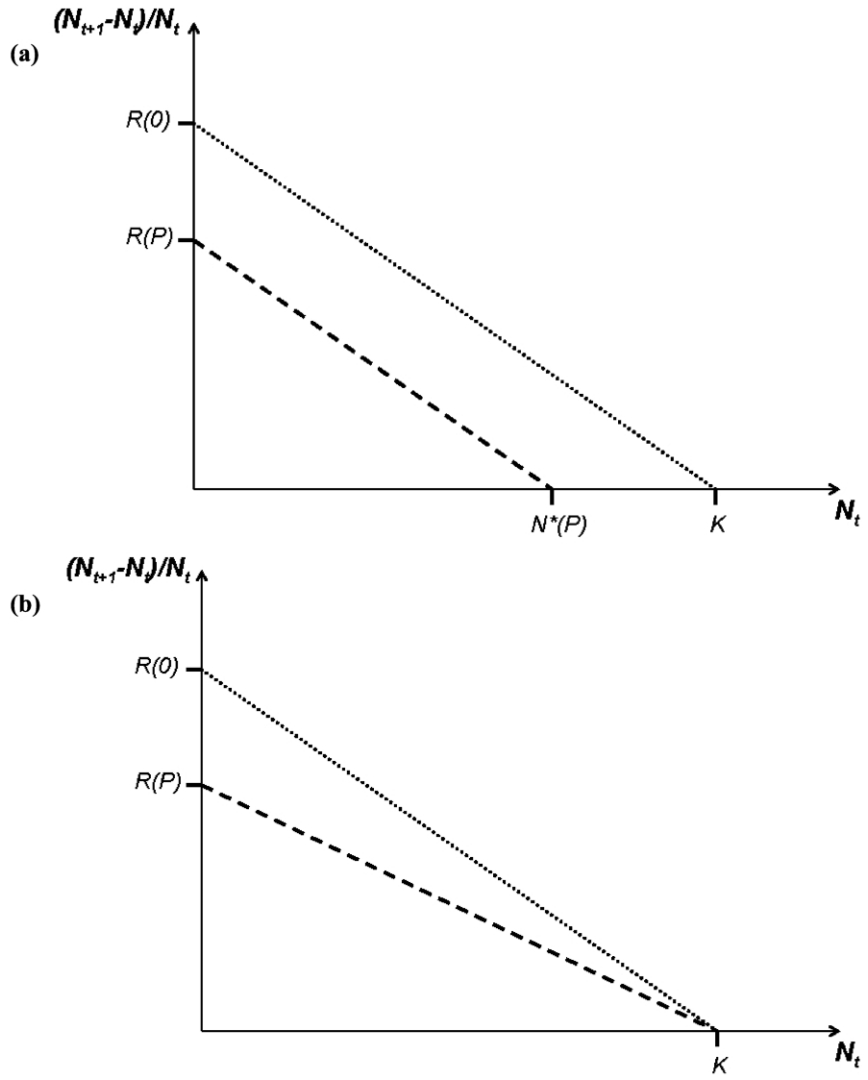

Figure 1: Functional relationship of per capita population growth rate ($[N_{t+1} - N_t]/N_t$; *Y*-axes) and popuation size (N_t; *X*-axes) for (*a*) the independent disease risk model and (*b*) the competing disease risk model. Dotted lines represent the disease-free case, and dashed lines represent the models including disease. Synergistic effects of disease and other risk factors would result in a case where $R(0) = R(P)$ and $N \times (P) < K$. We do not examine this case separately.

We modeled density-independent environmental disturbances by picking "bad years" at random but with a specified likelihood (inverse of average return interval). We varied the average return interval for bad years between 1 and 35 years to assess how disturbance frequency affects population dynamics under the different disease scenarios. The effect of a bad year was to kill 20% of the buffalo population regardless of current buffalo population size, which is well within mortality rates observed at Kruger National Park during droughts in 1982–1983 and the early 1990s (R. Bengis, personal communication). The rainfall distribution was set to the values observed at HIP.

We ran all models 1,000 times for 200 time steps, starting at $N_0 = 10$ buffalo, except for models incorporating density-independent disturbances, which started at $N = K = 5{,}300$. When no rainfall variation is added, the buffalo population reaches carrying capacity after 140 years. Long-term mean population size was therefore computed as the mean population size over the last 60 years of each model run, averaged across all model runs. Similarly, population variability was calculated as the coefficient of variation of population size between years 141 and 200, averaged over all model runs. We used Mathematica 4.2 software to code the population models presented here.

Different sources of mortality (disease, density-dependent effects) may affect different age groups of animals, so omitting population age structure from our models might affect our results. To control for this possibility, we also ran an age-structured version of the models (appendix in the online edition of the *American Naturalist*) but found that model predictions were qualitatively the same (fig. A2 in the online edition of the *American Naturalist*).

Results

Rainfall Variability at HIP

Rainfall at HIP varies widely between 390 and 1,250 mm, with a strong interdecadal wet-dry oscillation. The wavelet plot using monthly data is dominated by the seasonal variability in rainfall, while the wavelet analysis of annual rain data highlights the longer-term oscillations (fig. 2). Rainfall is distributed lognormally; the mean and SD of the lognormal rainfall distribution correspond to a long-term average annual rainfall of 722 mm and variance of 165 mm. The period of the wet-dry oscillation may be decreasing from approximately 18 years (between the late 1940s and about 1970) to 13 years in more recent years (fig. 2). We found no evidence of change in year-to-year variability of rainfall.

Disease Effects in the Buffalo/TB System

A total of 3,265 buffalo were tested for TB between 2000 and 2005 from 42 herds and herd fragments. There were 705 animals that tested TB-positive, and the average herd prevalence was 23%, ranging from no infection to 73%. Tuberculosis severity was determined for 403 of the TB-positive animals.

Evidence for Mortality due to TB as a Competing Risk Factor. Are deaths due to TB concentrated in the more vulnerable age groups (juveniles, senescents)?

Infection risk. Buffalo of all age groups are equally likely to be infected with TB, except juveniles younger than 3 years old, which have lower disease prevalence (fig. 3*a*). This is the typical pattern for a chronic disease, with low prevalence in juveniles because of limited exposure time. Selective culling may affect age prevalence patterns, so we examined data from herds that had not been handled before in a separate analysis. The age prevalence pattern in unmanipulated herds also does not reveal any evidence for increased infection risk in the more vulnerable age groups (fig. A3 in the online edition of the *American Naturalist*).

Mortality risk in infected animals. Disease severity in the youngest and oldest age group (0–1 and ≥18 years) does appear to be slightly higher than in the other age groups (fig. 3*b*), but these differences were not statistically significant (Kruskal-Wallis ANOVA by ranks; independent [grouping] variable: age group, response variable: TB severity; Kruskal-Wallis test: $H = 4.105308$, df $= 8$, $N = 403$, $p = .8475$). Contrasting the most vulnerable age groups against all the other age groups did not alter this result (Mann-Whitney U-test, $N_{\text{vulnerable}} = 24$, $N_{\text{other}} = 379$, $Z = 1.262238$, $p = .206864$). Given our current small sample sizes of very old and very young animals, we cannot evaluate whether TB severity is actually higher in these age groups; if it is, the effect is not very large (average severity in vulnerable age groups $= 1.56$; in other animals $= 1.26$). We thus found no evidence for an increased infection risk in juvenile or senescent buffalo, corroborating previous findings (Jolles et al. 2005). Results on differential mortality risks due to disease in juvenile and senescent buffalo compared with all other age groups are inconclusive.

Is There Evidence for Compensatory Survival in TB-Negative Buffalo? Tuberculosis-negative adult buffalo from high-prevalence herds were older, on average, than TB-negative adults from low-prevalence herds (Mann-Whitney U-test; TB-negative adults from herds with prevalence <0.1, $N = 410$, mean age approximately 11–12 years; TB-negative adults from herds with prevalence ≥ 0.5, $N = 57$, mean age approximately 13 years; $Z = 3.209$, $p = .0013$). This result is robust to excluding all animals from herds that had been previously captured (Mann-Whitney U-test; TB-negative adults from unhandled herds with prevalence <0.1, $N = 82$, mean age approximately 11 years; TB-negative adults from unhandled herds with prevalence ≥ 0.5, $N = 35$, mean age approximately 13 years; $Z = 2.033$, $p = .0421$) and is not due to a difference in adult age between high- and low-prevalence herds overall (Mann-Whitney U-test; all adult buffalo from herds with prevalence <0.1, $N = 441$; all adult buffalo from herds with prevalence ≥ 0.5, $N = 211$; $Z = 1.124$, $p = .261$). Because older males leave the breeding herds earlier in the dry season than younger males, a bias in herd TB prevalence by capture month could lead to a spurious correlation between prevalence and age. However, there is no correlation between capture month and herd TB prevalence (linear regression, $N_{\text{herds}} = 42$, F ratio $= 0.111$, $p = .741$). The result is also robust to including herds with up to 15% or 20% TB prevalence in the "low-prevalence" group but not to shifting the boundary of the high-prevalence group downward. Sensitivity to the definition of the "high-prevalence" group is not inconsistent with the interpretation that TB-negative buffalo may be compensating for TB mortalities in their herd mates; it likely takes time for the effects of compensation to become de-

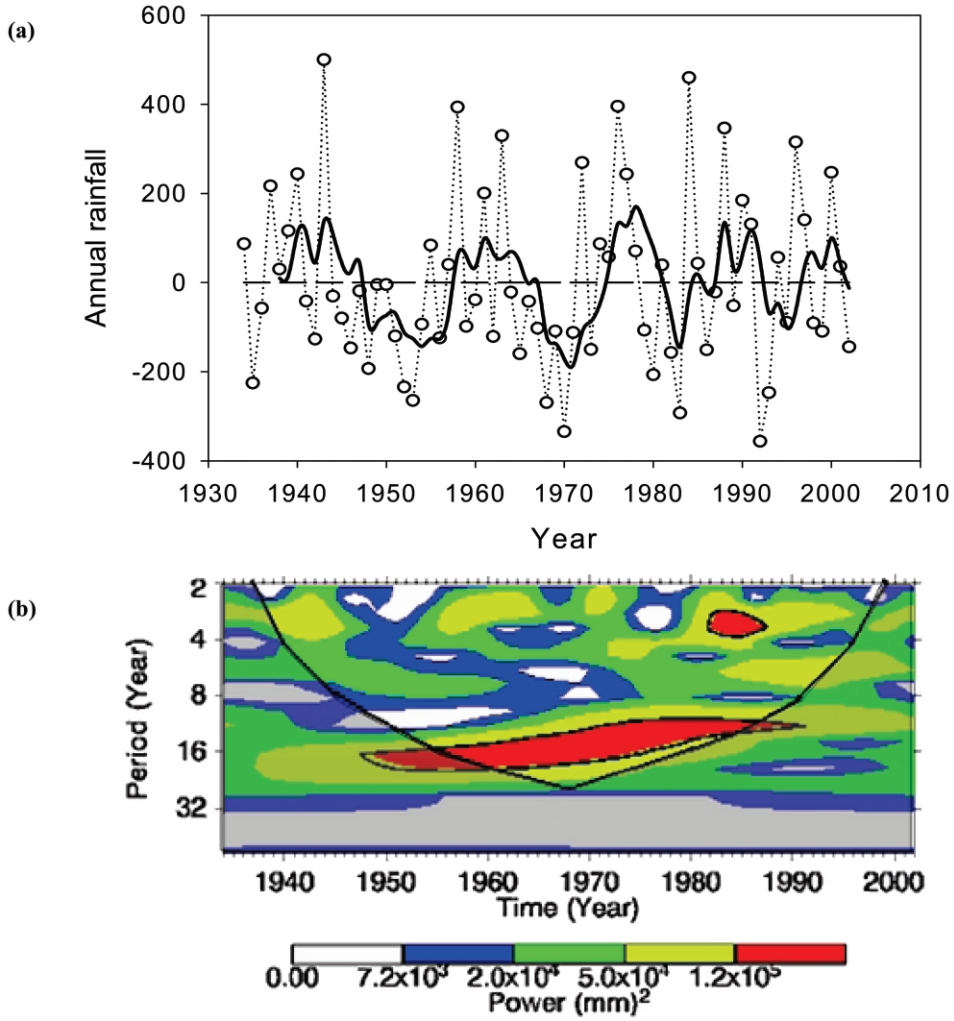

Figure 2: Rainfall at HIP from up to seven recording stations, 1934–2002, showing (*a*) annual rainfall normalized to the long-term mean. The dotted line indicates annual records, and the solid line indicates the 5-year moving average of the preceding conditions. *b*, Wavelet power spectrum for annual rainfall at HIP. The contour levels are chosen so that 75%, 50%, 25%, and 5% of the wavelet power is above each level, respectively. Black contour is the 5% significance level, using a red-noise (autoregressive lag1) background spectrum. The shaded area represents the cone of influence, below which results should be interpreted with caution because of edge effects. Wavelet software by C. Torrence and G. Compo is available at http://paos.colorado.edu/research/wavelets.

tectable in a herd, and the highest-prevalence herds are probably also those that have been infected the longest. Sensitivity of between-group comparisons to group delineations does call for caution in interpreting results.

Is There Evidence for Compensatory Fecundity in TB-Negative Females? Lactation rates (proportion lactating) in TB-negative females are positively correlated with herd TB prevalence when the seasonal decline in lactation is taken into account (linear regression, $N_{\text{herds}} = 33$; TB prevalence: F ratio = 5.024, $p = .0325$, parameter = 0.335; month: F ratio = 14.681, $p = .0006$, parameter = −0.051). The effect of TB prevalence on lactation rate in TB-negative females is not merely a reflection of a similar trend across all females: When both TB-positive and TB-negative females are included in the analysis, the only significant factor affecting lactation rate is month (linear regression, $N_{\text{herds}} = 35$; TB prevalence: F ratio = 1.435, $p = .240$, parameter = 0.180; month: F ratio = 7.810, $p = .0087$, parameter = −0.039). Throughout these analyses, capture year and area (as a covariate) were eliminated from the final models because they had no significant effects on lactation rate, and groups where fewer than five fe-

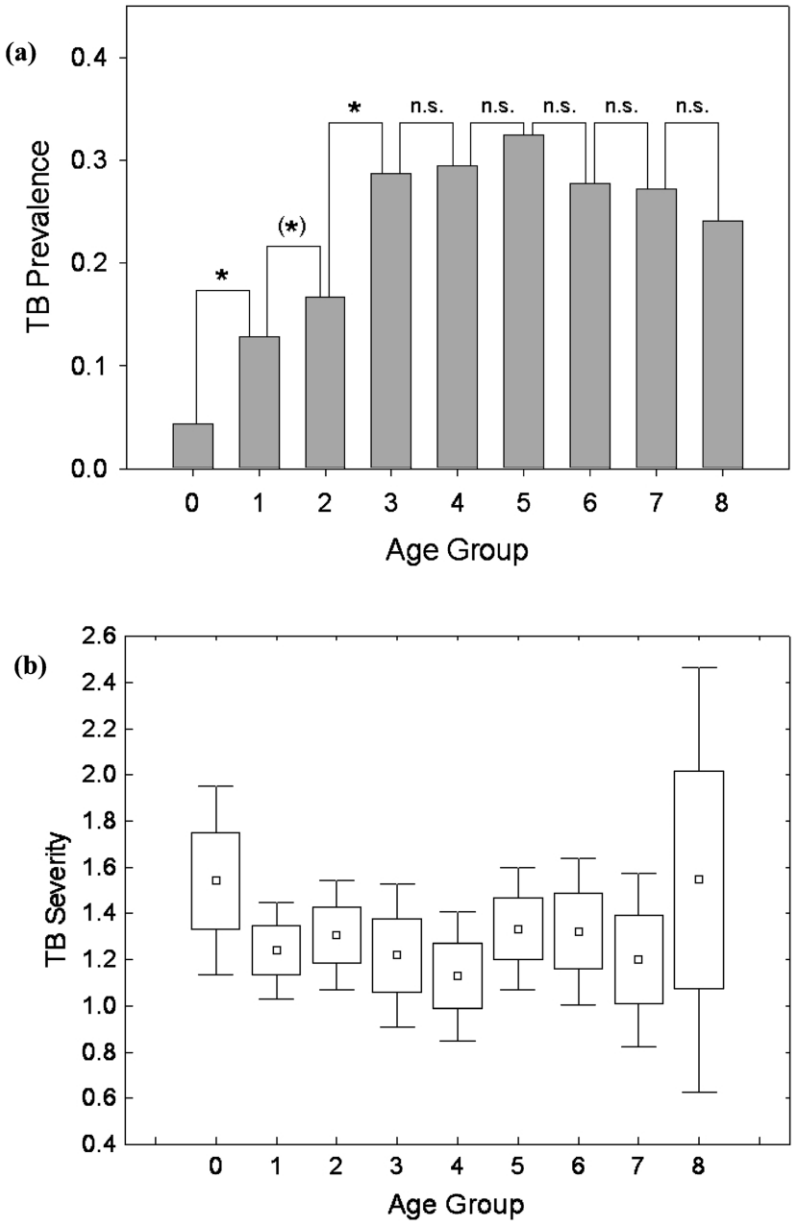

Figure 3: *a*, TB prevalence and buffalo age group. N_0 (0–1 year) = 372, N_1 (1–2 years) = 500, N_2 (2–3 years) = 540, N_3 (3–4 years) = 223, N_4 (4–5 years) = 295, N_5 (5–9 years) = 478, N_6 (9–13 years) = 423, N_7 (13–17 years) = 266, N_8 (18+ years) = 137. Buffalo typically acquire TB infection by 4 years of age, after which time TB prevalence does not change significantly with age group (χ^2 tests for age groups: 0 vs. 1, $\chi^2 = 18.49$, $p < .0001$; 1 vs. 2, $\chi^2 = 3.08$, $p = .0794$; 2 vs. 3, $\chi^2 = 14.18$, $p = .0002$; 3 vs. 4, $\chi^2 = 0.04$, $p = .8443$; 4 vs. 5, $\chi^2 = 0.73$, $p = .3926$; 5 vs. 6, $\chi^2 = 2.42$, $p = .1198$; 6 vs. 7, $\chi^2 = 0.03$, $p = .8654$; 7 vs. 8, $\chi^2 = 0.42$, $p = .5185$). *b*, TB severity and age group. Means are shown with SE (*boxes*) and 95% confidence interval (=1.96 × SE; *lines*). N_0 (0–1 year) = 12, N_1 (1–2 years) = 52, N_2 (2–3 years) = 73, N_3 (3–4 years) = 50, N_4 (4–5 years) = 54, N_5 (5–9 years) = 75, N_6 (9–13 years) = 51, N_7 (13–17 years) = 25, N_8 (18+ years) = 11.

males had been checked for lactation were excluded. Culling of buffalo for disease control might affect fecundity in the remaining females, so we reran our analysis excluding herds that had been handled before. Despite the smaller sample size of herds, the effect of TB prevalence on lactation rate in TB-negative females remains close to statistically significant (linear regression, $N_{\text{herds}} = 14$; TB prevalence: F ratio = 3.670, $p = .0818$, parameter = 0.322; month: F ratio = 8.550, $p = .0138$, parameter = −0.044). There is no effect of herd TB

prevalence on pregnancy rates of TB-negative females. Given similar pregnancy rates, one would expect similar lactation rates across herds. Higher lactation rates in TB-negative females from high-prevalence herds therefore point to improved calf survival to weaning and/or delayed weaning (which should in turn improve calf survival). Our results are thus consistent with fecundity compensation in TB-negative females via improved calf survival rather than higher conception rates.

Modeling Results

Density-Dependent Effects of Environmental Variation. Long-term average buffalo population size declines with increasing variability in rainfall (fig. 4*a*). The slope of the population size response curve is steepest between rainfall variation of 75 and 325 mm. Rainfall variability at HIP, at 165 mm, lies within this sensitive range. Adding disease to the model makes no difference if disease is modeled as a competing risk factor. If disease effects are independent, host population size is reduced linearly with increasing disease prevalence (fig. 4*a*), and the effect of disease does not depend on the level of environmental variability. Population variability increases sharply with rainfall variability up to approximately 300 mm and then plateaus with only a very gentle downward slope as rainfall variability increases further (fig. 4*b*). This plateau is expected, because population variability is limited by the maximum per capita growth rate. The slight decrease in population variability results from an increase in extinctions among modeled populations at very high rainfall variabilities. Including disease in the model reduces host population variability but does not change the shape of the response curve qualitatively. The response of population variability to disease prevalence is nonlinear: the reduction in population variability declines with increasing disease prevalence (fig. 4*b*). Competing risk and independent disease models yield very similar results, with independent disease effects reducing host population variability slightly more than disease as a competing risk factor.

Density-Independent Effects of Environmental Variation. Average buffalo population size declines exponentially with disturbance frequency (fig. 4*c*, 4*d*). For the disturbance magnitude modeled here (20% mortality), average population size drops off steeply when the disturbance return interval is <15–20 years. As in the density-dependent (variable rainfall) model, independent disease mortality leads to a linear reduction in host population size, and there is no interaction between the effects of environmental variability and disease (fig. 4*c*). However, when density-independent environmental disturbances are present, competing disease risks also affect host population size. In contrast to the independent case, the relationship between disease prevalence and host population size is nonlinear; disease effects increase with disturbance frequency (fig. 4*d*). Thus, in the competing risks case, disease effects on population size are subtle when disease prevalence is low and disturbances infrequent but can increase precipitously as infection spreads and/or disturbances recur more often. Table 1 summarizes the predicted effects of disease on the host population for independent and competing disease risks and for environments with no variation, density-dependent, or density-independent effects of environmental variability.

Discussion

The net effect of TB in buffalo probably lies between the extremes of fully competing disease risks and complete independence of disease effects from other risk factors. Tuberculosis does not simply remove animals that were about to die of other causes anyway. It kills some prime-age adults that would have had excellent prospects for survival in the absence of the disease, and it reduces fecundity in females that have not yet reached senescent age. To this extent, disease effects are likely additive to risk factors underlying density dependence, such as malnutrition and associated pathologies (e.g., pneumonia in old, emaciated buffalo). On the other hand, TB does also infect and kill or prevent reproduction in senescent buffalo, which might have succumbed to starvation, predation, or another disease even in the absence of TB. These cases might be better described by the competing risks model. At the herd level, uninfected buffalo may profit from increased mortality in their TB-positive companions. Tuberculosis-negative buffalo in herds with high prevalence appear to have lower mortality rates and higher fecundity (driven by improved calf survival) than those in herds with low TB prevalence. If food supply regulates buffalo populations, then this may simply be a consequence of reduced competition for food resources in high-TB-prevalence herds. Alternatively, TB may selectively kill buffalo suffering from severe infections with other parasites, effectively cleansing the herd of parasites (A. E. Jolles, R. S. Etienne, W. C. Turner, and H. Olff, unpublished manuscript), which might improve survival rates. Extrapolating from disease effects on vital rates to population-level impacts may thus be complicated by competing risk factors at the individual level and compensatory survival of healthy animals at the herd level.

Our modeling results demonstrate that different assumptions about the nature of disease effects on host vital rates and their interactions with environmental variability lead to contrasting predictions for the impact of diseases on host population dynamics. The assumption of inde-

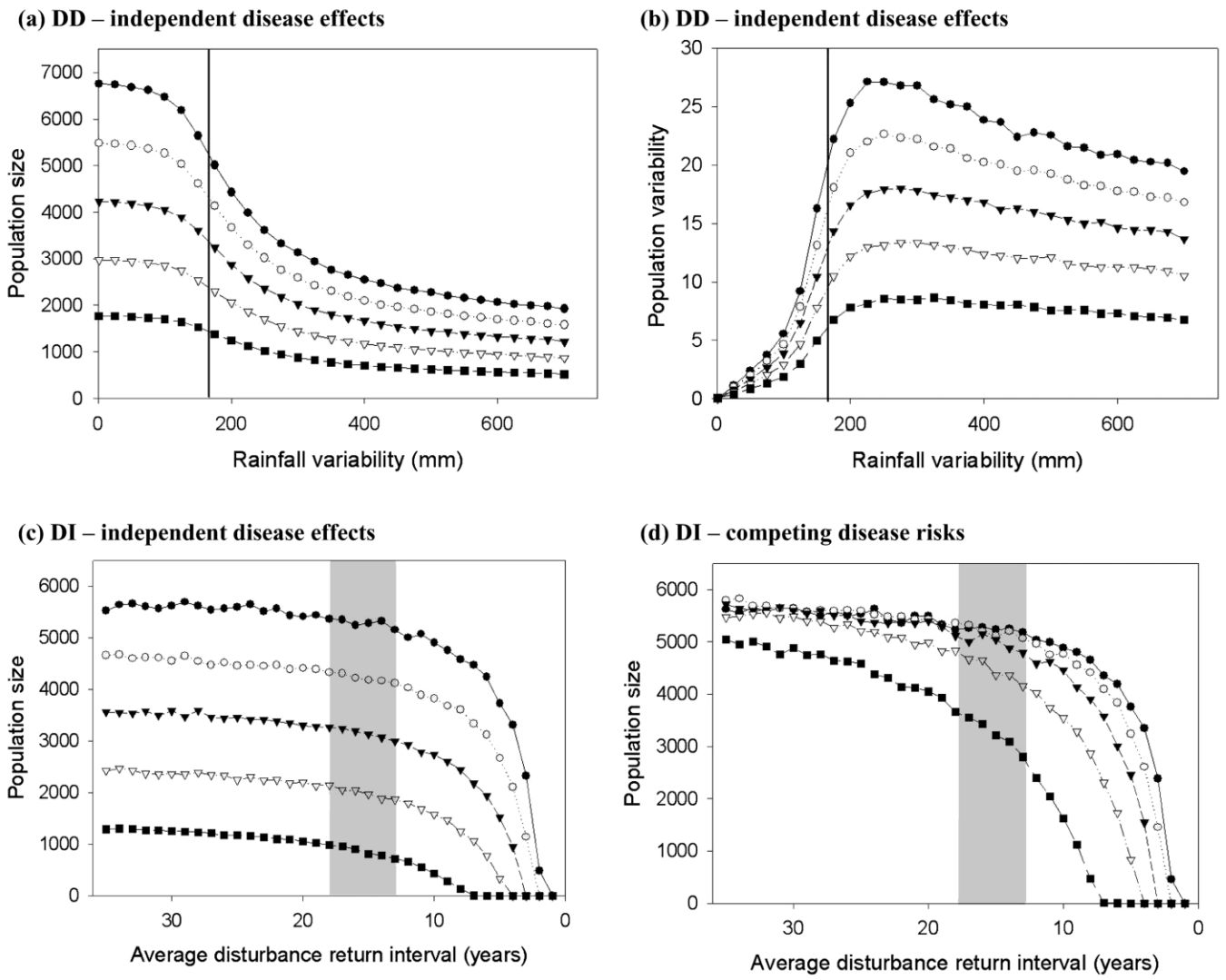

Figure 4: Model output for effects of disease and environmental variability on buffalo population size and variability. *Solid circles*, 0% TB prevalence; *open circles*, 25% TB; *solid triangles*, 50% TB; *open triangles*, 75% TB; *solid squares*, 100% TB. Effects of density-dependent environmental variation and independent disease effects on (*a*) buffalo population size and (*b*) population variability. The solid line represents the rainfall variability observed at HIP. Effect of density-independent variation and disease on buffalo population size, assuming (*c*) independent disease effects and (*d*) competing disease risks. The shaded area represents the range of average drought return intervals observed at HIP.

Table 1: Summary of disease effects on host population growth rate, population size, and population variability (coefficient of variation [CV])

	None	Density dependent	Density independent
Independent disease risks:			
R_{max}	Linear reduction	Linear reduction	Linear reduction
N	Linear reduction	Linear reduction	Linear reduction
CV(N)	None	Nonlinear reduction	
Competing disease risks:			
R_{max}	Linear reduction	Linear reduction	Linear reduction
N	None	None	Nonlinear reduction
CV(N)	None	Nonlinear reduction	

Note: Column headings refer to different scenarios for environmental variation (no environmental variation, density-dependent environmental variation, and density-independent environmental variation).

pendent disease effects, if erroneous, will overestimate disease impacts on host populations. The assumption of constant environments, on the other hand, may result in underestimating disease impacts, if disease effects on host vital rates act as competing risk factors. These almost ubiquitous assumptions are most likely to be accurate in the case of epidemic diseases, often with high host mortality rates, that sweep through their host populations at timescales that are short compared with host generation time. Because the epidemic's effects on the host population are essentially instantaneous, a constant environment may be a reasonable approximation. Mortality due to disease is determined simply by the transmission process, independent of morbidity caused by other factors and too rapid for compensation due to decreased competition to take effect. These conditions are particularly characteristic of newly introduced diseases and their naive host populations and of epidemic diseases of short-lived host species. By contrast, the common assumptions of independent disease effects and constant environments are probably less appropriate for chronic endemic infections, particularly in long-lived host species. Strongly seasonal diseases, such as many childhood diseases in humans, present an interesting intermediate scenario within the epidemic-endemic spectrum. Their dynamics tend to be fast relative to host life cycles, suggesting disease effects independent of risk factors that operate more sluggishly via host morbidity. On the other hand, seasonal forcing will tend to synchronize windows of opportunity for multiple dynamically similar pathogens, causing them to compete for the same, limited susceptible pool. Seasonal pathogens might therefore function as competing disease risks among each other while remaining independent of many other risk factors. Competitive interactions among seasonal pathogens can have substantial disease dynamic consequences (Rohani et al. 1998, 2003). We hypothesize that they may also modify disease impacts on the host population. Model assumptions on environmental variability and independent or competing disease risks deserve careful and explicit consideration for each study system.

In his analysis of disease impacts on natural host populations, Holmes (1982) pointed out that diseases appeared able to regulate invertebrates, particularly insects, but usually did not seem to have large effects on vertebrate hosts. Holmes attributed this difference to independent disease effects in invertebrates and competing risks in vertebrates. Our modeling results suggest an alternative explanation: the same pattern would emerge if disease effects usually functioned as competing risks in both groups, but invertebrate population dynamics were driven primarily by density-independent factors, whereas vertebrate populations were typically regulated by density-dependent factors. Predicting disease impacts on host population dynamics can thus not be divorced from the long-standing debate over density-dependent versus density-independent population regulation (Davidson and Andrewartha 1948; Nicholson 1954).

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