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CHAPTER 24

INFECTIOUS DISEASE IN SPATIALLY EXPANDING POPULATIONS: A MODEL FOR REINTRODUCED SPECIES

By

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ABSTRACT

The introduction of chronic infectious diseases by reintroduced populations is a serious hazard in conservation biology, threatening the original host and other spillover species. Beyond the usual epidemiological methods, analysis of this problem must include the reintroduction dynamics of the host. In this chapter we review and extend a previous study (Bar-David *et al.* 2006) that investigated the simultaneous expansion of a colonizing population and a disease introduced by that population, focusing on interventions for extermination or containment of the disease. Our previous study used a spatially-explicit individual-based model of a reintroduced population of Persian fallow deer in northern Israel, and a hypothetical but credible threat of a disease with the epidemiological characteristics of bovine tuberculosis. Our simulations supported the general concept that the outcome of simultaneous host and disease invasion falls into one of three regimes that depend on the relative expansion velocities of the epidemic and the reestablishing host population. We further explored whether each of these regimes has its own implications for management strategies aimed at curtailing the establishment of a disease reservoir. We found that stopping further releases in the reintroduction program, even at an initial stage of the program, had little effect on eradication of a chronic disease of moderate-to-high transmissibility. For a situation where the host and disease were introduced in the same location, focusing vaccination efforts in a core region around the introduction site appeared more effective than spreading a comparable number of vaccine doses over the entire population range. Based on model simulation we concluded that recognizing which of the three general regimes best describes a particular outbreak is central to finding the most efficient strategy needed to contain the disease.

INTRODUCTION

Beyond preserving the current distribution of biodiversity, conservation biology increasingly focuses on restoring species to areas from which they have been extirpated. Reintroductions—defined as releases of animals into areas within their original geographic range, where populations have significantly declined or disappeared during historical times due to natural catastrophes or human interference (Kleiman 1989)—have become an important component of conservation programs. In the past two decades the number of programs aimed at reintroducing species into the wild for conservation purposes has been increasing, and much effort has been invested to ensure their success (Griffith et al 1989; Beck *et al.* 1994).

In spite of the many attempts at reintroduction, the success rate is low (<50%, Griffith et al 1989; Beck *et al.* 1994). High costs and efforts, logistical difficulties and shortage of habitats often make these projects infeasible (Kleiman 1989). Among the threats to the success of these projects is infectious disease, which can pose a serious hazard to the establishment process of reintroduced populations and to the long-term persistence of the species in the wild (Smith 1982; Scott 1988; Viggers *et al.* 1993; McCallum and Dobson 1995; Cunningham 1996; Woodroffe 1999; Lafferty and Gerber 2002). Moreover, infectious diseases brought into the ecosystem by the reintroduced population imperil more than just the establishing population itself. Even if a disease has only a marginal impact on the reintroduced population (i.e. on individual survival or reproduction), the associated pathogens may spread to other host species that have no evolved defenses (Cunningham 1996; Lafferty & Gerber 2002; Prenter *et al.* 2004). Furthermore, the reintroduced population might become a reservoir host for the introduced pathogen, leading to repeated outbreaks of disease (Dobson & Foufopoulos 2001) and hence to direct and indirect effects on other species in the ecosystem, as well as the stability of the ecosystem in the long term (Scott 1988; Woodroffe 1999). Thus, understanding the phenomenon of disease spread in a reintroduced population has important implications for species conservation and ecosystem management. In this chapter we review and extend a previous study (Bar-David *et al.* 2006) in which we investigated the simultaneous expansion of a colonizing population and a disease introduced by that population, focusing on the implications of various management scenarios for management of a potential epidemic.

Reintroduction projects consist of single or repeated releases of individuals into natural habitats (Griffith *et al.* 1989; Beck *et al.* 1994). Hence, populations undergoing reintroduction present unique patterns (relative to established populations) of mixing and spatial spread as part of their establishment process: e.g., the spread of reintroduced European otters, *Lutra lutra* (Sjöåen 1997) or mountain gazelles, *Gazella gazella* (Dunham 1998). If the population has a positive intrinsic growth rate (r_p) in the new environment, as we assume throughout this paper, then it can spread into the surrounding landscape in a wavelike fashion with, under certain circumstances, a characteristic wavefront velocity (Mollison 1991; van den Bosch *et al.* 1992; Shigesada and Kawasaki 1997). Patterns of space use and range expansion of reintroduced populations are affected by the interaction of landscape-related parameters (such as topography, habitat quality and distribution and human-induced landscape alteration) with population characteristics such as growth rate and dispersal traits: e.g., the spread of reintroduced beaver, *Castor fiber* (Hartman 1995) and the spread of Persian fallow deer, *Dama mesopotamica* (Dolev *et al.* 2002; Bar-David *et al.* 2005a).

Invasion of an infectious disease into an established host population follows analogous principles. A disease can invade successfully only if the basic reproduction number, R_0 (defined as the expected number of secondary cases produced by one infectious case in a wholly susceptible

population), is greater than 1 (Hudson *et al.* 2001; Getz and Lloyd-Smith 2006). The range expansion of infectious disease, following disease establishment, is influenced by landscape features and characteristics of the disease and host, such as transmissibility, the density and distribution of susceptibles, dispersal traits, and host vigor (Tilman & Kareiva 1997; Hess *et al.* 2001; Jules *et al.* 2002). Again, this expansion will have a characteristic wavefront velocity under certain circumstances (Mollison 1991).

Most studies of the spatial dynamics of infectious disease have focused on established host populations (e.g., see Getz *et al.* 2006, and references therein), either at steady state or fluctuating through time. However, reintroduced host populations are expanding their geographical range during their establishment process, due to continuous dispersal of individuals from the release site, and to the establishment of home ranges and population activity centers. The question of how disease range expansion is influenced by the spatial dynamics of a colonizing host population (either introduced or reintroduced) has only recently been considered from a theoretical point of view. Hilker *et al.* (2005) present a thorough analytic treatment of the impact of a lethal disease on invasion dynamics of a host species, under the assumptions of homogeneous landscape, diffusive host movement and a strong Allee effect in host demographics. We explored the simultaneous expansion of a colonizing population and a chronic non-lethal disease introduced with it (Bar-David *et al.* 2006). We described expected outcomes of such introductions for three qualitatively distinct regimes (hereafter "conceptual regimes"), that depend on the relative velocities at which the population and the epidemic expand. Because epidemic velocity increases with disease transmissibility, the three regimes can be interpreted as different levels of transmissibility (and may represent uncertainty regarding a particular disease, or different diseases). The three conceptual regimes, depicted schematically in Figure 1, are as follows:

(1) If transmissibility is low the disease cannot persist (R_0<1), although due to stochasticity it may initially expand its range around the point of introduction before disappearing.
(2) If transmissibility is moderate, such that R_0>1 but the wavefront velocity for the population, v_p, is higher than that for the disease, v_d, then the disease wavefront lags behind that of the expanding host population.
(3) If transmissibility is sufficiently high that $v_d > v_p$, then the disease wavefront will closely follow the host wavefront.

Furthermore, we suggested that each of these three conceptual regimes has its own implications for management strategies aimed at preventing the establishment of a disease reservoir. When transmissibility is low (regime 1) the disease is likely to go extinct without any intervention. Some interventions are suggested, however, to minimize the possibility of spread to other species. Regimes 2 and 3 require more attention, because they incur a potential for disease establishment in the reintroduced population. In regime 2, the disease wavefront lags behind that of the population, so management measures should be focused on the infected core of the population to prevent the disease from spreading to the outer, disease-free zone. When transmissibility is high (regime 3) and the disease wavefront tracks the population closely, interventions should cover the entire range of the host. The goal of interventions may be to eradicate the disease or, sometimes, more realistically, to establish disease-free subpopulations that can be isolated in some way, while containing the disease in areas where prevalence is high.

Here, we illustrate these management scenarios in the context of the potential spread of bovine tuberculosis (*Mycobacterium bovis*; BTB) in a reintroduced population of Persian fallow deer (*Dama mesopotamica*) in northern Israel. These management scenarios were simulated by using a spatially-explicit individual-based model that predicts the dynamics of the simultaneous

expansion of the deer population and BTB infection (Bar-David *et al.* 2006). We also discuss the extent to which particular management strategies might contain the disease, focusing on their spatial aspects and the implications for ecosystem conservation.

THE PERSIAN FALLOW DEER AND BOVINE TUBERCULOSIS

The Persian fallow deer, mentioned in the Bible (Deuteronomy XVII) and previously abundant throughout Western Asia (Chapman & Chapman, 1997), is currently listed as Endangered (IUCN 1996). It had declined throughout its range in recent centuries, due to over hunting and habitat loss, and by 1940 was considered extinct. In 1956 two small remnant populations, of about a dozen animals each, were found along the Dez and Karaeh rivers in Kuzistan province, Iran, from which a captive breeding core was initiated in Opel Zoo, Germany. This population served as the basis for the world captive herd (Jantschke 1991). In 1976, the Israel Nature and Park Authority (INPA) established a breeding core of Persian fallow deer from seven (two male, five female) deer imported from Iran (offspring of the Opel zoo herd) and Germany for future reintroduction. By 1995, the Israeli breeding-core population, at Hai-Bar Carmel, had increased to >150 animals (62 adult females) and was considered large enough to support a reintroduction attempt (Saltz 1996).

In 1996, the reintroduction project, managed by the INPA, began in the upper west Galilee region of northern Israel (Saltz 1998). The reintroduction project followed the IUCN guidelines for reintroduction (IUCN 1998; Kleiman 1989) and is based on a long-term approach developed by Saltz (1998). The program consisted of transfers from the permanent breeding core to a habituation enclosure at the release site and "soft" releases (Kleiman 1989) into the wild. Twice a year, during spring and autumn, about 10 deer were selected from the breeding core according to their age and sex (average of 5 males and 5 females each time) and transferred to the habituation enclosure in Nahal Kziv Nature Reserve. The enclosure covered 11 ha with a natural habitat representative of the study area. After approximately 3 months in the habituation enclosure, the deer were released to the wild. The reintroduced population has been intensively studied since the beginning of the reintroduction program and data have been collected on its demography, space use patterns, and home range establishment (Dolev *et al.* 2002; Perelberg *et al.* 2003; Bar-David *et al.* 2005b). Five years after the project onset, the free-ranging population was estimated to consist of more than 100 individuals, including fawns born in the wild (Bar-David *et al.* 2005b), while occupying a range of more than 100 km² in the Galilee region. Other than the population reintroduced in Israel, only one population, estimated at about 24 animals, exists in the wild, in Iran (Perelberg *et al.* 2003).

Bovine tuberculosis (*Mycobacterium bovis*; BTB) is a chronic infectious disease, and is one of the most important pathogens of wild mammals worldwide (Morris *et al.* 1994). The disease was eradicated from the State of Israel during the mid 20th century, but its occurrence in Asia (e.g. Prasad *et al.* 2005), Africa (e.g. Ayele *et al.* 2004) and Europe (e.g. European Wildlife Disease Association, 2001) makes it a credible threat to the Israeli deer population. Moreover, BTB is known to easily invade long-lived social ungulates (Cross *et al.* 2005) and has been detected in European fallow deer (*Dama dama*), which appear to be a reservoir host of *M. bovis* (Morris *et al.* 1994; Mackintosh *et al.* 2004). Introduction of BTB by a reintroduced population carries risks to the broader ecosystem. The disease may have relatively minor effects on some reservoir species yet still cause major problems, through disease spillover, to other hosts including humans and livestock (Bengis 1999). There is substantial incentive to contain BTB shortly after its introduction, because once established in wildlife reservoirs, it has been proven to be exceedingly difficult to eradicate (Aranaz *et al.* 2004). This is particularly important in countries where

eradication programs have substantially reduced the incidence of BTB, but sporadic outbreaks still occur (Caffrey 1994; Aranaz *et al.* 2004; Simpson 2002).

Control of BTB based on test-and-remove principles, although very successful in cattle and farmed deer (Griffin *et al.* 2004), will have a very limited role for the control of BTB in free-ranging wildlife until improved diagnostic tests are developed (de Lisle *et al.* 2002). Moreover, in cases where the infected species are protected, non-lethal interventions are far preferable. Vaccination has been recognized as a possible means of controlling BTB in wildlife (Griffin & Mackintosh 2000), and a recent review found that the bacillus Calmette-Guerin (BCG) vaccine produced significant levels of protection against both infection and disease (Mackintosh *et al.* 2004), and hence may be used in wildlife, including deer. However, the long-term effectiveness of BCG vaccine is unknown for many host species (de Lisle *et al.* 2002). Moreover, broad-scale vaccination of wildlife populations presents considerable challenges (McCallum & Dobson 1995; Woodroffe 1999; Lafferty & Gerber 2002), especially in areas where more than one species might be infected with BTB and hence should be controlled (de Lisle *et al.* 2002).

METHODS

The Model

To explore the implications of the three conceptual regimes for management strategies aimed at restricting the establishment of a disease reservoir, we considered the potential spread of a non-lethal infectious disease in a reintroduced population. We used an existing spatially-explicit individual-based model that predicts numerical growth and spatial expansion of a reintroduced population of Persian fallow deer in northern Israel ("the deer model", Bar-David *et al.* 2005a) and extended it to simulate a hypothetical outbreak of BTB, a plausible threat to the population (Bar-David *et al.* 2006).

The deer model predicts the colonization process of a reintroduced female Persian fallow deer population by simulating movements of dispersing individual female deer released or born in the wild and their subsequent home range establishment and home range shift (i.e. a change in its spatial orientation over time). It also simulates demographic dynamics of female deer—individual survival and reproduction. The model was developed based on empirical data obtained during the first three years of the reintroduction project (1996-1999; Dolev *et al.* 2002, Perelberg *et al.* 2003; Bar-David *et al.* 2005b) and on the realistic landscape within the studied area. The study area, a 630 km² rectangular section of the Galilee region in Israel (between 32°54'-33°05'N and 35°09'-35°28'E) is represented by landscape template: a 213 by 300 1-hectare pixel grid, where each pixel is scored for deer habitat suitability. At each time step (one year) the following processes are simulated including stochastic elements (for details and parameter definition see Bar-David *et al.* 2005a):

- Release of female deer from a habituation enclosure (10 females per year for the first five years, and five females per year during the following five years—see Saltz 1998).
- Dispersal of female deer, newly released or wild-born, from the site of release or birth, in a "search" for suitable habitat to establish a home range. The factors that influence home range establishment include landscape parameters (according to the landscape template) and presence of conspecifics (as was quantified based on field data). The initial direction of movement is determined randomly at the start of the movement.

- Home range adjustment: released females could shift the spatial orientation of their home range during the first three years after release.
- Age-dependent survival and reproduction of individual females. Individuals that failed to establish a home range during a yearly time step were removed from the model.

The outputs of the deer model were validated by comparing them to the actual spatial and demographic performance of the reintroduced population at five years after project onset (i.e. two years beyond the period on which parameters were based). The model successfully identified much of the area occupied by the deer during that time, as well as the main "activity centers", or areas that are densely populated (Bar-David *et al.* 2005a). Because the detailed predictions regarding deer range expansion were validated from field data, we concluded that the model is an appropriate basis for exploring simultaneous host and disease invasions and associated management strategies.

We extended the deer model by adding another layer describing the dynamics of disease transmission among individual fallow deer. The disease is modeled as an SEI process (Susceptible, Exposed but not infectious or Infectious, Hudson *et al.* 2001; Getz and Lloyd-Smith 2006), as appropriate for BTB. The extended model and its parameters are described in detail in Bar-David *et al.* (2006); the following presents a brief overview.

All simulations start with one infected individual among the first group released. Transmission between deer is modeled as a stochastic horizontal process that depends on the spatial structure in Persian fallow deer populations, i.e. the risk of transmission increases with the degree of home range overlap among deer, which represents the level of interaction among individuals (Perelberg 2000). We assumed that the risk of infection to each susceptible deer is proportional to the fraction of potential contacts that are infectious only in its immediate surroundings, where each individual's total contact rate with other deer is density-independent. Hence, the force of infection (λ) for individual *i* is calculated as:

$$\lambda_i(t) = \frac{\beta \sum_k V_{ik}(t)}{\sum_j W_{ij}(t) + \sum_k V_{ik}(t)}, \quad (1)$$

where β is the transmission parameter, $W_{ij}(t)$ and $V_{ik}(t)$ are the areas of overlap of each susceptible individual *i* with other susceptible (or vaccinated, see below) individuals ($j = 1,...,n_S, j \neq i$) and infectious individuals ($k = 1,...,n_I$), respectively, within its immediate surroundings.

Assuming that infection is a constant hazard process within each time step, the probability that individual *i* is infected in any given time step is now given by the expression:

$$\Pr(\text{Infection of individual } i \text{ during timestep } t) = 1 - \exp(-\lambda_i(t)) \quad (2)$$

Values of β were defined based on measured rates of BTB transmission in herds of farmed fallow deer (Wahlström *et al.* 1998; see details in Bar-David *et al.* 2006). We used values of β in the range 0.1-1.0 to represent settings with low (0.1), moderate (0.5) and high (1.0) disease transmissibility. We simulated a one-year incubation period before an infected individual becomes infectious (Wahlström *et al.* 1998). Fawns born to infectious females could become infected via maternal transmission, during their first year of life while they are still in their

mothers' close vicinity, with probability β_{mat} = 0.25 (after McCarty & Miller, 1998) unless stated otherwise.

Potential influences of disease on survival, reproduction, and movement patterns of infected individuals were not modeled, in keeping with reports that BTB has relatively minor impacts for several ungulate maintenance hosts (McCarty & Miller, 1998; Rodwell *et al.* 2001).

Management strategies

Using the extended model, we simulated 5 different management strategies aiming to control disease spread in the reintroduced population:

(a) Vaccinating all released deer.
(b) Stopping further releases of deer once the disease was recognized.
(c) Vaccinating all released deer and a proportion of all wild-born young, i.e., the probability of finding a fawn in the wild and vaccinating it was set to 0.7 (p_{vacc}=0.7).
(d) Vaccinating all released deer and all wild-born fawns while focusing the efforts in a specific zone around the area of introduction—within a radius of 3.4 km from the release site, which is approximately two average home range diameters.
(e) Vaccinating all released deer and all wild-born young in the entire area occupied by the deer, i.e. complete coverage of the population (p_{vacc}=1).

We explored the potential efficacy of these management strategies, as a function of disease transmissibility, representing moderate (β=0.5) and high (β=1) transmissibility (regimes 2 and 3). All strategies were applied constantly beginning from the third year after initial release (i.e. after 20 individuals had been released over the first two years), assuming a two-year delay to identify and respond to the disease in the wild population.

Vaccination was assumed in the model to be 100% effective and to provide life-long protection. This is beyond the effectiveness of the currently available vaccine (Mackintosh *et al.* 2004), but was simulated as a theoretical exercise to assess the maximum impact of different vaccination programs, and whether we may expect future vaccines to have the potential to control a BTB outbreak. In the vaccination simulations, the vaccine could affect only susceptible individuals, e.g. the status of fawns already infected by maternal transmission was not altered by vaccination. For the vaccinated individuals, the force of infection (λ) was set to zero, i.e. Pr (the probability that vaccinated individual i is infected at time t)=0; equation 2), while for the susceptibles λ was calculated by including contacts with vaccinated individuals in the uninfected group ($W_{ij}(t)$; equation 1).

The model simulation ran for 20 years, covering roughly three deer generations (earliest age of reproduction is 2-3 years, with individuals living as long as 10-15 years), a reasonable time interval to consider short to mid-term disease management scenarios. For each management scenario, 250 stochastic realizations were simulated. At each time step, the following outputs were examined:

1. The number of infectives.
2. The proportion of model runs in which the disease had gone extinct.
3. The average spatial distribution of the population (generating a map of the overall occupancy of the study area, with each grid pixel representing the average number of females that occupy the pixel as part of their home range).

4. The average spatial distribution of infectives (generating a map that represents the infectives' use of the study area).

It is important to note that the model includes only female deer. As males may play a major role in disease transmission (O'Brien *et al.* 2002) (e.g. as mixing agents due to possible life-long movements), we expect our results to underestimate the effects of disease. Because the model describes a reintroduced population, however, all individuals are mixing and dispersing due to the population expansion process, so that the relative importance of males is likely to be diminished compared with an established population where males account for most dispersal. However, since the relative importance of males for disease transmission in colonizing populations is ultimately unknown, these simulations are intended as an illustration of the types of phenomena that may be observed, and as a tool for investigating the potential of various interventions for managing the disease.

RESULTS

The three conceptual regimes for the dynamics of disease invasion in a colonizing host population (Fig. 1) were evident in our simulations of a hypothetical outbreak of BTB in a reintroduced population of Persian fallow deer in northern Israel (Fig. 2-4). The model simulations indicated that the range of transmissibility determined in empirical studies of BTB in European fallow deer (Wahlström *et al.* 1998) led to simulated outbreaks spanning all three possible outcomes for the simultaneous invasion. For low transmissibility (the low end of the estimated values, β=0.1), the disease range initially expanded slightly, but ultimately decreased (Fig. 2), with high probability of extinction (p_{ext}) over the 20-year simulation. However, the outbreak did persist due to stochasticity in some simulations (e.g. p_{ext} <0.6 after 10 years, p_{ext} <0.85 after 20 years). Moderately and highly transmissible diseases exhibited infrequent extinction and faster growth: for β=0.5 the disease took hold, but its wavefront lagged behind the wavefront of the host population (Fig. 3). At the high end of the estimated range of transmissibility (β=1), the disease closely tracked the expanding host population (Fig. 4), and persisted for 20 years in more than 95% of simulations, with more than 50% of all females infected on average (79$\pm$32 out of 133$\pm$25 individuals [mean$\pm$SE]) (Fig. 4e). These results demonstrate clearly that transmissibility values throughout the plausible, empirically-determined range for BTB in fallow deer lead to highly disparate outcomes for disease invasion and persistence in a reintroduced population.

Investigating strategies to manage the outbreak (Fig. 5-7), we found that stopping further releases in the reintroduction program (after 20 individuals have been released over the first two years) had minimal effect on eradication of a chronic disease, increasing the probability of disease extinction within 20 years by only 5-10% for any transmissibility scenario. When transmissibility was moderate (β=0.5, Fig. 5) or high (β=1), the disease expanded and persisted in the population in 70% (p_{ext} <0.3) and 90% (p_{ext}<0.1) of the simulations, respectively, with an average of more than 50% of all females infected in the latter case (27$\pm$32 out of 46$\pm$15 individuals [mean+SE]) (Fig. 6).

When animal releases were continued, varying degrees of control were achieved with vaccination interventions. If all individuals released after the first two years were vaccinated, the disease range, on average, considerably decreased (in comparison to the "no intervention strategy", Fig 7), however, the probability of disease extinction increased only marginally (for β=0.5, p_{ext} =0.28, see Fig. 5; for β=1, p_{ext} =0.06). More substantial impacts on disease spread in the colonizing population were possible when wild-born young were vaccinated in addition to released individuals (Fig 5-7).

Spatially-targeted vaccination appeared more effective than comparable levels of coverage through the entire population range: Vaccinating all wild-born young (with efforts focused in a core region, within a radius of 3.4 km around the introduction site) proved superior on average to vaccinating 70% of wild-born young in the entire population (Fig. 5). Moreover, the spatial range of the disease in the latter scenario was wider, on average, than for the spatially-targeted policy (Fig 7). The effect of spatially-targeted vaccination was most noticeable for the moderately transmissible disease, i.e regime 2 (for β=0.5, p_{ext} =0.67 vs. p_{ext} =0.56, respectively—Fig. 5; for β=1, p_{ext}=0.37 vs. p_{ext}=0.25, respectively). However, variation in the number infected at year 20 was greater for the spatially targeted policy due to some epidemics that escaped the buffer zone (see Fig. 6 for β=0.5).

For a highly transmissible disease (regime 3), only a vaccination strategy with complete coverage of all wild-born and released individuals could cause a substantial increase in the probability of disease extinction within 20 years (for β=1, p_{ext}=0.56). For moderate disease this strategy led to a notable increase in the effect of the intervention but not to eradication because of maternal transmission (for β=0.5, p_{ext}=0.74, Fig. 5 and Fig. 6). Reducing maternal transmission to zero, in addition to the complete-coverage intervention, stopped all transmission and caused disease extinction by year 13 (for β=0.5, Fig. 5 and Fig. 6).

DISCUSSION

Infectious disease is a concern for conservation efforts (Viggers *et al.* 1993; Cunningham 1996; Lafferty & Gerber 2002), since "the relocation of wild animals never consists of the movement of a single species. Rather it always entails relocations of a 'biological package' consisting of the animal itself (host) and its passenger organisms, potentially including viruses…or other pathogens" (Davidson and Nettles, 1992), so the risks of disease should be considered seriously in reintroduction programs. To reduce these risks, a series of measures was recommended by Viggers *et al.* (1993) to be taken prior to release: (1) quarantine: the isolation of animals for a period that is dependent on the maximum incubation period of diseases known to affect that species; (2) diagnosis of disease: a full clinical examination conducted by an experienced wildlife veterinarian, including tests such as radiology, fecal examination, serology and microbial cultures; and (3) vaccination: depends on the host, the relative risk of disease and the efficacy of the vaccine.

Davidson and Nettles (1992) present a system for evaluating the disease risk when translocating wild animals, based on the probability that a parasite carried by the translocated animals will become established at the site of release and be pathogenic to either the target or other species. While it is often impossible to accurately quantify these hazards before undertaking wildlife translocations, it is important that persons involved in these conservation programs be aware of such risks (Conningham 1996) and, moreover, be prepared with a suite of management options to be implemented if disease should be identified. Understanding the dynamics of disease invasion in reintroduced populations can aid in designing such strategies.

Disease management of free ranging wildlife presents considerable challenges (McCallum & Dobson 1995; Woodroffe 1999; Lafferty & Gerber 2002). In our simulations, stopping further releases in the reintroduction program—even at an early stage of the program—had little effect on eradication of a chronic disease of moderate-to-high transmissibility, suggesting that additional management interventions are required. If the release program is continued, then vaccination interventions could be effective in combating disease spread in the colonizing

population, but only when wild-born young were vaccinated in addition to all released individuals. Note that these findings apply to an idealized vaccine with 100% efficacy; programs using currently available, less-effective vaccines will face greater challenges. Since vaccination throughout the entire spatial range of the population might not be feasible due to landscape-related parameters and logistical constraints, it is useful to assess reduced strategies. For a situation where the host and disease were introduced in the same location, focusing vaccination efforts in a core region around the introduction site appeared more effective than achieving comparable overall coverage by incomplete vaccination through the entire population range.

Our conclusions regarding management should apply generally to chronic, non-lethal diseases affecting reintroduced populations, but may not hold for acute or lethal diseases. In cases where the disease wavefront lags behind that of the population (regime 2), future studies should examine the effectiveness of 'cordon sanitaire' strategies that may prevent further expansion of the disease, thereby maintaining a disease-free portion of the population that could continue expanding. Such strategies might include applying vaccination or test-and-remove policies around the leading edge of the epidemic, or fencing in the diseased population. Fencing may lead to segregation of populations and hence limit the spread of disease or its spillover between species (e.g. foot and mouth disease in South Africa, Thomson *et al.* 2003). However, fences have significant environmental, social and economic costs, which are sometimes thought to outweigh their benefits (reviewed by Thomson *et al.* 2003). If fencing is considered as a management strategy for expanding populations, the actual frontiers of population and disease—as well as their expansion rates—must be assessed accurately, so that fences can be located beyond the frontier of the disease. Allowance for error is advisable, as the fencing exercise is futile if the disease is not contained. Also, future studies could examine the effectiveness of concentrating intervention efforts in specific sites such as the introduction site or population activity centers that have the potential to develop into disease foci (Bar-David *et al.* 2006).

We suggest that recognizing which of the conceptual regimes best describes a situation in the field can aid in choosing the most efficient and feasible management strategy. Hence it is important to consider how the applicable regime could be determined in a field situation. Assuming that accurate diagnostic tests exist for free ranging wildlife, we suggest that individuals should be tested along transects radiating outward from the introduction site, to ascertain the relative positions of the disease and population wavefronts. It is crucial to conduct these tests along transects in several directions, because of possible landscape-driven variation in the relative velocity at which the population and disease expand (v_d/v_p). For example, variation driven by human landscape development was observed for the deer population in northern Israel (Bar-David *et al.* 2006). Settlements on one boundary of the deer population range inhibited population expansion in that direction. In simulations with moderate transmissibility, the disease wavefront caught up with the population wavefront in this inhibited direction (akin to reaching the shore of an island), while in other directions the population continued expanding and the disease lagged behind it. In such settings, a combined approach using different regime-specific management strategies in different regions will be optimal.

When identifying a disease in a new environment, e.g. introduced by a colonizing population, a main challenge for wildlife managers is to assess disease transmissibility in the host population. Uncertainty regarding a disease's transmissibility can challenge the managers' ability to assess the likelihood of long-term persistence of the disease and the rate of its spread within a population. For example, within a range of disease transmissibility drawn from analysis of BTB in fallow deer, different values led to simulated outbreaks spanning all three dynamical regimes for the simultaneous invasion. Such uncertainties have important implications for the disease

persistence within the colonizing population, and hence for the threat to other species in the ecosystem.

In conclusion, the establishment process of reintroduced populations leads to unique patterns of mixing and spatial spread that may govern the invasion dynamics of infectious diseases. In this study we focused on a hypothetical BTB epidemic in the Persian fallow deer population recently reintroduced in northern Israel. The range of patterns observed in our simulations could describe the likely spatial dynamics of other systems with chronic non-lethal diseases infecting reintroduced hosts. Moreover they could describe disease dynamics in introduced (invasive) species.

Since pathogens are a major threat to the persistence of endangered reintroduced populations, management strategies should seek to eradicate a disease soon after its invasion. Moreover, since the impact of a novel disease introduced to an ecosystem by colonizing populations goes beyond the threat to the original host species, it is important to control the disease before it might spill over to other species and hence jeopardize the broader ecosystem. Understanding the spatial dynamics of disease within an expanding host population is an important component of planning management strategies aiming to control such situations.

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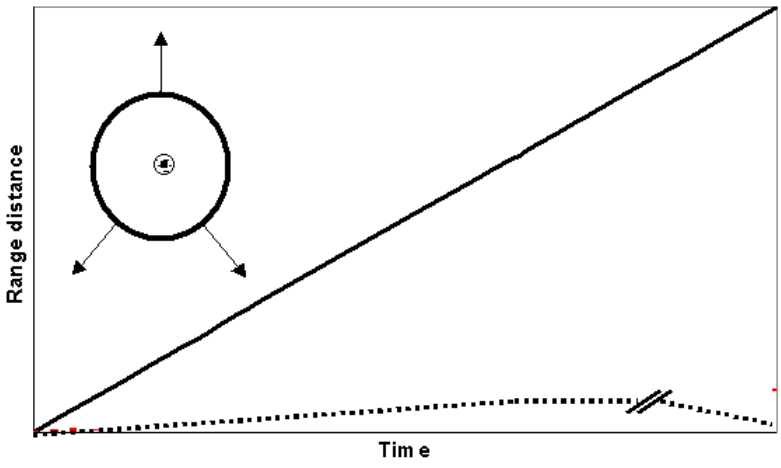
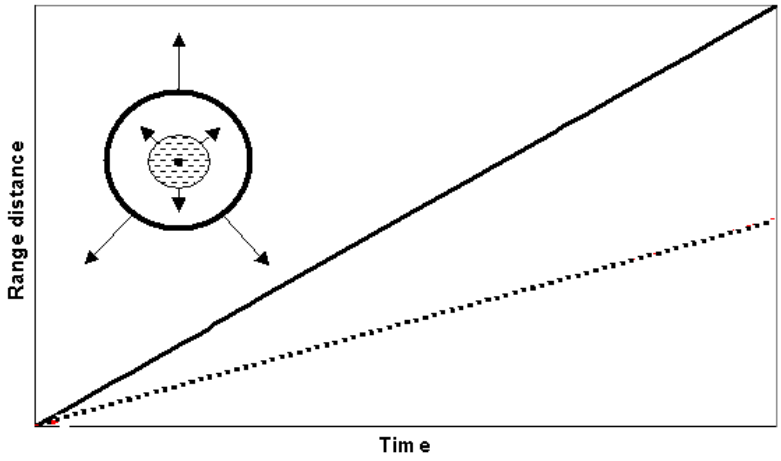
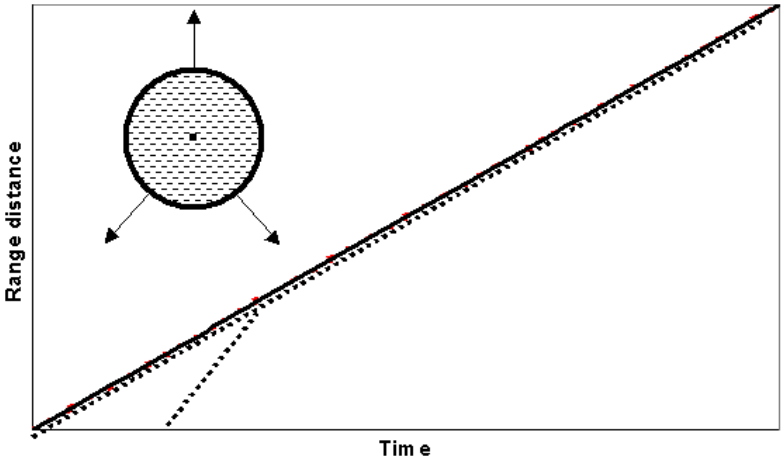
Figure 1. Simultaneous invasion of host and disease: expectations in an idealized homogeneous landscape. Schematic representation of range expansion versus time for a colonizing host population (solid lines) and disease (dashed lines), for three ranges of disease transmissibility. Inset diagrams show spatial spread of the population (white area enclosed by heavy circle) and disease (speckled area) from the introduction site (black square), with arrows depicting the rate of expansion. Wavefronts of population and disease are assumed to advance with characteristic velocities v_p and v_d, respectively. Three scenarios of increasing transmissibility are depicted: (a) $R_0<1$, (b) $R_0>1$ and $v_d<v_p$, (b) $R_0>1$ and $v_d>v_p$. In (c), two disease range curves are shown, representing disease introduction at different times. Figure re-printed with permission from Bar-David *et al.* (2006).



a. Low transmission coefficient



b. Intermediate transmission coefficient



c. High transmission coefficient

Figure 2. Spatial expansion of simultaneously invading host population and disease of low transmissibility (β=0.1) in a real landscape.

Range patterns based on model projections to the end of 5, 10, 15 and 20 years since the onset of the reintroduction project of the Persian fallow deer on the northern Israel landscape (a-d), for low disease transmissibility β=0.1. Black denotes home ranges of all deer, grey denotes home ranges of infected individuals; pixels were colored if the average number of individuals occupying them exceeded 0.5 over 250 runs. All simulations started with one infected individual among the first group released (star in (a) indicates release site). Each pixel represents 100 by 100 m (total of 213 by 300 pixels). (e) The total population size (line plot) and number of infected individuals (boxplot), as predicted by 250 realizations of the model with β=0.1. The line and error bars show the mean and standard error of the total population size. The box lines show the median and interquartile range (IQR) of the number infected, and whiskers show the extreme values within 1.5×IQR of the boxes. Results beyond the whiskers are shown by crosses (+). Figure re-drawn from Bar-David *et al.* (2006).

β=0.1

a. Year 5

b. Year 10

c. Year 15

d. Year 20

e. Number of infected individuals and population size

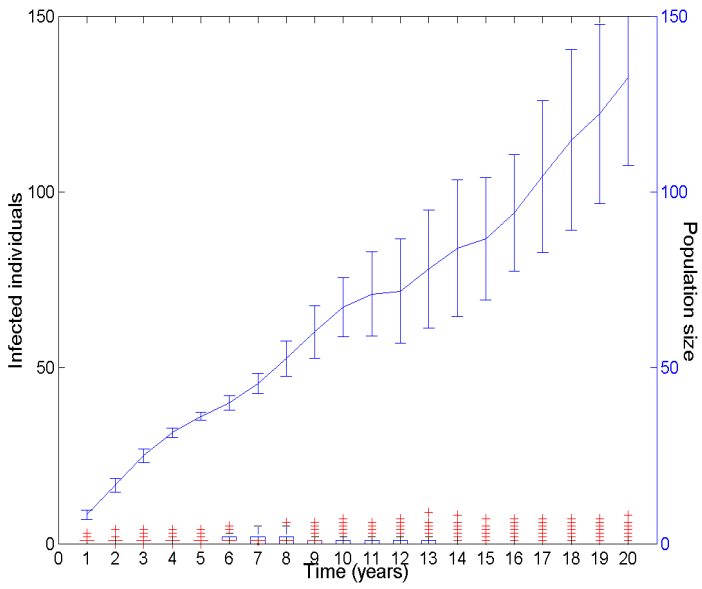


Figure 3. Spatial expansion of simultaneously invading host population and disease of moderate transmissibility (β=0.5) in a real landscape.

As in Figure 2, but for moderate disease transmissibility β=0.5. The population size is shown in Figure 2e. Figure re-drawn from Bar-David *et al.* (2006).

β=0.5

a. Year 5

b. Year 10

c. Year 15

d. Year 20

e. Number of infected individuals

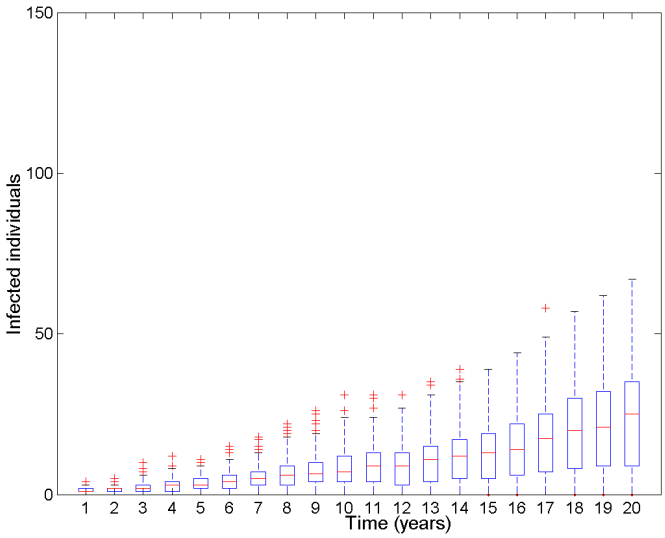


Figure 4. Spatial expansion of simultaneously invading host population and disease of high transmissibility (β=1) in a real landscape.

As in Figure 2, but for high disease transmissibility β=1. The population size is shown in Figure 2e. Figure re-drawn from Bar-David *et al*. (2006).

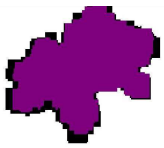
β=1

a. Year 5

b. Year 10

c. Year 15

d. Year 20



e. Number of infected individuals

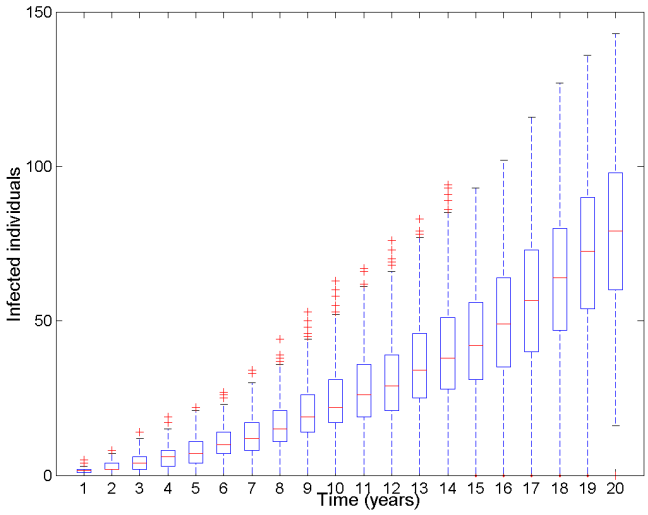


Figure 5. Proportion of disease outbreaks under various management policies. Proportion of disease invasions gone extinct (out of 250 runs) versus time, for a disease of moderate transmissibility (β=0.5) under various management policies:

(a) vaccination of all released deer; (b) Stopping further releases of deer; (c) vaccination of all released individuals, and of wild-born fawns with probability p_{vacc}=0.7; (d) vaccination of all released individuals, and of all wild-born young (with p_{vacc}=1) within a radius of 3.4 km from the release site; (e) vaccination of all released individuals, and of all wild-born young (p_{vacc}=1) in the entire population; (f) as in (e) with no maternal transmission (β_{mat}=0). Star indicates control (no intervention). All management strategies were applied from the third year after initial release onwards. Figure re-printed with permission from Bar-David *et al*. (2006).

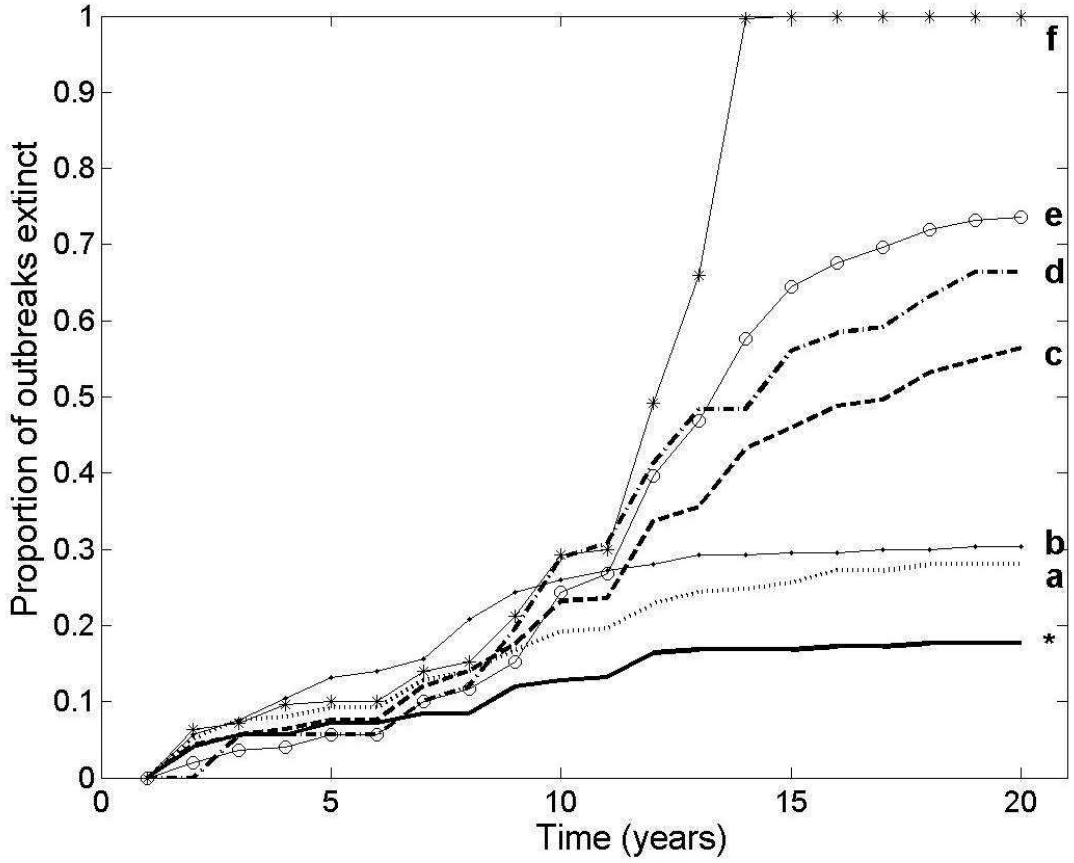
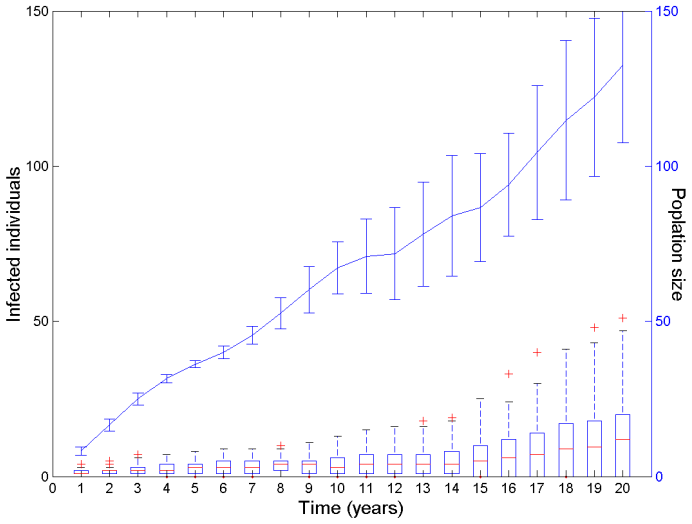


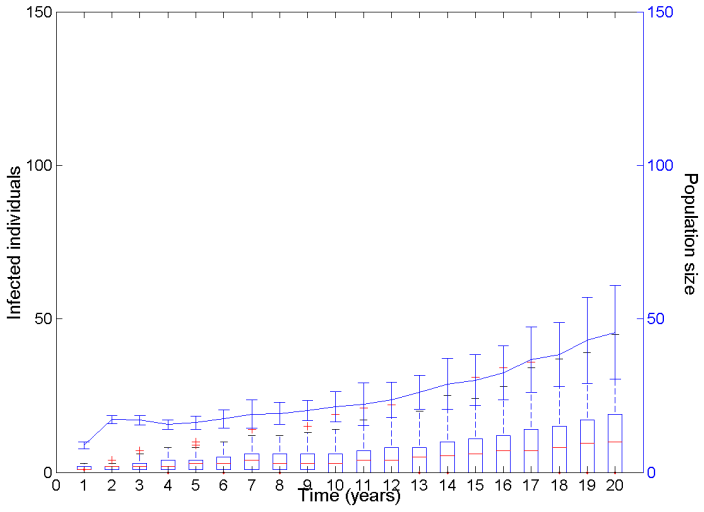
Figure 6. Time series of total population size and number infected for a disease of moderate transmissibility (β=0.5) under various management policies.

The total population size (line, with error bars standard error) and number infected (boxes) under various management policies (average of 250 runs): (a) vaccination of all released individuals; (b) no further individuals released; (c) vaccination of all released individuals, and of wild-born fawns with probability p_{vacc} =0.7; (d) vaccination of all released individuals, and of all wild-born young (with p_{vacc} =1) within a radius of 3.4 km from the release site; (e) vaccination of all released individuals, and of all wild-born young (p_{vacc} =1) in the entire population; (f) as in (e) with no maternal transmission (β_{mat}=0). All management strategies were applied from the third year after initial release onwards. The box lines show the median and interquartile range (IQR) of the number infected, and whiskers show the extreme values within 1.5×IQR of the boxes. Results beyond the whiskers are shown by crosses (+). Figure re-printed with permission from Bar-David *et al.* (2006).

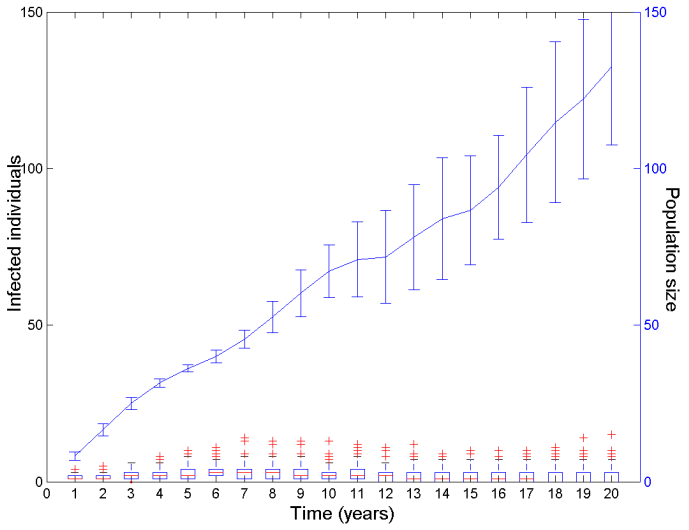
a. Vaccination of released individuals



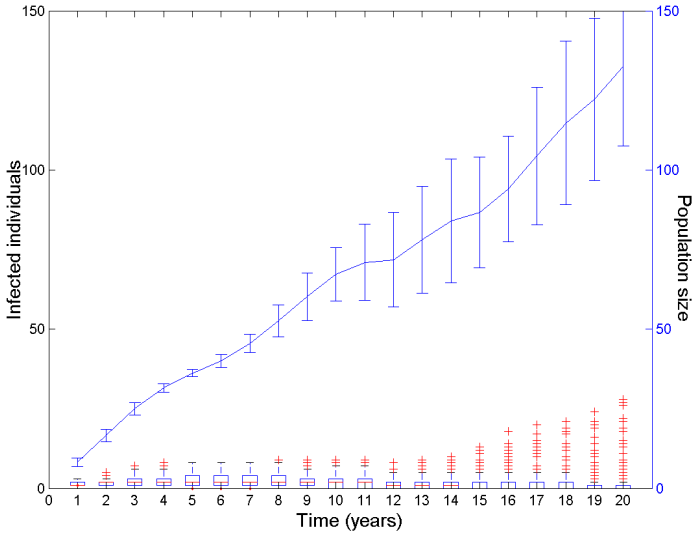
b. Stop releasing



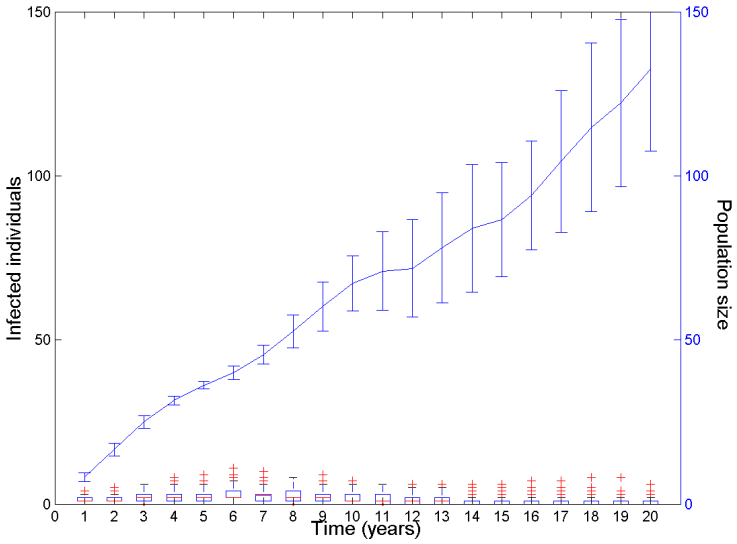
c. Vaccination of released individuals and the young born in the wild (p_{vacc} =0.7)



d. Vaccination of all released individuals and all the young in the wild (with p_{vacc} =1) within 3.4 km from release site



e. Vaccination of all released individuals and all the young (p_{vacc} =1) in all the area of distribution



f. Vaccination of all released individuals and all the young in the wild, no vertical transmission

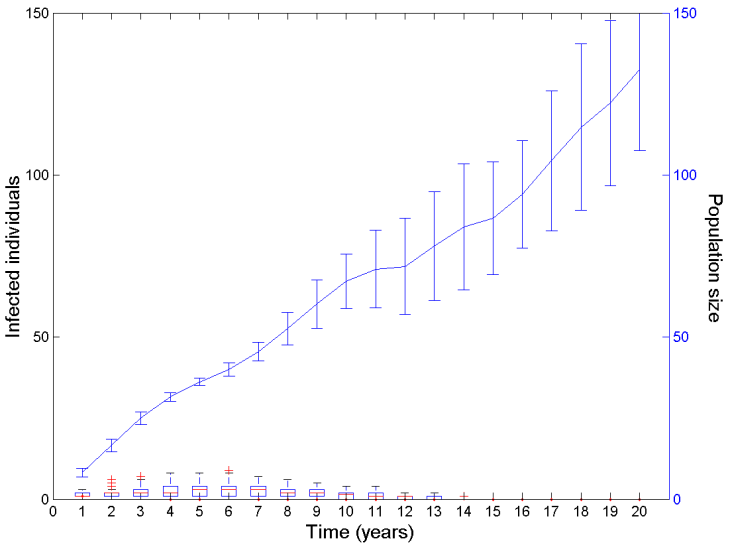
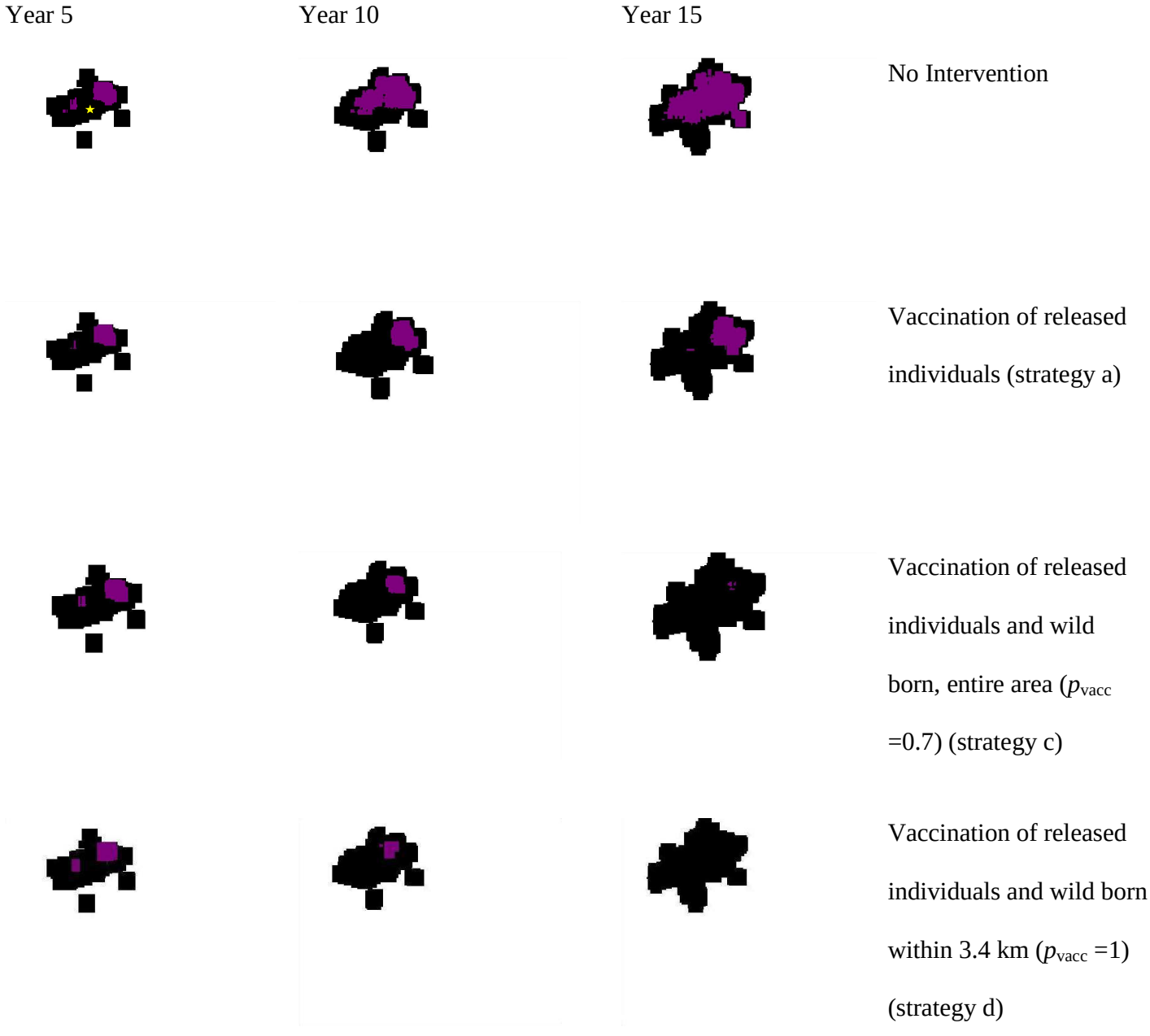


Figure 7. Spatial expansion of simultaneously invading host population and disease of moderate transmissibility (β=0.5) under several management policies, described in the text.

Range patterns are based on model projections to the end of 5, 10 and 15 years since the onset of the reintroduction project of the Persian fallow deer. Black denotes home ranges of all deer, grey denotes home ranges of infected individuals; pixels were colored if the average number of individuals occupying them exceeded 0.5 over 250 runs. All simulations started with one infected individual among the first group released (star indicates release site. Each pixel represents 100 by 100 m (total of 213 by 300 pixels):



d. Vaccination of released individuals and wild born, entire area (p_{vacc} =1) (strategy e)