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Persistence of canine distemper virus in the Greater Yellowstone Ecosystem's carnivore community

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Abstract. Canine distemper virus (CDV) is an acute, highly immunizing pathogen that should require high densities and large populations of hosts for long-term persistence, yet CDV persists among terrestrial carnivores with small, patchily distributed groups. We used CDV in the Greater Yellowstone ecosystem's (GYE) wolves (*Canis lupus*) and coyotes (*Canis latrans*) as a case study for exploring how metapopulation structure, host demographics, and multi-host transmission affect the critical community size and spatial scale required for CDV persistence. We illustrate how host spatial connectivity and demographic turnover interact to affect both local epidemic dynamics, such as the length and variation in inter-epidemic periods, and pathogen persistence using stochastic, spatially explicit susceptible–exposed–infectious–recovered simulation models. Given the apparent absence of other known persistence mechanisms (e.g., a carrier or environmental state, densely populated host, chronic infection, or a vector), we suggest that CDV requires either large spatial scales or multi-host transmission for persistence. Current GYE wolf populations are probably too small to support endemic CDV. Coyotes are a plausible reservoir host, but CDV would still require 50 000–100 000 individuals for moderate persistence (>50% over 10 years), which would equate to an area of 1–3 times the size of the GYE (60 000–200 000 km^2). Coyotes, and carnivores in general, are not uniformly distributed; therefore, this is probably a gross underestimate of the spatial scale of CDV persistence. However, the presence of a second competent host species can greatly increase the probability of long-term CDV persistence at much smaller spatial scales. Although no management of CDV is currently recommended for the GYE, wolf managers in the region should expect periodic but unpredictable CDV-related population declines as often as every 2–5 years. Awareness and monitoring of such outbreaks will allow corresponding adjustments in management activities such as regulated public harvest, creating a smooth transition to state wolf management and conservation after >30 years of being protected by the Endangered Species Act.

Key words: canine distemper virus; Canis latrans; Canis lupus; *critical community size; Greater Yellowstone Ecosystem; multi-host transmission; spatial connectivity; Yellowstone National Park, USA.*

Introduction

Acute, highly immunizing pathogens are generally thought to require large populations of hosts for long-term persistence. This conclusion stems from the extensive study of measles, which requires a threshold population size of between 250 000 and 500 000 people to persist in developed countries (Bartlett 1957, Keeling and Grenfell 1997). However, there are examples of acute, highly immunizing pathogens that surprisingly manage to persist among low-density, patchy host populations. For example, canine distemper virus (CDV), a close relative of measles, persists among terrestrial carnivores that tend to occur at relatively low densities (e.g., most species, <1 per km^2; Table 1), live in small social groups (i.e., 1–20), tend to be territorial, and are patchily distributed. Under these conditions, acute, highly immunizing pathogens like CDV probably require large spatial scales or multi-host transmission for persistence. We use the example of CDV persistence in Yellowstone National Park's (YNP) carnivores as a case study for exploring the factors necessary for the persistence of an acute, highly immunizing pathogen in low-density host populations. This is an important case study because wolves around the Greater Yellowstone Ecosystem (GYE), still fully listed under the Endangered Species Act at the time of this project's inception, had undergone periodic population declines coincident with CDV outbreaks (Almberg et al. 2009).

Several serological surveys, spanning 20 years, suggest that sympatric coyotes (*Canis latrans*; Gese et al. 1997, Almberg et al. 2009), wolves (*Canis lupus*; Almberg et al. 2009), and cougars (*Puma concolor*; Biek et al. 2006) in northern YNP experienced at least three (1989, 1999,

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and 2005) synchronous, multi-host outbreaks of CDV (Fig. 1). Between these discrete epidemics, there was no evidence from coyotes or cougars to suggest that CDV persisted locally in the Northern Range of YNP, a 1000-km^2 region in the north of the park where the surveys were conducted. In contrast, continuous sampling of wolves from 1997 to 2008 on both the Northern Range and interior of YNP yielded evidence for a small amount of inter-epidemic seroconversion, as well as a possible separate outbreak of CDV in the interior of the park in 2002 (Fig. 1; Almberg et al. 2009). These anomalous patterns of exposure prompted us to ask how, where, and at what scale CDV might be persisting in the regional carnivore community. Past CDV outbreaks were highly correlated with poor wolf pup survival (Smith et al. 2006, Smith and Almberg 2007, Almberg et al. 2009), which also motivated us to ask how frequently managers might expect to see short-term, disease-induced population declines.

Canine distemper virus (genus *Morbillivirus*, family Paramyxovirus) is a generalist pathogen capable of infecting a wide range of carnivores including members of *Canidae*, *Felidae*, *Mustelidae*, and *Procyonidae*. CDV is primarily transmitted through the direct exchange of oral and nasal exudates, although transmission might also occur through the ingestion of infectious saliva deposited at a communal food source. There is only a very narrow timeframe under which this latter form of transmission would be plausible because CDV is highly unstable in the environment (Greene and Appel 2006). CDV induces a relatively short period of latency and infectiousness, there is no known carrier state, it often causes significant mortality, and it is highly immunizing (Williams 2001, Greene and Appel 2006).

Bartlett's (1957) early work on human measles showed that there exists a host threshold population size below which measles fails to persist. This concept of critical community size has been extended to wildlife diseases but is complicated by the complex relationship between population size and recruitment (i.e., density-dependent recruitment effects; Lloyd-Smith et al. [2005]). In addition to host population size, previous work has shown that host population and metapopulation structure (Grenfell and Harwood 1997, Swinton et al. 1998, Park et al. 2002), spatial connectivity among groups (Swinton et al. 1998, Keeling 2000, Park et al. 2002, Ferrari et al. 2008, Jesse et al. 2008), host demographic turnover (Choisy and Rohani 2006, Conlan and Grenfell 2007), spatial heterogeneity (Park et al. 2001, Hagenaars et al. 2004), and the presence of multiple host species (McCormack 2006, McCormack and Allen 2007) can play an important role in pathogen persistence. For a given host population size, these studies found that pathogens persist best in hosts having many, relatively large social groupings or sub-populations, moderate levels of spatial and/or population connectivity, relatively high, continuous demographic turnover, and low spatial heterogeneity (in terms of host distribution). In the case of generalist pathogens such as CDV, the presence of multiple hosts capable of interspecies disease transmission is likely to increase the probability of long-term pathogen persistence (McCormack 2006, McCormack and Allen 2007). Our study adds to this existing body of knowledge by specifically addressing the effects of pulsed reproduction, the interaction between spatial connectivity and demographic turnover, and multi-host transmission in the context of pathogen persistence among hosts with small group sizes.

The characteristics of terrestrial carnivores such as wolves and coyotes are not expected to favor the persistence of acute, immunizing infections like CDV. Wolves and coyotes typically live at low densities relative to other terrestrial mammals, live in small social groups (if social), and are territorial, thereby adding spatial structuring that imposes limits on the degree of landscape connectivity. With these constraints in mind, we asked a series of questions pertaining to the conditions under which CDV is likely to persist within the GYE, the 60 000-km^2 region encompassing YNP, Grand Teton National Park, and a mosaic of public and private lands. Following the terminology of Haydon et al. (2002; i.e., a *maintenance population* is a single host species whose population is greater than the critical community size; a *maintenance community* is a collection of host species that together constitute a population greater than the critical community size; and a *reservoir* is a maintenance population or community that is responsible for spillover to the target species of interest), these questions were as follows:

1) Given plausible estimates of group size, host survival, and spatial connectivity, can GYE wolves alone function as a maintenance population for CDV? If not, how do spatial connectivity, demographic turnover, and time since the last epidemic affect the magnitude of subsequent outbreaks fueled by a reservoir species?

2) What is the critical community size of a plausible, alternate reservoir host, such as coyotes, and what does this suggest about the geographic scale over which CDV is operating?

3) How would the addition of a second host affect our estimate of the critical community size within any one host species and the spatial scale over which disease may be persisting?

Study area on which models were based

YNP is an 8991-km^2 tract of protected land situated within northwestern Wyoming and including parts of Montana and Idaho, in the western United States. YNP is surrounded by the GYE, a 60 000-km^2 area that includes Yellowstone and Grand Teton National Parks, national forests, wildlife refuges, and a mosaic of state and private lands. The GYE is mountainous (elevation range: $<$1000 to $>$4000 m), characterized by steep abiotic gradients in elevation, soil, and climate, and covered in a mosaic of shrubland, grassland, riparian zones, alpine meadows, mixed coniferous forests, as well as agricultural and urban development. Land and wildlife management

TABLE 1. Density estimates and hypothesized maintenance capacities of carnivore species susceptible to canine distemper in Yellowstone National Park (YNP) and the Greater Yellowstone Ecosystem (GYE).

Carnivore species	Local density estimates (no./km^2)	Location from which estimates were derived	Hypothesized maintenance capacity in the GYE
Gray wolf (*Canis lupus*)	0.002–0.099	YNP, GYE	low
Coyote (*Canis latrans*)	0.194–0.726	GYE	medium
Red Fox (*Vulpes vulpes*)	0.43–1.7‡	Poland; Spain; Ontario, Canada	low
Cougar (*Puma concolor*)	0.002–0.009	YNP	low
Black bear (*Ursus americanus*)	0.056–0.072	YNP	low/none§
Grizzly bear (*Ursus arctos*)	0.017	YNP	low/none§
American badger (*Taxidea taxus*)	≤1.1	southeast Wyoming, USA	low
River otter (*Lontra canadensis*)	0.26/km of waterway	western Idaho, USA	low
American marten (*Martes americana*)	0.4–2.4	southeast Ontario; Maine, USA	low
Short-tailed weasel (*Mustela erminea*)	2–6	southern Ontario	low
Long-tailed weasel (*Mustela frenata*)	0.7–9	western Colorado, USA; Pennsylvania, USA	low
Wolverine (*Gulo gulo*)	0.004–0.005	GYE	low/none
Striped skunk (*Mephitis mephitis*)	0.7–4.8¶	eastern and midwestern United States	low
Raccoon (*Procyon lotor*)	2–20¶	eastern and midwestern United States	low/medium

† Rationale for maintenance host classification includes (1) low-density/small populations, (2) high-density/large populations, (3) small group size (i.e., median group size ≤ 4) or solitary, (4) large group sizes, (5) habitat specialist (patchy distribution), (6) habitat generalist (wide distribution), (7) seasonal (undergo long period of hibernation/torpor).

‡ Red fox densities in the Rocky Mountains are expected to be much lower than the estimates reported here and are probably less than the local estimates for coyotes.

§ Bears can seroconvert, but it is not clear whether they ever become infectious.

¶ Raccoon and striped skunk densities in the Rocky Mountains are expected to be much lower, and their distribution is expected to be restricted to lower elevation valley bottoms and urban centers.

within the region is multi-jurisdictional, falling under a mixture of private, state, and federal control.

YNP and the GYE are home to an intact suite of terrestrial carnivores, including gray wolves, coyotes, red foxes (*Vulpes vulpes*), grizzly (*Ursus arctos*) and black bears (*Ursus americanus*), cougars, badgers (*Taxidea taxus*), river otters (*Lontra canadensis*), American martens (*Martes americana*), short- (*Mustela erminea*) and long-tailed weasels (*Mustela frenata*), wolverines (*Gulo gulo*), striped skunks (*Mephitis mephitis*), and raccoons (*Procyon lotor*) (Yellowstone National Park 2008). While GYE-specific density estimates have been published for wolves, coyotes, cougars, and grizzly and black bears, less is known about the local densities and distribution of the other carnivores (Table 1). Although carnivore densities probably scale inversely with body size, most of their distributions are quite variable and habitat specific.

Domestic dogs are common pets in the GYE and can be brought into the national parks with visitors as long as they remain leashed and kept within 30 meters of roadways. However, as there were only 18 possible or probable cases of CDV among domestic dogs in Montana recorded between 1994 and 2008 (Montana Veterinary Diagnostic Lab, *unpublished data*), domestic dogs are an unlikely reservoir host for CDV within and around the GYE. We chose to focus on wolves because of the biological and political importance of understanding the factors affecting the population formerly listed on the Endangered Species List and now newly recovered population within the region. Furthermore, we focused on coyotes (for which we had the additional benefit of having region-specific population and demographic data) as the most plausible dominant, single-species CDV reservoir host in the GYE due to their wide distribution, relatively high density, and sociality, which ensures frequent contact necessary for disease transmission. Although all the aforementioned GYE carnivores are susceptible to CDV (see Table 1), we think the majority of these species either have insufficient numbers, contacts (driven by density and sociality), and/or distributions for them to constitute plausible maintenance populations (Haydon et al. 2002). For example, mustelids appear to be highly susceptible to CDV (Deem et al. 2000, Williams 2001) but are probably too weakly connected among themselves or to other host species to play a dominant role in CDV dynamics. Raccoons are a likely reservoir host in the eastern United States, but in the intermountain west tend to be found at lower densities and are patchily distributed.

To address our questions regarding the persistence of CDV in the GYE, we developed a series of discrete, stochastic, spatially explicit, group-based susceptible–exposed–infectious–recovered (SEIR) simulation models. We manipulated model parameters to explore the relative importance of population size, host demographic rates, and spatial connectivity in affecting the probability of pathogen persistence. After addressing the theoretical relationships between these variables and persistence, we used estimated hypothetical ranges of parameter values to ask our specific questions regarding

TABLE 1. Extended.

Rationale†	References
4, 6, but 1	U.S. Fish and Wildlife Service et al. (2008), Smith and Bangs (2009); Yellowstone Wolf Project, *unpublished data*
2, 4, 6	Berger and Gese (2007)
6 but 1, 3	Larivière and Pasitschniak-Arts (1996)
1, 3, 5	Murphy (1998), YNP (2008)
6 but 1, 3, 7	YNP (2008)
6 but 1, 3, 7	YNP (2008)
1, 3, 5, 7	Goodrich and Buskirk (1998)
1, 3, 5	Melquist and Hornocker (1983)
1, 3, 5	Soutiere (1979), Clark et al. (1987)
2 but 3, 5/6	King (1983)
2 but 3, 5/6	Quick (1951), Sheffield and Thomas (1997)
1, 3, 5	Inman et al. (2007, 2008)
1, 3, 5, 7	Wade-Smith and Verts (1982)
2 but 3, 5	Lotze and Anderson (1979)

the probability and spatial scale of CDV persistence among wolves, coyotes, or among multiple host species.

METHODS

Single-species model structure

We assumed the host population was structured into g social groups (packs) evenly distributed on a square lattice with n individuals per group. Hosts experienced a fixed probability of daily survival and an annual birth pulse equivalent to the sum of all mortality experienced in the previous biological year, thus maintaining the total population size from one year to the next. This allowed us to directly manipulate the degree of demographic turnover within our host population. We assumed disease transmission to be density dependent, whereby the force of infection (λ), or the per capita probability of infection, was proportional to the number of infectious individuals within a spatial range of contact (McCallum et al. 2001). We calculated the daily probability of infection for all susceptibles in pack i as a function of within-pack transmission and between-pack transmission such that

$$\lambda_i = 1 - \exp\left[-\left(\beta I_i + \beta \sum_{j \in S_i} (I_j e^{-\varepsilon d_{ij}})\right)\right]$$

where β represents the transmission coefficient (equal to the contact rate multiplied by the probability of infection given a contact between an infectious and susceptible individual), d_{ij} is the distance between packs i and j, ε scales the connectivity among packs, and j is in the set of S_i packs within a 50-km radius of pack i (the radius was set as the maximum daily dispersal distance that could be expected of wolves or coyotes; Boyd and Pletscher [1999], Harrison [1992]), excluding pack i.

We began each simulation with three infected individuals in a randomly selected pack in a completely susceptible population. Once infected, individuals would move into an exposed but not infectious class. We adopted a multi-compartmental approach (Keeling and Rohani 2008:94) to model more realistic distributions of latent and infectious periods (Keeling and Grenfell 1997, Lloyd 2001, Wearing et al. 2005). We assumed that the distribution of latent (LP) and infectious periods (IP) were roughly normal (coyote, $\mu = 6$ days, $\sigma^2 = 1$; wolf, $\mu =$ 10 days, $\sigma^2 = 1$) and negative binomial (coyote, NegBin(r

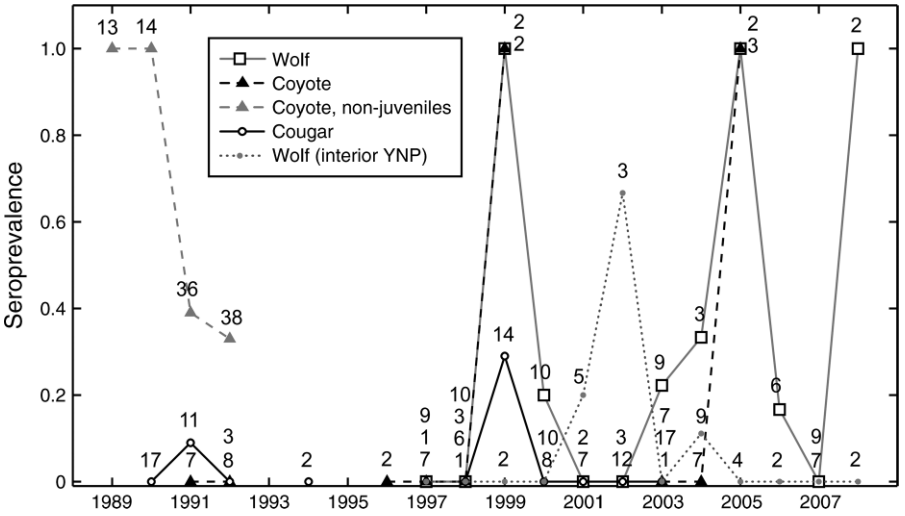

FIG. 1. Canine distemper virus (CDV) seroprevalence among wolves (*Canis lupus*), coyotes (*Canis latrans*), and cougars (*Puma concolor*) from the Northern Range (NR) and interior regions of Yellowstone National Park (YNP), USA, 1989–2008. All samples, with the exception of the coyote data (gray triangles) from Gese et al. (1997), are from juvenile animals (<2 years old) and thus can be interpreted as seroconversions for a given year; data for cougars are from Biek et al. (2006). Numerals adjacent to data points represent sample sizes of wolves, and where stacked, are in the species order of the legend. Small sample sizes among NR wolves in 1999, 2005, and 2008 reflect poor pup survival, which was likely the result of the CDV outbreaks (Almberg et al. 2009; Wolf Project, *unpublished data*).

TABLE 2. Parameter values used in the simulations of canine distemper virus in coyote and wolf populations of the Greater Yellowstone Ecosystem.

Parameter	Coyote	Wolf	References
Mean pack size (n)	10	14	Berger and Gese (2007), U.S. Fish and Wildlife Service et al. (2008), Smith and Bangs (2009); Yellowstone Wolf Project, *unpublished data*
Mean pack territory size	13 km^2	300–400 km^2	Berger and Gese (2007), U.S. Fish and Wildlife Service et al. (2008), Smith and Bangs (2009); Yellowstone Wolf Project, *unpublished data*
β, per capita daily transmission rate†	0.16 (also, 0.032, 0.063)	0.3 (also, 0.034, 0.085)	from estimates†
Annual mean survival rate, s†	0.35, 0.45, 0.55, 0.65	0.45, 0.55, 0.65, 0.75	Berger and Gese (2007), U.S. Fish and Wildlife Service et al. (2008), Smith and Bangs (2009); Yellowstone Wolf Project, *unpublished data*
Daily infectious survival rate, s_{dd}	0.9797	0.9797	Appel (1969, 1970), Greene and Appel (2006), Williams (2001)
Latent period (LP; days)	$\mu = 6$, $\sigma^2 = 1$, range = 5–8	$\mu = 10$, $\sigma^2 = 1$, range = 8–12	Appel (1969, 1970), Greene and Appel (2006), Williams (2001)
Infectious period (IP; days)	$\mu = 9$, mode = 7, $\sigma^2 = 17$	$\mu = 13$, mode = 9, $\sigma^2 = 45$	Appel (1969, 1970), Greene and Appel (2006), Williams (2001)

† Simulations were done over several different values of β and annual survival rates since we did not have precise empirical estimates of these values.

$= 2$, $p = 0.33$); wolf, NegBin($r = 2$, $p = 0.2$) [where r refers to the number of "heads" needed in a series of coin tosses before the tosses stop, and p refers to the probability of "heads" in each coin toss]), respectively (Table 2; Appendix A: Figs. A1 and A2). Less is known about the distribution of the latent period than of the infectious period (which is known to have a right tail) for canine distemper virus (CDV); thus we made the simplifying assumption that latent periods were normally distributed. These distributions were chosen to capture the majority of latent and infectious periods observed among domestic dogs (however, see *Discussion* and Appendix B for an explanation of how an extra class of extended infectiousness affects our conclusions) (Appel 1969, 1970, Williams 2001, Greene and Appel 2006). While infectious, individuals experienced an increased probability of mortality, δ (or a diseased daily survival rate, s_{dd}). Finally, individuals surviving infection advanced to recovery where they remained until death. We assumed the ordering of events within a daily time step as follows: transmission, movement between disease compartments, followed by death. The annual birth pulse was applied once a year at the end of the last daily time step.

Our model was stochastic in that binomial probabilities governed the random outcomes of host survival, the force of infection, and the transitions between disease states. Unless otherwise noted, we ran a minimum of 40 simulations for each combination of test parameters. We coded and ran all simulations using MATLAB computing software (R2007a; MathWorks, Natick, Massachusetts, USA).

Parameterization

We based simulated annual wolf and coyote survival probabilities (s) on geometric means of published age-specific survival probabilities in Greater Yellowstone's ecosystem (GYE) (Table 2; Berger and Gese 2007, Smith et al. 2010). Similarly, simulated wolf and coyote pack and territory sizes (Table 2) represented the mean of a range of values from locations in the GYE and were meant to include both the maximum densities following a birth pulse plus a small number of transients or dispersers (Berger and Gese 2007, U.S. Fish and Wildlife Service et al. 2008, Smith and Bangs 2009; Yellowstone Wolf Project, *unpublished data,*).

As we had no empirical estimates of contact rates or the probability of infection given a contact between a susceptible and infectious individual, the two components of the transmission coefficient, β, we made several simplifying assumptions. CDV transmission via oral exudates can take place both through social greetings where face-licking is common or at a communal feeding source such as a carcass. Wolves are obligate pack animals that primarily hunt and consume prey communally (Mech and Boitani 2003), whereas coyotes exhibit much more social plasticity, with some living in packs and others living as transients, and often hunting solitarily (although they can hunt and scavenge communally; Murie [1940]). Based on these socio-ecological differences, we assumed that within a pack, wolves made a greater number of effective contacts per day with one another than coyotes. Furthermore, we assumed that given a single initial infection within a pack, that on average, nearly all wolves within that pack became exposed by day 10 ($\beta = 0.3$), and nearly all coyotes by day 14 ($\beta = 0.16$) (these are admittedly guesses, but they were guided both by the knowledge that CDV is very contagious and that within packs, contacts can happen multiple times a day). The within-

pack basic reproductive ratio, R_0, or the mean number of secondary cases of infection caused by a single infectious individual within an entirely susceptible pack ($R_0 = n[1 - e^{-\beta/\gamma}]$, where n is the number of individuals within a pack minus 1, β is the transmission rate, and $1/\gamma$ is the duration of infectiousness [Keeling and Grenfell 2000]), was ~12 and ~6 for wolves and coyotes, respectively. These estimates fall within the range of R_0 estimates for other morbillivirus infections (human measles $R_0 = \sim 11$–15 [Hope-Simpson 1952, Anderson and May 1992]; harbor seal phocine distemper virus [PDV] $R_0 = \sim 2.8$ [Swinton et al. 1998]).

As the exact value of β will certainly affect the speed with which a pathogen spreads among a group of hosts, we conducted a sensitivity analysis where we ran simulations over three values of β for each species (wolf, $\beta = 0.034$, 0.085, 0.3; coyote, $\beta = 0.032$, 0.063, 0.16) equivalent to within-pack R_0 values of 3, 7, and 12 and 2, 3, and 6 for wolves and coyotes, respectively. We adopted estimates for the duration of latency and infectiousness from clinical studies of CDV infection in domestic dogs (Appel 1969, 1970,Williams 2001, Greene and Appel 2006). As physiological disease processes exhibit evidence of allometric scaling (Cable et al. 2007), we scaled these dog-CDV disease parameters via a power law ($\text{time}_{\text{ir}} = cM^{1/4}$, where time_{ir} is time to infectiousness or recovery, c is a canid-specific scaling constant, and M is host mass in kilograms) to account for differences in size between wolves, coyotes, and domestic dogs.

Although we did not have empirical estimates of spatial connectivity, ε, between packs, we assumed that it was much less than that of within-pack connectivity. Spatial connectivity is likely a function of a species' degree of territoriality, its local density, geographic features of the surrounding landscape, and its rate and distance of dispersal. We made the simplifying assumption that spatial connectivity was uniform across a population, and ran simulations over a wide range of constant connectivity values. This assumption probably makes our estimates of the necessary spatial scale and critical community size smaller than one may expect for patchily distributed hosts. It is worth noting here that connectivity, ε, enters the transmission function as, $e^{-\varepsilon d_{ij}}$ such that increasing values of ε indicate lower connectivity or increasing isolation. Connectivity can be thought of as the fraction of influence allotted to neighboring packs, j, scaled by their distance to pack i, over the risk of infection within pack i.

Two-host model

Rather than attempting to simulate another specific host species for which we had little demographic or disease-related information, we created a two-host model with two overlapping, coyote-like hosts, with identical demographic and disease characteristics. The two-host model was very similar to the single-host model. Each of the two hosts had 10 individuals per g packs on the lattice landscape. We assumed a 0.55 survival rate for both hosts and ran simulations over a smaller range of connectivity ($\varepsilon = 2$, 3, 4, 4.5). The probability of infection, λ_{ki}, for host species k, and pack (or landscape patch) i, was modified such that it included both intra- and interspecies (between species k and l) transmission scaled by distance (d) between landscape patches:

$$\lambda_{ki} = 1 - \exp\left[-\left(\left[\beta I_{ki} + \beta \sum_{kj \in S_i} (I_{kj} e^{-\varepsilon d_{kij}})\right] + \left[\beta' I_{li} + \beta' \sum_{lj \in S_i} (I_{lj} e^{-\varepsilon d_{lij}})\right]\right)\right].$$

We varied β', or the transmission coefficient for interspecies transmission, to consider the effects of interspecies transmission (i.e., $\beta' = 0.001$, 0.01, 0.1) on the probability of disease persistence. Additionally, we ran simulations assuming that intra- and interspecies transmission were identical ($\beta = \beta' = 0.16$), which is equivalent to doubling the density of a single-host species per landscape patch.

Simulations and data collection

To address questions of critical community size among wolves and coyotes, we ran simulations over a range of survival and spatial connectivity values for increasing population sizes. Group size remained fixed throughout our simulations, so an increase in the number of groups was directly proportional to an increase in population size. Critical community size was defined as the minimum population size (or number of packs), for a given set of parameter values necessary to ensure that persistence was more probable than not (persistence > 0.5) after 10 years. We defined an inter-epidemic period as the period of infection-free time between two consecutive outbreaks experienced by a single pack. The length and variation in inter-epidemic periods, both within and between packs, provides information about the frequency and regularity with which packs experience infection at a given location. Short inter-epidemic periods with little variation suggest a strong and frequent wavelike pattern of disease spread; longer and more variable inter-epidemic periods suggest a less regular, more patchy spread of disease. Assuming a population of 10 000 coyote packs, we randomly selected 400 packs to monitor inter-epidemic periods over a 50-year period during which CDV persisted. We ran five simulations for each combination of host survival and spatial connectivity.

To address the question of how wolf demographics, spatial connectivity within the population, and time since the last epidemic affect the magnitude of a subsequent outbreak, we ran a series of simulations (20 simulations per combination of survival and

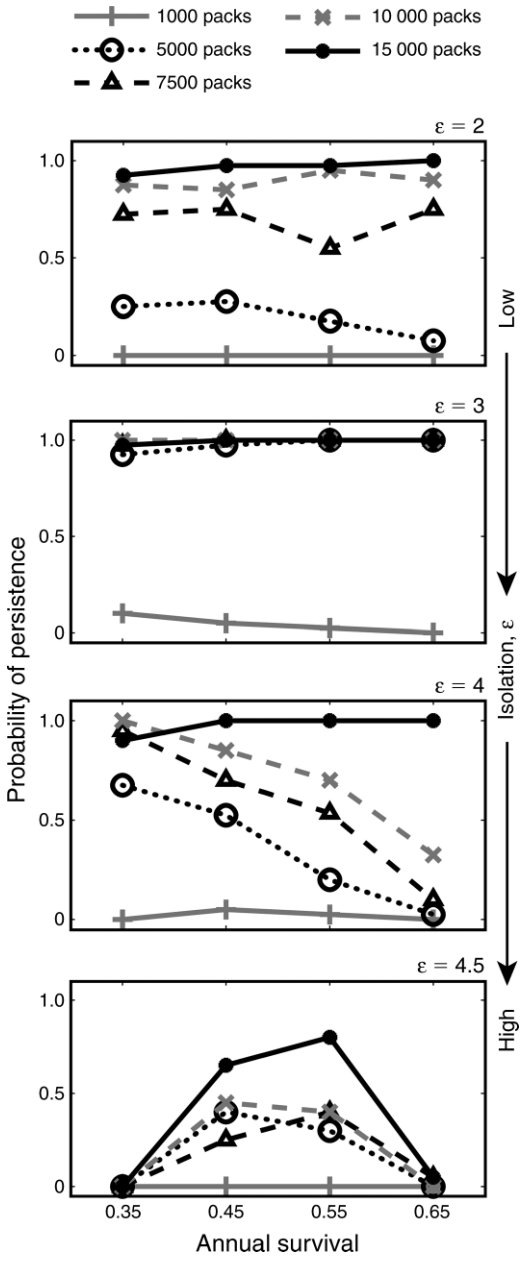

FIG. 2. Probability of CDV persistence over 10 years as a function of spatial isolation, ε, and annual survival over a range of coyote population sizes. (Simulations assume a single host species; $n = 10$, per capita daily intraspecies transmission rate $\beta = 0.16$, daily infectious survival rate $s_{dd} = 0.9797$, duration of exposure [mean latent period, LP(μ)] = 6 days, and duration of infectiousness [mean infectious period, IP(μ)] = 9 days.)

connectivity) where we let an epidemic run its course through a population of 64 packs of wolves in the first year. Then, we ran simulations where we forced the reintroduction of CDV infections in years 1, 2, and 3 after the initial epidemic. The number of packs infected in these subsequent outbreaks served as a measure of epidemic size/extent.

RESULTS

Effects of metapopulation structure and host demographics on CDV persistence

Consistent with other studies, increasing numbers of host groups and total population size increase the probability of pathogen persistence (Fig. 2; Appendix A: Fig. A3), assuming that inter-pack connectivity (and hence inter-pack transmission) is within an intermediate range.

Disease persistence is highly sensitive to the degree of spatial connectivity within the host population. For very high levels of connectivity (i.e., low isolation, $\varepsilon = 1$–2), canine distemper virus (CDV) moves through the entire population in a rapid synchronous wave (Fig. 3A), exhibiting dynamics similar to a non-spatial SIR model, and often burning out before the next birth-pulse of susceptibles. Under such scenarios (i.e., $\varepsilon = 2$), the median inter-epidemic period (disease-free time between two consecutive outbreaks within a pack) is ~1 yr with low variance, meaning that a single pack within a population of 10 000 packs would experience, on average, an outbreak every other year (Fig. 4). CDV persistence is maximized assuming an intermediate range of spatial connectivity ($\varepsilon = 3$–4) (Fig. 2; Appendix A: Fig. A3); the median inter-epidemic period and its variance increase considerably (Fig. 4) as CDV progresses more slowly and less uniformly across space (Fig. 3B). For low connectivity ($\varepsilon = 4$–5) and intermediate host turnover ($s = 0.45$, 0.55), the median inter-epidemic period is 3–5 years, with ranges as great as 0–28 years, translating to a very slow and patchy progression of CDV across space (Fig. 3C). However, very low spatial connectivity also increases the probability that an infected host recovers prior to transmitting the pathogen to a neighboring social group, thus increasing the probability of pathogen extinction.

Demographic turnover is a function of both host reproduction and survival. Our model assumed that reproduction fully compensated for the previous year's mortality, a simplification that allowed for the host population size to be impacted by natural and disease-induced mortality within a year but that maintained the host population size at a constant level from one year to the next. This assumption is roughly consistent with the demographics of wolves in Yellowstone National Park (YNP), where they have been increasing or stable in population size since 1995 with occasional but short-term reductions during CDV outbreaks (Smith et al. 2008, Almberg et al. 2009). It is worth noting that host survival operates on a daily timescale and, for a host with pulsed reproduction, directly affects the number of susceptible, exposed, and recovered hosts alive in the population throughout a year. By contrast, reproduction operates on an annual timescale, affecting the number of incoming susceptibles at the beginning of the year. We found that if host survival is very low ($s = 0.35$) and the pathogen does not die out due to a severely diminished host population, high levels of demographic

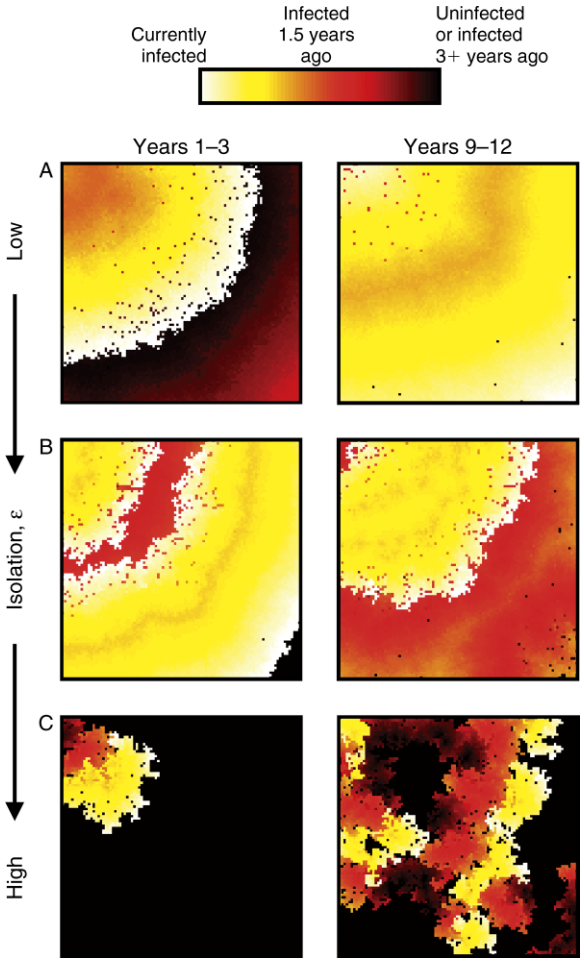

FIG. 3. Progression of CDV through time over landscapes of 10 000 coyote packs, assuming different levels of spatial connectivity. Each row reflects simulated disease dynamics assuming a different level of connectivity (ranging from low to high isolation: A, $\varepsilon = 2$; B, $\varepsilon = 3$; and C, $\varepsilon = 4.5$). The two columns represent time series of infection history from years 1–3 and 9–12, respectively, following disease introduction. The time series is represented by the color scale ranging from uninfected during the three years (black), infected 1.5 years ago (orange), to currently infected (white). (Simulations assume a coyote host: $n = 10$, $\beta = 0.16$, $s_{dd} = 0.9797$, LP(μ) = 6 days, and IP(μ) = 9 days.)

turnover yield slightly larger epidemics in terms of numbers of infections and infected packs (Fig. 5). By contrast, relatively high survival rates ($s = 0.65$–0.75) result in less turnover, a higher proportion of surviving immune individuals, and slightly smaller epidemics.

The effect of host demographic turnover on the probability of CDV persistence is related to these epidemic dynamics, but interacts with the degree of spatial connectivity within the population. When spatial connectivity is relatively high ($\varepsilon = 2$–3), demographic turnover has very little effect on the probability of long-term persistence (Fig. 2). Instead, CDV persistence is driven almost entirely by the host population size. As connectivity begins to drop ($\varepsilon = 4$), decreasing demographic turnover (i.e., high survival and smaller reproductive pulses) has a negative effect on persistence for all but the largest host populations (i.e., $\geq$15 000 packs). When connectivity is weak ($\varepsilon = 4.5$) disease persistence depends more on the balance of within-group dynamics (the number of incoming susceptibles, existing immunes, and their survival over the year), and only intermediate demographic turnover ($s = 0.45$–0.55) favors disease persistence. Low connectivity means that pathogens must spend more time within a patch before inter-patch transmission, making it more difficult for the pathogen to invade and persist amidst its spatially structured host.

Applications to CDV within the Greater Yellowstone Ecosystem

CDV persistence in wolves.—Assuming the most recent, and thus largest estimates of the gray wolf population in the Greater Yellowstone Ecosystem (GYE) (453 wolves; U.S. Fish and Wildlife Service et al. 2008), and simulating over a range of survival and spatial connectivity estimates, CDV cannot persist in local wolf populations given their annual pulses of reproduction and the lack of any known carrier state (Fig. 6). Even when we expand the potential number of hosts to include the entire population of wolves in the Northern Rocky Mountains (~1500 wolves in 192 packs; U.S. Fish and Wildlife Service et al. 2008), long-term persistence is still very unlikely with wolves as the sole maintenance population. These conclusions are not dependent on a specific value of β; rather, lower

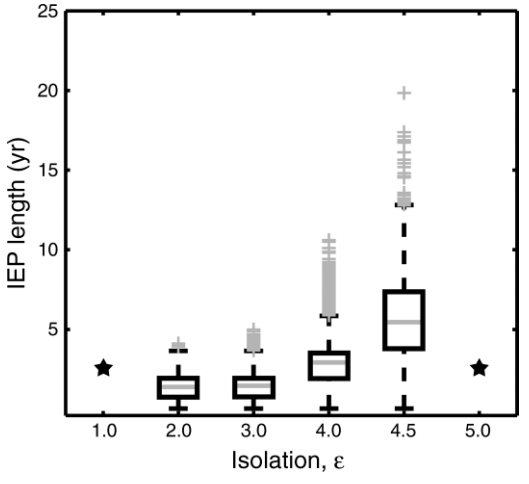

FIG. 4. Box plot of the inter-epidemic period (IEP) in years as a function of inter-pack isolation among coyotes (10 000 packs, $\beta = 0.16$, $n = 10$ coyotes per pack; IEPs were collected from 400 randomly sampled packs over five simulations run for 50 years). Each box encapsulates the interquartile range, the gray horizontal line is the sample median, the whiskers represent 1.5× interquartile range, plus signs are outliers, and stars denote levels of isolation for which there was no persistence. Note that the x-axis is not a linear scale.

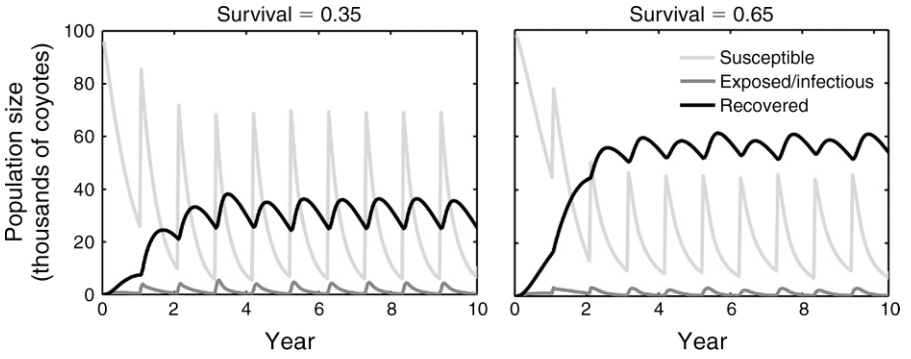

FIG. 5. Epidemic dynamics as a function of host (coyote) survival rate. Host survival, or the degree of demographic turnover, affects the proportion of susceptible, recovered, and infected individuals within the population during a year. Lines represent mean values from 40 simulations in a population of 10 000 coyote packs ($n = 10$ coyotes per pack, $\beta = 0.16$, $\varepsilon = 3$, annual survival = 0.55, $s_{dd} = 0.9797$, LP(μ) = 6 days, and IP(μ) = 9 days).

transmission rates demand higher levels of connectivity for maximum persistence, but burnout of CDV is still inevitable.

As wolves alone do not permit the persistence of CDV, the following results describe epidemic dynamics among wolves assuming spillover from a reservoir host species. Spatial connectivity largely controls the size and extent of outbreaks, regardless of whether it takes place in an entirely susceptible or partially immune population (Fig. 7). CDV infects a greater proportion of packs when the wolf population is assumed to be highly connected. If the population is either highly ($\varepsilon = 3$) or poorly ($\varepsilon = 6$) connected, there is no effect of time since the last outbreak on the number of packs infected in subsequent epidemics (Fig. 7). For cases of intermediate connectivity among wolves (i.e., $\varepsilon = 4$–5), the size of an outbreak triggered in the first or second year after an initial epidemic is always significantly smaller, sometimes as much as 49% smaller (for year 1, $s = 0.75$, $\varepsilon = 4$). However, the effect of time since the last outbreak quickly diminishes after the first 1–2 years (Fig. 7). For example, assuming intermediate connectivity ($\varepsilon = 4$), a mean of only 50% or 80% of the packs in the population experience infection in the year immediately following an initial epidemic (when $s = 0.75$ or 0.45, respectively), whereas these proportions rise to 81% or 91% when the subsequent infection is delayed until year 2 (when $s = 0.75$ or 0.45, respectively; $n = 20$ simulations). As expected, increasing survival has a negative impact on the size of subsequent epidemics. Reduced population turnover (i.e., high survival and low reproduction) yields smaller subsequent epidemics both in numbers of hosts

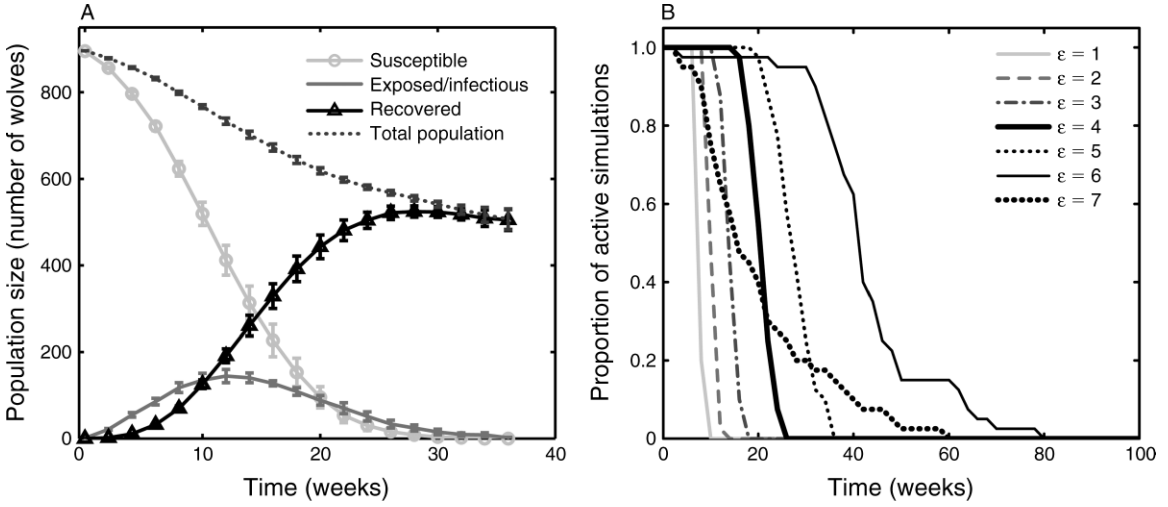

FIG. 6. (A) Simulated epidemic dynamics of CDV among Greater Yellowstone Ecosystem (GYE) wolves. CDV cannot persist among GYE wolves alone ($\varepsilon = 5$, $\beta = 0.3$, $s = 0.65$, $s_{dd} = 0.9797$, $g = 64$ packs, and $n = 14$ individuals/pack). Lines represent the mean values from 40 simulations (among active simulations only), and error bars encompass the 95% CI. (B) Proportion of 40 simulations with active CDV infections among wolves over time assuming different values of spatial isolation, ε.

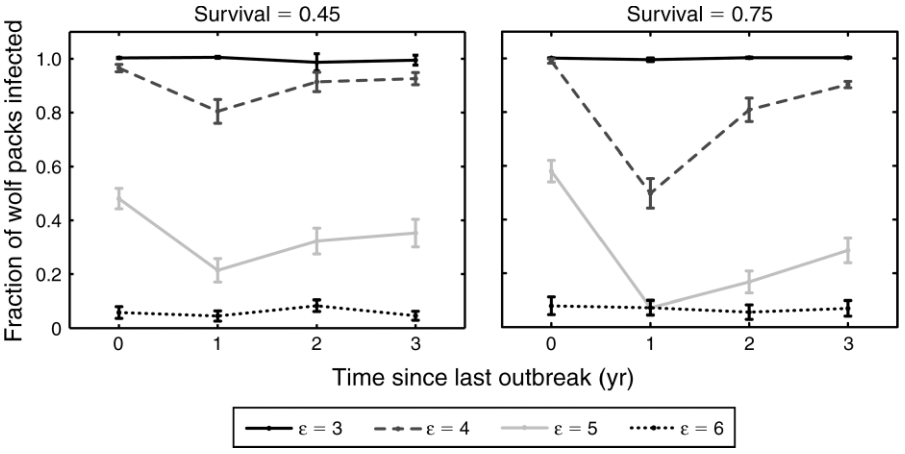

FIG. 7. Epidemic size, defined as the fraction of 64 total packs infected in the wolf population (mean with 95% CI), as a function of time since the last epidemic, host survival, and spatial isolation, ε ($n = 20$ simulations). The initial CDV epidemic was started in a wholly susceptible population and is displayed under time "0." Increasing values of ε denote increasing isolation (decreasing connectivity). Wolf demographic parameters were used for these simulations: $n = 14$ wolves per pack, $\beta = 0.3$, $s_{dd} = 0.9797$, LP(μ) = 10 days, and IP(μ) = 13 days.

infected and the proportion of packs in the population experiencing infection (Fig. 7).

Critical community size among coyotes

Given a range of intermediate, plausible estimates for survival ($s = 0.45$–0.55) and inter-pack connectivity ($\varepsilon = 3$–4.5, i.e., a completely susceptible pack would have between 0.018–0.077 per capita daily risk of infection if an adjoining pack were completely infected), we estimate that there would need to be a minimum of 5000–10 000 packs of coyotes, or between 50 000 and 100 000 individuals, to support a 50% probability of pathogen persistence over 10 years (Fig. 2). If we assume relatively low spatial connectivity ($\varepsilon = 4.5$), which yields a range of inter-epidemic periods consistent with those observed from the coyote serological data (i.e., 5- and 9-year gaps between consecutive CDV outbreaks; Figs. 1 and 4), the critical community size for CDV among coyotes would have to be a minimum of 15 000 packs to achieve a reasonable probability of long-term pathogen persistence (Fig. 2). Smaller values of the transmission rate, β, yield similar minimum critical community size estimates, although they require higher levels of connectivity ($\varepsilon = 2$) to ensure persistence at all.

CDV persistence amidst multiple hosts?

In the simplest case where we assume two overlapping, homogeneously distributed host species with identical host disease and demographic characteristics, a second host generally increases the probability of disease persistence at smaller geographic scales (Fig. 8). However, the precise effect of a second host on disease persistence depends on the degree of, and interaction between, intraspecies transmission and interspecies

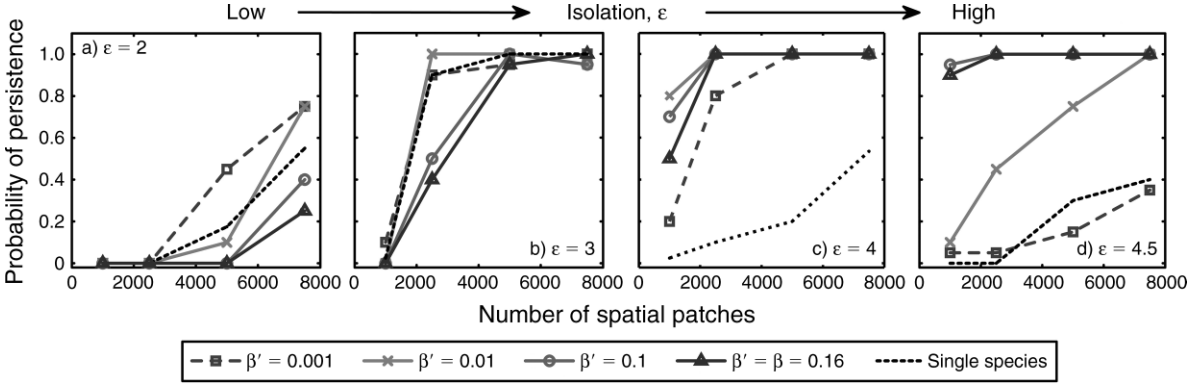

FIG. 8. Probability of CDV persistence over 10 years as a function of interspecies transmission rates (β′), intraspecies connectivity (isolation, $\varepsilon = 2$, 3, 4, and 4.5 in panels (a), (b), (c), and (d), respectively), and the number of packs, or spatial patches in the population. The probability of pathogen persistence for the single-host scenario is plotted for comparison. For simplicity, the two hosts are assumed to be identical in their host disease and demographic characteristics: $n = 10$ animals per pack, $\beta = 0.16$, $s = 0.55$, $s_{dd} = 0.9797$, LP(μ) = 6 days, and IP(μ) = 9 days.

connectivity (Fig. 8). It is important to note that the spatial coupling parameter, ε, affected both intra- and interspecies spatial connectivity in our model (they were assumed to be equal for the sake of simplicity). In other words, spatial connectivity set the radius over which hosts could contact their own neighbors and those of the additional host species. As intra-host transmission rates were fixed ($\beta = 0.16$), manipulating spatial connectivity was the primary means of affecting the degree of intraspecies transmission. By contrast, interspecies transmission was most explicitly affected by manipulating the interspecies transmission rate.

To clarify the relationships between CDV persistence, host density, population size, spatial scales of disease circulation, intraspecies connectivity, and the effects of multi-host transmission, we will break up the remaining results as follows. To begin, we will first report the simple effects of increasing the local density of hosts by comparing the persistence of CDV assuming $\beta = \beta'$ (where β' is interspecies transmission; i.e., equivalent to doubling the density of a single host species) to that when we assume the same population size in a single-host species, distributed over twice the spatial arena. Next, we will present the synergistic effects of multi-host transmission when we assume that $\beta' < \beta$.

Some of the two-host system's effects on CDV persistence stem from doubling the density of hosts per landscape patch. The level of connectivity within species determines whether doubling host density (i.e., $\beta = \beta'$) increases or decreases persistence over that when we assume a single-host species with the same total population size, distributed over twice the geographic space. When intraspecies connectivity is relatively high ($\varepsilon = 2$–3), doubling the density of hosts substantially reduces the probability of persistence when compared with the same population size distributed over twice the spatial scale (Fig. 8a, b; e.g., when $\varepsilon = 2$, we find 0% persistence for $\beta = \beta'$ at 5000 spatial patches [$n = 100\,000$ hosts] vs. 55% persistence for the single-host case at 7500 spatial patches [$n = 75\,000$ hosts]). When intraspecies connectivity is relatively low ($\varepsilon = 4$–4.5), doubling the host density greatly improves persistence over the scenario with half the host density but equivalent population size (Fig. 8c, d; e.g., when $\varepsilon = 4.5$, we find 100% persistence for $\beta = \beta'$ at 2500 spatial patches [$n = 50\,000$ hosts] vs. 30% persistence for the single host case at 5000 spatial patches [$n = 50\,000$ hosts]).

When $\beta' < \beta$, the addition of a second host species generally has a different effect than doubling the group size of a single host species ($\beta = \beta'$). When intraspecies connectivity is high ($\varepsilon = 2$), low levels of interspecies transmission ($\beta' = 0.001$–0.1) results in better CDV persistence than doubling the group size of the single host ($\beta = \beta'$). In this case, however, a second host species never improves persistence as much as doubling the geographic space, given the same population size of hosts (i.e., we find 0% persistence for $\beta' = 0.001$ amidst 2500 spatial patches [$n = 50\,000$ hosts] vs. 18% persistence for the single host scenario amidst 5000 spatial patches [$n = 50\,000$ hosts]). As intraspecies connectivity decreases ($\varepsilon = 4$–4.5), CDV persistence is greatly improved both at small spatial scales and for relatively small population sizes, even when compared to the equivalent population size distributed at a larger spatial scale (i.e., the single-host scenario; Fig. 8c, d). Furthermore, there is a small region of the parameter space where there is a synergistic effect of the second host species, and the second host improves CDV persistence beyond the effect of doubling the host density or doubling the spatial scale (e.g., Fig. 8c where $\varepsilon = 4$, persistence is 70–80% for $\beta' = 0.01$–0.1 vs. only 50% for $\beta = \beta'$ at 1000 spatial patches [$n = 20\,000$ hosts], and only 10% for the single-host case amidst 2500 patches [$n = 25\,000$ hosts]).

Discussion

Acute, highly immunizing pathogens utilize multiple evolutionary strategies to persist in low-density host populations including (1) inducing a carrier state or extended period of infectiousness in a small portion of individuals, (2) having a resistant environmental state (e.g., anthrax), (3) having the ability to rapidly change antigenic surfaces (e.g., influenza viruses), and (4) moving among different host populations and/or species. Options 2 and 3 have not been documented for any of the morbilliviruses. We explored the effects of having a separate class of individuals experiencing an extended period of infectiousness, which we discuss in *Discussion: CDV within the Greater Yellowstone Ecosystem*, but as this alone does not assure persistence amidst a low-density host species except amidst very large populations, we focus on host metapopulation structure and multi-host transmission as the key factors permitting CDV's long-term persistence.

This modeling study addressed the spatial scale that CDV would require for persistence within the GYE focusing on coyotes and wolves as potential maintenance/reservoir and spillover hosts, respectively. Our model results suggest that CDV is unlikely to persist in Northern Rocky Mountain wolves alone and that spillover from a reservoir is probably unpredictable but capable of triggering medium-to-large-sized epidemics. If CDV is persisting among coyotes, many individuals are needed, and the scale of disease circulation is probably very large and patchy (Fig. 3C; Appendix C: Video 1). More generally, while simulated metapopulation structure and host demographics can theoretically permit the persistence of acute, highly immunizing pathogens amidst low-density host populations, the large population sizes required make it unlikely that pathogens such as CDV are maintained amidst a single host species. Multi-host transmission is likely an essential evolutionary strategy for the long-term persistence of CDV among its low-density carnivore hosts.

Metapopulation structure, including the number of host patches, the size of patches, and the degree of connectivity between them, is critical to disease spread and persistence. These concepts have been explored before, although most extensively on systems with much larger groups, such as with haul-outs of several hundred to several thousand harbor seals or cities with hundreds of thousands of human hosts (Bartlett 1957, Swinton et al. 1998, Park et al. 2002). However, when a metapopulation patch, from the perspective of the pathogen, is a relatively small group of territorial hosts, and the pathogen is fast acting and highly immunizing, the conditions under which the pathogen can persist are considerably narrowed. In particular, persistence is highly sensitive to the interacting time scales of infection, transmission within and between patches, and host reproduction.

As others have also noted (Keeling 2000, Park et al. 2001, 2002, Keeling and Rohani 2002), pathogen persistence amidst a metapopulation of hosts is maximized for intermediate levels of spatial connectivity. When connectivity is too low, the pathogen often fails to spread to neighboring packs prior to host recovery; when it is too high, the pathogen rapidly burns through the host population in a synchronous wave, exhausting most or all susceptibles at a much faster rate than they are being replenished through reproduction. An intermediate range of spatial connectivity favors persistence as it balances pathogen transit time among patches, the timescale of the infection within the host, and the total number of host patches in the population against the recruitment of susceptibles. This balance becomes even more delicate when reproduction takes place in a single, annual birth pulse, as is the case with many temperate wildlife species. Intermediate-to-low connectivity creates patchy, spatially asynchronous disease dynamics that facilitate rescue effects following local burnouts (Keeling 2000, Ferrari et al. 2008).

Although the effects of host demographics and spatial coupling on persistence have each been addressed separately, to our knowledge, no one has pointed out the interaction between the two. When connectivity within a population is high, demographic turnover has no effect on persistence; the pathogen spreads so quickly that it simply needs huge population sizes to prevent extinction prior to the next birth pulse. As connectivity begins to decrease, so does the probability of inter-pack transmission, making stochastic extinction more likely in all cases except when host turnover is high. High demographic turnover increases the density of susceptibles at the start of the year facilitating interannual persistence. However, when connectivity is very low, high demographic turnover, too, can actually be detrimental to persistence. Ultimately, both small reproductive pulses (associated with high survival) and low annual survival (even when associated with large reproductive pulses) result in reduced numbers of susceptibles over the course of a year, either through a small annual input of new susceptibles or through the elevated mortality of susceptibles (and exposed individuals, too), respectively. When connectivity is low, these conditions make inter-pack transmission difficult and stochastic burnout more likely. Persistence under low population connectivity is only favored when turnover is intermediate, providing just enough susceptibles to counteract their rate of mortality throughout the year.

Although our representation of demographic turnover was simplistic, it is roughly consistent with what we have observed among YNP wolves (stable or growing populations or, following CDV outbreaks, short-term population declines followed by full recovery in 1–2 years; Smith et al. 2008, Almberg et al. 2009) and what we know about the compensatory nature of coyote reproduction (for a review, see Knowlton et al. [1999]). However, we can imagine a number of alternative scenarios for canids or other carnivore species where reproduction does not compensate for annual mortality: a growing population may have high survival and high reproduction; a declining population may have low survival and low reproductive output; or, although a population may be at equilibrium, disease mortality may be additive and cause short-term population declines. A pathogen's response to any of these alternative scenarios should be governed by the relationship between the numbers of incoming susceptibles, existing immunes, and the host's annual survival. As illustrated in our simulations, the pathogen needs sufficient numbers of incoming susceptibles (resource replenishment) to counteract the diminishing effect of annual mortality within the year. If disease-induced mortality is additive, then we might expect the pathogen to have an even more difficult time persisting overall because of the reduced host population following an outbreak.

CDV within the Greater Yellowstone Ecosystem

If our assumptions about CDV in canids are correct, namely, that there are no long-term carrier states for the virus and that CDV induces life-long immunity, CDV cannot currently be maintained in the GYE wolf population alone. Serological evidence indicates that CDV cycled through the coyote and cougar populations in YNP prior to wolf reintroduction in 1995 (Fig. 1; Gese et al. 1997, Biek et al. 2006), suggesting that wolves were at least not a necessary part of the maintenance host community at that time.

If wolves are not capable of maintaining CDV, then the CDV outbreaks observed among YNP wolves were most likely triggered by spillover from alternate host species. In our simulations, spatial connectivity played the biggest role in determining whether a single, successful spillover infection resulted in a large vs. small outbreak among wolves. Beyond this, the relative size of any subsequent outbreak was affected by the interaction between turnover and time since the initial outbreak. High turnover increased the rate at which the population was capable of experiencing another relatively large,

subsequent outbreak (Fig. 6). Similarly, as the time since the initial outbreak increased, so did the size and extent of subsequent epidemics.

Inter-epidemic seroconversion among wolves in YNP (Fig. 1) is suggestive of either multiple, failed epidemics initiated through spillover infections or a spatial and temporal progression of CDV across YNP (Almberg et al. 2009). Our simulations suggested that these are plausible results given relatively low spatial connectivity and relatively high survival among wolves. In reality, spatial connectivity is probably variable over years and locations, influenced by fluctuating wolf densities or landscape heterogeneities. If this is the case, low connectivity for a given year or location may result in very small, localized outbreaks that fail to turn into pandemics within the larger wolf population.

Although our model implicitly assumed a successful spillover event, the likelihood of a spillover event is in and of itself a critical determinant of whether a CDV outbreak is likely to occur among wolves. The likelihood of a spillover event to wolves is a function both of the probability that CDV is locally present in some other host and the probability of a successful contact between an infected alternate host and a susceptible wolf. Spatial connectivity within alternate host populations can drive the return of CDV to a given locale, as seen through our simulations of inter-epidemic periods among coyotes (Fig. 4). In fact, when spatial connectivity is relatively low, which is what would generally be expected for terrestrial, territorial carnivores, we found considerable variability among inter-epidemic periods, making it very difficult to predict the timing of a subsequent local outbreak. Furthermore, demographic turnover in wolves would be expected to govern the probability that an infectious contact from an alternate host happens with a susceptible wolf. While these probabilities remain unknown, it is likely that they increase with the number of years since the last outbreak (as the number of susceptibles increases).

Coyotes, by virtue of their relative abundance and wide distribution, are much more likely to be part of the local maintenance community for CDV than wolves. If we assume a dominant, single-species coyote reservoir, CDV is likely persisting amidst a *minimum* of 5000–10 000 packs, or between 50 000–100 000 individuals. Assuming a mean coyote territory size of 13 km^2 (Berger and Gese 2007) and that packs are densely and uniformly distributed on the landscape, this population estimate roughly translates to a minimum geographic area of 60 000–195 000 km^2, approximately one to three times the size of the GYE. With added spatial and demographic heterogeneity, the critical community size and spatial scale necessary for persistence may be considerably larger.

While CDV can cause a rare condition in domestic dogs called "old dog encephalitis," a long-term CDV infection of the central nervous system, it is not believed that these individuals are ever infectious beyond the typical infectious period (Imagawa et al. 1980, Vandevelde and Zurbriggen 1995, Zurbriggen et al. 1995). However, although no long-term carrier state has been documented for CDV, it has been noted that a small proportion of domestic dogs may shed from 30–90 days (Greene and Appel 2006) as opposed to the typical 7–14 days on which our model was based. If we assume that between 5% and 15% of all infected coyotes experience this longer duration of infectiousness, persistence improves and our estimated critical community size is reduced to between 2500 and 7500 coyote packs for most combinations of demographic turnover and connectivity (Appendix B). However, even when 15% of infectious individuals are extended shedders, CDV still has difficulty persisting over 10 years among populations of $\leq$7500 packs when they are characterized by low connectivity ($\varepsilon = 4.5$) and relatively low turnover (e.g., persistence $\leq$ 0.80 and 0.45 for $s = 0.55$ and 0.65, respectively).

The large populations required for CDV persistence tends to refute the hypothesis that domestic dogs might constitute a viable CDV reservoir in and around the GYE. Unlike in much of sub-Saharan Africa where CDV, rabies, and other canid pathogens are thought to be maintained by extremely large populations of unvaccinated domestic dogs (Laurenson et al. 1998, Rhodes et al. 1998, Cleaveland et al. 2007), the unvaccinated population of dogs in the United States is comparatively small. There are no published estimates of dog densities or vaccination compliance for the GYE; however, even if we assume less-than-average vaccination coverage among working ranch dogs, it is still unlikely that there are enough animals to maintain CDV.

It is most likely that CDV is maintained among multiple hosts and that multi-host transmission is important to long-term CDV persistence. The results of our simple simulations support the work of others to suggest that the inclusion of a second competent host species, with density-dependent transmission, generally increases the probability of pathogen persistence (Dobson 2004, McCormack 2006, McCormack and Allen 2007). The addition of a second competent host should generally reduce the critical community size within any one host species, as well as reduce the minimum spatial scale necessary for long-term disease persistence. From the perspective of the pathogen, multiple host species not only create the potential for higher densities of hosts, which would not otherwise exist among low-density host species, but they also add meta-population structuring, either providing another dimension of space (i.e., where multiple species represent vertical layers of space; Craft et al. 2008) or facilitating "rescue effects" when CDV burns out in any one species (Dobson 2004). As terrestrial carnivores typically exist at low densities, live in small social groups (if social), and are territorial, it seems that multi-host transmission is critical to ensuring long-term CDV persistence.

We found that for relatively high levels of within-species connectivity, weak coupling between the two species improved persistence over that of the single- and double-host density scenarios at a given spatial scale. Weak interspecies transmission helps to create a spatial–temporal lag in the infection dynamics between the two species, creating an effect analogous to that of increasing geographic space (Fig. 9A, B; Appendix C: Video 2a, b). We found that in the context of relatively low spatial connectivity ($\varepsilon = 4$), there are also some cases where multi-host transmission ($\beta' < \beta$) substantially improves persistence over both the single-host and double-density scenarios, even at very small spatial scales (1000 patches) and population sizes (20 000 hosts; Fig. 8c). This is also likely the result of decoupled disease dynamics between the two host species, facilitating rescue effects following localized burnouts (Fig. 9C; Appendix C: Video 3). In general, though, decreasing intraspecies connectivity is compensated for by increasing levels of interspecies transmission, facilitating persistence primarily by increasing the density of accessible hosts per landscape patch.

Despite our simulations across a broad range of connectivity and interspecies transmission rates, in our current model formulation, infection dynamics remained highly synchronized between host species (e.g., Fig. 9; Appendix C: Video 3 represents one of the most "asynchronous" examples). While this is consistent with the synchronous multi-host patterns observed in our empirical data from the Northern Range of Yellowstone (Fig. 1), these may not be the dynamics we would intuitively expect at large scales in the real world. A mechanistic model of transmission (Keeling and Rohani 2002) might allow for greater asynchrony in infection dynamics between species, yielding even better persistence at even smaller spatial scales. More importantly, we would expect differences between species' distributions, densities, home ranges (both in size and spatial relation to one another), and connectivity, as well as their demographics and disease characteristics, to drive spatial asynchrony in infection dynamics between species. Our model structure, which assumed homogeneously distributed, identically sized, and completely superimposed home ranges, constrained our ability to capture these inherent sources of heterogeneity. Furthermore, we lacked the empirical data needed to parameterize a multi-host model for some of the smaller candidate host species in the GYE. However, if these heterogeneities were to translate to greater spatial asynchrony, we might expect increased opportunities for rescue effects following localized burnouts in any one species.

In reality, ranges of low intraspecies connectivity ($\varepsilon = 4$–4.5) and relatively low interspecies transmission rates ($\beta' = 0.001$–0.01) probably best characterize the potential hosts in the GYE. Within this two-host parameter space of our model, we found that a minimum geographic space roughly 0.5–1.5 times the size of the GYE (32 500–97 500 km^2) encompassing

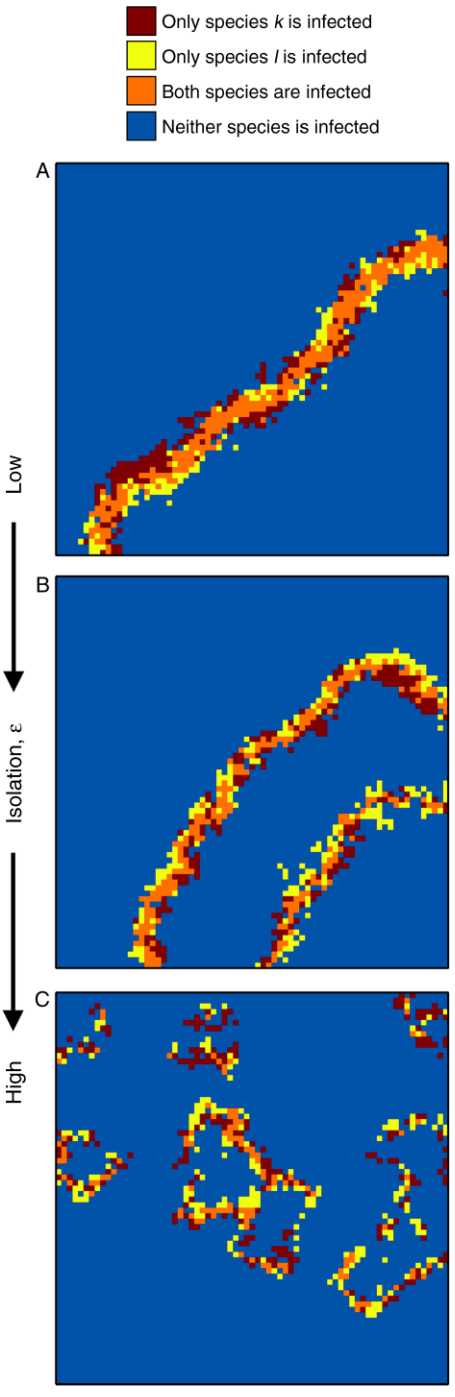

FIG. 9. Snapshots in time of multi-host CDV dynamics amidst 5000 landscape patches assuming low interspecies transmission ($\beta' = 0.001$) and different levels of intraspecies connectivity (in order of increasing isolation: A, $\varepsilon = 2$; B, $\varepsilon = 3$; and C, $\varepsilon = 4$). For simplicity, the two hosts are assumed to be identical in their host disease and demographic characteristics: $n = 10$ animals per pack, $\beta = 0.16$, $s = 0.55$, $s_{dd} = 0.9797$, LP(μ) = 6 days, and IP(μ) = 9 days.

2500–7500 coyote territories with ~50 000–150 000 hosts would be needed for CDV persistence (Fig. 8c, d, and assuming 13-km^2 coyote territories). Thus, while our estimated critical community size for just one of the two host species (only 25 000–75 000 individual coyotes) and the associated geographic scale are much smaller when multi-host transmission is assumed, our simplified two-host model suggests that we would need a similar number of total hosts as estimated under our single-host model. However, this particular result is likely an artifact of our assumption that our two hosts were identical. The competency of the second host (as determined by its densities, disease characteristics, connectivity, and demographic turnover), relative to the first, would likely determine whether additional or fewer individuals would be needed as compared to the scenario of a single-host reservoir. Heterogeneity among species would certainly affect our estimates of critical community size and the spatial scale of disease persistence; as these remain unknown and unexplored in our present study, it is difficult to ascribe much confidence to any numeric estimate of critical community size or geographic scale in our simplistic, two-host system.

The exact combination of host species comprising the CDV maintenance community responsible for the outbreaks among YNP wolves, coyotes, and cougars is unknown; however, coyotes, raccoons (thought to be the dominant reservoir host for CDV in the eastern United States), and perhaps some of the mustelid species are the most likely candidates. The combination of, and variation in, host species' distributions, demographic rates, intra- and interspecies contact rates, and spatial movements should theoretically affect details such as the frequency of disease outbreaks, the likelihood of multi-host spillover, and the patchiness of infection and outbreaks across the landscape. Our simulations suggest that CDV may be able to persist locally among multiple hosts at relatively small spatial scales. If this were the case, with continuous disease monitoring across a wide range of hosts and locales within the GYE, we might detect frequent, multi-host CDV outbreaks scattered across the landscape. Furthermore, if in the future we were able to isolate CDV from multiple host species throughout the GYE over time, we would be in a better position to explicitly ask how frequently CDV is being transmitted within and between different species over geographic space.

Management implications

It is likely that CDV is persisting among multiple, wild host species and/or over a large geographic scale, making any system-wide attempt at eradication or control impractical and impossible. Moreover, what little information is available suggests that at least for wolves, there is little need for explicit intervention. Following the large CDV outbreaks in YNP in 1999, 2005, and 2008, during which local pup survival rates fell as low as 13% and the overall population declined ~30% in the short-term, wolf populations rebounded and continued to grow (Smith et al. 2008, Almberg et al. 2009, Smith et al. 2010; Wolf Project, *unpublished data*). Currently, no information is available on whether CDV is significantly impacting any of the other GYE carnivore populations.

While these short-term population declines do not appear to threaten the long-term persistence of wolf populations within the GYE, they may have important implications for current wolf management. It is prudent that Idaho and Montana have committed to manage their share of the Northern Rocky Mountain wolf population well above (Montana, 328–657 wolves [Montana Fish Wildlife and Parks 2003:132]; Idaho, 518–732 wolves [Idaho Department of Fish and Game 2008:1]) the minimum threshold population size that could trigger endangered species review (15 breeding packs with 150 wolves; U.S. Fish and Wildlife Service [2009]), so as to accommodate periodic and unpredictable population declines due to CDV or other stochastic mortality factors. Awareness and monitoring of such outbreaks will allow corresponding adjustments in management activities such as regulated public harvest, creating a smooth transition to state wolf management and conservation after over 30 years of being protected by the Endangered Species Act.

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APPENDIX A

Supporting figures of model structure and output (*Ecological Archives* A020-075-A1).

APPENDIX B

Extended infectiousness (*Ecological Archives* A020-075-A2).

APPENDIX C

Supporting video files of model dynamics (*Ecological Archives* A020-075-A3).