

RESEARCH ARTICLE

Modelling management strategies for chronic disease in wildlife: Predictions for the control of respiratory disease in bighorn sheep

Emily S. Almborg¹ | Kezia R. Manlove²  | E. Frances Cassirer³ | Jennifer Ramsey¹ | Keri Carson¹ | Justin Gude¹ | Raina K. Plowright⁴ 

¹Montana Fish, Wildlife, and Parks, Bozeman, MT, USA

²Department of Wildland Resources & Ecology Center, Utah State University, Logan, UT, USA

³Idaho Department of Fish and Game, Lewiston, ID, USA

⁴Department of Microbiology and Immunology, Montana State University, Bozeman, MT, USA

Correspondence

Kezia Manlove
Email: kezia.manlove@usu.edu

Funding information

Defense Advanced Research Projects Agency, Grant/Award Number: D18AC00031; Cooperative State Research, Education, and Extension Service, Grant/Award Number: UTA01427; Federal Aid for Wildlife Research program; U.S. National Science Foundation, Grant/Award Number: DEB-1716698; National Institute of Food and Agriculture, Grant/Award Number: 1015891; Nevada Department of Wildlife; U.S. Geological Survey, Grant/Award Number: #G21AC10105-00 and #G18AC00366

Handling Editor: Hamish McCallum

Abstract

1. Controlling persistent infectious disease in wildlife populations is an ongoing challenge for wildlife managers and conservationists worldwide, and chronic diseases in particular remain a pernicious problem.
2. Here, we develop a dynamic pathogen transmission model capturing key features of *Mycoplasma ovipneumoniae* infection, a major cause of population declines in North American bighorn sheep *Ovis canadensis*. We explore the effects of model assumptions and parameter values on disease dynamics, including density- versus frequency-dependent transmission, the inclusion of a carrier class versus a longer infectious period, host survival rates, disease-induced mortality and recovery rates and the epidemic growth rate. Along the way, we estimate the basic reproductive ratio, R_0 , for *M. ovipneumoniae* in bighorn sheep to fall between approximately 1.36 and 1.74.
3. We apply the model to compare efficacies across a suite of management actions following an epidemic, including test-and-remove, depopulation-and-reintroduction, range expansion, herd augmentation and density reduction.
4. Our results suggest that test-and-remove, depopulation-and-reintroduction and range expansion could help persistently infected bighorn sheep herds recovery following an epidemic. By contrast, augmentation could lead to worse outcomes than those expected in the absence of management. Other management actions that improve host survival or reduce disease-induced mortality are also likely to improve population size and persistence of chronically infected herds.
5. *Synthesis and applications.* Dynamic transmission models like the one employed here offer a structured, logical approach for exploring hypotheses, planning field experiments and designing adaptive management. We find that management strategies that removed infected animals or isolated them within a structured metapopulation were most successful at facilitating herd recovery from a low-prevalence, chronic pathogen. Ideally, models like ours should operate iteratively with field experiments to triangulate on better approaches for managing wildlife diseases.

KEYWORDS

basic reproductive ratio, bighorn sheep, chronic carriage, depopulation, disease model, *Mycoplasma ovipneumoniae*, test-and-cull, wildlife disease management

1 | INTRODUCTION

Managing emerging infectious disease in wildlife is an important and difficult task for conservation and management agencies around the world, and the need for strategies to control chronic diseases like white-nose syndrome (Langwig et al., 2012), chronic wasting disease (Uehlinger et al., 2016) or bovine tuberculosis (le Roex et al., 2016) is urgent. However, dynamic models describing pathogen transmission and persistence are rarely harnessed to inform wildlife management (Joseph et al., 2013). This is an important gap, since mechanistic models of pathogen transmission present a structured, logical approach towards exploring hypotheses, and their predictions serve as a basis for planning field experiments and adaptive management.

One context where transmission models of long-term infections could prove particularly useful is in the management of bighorn sheep pneumonia (Cassirer et al., 2013; Cassirer & Sinclair, 2007). Bighorn sheep *Ovis canadensis* have experienced dramatic population declines over the last 150 years (Cassirer et al., 2018), due in part to the bacterial pathogen *Mycoplasma ovipneumoniae*. *M. ovipneumoniae* is a respiratory pathogen primarily affecting domestic and wild Caprinae including sheep, goats and muskox *Ovibos moschatus*. Infections produce respiratory symptoms, and transmission requires close or direct contact because the pathogen degrades rapidly outside the host. *M. ovipneumoniae* occurs at high prevalence (Manlove et al., 2019) and diversity (Kamath et al., 2019) in domestic sheep, where it imposes small but detectable consequences on health and vital rates (Besser et al., 2019; Manlove et al., 2019). In contrast, *M. ovipneumoniae* spillover into bighorn sheep herds can trigger epidemics of acute, microbially diverse pneumonia (Besser et al., 2008) with mild to severe mortality. Most bighorn sheep who survive acute infections become immune to disease from the infecting *M. ovipneumoniae* strain, but not necessarily immune to infection, and there is no evidence that this immunity transfers to newborn lambs (Plowright et al., 2013). The pathogen's long-term persistence in bighorn sheep populations is especially problematic. Some individuals continue to harbour *M. ovipneumoniae* in their upper respiratory tracts (Plowright et al., 2017) and these 'chronic carriers' can spark transmission to susceptible lambs in communal nursery groups, leading to years-to-decades of poor recruitment that prevents population recovery. Wildlife management agencies invest heavily in spillover risk mitigation by limiting interactions between domestic sheep and goats and bighorn sheep; however, the management of chronic disease is also imperative for recovering historic bighorn sheep population numbers and minimizing the risks that infected herds pose to nearby populations.

Previous epidemiological models of bighorn sheep pneumonia accounted for long-term effects of pathogen introduction on herd

viability (Cahn et al., 2011; Clifford et al., 2009). However, these efforts did not engage with the disease transmission process per se (but see Hobbs & Miller, 1992), and their construction preceded discovery of the immunity and chronic carriage patterns described above. In the absence of models that incorporate these new insights, the best approach for limiting long-term effects of pathogen persistence on bighorn sheep populations remains unclear.

Here, we present epidemiological models of *M. ovipneumoniae* transmission in bighorn sheep populations that capture major hypotheses regarding chronic carriage. We use the models to compare five strategies for managing post-spillover disease in bighorn sheep—test-and-remove, depopulation-and-reintroduction, range expansion, herd augmentation and density reduction—and evaluate each action's capacity to influence *M. ovipneumoniae* fade-out and bighorn sheep population recovery. Options for wildlife disease management are limited, and we selected these tools because of their historical, proposed or more recent use by wildlife management agencies to bolster herds struggling with chronic respiratory disease. We evaluate each action's capacity to influence the probability of *M. ovipneumoniae* extinction, and to produce bighorn sheep population recovery in the absence of additional spillover.

2 | MATERIALS AND METHODS

2.1 | System ecology

Bighorn sheep are a group-living North American ungulate. Individuals usually reside in sexually segregated groups throughout most of the year, except around the mating season (which for Rocky Mountain bighorns, *O. c. canadensis* typically occurs from mid-November to mid-December). Longevity regularly exceeds 15 years among females and 10 years among males. Females typically give birth to a single lamb each year from age 2 or 3 until their final year of life. Births are pulsed in the spring, after which ewes and lambs form nursery groups of varying stability. These nursery groups are the critical unit of seasonal transmission among lambs during the chronic phase of the disease (Manlove et al., 2014).

2.2 | Simulation model

We developed a stochastic, susceptible-exposed-infectious-chronic/recovered (SEIC/R) population model of *M. ovipneumoniae* within a single Rocky Mountain bighorn sheep herd. The model operated on a fixed weekly time step within an annual cycle. Animals moved among a set of demographic- and infection-status-defined states, with state transitions at each time step determined by stochastic

draws from binomial distributions with probabilities extracted from the existing ecological literature (Table S1).

2.2.1 | Host demography

The model considered three demographic groups—ewes, rams and lambs less than 1 year of age—which were chosen based on their distinct contributions to demography and disease burden. A single disease-free survival rate was calculated for adult ewes and rams using weighted geometric averages of sex and age-specific estimates (Table S1). Eighty per cent of ewes gave birth to a single lamb each year. Population sizes were constrained by a carrying capacity (here, set to 350) which operated through density-dependent lamb survival in a theta-logistic growth model, $\frac{\text{LambSurvival}_0}{1+(N/K)^\theta}$ (Gilpin & Ayala, 1973). Lamb survival in the absence of infection (and at low population density) was calculated as the geometric average of several field-based estimates (Table S1).

2.2.2 | Host social structure

Disease dynamics in rams were independent of disease dynamics in ewes and lambs, except during the 1-month breeding season when sexes were allowed to mix. All lambs were born in a single pulse on 15 May, and aged into the adult classes with a 50:50 sex ratio on 14 May the following year. We assumed nursery groups were well mixed except in the case of the Range Expansion management action, in which case connectivity between groups was limited to between-group movement by males.

2.2.3 | Pathogen transmission

We used a chain binomial model that forced individuals to progress through a sequence of exposed and infected substates to create incubation and infection periods with approximately log-normally distributed durations (Wearing et al., 2005). Incubation ('E') periods averaged 3 weeks, and acutely infectious periods averaged 19 weeks (across all animals regardless of fate), or 12 weeks for adults and 7 weeks for lambs whose eventual fate was death (Appendix S1 Section 1 and Figures S1 and S2). Ewes and rams experienced an elevated disease-induced mortality rate while acutely infectious, and lambs experienced a separate, higher, rate. Individuals within the susceptible, exposed (latent), chronic and recovered states experienced healthy survival rates. Following acute infection, surviving adults became either permanent chronic carriers or permanently recovered-and-immune. We assumed that chronic carriers transmitted pathogens at one-fourth the rate of their acutely infected peers (Manlove et al., 2017). Lambs experienced acute infection but did not become chronically infected unless they were still infectious when they aged into the adult

class. Individuals were exposed through a stochastic transmission process (Appendix S1 Section 2).

The probability of transmission at each time step, λ , assumed random mixing year-round (no distinct subgroups) for ewes and lambs; rams had a separate probability of transmission, except during the 4-week breeding season when sexes co-mingled (Appendix S1 Section 3). Transmission occurred first within each time step, followed by transitions among infection states, and finally, host survival.

We also developed a simpler SEIR model that was identical to the SEIC/R model in all ways except that it excluded the chronic carrier state and lengthened the average infectious period before individuals transitioned to recovery (Appendix S1 Section 4).

2.2.4 | Simulation procedure

We used published rates to parameterize the model wherever possible (Table S1). Epidemics began with the introduction of three infectious animals following a 100-year burn-in period during which population dynamics reached equilibrium. We ran 100 replicate simulations for each transmission structure/management combination and calculated (a) the proportion of simulations in which the pathogen faded out (i.e. the pathogen went extinct even as the host population persisted), (b) the proportion of simulations in which the host population went extinct and (c) the mean host population size through time. Population status was recorded once a year in October. The model was written and implemented de novo in R (R Core Team, 2017; Figure 1).

2.3 | Epidemic growth rates and estimation of R_0

In order to parameterize the model, we first needed to estimate a key epidemiological quantity: the basic reproductive ratio, R_0 . R_0 describes the number of new cases that a single infected individual is expected to produce in an otherwise fully susceptible population. Its exact calculation depends on the particular life histories of the host and pathogen in question, but it can be estimated to a first approximation based on the rate at which new cases are produced during an epidemic event. The best-resolved data that speak to that rate in bighorn sheep originate from recurrent lamb pneumonia events, and those were the data we relied on here. We used time series of seasonal lamb pneumonia epidemics, aggregated over 19 years in 16 populations from Hells Canyon, a well-studied bighorn sheep metapopulation (Cassirer et al., 2013; Cassirer & Sinclair, 2007). Data were gathered in accordance with standard Idaho Department of Fish and Game and Washington Department of Fish and Wildlife field protocols. We first constructed time series of logged weekly mortality counts (which we took as a reasonable proxy for weekly new cases; King et al., 2015) and identified a change-point in the time series using the piecewise.linear function in R's `sizeR` package (Sonderregger et al., 2009). We constrained

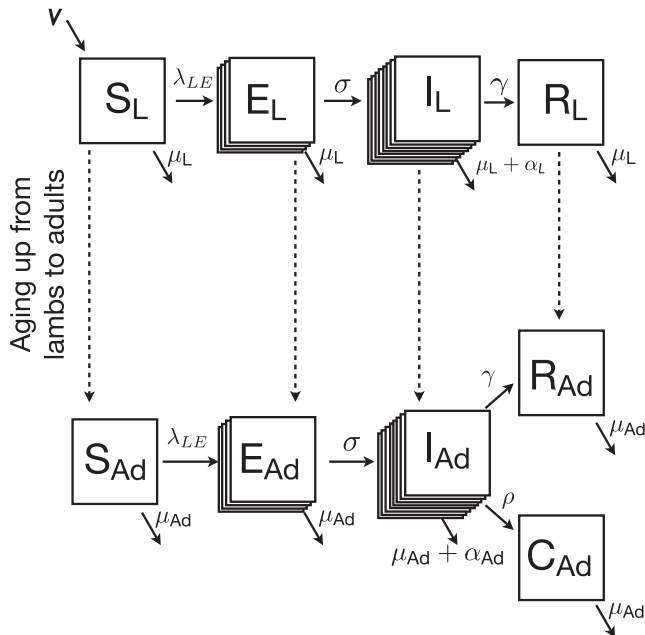


FIGURE 1 SEIC/R model dynamics. The model considers two age classes, lambs and adults. All lambs are born susceptible (S), and all individuals are subject to a background mortality rate accounting for factors other than disease (μ_L or μ_{Ad}). The stacks of boxes under the E and I compartments represent the chain binomial structure of these states. Both acute and chronically infected animals transmit pathogens, but chronically infected animals do so at a lower rate (τ) than their acutely infected counterparts. Exposed individuals transition to acutely infected (I) according to a log-normal distribution. Acutely infected animals experience an additional disease-induced mortality burden (α_L for lambs and α_{Ad} for adults). Lambs surviving acute infections become recovered and immune (R_L); adults surviving acute infection become randomly recovered (R_{Ad}) or chronically infected (C_{Ad}), with probability ρ . Here, we show ewes and rams as a single ‘adult’ group for simplicity, but they are treated separately in the model

our analysis to the exponential growth phase prior to the change-point, and fit a linear regression of logged weekly mortalities as a function of time. We exponentiated the resulting slope coefficient estimate to get the epidemic’s exponential growth rate and calculated R_0 following the formulation of Wearing et al. (2005), which allows for a chain binomial structure similar to the one in our simulation model. We used that estimate of R_0 to solve for β under both frequency- and density-dependent transmission by adjusting relationships from Lloyd-Smith et al. (2005) and Keeling and Rohani (2011) (Appendix S1 Section 5).

2.4 | Management experiments

We explored six different management strategies: test-and-remove, depopulation-and-reintroduction, density reduction, augmentation, range expansion and no action (Table S2). Of these strategies, both test-and-remove and depopulation-and-reintroduction

targeted infectious individuals, and could eliminate the pathogen entirely if employed perfectly (i.e. 100% test-and-remove or depopulation). We modelled the consequences of handling <100% of the herd, since capturing every individual is often not possible. Density reduction could reduce transmission rates if transmission was density dependent, and could result in the chance removal of infected individuals. Range expansion could decrease (density-dependent) transmission through reduced local host densities and allowed for asynchronous disease dynamics among subgroups. We let range expansion increase the population’s overall carrying capacity, under an assumption that expansion was directed towards appropriate, unoccupied habitat. Augmentation has typically been used to increase genetic diversity or population size in an effort to mitigate Allee effects, but in the context of an infectious disease, it increases the number and density of susceptible hosts and thus could also increase the transmission rate within the newly augmented population.

Specific simulation protocols for all actions are described in Table S2. Management was implemented 20 years after pathogen introduction and simulations without any management served as controls.

2.5 | Sensitivity analysis

We evaluated the sensitivity of three outputs—probability of host extinction, probability of pathogen fade-out and host population persistence and host population size—to seven model parameters: background host survival rates, probability that acutely infected animals became chronic carriers, the basic reproductive ratio (R_0), whether transmission was frequency or density dependent, relative contribution of chronic carriers to force of infection, disease-induced mortality rate and recovery rate. For recovery rate, we left the chain binomial structure of the I state intact, but adjusted the waiting time for transitions between compartments. Parameters were sampled from uniform distributions over the ranges in Table S1.

Reasonable value ranges were identified for all parameters (Table S1) and partitioned into eight equal segments. We surveyed the parameter space through 250 samples drawn according to a Latin hypercube (Wu et al., 2013) to obtain comprehensive coverage. We simulated 250 time series for each parameter combination and calculated median host population size and host and pathogen extinction probabilities across the replicate simulations 50 years post-invasion. In order to avoid influence from simulations with early pathogen fade-out, we included only those where the pathogen persisted at least 4 years following introduction (resulting in removal of approximately 15% of the simulations). Using the remaining parameter combinations, we calculated the partial rank correlation coefficient (PRCC) between each parameter value and each output probability as implemented in R’s *sensitivity* package (Pujol et al., 2017).

3 | RESULTS

3.1 | Estimation of R_0 and β

Figure S3 (Appendix S1 Section 6) shows lamb mortality time series, along with change-point regions and model fits for the exponential growth phase. The piecewise regression identified a significant change-point in number of weekly mortalities on 14 June (95% CI [26 May, 22 June]). The linear model of logged weekly mortalities prior to 14 June produced an exponentiated slope estimate of 1.032 (95% CI [1.020, 1.044]), which corresponds to an R_0 estimate of 1.53 (95% CI [1.36, 1.74]).

3.2 | Simulation experiments

Simulations in our specific parameter space (Table S1) under the SEIC/R model consistently produced large die-off events and pathogen persistence (under density-dependent transmission, the median epidemic infected 36.8% of the population at its apex and persisted for 34.8 years; under frequency-dependent transmission, the median epidemic infected 89.9% of the population at its apex and persisted for 38.0 years; Table S3). SEIR dynamics in the same parameter space showed dramatically lower epidemic size and persistence (Appendix S1 Section 7), which were inconsistent with the dynamics of the system on which the model was based (Cassirer et al., 2013, 2018; Manlove et al., 2016). This led us to abandon the SEIR model in favour of the more complex SEIC/R structure, which is our focus throughout the remainder of this investigation.

In the absence of management, system dynamics were strongly influenced by the structure of the transmission function (Figure 2). Under density-dependent transmission, population recovery was largely driven by pathogen fade-out and resurgence of a fully susceptible population to the pre-epidemic carrying capacity (Figure 2b). Under frequency-dependent transmission, populations declined to lower levels, were more likely to go extinct, were dominated by recovered individuals and were slower to rebound to pre-epidemic numbers (Figure 2c).

Despite the gross differences in density- and frequency-dependent transmission, management action performances ranked similarly across both transmission structures. Test-and-remove or depopulation-and-reintroduction implemented on a high proportion of the population (i.e. $\geq 80\%$) accelerated pathogen fade-out (Figure 3a,b; Appendix S1 Section 8, Figures S6 and S7 for results from full range of management intensities). Density reductions (i.e. 50%) and range expansion (here, into two distinct groups) also increased the probability of pathogen fade-out, although to a lesser extent. Importantly, augmentation—regardless of whether introduced animals were immune or susceptible—actually increased pathogen persistence (Figure 3a,b; Figures S8 and S9).

The degree and speed of population recovery following management depended on whether the pathogen faded out, and on the host population's size when fade-out occurred. Herds took longer to recover under frequency-dependent transmission because frequency-dependent population declines were more dramatic, yielding smaller population sizes at the time of management (Figure 4).

When it succeeded in eliminating the pathogen, depopulation-and-reintroduction incited rapid recovery of herd size (Figure 3c,d). Range expansion generated robust population growth despite

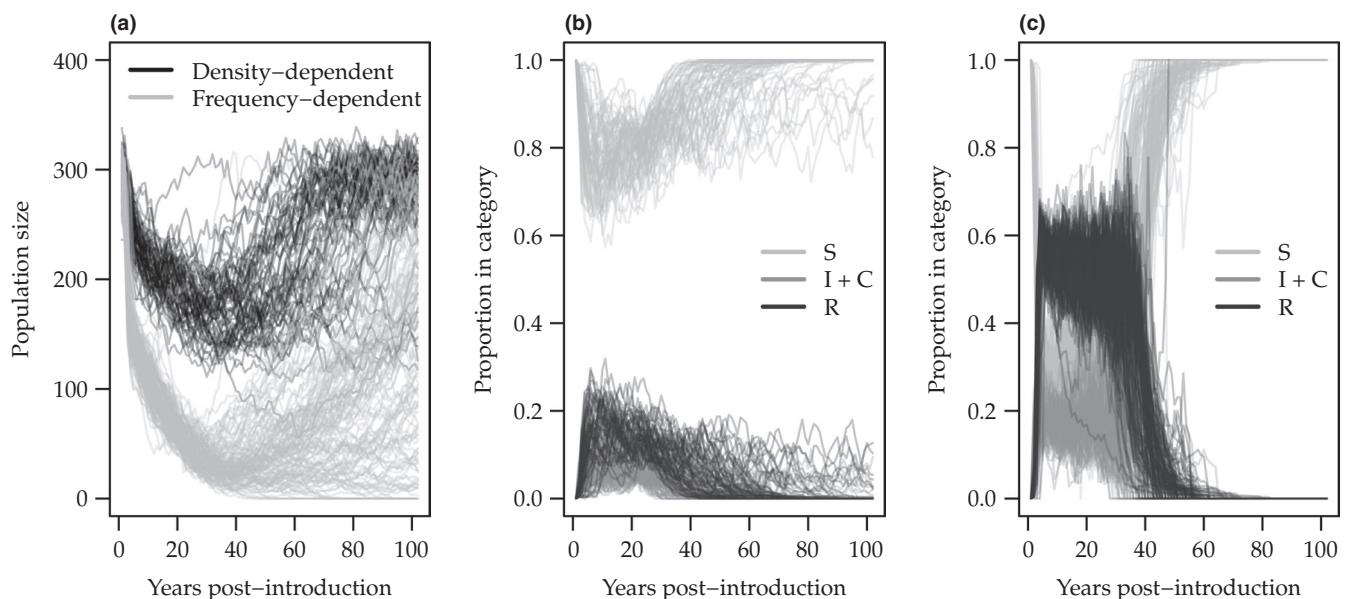


FIGURE 2 Model forecasted host-pathogen dynamics under the SEIC/R model without management. (a) Population trajectories. (b) Host-pathogen dynamics under density-dependent transmission. (c) Host-pathogen dynamics under frequency-dependent transmission. S, susceptible; I, acutely infectious; C, chronic carrier; R, recovered (immune). Simulations relied on the parameters listed in Table S1. Pathogens were introduced at year 0, and we tracked trajectories forward for 100 years. Figure S4 contains a parallel diagram for the SEIR model

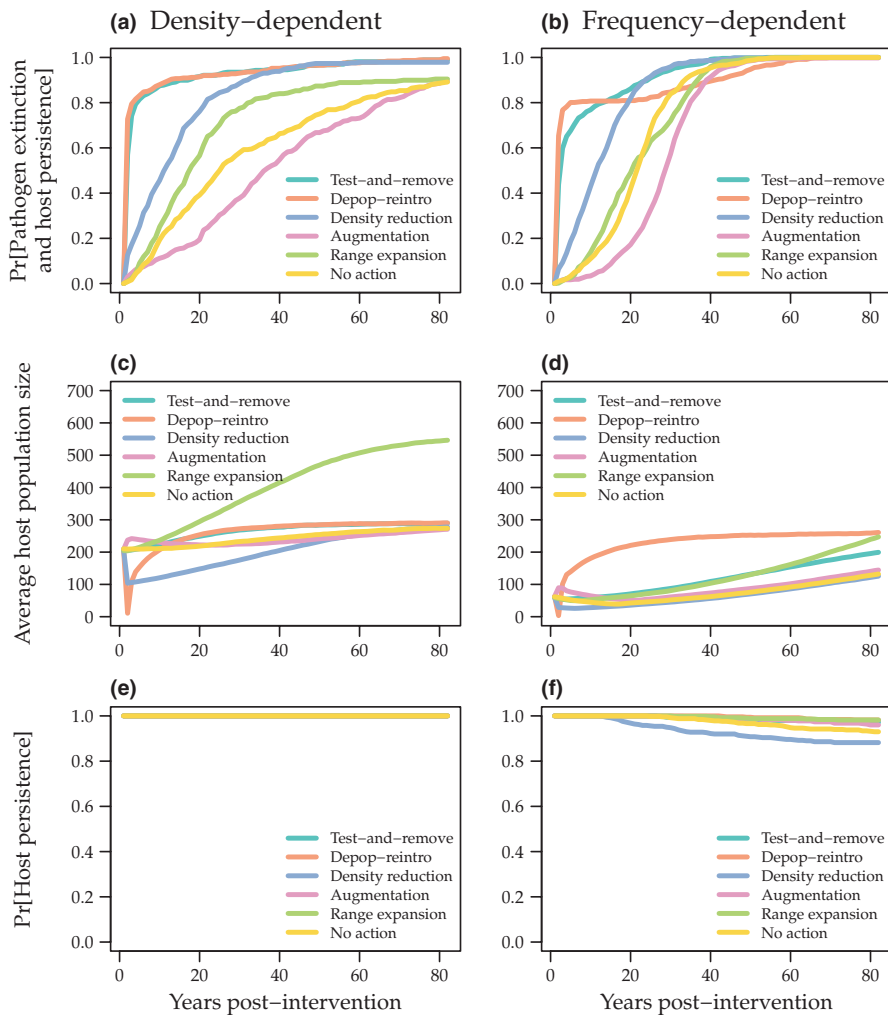


FIGURE 3 Epidemiological responses to different management regimens under the SEIC/R model. Lines represent (a & b) pathogen fade-out probabilities, (c & d) average population size associated with different management approaches and (e & f) host extinction probabilities associated with each management action for density- and frequency-dependent expansion (left and right columns respectively). Lines for test-and remove and depopulation-and-reintroduction represent scenarios in which 95% of animals were tested, and 95% of animals were removed respectively. These simulations assumed $R_0 = 1.53$, and 22% of surviving infectious individuals became carriers. Management occurred 20 years post-pathogen introduction, and results are plotted over time since management intervention

infection and was (by definition) the only tool able to produce long-term growth beyond the pre-outbreak carrying capacity (Figure 4i), though this was more common under density-dependent than frequency-dependent transmission. Test-and-remove consistently led to faster population recovery than augmentation, density reductions or no management. Augmentation led to short-lived population increases, followed by declines as new susceptibles became infected and died. Density reductions engendered an initial population decline associated with the management action itself, and herd size usually fell short of the no management scenario in the long term.

Density reduction, augmentation and the no management option brought about slight increases in the risk of host extinction when transmission was frequency dependent (Figure 3f). Parallel risks associated with test-and-remove, depopulation-and-reintroduction and range expansion were all negligible.

3.3 | Sensitivity analysis

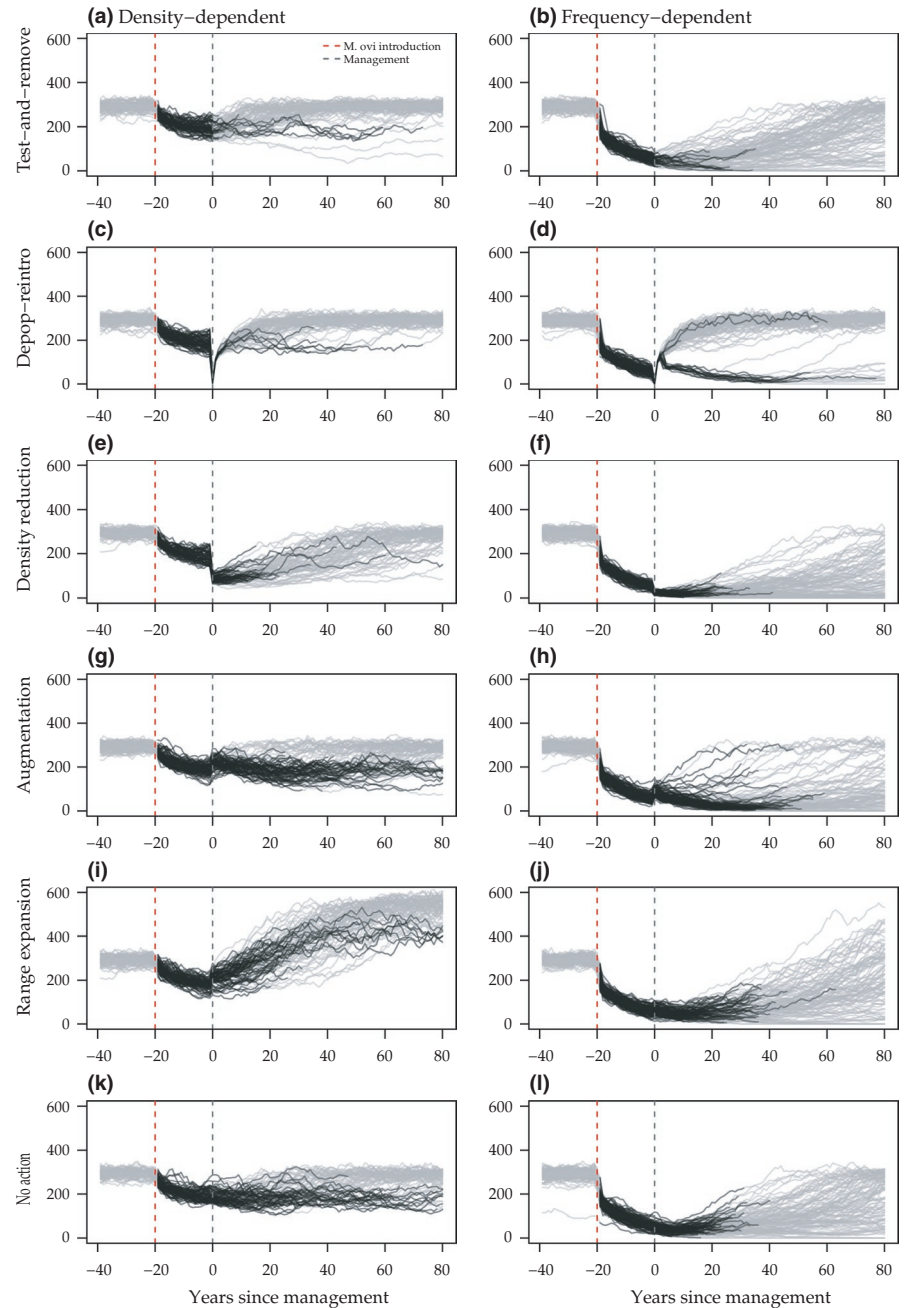
Both host persistence and pathogen fade-out were most sensitive to background host survival rates and disease-induced mortality rates

(Figure 5a,c). Average host population size was most sensitive to host survival (Figure 5b). Increasing host survival resulted in improved host population persistence and size, but decreased the probability of pathogen fade-out. Similarly, as disease-induced mortality decreased, host persistence increased and the probability of pathogen fade-out declined. Increased shedding from carriers (bringing the probability of transmission given contact with a carrier closer to probability of transmission given contact with an acutely infected individual), faster epidemic growth rates and frequency-dependent transmission were all detrimental to host persistence and population size. Host population persistence also declined when a higher proportion of adults became chronic carriers. The pathogen was most likely to fade out when there were fewer chronic carriers, faster recovery rates and (marginally) when transmission was frequency dependent. A description of how sensitivities changed with time since the epidemic is included in Appendix S1 Section 9 and shown in Figure S11.

4 | DISCUSSION

Implementing adaptive management to control wildlife disease is an iterative process of prediction, monitoring, evaluation and

FIGURE 4 Plots of bighorn sheep population size over time following the spillover of *Mycoplasma ovipneumoniae* in year -20, and the implementation of disease management in year 0, indicated by the vertical grey line. Each line is a simulation, and lines are color-coded by infection status where grey indicates no infection (i.e. pathogen fade-out) and black indicates the presence of active infections. Density-dependent transmission is shown in the left column, and frequency-dependent transmission in the right



refinement. Here, we estimated R_0 and used a predictive model of long-term pathogen transmission to systematically explore management options for *M. ovipneumoniae*, a persistent infectious pathogen of bighorn sheep, with the goal of increasing host population size. As empirical data on herd responses to management actions accumulate, they can be compared to these predictions, providing a basis to refine and improve model forecasts in the future.

4.1 | Strategies for managing bighorn sheep pneumonia

The model suggested that a management action's ability to produce post-epidemic population recovery depended on two factors: (a)

how effectively the action curtailed pathogen transmission and (b) the size of the host population immediately following management implementation, as determined by both the severity of the initial epidemic and alterations in population size due to the action itself (e.g. through removal or augmentation).

The models highlight one critical knowledge gap: Whether transmission is frequency- or density-dependent. Actions were less effective and population outcomes were worse when transmission was frequency dependent, because by definition, shifts in population density did not alter transmission rate. That said, overall disease dynamics—and thus the likelihood that managers would undertake actions at all—varied substantially between the two transmission structures. In some well-studied bighorn sheep populations, lamb mortality rates vary more among nursery groups than among

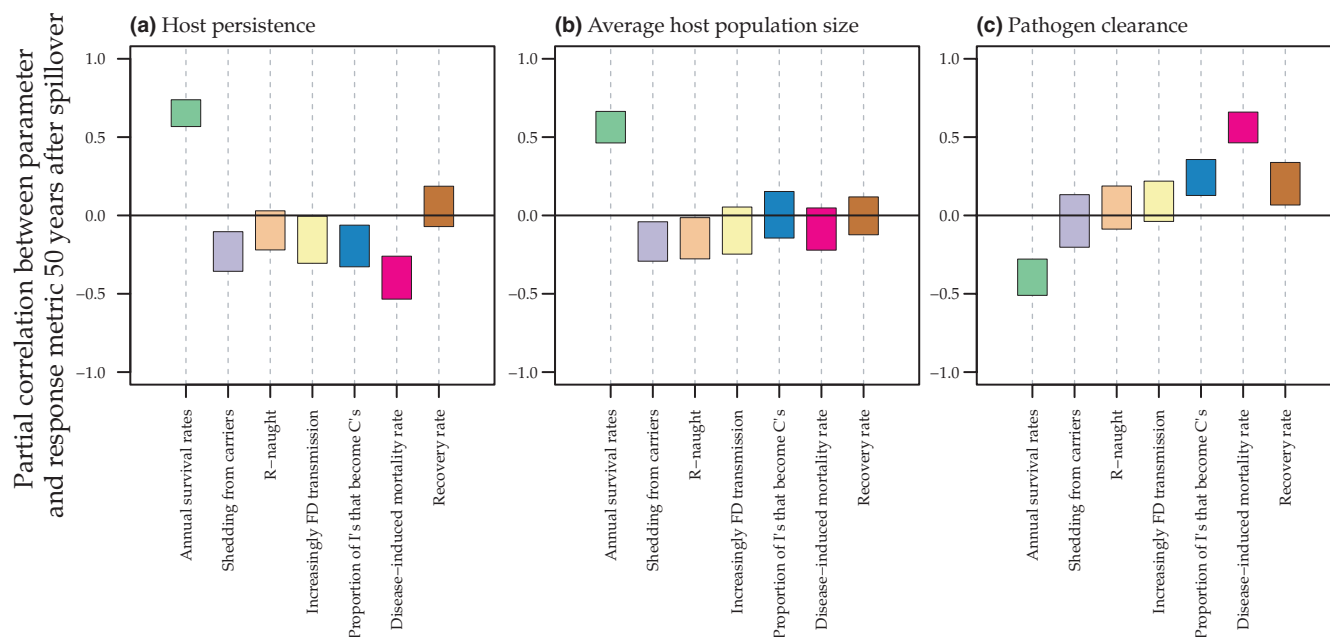


FIGURE 5 Sensitivities of bighorn sheep population persistence, population size and pathogen clearance to seven epidemiological parameters

populations or years in the presence of *M. ovipneumoniae* transmission, and nursery group sizes hold steady even as population sizes decline (Manlove et al., 2014). This suggests a pathway for behaviourally mediated frequency-dependent transmission (Cassirer et al., 2013). Mechanistic understanding of how transmission scales from density to frequency dependence in this system and others is an area of ongoing research.

More severe initial population die-off events were associated with delayed population recovery following pathogen fade-out across the board (Figure 4). Population sizes rebounded fastest when actions targeted removal of infected hosts (as in the cases of test-and-remove and depopulation-and-reintroduction; Figure 4c,d), or increased carrying capacity as defined in the model (as in the case of range expansion, Figure 4i). This is consistent with experimental and observational field studies reporting marked improvement in recruitment following complete clearance of *M. ovipneumoniae* among ewes (Garwood et al., 2020; Spaan et al., 2021). When depopulation-and-reintroduction efforts succeeded at removing all infected individuals, they had the added benefit of boosting the post-management population size, further accelerating population resurgence. Range expansion had limited effects on pathogen clearance, but allowed for better population recovery, likely through an increased carrying capacity and asynchronous disease dynamics among the subpopulations. Density reductions improved the probability of pathogen fade-out, but at the cost of host population size and persistence, and delayed recovery time. Augmentation of infected herds bolstered population size in the short term, but eventually led to significant reductions in pathogen clearance and longer term depressions in population size and persistence. In reality, outcomes of augmentation efforts

could be even worse than suggested here (for instance, due to novel strain introduction events associated with post-release exploratory movements of animals unfamiliar with the reintroduction site) (Cassirer et al., 2017).

Increasing background host survival and reducing disease-induced mortality rates could improve host persistence and population size, despite infection (Figure 5). This underscores the merit in considering other management tools that boost survival and diminish disease severity in infected herds. Reducing the proportion or shedding potential of carriers, or limiting contact rates through changes in host densities could achieve more modest improvements in host population size. The degree of herd substructuring (the number, size and connectivity among subgroups) and the stability of group membership likely also determine the efficacy of test-and-remove, depopulation-and-reintroduction and density reductions. If within-group mortality patterns are known, test-and-remove or depopulation efforts could be targeted to specific groups, affecting a lower proportion of animals across the herd as a whole. However, while the complexities of herd substructuring warrant further exploration, they are beyond the scope of this study.

Even when model parameters were held constant, simulations produced variable population sizes, pathogen prevalences and serological dynamics (Figures 2 and 4). This is consistent with the high variability in dynamics observed empirically (Cassirer et al., 2018). Replicated management interventions, followed by empirical data collection that informs updates to model parameters or structure, are required to fully understand variation in efficacies of management efforts already underway (Garwood et al., 2020; Lula et al., 2020).

4.2 | Considerations when managing emerging infectious diseases in wildlife

The ultimate goal of management for many wildlife diseases, including bighorn sheep pneumonia, is to increase herd abundance to sustainable levels. Many context-specific circumstances inform the particular tactics used to achieve this goal (Sells et al., 2016), including the importance of conserving population genetic and ecological adaptation, the degree of connectivity with neighbouring populations and their infection statuses, agency and public tolerance of population extinction, costs and logistical feasibility.

Given this array of considerations, there is no single 'best' management intervention. However, the greater the effect of management on the underlying factors limiting population recovery, the more likely that action will be to facilitate population growth. Tools that speed pathogen extinction, increase host survival, reduce disease-induced mortality and increase host carrying capacity are likely to improve population recovery. Delineating how each management action operates can begin to clarify how several actions—for example, test-and-remove plus augmentation or range expansion—might be used in concert. Management options not identified here could also prove effective if they address the limiting factors listed above.

4.3 | Model limitations

Our model scenarios explored population responses to interventions following relatively high-virulence epizootics. Model predictions may not apply to low-severity events, which are less likely to be prioritized for disease management. Our model is also subject to several other limitations. First, our estimation of R_0 relies on data from annually recurrent lamb epidemics, and we assume that transmission rates among naive lambs reasonably approximate transmission rates among naive adults. There are limited high-resolution data on adults during acute epidemic events. Fortunately, our results are not overly sensitive to epidemic growth rate (Figure 5), so even if rates are not precisely consistent between lambs and adults, the rank of the management actions explored here would be unlikely to change. However, the actual outcomes of management actions themselves might differ (for instance, density dependence might be more important, and fade-out might be less likely to occur).

Second, we assume no continuing risk of spillover from neighbouring reservoir hosts. Wild and domestic sheep and goats are potential reservoirs of *M. ovipneumoniae* and pathogen clearance from any bighorn herd hinges on avoiding new spillover events. Several management tools including augmentation, depopulation-and-reintroduction and range expansion may inherently increase spillover risk if translocated animals roam widely and contact reservoir hosts (Clapp et al., 2014). Actions to mitigate these risks should be sustained before, during and after management efforts.

Third, our population model does not incorporate the potential for Allee effects when populations are small. Allee effects

can play an important role in bighorn sheep population dynamics (Hogg et al., 2006), and may accelerate host extinction in the face of disease-induced population declines (Deredec & Courchamp, 2006). If population size is very low following pathogen clearance, additional actions not accounted for in the model, such as natural or assisted augmentation, may be required for recovery.

Fourth, some of the patterns reported here could stem from the model's demographic structure, instead of the pathogen transmission process per se. For instance, we did not investigate mechanisms contributing to carrying capacity (including whether individuals modify or expand their range use to alleviate habitat limitation as numbers and densities increase), nor did we explore how year-to-year variation in population carrying capacity might alter system dynamics. Variable carrying capacity is likely important in some regions of bighorn sheep range, and could change results, especially given the powerful reliance of modelled outcomes on host survival rates. However, the extent to which carrying capacity truly limits bighorn sheep populations—especially those with active disease—remains unknown. Exploring the carrying capacity–disease interface fully is beyond our current scope.

Fifth, some elements of the underlying disease process remain poorly understood. In particular, assumptions regarding the existence of completely and partially recovered classes (Plowright et al., 2017), a common probability of becoming a chronic carrier applied to all adults, a limited cost of infection on carrier survival (e.g. Dekelaita et al., 2020) and a transmission function that is either completely density- or completely frequency dependent all deserves further inquiry. Moreover, relationships between states and parameters within this model are inherently nonlinear, violating some of the independence assumptions associated with the PRCC and potentially confounding our sensitivity estimates.

Finally, variation in virulence among *M. ovipneumoniae* strains is an emerging area of research and other factors not considered here, such as the polymicrobial nature of pneumonia events in bighorn sheep, may also affect disease outcomes.

4.4 | Next steps

Pneumonia epidemics are relatively infrequent events in bighorn sheep populations, yet their consequences threaten long-term viability in many parts of their range. Wildlife management agencies continue to implement a wide variety of post-epidemic management strategies in an effort to facilitate herd recovery, and these can be used to empirically evaluate and inform this model. The model will be most useful if it is applied in iteration with field research and monitoring to evaluate model assumptions, update model parameter estimates and improve predictions in the future. This model lays out a systematic approach for thinking about disease management and predicting and evaluating biological outcomes in this system and others.

ACKNOWLEDGEMENTS

We thank the Western Association of Fish and Wildlife Agencies' Wild Sheep Working Group, the Wild Sheep Foundation, Federal Aid to Wildlife Restoration and numerous state and federal wildlife management agencies for their diligent work addressing bighorn sheep pneumonia and for discussions that contributed to model formulation. K.R.M. was funded by USDA UAES Project # UTA01427, Nevada Department of Wildlife and the U.S. Geological Survey (Grant #G21AC10105-00 and #G18AC00366). R.K.P. was funded by DARPA PREEMPT # D18AC00031, the U.S. National Science Foundation (DEB-1716698) and the USDA National Institute of Food and Agriculture (Hatch project 1015891).

CONFLICT OF INTEREST

The authors have no conflicts of interest to report.

AUTHORS' CONTRIBUTIONS

E.S.A., K.R.M., E.F.C. and R.K.P. conceived the ideas and designed the methodologies; E.S.A. conducted initial model exploration and ran management simulations; E.S.A. and K.R.M. designed and K.R.M. implemented the sensitivity analysis; K.R.M. and E.S.A. drafted the manuscript; and all authors contributed comments to multiple drafts.

DATA AVAILABILITY STATEMENT

Data available from the Dryad Digital Repository <https://doi.org/10.5061/dryad.s1rn8pk8x> (Manlove et al., 2021).

ORCID

Kezia R. Manlove  <https://orcid.org/0000-0002-7200-5236>

Raina K. Plowright  <https://orcid.org/0000-0002-3338-6590>

REFERENCES

- Besser, T. E., Cassirer, E. F., Potter, K. A., VanderSchalie, J., Fischer, A., Knowles, D. P., Herndon, D. R., Rurangirwa, F. R., Weiser, G. C., & Srikumaran, S. (2008). Association of *Mycoplasma ovipneumoniae* infection with population-limiting respiratory disease in free-ranging Rocky Mountain bighorn sheep (*Ovis canadensis canadensis*). *Journal of Clinical Microbiology*, 46(2), 423–430. <https://doi.org/10.1128/JCM.01931-07>
- Besser, T. E., Levy, J., Ackerman, M., Nelson, D., Manlove, K., Potter, K. A., Busboom, J., & Benson, M. (2019). A pilot study of the effects of *Mycoplasma ovipneumoniae* exposure on domestic lamb growth and performance. *Plos one*, 14(2), e0207420.
- Cahn, M. L., Conner, M. M., Schmitz, O. J., Stephenson, T. R., Wehausen, J. D., & Johnson, H. E. (2011). Disease, population viability, and recovery of endangered Sierra Nevada bighorn sheep. *The Journal of Wildlife Management*, 75(8), 1753–1766. <https://doi.org/10.1002/jwmg.232>
- Cassirer, E. F., Manlove, K. R., AlMBERG, E. S., Kamath, P. L., Cox, M., Wolff, P., Roug, A., Shannon, J., Robinson, R., Harris, R. B., Gonzales, B. J., Plowright, R. K., Hudson, P. J., Cross, P. C., Dobson, A., & Besser, T. E. (2018). Pneumonia in bighorn sheep: Risk and resilience. *The Journal of Wildlife Management*, 82(1), 32–45. <https://doi.org/10.1002/jwmg.21309>
- Cassirer, E. F., Manlove, K. R., Plowright, R. K., & Besser, T. E. (2017). Evidence for strain-specific immunity to pneumonia in bighorn sheep. *The Journal of Wildlife Management*, 81(1), 133–143. <https://doi.org/10.1002/jwmg.21172>
- Cassirer, E. F., Plowright, R. K., Manlove, K. R., Cross, P. C., Dobson, A. P., Potter, K. A., & Hudson, P. J. (2013). Spatio-temporal dynamics of pneumonia in bighorn sheep. *Journal of Animal Ecology*, 82(3), 518–528. <https://doi.org/10.1111/1365-2656.12031>
- Cassirer, E. F., & Sinclair, A. R. E. (2007). Dynamics of pneumonia in a bighorn sheep metapopulation. *Journal of Wildlife Management*, 71(4), 1080–1088. <https://doi.org/10.2193/2006-002>
- Clapp, J. G., Beck, J. L., & Gerow, K. G. (2014). Post-release acclimation of translocated low-elevation, non-migratory bighorn sheep. *Wildlife Society Bulletin*, 38(3), 657–663. <https://doi.org/10.1002/wsb.441>
- Clifford, D. L., Schumaker, B. A., Stephenson, T. R., Bleich, V. C., Cahn, M. L., Gonzales, B. J., Boyce, W. M., & Mazet, J. A. (2009). Assessing disease risk at the wildlife–livestock interface: A study of Sierra Nevada bighorn sheep. *Biological Conservation*, 142(11), 2559–2568. <https://doi.org/10.1016/j.biocon.2009.06.001>
- Dekelaita, D. J., Epps, C. W., Stewart, K. M., Sedinger, J. S., Powers, J. G., Gonzales, B. J., Abella-Vu, R. K., Darby, N. W., & Hughson, D. L. (2020). Survival of adult female bighorn sheep following a pneumonia epizootic. *The Journal of Wildlife Management*, 84(7), 1268–1282. <https://doi.org/10.1002/jwmg.21914>
- Dereced, A., & Courchamp, F. (2006). Combined impacts of Allee effects and parasitism. *Oikos*, 112(3), 667–679. <https://doi.org/10.1111/j.0030-1299.2006.14243.x>
- Garwood, T., Lehman, C., Walsh, D., Cassirer, E. F., Besser, T. E., & Jenks, J. (2020). Removal of chronic *Mycoplasma ovipneumoniae* carrier ewes eliminates pneumonia in a bighorn sheep population. *Ecology and Evolution*, 10(7), 3491–3502. <https://doi.org/10.1002/ece3.6146>
- Gilpin, M. E., & Ayala, F. J. (1973). Global models of growth and competition. *Proceedings of the National Academy of Sciences of the United States of America*, 70(12), 3590–3593. <https://doi.org/10.1073/pnas.70.12.3590>
- Hobbs, N. T., & Miller, M. W. (1992). Interactions between pathogens and hosts: Simulation of pasteurellosis epizootics in bighorn sheep populations. In D. R. McCullough, & R. H. Barrett (Eds.), *Wildlife 2001: Populations* (pp. 997–1007). Springer.
- Hogg, J. T., Forbes, S. H., Steele, B. M., & Luikart, G. (2006). Genetic rescue of an insular population of large mammals. *Proceedings of the Royal Society B: Biological Sciences*, 273(1593), 1491–1499. <https://doi.org/10.1098/rspb.2006.3477>
- Joseph, M. B., Mihaljevic, J. R., Arellano, A. L., Kueneman, J. G., Preston, D. L., Cross, P. C., & Johnson, P. T. (2013). Taming wildlife disease: Bridging the gap between science and management. *Journal of Applied Ecology*, 50(3), 702–712. <https://doi.org/10.1111/1365-2664.12084>
- Kamath, P., Manlove, K. R., Cassirer, E. F., Cross, P. C., & Besser, T. E. (2019). Genetic structure of *Mycoplasma ovipneumoniae* informs pathogen spillover dynamics between domestic and wild Caprinae in the western United States. *Scientific Reports*, 9(1), 1–14. <https://doi.org/10.1038/s41598-019-51444-x>
- Keeling, M. J., & Rohani, P. (2011). *Modeling infectious diseases in humans and animals*. Princeton University Press.
- King, A. A., Domenech de Cellès, M., Magpantay, F. M., & Rohani, P. (2015). Avoidable errors in the modelling of outbreaks of emerging pathogens, with special reference to Ebola. *Proceedings of the Royal Society B: Biological Sciences*, 282(1806), 20150347. <https://doi.org/10.1098/rspb.2015.0347>
- Langwig, K. E., Frick, W. F., Bried, J. T., Hicks, A. C., Kunz, T. H., & Kilpatrick, A. M. (2012). Sociality, density-dependence and microclimates determine the persistence of populations suffering from a novel fungal disease, white-nose syndrome. *Ecology Letters*, 15(9), 1050–1057. <https://doi.org/10.1111/j.1461-0248.2012.01829.x>

- le Roex, N., Cooper, D., van Helden, P. D., Hoal, E. G., & Jolles, A. E. (2016). Disease control in wildlife: Evaluating a test and cull programme for bovine tuberculosis in African buffalo. *Transboundary and Emerging Diseases*, 63(6), 647–657. <https://doi.org/10.1111/tbed.12329>
- Lloyd-Smith, J. O., Schreiber, S. J., Kopp, P. E., & Getz, W. M. (2005). Superspreading and the effect of individual variation on disease emergence. *Nature*, 438(7066), 355–359.
- Lula, E. S., Lowrey, B., Proffitt, K. M., Litt, A. R., Cunningham, J. A., Butler, C. J., & Garrott, R. A. (2020). Is habitat constraining bighorn sheep restoration? A case study. *The Journal of Wildlife Management*, 84(3), 588–600. <https://doi.org/10.1002/jwmg.21823>
- Manlove, K. R., Almborg, E. S., Cassirer, E. F., Ramsey, J., Carson, K., Gude, J., & Plowright, R. K. (2021). Data from: Modeling management strategies for chronic disease in wildlife: Predictions for the control of respiratory disease in bighorn sheep. *Dryad Digital Repository*, <https://doi.org/10.5061/dryad.s1rn8pk8x>
- Manlove, K., Branan, M., Baker, K., Bradway, D., Cassirer, E. F., Marshall, K. L., Miller, R. S., Sweeney, S., Cross, P. C., & Besser, T. E. (2019). Risk factors and productivity losses associated with *Mycoplasma ovipneumoniae* infection in United States domestic sheep operations. *Preventive Veterinary Medicine*, 168, 30–38. <https://doi.org/10.1016/j.prevetmed.2019.04.006>
- Manlove, K. R., Cassirer, E. F., Cross, P. C., Plowright, R. K., & Hudson, P. J. (2014). Costs and benefits of group living with disease: A case study of pneumonia in bighorn lambs (*Ovis canadensis*). *Proceedings of the Royal Society B: Biological Sciences*, 281(1797), 20142331. <https://doi.org/10.1098/rspb.2014.2331>
- Manlove, K., Cassirer, E. F., Cross, P. C., Plowright, R. K., & Hudson, P. J. (2016). Disease introduction is associated with a phase transition in bighorn sheep demographics. *Ecology*, 97(10), 2593–2602. <https://doi.org/10.1002/ecy.1520>
- Manlove, K. R., Cassirer, E. F., Plowright, R. K., Cross, P. C., & Hudson, P. J. (2017). Contact and contagion: Probability of transmission given contact varies with demographic state in bighorn sheep. *Journal of Animal Ecology*, 86(4), 908–920. <https://doi.org/10.1111/1365-2656.12664>
- Plowright, R. K., Manlove, K. R., Besser, T. E., Páez, D. J., Andrews, K. R., Matthews, P. E., Waits, L. P., Hudson, P. J., & Cassirer, E. F. (2017). Age-specific infectious period shapes dynamics of pneumonia in bighorn sheep. *Ecology Letters*, 20(10), 1325–1336. <https://doi.org/10.1111/ele.12829>
- Plowright, R. K., Manlove, K. R., Cassirer, E. F., Cross, P. C., Besser, T. E., & Hudson, P. J. (2013). Use of exposure history to identify patterns of immunity to pneumonia in bighorn sheep (*Ovis canadensis*). *PLoS ONE*, 8(4), e61919. <https://doi.org/10.1371/journal.pone.0061919>
- Pujol, G., looss, B., & Janon, A. (2017). *sensitivity: Global sensitivity analysis of model outputs*. R package version 1.15.0. Retrieved from <https://CRAN.R-project.org/package=sensitivity>
- R Core Development Team. (2017). *R: A language and environment for statistical computing*. R Foundation for Statistical Computing.
- Sells, S. N., Mitchell, M. S., Edwards, V. L., Gude, J. A., & Anderson, N. J. (2016). Structured decision making for managing pneumonia epizootics in bighorn sheep. *The Journal of Wildlife Management*, 80(6), 957–969. <https://doi.org/10.1002/jwmg.21088>
- Sonderogger, D. L., Wang, H., Clements, W. H., & Noon, B. R. (2009). Using SiZer to detect thresholds in ecological data. *Frontiers in Ecology and the Environment*, 7(4), 190–195. <https://doi.org/10.1890/070179>
- Spaan, R. S., Epps, C. W., Crowhurst, R., Whittaker, D., Cox, M., & Duarte, A. (2021). Impact of *Mycoplasma ovipneumoniae* on juvenile bighorn sheep (*Ovis canadensis*) survival in the northern Basin and Range ecosystem. *PeerJ*, 9, e10710. <https://doi.org/10.7717/peerj.10710>
- Uehlinger, F. D., Johnston, A. C., Bollinger, T. K., & Waldner, C. L. (2016). Systematic review of management strategies to control chronic wasting disease in wild deer populations in North America. *BMC Veterinary Research*, 12(1), 173. <https://doi.org/10.1186/s12917-016-0804-7>
- Wearing, H. J., Rohani, P., & Keeling, M. J. (2005). Appropriate models for the management of infectious diseases. *PLoS Medicine*, 2(7), e174. <https://doi.org/10.1371/journal.pmed.0020320>
- Wu, J., Dhingra, R., Gambhir, M., & Remais, J. V. (2013). Sensitivity analysis of infectious disease models: Methods, advances and their application. *Journal of the Royal Society Interface*, 10(86), 20121018. <https://doi.org/10.1098/rsif.2012.1018>

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Almborg, E. S., Manlove, K. R., Cassirer, E. F., Ramsey, J., Carson, K., Gude, J., & Plowright, R. K. (2021). Modelling management strategies for chronic disease in wildlife: Predictions for the control of respiratory disease in bighorn sheep. *Journal of Applied Ecology*, 00, 1–11. <https://doi.org/10.1111/1365-2664.14084>