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## RESEARCH ARTICLE

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# Parsing the effects of demography, climate and management on recurrent brucellosis outbreaks in elk

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**Handling Editor:** Silke Bauer**Abstract**

1. Zoonotic pathogens can harm human health and well-being directly or by impacting livestock. Pathogens that spillover from wildlife can also impair conservation efforts if humans perceive wildlife as pests. Brucellosis, caused by the bacterium *Brucella abortus*, circulates in elk and bison herds of the Greater Yellowstone Ecosystem and poses a risk to cattle and humans. Our goal was to understand the relative effects of climatic drivers, host demography and management control programmes on disease dynamics.
2. Using >20 years of serologic, demographic and environmental data on brucellosis in elk, we built stochastic compartmental models to assess the influences of climate forcing, herd immunity, population turnover and management interventions on pathogen transmission. Data were collected at feedgrounds visited in winter by free-ranging elk in Wyoming, USA.
3. Snowpack, hypothesized as a driver of elk aggregation and thus brucellosis transmission, was strongly correlated across feedgrounds. We expected this variable to drive synchronized disease dynamics across herds. Instead, we demonstrate asynchronous epizootics driven by variation in demographic rates.
4. We evaluated the effectiveness of test-and-slaughter of seropositive female elk at two feedgrounds. Test-and-slaughter temporarily reduced herd-level seroprevalence but likely reduced herd immunity while removing few infectious individuals, resulting in subsequent outbreaks once the intervention ceased. We simulated an alternative strategy of removing seronegative female elk and found it would increase herd immunity, yielding fewer infections. We evaluated a second experimental treatment wherein feeding density was reduced at one feedground, but we found no evidence for an effect despite a decade of implementation.
5. *Synthesis and applications.* Positive serostatus is often weakly correlated with infectiousness but is nevertheless used to make management decisions including lethal removal in wildlife disease systems. We show how this can have adverse consequences whereas efforts that maintain herd immunity can have longer-term protective effects. Climatic drivers may not result in synchronous disease

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dynamics across populations unless vital rates are also similar because demographic factors have a large influence on disease patterns.

#### KEYWORDS

*Cervus*, disease ecology, metapopulation dynamics, partially observed Markov process, pathogen transmission, POMP model, supplemental feeding, test and remove, Yellowstone, zoonotic

## 1 | INTRODUCTION

Controlling disease spread is especially problematic in the case of wide-ranging wildlife populations. Part of the problem is that disease surveillance typically relies on serological testing, the results of which can only be properly interpreted within the context of a specific combination of test, host and pathogen (Gilbert et al., 2013). Assuming test accuracy, a common misconception is that positive serostatus denotes current infection. Instead, seropositivity indicates detectable antibodies due to previous exposure. Conversely, seronegativity could mean no exposure, recent exposure within the period required to seroconvert, or historical exposure followed by the loss of detectable antibodies. Evidence from human systems shows that antibodies to many pathogens decline in the months or years following infection (Edwards, 2005; Gijzen, Land, Goossens, Slobbe, & Bruggeman, 2002) and in cases like brucellosis long-term immunity can be retained in test-negative individuals through adaptive cell-mediated responses (Yingst & Hoover, 2003). Consequently, serostatus alone is not a reliable indicator of infection status, especially when antibodies are short-lived relative to the lifespan of the host. Such is the case with brucellosis in elk (*Cervus canadensis*), caused by the bacterium *Brucella abortus*. Detectable antibodies are lost over time, and modelling results suggest that immunity to reinfection may be retained (Benavides et al., 2017).

'Brucellosis' refers to infection by members of the genus *Brucella* and is one of the most common zoonotic diseases worldwide (Boschioli, Foulongne, & O'Callaghan, 2001). In the Greater Yellowstone Ecosystem of the western USA, elk and bison (*Bison bison*) are reservoirs of *B. abortus* which arrived with cattle over a century ago (Meagher & Meyer, 1994). There is low spillover risk from bison to cattle (National Academies of Sciences, Engineering, & Medicine, 2017) despite seasonal movements of bison out of the park as influenced by climate and population size (Kilpatrick, Gillin, & Daszak, 2009). Elk, however, are widely distributed inside and outside the park, and brucellosis periodically spills back from elk to cattle (Kamath et al., 2016) at significant cost to the affected cattle industry. The pathogen is transmitted by direct contact with fetal tissues and fluids, resulting from disease-induced abortions (National Research Council, 1998). Live births from infected mothers can also cause horizontal transmission if other herd members inspect the newborn calf or birth tissues, although parturient elk sequester themselves and their newborn calves (Van Campen & Rhyan, 2010). Vertical transmission is not thought to be important. Bison and elk born to seropositive

mothers can have detectable antibodies, but these disappear after several months and do not provide lifelong immunity (Rhyan et al., 2009; Thorne, Morton, Blunt, & Dawson, 1978). Thus elk-to-elk and elk-to-cattle transmissions are most likely during and after abortion events, which primarily occur between March and May (Cross et al., 2015) and in the first year following infection (Thorne et al., 1978).

Elk-to-elk transmission of brucellosis is facilitated by 23 feedgrounds in Wyoming that aggregate large herds during part of the transmission season. Hay is provided daily at these diversionary locations to reduce depredation of private haystacks and minimize commingling with cattle in winter as part of a disease-risk mitigation strategy. Feedgrounds reduce local spillover risk to cattle in the short term (Brennan, Cross, Portacci, Scurlock, & Edwards, 2017), yet simultaneously contribute to disease persistence (Scurlock & Edwards, 2010). The seasonality of transmission, coinciding with winter feeding and high site fidelity of elk to particular feedgrounds, creates a metapopulation structure where feedground herds are subpopulations within which brucellosis circulates. This presents a fortuitous study system for investigating the drivers of pathogen transmission. Drivers can be broadly categorized as those that are exogenous, or 'external' to the host and pathogen, like climatic variables, and those that are endogenous, or 'internal', like vital rates or epidemiological processes. Interactions between the two can make it difficult to infer the underlying processes from the observed serological patterns (Koelle & Pascual, 2004; Paull et al., 2017). In the context of a metapopulation, strong environmental forcing might generate a Moran effect, with strong synchrony in outbreak size or timing across subpopulations (Moran, 1953). Yet, if disease trends are sensitive to stochasticity, vital rates, or epidemiological rates, then we might instead expect asynchrony despite common external forcing (Rohani, Earn, & Grenfell, 1999). Exogenous effects also depend on conditions within the host population. Strong forcing could facilitate pathogen transmission, but not if herd immunity is already high.

Previous work suggested that deep snowpack increases elk-to-elk brucellosis transmission (Cross, Edwards, Scurlock, Maichak, & Rogerson, 2007) and that dispersing haypiles across greater area on the feedground could reduce elk density by 83% and contagious contacts by 91% (Creech et al., 2012). The Wyoming Game and Fish Department (WGFD) has thus experimented with 'low-density feeding' in addition to a test-and-slaughter programme during late winter from 2006 to 2010 at three feedgrounds. The effectiveness of these actions had not been fully evaluated, which motivated our current work. We modelled the underlying infection dynamics of brucellosis in free-ranging, winter-fed elk using compartmental

SIR models and explored the relative influences of demographic and environmental drivers on transmission. This provided a baseline understanding of seroprevalence trends within a metapopulation context while accounting for the ambiguity of serological status. Against this backdrop, we assessed two management interventions in relation to their intended effectiveness in reducing disease prevalence: 'low-density' feeding and test-and-slaughter.

## 2 | MATERIALS AND METHODS

### 2.1 | Study area and data collection

Our study area is western Wyoming, south of Yellowstone National Park, USA, at winter feedgrounds that are used by approximately 80% of the region's elk annually (Figure 1; Dean et al., 2004). Elk captures occurred principally in February of each year for the purpose of disease surveillance. Blood was drawn only from female elk because males are insignificant as vectors of infection (National Research Council, 1998). Serological testing was performed in accordance with the National Veterinary Services Laboratory protocols as described by Maichak et al. (2017). Elk calves were excluded from serological testing. Serologic test results were aggregated by site and year. Greys River, Dell Creek, and Muddy Creek feedgrounds each had 15–25 years of serology data with robust sample sizes, despite periodic gaps (Table S1). Demographic data included adult counts by sex and the number of calves present. Attendance at these feedgrounds ranged from 100 to 700 adult female elk per year. Counts and age/sex classifications were recorded during peak-winter along feedlines, when feedground attendance by elk is presumed highest. One additional feedground, Scab Creek, provided sufficient data with which to test our top model and parameter estimates.

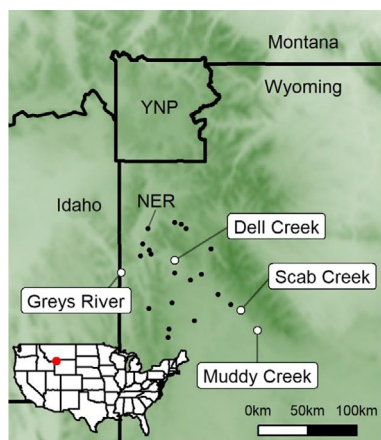
Beginning in 2009 'low-density' feeding practices were adopted at Greys River feedground. Reliable feed distribution and elk density

data were unavailable and so we characterized the experimental treatment as a categorical (before-and-after) variable. Test-and-slaughter of seropositive female elk took place at Muddy Creek and Scab Creek, where capture and testing rates ranged from 29% to 62% of attending female elk per year (Table S2; Scurlock, Edwards, Cornish, & Meadows, 2010). At Muddy Creek 107 seropositive female elk were removed over 5 years (2006–2010) when the female count averaged 260. At Scab Creek, 58 seropositive female elk were removed over 2 years (2009–2010) when the female count averaged 486.

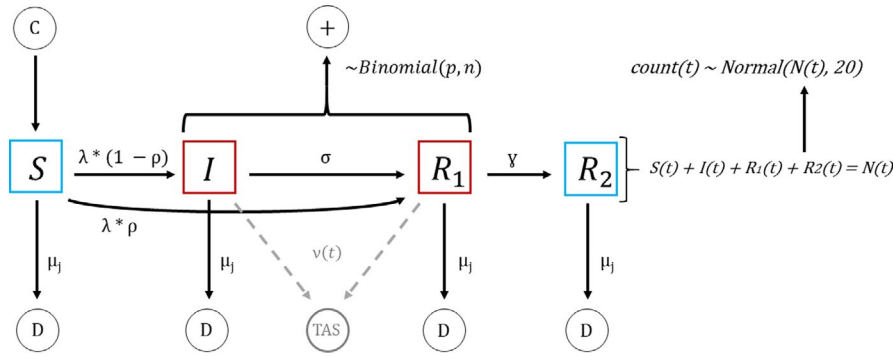
### 2.2 | Partially observed Markov process models

Deterministic compartmental models are central to the study of disease dynamics. Although statistical inference is simpler with deterministic models, 'many infectious systems are fundamentally individual-based stochastic processes, and are more naturally described by stochastic models' (Roberts, Andreasen, Lloyd, & Pellis, 2015). Partially observed Markov process (POMP) models combine the mechanistic processes in compartmental SIR models with probabilistic models linking the observed data to the latent process (King, Nguyen, & Ionides, 2016). Our latent process was a four-compartment model (Figure 2), alternatively described as a series of discretized equations (Supporting Information). We modelled a discrete-time process at annual intervals because disease transmission and birth pulses are seasonal and infected females are likely to abort, and thus transmit infection, in the following year. Additionally, 90% of our data were collected in February, a length of time less than the average time to seroconvert following exposure (Thorne et al., 1978) and prior to peak transmission season (Cross et al., 2015).

The compartments of our models include susceptible and seronegative ( $S$ ), infected, infectious, and seropositive ( $I$ ), seropositive but no longer abortive ( $R_1$ ) and seroreverted–seronegative and recovered with immunity ( $R_2$ ). Entry occurs via calf recruitment. Because we modelled female elk only, the number of calves ( $C$ ) in year  $t$  was the number observed divided by two under the assumption of equal sex ratio in calves (Johnson, 1951). Hunting is the dominant source of mortality in this population and so individuals across all compartments experienced an equal probability of mortality  $\mu_j$  within each defined period of the timeseries ( $j = 1-3$  periods depending on feedground) when there was a new management objective for that hunt unit. Susceptibles are exposed at a rate corresponding to the force of infection ( $\lambda$ ), but not all that are exposed and seroconvert become infectious (abort), which allows a proportion to transition straight from  $S$  to  $R_1$  ( $\rho$ ). Elk that do become infectious recover with probability  $\sigma$  and detectable antibodies are lost with probability  $\gamma$ . Because serology does not distinguish between compartments  $I$  and  $R_1$ , the test-and-slaughter models (Muddy Creek and Scab Creek) included  $v$ , the probability of seropositives exiting  $I$  and  $R_1$  in years with removals. Conditional on being in compartments  $I$  and  $R_1$ , the probability of removal was equal to the proportion of females captured for testing at a feedground in a given year. This approach is integer-based, therefore probabilities and rates were incorporated into the process model using random draws



**FIGURE 1** Wyoming has 23 winter feedgrounds for elk located south of Yellowstone National Park (YNP). The National Elk Refuge (NER) is operated by the U.S. Fish and Wildlife Service, while the remainder is operated by the Wyoming Game and Fish Department. Greys River, Dell Creek, Muddy Creek and Scab Creek feedgrounds contributed to our analyses



**FIGURE 2** Flow diagram for the disease process model with four compartments: S, susceptible; I, infectious; R<sub>1</sub>, recovered but seropositive; and R<sub>2</sub>, having lost detectable antibodies and immune. Seropositive states outlined in red; seronegative in blue. Female elk are born naïve and enter via calf recruitment (C). All compartments experience an equal period-dependent probability of mortality ( $\mu_j$ ). Susceptible elk are exposed at a rate corresponding to the force of infection ( $\lambda$ ), but not all elk that seroconvert will abort, which allows a proportion ( $\rho$ ) to transition straight from S to R<sub>1</sub>. Recovery occurs with probability  $\sigma$  and detectable antibodies are lost with probability  $\gamma$ . Conditional on being seropositive, the probability of removal  $\nu(t)$  for test-and-slaughter (TAS) models equaled the proportion of the herd captured for testing in a given year. The measurement model assumed that the number of positive tests (+) was a binomial draw and the probability of the observed female elk count was drawn from a normal distribution

from an eulermultinomial distribution within the software package ‘POMP’ (King et al., 2018) in R (R Core Team, 2018).

The force of infection,  $\lambda$ , took one of three basic forms each corresponding to a model where transmission was internally driven (endogenous), driven by climate (exogenous), or driven by both factors (combination). In the endogenous model, we assumed  $\lambda_1$  is equal to the product of a constant transmission parameter  $\beta$ , and the sum of the annual number of infected I and imported infections from outside the herd  $i$ , divided by the population size  $N$  raised to a scaling parameter  $\theta$ . The scaling parameter describes the degree to which the transmission process is density-dependent ( $\theta = 0$ ) or frequency-dependent ( $\theta = 1$ ) (Cross et al., 2013). In the exogenous forcing model, we assumed  $\lambda_2$  is related to a winter severity covariate  $\psi$  that varied annually and by feedground. The final form was a combination of the previous two.

$$\lambda_1(t) = \frac{\beta [I(t) + i]}{N(t)^\theta} \quad \text{endogenous}$$

$$\lambda_2(t) = \frac{[\beta' * \psi(t)] [I(t) + i]}{N(t)^\theta} \quad \text{exogenous}$$

$$\lambda_3(t) = \frac{\{\beta + [\beta' * \psi(t)]\} [I(t) + i]}{N(t)^\theta} \quad \text{combined}$$

The observed process was the number of seropositive test results divided by the total number tested for a given feedground in a given year (‘apparent seroprevalence’). The probability of the data (number of seropositive test results) in year  $t$  was binomially distributed and conditional on the probability  $p(t)$ , which was the ‘true seroprevalence’ from the latent process and  $n(t)$ , the total number of tests. We also modelled female elk counts to ensure that our model predictions conformed both to the observed disease and population trends. Observed counts were modelled as a draw from a normal distribution with a mean at the ‘true population size’  $N$  (the sum of the four compartments), and

a standard deviation of 20, which represents approximately 5% of an intermediate-sized feedground herd.

### 2.3 | Incorporating winter severity

Based on previous studies, we expected that environmental conditions causing larger elk aggregations for longer periods during late winter should result in more transmission (Creech et al., 2012; Cross et al., 2007). We thus tested models in which ‘heavy snow’ and ‘late green-up’ contributed to environmentally-driven transmission ( $\psi$ ) via the force of infection. Snow-depth data were unavailable across the temporal and spatial extent of our study area so we used snowmelt water equivalent (SWE) values from nearby SNOTEL sites for each feedground between March and June. These values were strongly correlated with one another across sites within each year (Figure S8). We summed the SWE values of the first day in each of these months to arrive at a single value per site and year.

Often the nearest SNOTEL stations are several kilometers from the feedground and hundreds of meters higher in elevation, so we also calculated green-up metrics using normalized difference vegetation index (NDVI) MODIS data and the  $3 \times 3$  square of pixels around each feedground where each pixel was  $250 \times 250$  m. We excluded pixels that included roads or buildings. We fit double logistic curves to NDVI time series to calculate these metrics following the methods of Bischof et al. (2012) and Merkle et al. (2016). Metrics were strongly correlated so we only investigated the date of ‘spring start’, which we defined as the peak values of the second derivative of the spring side of the NDVI curve (Johnston, Beaver, Merkle, & Chong, 2018). Annual SWE values were standardized across the years 1991–2018 for each SNOTEL station corresponding to an individual feedground, whereas NDVI values were standardized across 2000–2017 (beginning when these data were first available). Standardized values were then exponentiated because  $\lambda$  is a rate, which cannot be negative.

## 2.4 | Candidate models

All of our models follow the four-compartment plan (Figure 2). Alternative models featuring no seroreversion or seroreversion without retained immunity did a poor job of describing the data and received less support using AIC in a preliminary analysis (Figures S1, S2). The possibility of a 'low-density feeding' treatment effect was tested at Greys River feedground with models where  $\lambda$  was allowed to vary 'before' and 'after' treatment initiation in 2009. Testing all possible combinations for a time-dependent low-density feeding treatment effect yielded five additional models (Table S3).

## 2.5 | Inference, comparison, and constraints

We used sequential Monte Carlo to obtain the log likelihood following the maximum-likelihood approach of Ionides, Nguyen, Atchadé, Stoev, and King (2015), and iterated filtering in the software package 'POMP' (King et al., 2018). A broad exploration of parameter space was initiated using 100 sets of parameter values, with each value drawn from a uniform distribution. Likewise, initial starting conditions were generated for the four compartments (full details in Supporting Information). During iterative filtering ('MIF2' in 'POMP'), all parameters were perturbed except  $\rho$  and  $\gamma$ . We used 20,000 particles, 800 iterations and 20 replicates. For each replicate, we ran 20 particle filters with 20,000 particles to calculate the log likelihood and standard error of the Monte Carlo approximation. The standard error for the log likelihoods of all models was  $<0.1$ .

With limited data at Scab Creek, we used it to test our top model and a reduced range of parameter estimates based on the results of other feedgrounds. Diagnostic checks included monitoring the effective sample size of our filtering procedure, the conditional log likelihood at the last iteration of the MLE search and traceplots of the parameter estimates. We calculated the Akaike information criterion (AIC) and Akaike model weights (Burnham & Anderson, 2002), using the MLEs of each model for comparison. We further assessed parameter uncertainty following the methods of King, Cellès, Magpantay, and Rohani (2015; see Supporting Information).

## 2.6 | Testing expectations of synchrony

Assuming heavy snowfall causes elk to aggregate, thereby increasing transmission, we expected synchronous seroprevalence trends across feedgrounds because all feedgrounds experienced synchronous snowfall (Figure S8). Following model comparison, we simulated three hypothetical subpopulations with varying demographic rates and projected count and seroprevalence trends out 100 years to explore if we should expect synchronous trajectories across subpopulations. Hypothetical subpopulations received the same starting size ( $N = 400$ , female only) and initial conditions of the four disease compartments. We used the MLE values of parameters from the endogenous, exogenous and combined models for Greys River and held them constant across space and time. We used identical climate

values for each subpopulation, which was a vector sampled with replacement from our Greys River SWE data. Calf recruitment in year  $t$  was a random draw that broadly encompassed a plausible range of calf recruitment values from Rocky Mountain elk populations across the Western U.S. ( $\sim$ Uniform(0.1, 0.4); Raithe, Kauffman, & Pletscher, 2007) multiplied by the subpopulation size in year  $t$ . Mortality ( $\mu$ ) varied by subpopulation but was time-constant and took values (1/8, 1/9, and 1/10) that were found to yield decreasing, stable, or increasing count trends across subpopulations. Additional sources of stochasticity were (a) a multinomial draw on the number of new infectives at each time step, and (b) infectious individuals were imported as a Bernoulli draw with an annual probability corresponding to rate  $\iota$ . We compared the projections of our three transmission models.

## 2.7 | Comparing test-and-slaughter with other possible regimes at Muddy Creek

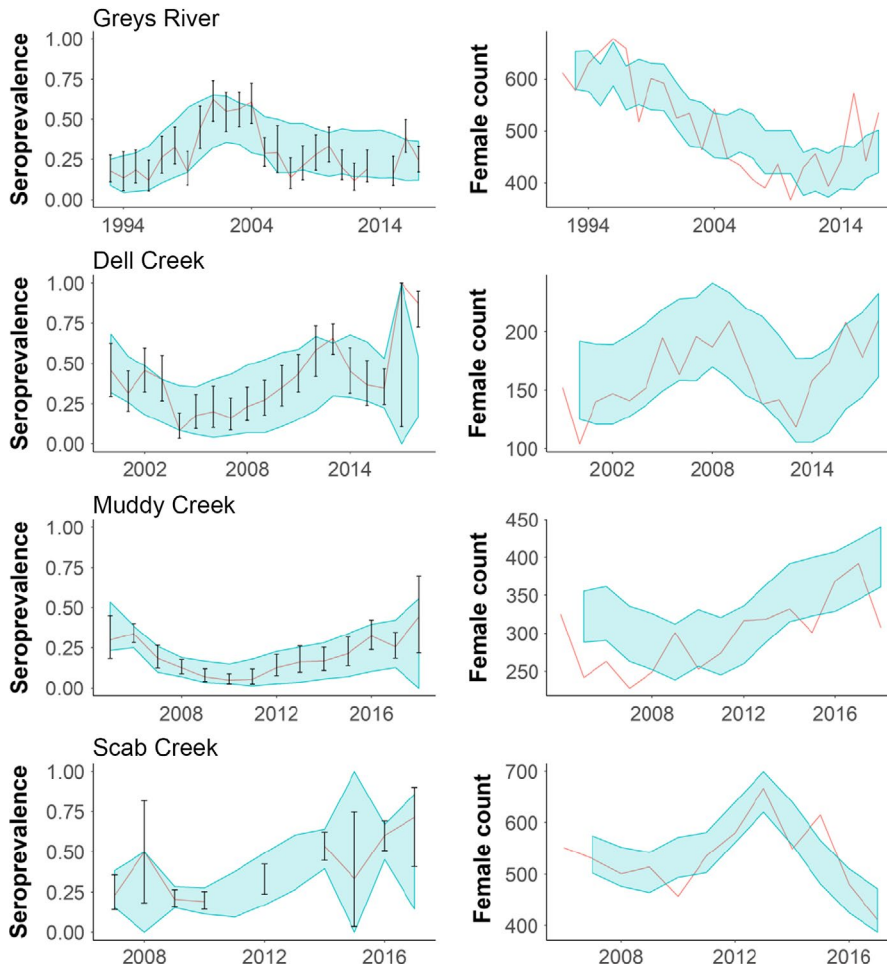
Using the MLE parameter values for our endogenous model at Muddy Creek, we estimated the number of abortive elk ( $I$ ) over the modelled 15-year period and constructed 90% prediction intervals, using the 5% and 95% quantiles of 2000 simulations of the model. We repeated this process for three hypothetical management regimes over the same time period: (a) no slaughtering; (b) slaughtering seronegative elk only; (c) indiscriminate culling. Removals (options 2 and 3) were set to maintain population sizes comparable to those observed when only seropositive female elk were slaughtered. Finally, we calculated the difference of median estimates over time between the 4 regimes and estimated the number of infectives removed during test-and-slaughter.

## 3 | RESULTS

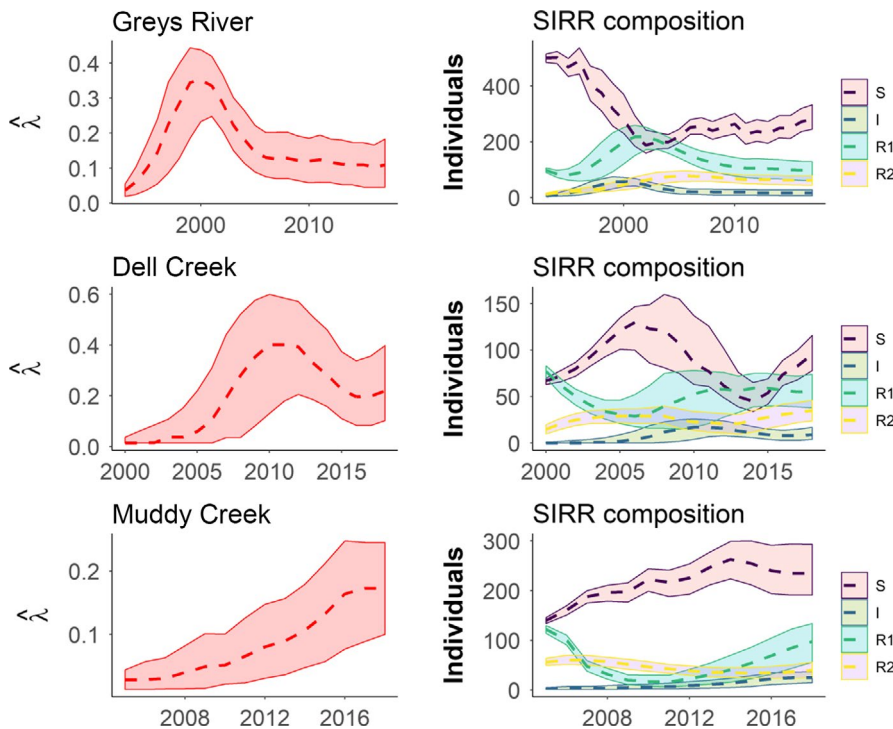
We found substantial temporal variability in seroprevalence within individual feedground herds suggesting recurrent outbreaks (Figure 3) that were asynchronous across subpopulations. At Greys River feedground, the site for which we had the most years of data, the endogenous model received the highest support by AIC, while at Dell Creek and Muddy Creek, exogenous models received similar model weight to the alternatives (Table S5). Substituting vegetation green-up for snow data did not substantially alter these results (Table S6), except that the exogenous model received stronger support at Dell Creek. This might suggest that NDVI improved on SWE for modelling. The incorporation of a treatment effect from low-density feeding practices at Greys River failed to improve model fit. There were insufficient data at Scab Creek to perform a formal model comparison, but the endogenous model and parameter estimates from other feedgrounds were in rough agreement (Figure 3).

Because  $\lambda$  depends on the relative fraction of susceptible and infectious individuals, it can vary substantially over time despite a constant transmission term (Figure 4). By simulating with the parameter





**FIGURE 3** Time series simulations for endogenous models at four feedgrounds showing disease trends (left) and female elk count trends (right). Red lines denote observed data; black error bars represent 90% binomial confidence intervals; blue shading indicates 90% prediction intervals from 2000 stochastic simulations with parameter values set at the maximum likelihood estimate



**FIGURE 4** Predictions from the endogenous models for Greys River (top), Dell Creek (middle), and Muddy Creek (bottom). Left, estimated force of infection over time with parameter values set at the maximum likelihood estimate. Right, corresponding estimates of the number of individuals in each of the four compartments over time for *S* (susceptibles), *I* (infecteds), *R*<sub>1</sub> (recovereds), and *R*<sub>2</sub> (lost antibodies, immune). Dashed lines represent median estimates and 90% prediction intervals from 2000 simulations are shaded

**TABLE 1** Model results using full time series and snowmelt water equivalent data as environmental covariate. At Greys River the endogenous model with a constant transmission term,  $\beta$ , received the greatest support by Akaike information criterion (AIC) and Akaike model weight. At Dell Creek and Muddy Creek, all three models were <2 dAIC different. The effect of a 'low-density' feeding treatment was tested with 5 models at Greys River, the only one of the three feedgrounds to adopt the practice

Feedground	Model	loglik	AIC	dAIC	Weight
Greys River	Endogenous	-64.22	152.44	—	0.75
Greys River	Endogenous, LD treat.	-63.94	155.88	3.44	0.13
Greys River	Combined	-65.40	156.79	4.35	0.08
Greys River	Combined, LD treat. B	-64.81	159.63	7.19	0.02
Greys River	Combined, LD treat. C	-65.83	161.65	9.21	0.01
Greys River	Combined, LD treat. A	-65.72	163.45	11	<0.01
Greys River	Exogenous	-69.90	163.80	11.36	<0.01
Greys River	Exogenous, LD treat.	-70.78	169.56	17.11	<0.01
Dell Creek	Exogenous	-45.99	115.97	—	0.44
Dell Creek	Endogenous	-46.07	116.15	0.17	0.4
Dell Creek	Combined	-45.97	117.94	1.97	0.16
Muddy Creek	Exogenous	-32.63	87.25	—	0.45
Muddy Creek	Combined	-32.10	88.20	0.94	0.28
Muddy Creek	Endogenous	-33.12	88.24	0.99	0.27

values at the MLE, it becomes apparent that relatively few infective elk are needed to achieve high levels of seroprevalence. This is consistent with the difficulty in detecting abortions at the feedgrounds and previous work which estimated that 16% of seropositive elk abort in any given year (95% CI: 0.10, 0.23; Cross et al., 2015).  $I$ , which we defined as abortive in our models, provided this additional point of comparison. Indeed, the sum of  $I/(I+R_1)$  for the full time series of the endogenous models from 2000 stochastic simulations had a median of 16.6% at Greys River (90% prediction interval (PI): 0.14, 0.19), 13.6% at Dell Creek (90% PI: 0.08, 0.18), and 17.0% at Muddy Creek (90% PI: 0.12, 0.20). Our models consistently estimated quick transitions from  $I$  to  $R_1$ , indicating that the majority of elk that do abort only do so in the first year following infection, consistent with work on captive elk (Thorne et al., 1978; see Supporting Information; Table 1).

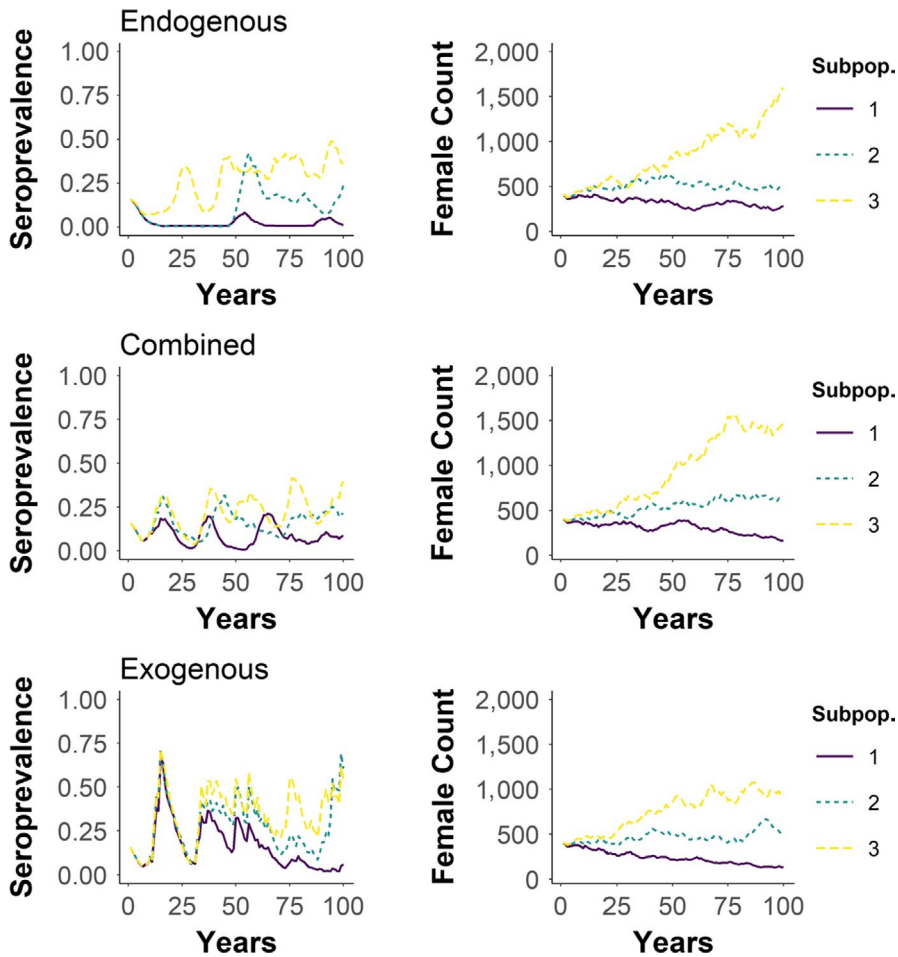
Our simulation revealed that if demographic rates vary between feedgrounds then asynchronous disease trends can emerge even when synchronous exogenous forces drive  $\lambda$ . As expected, the endogenous model predicted the greatest asynchrony across sites, but all models generated increasing asynchrony as time progressed and population growth trajectories diverged (Figure 5).

At Muddy Creek, we estimate that of 107 seropositive elk that were removed over 5 years, only 6 were infective, but this prevented an additional 20 infections in the following 8 years. These effects translate to two fewer infectives in the remaining population per year compared to models without test-and-slaughter (Figure 6). Annually removing 10% of female seronegative elk during the same 5-year period was predicted to generate a similar reduction to the number of infectives present during control efforts, but yield additional benefits over the remaining time period (37 fewer infectives compared to seropositive removal). The simulation of culling without

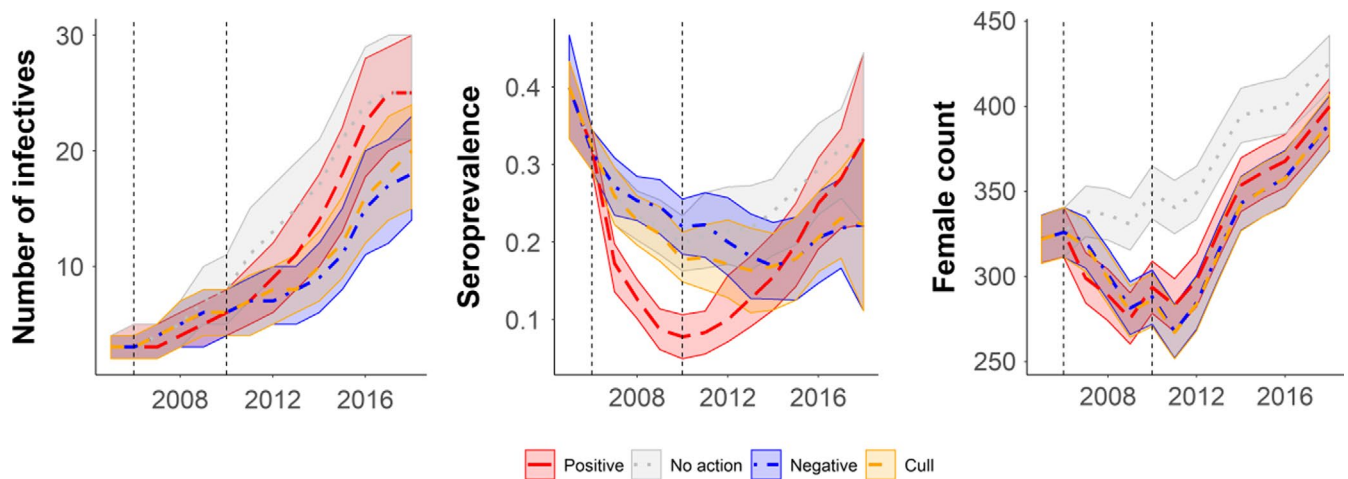
regard to serostatus of 7.5% of female elk per year fell between the other two predictions: it achieved fewer infectives compared to slaughter of seropositive elk, but underperformed compared to seronegative slaughter.

## 4 | DISCUSSION

We found brucellosis seroprevalence trends that were asynchronous across elk subpopulations despite their exposure to similar environmental forcing. Our mechanistic modelling tackled the 'inverse problem' of inferring the latent processes from the observed serological dynamics. Although brucellosis is widely considered a chronic ailment (Ahmed, Zheng, & Liu, 2016), our results suggest that disease transmission may be brief, followed by recovery. The time to seroconversion following exposure (approximately 1 month), the timing of testing (prior to disease-induced abortions), and the chances that a newly infected elk will actually abort (approximately 50%), along with quick recovery time and lifelong immunity, all contribute to a situation in which targeting seropositives rarely removes infectious individuals. Though at first counterintuitive, it follows that removing seronegative elk would have longer-term protective effects. This is consistent with brucellosis work in bison suggesting that the loss of herd immunity created by removal of seropositive individuals can result in ricochet effects (Ebinger, Cross, Wallen, White, & Treanor, 2011). Timing of interventions is also paramount. It appears that test-and-slaughter at Muddy Creek coincided with a 'fadeout period' when seroprevalence was high, but declining. Therefore, the number of infectious elk was low (Figure 4). If removals instead targeted seronegative elk when seroprevalence is high, this would drive



**FIGURE 5** Simulations for three hypothetical subpopulations over 100 years under the same starting conditions, including initial population size and disease parameters, but with varying death and replacement. The model drivers are endogenous (top), exogenous (bottom) and both combined (middle)



**FIGURE 6** Left: the estimated number of infective elk present at Muddy Creek feedground during 2005–2018 including 5 years of management intervention (2006–2010, denoted by vertical dashed lines) with four management options: test-and-slaughter of all seropositive female elk (red); no action (grey); test-and-slaughter of 10% of seronegative female elk (blue); indiscriminate culling of 7.5% of female elk (orange). Center: corresponding estimates for seroprevalence under the four regimes. Right: corresponding female count estimates. Coloured dashed/dotted lines represent median estimates; shaded areas are 50% prediction intervals from 2000 simulations

a spike in seroprevalence but a decline in newly infected elk, a longer period with reduced spillover risk, and thereafter a decline in seroprevalence. Achieving public support for such action might

require substantial outreach. Alternatively, sustained culling without regard to serostatus (through increased hunter harvest) might garner wider support. This result stands in contrast to a finding



that hunting can increase disease prevalence (Choisy & Rohani, 2006), but which involved a region of the parameter space that is unlikely in our system (large annual fluctuations in host population size and rapid, explosive spikes in prevalence).

Based on the simulation results of our hypothetical herds, we should not necessarily expect synchronous seroprevalence trends even in scenarios with strong climate forcing. Outbreaks might periodically align following severe winters, but intervening years exhibit asynchrony like that detected in the actual seroprevalence data. Severe winters can only trigger outbreaks if a large pool of susceptible female elk already exists. This underscores the importance of birth rate and population turnover to the disease dynamics of this system. These findings are consistent with existing literature (Lloyd & Sattenspiel, 2010), yet ours is the first application for long-lived, free-ranging wildlife. Lastly, we found no evidence that 'low-density feeding' has reduced the force of infection at Greys River feedground. Additional data on elk density and feed distribution would permit more explicit modelling. The course of an outbreak for any one of our subpopulations appears to exceed a decade, and our longest time-series was 25 years. In that context, small treatment effects may be difficult to detect.

These findings prompt a review of the options for reducing brucellosis transmission among feedground elk. A vaccination programme persisted at feedgrounds for decades, in part because its implementation coincided with a brief dip in seroprevalence, although it was later deemed ineffective (Maichak et al., 2017). Further vaccine development is hampered by the USDA's Select Agent Status for *Brucella* spp. (National Academies of Sciences, Engineering, & Medicine, 2017). Quarantine is infeasible for free-ranging elk and wide-scale fencing is problematic (Mysterud & Rolandsen, 2018). In general, removing infectives should reduce contagion in situations where 'infectiousness' can be accurately identified, rates of capture and monitoring are high, and mixing with other populations is minimal. Although all these conditions can exist in some wildlife systems (Garwood, 2018), it is more common that the inability to meet one or all of them diminishes the efficacy of this practice (Wolfe, Watry, Sirochman, Sirochman, & Miller, 2018).

Managing brucellosis in elk is ultimately about limiting risk to cattle because the disease does not pose a major threat to elk abundance. This means minimizing the risk of cattle encountering elk fetuses from brucellosis-induced abortions. Although feedgrounds contribute to the persistence of this dilemma, suggestions of closing them have met with opposition. After all, the feedgrounds divert elk from areas of their winter range where they would commingle with cattle. Our models suggest that this seasonal sequestration has created subpopulations (different feedground herds) within which recurrent brucellosis outbreaks occur, and when local seroprevalence is high the period of greatest spillover risk has likely passed. This reframing of risk, combined with spatial modelling of resource selection, should help identify risky times and places for cattle (Merkle et al., 2018). Finally, scavengers are effective in removing infective tissues (Maichak et al., 2009) and so conserving the scavenger guild is likely beneficial for reducing brucellosis contagion on open

rangeland. Nevertheless, these options remain limited while brucellosis is spreading through the growing elk populations in the GYE. Also, chronic wasting disease (CWD) has recently arrived to the GYE and so management actions aimed at controlling one will necessitate consideration of the impacts on both. For example, CWD could create a younger age structure and reduce population growth, but any management efforts to maintain the total abundance of (younger) elk could increase the frequency and intensity of brucellosis outbreaks. Our findings emphasize a need to move beyond traditional control measures and should serve as a warning to agencies that face the possibility of increasing brucellosis infections in elk elsewhere in North America or red deer (*Cervus elaphus*) in other countries. If infected subpopulations become interconnected then eradicating this troublesome disease could quickly become impossible without extremely costly and controversial culling campaigns.

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## AUTHORS' CONTRIBUTIONS

G.G.C., P.C.C., J.D.R., B.M.S. and J.T.d.T. conceived the idea for this article. Data acquisition was performed by J.A.M., J.D.R. and B.M.S. The article was primarily written by G.G.C., P.C.C. and J.T.d.T. All authors contributed critically to the drafts and gave final approval for publication.

## DATA AVAILABILITY STATEMENT

Data and supporting code available via USU Digital Commons <https://doi.org/10.26078/f0fc-jw55> (Cotterill, du Toit, & Cross, 2019).

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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