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Decision-making for mitigating wildlife diseases: From theory to practice for an emerging fungal pathogen of amphibians

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Abstract

1. Conservation science can be most effective in its decision-support role when seeking answers to clearly formulated questions of direct management relevance. Emerging wildlife diseases, a driver of global biodiversity loss, illustrate the challenges of performing this role: in spite of considerable research, successful disease mitigation is uncommon. Decision analysis is increasingly advocated to guide mitigation planning, but its application remains rare.
2. Using an integral projection model, we explored potential mitigation actions for avoiding population declines and the ongoing spatial spread of the fungus *Batrachochytrium salamandrivorans* (*Bsal*). This fungus has recently caused severe amphibian declines in north-western Europe and currently threatens Palearctic salamander diversity.
3. Available evidence suggests that a *Bsal* outbreak in a fire salamander (*Salamandra salamandra*) population will lead to its rapid extirpation. Treatments such as antifungals or probiotics would need to effectively interrupt transmission (reduce probability of infection by nearly 90%) in order to reduce the risk of host extirpation and successfully eradicate the pathogen.
4. Improving the survival of infected hosts is most likely to be detrimental as it increases the potential for pathogen transmission and spread. Active removal of a large proportion of the host population has some potential to locally eradicate *Bsal* and interrupt its spread, depending on the presence of *Bsal* reservoirs and on the host's spatial dynamics, which should therefore represent research priorities.

Stefano Canessa and Claudio Bozzuto contributed equally.
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5. *Synthesis and applications*. Mitigation of *Batrachochytrium salamandrivorans* epidemics in susceptible host species is highly challenging, requiring effective interruption of transmission and radical removal of host individuals. More generally, our study illustrates the advantages of framing conservation science directly in the management decision context, rather than adapting to it *a posteriori*.

KEYWORDS

amphibian, *Batrachochytrium salamandrivorans*, chytrid fungus, conservation management, disease spread, epidemiology, host–pathogen, integral projection model, salamander, transmission

1 | INTRODUCTION

Conservation biology has been called a "crisis discipline" aimed at solving problems about declining species (Soulé, 1985). Such problems typically consist of understanding how to manage natural systems, and conservation science seeks to suggest solutions by providing relevant information (Arlettaz et al., 2010). This decision-support role is best performed by trying to find answers to clearly formulated questions directly relevant to ecosystem management ("strong inference"; Burnham & Anderson, 2001; Chamberlin, 1890; Platt, 1964), rather than simply by collecting data and seeking patterns a posteriori (Nichols & Williams, 2006).

A particularly challenging problem for conservation science is the development of responses to emerging infectious diseases, which are increasingly driving biodiversity loss worldwide (Fisher et al., 2012). Infectious diseases often demand rapid decision-making in the face of scarce knowledge, limited time for learning, and challenges turning the available scientific knowledge into actions (Grant et al., 2017). For example, the amphibian chytrid fungus *Batrachochytrium dendrobatidis* was identified about 20 years ago (Longcore, Pessier, & Nichols, 1999); its role in global amphibian declines was clarified over the following decade (Skerratt et al., 2007); potential mitigation strategies were then considered (Scheele et al., 2014; Woodhams et al., 2011), yet to date implementation has been rare and success in maintaining susceptible populations of amphibians in the pathogen's presence remains elusive (Bosch et al., 2015; Geiger, Bregnard, Maluenda, Voordouw, & Schmidt, 2017). For this reason, a more critical evaluation of potential mitigation strategies for amphibian chytridiomycoses has been recently advocated (Garner et al., 2016; Grant et al., 2017), with the use of specific decision-analytic methods to assess research priorities and plan management actions (e.g. Converse et al., 2016; Gerber et al., 2017). The lack of applications of decision analysis in the treatment of emerging wildlife diseases such as amphibian chytridiomycoses contrasts with its common application in human healthcare management (e.g. Claxton & Sculpher, 2006; Nutt, King, & Phillips, 2010; Smith, Hillner, & Desch, 1993). However, this implementation gap may occur because conservation managers, researchers and decision-makers remain unsure about what a decision-analytic approach to emerging wildlife diseases entails and how to implement it in practice, including which research should be pursued to improve population viability.

Management decisions arise when, in order to achieve one or more objectives, a choice must be made among two or more alternative actions. Decision analysis is the ensemble of principles and methods to make such choices rationally in the face of uncertainty (Keeney, 1982). All revolve around a basic, iterative process: (1) state the decision problem at hand; (2) identify the key management objectives, with associated measures of success; (3) list the potential actions available; (4) use a model of the system to predict the expected outcome of respective actions, measured against the objectives; (5) recognise uncertainty and solve trade-offs; (6) make and implement a decision. To summarize, decision analysis requires science to perform its "strong inference" role firmly in the management decision context, with explicit statements about objectives, formalization of current (prior) knowledge and comparable predictions of the outcomes of management actions.

In this study, we put in practice this approach as advocated by recent studies (Garner et al., 2016; Grant et al., 2017; Russell, Katz, Richgels, Walsh, & Grant, 2017), following the decision-analytic process to explore the potential effect of mitigation actions for the recently discovered salamander chytrid fungus *Batrachochytrium salamandrivorans* (*Bsal*; Martel et al., 2013). Strong evidence suggests that this fungus is native to Asia and causes lethal chytridiomycosis in several species of Palearctic salamanders, threatening to cause loss and disturbance of biodiversity in Europe and North America (Martel et al., 2014). The recent arrival of *Bsal* in Europe has been implicated in the collapse of several populations of fire salamanders (*Salamandra salamandra*) in the north-western range of this species (Spitzen-van der Sluijs et al., 2016). A recent model of the dynamics of host populations suggests a potential rapid spread of *Bsal* across the range of fire salamanders in Central Europe (Schmidt, Bozzuto, Lötters, & Steinfartz, 2017), requiring urgent management decisions. In the United States, which host amphibian populations at high risk from *Bsal* (Richgels, Russell, Adams, White, & Grant, 2016), pre-arrival actions to restrict the potential importation of infected salamanders are being implemented while proactive management is considered (Grant et al., 2016). Here, we focused on the possible management context at the invasion front and epidemic stage (sensu Langwig et al., 2015; note that for consistency with their classification, we use "epidemic" rather than "epizootic" throughout). We modelled the host–pathogen dynamics

in a population of a vulnerable salamander species to seek answers to a key management question: how, if at all, can a *Bsal* epidemic be locally managed?

2 | MATERIALS AND METHODS

2.1 | Problem definition

For our study, we evaluated a range of possible management actions to respond to an infectious disease outbreak. We used the European fire salamander *S. salamandra* as the target species, since it is a widespread species in Europe at great extinction risk from *Bsal* (Stegen et al., 2017). We considered the management of a single salamander population over a short time frame of 3 months, chosen on the basis of the rapid *Bsal*-driven population crashes in fire salamanders (Schmidt et al., 2017; Stegen et al., 2017). We assumed optimal climatic conditions for *Bsal* growth and transmission (Stegen et al., 2017). We envisaged management would have two general objectives: minimizing the risk of population extinction and minimizing the potential for further geographic disease spread.

2.2 | Predicting disease impacts: Integral projection model

Predictions of the outcomes of mitigation actions are generally based on a simplified representation of the system (a model). Most conservation actions rely on implicitly drawing predictions from previous successes and failures ("experience-based model"; Dicks, Walsh, & Sutherland, 2014); however, an explicit mathematical description of the system provides a stronger basis to compare and update current knowledge, identify key uncertainties and address trade-offs (Russell et al., 2017). We adapted the dynamical population model by Schmidt et al. (2017) into an integral projection model (IPM; Ellner & Rees, 2006; all equations in Appendix S1). An IPM is a generalization of a classic stage-structured population model, where demographic processes are described by one or more continuous covariate(s) rather than discrete stages. This makes IPMs particularly suitable for fungal infections, where rates are influenced both by infection status and infection load, the latter typically measured continuously using quantitative PCR (Wilber, Langwig, Kilpatrick, McCallum, & Briggs, 2016). As an initial template we used the IPM developed by Wilber et al. (2016) for *B. dendrobatidis*. We parameterized our model using formal expert elicitation and available data from the literature. Using these sources of information, we then modified model components to reflect on how management could seek to influence key processes to mitigate *Bsal* impacts.

The model considers two disease-related compartments, $S(t)$ and $I(z, t)$, respectively the number of (uninfected) susceptible and infected individuals at each time step t (Figure 1). Infected individuals are classified according to their infection load z (Equation S2). The transitions over time and between states are defined by several functions (Figure 1 and Equation S2); below, we provide a brief summary of all functions used in our IPM. Given the short time frame of our management scenario, reflecting the speed of *Bsal*-driven local population declines in fire salamanders, we focused on a period of the year where recruitment would be negligible, and we also excluded density-dependent mortality effects. We also did not include a "recovered" state or a loss-of-infection function (the probability that an individual transitions from infected to uninfected), since available evidence suggests fire salamanders are unable to clear *Bsal* infection (Stegen et al., 2017).

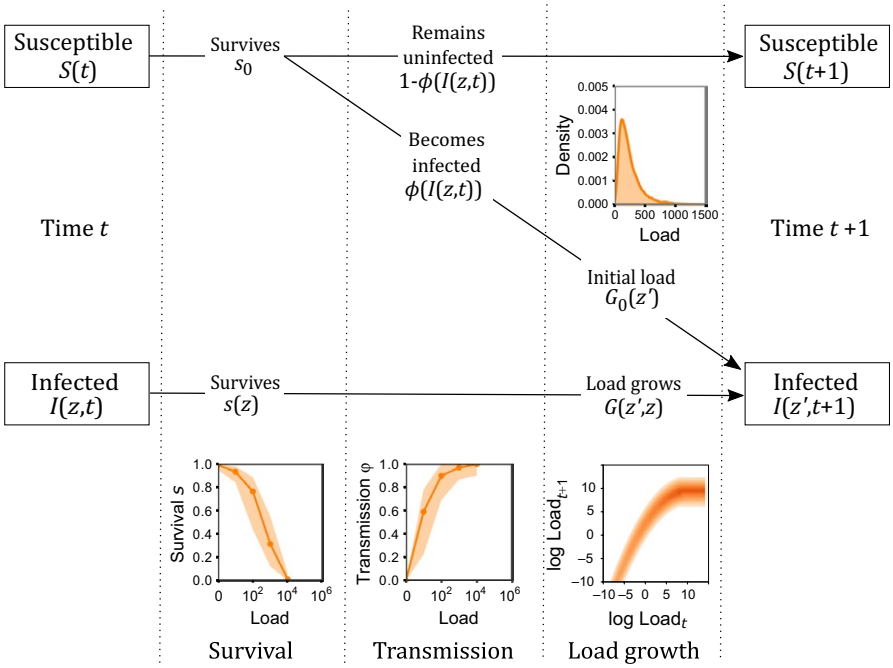

FIGURE 1 Summary flow chart for the fire salamander-*Bsal* integral projection model. The arrows indicate how hosts can transition within and between the susceptible and infected states from time t to time $t + 1$ (3 days apart); z and z' indicate infection loads at t and $t + 1$, respectively. Inserts represent the elicited parameter values; for Survival and Transmission (probability of transmitting infection from an infected to a susceptible host), curves indicate the most likely elicited values, with shaded areas indicating minimum–maximum ranges. For Initial Load, the insert represents the elicited probability distribution; for Load Growth, the insert represents the probability density function of *Bsal* load at time $t + 1$, given the load at time t

2.2.1 | Survival (Equation S4)

Parameter s_0 and the function $s(z)$ describe, respectively, the survival of uninfected and infected individuals from time t to $t + 1$. For infected individuals, survival is a function of the infection load z at time t.

2.2.2 | Transmission (Equations S3 and S5)

The function describes the probability that uninfected individuals at time t transition into the infected group at time $t + 1$, and depends on the load-related distribution of infected individuals in the population at time t and the load-dependent effect of infected individuals on the transmission probability. We assumed a mass-action, density-dependent transmission function for our population.

2.2.3 | Initial load (Equation S7)

$G_0(z')$ describes the probability density of individuals having an infection load z' upon infection.

2.2.4 | Load growth (Equations S8–S10)

$G(z', z)$ describes the probability density of infected individuals having an infection load z' at time $t + 1$, given load z at time t.

2.2.5 | Host movement

In addition to the dynamics of a closed population, we calculated—independently from these dynamics—how far *Bsal* would spread via infected dispersing individuals, given our current knowledge captured in the IPM functions. Starting with an initial load distribution $G_0(z')$, we calculated the life span of a pool of infected individuals given the load growth function and load-dependent survival (i.e. using the IPM kernel). We defined life span as the time taken for the cumulative survival probability to fall below 1%, so that, because of the initial load distribution, infected individuals would travel different distances before dying. Using this formulation, rather than the mean time to death for an infected individual, allows us to better express the uncertainty in the initial load function (see next section). We calculated the distance travelled by dispersing infected individuals based on their life spans and the mean distance travelled per day by fire salamanders in a typical central European habitat (Table S1).

To evaluate the ability to meet our objectives of minimizing the reduction in the density of susceptible individuals and pathogen spread, we calculated (1) the *Bsal* basic reproduction number R_0 ($R_0 < 1$ indicates a disease dying out, and $R_0 > 1$ implies a disease outbreak; see Wilber et al., 2016 for the derivation of R_0 as used in our study); (2) the ratio between the predicted final density of susceptible individuals under each action and the predicted density with neither infection nor mitigation; and (3) the movement distance of infected individuals.

2.3 | Parameterizing the model

Given the recent emergence of *Bsal* in Europe, its infection dynamics are not yet entirely understood, although information is rapidly being accrued. Therefore, we used a formal expert elicitation process to estimate the model parameters; this ensured that all evidence available was incorporated, while making explicit any additional uncertainty expressed by experts. We carried out the elicitation in a group of 10 experts (all listed co-authors except SC, CB and EG, who acted as facilitators) during a 4-day workshop, using a best-practice approach (Martin et al., 2012). For each parameter, each expert was initially asked to provide estimates individually (minimum, most likely and maximum values), then allowed to revise those after group discussions based on critically evaluated published and unpublished evidence. For the survival and transmission functions, experts were asked to estimate the respective probabilities at infection loads of 0, 10, 100, 1,000 and 10,000 genomic equivalents (a measure of infection load); for the initial load distribution, estimates of mean, dispersion and skewness; for the growth function, the maximum observable load and the load growth rate. Figure 1 shows a graphical depiction of the elicited values and fitted functions; further details can be found in Appendix S1, including parameter values in Table S1. The elicitation and discussion also highlighted limited knowledge of the contact rate among individual hosts (number of contacts within a 3-day period). We therefore chose to derive this parameter from the only published source describing a *Bsal* outbreak in the wild using individual host mark–recapture (Stegen et al., 2017). To this end, we used a final size relation for a simplified model (see Section 2.5). Details of the derivation are provided in Appendix S1.

2.4 | Predicting the outcomes of mitigation actions

To understand how management could seek to influence key disease processes, we considered a small set of potential management actions (Table 1), devised during our workshop and from literature (Garner et al., 2016; Grant et al., 2017; Scheele et al., 2014). Fundamentally, actions could be considered different combinations of modifications to pathogen transmission (reducing the probability that an uninfected individual becomes infected upon contact with an infected one), pathogen growth (slowing the growth of *Bsal* on infected individuals) and host density (reducing density prior to, or right after the arrival of *Bsal* in the population). Repeating the expert elicitation process, we thought critically about which model parameters each action would seek to modify, and by how much. Since no mitigation of *Bsal* has been attempted to date, the initial parameterization described above reflected a "no action" scenario, which we used as a baseline reference after group discussions among experts confirmed that the elicited functions approximated the dynamics observed in the field (Stegen et al., 2017). A further reference level was obtained by modelling the outcome metrics for an uninfected population. For all scenarios, we expressed uncertainty using probability distributions. Following a best-practice approach, we used beta-PERT distributions for all

TABLE 1 Summary of exploratory actions for *Bsal* mitigation and their implementation in the integral projection model. The column "Parameters modified" refers to the parameters in the integral projection model (IPM) equations (Appendix S1) and how they were modified to simulate the prospective management actions. "Data" indicate the modification that was applied directly to the values elicited from experts (e.g., the estimated transmission rates at different infection loads)

Action	Description	Parameters modified
(a) No action	Unmitigated course of *Bsal* outbreak in a population	—
(b) Improve body condition	Improve body condition of individuals, for example by food supplementation at larval stage, with the aim of increasing their resistance to infection at low infection burdens by 50%	$0.5 \cdot \beta(z)$ for $z \leq 100$ GE
(c) Probiotic treatment	Pre-emptive treatment of susceptible individuals, (a) increasing their resistance to infection at low infection burdens by 50%, and (b) slowing *Bsal* growth once infected by 80%	(a) $0.5 \cdot \beta(z)$ for $z \leq 100$ GE (b) $\lambda = (\sqrt[5]{0.2 \cdot \text{data}})^3$
(d) Antifungal treatment, perfect coverage	Treatment of both susceptible and infected individuals, (a) increasing the resistance of susceptible individuals to infection by 98%, and (b) slowing *Bsal* growth once infected by 80%	(a) $(1-0.98) \cdot \beta(z)$ (b) $\lambda = (\sqrt[5]{0.2 \cdot \text{data}})^3$
(e) Antifungal treatment, incomplete coverage	Treatment of both susceptible and infected individuals, (a) increasing the resistance of susceptible individuals to infection by 98% (only 80% of individuals in the population treated at each time step), and (b) slowing *Bsal* growth once infected by 80%	(a) $(1-0.80 \cdot 0.98) \cdot \beta(z)$ (b) $\lambda = (\sqrt[5]{0.2 \cdot \text{data}})^3$
(f) Pre-emptive removal—low thinning	Removal of 50% of individuals prior to entry of *Bsal*	$0.5 \cdot S_0$
(g) Pre-emptive removal—high thinning	Removal of 90% of individuals prior to entry of *Bsal*	$0.1 \cdot S_0$
(h) Post-detection removal	Removal of 90% of all individuals (per time step) starting immediately after entry of *Bsal*, i.e., imposing an additional mortality probability of 90%	$0.1 \cdot s(z)$

parameters elicited from experts (Vose, 1996). Furthermore, for the initial density derived from Stegen et al. (2017) we used a negative binomial distribution, and for the mean survival probability of infected individuals, also from Stegen et al. (2017), we used a beta distribution. We simulated 1,000 datasets by drawing random combinations of parameters from the respective distributions (data available from Canessa et al., 2018), and then fit the IPM functions using those values to assess model outcomes across the range of parametric uncertainty.

2.5 | Exploring the management-related parameter space

The set of actions presented in Table 1 was not a comprehensive evaluation of all potential actions. Rather, it reflected initial creative thinking about mitigation, and may be interpreted as a snapshot of a general sensitivity analysis, easier to discuss and link to management than a multi-dimensional but abstract exploration of the parameter space. This approach is particularly useful considering that decision analysis is an iterative process, where different components can be revisited as needed. For example, new actions could be devised using the initial results as an indication of the effects of manipulating different model parameters (N'Guyen et al., 2018).

Therefore, after observing the initial results we carried out a further exploration of possible model outcomes, with the aim of identifying the requirements of any new action, or combination thereof, which sought to influence specific model parameters. We used a simplified dynamical model, collapsing the continuous classification of infected individuals as a function of load into a single "infected" state, to obtain a discrete time Susceptible-Infected model (Equation S11). First, we studied the effects of management by modifying the equation that calculates R_0 for this model (Equation S12). Here, on the basis of our initial results, we assumed actions would seek to reduce transmission (β in Equation S12), initial host density (S_0 in Equation S12) and/or host survival (s_0 and $\bar{s}$ in Equation S12). We multiplied each of these parameters by a term indicating the proportional reduction caused by management ($1 - m$), and we calculated the proportional reductions that would result in $R_0 = 1$. Furthermore, as for the IPM model, we also calculated the

density ratio of susceptible hosts between a given reduction and no reduction (i.e., with and without management). For ease of comparison with the initial IPM results, we obtained the density ratios of susceptible hosts by iterating the simplified model (Equation S11). Further details, including a final size relation for the simplified model, can be found in Appendix S1.

3 | RESULTS

The results of our IPM simulations reflect the high virulence of *Bsal* in fire salamander populations, observed in field and laboratory studies to date and confirmed by the expert judgement used to parameterize the model (Figure 1, Table S1). In a "no action" scenario, susceptible hosts would almost inevitably become infected upon contact with infected individuals at high burdens of infection (>100 genomic equivalent) that occur soon after exposure, leading to a rather high *Bsal* basic reproduction number (median $R_0 \approx 9.6$). Host survival would decrease to almost certain death at intermediate to high infection loads. Therefore, an unmitigated *Bsal*-breakout is expected to lead to the effective extirpation of the host population within our 3-month time frame (Figure 2). The rapid growth of *Bsal* and consequential reduced host survival meant that, in the absence of mitigation, an infected dispersing individual would move on average less than 100 m during the study period (Figure 3a). However, rare extreme movements may be more relevant for disease spread, where one or a few individuals may reach longer distances. In our case, without mitigation, the mean distance for those rare individuals could be approximately double the mean movement, as illustrated by the uncertainty shown in Figure 3a. Note that our proportional formulation implies that a larger population will produce a greater absolute number of such long-range dispersers.

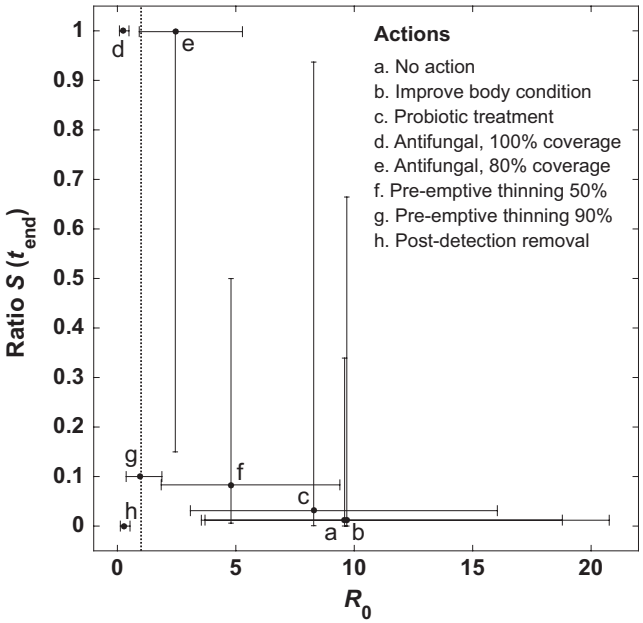

FIGURE 2 Comparison of predicted outcomes for potential *Bsal* mitigation actions in a fire salamander population over a 3-month period, obtained from the integral projection model (IPM). The *x*-axis indicates the basic reproduction number of *Bsal* (R_0), and the *y*-axis the host population decline, expressed as the ratio between the final number of susceptible individuals for a given action and that simulated for a scenario without infection. Values shown are median (markers) and 95% confidence intervals (CI) for each action (error bars). Note that, given the strong within-action correlation between R_0 and final density ratio (not shown), the error bars for the latter are the associated results of the 95% CIs in R_0: within a management action, the highest final density ratio is associated to the lower 95% CI bound of R_0, et vice versa

The potential actions described in Table 1, analysed using the IPM, were mostly unable to prevent population extirpation, even under optimistic parameterization (Figure 2). An "individual manipulation" that reduced transmission probabilities for low infection loads by 50% did not prevent the collapse of the population or reduce *Bsal* R_0 (Figure 2); a treatment such as our generalized "probiotic," that reduced transmission while slowing pathogen growth, actually worsened outcomes, failing to prevent the collapse of the host population while increasing R_0 and the distances across which infected hosts moved (Figures 2 and 3b,c). A highly effective "antifungal" treatment (treatment "d" in Figure 2) that reduced transmission by 98% was likely to avoid a population collapse within our time frame and eradicate the pathogen ($R_0 < 1$), although this treatment also increased host movement distances (Figures 2 and 3d). However, decreasing coverage (the proportion of individuals treated with the "antifungal") from 100% to 80% ("e" in Figure 2) was already sufficient to negate these results: although the collapse did not occur during our time frame, it was only delayed beyond our 3-month simulation period, since eradication could not be achieved ($R_0 > 1$), while still increasing host movements (Figures 2 and 3e). "Pre-emptive thinning" that manipulated host density by removing 50% of the individuals before *Bsal* entered the population was not effective under the conditions we simulated; when the proportion removed was increased to 90%, the chance of eradicating *Bsal* was approximately 50% (Figures 2 and 3f,g). Rapid and efficient "post-detection removal" of both susceptible and infected individuals starting immediately after *Bsal* entry obviously led to almost complete extirpation of the population, but was the only action likely to both eradicate *Bsal* and minimize host movements, and thus the risk of disease spread to other populations, which was otherwise largely unaffected by other actions (Figures 2 and 3h). We found only one case in which parametric uncertainty resulted in significant uncertainty between success and failure of the same action, i.e., for which the predicted R_0 included values lower and greater than 1: as mentioned above, this was pre-emptive removal of 90% of the population, which was equally likely to succeed or fail in eradicating *Bsal*. The application of the highly effective antifungal with 80% coverage had only a marginal chance of being successful (less than 2.5% of the simulation runs resulted in $R_0 < 1$; Figure 2).

In addition to the IPM model, we used a simplified model to further assess the efficacy of single and/or combined management actions. The simplified model without management produced $R_0 \approx 7.9$, in good agreement with $R_0 \approx 9.6$ (5.8–14.3 the 95% confidence interval, Figure 2) from the IPM model. Exploration of this simplified model confirmed that any potential action, or combination of actions,

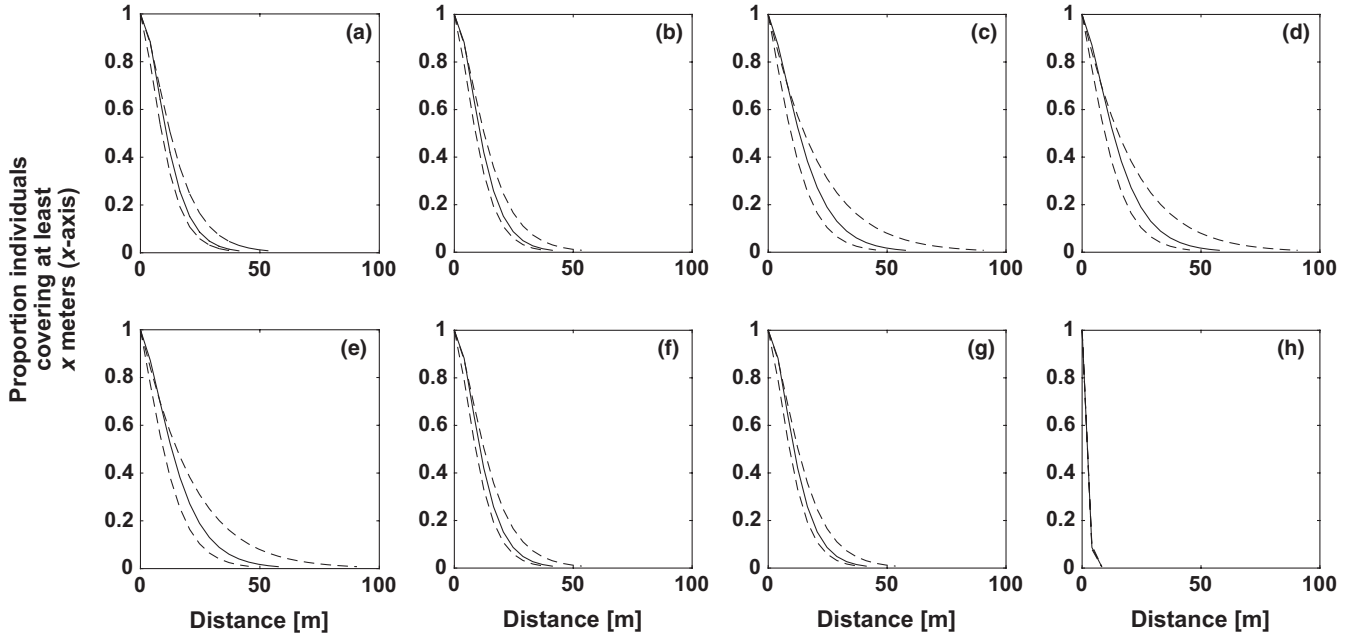

FIGURE 3 Distance covered by infected individuals during their life span, under different mitigation actions, obtained from the integral projection model (IPM). Action labels correspond to those indicated in Figure 2 and Table 1. The *y*-axis indicates the proportion of individuals that moved at least the distance given by the respective value on the *x*-axis. Dashed lines indicate minimum/maximum values

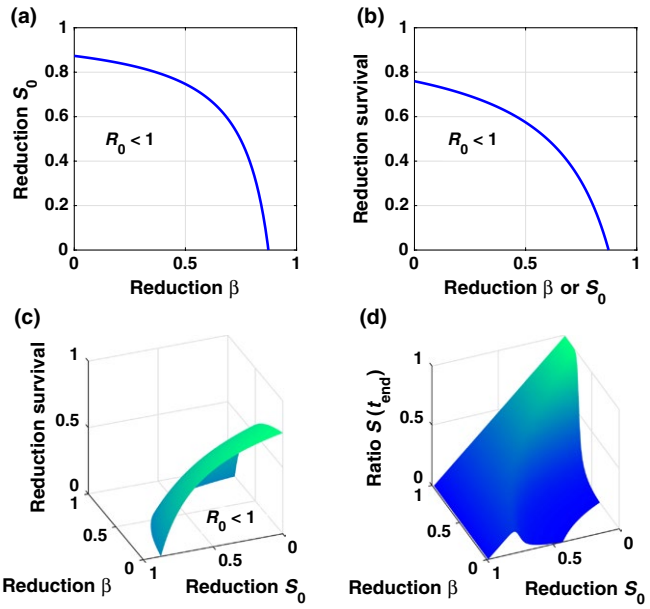

FIGURE 4 Results of management-related parameter space exploration, obtained from the simplified model. (a–c) The combinations of management effects (reduction in transmission β, initial host density S_0 or host survival) that are required to obtain $R_0 = 1$, corresponding to the blue line in (a) and (b), and the surface in (c). In (b), reducing transmission or initial density leads to the same graph (see Equation S12). In (c), parameter combinations under the plotted surface lead to $R_0 < 1$. (d) The ratios of final host densities (with and without management) as a function of two management parameters (with a quasi-extinction threshold of 0.01)

targeting host density, transmission and/or survival would require (very) high effectiveness to achieve $R_0 < 1$ and prevent a disease outbreak (Figure 4a–c). As suggested by our initial exploratory actions, management strategies targeting single parameters would need to reduce survival by at least 75% or initial density or transmission by at least 85%. Acting on several parameters at once would slightly reduce these requirements. For example, $R_0 = 1$ could be achieved by reducing transmission, initial host density and host survival by approximately 42% each (Figure 4c), or by reducing transmission and host survival by 87% each (Figure 4a). Avoiding the collapse of the host population (i.e., obtaining a high density ratio between susceptible individuals with and without intervention) would require a similarly high effectiveness (Figure 4d). As expected, reducing the initial density has approximately a linear effect on the final density; however, this reduction would still need to be paired with a highly effective reduction in transmission to result in a final viable population (Figure 4d).

4 | DISCUSSION

Our modelling approach revealed that mitigation actions at the *Bsal* invasion front and during a *Bsal* epidemic event are highly unlikely to be effective, at least for very susceptible species such as those in the genus *Salamandra*, particularly *S. salamandra* (see Sabino-Pinto et al., 2015). Treatments that seek to reduce transmission would require almost complete effectiveness (i.e., perfect interruption of transmission) and very high coverage, with >80% of the population treated within 3 days. Moreover, since current evidence suggests fire salamanders do not clear *Bsal* infection and do not acquire immunity (Stegen et al., 2017), unless the pathogen can be eradicated, even

highly effective treatments would likely only slow the decline of host populations. Treatments that only slow the growth of the pathogen, although they may appear intuitively appealing, effectively create a larger pool of active infected individuals and increase the potential for spread of the pathogen to other populations. This inherent risk in treatments that prolong survival but do not interrupt transmission is a recognized concern in the management of virulent pathogens (Read et al., 2015).

If the persistence of affected populations is unlikely to be achievable after *Bsal* entry, this objective may become irrelevant and the focus may shift to stopping the further spread of the pathogen to other populations, by interrupting its transmission and minimizing host movements. Our results suggest that these objectives might only be achieved with reasonable certainty by applying radical interventions, such as the almost complete removal of infected populations. Moreover, recent evidence suggests that *Bsal* reservoirs may exist, either in other amphibian species or as free-living encysted spores (Stegen et al., 2017). Once their role in the wild is clarified, such reservoirs can be incorporated into the model (Wilber et al., 2016). From a management perspective, since reservoirs increase the probability of infection, their presence may negate even the only potential benefit of removal-based management (minimizing spread by host movement). Removal actions could be revised to include amphibian reservoirs, but this may be less feasible for other taxa or environmental reservoirs. Additional knowledge about the site-specific density and encounter rates of host individuals may help refine predictions and understand the potential for pathogen spread and identify promising management options (e.g. spacing of quarantine fences and radius of capture searches for host removal).

Our initial comparison of actions was obviously not exhaustive and more creative thinking is to be encouraged (Grant et al., 2017). However, irrespective of the management strategy, our conclusions are likely to remain broadly applicable; ultimately any action that seeks to address an epidemic would rely on the manipulation of one of the processes described in the model, such as pathogen growth, host survival or rates of transition between infection states. Our exploration of the management-related parameter space using the simplified model suggests that management strategies that target multiple processes are likely to be necessary, and even if they can be devised, all those components would still need to be highly effective to achieve management objectives. Given the limited ability to mitigate epidemics, alternative actions aimed at preventing the entry of the pathogen remain a priority. At the local level, besides mandatory biocontrol precautions, more radical options could involve restriction of access by humans or isolation of host populations in-situ, for example through quarantine fences. Such tactics may however only reduce the risk of *Bsal* entry, not the ultimate outcome of an epidemic, and their effectiveness may be limited given the multiple possible passive and active vectors of *Bsal* (Stegen et al., 2017). Ex-situ rescue would likely still face the same challenges highlighted by our model at the time of reintroduction, unless the pathogen could be entirely removed or mechanisms of augmenting resistance were developed (e.g., vaccination; a possibility contrary to current evidence, at least for fire salamanders which do not appear to acquire immunity; Stegen et al., 2017).

Recognizing the current uncertainty surrounding those processes provides an ideal basis for rational planning of future research and implementation of adaptive management, by focusing on the uncertain parameters that directly influence the choice of management actions (Russell et al., 2017). For example, Wasserberg, Osnas, Rolley, and Samuel (2009) describe an adaptive management model for white-tailed deer affected by chronic wasting disease, where they determined a relationship between disease transmission and the effectiveness of culling. In the *Bsal* case, our results suggest, for example, that understanding whether a candidate antifungal can reduce *Bsal* transmission by 85% or 95% would be of immediate relevance for deciding whether to use it or not; conversely, understanding whether a probiotic-based treatment reduces transmission by 20% or 50% may reveal important biological processes, but this improved knowledge is still unlikely to make application of such a treatment an optimal management strategy. In terms of more general improvements to our model, better knowledge of the effect of reservoirs, host density and non-amphibian vectors in the transmission function may provide the greatest benefit for decision-making.

Perhaps the most urgent need is to clearly define the real, rather than theoretical, decision context for *Bsal* management. We were able to obtain useful information and to provide an initial assessment of potential actions in a hypothetical management situation. However, we also recognize that natural resource managers (the actual decision makers) face additional objectives and potential constraints, such as the social acceptability of host removal and the allocation of limited funding. These additional complexities will vary with the spatial and temporal scale of possible disease management, and will require the direct involvement of those decision makers.

Our study provides a first practical demonstration of the advantages of embedding scientific analysis of emerging diseases in a realistic decision context, as recently advocated for amphibian chytridiomycoses (Garner et al., 2016; Grant et al., 2017; Russell et al., 2017). Essentially, decision analysis required us to approach the problem from a manager's perspective, stating clear objectives, thinking creatively about actions and making comparable predictions about specific management actions, thus performing that ideal role of scientific "strong inference". Setting our model in this context allowed us to clarify potential actions and formalise current knowledge for use in a model that can be easily updated as new information becomes available. This approach thus creates the foundations for a transparent discussion about the potential of any proposed action to mitigate the effects of disease.

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AUTHORS' CONTRIBUTIONS

S.C., C.B. and B.R.S. conceived the ideas and designed methodology; all authors contributed to model parameterization, definition of mitigation actions and interpretation of results; S.C. performed all elicitation-related analyses and C.B. performed all IPM-related analyses; S.C. and C.B. wrote the manuscript with input from all authors. All authors contributed critically to the drafts and gave final approval for publication.

DATA ACCESSIBILITY

The full set of 1,000 combinations of random parameter values used for the IPM simulations is available from the Dryad Digital Repository https://doi.org/10.5061/dryad.0jh5p (Canessa et al., 2018).

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REFERENCES

Arlettaz, R., Schaub, M., Fournier, J., Reichlin, T. S., Sierro, A., Watson, J. E., & Braunisch, V. (2010). From publications to public actions: When conservation biologists bridge the gap between research and implementation. *BioScience*, *60*, 835–842. https://doi.org/10.1525/bio.2010.60.10.10

Bosch, J., Sanchez-Tomé, E., Fernández-Loras, A., Oliver, J. A., Fisher, M. C., & Garner, T. W. (2015). Successful elimination of a lethal wildlife infectious disease in nature. *Biology Letters*, *11*, 20150874. https://doi.org/10.1098/rsbl.2015.0874

Burnham, K. P., & Anderson, D. R. (2001). Kullback-Leibler information as a basis for strong inference in ecological studies. *Wildlife Research*, *28*, 111–119. https://doi.org/10.1071/WR99107

Canessa, S., Bozzuto, C., Grant, E. H. C., Cruickshank, S., Fisher, M., Koella, J., … Schmidt, B. R. (2018). Data from: Decision making for mitigating wildlife diseases: From theory to practice for an emerging fungal pathogen of amphibians. *Dryad Digital Repository*, https://doi.org/10.5061/dryad.0jh5p

Chamberlin, T. C. (1890). The method of multiple working hypotheses. *Science*, *15*, 92–96.

Claxton, K. P., & Sculpher, M. J. (2006). Using value of information analysis to prioritise health research. *Pharmacoeconomics*, *24*, 1055–1068. https://doi.org/10.2165/00019053-200624110-00003

Converse, S. J., Bailey, L. L., Mosher, B. A., Funk, W. C., Gerber, B. D., & Muths, E. (2016). A model to inform management actions as a response to chytridiomycosis-associated decline. *EcoHealth*, *14*, 1–12.

Dicks, L. V., Walsh, J. C., & Sutherland, W. J. (2014). Organising evidence for environmental management decisions: A '4S'hierarchy. *Trends in Ecology & Evolution*, *29*, 607–613. https://doi.org/10.1016/j.tree.2014.09.004

Ellner, S. P., & Rees, M. (2006). Integral projection models for species with complex demography. *The American Naturalist*, *167*, 410–428. https://doi.org/10.1086/499438

Fisher, M. C., Henk, D. A., Briggs, C. J., Brownstein, J. S., Madoff, L. C., McCraw, S. L., & Gurr, S. J. (2012). Emerging fungal threats to animal, plant and ecosystem health. *Nature*, *484*, 186–194. https://doi.org/10.1038/nature10947

Garner, T. W., Schmidt, B. R., Martel, A., Pasmans, F., Muths, E., Cunningham, A. A., … Bosch, J. (2016). Mitigating amphibian chytridiomycoses in nature. *Philosophical Transactions of the Royal Society B*, *371*, 20160207. https://doi.org/10.1098/rstb.2016.0207

Geiger, C. C., Bregnard, C., Maluenda, E., Voordouw, M. J., & Schmidt, B. R. (2017). Antifungal treatment of wild amphibian populations caused a transient reduction in the prevalence of the fungal pathogen *Batrachochytrium dendrobatidis*. *Scientific Reports*, *7*, 5956. https://doi.org/10.1038/s41598-017-05798-9

Gerber, B. D., Converse, S. J., Muths, E., Crockett, H. J., Mosher, B. A., & Bailey, L. L. (2017). Identifying species conservation strategies to reduce disease-associated declines. *Conservation Letters*. https://doi.org/10.1111/conl.12393

Grant, E. H. C., Muths, E. L., Katz, R. A., Canessa, S., Adams, M. J., Ballard, J. R., … White, C. L. (2016). Salamander chytrid fungus (*Batrachochytrium salamandrivorans*) in the United States – Developing research, monitoring, and management strategies. Open-File Report, U. S. Geological Survey, pp. 26. Reston, VA.

Grant, E. H. C., Muths, E., Katz, R. A., Canessa, S., Adams, M. J., Ballard, J. R., … White, C. L. (2017). Using decision analysis to support proactive management of emerging infectious wildlife diseases. *Frontiers in Ecology and the Environment*, *15*, 214–221. https://doi.org/10.1002/fee.1481

Keeney, R. L. (1982). Decision analysis: An overview. *Operations Research*, *30*, 803–838. https://doi.org/10.1287/opre.30.5.803

Langwig, K. E., Voyles, J., Wilber, M. Q., Frick, W. F., Murray, K. A., Bolker, B. M., … Hoyt, J. R. (2015). Context-dependent conservation responses to emerging wildlife diseases. *Frontiers in Ecology and the Environment*, *13*, 195–202. https://doi.org/10.1890/140241

Longcore, J. E., Pessier, A. P., & Nichols, D. K. (1999). *Batrachochytrium dendrobatidis* gen. et sp. nov., a chytrid pathogenic to amphibians. *Mycologia*, *91*, 219–227. https://doi.org/10.2307/3761366

Martel, A., Blooi, M., Adriaensen, C., Van Rooij, P., Beukema, W., Fisher, M., … Goka, K. (2014). Recent introduction of a chytrid fungus endangers Western Palearctic salamanders. *Science*, *346*, 630–631. https://doi.org/10.1126/science.1258268

Martel, A., Spitzen-van der Sluijs, A., Blooi, M., Bert, W., Ducatelle, R., Fisher, M. C., … Bossuyt, F. (2013). *Batrachochytrium salamandrivorans* sp. nov. causes lethal chytridiomycosis in amphibians. *Proceedings of the National Academy of Sciences of the United States of America*, *110*, 15325–15329. https://doi.org/10.1073/pnas.1307356110

Martin, T. G., Burgman, M. A., Fidler, F., Kuhnert, P. M., Low-Choy, S., McBride, M., & Mengersen, K. (2012). Eliciting expert knowledge in conservation science. *Conservation Biology*, *26*, 29–38. https://doi.org/10.1111/j.1523-1739.2011.01806.x

N'Guyen, A., Hirsch, P. E., Bozzuto, C., Adrian-Kalchhauser, I., Hôrková, K., & Burkhardt-Holm, P. (2018). A dynamical model for invasive round goby populations reveals efficient and effective management options. *Journal of Applied Ecology*, *55*, 342–352. https://doi.org/10.1111/1365-2664.12934

Nichols, J. D., & Williams, B. K. (2006). Monitoring for conservation. *Trends in Ecology & Evolution*, *21*, 668–673. https://doi.org/10.1016/j.tree.2006.08.007

Nutt, D. J., King, L. A., & Phillips, L. D. (2010). Drug harms in the UK: A multicriteria decision analysis. *The Lancet*, *376*, 1558–1565. https://doi.org/10.1016/S0140-6736(10)61462-6

Platt, J. R. (1964). Strong inference. *Science*, *146*, 347–353. https://doi.org/10.1126/science.146.3642.347

Read, A. F., Baigent, S. J., Powers, C., Kgosana, L. B., Blackwell, L., Smith, L. P., … Nair, V. K. (2015). Imperfect vaccination can enhance the transmission of highly virulent pathogens. *PLoS Biology*, *13*, e1002198. https://doi.org/10.1371/journal.pbio.1002198

Richgels, K. L. D., Russell, R. E., Adams, M. J., White, C. L., & Grant, E. H. C. (2016). Spatial variation in risk and consequence of *Batrachochytrium salamandrivorans* introduction in the USA. *Royal Society Open Science*, *3*, 150616. https://doi.org/10.1098/rsos.150616

Russell, R. E., Katz, R. A., Richgels, K. L., Walsh, D. P., & Grant, E. H. (2017). A framework for modeling emerging diseases to inform management. *Emerging Infectious Diseases*, *23*, 1. https://doi.org/10.3201/eid2301.161452

Sabino-Pinto, J., Bletz, M., Hendrix, R., Perl, R. B., Martel, A., Pasmans, F., … Steinfartz, S. (2015). First detection of the emerging fungal pathogen *Batrachochytrium salamandrivorans* in Germany. *Amphibia-Reptilia*, *36*, 411–416. https://doi.org/10.1163/15685381-00003008

Scheele, B. C., Hunter, D. A., Grogan, L. F., Berger, L., Kolby, J. E., McFadden, M. S., … Driscoll, D. A. (2014). Interventions for reducing extinction risk in chytridiomycosis-threatened amphibians. *Conservation Biology*, *28*, 1195–1205. https://doi.org/10.1111/cobi.12322

Schmidt, B. R., Bozzuto, C., Lötters, S., & Steinfartz, S. (2017). Dynamics of host populations affected by the emerging fungal pathogen *Batrachochytrium salamandrivorans*. *Royal Society Open Science*, *4*, 160801. https://doi.org/10.1098/rsos.160801

Skerratt, L. F., Berger, L., Speare, R., Cashins, S., McDonald, K. R., Phillott, A. D., … Kenyon, N. (2007). Spread of chytridiomycosis has caused the rapid global decline and extinction of frogs. *EcoHealth*, *4*, 125–134. https://doi.org/10.1007/s10393-007-0093-5

Smith, T. J., Hillner, B. E., & Desch, C. E. (1993). Efficacy and cost-effectiveness of cancer treatment: Rational allocation of resources based on decision analysis. *Journal of the National Cancer Institute*, *85*, 1460–1474. https://doi.org/10.1093/jnci/85.18.1460

Soulé, M. E. (1985). What is conservation biology? *BioScience*, *35*, 727–734.

Spitzen-van der Sluijs, A., Martel, A., Asselberghs, J., Bales, E. K., Beukema, W., Bletz, M. C., … Kinet, T. (2016). Expanding distribution of lethal amphibian fungus *Batrachochytrium salamandrivorans* in Europe. *Emerging Infectious Diseases*, *22*, 1286. https://doi.org/10.3201/eid2207.160109

Stegen, G., Pasmans, F., Schmidt, B. R., Rouffaer, L. O., Van Praet, S., Schaub, M., … Martel, A. (2017). Drivers of salamander extirpation mediated by *Batrachochytrium salamandrivorans*. *Nature*, *544*, 353–356. https://doi.org/10.1038/nature22059

Vose, D. (1996). *Quantitative risk analysis: A guide to Monte Carlo simulation modelling*. Chichester, UK: John Wiley & Sons Ltd.

Wasserberg, G., Osnas, E. E., Rolley, R. E., & Samuel, M. D. (2009). Host culling as an adaptive management tool for chronic wasting disease in white-tailed deer: A modelling study. *Journal of Applied Ecology*, *46*, 457–466. https://doi.org/10.1111/j.1365-2664.2008.01576.x

Wilber, M. Q., Langwig, K. E., Kilpatrick, A. M., McCallum, H. I., & Briggs, C. J. (2016). Integral Projection Models for host–parasite systems with an application to amphibian chytrid fungus. *Methods in Ecology and Evolution*, *7*, 1182–1194. https://doi.org/10.1111/2041-210X.12561

Woodhams, D. C., Bosch, J., Briggs, C. J., Cashins, S., Davis, L. R., Lauer, A., … Sheafor, B. (2011). Mitigating amphibian disease: Strategies to maintain wild populations and control chytridiomycosis. *Frontiers in Zoology*, *8*, 8. https://doi.org/10.1186/1742-9994-8-8

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