

APPENDIX A: DETAILED DESCRIPTIONS OF DEVELOPMENT OF MULTI-SCALE MODELS WITH EXPONENTIALLY- AND GAMMA-DISTRIBUTED EXTIRPATION TIME

Estimation of the hibernaculum extirpation time $1/\gamma$

The basic reproduction number cannot be calculated without an estimate of the hibernaculum extirpation time. As an order-of-magnitude guide, we examined hibernaculum-level case reports as follows. Frick et al. (2010) found that on average, there is 85% mortality of Little Brown bats in the first year following introduction of WNS to a hibernaculum, 65% mortality in the second year and 45% mortality in the third year, i.e., just ~3% of the population in a hibernaculum remained after 3 years. In addition, Turner et al. (2011) provided estimates of mortality based on bat surveys, which the U.S Fish and Wildlife Service used to estimate the number of dead bats (between 5.5 and 6.7 million) in January 2012 (U.S Fish and Wildlife Service, 2012). The survey documents the year of introduction of WNS to hibernacula in 5 states and the abundances of various bat species prior to, and after the introduction of WNS. To calculate the average hibernaculum decline, we used bat populations that were counted either one year before or any year after the introduction of WNS to the state (Turner et al. 2011). The average decline in Little Brown bat numbers is 96% in hibernacula where WNS has been present for 3 years or less (between 2008 and 2011). Therefore, we assumed a hibernaculum extirpation time $1/\gamma$ of 3 years in our simulations of the multi-scale SIR models. Acknowledging that this method can produce at best a rough estimate, we conducted simulations over a wide range of hibernaculum infectious periods (<1 year up to 10 years) in an effort to bound our estimate of the WNS epidemic final size (the initial propagation of an SIR epidemic resembles an SI epidemic).

Estimating the intrinsic growth rate λ of WNS within a single county

To estimate the intrinsic growth rate λ of WNS within a single county, we fitted a generalized linear model with Poisson distributed errors and identity link function to the New York-Pennsylvania hibernaculum infection history data set from 2005–2010 (Figs. A1 and A2). We assumed the cumulative number of infections by year t ($t=0, 1, \dots$) in a single county is a proxy for the number of infectious hibernacula in a county at year t at the beginning of the epidemic. Denoting the cumulative number of hibernaculum infections by year t by I_t , the number of newly infected hibernacula in year $t + 1$ is the difference between the cumulative number of infections up to year $t + 1$ and up to year t . We assumed that I_t predicted the number of new cases in year $t + 1$ in each county and the predicted relationship was a linear function of λ . When WNS reaches a susceptible county at year $t = 0$, the cumulative number of infections by year 0 is naturally zero, and so we assumed the mean number of new infections that have occurred by year 1 was unity. Furthermore, infection events are rare at the start of an epidemic, especially when there are very many possible susceptible sites per county for an infection to arise. Occurrences of rare events may be assumed to be independent and therefore Poisson distributed. Putting these assumptions together, the number of new infections per year per county is a Poisson random variable with mean $1 + \lambda I_t$. Thus, the variance of each incidence observation increases with the expected value of each observation and so smaller annual incidences that occur at the start of the epidemic are assumed to have smaller variance than annual incidences recorded in the years that follow. These considerations imply that a generalized linear model with Poisson distributed errors and identity link function is appropriate.

We remark in passing that the chain binomial model, not our model, is the conventional choice for discrete time epidemics, where the number of infectives at time $t + 1$ is binomially distributed with the number of trials equal to the number of susceptibles at time t and probability of infection $1 - \exp(-\beta I_t)$. The main reason we have not used this model is that when the infectious period is unknown, the exponential approximation to the intrinsic growth rate of the infection is a more appropriate model for an outbreak in its initial stages than the chain binomial model (Ferrari et al. 2005). Of course, if we had information on

the full WNS epidemic trajectory, then a chain binomial model might be an acceptable alternative. Our procedure is further justified by the fact that the cave incidence data were collected in the first five years of the epidemic, when the outbreak was in its initial stages. Finally, the binomial distribution is well approximated by the Poisson distribution when the number of trials is large and the probability of success (i.e., infection) is small. In the initial years of the epidemic, the number of susceptible hibernacula per county is very large relative to the number of infected hibernacula and the probability of infection is small. Hence, the assumption that susceptibles are not depleted by infection is reasonable because susceptible hibernacula outnumber infected hibernacula at the beginning of the outbreak in each county. While we acknowledge that alternative model specifications (e.g., including an intercept to the generalized linear model) might provide a better fit to the available data, our choice for model structure was driven by theoretical and conceptual considerations.

Counties that were infected for greater than one year were used to calculate R_0 . Eight counties (Albany, Essex, Luzerne, Mifflin, Schoharie, Sullivan [NY], Ulster and Warren Counties [PA]) of the hibernaculum infection history dataset satisfied this condition. 58 out of a possible 314 potential hibernacula in these 8 counties were infected by the winter of 2009–2010.

Macro-scale model

The heterogeneous landscape of the United States was represented as a graph, with counties containing potential hibernacula as nodes (Fig. A3). All nodes of the landscape network were assumed to be connected to one another (a complete graph). Links between counties i and j were weighted according to a generalized gravity dispersal kernel that accounted for landscape spatial heterogeneities and climate.

The probability that county j infects county i in a given year is

$$p_{ij} = \frac{1}{1 + \exp(\beta_0 + \beta_1 \frac{d_{ij}}{(n_i n_j)^{\beta_2}} + \beta_3 \tau_i)},$$

where the gravity term $\beta_1 d_{ij} / (n_i n_j)^{\beta_2}$ is the distance between the two counties (d_{ij}) divided by the product of potential hibernaculum numbers in counties i and j , multiplied by an estimated coefficient (β_1) and β_0 is the background infection rate. The effect of the length of winter was determined by the coefficient β_3 . The exponent β_2 determined the relative importance of hibernaculum numbers and distance between counties i and j . A small exponent leads to spatially diffuse spread whereas a large one makes long jumps to nodes with large numbers of hibernacula more likely to occur. The exponent may take any real value; therefore we refer to the model as “generalized”.

Uniting the spatial scales

To unite the disparate spatial scales, each county was assigned a state variable that represented whether it was susceptible, infected or removed as a result of an accumulation of local extirpation events. We calculated the number of years for epidemic burnout to occur for each county using the hibernaculum-scale SIR model with exponentially distributed infectious period, initialized with a single infectious hibernaculum and all other hibernacula susceptible within each county. Epidemic burnout within a county was assumed to have occurred when the number of infected hibernacula was exhausted (i.e., the number of infected hibernacula within that county had diminished to less than one). Once a county (node in the landscape graph) became infected, our simulations tracked the year of infection of each node. An infected county and all links originating from and terminating at it were removed from the network when the county epidemic burnout time (calculated from the hibernaculum level SIR model) had been reached. Consequently, all hibernacula within a county were removed from the graph and bats were assumed not to recolonize ‘removed’ areas. We repeated this procedure at each time step until no infected nodes remained, i.e., the macro-scale epidemic had terminated. Finally, it is important to note that while the hibernaculum extirpation time was fixed within each county, the duration of the county epidemic was a function of the number of caves within it, and thus epidemic duration was not homogeneous across counties.

Simulation of epidemics

To simulate propagation of WNS over the landscape network, we calculated the probability p_i that each susceptible county i was infected by at least one infected county at the start of each year,

$$p_i = \begin{cases} 1 - \exp\left(\sum_{j=1}^n \log(1 - p_{ij})\right), & n > 0, \\ 0, & n = 0, \end{cases}$$

where n is the number of infected counties at the start of the year. A susceptible county i became infected with WNS if p_i was greater than a uniform random number in the range 0 to 1 (a Bernoulli trial). Nodes and their links were removed at the end of each year, i.e., before the probabilities p_i were calculated that determined the number of new infections the next year. As the number of infected nodes decreased near the end of the epidemic, the probabilities of susceptible nodes becoming infected also decreased.

Model for gamma-distributed hibernaculum extirpation time

The basic hibernaculum-level SIR model described in the main text assumes that the hibernaculum extirpation time is exponentially distributed. An exponentially distributed infectious period overestimates the number of hibernacula in a population whose infection duration is much shorter than the mean of three years (Fig. A4, blue line). However, Lorch et al., (2013) suggest that hibernacula can remain contaminated with WNS due to the fungus remaining in the environment for up to 1–2 years following elimination of bats. Due to environmental contamination, the probability of elimination is more likely to increase over time, peaking about the mean of three years (Fig. A4, pink line) and thus the distribution of the hibernaculum infectious period may be more tightly concentrated about the mean of three years than assumed by an SIR model with exponentially distributed infectious period. Modeling the hibernaculum extirpation time as gamma-distributed is thus appropriate under the finite environmental contamination scenario. The gamma distribution function is given by

$$f(\tau) = \frac{(\gamma n)^n}{\Gamma(n)} \tau^{n-1} e^{-\gamma n \tau}.$$

The exponential distribution is a special case of the gamma distribution (when the shape parameter n is equal to one).

Mathematically, the SIR epidemiological process with gamma-distributed hibernaculum extirpation time may be represented using the method of stages (Anderson and Watson 1980, Lloyd 2001) whereby the infectious hibernaculum class is divided into n infectious disjoint compartments or stages I_n . The time spent in each stage is exponentially distributed. Biologically, initial stages (e.g., I_1, I_2) may represent hibernacula that are infectious due to presence of infectious bats and latter stages (e.g., I_{n-1}, I_n) may represent infectiousness due to presence of environmental substrate and absence of bats. All of the infectious compartments contribute to transmission at the hibernaculum level. The model is given by the following set of equations,

$$\begin{aligned} \frac{dS}{dt} &= -\beta S \sum_{i=1}^n I_i, \\ \frac{dI_1}{dt} &= \beta S \sum_{i=1}^n I_i - \gamma n I_1, \quad (1) \\ \frac{dI_2}{dt} &= \gamma n I_1 - \gamma n I_2, \\ &\vdots \\ \frac{dI_n}{dt} &= \gamma n I_{n-1} - \gamma n I_n, \\ \frac{dR}{dt} &= \gamma n I_n. \end{aligned}$$

In our formulation of the model, we assumed there were five infectious stages, which gives rise to an approximately normally distributed hibernaculum extirpation time. The estimate for R_0 was corrected for the gamma-distributed infectious period using the formula (Wearing et al. 2005),

$$R_0 = \frac{\lambda}{\gamma(1 - (\lambda / n\gamma + 1)^{-n})}$$

Model (1) was coupled to the county-level model by using the corrected R_0 to calculate the duration of the WNS epidemic within each county. Maximum likelihood was then used to estimate the macro-scale parameters and 10,000 simulations of the model were conducted.

Decline of Little Brown bat populations

The total number of Little Brown bats N_{t+1} in the northeast at time $t + 1$ was calculated using the formula $N_{t+1} = S_t N_0 / S_0$, where the number of susceptible hibernacula at time t in the region is denoted by S_t and the initial number of susceptible hibernacula is denoted by S_0 . As an approximation, we further assumed that the estimated pre-WNS population N_0 of ~6.5 million bats (Frick et al., 2010) was isotropically distributed among the 2,233 potential hibernacula in the 119 counties of the region. Assuming only susceptible hibernacula contain uninfected bats is conservative because the susceptible and infected bats that may inhabit infected hibernacula are not included in the population estimate. In susceptible counties, we assumed that the population size was constant each year as the Little Brown bat population was approximately stable prior to the introduction of WNS (Frick et al., 2010). In infected counties, the susceptible population declined according to the SIR model with exponentially distributed infectious period. The annual population decline rate was calculated using the formula $1 - N_{t+1}/N_t$.

To examine the implications of hibernacula remaining infectious indefinitely as a result of environmental contamination, we repeated these calculations using a multi-scale SI model. The SI model developed by Maher et al.,(2012) was used to calculate spread between counties. In infected counties, the susceptible population declined according to a hibernaculum-level SI model and the number of susceptible hibernacula per county was used as a proxy for the healthy bat population. Once all susceptible hibernacula were exhausted within a county, we assumed all bats had died from WNS. In contrast to the multi-scale SIR model, infected counties were not removed from the landscape graph following extinction of bats because hibernacula within counties were assumed to remain contaminated with WNS.

SUPPORTING FIGURES FOR METHODS

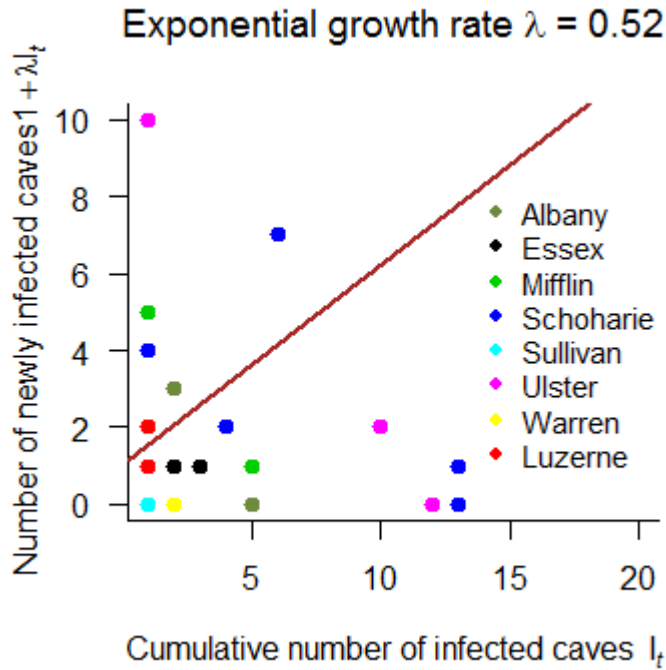


FIG. A1. Generalized linear model with Poisson distributed errors and identity link function fit to the New York-Pennsylvania hibernaculum infection history data set from 2005–2010. Colored points indicate the number of newly infected caves as a function of the cumulative number of infected caves from the previous year in Albany, Essex, Luzerne, Mifflin, Schoharie, Sullivan [NY] and Ulster and Warren Counties [PA].

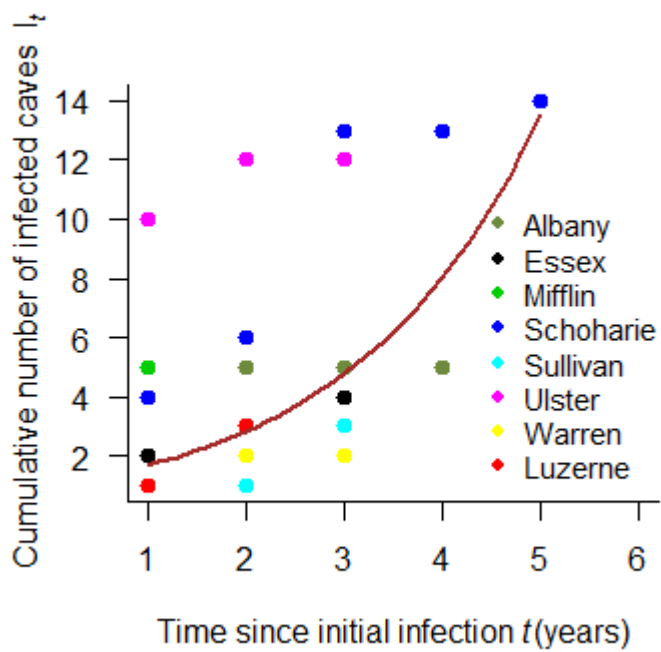


FIG. A2. Exponential growth of WNS in New York and Pennsylvania. Colored points indicate the hibernaculum infected cave histories as a function of the number of years since initial infection in Albany, Essex, Luzerne, Mifflin, Schoharie, Sullivan [NY] and Ulster and Warren Counties [PA].

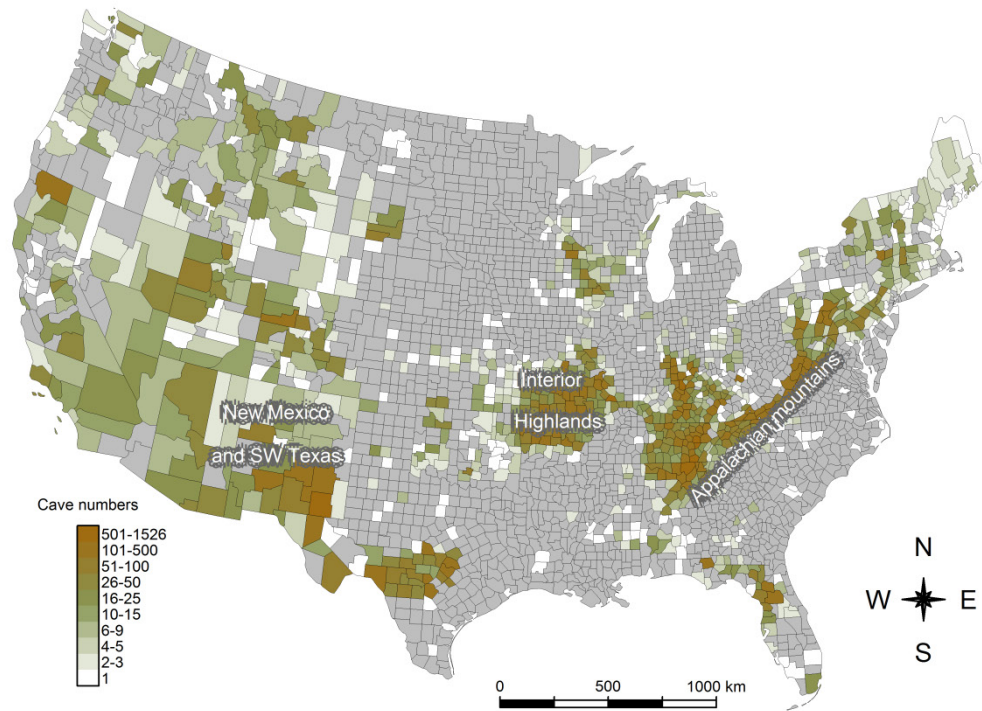


FIG. A3. The estimated geographic distribution of potential hibernacula in each county of the contiguous United States. The locations of county centroids represent nodes of a heterogeneous landscape graph. Nodes are heterogeneous as a result of differing numbers of caves (the proxy for hibernacula) and winter durations in each node. The Appalachian mountain range, interior highlands, New Mexico and southwest Texas contain large numbers of caves. Counties colored in gray do not contain any caves. Culver, et al.(1999) documented the distribution of caves in the United States, on which this map is based. Maher et al. (2012) describe how the geographic distribution of potential hibernacula was estimated.

Probability Distribution $f(\tau)$

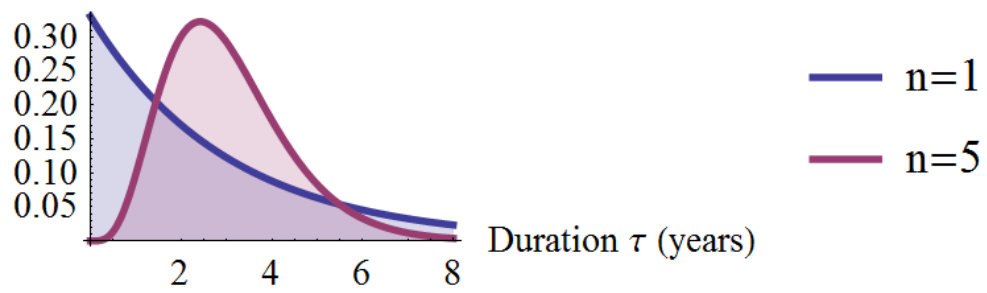


FIG. A4. Exponentially distributed infectious period ($n = 1$) compared with gamma-distributed infectious period ($n = 5$). If $n = 1$, the distribution of the infectious period is over-dispersed around the mean of 3 years and is more tightly concentrated about the mean if $n = 5$.

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