Popul Ecol (2015) 57:473–484
DOI 10.1007/s10144-015-0500-7

THE SOCIETY OF POPULATION ECOLOGY

ORIGINAL ARTICLE

Persistence of plague outbreaks among great gerbils in Kazakhstan: effects of host population dynamics

Lise Heier[2] · Hildegunn Viljugrein[1,2] · Geir O. Storvik[3]

Received: 31 March 2014 / Accepted: 12 June 2015 / Published online: 31 July 2015

Abstract Outbreaks of plague (*Yersinia pestis*) among great gerbils (*Rhombomys opimus*) generally require a high host abundance to be initiated. The duration of an outbreak is expected to depend on the subsequent development of this abundance; however, prediction is nontrivial due to the complexity of the gerbil–plague system. The aim of this study was to investigate how the duration of outbreaks depends on different types of host population dynamics generated from: a cyclic model; an autoregressive model giving irregular fluctuations; and a simple model with uncorrelated fluctuations. For each model, outbreak duration was studied under various levels of mean and variability of host abundance. Its focus on the effect of different gerbil dynamics sets this study apart from the few published studies on diseases in dynamic host populations. Plague outbreaks were simulated in a cellular automaton model based on statistical analysis of archived records of plague and host abundance. Temporal autocorrelation was found to make outbreak duration less sensitive to changes in mean abundance than uncorrelated fluctuations. Cyclicity had little effect on the mean duration of outbreaks, but resulted in a multimodal distribution. For all three types of gerbil dynamics, increased variability in gerbil abundance reduced the duration of outbreaks when the mean abundance was high (paralleling results on the risk of species extinction in fluctuating environments), but increased their duration when the mean abundance was lower. Spatial heterogeneity was briefly tested and produced longer outbreaks than the homogenous case. The results are relevant to predicting plague activity in populations of great gerbils.

Keywords Noise colour · Periodicity · *Rhombomys opimus* · Temporal variability · Time to extinction · *Yersinia pestis*

Introduction

Outbreaks of infectious disease, whether among animals or humans, have been studied extensively with the aims of control and eradication. A key finding is that the size of the host population is important for initiation of outbreaks and in their further development (see e.g., Anderson and May 1991; Dobson and Carper 1996; Diekmann et al. 2013). For a disease to persist, the host population must exceed a critical community size (CCS), which has been identified for several diseases (Ross 1911; Bartlett 1957, 1960; Heesterbeek and Roberts 1995; Swinton et al. 1998). However, all reasonable stochastic models show that the disease will eventually become extinct, even when above the CCS, because of stochastic burn-out; hence, many studies have instead focused on the duration of outbreaks, measured as the expected time to disease extinction. This has been modelled in both endemic and epidemic diseases and is well understood when host abundance is constant, or

Electronic supplementary material The online version of this article (doi:10.1007/s10144-015-0500-7) contains supplementary material, which is available to authorized users.

✉ Lise Heier
lh@liseheier.net

[1] Norwegian Veterinary Institute, PO Box 750 Sentrum, 0106 Oslo, Norway

[2] Centre for Ecological and Evolutionary Synthesis (CEES), Department of Biosciences, University of Oslo, PO Box 1066 Blindern, 0316 Oslo, Norway

[3] Department of Mathematics, University of Oslo, PO Box 1053 Blindern, 0316 Oslo, Norway

influenced only by constant birth, immigration rates, or by the disease; see e.g., Nåsell (1999a, b, 2005); Clancy et al. (2001); Diekmann et al. (2013).

The effect of a *dynamic* host abundance has been less explicitly studied. Although the question can be addressed by, for instance, an SIR (susceptible–infectious–recovered) disease model with variable birth and death rates, so far there have been few such studies and few results from field data. What has been shown is that seasonal variation in transmission rates reduces the persistence of the disease, explained by a larger probability of disease extinction when transmission is low (Grassly and Fraser 2006). In a field study of hantavirus outbreaks in bank vole (*Myodes glareolus*) populations with a three-year periodic cycle, it was found that both the duration of outbreaks and the survival of the virus were affected by the length of the low-density period (Sauvage et al. 2003). In a modelling study of the persistence of plague in a rodent community in California, increased stochastic environmental variation was found to increase the rate of disease extinction (Foley and Foley 2010).

Analogous to the persistence of infectious diseases in a fluctuating host population is the persistence of an animal or plant species in a fluctuating environment (Hanski 1999). In general, the probability of a species becoming extinct increases with the temporal variability of the environment (Lande 1993; Inchausti and Halley 2003). Long-term environmental fluctuation, that is, variability that is temporally correlated, also increases the probability of extinction in most situations (Inchausti and Halley 2003; Schwager et al. 2006). Moreover, the regularity of the fluctuations has been found to be important to the extinction risk (Wichmann et al. 2003).

The present study extends our current knowledge of diseases in dynamic host populations by focussing on different properties of host abundance dynamics: we investigated the effects of periodicity, other temporal correlation, variability, and mean population size on the duration of disease outbreaks. As the host can be seen as analogous to a fluctuating environment, this study has clear parallels to studies of the risk of species extinction.

Our study is based on the rodent–plague system in the Pre-Balkhash area in Kazakhstan. Plague, caused by *Yersinia pestis*, is well known for the medieval Black Death pandemic and is present today in natural reservoirs of infection in several parts of the world (Gage and Kosoy 2005). In Kazakhstan the disease causes outbreaks in populations of great gerbils (*Rhombomys opimus*) at irregular intervals. These outbreaks have been shown to be tightly coupled with the population size of the gerbils, which shows considerable multiannual fluctuation. An onset of a plague outbreak is possible when gerbil abundance exceeds a certain threshold for one to 2 years (Davis et al. 2004, 2007). When the population returns to a low level, an ongoing outbreak fades out. Great gerbils are considered to be a relatively plague-resistant species (Gage and Kosoy 2005) and, although plague causes some mortality during outbreaks, the prevailing view is that gerbil numbers are not strongly affected by the disease (Gage and Kosoy 2005; Kausrud et al. 2007).

Gerbil population dynamics vary among different regions of Kazakhstan with respect to periodicity, mean abundance, and variability (Dubyanskiy et al. 2003). The dynamics may additionally change over decades and centuries due to climatic change. Thus, the pattern of plague outbreaks may also change over space and time. One implication is that some regions may have more persistent plague activity than others, possibly acting as a source for outbreaks elsewhere. Another implication is that the plague pressure in Central Asia may be altered by current climatic changes. Due to complex interactions in the gerbil–plague dynamic system, it is not trivial how the interplay of mean levels, variability, temporal correlation, and periodicity of host population affects the duration of outbreaks. Knowledge of these relationships can help to predict the duration of outbreaks under different gerbil dynamic scenarios in regions other than Pre-Balkhash and in a changed future climate.

In the present study, we investigated the duration of plague outbreaks under three different models of gerbil dynamics: one that reproduces the regular cycles observed in parts of Pre-Balkhash; one with irregular, autocorrelated variation (reddened noise); and a simple white noise model for comparison. For each model, time series of gerbil dynamics were simulated for a range of mean abundance levels and variability values under the assumption that plague does not significantly influence gerbil dynamics. For each time series, plague outbreaks were then simulated by the use of a cellular automaton, and the mean duration of outbreaks was estimated. As a basis for the models, we used a historical dataset on the Pre-Balkhash plague system. This dataset has been used in previous studies (see e.g., Davis et al. 2004; Stenseth et al. 2006; Reijniers et al. 2014) to extract information about the biological system from the data; here, we explore a feature of the system (duration of outbreaks) under both the current and changed conditions (gerbil population dynamics). Complex structures in the gerbil–plague dynamic system are captured by the cellular automaton model for plague together with the gerbil abundance models. The simulation results are compared with analogous results in conservation biology and are discussed in the context of climate change.

Materials and methods

To study the effect of different gerbil population dynamics on the duration of plague outbreaks, the modelling is separated into two parts. The first consists of models of

gerbil abundance, which we assumed to fluctuate in time but to be homogeneous across space (see below). The second part is a model for plague occurrence given gerbil abundance, and is spatially explicit (model modified from Heier et al. 2011).

Both parts of the modelling are based on historical data from the Pre-Balkhash area, a semi-arid and mostly uninhabited area covering 45,000 km^2 south of Lake Balkhash (see Section S1 in the Electronic supplementary material (ESM)). Here, the great gerbil is a numerically dominant species and outbreaks of plague can cover large parts of the area. The dataset contains estimates of gerbil abundance, flea abundance, plague prevalence and so on at a number of locations for each spring and autumn from 1949 to 1995. Despite the long surveillance period, drawing inferences from these data is challenging because of the large number of missing values and the highly varying sampling intensity. While plague occurrence has been found to depend on gerbil population size (Davis et al. 2004) and previous plague occurrence in the area (Heier et al. 2011), seasonal effects on plague were not found to be statistically significant in the available data. Hence, seasonal effects were not included in the present plague model, yet are indirectly incorporated through the gerbil dynamics. Data on flea abundance are missing from large parts of the dataset, and an assessment of a model with or without flea abundance was inconclusive (L. Heier, unpublished data); flea abundance was hence omitted from the present model. However, flea abundance follows gerbil abundance quite closely (Frigessi et al. 2005), so plague is likely to be relatively well predicted solely by gerbil abundance.

Simulating great gerbil dynamics

Great gerbils inhabit burrow systems in semi-arid regions of Central Asia. The burrow systems are permanent and, as the gerbil numbers fluctuate, are alternately abandoned and reoccupied. The Pre-Balkhash dataset contains estimates of the proportion of burrows occupied by great gerbils at a given time and location, in addition to gerbil population density estimates. The proportion of burrows occupied was estimated by researchers inspecting 30 selected burrows at each location. In our study, as in Heier et al. (2011), we used these estimates rather than population density estimates, as the former have demonstrated more explanatory power for plague outbreaks than the latter. In the present work, the term 'abundance' will be used for this proportion.

Observed variation of great gerbil abundance, as recorded in the Pre-Balkhash dataset, formed a basis for the modelling of great gerbil dynamics. The temporal fluctuations of the gerbil abundance are considerable (Fig. 1); in the Bakanas part of Pre-Balkhash, abundance fluctuates regularly between about 0.1 and 0.8 with a mean of 0.36 (see Section S2 in the ESM for estimation). In the remaining parts of Pre-Balkhash, the fluctuations are less regular and less spatially homogenous; here, the spatial mean varies typically between 0.2 and 0.7 (see Fig. 1), with a temporal mean of 0.41. For Pre-Balkhash as a whole, the temporal mean abundance is 0.38. The extremely low abundance in the early 1980s across Pre-Balkhash is thought to have been caused by an infectious disease other than plague (V. Ageyev, personal observation). In addition to interannual variation, there is variation within the year. Abundance is at its lowest in early spring after high winter mortality, increases during spring and summer due to reproduction and reaches a peak in the autumn.

The gerbil abundance shows a high spatial correlation in Pre-Balkhash (see Kausrud et al. (2007) and Section S3 in the ESM); in years with high abundance, nearly all sampled locations had a high abundance, and vice versa in years with low abundance. This spatial correlation lay behind our model assumption that gerbil abundance is spatially homogeneous. However, there were also years when parts of the area had a higher or lower abundance than others. For this reason, we have included one model with simple spatial heterogeneity (see Section S9 in the ESM) for comparison with the homogeneous models.

Three models for gerbil dynamics were used in plague simulations: a simple white noise model; a biannual autoregressive model, AR(1), giving temporally correlated and irregular fluctuations; and a model with regular cycles, based on a sine function with a flexible (stochastic) period. Commonly, regular cycles are modelled by the use of AR(2) models [or AR(3) or AR(4) on a biannual scale with seasonality]. Here, however, the sine model was chosen for three reasons. Firstly, simulations from it resembled the observed data more closely. Secondly, modelling the exact density-dependent structure of gerbil dynamics was not necessary to address the scope of this study, that is, to describe the effect that different dynamics have on plague outbreaks. Thirdly, a model with quite regular cycles was desirable as a contrast to the other two models. Seasonal variation was included in the models as spring and autumn showed systematic differences in the original data.

In the three models for gerbil dynamics, the following notation is used:

- t is biannual time (odd numbers = spring, even numbers = autumn);
- x_t is the logit-transformed gerbil abundance at time t. The logit function, $f(g) = \log(g/(1 - g))$, transforms any number between 0 and 1 to a number between $-\infty$ and ∞;

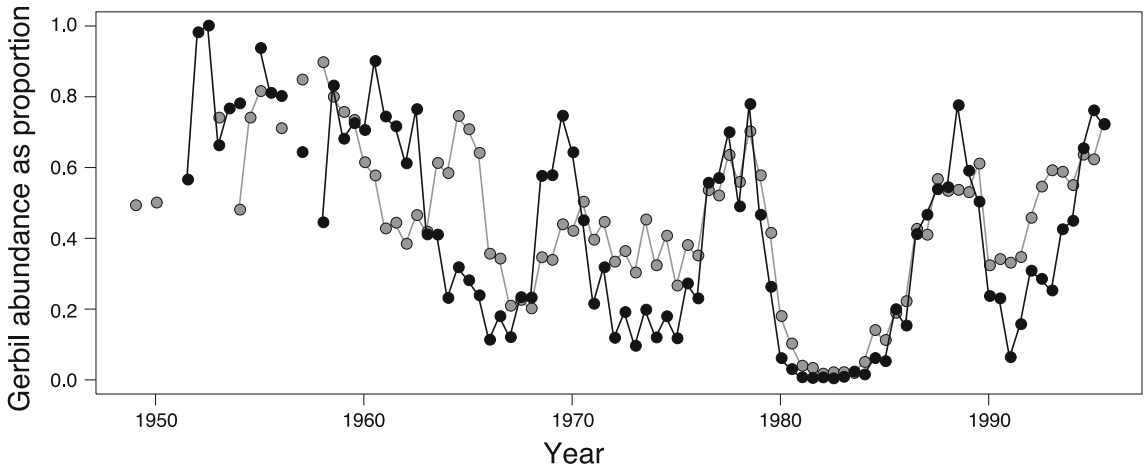

Fig. 1 Original gerbil abundance data. *Black points* indicate data aggregated over the *Bakanas area*, which covers about half the Pre-Balkhash. Regular cycles can be seen. *Grey points* indicate data aggregated over the Pre-Balkhash area outside Bakanas, where the fluctuations are less regular. Observations were made in spring and autumn, and seasonal variation can be seen as a zigzag pattern, that is, gerbil abundance is generally lower in spring than in autumn. The number of observations varied greatly over the time period and was generally low until 1959 (implying higher uncertainty), with some seasons missing altogether

– $s(t)$ is the season at time t (1 = spring, 2 = autumn);
– ε_t is an i.i.d. random term at time t.

White noise model, that is, short-term variation only:

$$\begin{aligned} x_t &= \mu_{s(t)} + \varepsilon_t \\ \varepsilon_t &\sim \mathrm{N}(0,\ \sigma) \end{aligned} \tag{1.1}$$

where $\mu_{s(t)}$ is the temporal mean for spring [$s(t) = 1$] and autumn [$s(t) = 2$], while σ is the standard deviation (SD) of the normally distributed noise.

Model with autocorrelated, irregular fluctuations, that is, long-term and short-term variation:

$$\begin{aligned} x_t &= \alpha_{0,s(t)} + \alpha_1 x_{t-1} + \varepsilon_t \\ \varepsilon_t &\sim \mathrm{N}(0, \sigma) \end{aligned} \tag{1.2}$$

where $\alpha_{0,s(t)}$ and α_1 are constants, the latter being an autoregression coefficient of first order.

Model with regular cycles in addition to irregular long-term and short-term variation:

$$\begin{aligned} x_t &= \alpha_{0,s(t)} + \alpha_1 x_{t-1} + b\sin(2\pi f(t+\theta_t)) + \varepsilon_t \\ \theta_t &\sim \mathrm{N}(\theta_{t-1}, \tau) \\ \varepsilon_t &\sim \mathrm{N}(0, \sigma) \end{aligned} \tag{1.3}$$

where now b is the amplitude and f is the frequency of the cycles; θ_t is the phase offset, varying stochastically with time and thus giving a variable length of the cycles; and τ measures the amount of variability in the period of the cycles.

Simulations from these models provided time series of gerbil abundances for use in the simulations of plague outbreaks. Parameter values for Models (1.1) and (1.2) were obtained by fitting the models to data from the whole Pre-Balkhash area; for Model (1.3), data from the Bakanas subarea were used (Table 1, and Section S4 in the ESM). The Bakanas subarea showed more regular cycles than the rest of Pre-Balkhash, and we used this as a basis for Model (1.3) in order to make the parameter values as realistic as possible. In the simulations, we initialised Models (1.2) and (1.3) by setting x_1 equal to the mean abundance for the spring season in each model, found analytically for Model (1.2) and by simulating 1,000,000 time steps for Model (1.3). The initial value for θ_1 in Model (1.3) was 0.

Table 1 Parameter values for Models (1.1–1.3). The period in Model (1.3) is $1/f = 19.12$ time steps = 9.6 years

Parameter	Estimate
Model (1.1): white noise	
μ_1	−0.63
μ_2	−0.34
σ	1.18
Model (1.2): autocorrelated, irregular fluctuations	
$\alpha_{0,1}$	−0.37
$\alpha_{0,2}$	0.29
α_1	0.93
σ	0.42
Model (1.3): regular cycles	
$\alpha_{0,1}$	−0.59
$\alpha_{0,2}$	0.36
α_1	0.89
b	0.51
f	0.052
τ	0.50
σ	0.38

In order to study the effect of different levels of temporal mean and variability of gerbil abundance on plague outbreaks, we manipulated the mean and variability after the simulation of gerbil abundance data. Firstly, the simulated data (on logit scale) were standardized by subtraction of the mean and division by SD (see below). Next, variability was manipulated by multiplying the standardized data by a rescaling factor; numbers from 0 to 2 in steps of 0.2 were used. Lastly, mean abundance was set by adding a constant to the data; here, numbers from −1.8 to 1.2 in steps of 0.2 were used. The data were then transformed to the original scale (proportions between 0 and 1) by the inverse logit function. The chosen mean abundances on the logit scale correspond to mean abundances between 0.14 and 0.77 on the original scale at zero variability. Examples of simulations from the models are shown in Fig. 2.

The variability in each model, before manipulation, was found by simulating 100,000 time steps and calculating the SD of the result (on logit scale). SD was 1.19 in Model (1.1), 1.17 in Model (1.2), and 1.43 in Model (1.3). The higher variability in Model (1.3) is partly due to the regularity of the cycles, which places more values at high and low phases, and fewer close to the mean.

In order to investigate the effect of regularity of the fluctuations, it was necessary to assess in all three models the 'noise colour', which describes the relative amount of long-term vs. short-term variation in the dynamics. Models (1.2) and (1.3) might differ not only in regularity, but also in proportion of long-term variation, and the results must be viewed against this background. To this end, we used a measure often referred to as the spectral exponent (here we call this γ; see Section S5 in the ESM). In white noise, $\gamma = 0$; whenever $\gamma > 0$, we use the term *reddened* noise as per Inchausti and Halley (2003). The higher the γ, the higher the predominance of long-term variation in the dynamics.

Simulating plague occurrence given gerbil abundance

The spatial model for plague occurrence in Heier et al. (2011) provides a basis for cellular automaton simulations of plague outbreaks in a grid representing a geographical area. Each cell corresponds to a square of 20 × 20 km^2 and each time step to 6 months, which is the resolution of the data in the Pre-Balkhash dataset. In the model, the probability that a square will be infected by plague at a certain time is given by the presence or absence of plague in that square and its eight neighbours 6 months earlier, and by past great gerbil abundance. The model is the result of an extensive model selection process in Heier et al. (2011), including models with separate formulations for invasion and persistence, a host abundance threshold for invasion of plague, climatic variables and so on. Although these variables are likely to be important, their effect could not be ascertained by the available data. Yet, the spatial formulation of the present model, together with the gerbil dynamic models, enables complex structures to be described.

To apply Heier et al.'s (2011) model in the present simulations, we made two modifications. Firstly, because it is not possible to infer true absence of plague at a location with the limited sample sizes employed in the Pre-Balkhash data, the definition of presence and absence of plague was changed to prevalence above or below a chosen threshold of 0.001. This level was chosen because it gave the clearest results in the parameter estimation of Model (2) (see below); however, a range of different levels gave similar results (see Section S6 in the ESM). Secondly, the weak spatial correlation was excluded (see Section S6 in the ESM). Note, however, that indirectly, there will be spatial correlation due to the dependence of plague presence in neighbouring squares at the previous time point. Thus, the following model was used:

$$\begin{aligned}\operatorname{logit}(P(y_{i,t}=1)) &= \beta_0 + \beta_1 y_{i,t-1} + \beta_2 n^{y}_{i,t-1} \\ &\quad + \begin{cases} \beta_{3,0} g_{t-1} & \text{if } y_{i,t-1}=0 \\ \beta_{3,1} g_{t-1} & \text{if } y_{i,t-1}=1 \end{cases} \end{aligned} \quad (2)$$

where

- $y_{i,t}$ is presence or absence of plague in square i at time t, that is, $y_{i,t} = 1$ when the prevalence was above the chosen threshold of 0.001, and $y_{i,t} = 0$ when it was below;
- t is biannual time; odd numbers = spring, even numbers = autumn;
- $n^{y}_{i,t-1}$ is the extent of plague in neighbouring squares half a year earlier, that is, the proportion of the eight neighbouring squares having plague prevalence above the threshold, where the corner squares were given a weight = 0.4 relative to the adjacent squares;
- g_{t-1} is the gerbil abundance half a year earlier. g_t is related to x_t in Models (1.1–1.3), x_t being the logit-transform of the abundance g_t at time t;
- βs are regression coefficients.

Parameter values for Model (2) were obtained by estimation based on the Pre-Balkhash dataset (Table 2). Estimation was performed using the glm function in the R software (R Development Core Team 2011). Uncertainty in prevalence data due to limited sample sizes was accounted for by imputation, and the results were summarized using the package mitools (Lumley 2010), as in Heier et al. (2011). For further details on the estimation procedure and graphs illustrating the model, see Section S6 in the ESM.

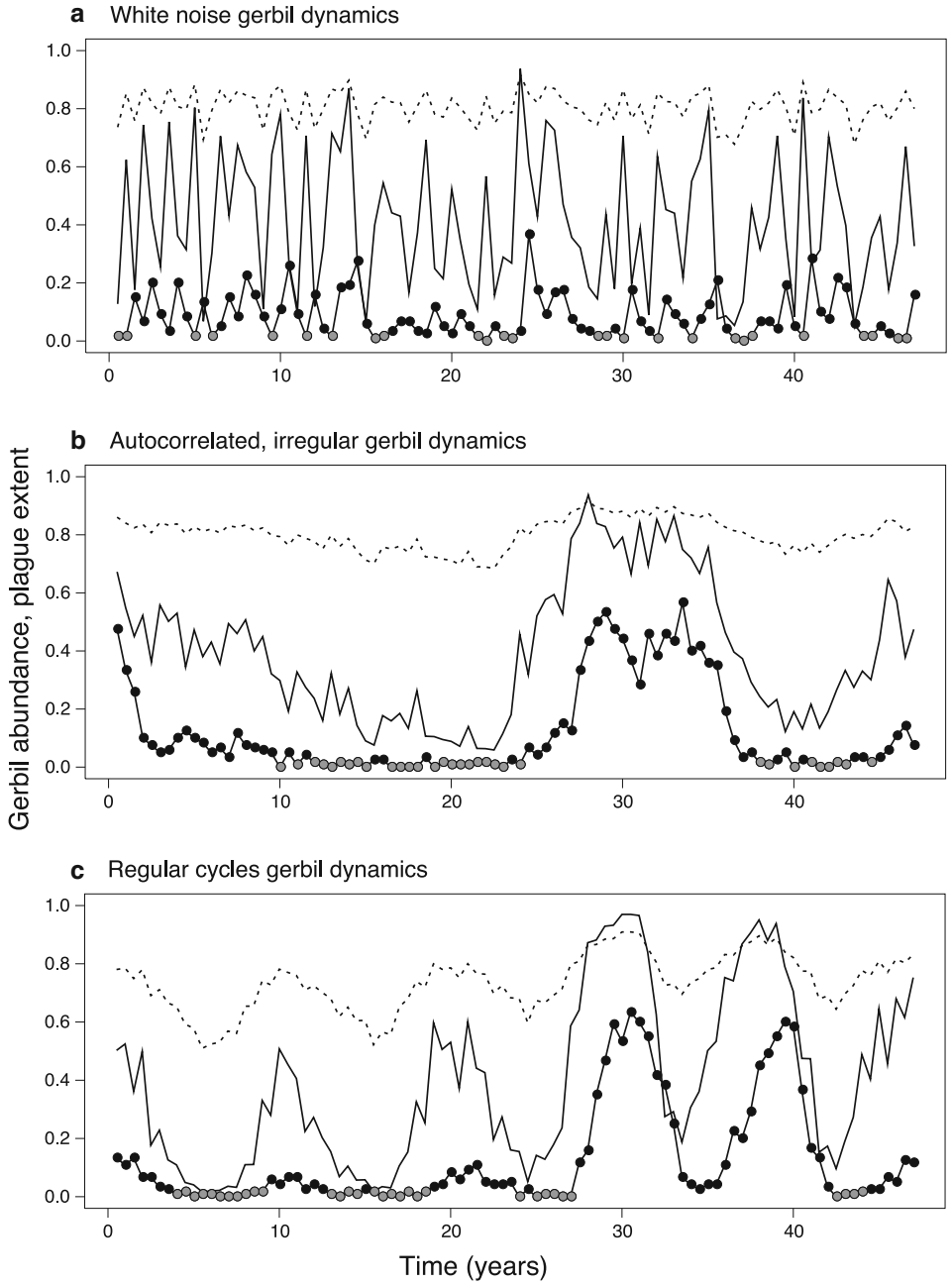

Fig. 2 Dynamics of gerbil abundance and plague extent. *Lines without points* indicate gerbil dynamics simulated from: **a** white noise model [Model (1.1)]; **b** model giving autocorrelated, irregular fluctuations [Model (1.2)]; **c** regular cycles model [Model (1.3)]. *Solid lines* show dynamics with the same variability and mean level as in the original data; *broken lines* illustrate simulations with smaller variability but a higher mean level. *Lines with points* indicate simulated plague outbreaks based on the *Solid line* gerbil dynamics; the *y*-axis shows the proportion of squares with plague at each time step. *Black* vs. *grey* points show plague activity above vs. below the threshold of outbreak following its present definition (that is, plague in at least three squares)

Table 2 Parameter values for Model (2). Standard errors are given in parentheses

Parameter effects		Estimates (SE)
β_0	Constant term	−5.20 (0.53)
β_1	Plague prevalence > 0.001 previous season	3.12 (0.91)
β_2	Proportion of neighbouring squares with prevalence > 0.001 previous season	2.13 (0.59)
$\beta_{3,0}$	Past gerbil abundance if $y_{i,t-1} = 0$ (possibility of invasion)	4.77 (0.91)
$\beta_{3,1}$	Past gerbil abundance if $y_{i,t-1} = 1$ (possibility of persistence)	1.45 (1.21)

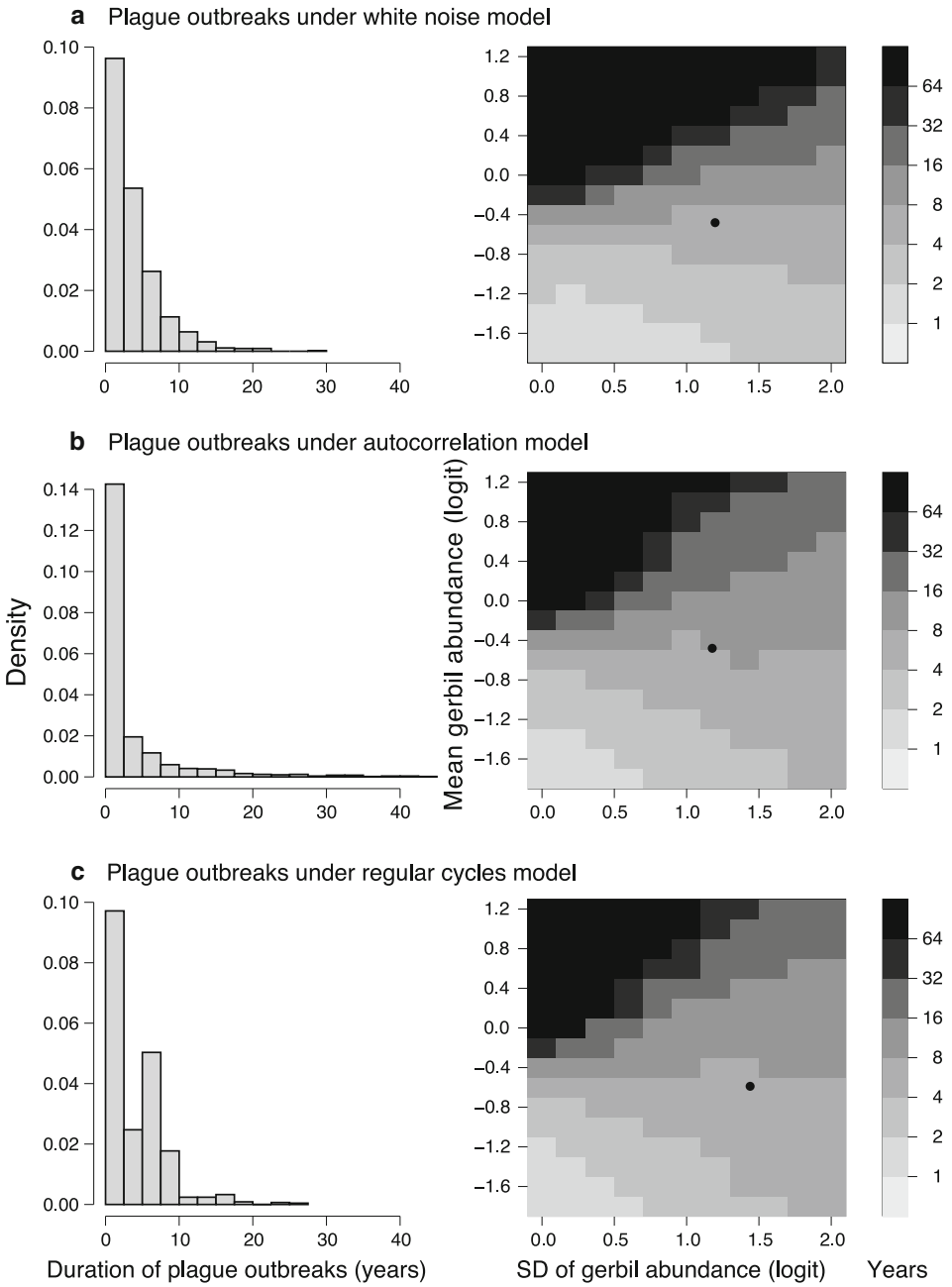

Fig. 3 Duration of simulated plague outbreaks given gerbil dynamics with: **a** white noise only; **b** autocorrelated, irregular fluctuations; **c** regular cycles. *Left panels* show the distribution of duration of plague outbreaks for mean abundance = 0.4 (logit mean abundance = −0.40) and SD = 1 (logit scale). *Right panels* show mean duration as shades of *grey*. The axes show mean and SD of gerbil abundance. The *black point* indicates gerbil dynamics similar to the original data; logit mean abundance = −0.48 in whole Pre-Balkhash and −0.59 in Bakanas (see 'Materials and methods')

With this model, the persistence or fade-out of an outbreak of plague depends on the gerbil abundance. A high abundance will increase the number of squares with plague, whereas a low abundance will decrease it, exact levels depending on the number and configuration of cells already infected. Given a grid size and definition of plague outbreaks as described below, an outbreak can be expected to persist from one season to the next when gerbil abundance is above 0.28 (L. Heier, unpublished data), and to fade out when gerbil abundance drops below this value, although the process may take several years. This is in agreement with field observations that fade-out of plague outbreaks follows depressions in gerbil abundance.

Outbreaks of plague were simulated on a grid consisting of 10×12 cells so that he total area of the grid

corresponded roughly to the area of the Pre-Balkhash plague focus. The cells used in the simulations were arranged in a rectangle, whereas the area of the plague focus has an irregular shape (see Section S1 in the ESM).

An extra layer of cells was included around the rectangle of interest and set to be plague-free at all time steps. These cells were used in the calculation of the probability of plague in edge cells, specifically in the calculation of the proportion of neighbouring cells infected with plague at the previous time step (see Model (2)). This boundary condition (see Fu and Milne 2004 and White et al. 2007) meant that plague could not invade from outside, corresponding to natural barriers, such as large lakes.

For each gerbil dynamic model [Models (1.1–1.3)] and for each combination of gerbil abundance mean and variability (see above), a simulation of gerbil dynamics and plague outbreaks was run, making a total of $3 \times 11 \times 16 = 528$ plague simulations. To cancel any effect of initial conditions of gerbil dynamics, each plague simulation was initiated when the gerbil dynamic simulation had completed 75 time steps. At the start of each plague simulation, all cells in the grid were set to be plague-free ($y_{i,1} = 0$). At each time step, plague occurrences were simulated from Model (2) based on plague occurrences at the previous time step and simulated gerbil abundance. Each plague simulation ran for 10,000 time steps, producing a long time series of recurring outbreaks of plague.

To make summary statistics of the duration of outbreaks, the duration of each outbreak in the 10,000 time steps was recorded. An outbreak was defined as a period of time when there was plague in at least three cells (2.5 % of the area) (see Bartlett 1957). This threshold is arbitrary, and both a higher or a lower value could have been chosen as long as it separated time periods with extensive plague activity from periods with little or no activity; the qualitative effect of different gerbil dynamics on outbreak duration did not depend on the exact threshold level.

The mean duration of outbreaks was found for each combination of mean abundance, variability, and gerbil dynamic type [Models (1.1–1.3)]. The distribution of outbreak durations for each type of gerbil dynamic and for various levels of variability and mean abundance was assessed by histograms to check for skewness and multimodality. Of these histograms, one from each gerbil dynamic is shown in the results section.

Results

Examples of simulated plague outbreaks are shown in Fig. 2, together with the three types of gerbil dynamics underlying them. With white noise dynamics [Model (1.1)], the gerbil abundance could fluctuate greatly from one time step to the next, and plague outbreaks were small and closely spaced. With autocorrelated, irregular fluctuations [Model (1.2)], the autocorrelation ensured that changes were generally slower and plague outbreaks could build up to cover a larger area. With regular cycle dynamics [Model (1.3)], the plague outbreaks followed the regular pattern of the host's abundance. (An example of the spatial development of a simulated plague outbreak is shown in Section S7 in the ESM.)

The noise colour for the white noise dynamics [Model (1.1)] was found to be close to white ($\gamma = 0.12$). The gerbil dynamics with autocorrelated, irregular fluctuations [Model (1.2)] had a reddened noise ($\gamma = 1.62$); that is, a substantial amount of long-term vs. short-term variation. The regular cycles model [Model (1.3)] had approximately the same noise colour ($\gamma = 1.68$).

The distribution of the duration of outbreaks was highly skewed for all gerbil dynamics (most outbreaks were of short duration) (Fig. 3, left panels). For regular cycles, the distribution was multimodal with modes corresponding to single or multiple population cycles (mean cycle length: 9.6 years). The difference between mode values (e.g., 5.0–7.5 years) and cycle length is due to inter-epizootic periods. The distributions shown in Fig. 3 correspond to gerbil abundance mean and SD equal to 0.4 and 1 (on logit scale), respectively, but other combinations of gerbil abundance mean and SD resulted in similar distributions. These results show that it is difficult to define a 'typical' outbreak. We have used the mean as a summary statistic in order to compare the effect of different host abundance dynamics, but outbreaks of much longer and shorter durations were frequent.

The mean duration of the simulated plague outbreaks was found to depend on the degree of autocorrelation as well as the mean and SD of host abundance (Fig. 3, right panels). Cyclicity had little effect on the mean outbreak duration. The dependence on host abundance mean and SD was found to be qualitatively similar for all three types of dynamics. At a mean abundance of 0.38 (logit mean abundance $= -0.5$), the mean outbreak duration was similar (4 years) at all levels of variability. An increase in mean abundance invariably led to an increase in the mean duration of outbreaks. At SD $= 0$, the mean outbreak durations had a wide range from only 0.7 years at mean abundance $= 0.14$ (logit mean abundance $= -1.8$) up to continuous circulation (5000 years) at mean abundance ≥ 0.6 (logit mean abundance ≥ 0.4). At SD > 0, the range of mean outbreak durations became narrower. At SD $= 2$ (logit scale), the range was from 1.4 to 32 years for white noise dynamics, corresponding to mean abundance from 0.25 to 0.67 (logit mean abundance from -1.8 to 1.2; the variability affects the mean abundance on linear scale); and

from 2.1 to 11 years for both autocorrelated, irregular dynamics and for regular cycle dynamics.

A few additional plague simulations were performed, based on modified versions of the gerbil abundance models (see Section S8 in the ESM). The results supported the conclusions in the present section. A simulation with simple spatial heterogeneity of gerbil abundance (Section S9 in the ESM) showed that except at very low mean gerbil abundance, spatial heterogeneity caused longer mean durations of outbreaks than homogenous versions.

Discussion

The mean duration of plague outbreaks among great gerbils was found to depend on mean host abundance, temporal variability, and the presence of temporal autocorrelation. The model for plague outbreaks was based on a spatio-temporal regression analysis, predicting plague occurrence at given levels of gerbil abundance.

We assumed that plague does not significantly influence gerbil abundance, the prevailing view today (Gage and Kosoy 2005; Kausrud et al. 2007). In fact, a gerbil population cycle is observable in the data in the absence of any outbreaks of plague. However, the results in Begon et al. (2006) suggest that the effect of plague infection on host survival may be substantial, although it is not known whether this is compensatory or additive to other mortality factors. Plague infection may be one of many factors contributing to the gerbil cycles, such as high fecundity combined with interactions with food supply and levels of predators, and interannual variation in climate and vegetation (Kausrud et al. 2007, 2010).

There is evidence that even small effects of a disease can contribute to the overall dynamics of the host species, for instance, by delaying maturity, which can produce multi-annual cycles (Telfer et al. 2005; Smith et al. 2008). The effect on outbreak duration will depend on the nature of the changed population dynamics. Independently of this, if the population dynamics change in infected but not in uninfected ares, the resultant spatial heterogeneity may contribute to more persistent outbreaks according to the present results.

Comparison with general studies of extinction time

The mean duration of plague outbreaks increased with the mean abundance of gerbils for all three types of gerbil population dynamics modelled here. This is a consequence of the fact that both parameters $\beta_{3,0}$ and $\beta_{3,1}$ in Model (2) were positive, meaning that the probability of plague occurrence in a grid cell increased with gerbil abundance. Theoretical work on disease predicts the same effect (e.g., Nåsell 1999b, 2005), and the results are in line with models and observations showing that endemicity depends on population size (Bartlett 1957, 1960).

High temporal variability in gerbil abundance shortened the duration of outbreaks when the mean abundance was high and increased it when it was low. In other words, as the temporal variability in the gerbil abundance increased, the difference in the mean duration of outbreaks at high and low mean abundance became less pronounced. This can be explained as follows. High variability increases the probability of both high and low levels of gerbil abundance; high levels will increase plague activity, whereas low levels will decrease it. In cases of high mean abundance, an increased variability will increase the probability of abundance depressions that are sufficiently long and deep to end an ongoing outbreak. In cases of low mean abundance, variability will increase the probability of abundance peaks that will enable a plague outbreak. The result for high mean abundance is analogous to results in conservation biology. Models and empirical data have demonstrated that the risk of species extinction increases with temporal variability in the environment (Lande 1993; Foley 1994; Hakoyama and Iwasa 2000; Alvarez 2001; Inchausti and Halley 2003). The result for low mean abundance is unique to our study, but does not contradict the results from conservation biology. Low mean gerbil abundance corresponds to an unfavourable environment that is unsuitable for the species in question; only if there is temporal variability can the species establish itself for short periods of time.

The effect of temporal correlation, present in Models (1.2) and (1.3) but not in Model (1.1), was similar to the effect of temporal variability: it reduced the mean duration of plague outbreaks when mean abundance was high, and increased it when mean abundance was low. Empirical studies have shown that the probability of species extinction increases with both the strength of the variability and the amount of long-term vs. short-term variation, that is, the noise colour exponent (Inchausti and Halley 2003). Further, Johst and Wissel (1997) show in a modelling study that the increase in the probability of extinction with noise redness is stronger when variability is high. However, temporal correlation may also *reduce* the probability of extinction. In a simulation study, Schwager et al. (2006) show that this may happen if short periods of extremely poor environmental conditions are possible, or if the population is highly sensitive to the environment (over-compensatory density regulation: see Ovaskainen and Meerson 2010 for a review). Our results show both an increasing and a decreasing effect of temporal correlation on the probability of extinction. When mean gerbil abundance is high, periods of extremely low levels of gerbil abundance are rare and, with little temporal correlation, too short to cause disease extinction. Increased temporal correlation will

prolong these periods and thus increase the probability of extinction. When mean abundance is low, periods of extremely low gerbil abundance are more frequent, and temporal correlation will here reduce the probability of extinction by separating years with poor conditions from years with good conditions, making outbreaks last longer than under corresponding white noise dynamics.

Cyclicity in the gerbil abundance dynamics had little effect on the mean duration of outbreaks. This is in contrast to Wichmann et al. (2003), where a fluctuating environment with long, regular cycles produced a shorter extinction time for a population than did irregular red or white noise. However, we found that cyclicity produced a multimodal distribution of outbreak durations, where the duration corresponded to one or several cycles of gerbil dynamics. This contrasted with the non-cyclic case, where the distribution was highly skewed with many outbreaks of short duration as well as some of very long.

Additionally, the different types of gerbil abundance dynamics were observed to affect the spatial extent of outbreaks and the duration of inter-epizootic periods. Although not the focus of the present study, these two aspects of disease dynamics deserve to be studied more closely in future work.

Predictions of plague in Kazakhstan

The present simulation results can be used to predict the duration of outbreaks of plague under gerbil dynamic scenarios differing from those observed in the Pre-Balkhash area so far. A relevant issue is how the gerbil dynamics will be affected by ongoing climate changes, and resultant effects on plague outbreaks. Mean temperatures and yearly precipitation in Central Asia are predicted to change towards 2100 (IPCC 2013) and temporal variability is generally expected to increase (Collins et al. 2013). Once the response of the gerbil dynamics to these changes has been established, predictions can be made for plague dynamics, at least in part. It is important, however, to bear in mind that the ecological system is complex and that many parameters are unknown, each of which may affect the plague dynamics (e.g., plague–vector–host interaction, population structure, alternative hosts, effect of climate on all components of the system, and human activities). The following are examples of possible chains of reasoning.

Changes in mean temperature and precipitation may increase or decrease the suitability of the great gerbil habitat, depending on local conditions. This may increase or decrease their temporal mean abundance locally, which in turn will increase or decrease the duration of plague outbreaks in those areas. On a large spatial scale, however, overall plague activity may remain unchanged as climate change may lead merely to a shift in the geographical distribution of great gerbils. It has been argued that the predicted increase in spring temperatures will increase plague activity in Central Asia (Stenseth et al. 2006), but this prediction assumes that mean levels of gerbil abundance would not change locally.

As for increased variability, its effect depends on the response of gerbil dynamics. If gerbil abundance follows the climatic fluctuations, increased variability will stabilize the duration of plague outbreaks, that is, it will lead to longer outbreaks in areas where they are currently short, and vice versa. Increased climate forcing may also make the noise colour of gerbil dynamics more like that of the environment, which in the case of temperature is reddened with exponent $\gamma \approx 0.5$ on time scales appropriate to population dynamics (Pelletier 2002). Further, a synchronization of gerbil dynamics over larger areas might be expected, assuming that weather conditions occur on a large spatial scale. According to the current results, this will lead to shorter plague outbreaks. The burn-out of plague outbreaks is important, because the disease does not always re-emerge when gerbil abundance increases after low levels. The disease may skip a peak of gerbil abundance, which in turn may lead to a reduced amount of infective agent in the environment. Survival of the bacterium in the soil or in dead hosts are two of several hypotheses on how it persists during interepizootic periods (Gage and Kosoy 2005; Easterday et al. 2012; Schmid et al. 2012).

Conclusions

This study extends current knowledge on diseases in dynamic host populations by focussing on the effect of different host dynamics on the duration of disease outbreaks. In part, the results parallel results from conservation biology; at high mean gerbil abundance, the mean duration of plague outbreaks was reduced by variability and temporal correlation, while at low mean gerbil abundance, the mean duration was increased by the same factors; that is, they had a stabilizing effect on the mean duration of outbreaks. Cyclicity, on the other hand, had little effect on the mean duration of outbreaks, but resulted in a multimodal distribution of duration. The results are relevant to predicting the duration of plague outbreak in cases where gerbil population dynamics are known or can be predicted.

Author contributions L.H. designed the study, performed all analyses and undertook the main writing. H.V. advised on the design of the study and the text. G.S. advised on the modelling and the text. All authors discussed the analyses and have read and approved the final manuscript.

Acknowledgments The authors thank Nils Chr. Stenseth, Boris Schmid, Kyrre L. Kausrud, and Thomas Marcussen for comments and suggestions on the manuscript. Trond Reitan is acknowledged for his assistance on model selection in BUGS and for comments on the manuscript. Three anonymous reviewers have given valuable comments and advice.

References

Alvarez LHR (2001) Does increased stochasticity speed up extinction? J Math Biol 43:534–544

Anderson RM, May RM (1991) Infectious diseases of humans. Oxford University Press, Oxford

Bartlett MS (1957) Measles periodicity and community size. J Royal Stat Soc Ser A Gen 120:48–70

Bartlett MS (1960) The critical community size for measles in the United-States. J Royal Stat Soc Ser A Gen 123:37–44

Begon M, Klassovskiy N, Ageyev V, Suleimenov B, Atshabar B, Bennett M (2006) Epizootiologic parameters for plague in Kazakhstan. Emerg Infect Dis 12:268–273

Clancy D, O'Neill PD, Pollett PK (2001) Approximations for the long-term behavior of an open-population epidemic model. Methodol Comput Appl Probab 3:75–95

Collins M, Knutti R, Arblaster J, Dufresne J-L, Fichefet T, Friedlingstein P, Gao X, Gutowski WJ, Johns T, Krinner G, Shongwe M, Tebaldi C, Weaver AJ, Wehner M (2013) Long-term climate change: projections, commitments and irreversibility. In: Stocker TF, Qin D, Plattner G-K, Tignor M, Allen SK, Boschung J, Nauels A, Xia Y, Bex V, Midgley PM (eds) Climate Change 2013: The physical science basis Contribution of Working Group I to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. Cambridge University Press, Cambridge and New York

Davis S, Begon M, De Bruyn L, Ageyev VS, Klassovskiy NL, Pole SB, Viljugrein H, Stenseth NC, Leirs H (2004) Predictive thresholds for plague in Kazakhstan. Science 304:736–738

Davis S, Leirs H, Viljugrein H, Stenseth NC, De Bruyn L, Klassovskiy N, Ageyev V, Begon M (2007) Empirical assessment of a threshold model for sylvatic plague. J R Soc Interface 4:649–657

Diekmann O, Heesterbeek H, Britton T (2013) Mathematical tools for understanding infectious diseases dynamics. Princeton University Press, Princeton

Dobson AP, Carper ER (1996) Infectious diseases and human population history - Throughout history the establishment of disease has been a side effect of the growth of civilization. Bioscience 46:115–126

Dubyanskiy VM, Pole SB, Klassovskiy NL (2003) Environmental and statistical characteristics of the dynamics of the great gerbil spring abundance in geographic populations of the Central Asian natural focus of plague. Vestnik KazNU im Al-Farabi Ser Ekol 2:127–131 **(in Russian with English abstract)**

Easterday WR, Kausrud KL, Star B, Heier L, Haley BJ, Ageyev V, Colwell RR, Stenseth NC (2012) An additional step in the transmission of Yersinia pestis? ISME J 6:231–236

Foley P (1994) Predicting extinction times from environmental stochasticity and carrying-capacity. Conserv Biol 8:124–137

Foley P, Foley J (2010) Modeling Susceptible Infective Recovered dynamics and plague persistence in California rodent-flea communities. Vector Borne Zoonotic Dis 10:59–67

Frigessi A, Holden M, Marshall C, Viljugrein H, Stenseth NC, Holden L, Ageyev V, Klassovskiy NL (2005) Bayesian population dynamics of interacting species: great gerbils and fleas in Kazakhstan. Biometrics 61:230–238

Fu SC, Milne G (2004) A flexible automata model for disease simulation. In: Sloot PMA, Chopard B, Hoekstra AG (eds) 6th International Conference on Cellular Automata for Research and Industry. Amsterdam, pp 642–649

Gage KL, Kosoy MY (2005) Natural history of plague: perspectives from more than a century of research. Annu Rev Entomol 50:505–528

Grassly NC, Fraser C (2006) Seasonal infectious disease epidemiology. Proc R Soc B-Biol Sci 273:2541–2550

Hakoyama H, Iwasa Y (2000) Extinction risk of a density-dependent population estimated from a time series of population size. J Theor Biol 204:337–359

Hanski I (1999) Metapopulation ecology. Oxford University Press, USA

Heesterbeek JAP, Roberts MG (1995) Mathematical models for microparasites in wildlife. In: Grenfell BT, Dobson AP (eds) Ecology of infectious diseases in natural populations. Cambridge University Press, Cambridge, pp 90–122

Heier L, Storvik GO, Davis SA, Viljugrein H, Ageyev VS, Klassovskaya E, Stenseth NC (2011) Emergence, spread, persistence and fade-out of sylvatic plague in Kazakhstan. Proc R Soc B-Biol Sci 278:2915–2923

Inchausti P, Halley J (2003) On the relation between temporal variability and persistence time in animal populations. J Anim Ecol 72:899–908

IPCC (2013) Annex I: Atlas of global and regional climate projections. In: Van Oldenborgh GJ, Collins M, Arblaster J, Christensen JH, Marotzke J, Power SB, Rummukainen M, Zhou T (eds) Climate Change 2013: The physical science basis Contribution of Working Group I to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. Cambridge University Press Cambridge, United Kingdom and New York

Johst K, Wissel C (1997) Extinction risk in a temporally correlated fluctuating environment. Theor Popul Biol 52:91–100

Kausrud KL, Viljugrein H, Frigessi A, Begon M, Davis S, Leirs H, Dubyanskiy V, Stenseth NC (2007) Climatically driven synchrony of gerbil populations allows large-scale plague outbreaks. Proc R Soc B-Biol Sci 274:1963–1969

Kausrud KL, Begon M, Ben Ari T, Viljugrein H, Esper J, Büntgen U, Leirs H, Junge C, Yang B, Yang MX, Xu L, Stenseth NC (2010) Modeling the epidemiological history of plague in Central Asia: palaeoclimatic forcing on a disease system over the past millennium. BMC Biol 8:112

Lande R (1993) Risks of population extinction from demographic and environmental stochasticity and random catastrophes. Am Nat 142:911–927

Lumley T (2010) mitools: tools for multiple imputation of missing data. R package version 2.0. http://cran.r-project.org/web/packages/mitools/. Accessed 1 Mar 2014

Nåsell I (1999a) On the quasi-stationary distribution of the stochastic logistic epidemic. Math Biosci 156:21–40

Nåsell I (1999b) On the time to extinction in recurrent epidemics. Royal-Statistical-Society Epidemics Workshop. Isle Skye, Scotland, pp 309–330

Nåsell I (2005) A new look at the critical community size for childhood infections. Theor Popul Biol 67:203–216

Ovaskainen O, Meerson B (2010) Stochastic models of population extinction. Trends Ecol Evol 25:643–652

Pelletier JD (2002) Natural variability of atmospheric temperatures and geomagnetic intensity over a wide range of time scales. Proc Natl Acad Sci USA 99:2546–2553

R Development Core Team (2011) R: a language and environment for statistical computing. R Foundation for Statistical Computing,

Vienna, Austria. http://www.R-project.org. Accessed 1 Mar 2014
Reijniers J, Begon M, Ageyev VS, Leirs H (2014) Plague epizootic cycles in Central Asia. Biol Lett 10:20140302
Ross R (1911) The prevention of malaria, 2nd edn. Murray, London
Sauvage F, Langlais M, Yoccoz NG, Pontier D (2003) Modelling hantavirus in fluctuating populations of bank voles: the role of indirect transmission on virus persistence. J Anim Ecol 72:1–13
Schmid BV, Jesse M, Wilschut LI, Viljugrein H, Heesterbeek JAP (2012) Local persistence and extinction of plague in a metapopulation of great gerbil burrows, Kazakhstan. Epidemics 4:211–218
Schwager M, Johst K, Jeltsch F (2006) Does red noise increase or decrease extinction risk? Single extreme events versus series of unfavorable conditions. Am Nat 167:879–888
Smith MJ, White A, Sherratt JA, Telfer S, Begon M, Lambin X (2008) Disease effects on reproduction can cause population cycles in seasonal environments. J Anim Ecol 77:378–389
Stenseth NC, Samia NI, Viljugrein H, Kausrud KL, Begon M, Davis S, Leirs H, Dubyanskiy VM, Esper J, Ageyev VS, Klassovskiy NL, Pole SB, Chan KS (2006) Plague dynamics are driven by climate variation. Proc Natl Acad Sci USA 103:13110–13115
Swinton J, Harwood J, Grenfell BT, Gilligan CA (1998) Persistence thresholds for phocine distemper virus infection in harbour seal Phoca vitulina metapopulations. J Anim Ecol 67:54–68
Telfer S, Bennett M, Bown K, Carslake D, Cavanagh R, Hazel S, Jones T, Begon M (2005) Infection with cowpox virus decreases female maturation rates in wild populations of woodland rodents. Oikos 109:317–322
White SH, del Rey AM, Sanchez GR (2007) Modeling epidemics using cellular automata. Appl Math Comput 186:193–202
Wichmann MC, Johst K, Moloney KA, Wissel C, Jeltsch F (2003) Extinction risk in periodically fluctuating environments. Ecol Model 167:221–231