Science **Supporting Online Material**

Predictive Thresholds for Plague in Kazakhstan

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Material and Methods

Field data. The plague microbe, its various hosts, and the many flea species that transmit the disease between rodents and from rodents to humans have been monitored intensively by scientists in Kazakhstan since 1949. Monitoring effort is directed towards detecting plague in rodents and their fleas. When plague is found near human communities, insecticides are pumped into burrow systems to kill the fleas. This is followed by rodent removal. However, the sites from which our data come are remote and no control actions were undertaken when plague was detected.

Prevalence data and abundance data (proportion of burrow systems occupied and number of gerbils per burrow system) were sampled independently. Estimates of occupancy were based on transects of 30 burrow systems. A further 10 burrows, within walking distance of the transect, were observed to obtain counts of the maximal number of simultaneously visible gerbils. Gerbil densities were calculated as the product of the number of burrow systems per hectare, the proportion of occupied burrow systems and the average number of gerbils per burrow system.

Estimates of flea density require the digging up of burrow systems of the great gerbil and are therefore less common than estimates of gerbil density. Estimates of flea density were usually taken near four key areas regularly monitored for plague bacteria while estimates of gerbil density are relatively uniformly distributed over the plague focus. To estimate the number of fleas per burrow, 10 burrows systems were visited and all migrating fleas were collected from burrow entrances. The burrow systems were then dug out to the level of the feeding chambers in an attempt to collect those fleas not at the burrow entrances. Estimates of flea density were calculated as for gerbil density with average number of fleas per burrow system replacing average number of gerbils per burrow system. The estimates of flea abundance represent fleas of all species (there are more than one *Xenopsylla* species involved in transmission of plague) and does not take into account the fleas carried by the gerbils themselves. For the latter half of the time series only, an average number of fleas per gerbil may be calculated for each sector as the ratio of number of rodent fleas tested for plague to the number of gerbils tested.

For the prevalence data, gerbils were sampled using snap-traps, and together with their fleas, tested for plague using a bacteriological test (isolation attempts of plague from blood, spleen, liver or flea homogenates). For any method of monitoring disease a threshold rate of infection below which the disease is not detected is inevitable and the success of isolation attempts is certainly no exception. In the 1970's serological methods of detection became available and gerbils were also tested for plague antibody. The latter results are unreliable as indicators of present infection, but useful in confirming the absence of plague from a population since they identify hosts that have ever been infected rather than those infected at the time of sampling. In

years when plague is active the frequency with which it is isolated bacteriologically, relative to the proportion of great gerbils testing seropositive, indicates that the serological test is the more sensitive. In the present study success or failure in isolating the bacteria from blood and organs of a sample of gerbils is used to infer the presence and absence of plague, and on this basis there is support for an epidemiological threshold in terms of host abundance. An alternative perspective is that the results arise from a detection threshold and there is simply a positive correlation between prevalence and abundance with some delay. Against this interpretation is that when serological data on gerbils is available (Fig. S1) it confirms that during periods when all isolation attempts fail, plague was also absent serologically. Taken together with the sample sizes (Fig. *S1*) then if infection does persist, it is in a tiny fraction of rodents. Hence the data show qualititative shifts between periods when plague is inactive and plague epizootics, and this indicates a real epidemiological threshold is operating.

The finest spatial scale recorded in the data is the sector, an area covering 100 square kilometres. A 'large square' contains 16 sectors. The number of samples collected from a particular sector in a particular year is variable and only a proportion of sectors were visited each season. There were two areas at which data were collected more or less every season. To produce the time series shown in the main text, data on prevalence and occupancy were aggregated over the large squares that encompass these semi-permanent sites. Surveillance occurred from spring through to fall though not in the hottest months of summer. This coincides with the times of year when gerbils are most active—breeding, dispersing and colonizing empty burrow systems. Data from the same calendar year were pooled to obtain (a) an annual estimate of gerbil abundance and (b) a binary variable representing whether or not plague was detected that year.

Data analysis. Relationships between annual estimates of abundance (occupancy and density) and the probability that plague was detected in gerbils (1 = plague detected that year, 0 = plague not detected) were assessed with generalized nonlinear regression models (*S2*) with binomial error. To account for serial dependence among years, year was added as a first-order autoregressive variable in a generalized nonlinear autoregression model (*S3*). First-order autoregressive linear logistic regression models were also fitted for comparison with the non-linear set. Delays of up to five years were included in the set of models considered. The data set was restricted to those years for which occupancy had already been monitored for five years. Missing values for spring/fall occupancy were replaced by an average of the previous and subsequent spring/fall values. Years where less than 100 gerbils were captured were omitted from the analyses because prevalence among gerbils was regularly less than 0.01. Model selection was based on Akaike's information criterion (AIC) which may be defined as $-2\ln(L(\hat{\theta}|y))+2K$ where $L(\hat{\theta}|y)$ is the likelihood of the model with parameter values $\hat{\theta}$ given the data y and K is the number of parameters (*S4*). A common interpretation of this formula is that the first term represents a measure for lack of fit, while the second term is a "penalty" for increasing the "size" of the model (there is a trade-off between describing the data well and the principle of parsimony). The criterion has a solid theoretical underpinning, based on a data analysis philosophy that no model is true; rather the truth is far more complex then any model used (*S4*). AIC can be used to compare different types of candidate models, given the response data (y) are equal. Models that differed in AIC by 2 or less were considered to be equally good approximations of the data. Direct comparison of AIC values between and within the two right-hand columns in Table S1 is valid. The AIC values for the first-order generalized nonlinear autoregression models were generally better than those of the respective generalized nonlinear

models. Detailed results for these models are given in Table S1. Confidence intervals for the model based on occupancy with one and two year delays were calculated using the profile likelihood (*S5*, *S6*). The analyses were performed using the GAR functions in the R-program. R is a fast S-Plus clone freely available to the public (http://cran.r-project.org).

References and Notes

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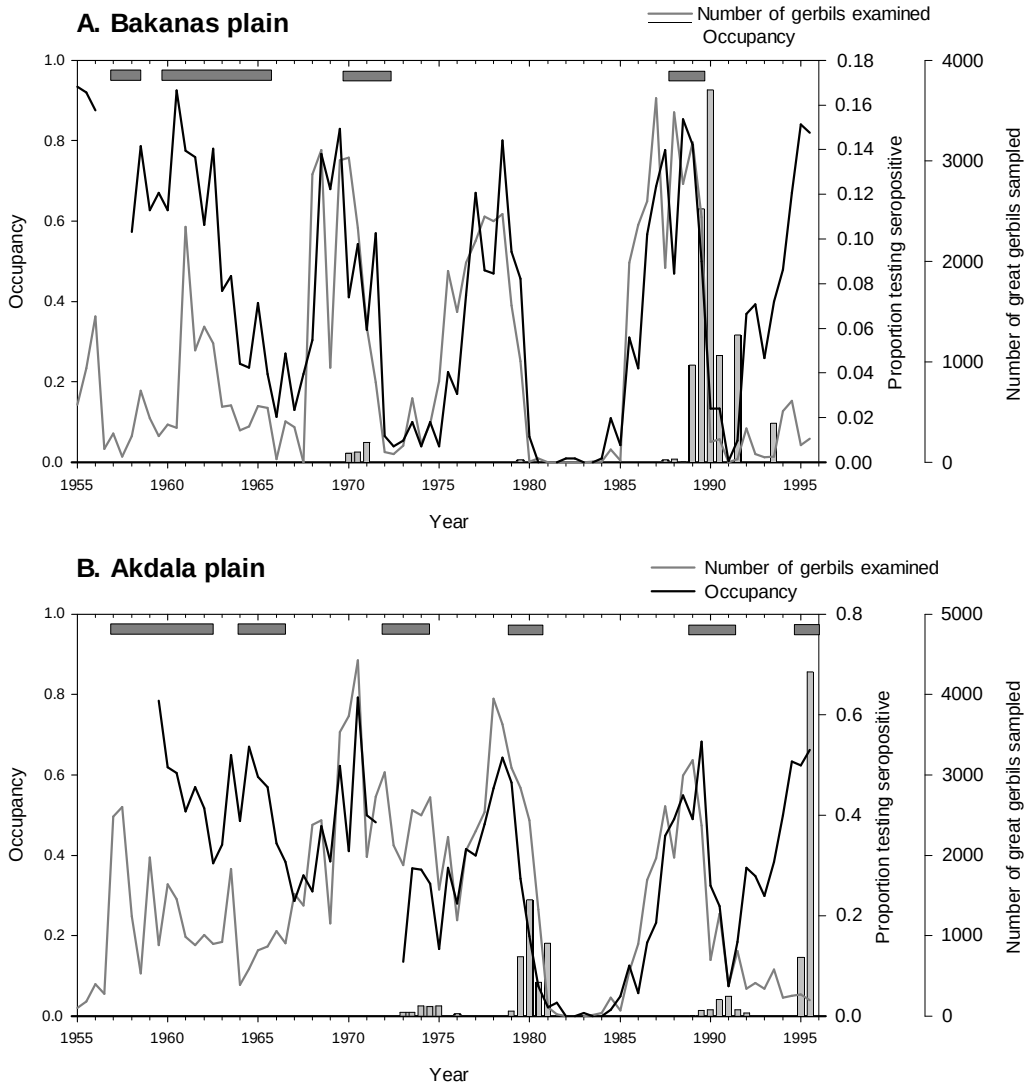

Fig. S1. Great gerbil occupancy, number of gerbils examined and the results of the serological testing for the sites in (**A**) Bakanas plain, and (**B**) Akdala plain. Serological results are first reported in 1970. The horizontal bars along the tops of the axes represent periods in which plague was successfully isolated from gerbils (see Fig. 1 of main text). We note that in 1979 a single rodent tested seropositive at the site in Bakanas plain.

Table S1. Performance of generalized nonlinear autoregression models.

Delays included in model	AIC for threshold model	AIC for logistic model
Occupancy		
1	28.46	61.56
2	25.72	56.55
3	32.46	74.71
1 and 2*	25.01	53.11
2 and 3	†	58.16
1 and 2 and 3	26.42	54.39
Density		
1	30.71	80.34
2	26.54	75.66
3	36.68	84.25
1 and 2	25.56	76.8
2 and 3	28.53	77.66
1 and 2 and 3	30.06	78.61

*Parameter estimates and 95% confidence intervals for this model are γ = 0.476 (0.355, 0.572), η = 0.242 (0.127, 0.497) and β = 0.852 (0.226, 1.768). The respective weights for the one and two-year delays are 0.586 (0.379, 0.953) and 0.867 (0.582, 1.000).
†Model failed to converge.