Nonlinear effect of climate on plague during the third pandemic in China

Supporting Information

Lei Xu, Qiyong Liu, Leif Chr. Stige, Tamara Ben Ari, Xiye Fang, Kung-Sik Chan, Shuchun Wang, Nils Chr. Stenseth and Zhibin Zhang

Additional modelling material for Model A (separate models for northern and southern China)

Figure S1. Effects of predictor variables in model A for northern China.

A: Smooth effect of year ($F_{8.78,\ 432.6}$=11.61, p<0.01). B: Smooth effect of longitude and latitude of grids centre ($F_{20.8,\ 432.6}$=5.14, p<0.01). C: Smooth effect of the natural logarithm of the number of observed plague cases in the same quadrate in previous year ($F_{3.90,\ 432.6}$=17.13, p<0.01). D: Smooth effect of current year's dryness/wetness ($F_{2.47,\ 432.6}$=7.05, p<0.01), also shown on Fig. 2 in main text. E: Smooth effect of previous year's dryness/wetness ($F_{2.55,\ 432.6}$=2.68, p<0.05), also shown on Fig. 2. F: Smooth effect of the natural logarithm of the number of plague cases observed in the 8 surrounding quadrates in previous year ($F_{3.89,\ 432.6}$=5.70, p<0.01). Tick marks at the bottom of the plot show the locations of the data points along the x axis.

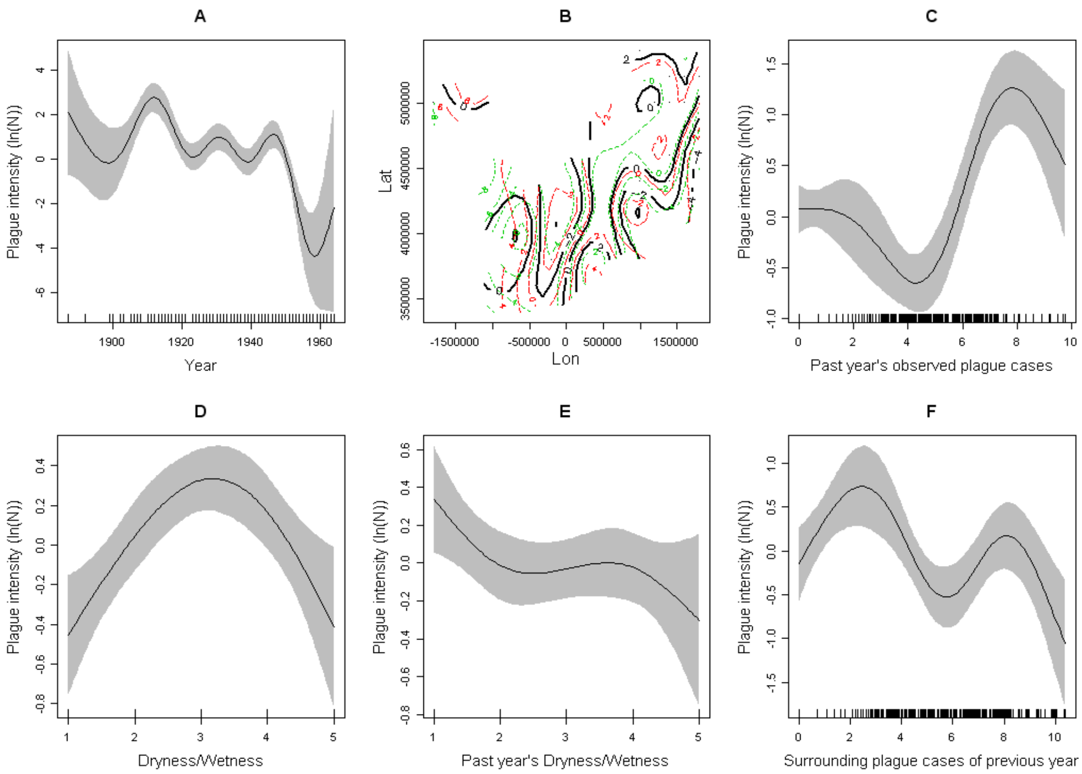


Figure S2. Residual diagnostics for model A for northern China.

A: Autocorrelation function (ACF) of annual averages of residuals. B: Residual semi-variogram. These plots indicate whether there is any remaining temporal and/or spatial correlation in the residuals; for correctly specified models, these plots will not contain any systematic patterns, otherwise any systematic pattern may provide clues for further improvements of the model specification. ACF is useful for checking whether the residuals have any temporal structure. If there is no remaining residual spatial autocorrelation, the semivariogram should be an approximately flat line. In the presence of positive (negative) spatial autocorrelation, the semivariogram will tend to curve upwards (downward).

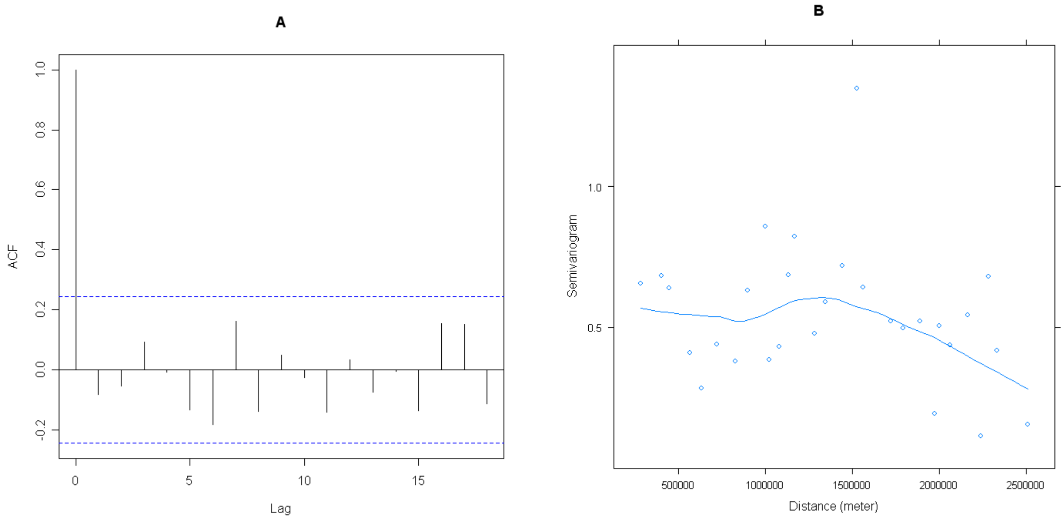


Figure S3. Effects of predictor variables in model A for southern China.

A: Smooth effect of year ($F_{8.13,\ 580.7}$=8.57, p<0.01). B: Smooth effect of longitude and latitude of grids centre ($F_{18.9,\ 580.7}$=7.71, p<0.01). C: Smooth effect of the natural logarithm of the number of observed plague cases in the same quadrate in previous year ($F_{3.65,\ 580.7}$=15.62, p<0.01). D: Smooth effect of current year's dryness/wetness ($F_{2.88,\ 580.7}$=6.29, p<0.01), also shown on Fig. 2 in main text. E: Smooth effect of previous year's dryness/wetness ($F_{1.93,\ 580.7}$=3.00, p<0.05), also shown on Fig. 2. F: Smooth effect of the natural logarithm of the number of plague cases observed in the 8 surrounding quadrates in previous year ($F_{3.86,\ 580.7}$=6.30, p<0.01). Tick marks at the bottom of the plot show the locations of the data points along the x axis.

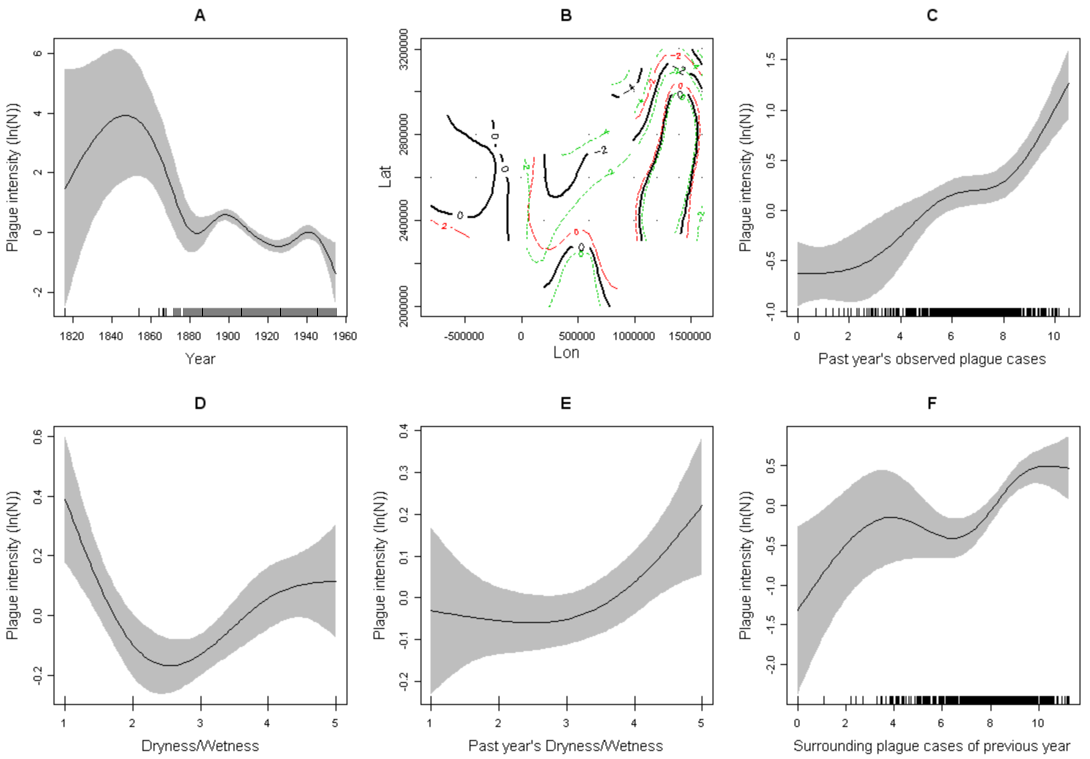
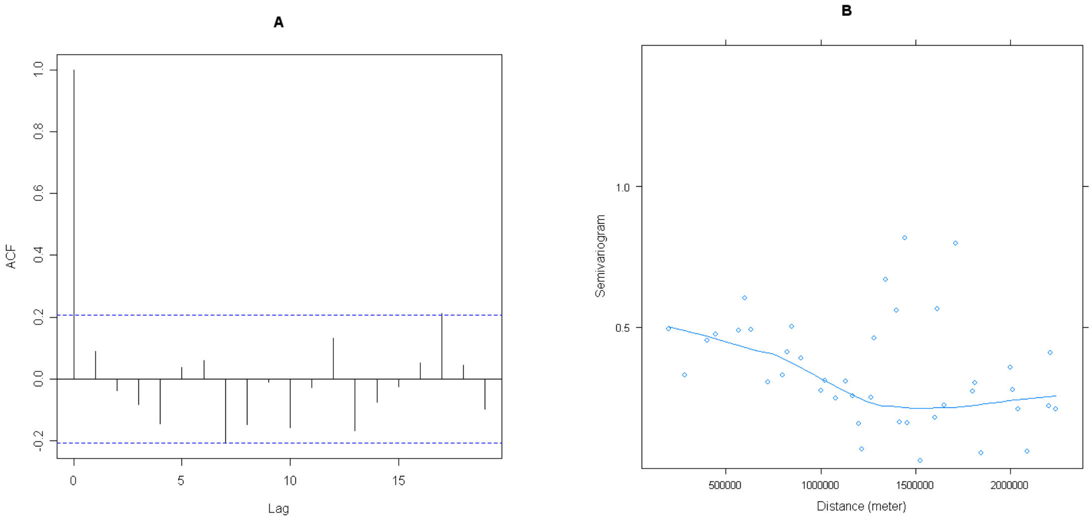


Figure S4. Residual diagnostics for model A for southern China.

A: Autocorrelation function (ACF) of annual averages of residuals. B: Residual semi-variogram. See Figure S2 for interpretation of residual diagnostics plots.



Additional modelling material for Model B (whole-China)

Figure S5. Effects of predictor variables in model B.

A: Smooth effect of year ($F_{14.4,\ 906.8}$=8.45, p<0.01). B: Smooth effect of the natural logarithm of the number of observed plague cases in the same quadrate in previous year ($F_{3.59,\ 906.8}$=32.83, p<0.01). C: Smooth effect of the natural logarithm of the number of plague cases observed in the 8 surrounding quadrates in previous year ($F_{3.55,\ 906.8}$=3.49, p<0.01). In addition, the model included two spatial terms (Fig. 3, main text): a spatially-variable effect of previous-year dryness/wetness index ($F_{89.0,\ 906.8}$=2.52, p<0.01) and a spatially-variable effect of current-year dryness/wetness index ($F_{78.8,\ 906.8}$=3.13, p<0.01).

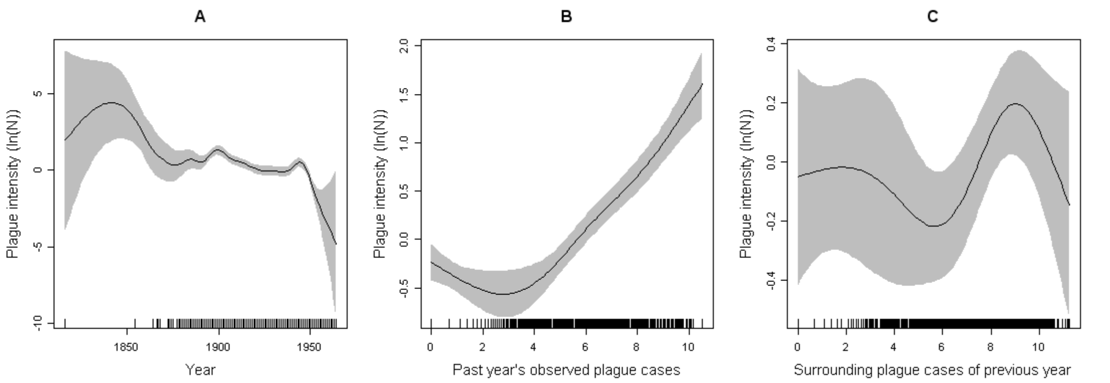
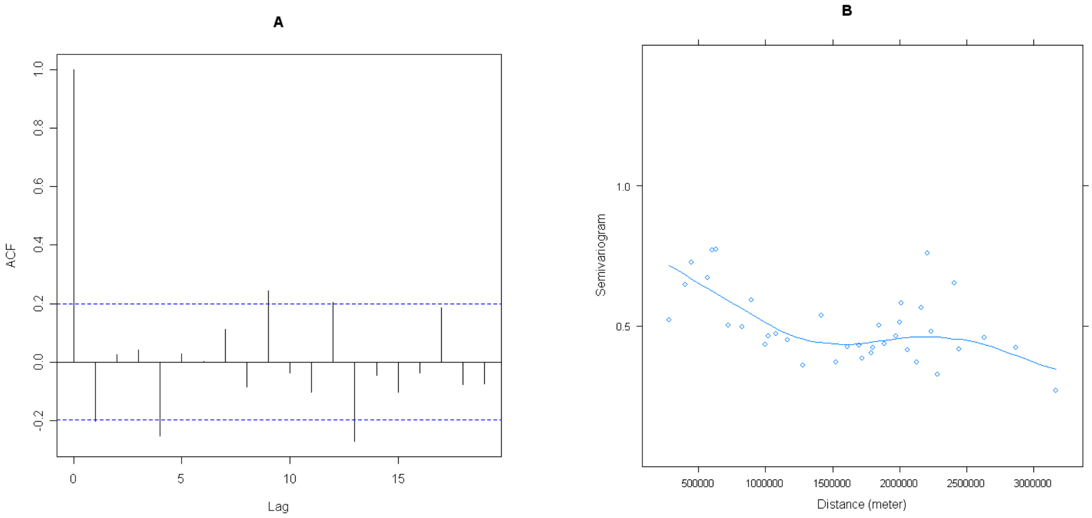


Figure S6. Residual diagnostics for model B. A: Autocorrelation function (ACF) of annual averages of residuals. B: Residual semi-variogram. See Figure S2 for interpretation of residual diagnostics plots.



Additional model diagnostics: cross validation

As a conservative way of evaluating the predictive power of alternative model formulations, we computed leave-one-year-out cross validation (CV) errors. The CV procedure was:

(i) Fit the model to a reduced data set with data for one year removed,

(ii) Make predictions for the observations not used when fitting the model,

(iii) Calculate prediction errors (predicted-observed values) for these observations,

(iv) Repeat i-iii for all years (one year left out at a time), and

(v) Calculate:

Mean CV error = $\sqrt{\frac{1}{n}\sum_{i=1}^{n}(\ln(\hat{y}_i+1)-\ln(y_i+1))^2}$,

Where $\hat{y}_i$ and y_i denote predicted and observed number of plague cases for a given year and location, respectively, and n is total sample size.

We used CV specifically to investigate whether the models might be over-fitted. For model A we compared alternative restrictions on the maximum numbers of degrees of freedom (df) for the effects of plague intensity in the same and in the neighbouring quadrates the previous year (*d* and *e* terms in equation in main text) and for the baseline spatial effect (*c* term in the same equation). Table S1 gives the resulting mean CV errors. Although mean CV error could have been reduced slightly by choosing somewhat different restrictions on the df, the results give no indication of any dramatic effects of over-fitting. The estimated partial effects of dryness/wetness generally remained qualitatively similar to the presentation given in Fig. 2 when these restrictions were altered. However, the effect of previous-year dryness/wetness did not reach statistical significance (i.e., $p>0.05$) for northern China when maximum df for the spatial *c*-term was increased to 34 (giving the lowest CV error) or the maximum df for the autoregressive *d*- and *e*-terms were reduced to 1 or 3 (more easily interpretable, but higher CV error).

Table S1. Mean CV errors of alternative formulations of model A for northern and sourthern China. The alternative formulations differed in the restrictions on the number of degrees of freedom (= number of knots – 1) on the smooth effects (*c*-, *d*-, and *e*-terms in equation in main text). Df = 1: linear effect.

			Max. df of *d*- and *e*-terms		
			1	3	4[1]
Northern China	Max. df of *c*-term	14	2.152	2.140	2.110
		24[1]	2.163	2.126	2.071
		34	2.031	2.002	1.990
Southern China	Max. df of *c*-term	14	1.877	1.895	1.891
		24[1]	1.848	1.874	1.867
		34	1.840	1.873	1.874

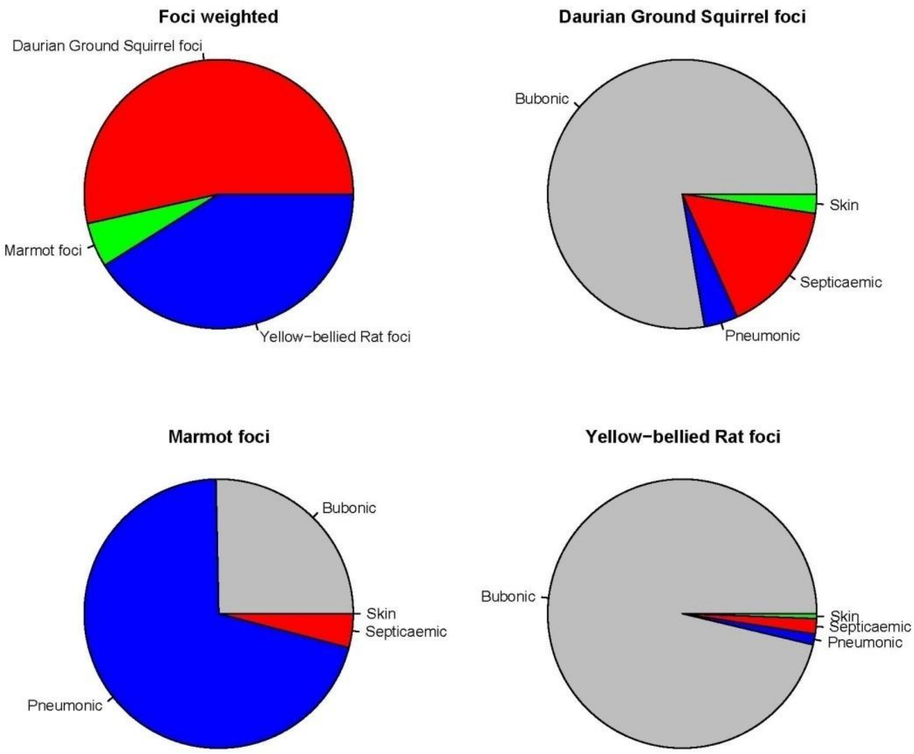
[1]Max. df used for model presented in the main text.

For model B the mean CV error of the model presented in the main text was 1.935. This was better than a sample-size-weighted mean of CV errors of model A fitted to northern and southern China separately $((476\cdot2.071^2+621\cdot1.867^2)/(476+621))^{0.5} = 1.958$. This suggests that the more complex model B explains variability (presumably spatial variability in the effects of climate) not captured by model A.

Additional information on plague data: types of plague cases in China

Pneumonic plague was much rarer than bubonic plague; incomplete records from 1947 to 1962 include 267 pneumonic plague cases out of 4,123 plague cases. However, in the marmot foci in northern China, more than 70 percent of the 221 recorded cases were pneumonic plague, within the same period.

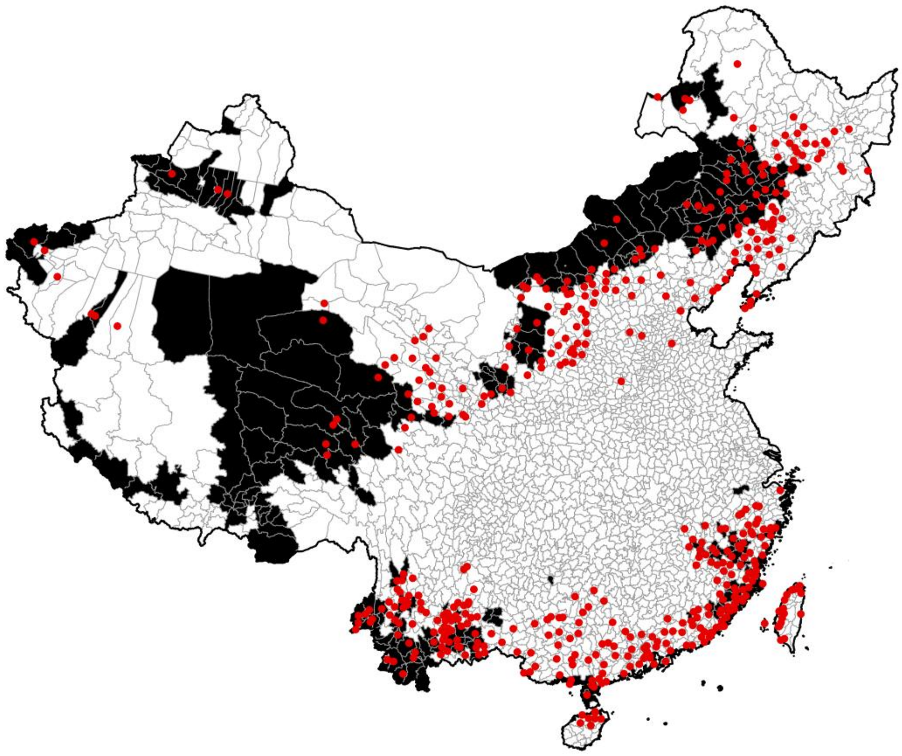
Figure S7. Pie charts of "Foci Weighted" shows the distribution of different types of human plague cases in Daurian Ground Squirrel foci, Marmot foci and Yellow-bellied Rat foci. Types of plague case in each kind of foci are for whole-China.



Additional information on plague data: distribution of human plague cases and natural plague foci in China

Figure S8 shows that occurrences of human plague cases were closely related to the locations of natural plague foci in China.

Figure S8. Plague-infected counties and natural plague foci in China. Red points indicate the municipal centres of counties with reports of human plague. Black areas indicate the distribution of natural plague foci in China (areas where *Yersinia pestis* strains have been isolated from local animal reservoirs).



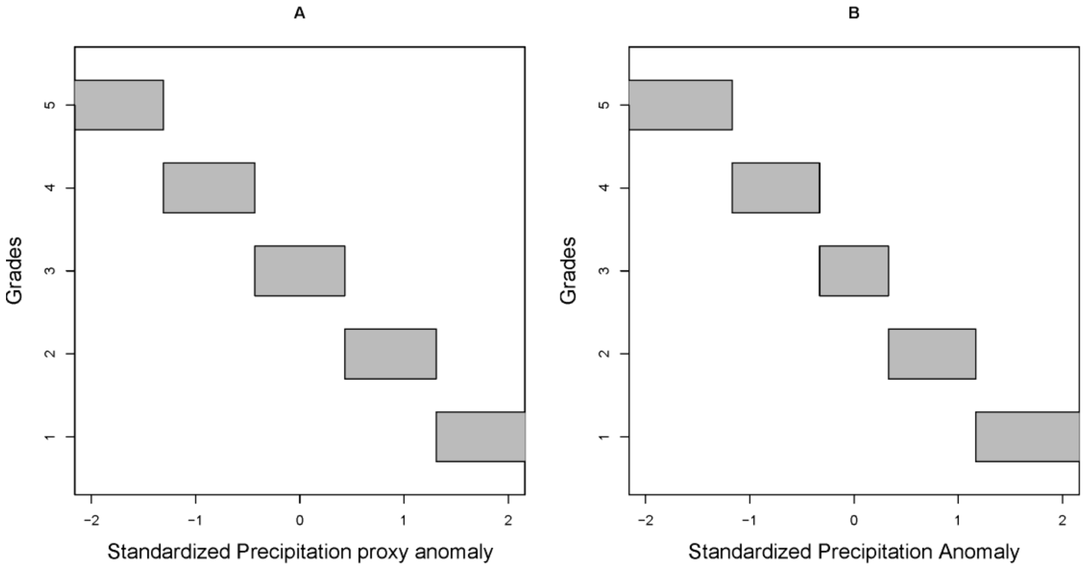
Additional information on climate data: Dryness/Wetness index

The spatial-temporal dryness/wetness (D/W) index (a proxy of precipitation) data were derived from the widely used book "*Yearly Charts of Dryness/Wetness in China for the Last 500-Year Period"* (Central Meteorological Bureau, 1981). The book was comprised of information from more than 2200 local annals and other historical records, supplemented with instrumental data for the most recent time period. The dryness/wetness of each year in each of a total of 120 stations across China was scaled into 5 grades from 1 (extremely wet) to 5 (extremely dry).

For years prior to 1951, grade classification was defined based on descriptions in historical documents about intensity and temporal extent of dryness or wetness around local stations in spring, summer and autumn. The 5 grades were defined based on qualitative information from each station, such as follows: Grade 1: *heavy rains lasting from spring to summer, serious floods*; Grade 2: *heavy rains in August*; Grade 3: *good crop harvest* or *no record of flood or drought*; Grade 4: *drought in spring*; Grade 5: *severe drought from April to August*. The frequencies of Grades 1 to 5 are approximately <10%, 20-30% (average 25%), 30-40% (average 35%), 20-30% (average 25%) and <10%. Assuming that precipitation is normally distributed, Grade 1 corresponds to precipitation >1.31 standard deviation units (SD) above the long-term average, Grade 2 to precipitation between 0.43 and 1.31 SD, Grade 3 to precipitation between -0.43 and 0.43 SD, Grade 4 to precipitation between -1.31 and -0.43 SD, and grade 5 to precipitation <-1.31 SD. Under the same assumption, the scaling of the dryness/wetness index preserves an approximately (inverse) linear relationship with precipitation (Fig. S9A)

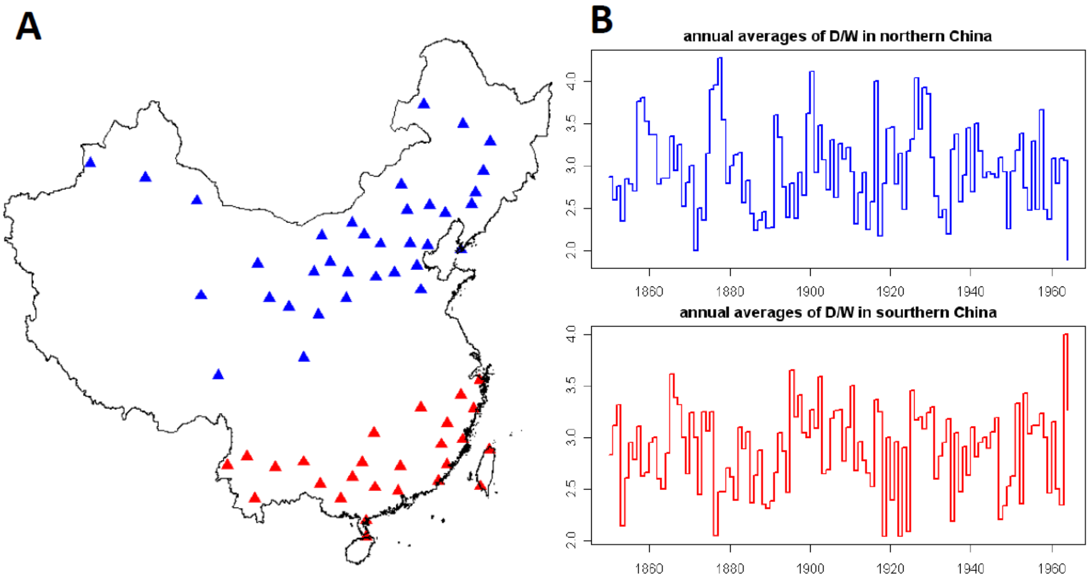
From 1951 onwards, the D/W proxy was classified into 5 grades based on May to September precipitation data collected using weather instruments. To keep the similar frequency of the data distribution, for this period the D/W index was defined as follows: Grade 1: precipitation anomaly >1.17 SD; Grade 2: 0.33 SD <precipitation anomaly <1.17 SD; Grade 3: -0.33 SD <precipitation anomaly <0.33 SD; Grade 5: precipitation anomaly < -1.17 SD. The D/W index for this period is also approximately linearly (reversely, as the D/W index increases with the drought) related to precipitation (Fig. S9B).

Figure S9. Relationship between standardized precipitation (or proxy) anomaly and five grades of D/W index. (A): Prior to 1951 based on quantitative information. (B) After 1951 based on weather instrumental records.



We used D/W data from 67 stations covering the whole plague-report area; 38 stations were located in northern China and 29 in southern China (Fig. S10A). Fig. S10B shows the annual averages of the D/W index pooled from the stations in northern and southern China.

Figure S10. (A): The positions of 67 D/W stations used in our study, stations located in northern China are drawn as blue triangles while southern stations are represented as red triangles. **(B):** annual average D/W proxy values from stations in northern and southern China.



Temporal autocorrelation of D/W index

There are significant temporal auto-correlations in the D/W index for both northern and southern China (Table S2). The auto-correlations are generally much stronger in northern China than in southern China.

Table S2. Number of stations showing significant temporal auto-correlations in northern and southern China

Time-lags	1 year	2 year	3 year	4 year	5 year	Total for 3-5 years
North	16	6	11	10	11	32
South	8	7	8	3	6	17

Additional model diagnostics: effects of D/W with other time-lags than predicted

In our model of climate effects on plague, we only considered potential effects of the D/W index of the current and previous year. This is because time-lags of climate effects on plague have generally been found to be of one-year duration at most (Stenseth et al., 2006; Enscore et al., 2002). Also, longer time-lags may not be biologically plausible. Nevertheless, as additional model diagnostics, we examined whether other time-lags of D/W (lags from -5 to 5) may have explanatory power beyond the information contained in the current and lag-1 of D/W. Significant effects at non-plausible time-lags might be indicative of spurious D/W-plague relationships.

First, we tested whether D/W at different time-lags entered significantly as predictor variables in generalized additive models with the response variable being the residuals from Model A (accounting for effects of current-year and previous-year D/W):

$$R_{i,j} = a + f(D/W_{i-t,j}) + \varepsilon_{i,j} \qquad \text{(A.1)}$$

Here, $R_{i,j}$ is the residual from model A for location *j* in year *i*, *a* is the intercept, *f* is a natural cubic spline function of the D/W index for the given location in year *i-t*, and $\varepsilon_{i,j}$ is the error term.

Model results are shown in Table S3. We see that in northern China, D/W at lag 3 years (*i.e.*, D/W three years before plague observations) showed significant effect on residual plague intensity, but the adjusted R-sq. is very small (= 0.02). We also found that the D/W index at lag -4 years (*i.e.*, D/W four years *after* plague observations) showed significant effect, but the adjusted R-sq. is also very small (= 0.02). In southern China, we found that D/W at lags 3 years and -5 years showed significant effects on residual plague intensity, but the effects are also small (adjusted R-sq = 0.01). We hypothesize that these effects are caused by the temporal autocorrelation of the D/W index (Table S2) combined with inaccuracies in the D/W data.

Table S3. Time-lagged D/W effects on residuals of Model A, including the *p*-value, adjusted R square and deviance explained. In this table, time-lag(t) is the D/W in t years before, the same as table S4. Positive lags represent (apparent) effects on plague of previous-years' D/W, negative lags represent subsequent-years' D/W.

Time-lag (t)	5	4	3	2	1[1]	0[1]	-1	-2	-3	-4	-5
Northern											
p-value	0.16	0.54	0.02*	0.90	0.39	0.49	0.39	0.22	0.58	0.01*	0.09
R-sq	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.00
Dev. explained	0.00	0.00	0.02	0.00	0.01	0.00	0.01	0.01	0.00	0.03	0.01
Southern											
p –value	0.35	0.52	0.05*	0.92	0.71	0.50	0.71	0.15	0.35	0.44	0.03*
R-sq	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.01
Dev. explained	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.01

[1]It is reasonable that the effects D/W index of the current year and previous year are zero because these effects have been accounted for in Model A.

We therefore devised a test of the independent effects of D/W at different time-lags, accounting for the autocorrelation in the D/W series. To do so, we first removed the linear effects of current-year and previous-year D/W from the lag *t* of D/W,, by regression:

$$D/W_{i-t,j} = a_j + \beta_{0,t,j} D/W_{i,j} + \beta_{1,t,j} D/W_{i-1,j} + \varepsilon_{i,j} \qquad \text{(A.2)}$$

Here, *t* varies from 5 to -5 without 1 and 0. The residuals from model A.2 are the adjusted lag -*t* of *D/W*, denoted as $\overline{D/W_{\iota-t,J}}$. Then we tested whether D/W_{i-t} may have additional explanatory power by regressing the residuals from model A on the adjusted D/W_{i-t} via the following model (notation as in equation A.1):

$$R_{i,j} = a + f\left(\overline{D/W_{\iota-t,J}}\right) + \varepsilon_{i,j} \qquad \text{(A.3)}$$

Models results (Table S4) suggest that, after adjusting for the autocorrelation in the D/W index, no other lags of the D/W index than 0 or 1 are associated with the plague intensity.

Table S4. Results from model A.3, including the *p*-values of the term *f*, the adjusted R-square values and the deviance explained. For both northern and southern China, the autocorrelation-adjusted D/W show no significant lagged effects ($p>0.05$) beyond the effects at lags 0 and 1 years. Positive lags represent (apparent) effects on plague of previous-years' D/W, negative lags represent subsequent-years' D/W.

Time-lag (t)	5	4	3	2	-1	-2	-3	-4	-5
Northern									
p-value	0.69	0.45	0.09	0.97	0.70	0.14	0.55	0.118	0.32
R-sq	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.01	0.00
Dev. explained	0.04	0.14	1.43	0.00	0.03	1.05	0.08	1.29	0.24
Southern									
p –value	0.39	0.65	0.23	0.94	0.6	0.09	0.99	0.65	0.34
R-sq	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00
Dev. explained	0.18	0.05	0.56	0.00	0.13	1.5	0.00	0.05	0.512

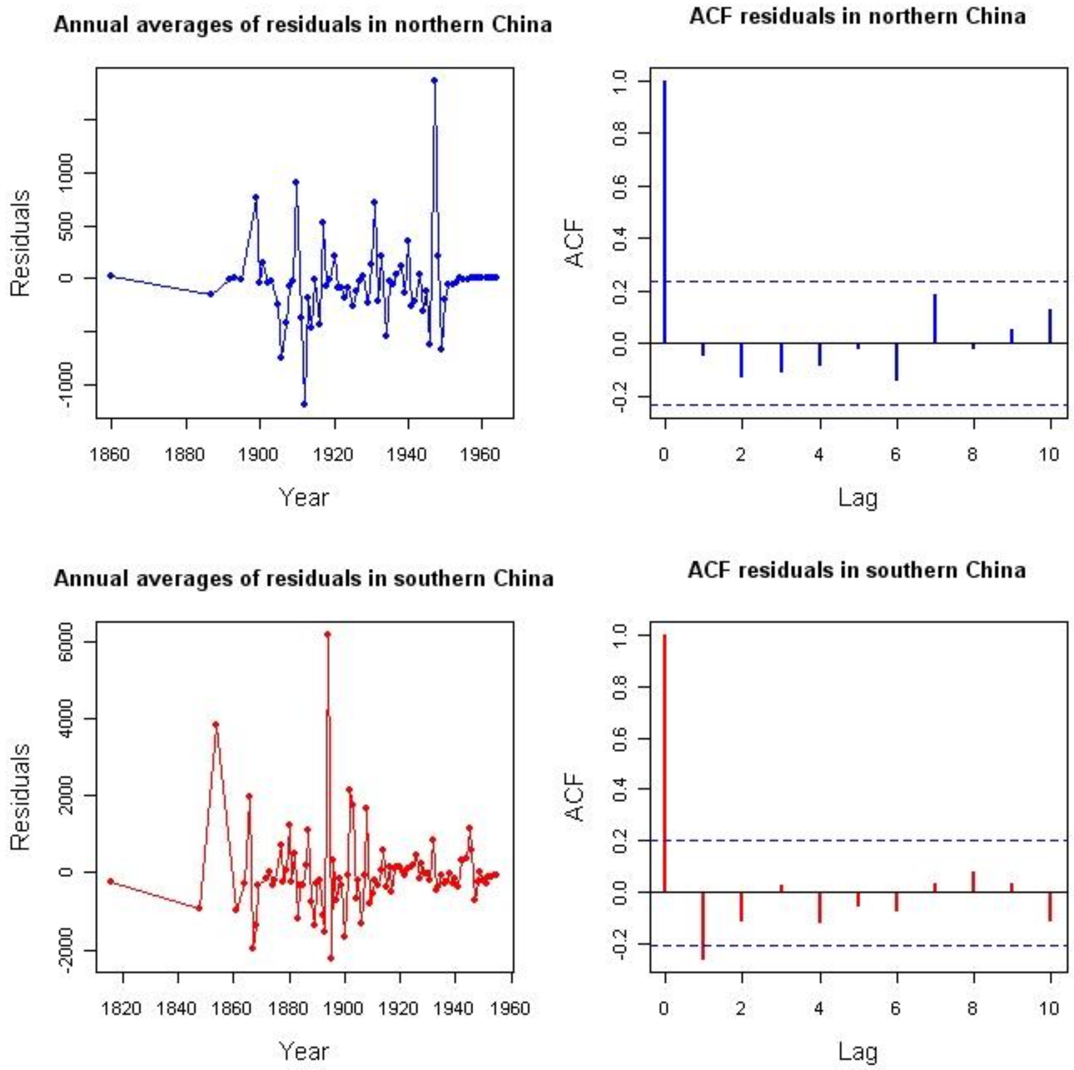
Additional model diagnostics: low-frequency trends

To test whether the modelled effect of the D/W index is caused by low-frequency trends in both plague and D/W, we built a model based on Model A but with no effects of D/W (of neither current nor preceding year):

$$P_{i,j} = a + b_i + c(Lon_j, Lat_j) + d(\hat{P}_{i-1,j}) + e(N_{i-1,j}) + \varepsilon_{i,j} \quad \text{(A.4)}$$

The notations are similar to those in model A. The residuals from this model show no significant temporal autocorrelation (Fig. S11), suggesting that the detected effects of D/W on plague intensity in model A are not caused by some low-frequency trend.

Figure S11: Residual time series plots and residual autocorrelation function (ACF) for model A.4 fitted to northern and southern China.



References:

1. Central Meteorological Bureau (1981) *Yearly Charts of Dryness/Wetness in China for the Last 500-Year Period* (Cartographic Publishing House, Beijing).

2. Stenseth NC, et al. (2006) Plague dynamics are driven by climate variation. *Proc Natl Acad Sci USA* 103:13110-13115.

3. Enscore RE, et al. (2002) Modelling relationships between climate and the frequency of human plague cases in the southwestern United States, 1960-1997. *Am J Trop Med Hyg* 66:186-196.