Effects of meteorological factors on scrub typhus in a temperate region of China

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SUMMARY

Scrub typhus is emerging and re-emerging in many areas: climate change may affect its spread. To explore the effects of meteorological factors on scrub typhus, monthly cases of scrub typhus from January 2006 to December 2012 in the Laiwu district of temperate northern China were analysed. We examined the correlations between scrub typhus and meteorological factors (and their delayed effects). We built a time-series adjusted negative binomial model to reflect the relationships between climate variables and scrub typhus cases. The key determinants of scrub typhus transmission were temperature, relative humidity and precipitation. Each 1 °C increase in monthly average temperature in the previous 3 months, each 1% increase in monthly relative humidity in the previous 2 months and each 1 mm increase in monthly precipitation in the previous 3 months induced 15·4%, 12·6% and 0·7% increases in the monthly number of cases, respectively. In conclusion, scrub typhus is affected by climate change in temperate regions.

Keywords: Climate, scrub typhus, temperate.

INTRODUCTION

Scrub typhus, caused by *Orientia tsutsugamushi*, is a potentially fatal infectious disease [1]. It is prevalent in the western Pacific, southern Asia, and northeastern Australia. The causative agent is transmitted to humans during the bite of chiggers (larval trombiculid mites) [2, 3]. New foci of disease transmission have been reported in southern India [1] and northern China [4–7]. Cases of scrub typhus acquired in Asia during 'eco-tourism' have been increasingly reported in Europe, America [8, 9] and Australia [10]. As tourism increases, other remote foci of vectors and

organisms may also be identified. Early diagnosis and treatment are important for the prevention of serious complications associated with the disease [1].

The life-cycle of trombiculid mites includes seven stages [egg, deutovum, larva (chigger), protonymph, deutonymph, tritonymph, adult], of which only chiggers are parasitic [11] and requires host body or tissue fluid [12]. Nymphs and adults are free living in the soil, feeding mainly on the eggs and larvae of arthropods [11]. Forest clearings, riverbanks, and grassy regions provide optimal conditions for mites [13, 14]. Transmission of scrub typhus depends on the seasonal activities of both chiggers and humans. Chigger activity is determined by temperature and humidity, both of which are relatively stable and high in the tropics [15]. However, this is not the case in temperate zones. For example, transmission in northern Japan is markedly seasonal, but occurs year-round in the

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south of the country [2, 16, 17]. Transmission has also been found to be seasonal in Korea [18] and northern China, where transmission primarily occurs in autumn [18–20]. These data indicate that the incidence of scrub typhus in different regions may be influenced by each region's peculiar climatic conditions [18].

Reports published in *The Lancet* in November 1993 first began to link the increases in the number of cases of vector-borne diseases to heavy rainfall and increases in temperature [21–23]. Since then, research has connected climate change with increased outbreaks of viral illnesses such as West Nile virus and dengue fever, as well as bacterial illnesses such as cholera, salmonellosis [24], and dysentery [25]. The increases in temperature and rainfall predicted to occur with global warming are also causing concern for increases in vector-borne diseases, particularly the endemic arboviruses [26]. The relationships between scrub typhus and meteorological factors have been documented to a limited extent in studies from Korea [27], Taiwan [28–31] and Japan [2, 32]. In order to better determine the strength of the associations between climate variations and scrub typhus, we investigated the relationship between climate variables and notified cases of scrub typhus in Laiwu, China, which has temperate climatic conditions.

MATERIALS AND METHODS

Study area

Shandong Province experienced the earliest emergence of scrub typhus and has become a serious focus for the disease in northern China. Scrub typhus is hyperendemic in the Laiwu District of Shandong Province. The incidence in Laiwu is higher than that of any other districts, and about ten times greater than the average incidence in Shandong Province overall. Laiwu, located between 117° 19′–117° 58′ E and 36° 02′–36° 33′ N, lies in central Shandong Province. It borders the provincial capital of Jinan to the north and Mount Tai to the southwest. As of 1 November 2010, Laiwu had a total area of 2246 km^2 and a population of 1·2985 million [33]. It has three primary regions: tourist resorts in the north, ginger and garlic processing, storing, and transporting areas in the centre, and steel processing and logistics areas in the south. Laiwu has a warm, temperate semi-humid monsoon climate. The gross domestic product *per capita* was 48 518 CNY (US$7719) in 2012.

Data collection

Disease surveillance data

Scrub typhus is diagnosed when a patient satisfies at least three of the following criteria: (1) a history of field exposure in the previous 1–3 weeks; (2) sudden-onset high fever, accompanied by characteristic eschar or ulcer; (3) enlarged lymph nodes, skin rash, splenomegaly, or hepatomegaly; (4) an agglutination titre >1:160 in the Weil–Felix test using the OX-K strain of *Proteus mirabilis*; and (5) a ⩾fourfold increase in titre against *O. tsutsugamushi* by indirect immunofluorescence antibody assay (IFA) [34]. In addition, a therapeutic response to specific antibiotics with rapid defervescence is also strongly suggestive of scrub typhus.

Scrub typhus has been a notifiable disease in Shandong since 2006. We obtained the computerized dataset on the notified scrub typhus cases in Laiwu for the period January 2006 to December 2012 from the Notifiable Infectious Diseases System of the Shandong Center for Disease Control and Prevention. The notification system records detailed information of each case including the onset date, diagnosis date and notification date. The onset date of scrub typhus, which was more useful for epidemiological study than the dates of diagnosis or notification, was used in this study. Basic population data for Laiwu from 2006 to 2012 were obtained from Shandong Statistical Yearbooks.

Meteorological data

Meteorological factors used were monthly average temperature (°C), relative humidity (%), precipitation (mm), sunshine (h), and evaporation (mm). Given that the effects of climate variation are delayed, the meteorological data were extracted for the years starting from 2005, 1 year prior to the disease becoming notifiable. The data were provided by the Shandong Bureau of Meteorology.

Data analysis

After a descriptive summarization for each variable, Spearman's correlation analyses were performed to determine association between climatic variables and the number of cases over the study period. To examine delayed effects of meteorological factors on scrub typhus cases, delays of 0–6 months were included.

Time-series adjusted negative binomial regression analysis was performed to quantify the relationship
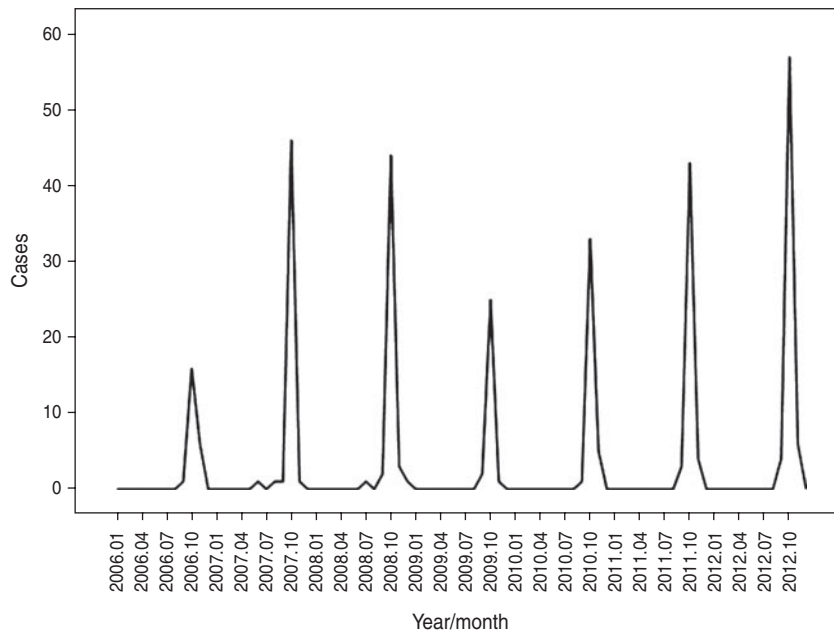
Fig. 1. Scrub typhus cases in Laiwu, China from 2006 to 2012.

between weather variables and cases of scrub typhus, allowing for consideration of autocorrelation, delayed effects, seasonality and long-term trend. Autocorrelation analyses of notified cases were conducted by calculating the autocorrelation function (ACF) and partial autocorrelation function (PACF), two useful qualitative tools, to assess the presence of autocorrelation for each period of delay. Autocorrelation is the linear dependence of a variable with itself at two points in time, and autocorrelation between any two observations depends only on the time lag (h) between them. Correlation between two variables can result from a mutual linear dependence on other variables (confounding). Partial autocorrelation is the autocorrelation between yt and $yt-h$ after removing any linear dependence on $y1, y2, \ldots, yt-h+1$. Moreover, as a more quantitative method, the Box–Ljung statistic was calculated to test for autocorrelation at multiple delays jointly [35].

Taking into account the strong correlations that exist between climate variables, multicollinearity diagnostics were applied to exclude some meteorological factors before building the model. Multicollinearity can be identified by tolerance and the variance inflation factor (VIF). Tolerance = $1 - R_j^2$, VIF = 1/tolerance, where R_j^2 is the coefficient of determination of a regression of explanator j on all the other explanators. A tolerance of <0·20 or <0·10 and/or a VIF of 5 or 10 and above indicates a multicollinearity problem [36].

Transmission of scrub typhus has been shown to be seasonal in northern Japan [2, 16, 17], Korea [18], and northern China [19, 20]. Scrub typhus in Laiwu, China also has a characteristic seasonal distribution (Fig. 1). Therefore, seasonality should be considered in the statistical analysis of relationships between weather variables and the disease. In this study, potential seasonal variation was controlled by adjusting a categorical seasonal variable in the model. Seasons in Laiwu were defined according to local weather [37]: 1=summer and autumn (June–October), and 2 = winter and spring (November–May). Long-term trend has often been considered when investigating the relationship between diseases and meteorological variables, and air pollution [38–40]. The 'year' variable included in the time-series adjusted negative binomial model was treated as an agent for long-term trend of scrub typhus. The diagnosis of the time-series adjusted negative binomial model was performed by goodness-of-fit and testing of forecasting ability. Data from 2006 to 2011 were used to build up the model and data from January to December 2012 were used to test the forecasting ability of the model. McFadden's R^2 was adopted to reflect the predictive power of the model. McFadden's R^2 was chosen because both negative binomial distribution and logistic regression are estimated by maximizing the likelihood function. McFadden's R^2 is a better choice than the Cox–Snell R^2 to measure the predictive power of logistic regression, as recommended by Allison [41].

McFadden's R^2 is defined as $R^2_{McF} = 1 - \ln(L_M)/\ln(L_0)$, where ln(.) is the natural logarithm, L_0 is the value of the likelihood function for a model with no predictors, and L_M is the likelihood for the model being estimated. All the analyses were performed using SPSS v. 16.0 (SPSS Inc., USA).

RESULTS

Descriptive analysis

The average annual incidence of scrub typhus was 3·40/100 000 in Laiwu from 2006 to 2012, with a marked monthly variation in the number of cases (Fig. 1). The prevailing disease occurred in autumn and peaked in October. In some years, there was a minor fluctuation from June to July, e.g. in 2007 and 2008 (Fig. 1). During the period 2005–2012, the monthly average temperature, relative humidity, precipitation, sunshine, and evaporation were 13·49 °C, 58·26%, 63·84 mm, 185·23 h, and 124·91 mm, respectively. Table 1 shows the mean, standard deviation and quartiles for climatic factors by calendar month from 2005 to 2012 in Laiwu, China. Monthly variations in mean values of climatic factors are also illustrated in Figure 2.

Autocorrelations analysis of monthly cases of scrub typhus

Autocorrelation analyses of scrub typhus cases from 2006 to 2012 for each month with delays of 1–11 months showed that the signature of the Box–Ljung statistic of the autocorrelation coefficients were between 0·611 and 0·762. In addition, ACF and PACF also indicated that the number of notified cases in each month was not related to the number of cases in any previous months (Fig. 3a, b). Thus, the delayed effects of cases were not considered when building the time-series adjusted negative binomial model.

Correlation between climate variables and cases of scrub typhus

Most of Spearman's correlation coefficients for the relationships between monthly cases of scrub typhus and meteorological factors from the current to previous 6 months were significantly different from zero (Table 2). Based on this, the delayed effect of each climate variable on scrub typhus was identified by the maximum coefficient (indicated in bold in Table 2). The delay phase for average temperature was 3 months, for relative humidity 2 months, for evaporation 4 months, for precipitation 3 months, and for sunshine was 2 months (negative) and 5 months (positive).

Time-series adjusted negative binomial regression analysis

Multicollinearity diagnostics were performed for meteorological variables with delayed effects on scrub typhus. No multicollinearity existed after removing sunshine delayed effects of 2 months and 5 months. Monthly average temperature delayed effects of 3 months (TL3M), relative humidity delayed effects of 2 months (HL2M), precipitation delayed effects of 3 months (PL3M), evaporation delayed effects of 4 months, season and the particular year were treated as explanatory variables, while the number of cases from 2006 to 2011 was treated as the dependent variable and the logarithm of population (unit 10^5) was treated as the offset variable to fit the time-series adjusted negative binomial model. Year and evaporation delayed effects of 4 months were not significantly associated, and were excluded from the model. The equation of the time-series adjusted negative binomial regression was

$$\ln[E(Y)] = -13\cdot432 + 0\cdot143\text{TL3M} + 0\cdot119\text{HL2M} + 0\cdot007\text{PL3M} + \begin{pmatrix} 1\cdot248 & (\text{if season} = 1) \\ 0 & (\text{if season} = 2) \end{pmatrix}.$$

The notified and model fit cases from 2006 to 2011, and the actual and predicted cases from January to December 2012, are illustrated in Figure 4. The log-likelihood function of the estimated time-series adjusted negative binomial model was −72·452, and the log-likelihood of the negative binomial model with intercept only was −168·779. Therefore, McFadden's R^2 of the time-series adjusted negative binomial model was 57·08%.

As shown in Table 3, TL3M, HL2M and PL3M were positively associated with the number of scrub typhus cases. The model suggested that each 1 °C increase in monthly average temperature in the previous 3 months led to a 15·4% [90% confidence interval (CI) 1·3–31·4] increase in the monthly number of cases, that each 1% increase in monthly relative humidity in the previous 2 months led to a 12·6% (90% CI 6·1–19·5) increase in the monthly number of cases, and that each 1 mm increase in monthly precipitation in the previous 3 months led to a 0·7% (90% CI 0·3–1·1) increase in the monthly number of cases.

Table 1. *Climatic variables by calendar month from 2005 to 2012 in Laiwu, China*

|	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sep.	Oct.	Nov.	Dec.	Year round
Average temperature (°C)													
Mean	−2·05	1·48	7·01	14·79	20·93	25·22	26·25	24·98	20·53	15·48	7·38	−0·08	13·49
s.d.	1·31	2·46	1·41	1·50	0·93	1·03	0·78	0·42	0·67	1·37	1·89	1·32	10·10
25th percentile	−2·65	−0·18	5·70	14·40	20·18	24·60	25·45	24·63	20·28	14·35	6·13	−1·48	4·08
50th percentile	−2·00	1·10	7·15	14·85	20·70	25·45	26·40	24·80	20·50	15·15	7·65	0·10	14·85
75th percentile	−0·90	3·45	8·38	16·03	21·53	26·10	26·90	25·48	21·08	16·45	9·03	0·88	23·10
Relative humidity (%)													
Mean	49·75	52·38	45·63	48·13	52·13	57·25	73·25	76·25	70·13	61·00	58·13	55·13	58·26
s.d.	8·63	6·78	6·12	4·61	2·85	5·95	3·11	2·60	2·95	5·63	7·04	8·41	11·10
25th percentile	42·50	47·00	39·25	44·50	50·00	52·25	71·25	74·25	67·50	4·15	53·25	46·00	50·00
50th percentile	49·00	51·50	46·00	49·00	51·00	55·50	72·50	75·50	70·00	13·15	56·50	58·00	57·00
75th percentile	58·00	60·00	51·50	51·75	54·75	63·00	74·50	79·25	72·00	26·00	64·00	61·50	68·50
Precipitation (mm)													
Mean	2·09	11·15	13·85	33·40	59·69	99·36	204·56	192·96	101·86	14·59	21·23	11·30	63·84
s.d.	2·44	7·83	12·14	19·43	37·86	54·91	94·07	90·46	89·03	10·79	34·41	11·91	83·97
25th percentile	0·00	3·83	1·10	21·65	40·78	48·95	129·65	114·83	30·33	55·25	0·85	1·63	6·10
50th percentile	1·20	10·20	13·35	31·70	51·00	78·50	183·05	171·60	75·85	61·50	8·20	7·10	27·95
75th percentile	4·58	19·53	27·08	45·58	91·50	158·48	250·55	275·85	199·60	66·00	26·85	18·50	87·85
Sunshine (h)													
Mean	168·65	146·44	212·75	236·29	254·24	212·66	158·14	155·74	156·00	187·18	169·53	165·19	185·23
s.d.	43·04	33·63	40·07	22·67	20·07	41·27	26·21	37·61	17·77	24·73	37·97	33·21	45·84
25th percentile	119·38	116·00	168·95	220·50	236·85	171·23	134·90	128·80	139·83	163·58	158·55	139·70	151·93
50th percentile	181·20	151·30	219·85	236·85	250·70	201·35	164·75	145·40	153·50	198·70	172·15	157·05	181·65
75th percentile	203·20	171·98	246·65	252·45	267·05	258·50	180·95	182·95	169·93	207·05	194·45	189·03	222·60
Evaporation (mm)													
Mean	39·66	53·85	120·19	185·49	232·19	230·38	165·78	139·68	118·56	105·69	66·68	40·85	124·91
s.d.	9·67	9·86	19·80	30·19	24·12	49·63	23·91	29·13	11·60	20·92	15·86	13·59	69·58
25th percentile	31·00	46·68	98·70	154·98	215·53	184·23	147·95	114·08	109·40	84·50	50·55	29·98	58·65
50th percentile	38·10	51·65	124·85	184·20	227·80	225·15	169·50	133·20	114·35	112·20	64·95	35·90	117·85
75th percentile	47·05	56·83	135·10	216·98	250·95	281·85	187·33	172·58	127·68	124·70	83·65	55·85	174·65

s.d., Standard deviation.
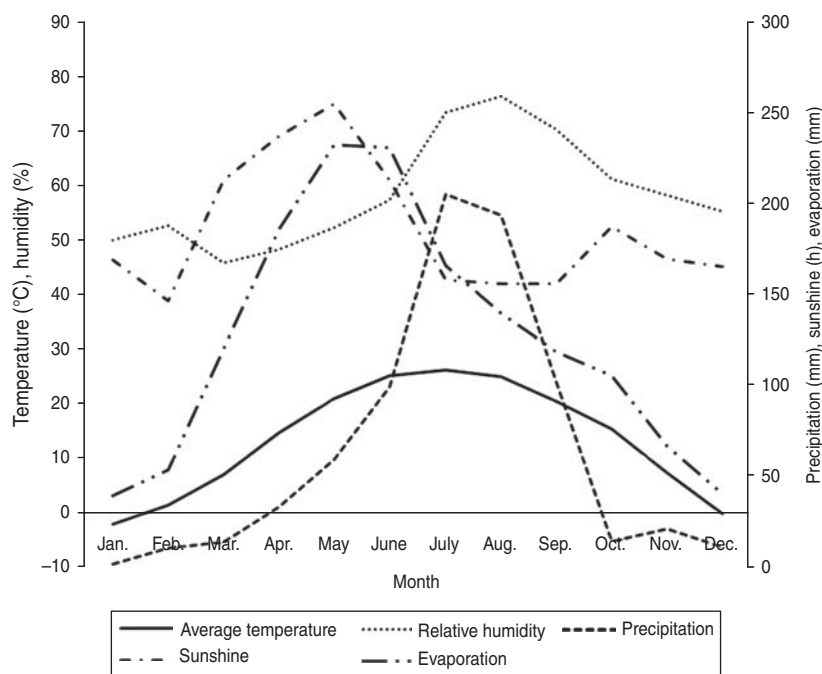
Fig. 2. Monthly means of climatic factors in Laiwu, China during 2005–2012.

DISCUSSION

Scrub typhus is hyper-endemic in the Laiwu region of China. Modern agriculture has developed rapidly in Laiwu, and it is known as the Native Land of Ginger in China. Moreover, Laiwu has been listed as a China Excellent Tourism City and a National Garden City. People contract scrub typhus by being bitten by chiggers infected with *O. tsutsugamushi* and such bites occur accidentally during agriculture or recreational field activities [42]. With the growth of tourism and agriculture in Laiwu, the frequency of outdoor activities has increased, and the risk of humans coming into contact with chiggers has also increased, especially in autumn.

The results of this study showed that weather variations may play a significant role in the transmission of scrub typhus in temperate regions. Correlation analysis showed that average temperature, relative humidity, precipitation and evaporation were significantly positively associated with the monthly number of cases of scrub typhus (Table 2). In addition, sunshine hours in the previous 1–3 months were negatively correlated with monthly cases of scrub typhus, while sunshine hours in the previous 4–6 months were positively correlated with the disease. Tsai & Yeh [31] observed in Taiwan that surface temperature correlated positively with scrub typhus incidence in five local climate regions (central western and southwestern Taiwan, as well as the Pescadore, Kinmen, and Matou Islands). Precipitation correlated positively with scrub typhus incidence in three local climate regions (central western and southwestern Taiwan, and the Kinmen Islands). Relative humidity correlated positively with scrub typhus incidence in two regions (southwestern Taiwan and the Kinmen Islands), whereas the correlation with scrub typhus incidence was negative in northwestern Taiwan. Sunshine hours correlated positively with scrub typhus incidence in three regions (central Western Taiwan, and the Kinmen, and Matou Islands) [31]. Therefore, the correlations between scrub typhus and climatic variables differ in different countries and areas.

After controlling for seasonal variation, delayed effects and long-term trend, the time-series adjusted negative binomial model revealed that the key determinants of scrub typhus transmission included average temperature (at a delay of 3 months), relative humidity (at a delay of 2 months) and precipitation (at a delay of 3 months) (Table 3). The positive relationships between scrub typhus and temperature and humidity were similar to those found in a study in Korea, which reported that the incidence of scrub typhus in a hyper-endemic region during the outbreak period was positively correlated with temperature and humidity during the summer [27]. However, there were
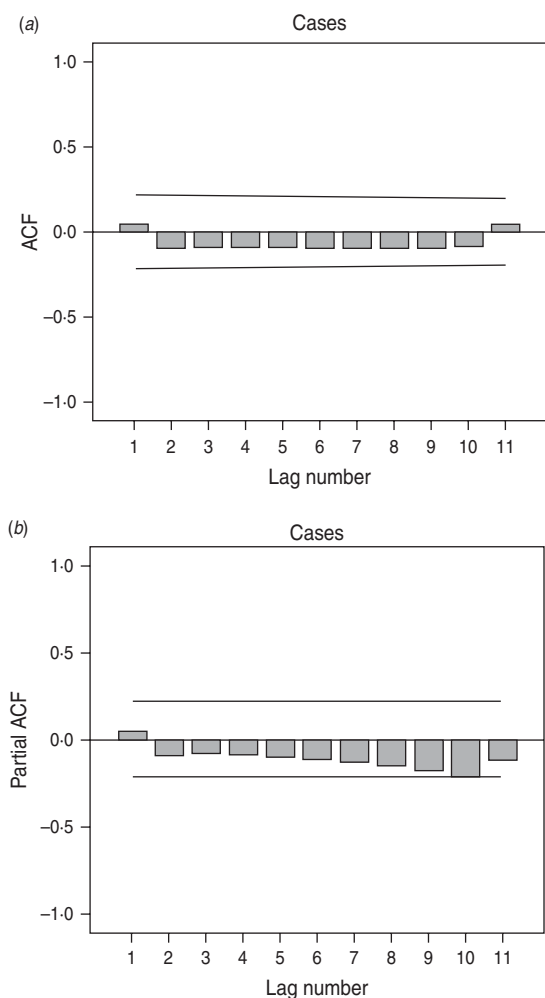
Fig. 3. (a) The autocorrelation function and (b) partial autocorrelation function of the number of cases in Laiwu, China. ▢, Coefficient. The horizontal lines indicate the upper and lower confidence limits.

no significant correlations between the monthly numbers of scrub typhus cases and meteorological factors for scrub typhus in Korea as a whole [27]. This might be because the seasonal distribution of scrub typhus varies in different geographical areas, so it may be too simplistic to study the disease at a national level. In our study we selected Laiwu District, a temperate region with the highest incidence of scrub typhus throughout northern China: by selecting this particular region, we may have overcome the problem described above.

Scrub typhus is a vector-borne disease, transmitted to humans by the bite of chiggers (larval trombiculid mites) [2, 3]. In Shandong Province, *Leptotrombidium scutellare* mainly appear from September to November, and this is the predominant species in the epidemic season of scrub typhus [43].

In addition, the peak incidence of scrub typhus coincides with the seasonal peak of *L. scutellare*, a chigger that naturally harbours *O. sutsugamushi* and can infest mice and humans [43]. *L. scutellare* larvae are frequently found in shaded and humid locations, but not on dry soil surfaces [44]. Frances and colleagues observed the seasonal occurrence of *L. deliense* attached to sentinel rodents in an orchard near Bangkok, Thailand. They found that the occurrence of *L. deliense* was influenced by rainfall, with more chiggers attached to rodents in the wetter months [45]. In Malaysia, field observation revealed that *L. akamushi* and *L. deliense* were sensitive to changes in temperature and humidity [46], and in the Pescadores Islands, *L. deliense* population numbers were positively correlated with temperature [47]. Therefore, climatic conditions during September–November might be appropriate to *L. scutellare* survival in Laiwu, China.

Because the incubation period of scrub typhus is about 6–21 days [48] (mean 10–12 days) after the initial chigger bite, climatic variables might not affect scrub typhus occurrence immediately. Delayed effects of meteorological variables on the number of scrub typhus cases were observed in our study and in another investigation conducted in Gifu prefecture, Japan. The Japanese study reported that the temperature in early summer had a significant effect upon the prevalence of the disease in early winter [32]. Moreover, we used data for disease onset rather than date of notification or diagnosis in this analysis, since the onset data would be expected to provide a more accurate estimation of the relationship between climate variables and the disease. In addition, although the date of infection could only be estimated, e.g. by estimating 1·5 weeks ahead of symptom occurrence, the exact onset date was more accurate than the estimated infection date when studying the effects of climatic factors on scrub typhus. After controlling for autocorrelation of cases, delayed effects of climate factors, seasonality and long-term trend, the time-series adjusted negative binomial model indicated that each 1 °C increase in monthly average temperature in the previous 3 months, each 1% increase in monthly relative humidity in the previous 2 months and each 1 mm increase in monthly precipitation in the previous 3 months were associated with 15·4%, 12·6% and 0·7% increases in the monthly number of cases, respectively. With the onset of global warming and frequent extreme weather events, our results are valuable for predicting and preventing scrub typhus.

Table 2. *Correlations between cases of scrub typhus and meteorological factors in Laiwu, China*

Previous no. of months	Meteorological factors				
	Temperature (°C)	Humidity (%)	Precipitation (mm)	Sunshine (h)	Evaporation (mm)
0	0·034	0·302**	−0·072	−0·179	−0·193
1	0·361**	0·548**	0·233*	−0·215*	0·053
2	0·620**	**0·713****	0·649**	**−0·357****	0·232*
3	**0·751****	0·527**	**0·707****	−0·152	0·460**
4	0·631**	0·097	0·459**	0·263*	**0·662****
5	0·310**	−0·290**	0·213	**0·559****	0·647**
6	−0·053	−0·474**	−0·045	0·533**	0·400**

Each value is Spearman's correlation coefficient for the relationship between the number of cases and the monthly value of meteorological factors in the previous 0–6 months.
** $P < 0.01$, * $P < 0.05$ (two-tailed).

Table 3. *Parameters estimated by the time-series adjusted negative binomial model for scrub typhus in Laiwu, China*

	Coefficient	S.E.	P	90% CI
Intercept	−13·432	1·6468	<0·001	−16·141 to −10·732
Temperature lag 3 months	0·143	0·0793	0·071	0·012 to 0·273
Relative humidity lag 2 months	0·119	0·0362	0·001	0·059 to 0·178
Precipitation lag 3 months	0·007	0·0025	0·005	0·003 to 0·011
Season = 1	1·248	0·3900	0·001	0·607 to 1·890
Season = 2*	0	—	—	—

CI, Confidence interval; S.E., standard error.
* Reference; lag 1/lag 2/lag 3: records occurred in the previous 1/2/3 months; season = 1, summer and autumn (June–October); season = 2, winter and spring (November–May).
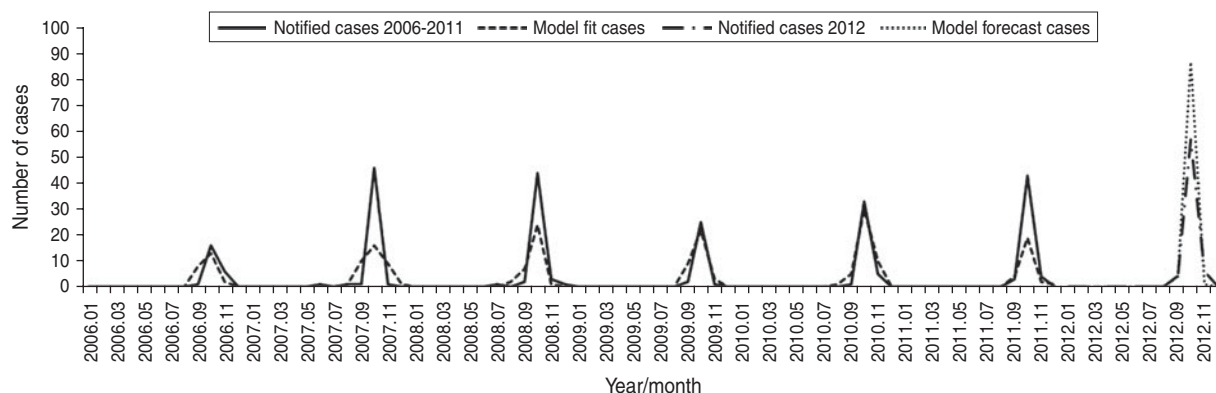

Fig. 4. Notified cases, model fit cases from 2006 to 2011, and predictive cases of scrub typhus in 2012 according to the time-series adjusted negative binomial model.

Some limitations of this study should be acknowledged. First, underreporting is inevitable in any infectious disease surveillance system. The notified cases are likely to be those who had severe symptoms and were admitted to hospitals [25]. This phenomenon may introduce systematic bias. However, since underreporting is likely to have been consistent over the study period, we believe the effects of bias to be relatively minor. Second, the occurrence of scrub typhus is complex. It is not only influenced by climate, but also by other factors such as environmental and socioeconomic factors [3]. Further studies including more local factors are needed to better understand the various effects of climate variables on vector-borne diseases.

In conclusion, the occurrence of scrub typhus is positively correlated with temperature in the previous 3 months, humidity in the previous 2 months and precipitation in the previous 3 months in Laiwu, China. Climate change, particularly global warming, coupled with the positive correlation between temperature and scrub typhus may increase the prevalence of scrub typhus in temperate regions. The control of scrub typhus is an ongoing challenge, and public health authorities need to make concerted efforts to monitor and control this disease. The findings of this research may assist local public health authorities to utilize the model developed in this study to predict scrub typhus outbreaks and to mobilize limited health resources to effectively control and prevent the disease during epidemic periods.

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DECLARATION OF INTEREST

None.

REFERENCES

1. **Razak A, et al.** Scrub typhus in Southern India: are we doing enough? *Tropical Doctor* 2010; **40**: 149–151.
2. **Okada N.** Tsutsugamushi disease found in the northern districts of Awaji Island – epidemiological study of the outbreak season temperature. *Kansenshogaku Zasshi* 2003; **77**: 60–67.
3. **Kuo CC, et al.** Spatial analysis of scrub typhus infection and its association with environmental and socio-economic factors in Taiwan. *Acta Tropica* 2011; **120**: 52–58.
4. **Chen SL, et al.** Observation on clinical characteristics of tsutsugamushi disease in the epidemic focus, Hebei Province. China [in Chinese]. *Chinese Journal of Vector Biology and Control* 2001; **12**: 65–66.
5. **Xu BL, et al.** The epidemiological investigation on the first outbreak of tsutsugamushi disease in Henan Province [in Chinese]. *Henan Journal of Prevention Medicine* 2006; **17**: 129–131.
6. **Yang LP, et al.** Electron-microscopic observation of mouse spleen tissue infected with Orientia tsutsugamushi isolated from Shandong, China. *Journal of Electron Microscopy* 2008; **57**: 169–174.
7. **Wu JB, et al.** Epidemiological analysis on the first outbreak of tsutsugamushi disease in Fuyang City of Anhui Province in 2008 [in Chinese]. *Chinese Journal of Disease Control and Prevention* 2009; **13**: 651–653.
8. **Silpapojakul K.** Scrub typhus in the Western Pacific region. *Annal Academic Medicine Singapore* 1997; **26**: 794–800.
9. **Watt G, Parola P.** Scrub typhus and tropical rickettsioses. *Current Opinion Infectious Diseases* 2003; **16**: 429–436.
10. **Currie B, O'Connor L, Dwyer B.** A new focus of scrub typhus in tropical Australia. *American Journal of Tropical Medicine and Hygiene* 1993; **49**: 425–429.
11. **Kawamura A, Tanaka H, Takamura A.** *Tsutsugamushi Disease: An Overview*. University of Tokyo Press, Tokyo, 1995.
12. **Lerdthusnee K, et al.** Scrub typhus: vector competence of *Leptotrombidium chiangraiensis* chiggers and transmission efficacy and isolation of *Orientia tsutsugamushi*. *Annals of the New York Academy of Sciences* 2003; **990**: 25–35.
13. **Kelly DJ, et al.** Scrub typhus: the geographic distribution of phenotypic and genotypic variants of Orientia tsutsugamushi. *Clinical Infectious Diseases* 2009; **48** (Suppl. 3): 203–230.
14. **Kim SH, Jang JY.** Correlations between climate change-related infectious diseases and meteorological factors in Korea. *American Journal of Preventive Medicine* 2010; **43**: 436–444.
15. **Watt G, Strickman D.** Life-threatening scrub typhus in a traveler returning from Thailand. *Clinical Infectious Diseases* 1994; **18**: 624–626.
16. **Matsui T, et al.** Evaluation of national tsutsugamushi disease surveillance – Japan, 2000. *Japanese Journal of Infectious Diseases* 2002; **55**: 197–203.
17. **Ogawa M, et al.** Scrub typhus in Japan: epidemiology and clinical features of cases reported in 1998. *American Journal of Tropical Medicine and Hygiene* 2002; **67**: 162–165.
18. **Bang HA, Lee MJ, Lee WC.** Comparative research on epidemiological aspects of tsutsugamushi disease (scrub typhus) between Korea and Japan. *Japanese Journal of Infectious Diseases* 2008; **61**: 148–150.
19. **Li J, Li XY, Liu YX.** Epidemiology and reservoirs of scrub typhus in China. *Practical Preventive Medicine* 2005; **12**: 1251–1253.
20. **Zhang M, Wang XJ, Zhao ZT.** Current epidemic status and issues on prevention and control of scrub typhus. *Chinese Journal of Epidemiology* 2011; **32**: 419–423.
21. **Nicholls N, et al.** El nino-southern oscillation and vector-borne disease. *Lancet* 1993; **342**: 1284–1285.
22. **Freier JE.** Eastern equine encephalomyelitis. *Lancet* 1993; **342**: 1281–1282.

23. **Rogers DJ, Packer MJ.** Vector-borne diseases, models, and global change. *Lancet* 1993; **342**: 1282–1284.

24. **Interagency Working Group on Climate Change and Health.** *A Human Health Perspective on Climate Change: A Report Outlining the Research Needs on the Human Health Effects of Climate Change*. Research Triangle Park, NC: Environmental Health Perspectives and National Institute of Environmental Health Sciences. 2010, pp. 45–55.

25. **Zhang Y, et al.** El Nino Southern Oscillation (ENSO) and dysentery in Shandong province, China. *Environmental Research* 2007; **103**: 117–120.

26. **Russell RC.** Vectors vs. humans in Australia – who is on top down under? An update on vector-borne disease and research on vectors in Australia. *Journal of Vector Ecology* 1998; **23**: 1–46.

27. **Kim SH, Jang JY.** Correlations between climate change-related infectious diseases and meteorological factors in Korea. *Journal of Preventive Medicine and Public Health* 2010; **43**: 436–444.

28. **Olson JG, Scheer EJ.** Correlation of scrub typhus incidence with temperature in the Pescadores Islands of Taiwan. *Annals of Tropical Medicine Parasitology* 1978; **72**: 195–196.

29. **Olson JG.** Forecasting the onset of a scrub typhus epidemic in the Pescadores Islands of Taiwan using daily maximum temperatures. *Tropical Geography Medicine* 1979; **31**: 519–524.

30. **Kuo CC, Huang CL, Wang HC.** Identification of potential hosts and vectors of scrub typhus and tick-borne spotted fever group rickettsiae in eastern Taiwan. *Medical and Veterinary Entomology* 2011; **25**: 169–177.

31. **Tsai PJ, Yeh HC.** Scrub typhus islands in the Taiwan area and the association between scrub typhus disease and forest land use and farmer population density: geographically weighted regression. *BMC Infectious Diseases* 2013; **13**: 191.

32. **Kasuya S.** Studies on tsutsugamushi disease in Gifu prefecture. 6. Correlation between number of patients and meteorological elements. *Kansenshogaku Zasshi* 1995; **69**: 1110–1117.

33. **The sixth China population census in Laiwu, 2010.** Laiwu city statistical information network (http://www.lwtjj.gov.cn/tj_weblm/pc_lm/rk2010/Read.Asp?Lt_NewsID=235). Accessed 6 May 2011.

34. **Yao JL.** Scrub typhus. In: Peng WW, ed. *Infectious Diseases*, 6th edn. Beijing: People's Medical Publishing House, 2004, pp. 118–121.

35. **Ljung GM, Box GEP.** On a measure of lack of fit in time series models. *Biometrika* 1978; **65**: 297–303.

36. **Robert M, O'Brien.** A caution regarding rules of thumb for variance inflation factors. *Quality and Quantity* 2007; **41**: 673–690.

37. **Bu QL, Wang QZ, Wang XL.** Climate change characteristics and effects on agricultural production in Laiwu. *Modern Ecological Agriculture* 2006; **15**: 58–60.

38. **Segala C, et al.** Winter air pollution and infant bronchiolitis in Paris. *Environmental Research* 2008; **106**: 96–100.

39. **Alessandrini E, et al.** Emergency ambulance dispatches and apparent temperature: a time series analysis in Emilia-Romagna, Italy. *Environmental Research* 2011; **111**: 1192–1200.

40. **Lin YK, et al.** Temperature, nitrogen dioxide, circulating respiratory viruses and acute upper respiratory infections among children in Taipei, Taiwan: a population-based study. *Environmental Research* 2013; **120**: 109–118.

41. **Allison P.** What's the best R-Squared for logistic regression? *Statistical Horizons* (http://www.statisticalhorizons.com/r2logistic). Accessed 13 February 2013.

42. **Jeong YJ, et al.** Scrub typhus: clinical, pathologic, and imaging findings. *Radiographics* 2007; **27**: 161–172.

43. **Liu YX, et al.** Epidemiological studies on host animals of scrub typhus of the autumn-winter type in Shandong Province, China. *Southeast Asian Journal of Tropical Medicine and Public Health* 2003; **34**: 826–830.

44. **Kimito U, et al.** A Wide and Heavy Infestation with Leptotrombidium scutellare Larvae in the Western Part of Kanagawa Prefecture, Japan (Trombidiformes, Trombiculidae). *Journal of the Acarological Society of Japan* 1994; **3**: 69–77.

45. **Frances SP, et al.** Seasonal occurrence of Leptotrombidium deliense (Acari: Trombiculidae) attached to sentinel rodents in an orchard near Bangkok, Thailand. *Journal of Medical Entomology* 1999; **36**: 869–874.

46. **Gentry JW, Yueh CS, Wah PO.** Preliminary observations on Leptotrombidium (Leptotrombidium) akamushi and Leptotrombidium (Leptotrombidium) deliensis in their natural habitat in Malaysia: (Acarina: Trombiculidae). *American Journal of Hygiene* 1963; **78**: 181–190.

47. **Van Peenen PF, et al.** Correlation of chigger abundance with temperature at a hyper endemic focus of scrub typhus. *Journal of Parasitology* 1976; **62**: 653–654.

48. **Lai CH, et al.** Epidemiology of acute Q fever, scrub typhus, and murine typhus, and identification of their clinical characteristics compared to patients with acute febrile illness in southern Taiwan. *Journal of the Formosan Medical Association* 2009; **108**: 367–376.