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Association between floods and typhoid fever in Yongzhou, China: Effects and vulnerable groups

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A R T I C L E I N F O

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A B S T R A C T

Background: Little information about the effects of floods on typhoid fever is available in previous studies. This study aimed to examine the relationships between floods and typhoid fever and to identify the vulnerable groups in Yongzhou, China.

Methods: Weekly typhoid fever data, flood data and meteorological data during the flood season (April to September) from 2005 to 2012 were collected for this study. A Poisson generalized linear model combined with a distributed lag non-linear model was conducted to quantify the lagged and cumulative effects of floods on typhoid fever, considering the confounding effects of long-term trend, seasonality, and meteorological variables. The model was also used to calculate risk ratios of floods for weekly typhoid fever cases among various sub-populations.

Results: After adjusting for long-term trend, seasonality, and meteorological variables, floods were associated with an increased number of typhoid fever cases with a risk ratio of 1.46 (95% CI: 1.10–1.92) at 1-week lag and a cumulative risk ratio of 1.76 (95% CI: 1.21–2.57) at lag 0–1 weeks. Males, people aged 0–4 years old, people aged 15–64 years old, farmers, and children appeared to be more vulnerable than the others.

Conclusions: Our study indicates that floods could significantly increase the risks of typhoid fever with lag effects of 1 week in the study areas. Precautionary measures should be taken with a focus on the identified vulnerable groups in order to control the transmission of typhoid fever associated with floods.

1. Introduction

In the context of global warming, the frequency and severity of natural hazards, such as floods, storms and droughts, are increasing due to climate change (Parry, 2007). Floods, the most common disaster worldwide, caused severe damage, tremendous casualties and huge economic losses every year (Birkholz et al., 2014). For example, floods and other hydrological disaster caused 64.7 million victims globally, accounting for 51.9% of total disaster victims in 2012 (Guha-Sapir et al., 2013). In addition to destruction, previous studies have found that floods would result in various human health impacts (Ahern et al., 2005; Reacher et al., 2004). In China, floods happen frequently during flood season due to large number of rivers and persistent precipitation. In 2012, floods in China affected more than 110 million people and resulted in direct economic loss of approximately 166.1 billion Yuan (Song, 2013). According to The Yearbook of Meteorological Disasters in China, several floods had occurred from 2005 to 2012 in Yongzhou, a city located in Hunan Province, China (Song, 2013).

Typhoid fever, a severe gastrointestinal infectious disease, is caused by infection of the bacterium *Salmonella* serovar *Typhi* (Mogasale et al., 2014). Being spread by faecal-oral transmission, typhoid fever is typically manifested itself in a syndrome of prolonged high fever, relative bradycardia, splenomegaly, and abdominal symptoms (Parry et al., 2002). Although control measures, e.g. the usage of vaccine and

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improvement of sanitation, have been implemented in many areas of the world, typhoid fever is still an epidemic disease in African, Asian, and South American regions (Crump and Mintz, 2010; Watson and Edmunds, 2015). In recent decades, there were approximately 10,000–20,000 reported typhoid fever cases annually in China (Yan et al., 2016). Hunan Province, a high prevalence area of typhoid fever, had an incidence of 2.34 per 100,000 in 2012 and ranked 4th in all provinces of China (DCFPH, 2011).

In recent years, some studies have examined the association between gastrointestinal infectious diseases and floods or extreme precipitation. For instance, a significant association between extreme precipitation and gastrointestinal illness-related hospital admissions was reported in Chennai with a cumulative risk ratio of 1.60 (95% CI: 1.29–1.98) (Bush et al., 2014). There were also some studies indicating increased risks of getting different kinds of gastrointestinal infectious diseases, such as cholera (Koley et al., 2014), bacillary dysentery (Ni et al., 2014), and hepatitis A virus infection (Gao et al., 2016) associated with floods. However, few previous studies have focused on the effects of floods on morbidity of typhoid fever, and the evidence on the association between floods and typhoid fever is still insufficient. Thus, the aim of our study was to quantify the lagged effects of floods on typhoid fever and to identify the vulnerable groups based on the time series data of typhoid fever and meteorological factors. Results will provide scientific information for exploring the health impact of floods and assist in developing control strategies to reduce the risk of gastrointestinal infectious diseases associated with floods.

2. Materials and methods

2.1. Study area and period

Yongzhou (24°39–26°51′N, 111°06–112°21'E) is located in the south of Hunan Province, China (Fig. 1). The main rivers in Yongzhou were Xiangjiang River and Xiaoshui River. Located in a subtropical humid monsoon climate zone, the city has an annual average temperature of 17.6–18.6 °C and an annual average precipitation of 1200–1900 mm. Numerous rivers and abundant precipitation provide favourable conditions for the formation of floods. Yongzhou was chosen as the study area for frequent floods and a high incidence of typhoid fever. In 2012, the incidence of typhoid fever in Yongzhou was 6.10 per 100,000, which was higher than the average of Hunan Province (2.34 per 100,000) and China whole population (1.30 per 100,000) (DCFPH, 2011). In the study area, floods only occurred in flood season (April to September), a period with more precipitation than the rest of the year. The study period covered flood season from 2005 to 2012.

2.2. Data collection

2.2.1. Disease surveillance data

Weekly number of typhoid fever cases in Yongzhou from 2005 to 2012 was collected from National Notifiable Disease Surveillance System (NDSS). Typhoid fever is a statutory category B notifiable infectious disease in China. All of typhoid fever cases used in our study had been diagnosed clinically and met diagnostic criteria (GB 16001–1995) (NHFPC, 1995). Some cases were confirmed by laboratory tests. After making a definite diagnosis, doctors must report every typhoid fever case within 24 h through the Direct Network Report system (NHFPC, 2006). The disease data include the number of typhoid fever cases in total population and in subpopulations by age, gender and occupation.

2.2.2. Flood data

Flood data from 2005 to 2012 in Yongzhou were obtained from the Yearbook of Meteorological Disasters in China (Dong, 2006, 2007; Song, 2010, 2011, 2012, 2013; Xiao, 2008, 2009). These yearbooks contained information of floods, including dates, affected area, affected population and economic losses. According to the yearbooks, Yongzhou experienced 12 floods from 2005 to 2012.

2.2.3. Meteorological data

Weekly meteorological data during the study period were collected from the China Meteorological Data Sharing Service System (http://cdc.cma.gov.cn/). The meteorological variables used in our study included weekly average temperature (WAT), weekly average relative humidity (WARH) and weekly total precipitation (WTP). The meteorological data used in this study was from the weather station in Lingling district, which was located at 26°14′N and 111°37′E.

2.3. Statistical analysis

In the descriptive analysis, time series plots were drawn to describe the distribution of the number of weekly typhoid fever cases and meteorological factors during the study period in Yongzhou.

To quantify the lagged and cumulative effects of floods on typhoid fever, a Poisson generalized linear model combined with a distributed lag non-linear model (DLNM) was conducted, with the number of weekly cases as the dependent variable and the floods as the independent variable. Poisson generalized linear regression model is a classical method to estimate the effects of environmental factors on health outcomes (Labrada-Martagon et al., 2013; Xu et al., 2014). DLNM is a modelling framework that can simultaneously represent non-linear exposure-response dependencies and delayed effects (Gasparrini

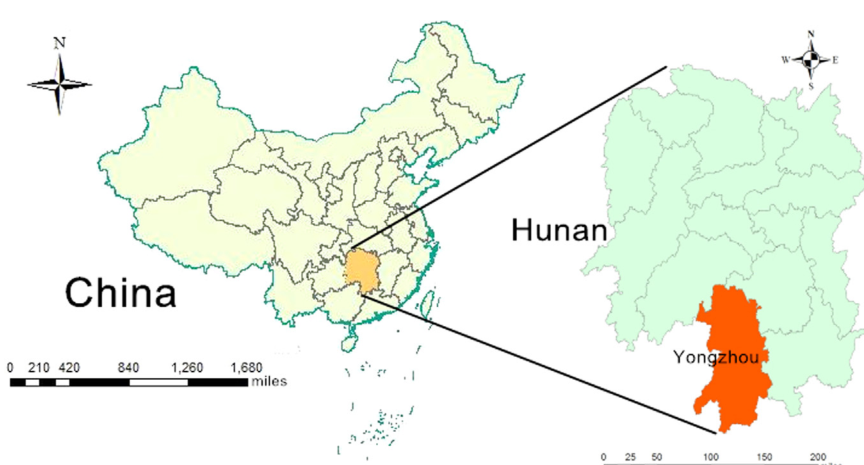

Fig. 1. Location of Yongzhou in Hunan Province, China.

et al., 2010). In recent years, DLNM models were used to examine the relationship between environmental exposure and infectious diseases (Limper et al., 2016; Xiang et al., 2017).

Cross-basis functions were established for floods and WAT in models. In the two cross-basis functions, linear function was used to investigate the relationship in the dimension of exposure, and polynomials function with four degrees of freedom (df) was used to investigate the relationship in the dimension of lags (Gasparrini, 2011). Natural cubic spline was used for time and week of year (woy) to control long-term trend and seasonality. Previous studies have discovered that meteorological variables influenced the transmission of typhoid fever (Cheng et al., 2013; Dewan et al., 2013). Therefore, WARH and WTP were also controlled in the models.

Considering delayed transport of bacterium in environment and the incubation period of typhoid fever, we explored a 4-week lag for floods and WAT when establishing cross-basis functions in models (Wang et al., 2012). The following model was conducted to detect the lagged and cumulative effects of floods on typhoid fever:

$$\log[E(Y_t)] = \alpha + cb(floods_{t,4}, \beta) + cb(WAT_{t,4}, \gamma) + ns(WARH, 3) + ns(WTP, 3) + ns(time, 3) + ns(woy, 4) + lag(res, 1)$$

Here, Y_t was the number of weekly typhoid fever cases in week t; α was the intercept; $cb(floods_{t,4},\beta)$ was the cross-basis function for floods; *floods* was a binary variable, non-flooded and flooded weeks were presented by 0 and 1, respectively; β was the effect estimate of floods; $cb(WAT_{t,4},\gamma)$ was the cross-basis function for weekly average temperature; γ was the effect estimate of weekly average temperature; $ns(WARH,3)$ and $ns(WTP,3)$ were natural cubic splines of weekly average relative humidity and weekly total precipitation to control the effects of them; $ns(time,3)$ and $ns(woy,3)$ were natural cubic splines of time and week of year to control long-term trend and seasonality; $lag(res,1)$ was first-order lagged variable of residual error to control the autocorrelation.

To identify the vulnerable groups, the above model was also developed for various subpopulations. The statistical significance of differences between effect estimates (β) of different vulnerable groups can be estimated by calculating the 95% CI as shown below:

$$\left(\hat{Q}_1 - \hat{Q}_2\right) \pm 1.96\sqrt{\left(\hat{SE}_1\right)^2 + \left(\hat{SE}_2\right)^2},$$

where $\hat{Q}_1$ and $\hat{Q}_2$ are the estimates (β) for the two different demographic categories, and $\hat{SE}_1$ and $\hat{SE}_2$ are their respective standard errors (Schenker and Gentleman, 2001).

Normality test and autocorrelation analysis were performed to test the residuals of the DLNM model. In addition, sensitivity analysis was conducted by using full-year data instead of the data in flood season, changing df in models, and changing lagged methods (single lag model, unconstrained DLNM model, and constrained DLNM model) to estimate whether the model was robust.

All statistical analysis in our study was conducted by using the R software (version 3.3.1). We used "dlnm" package to develop models (Gasparrini, 2011). The level of statistically significance was set at 0.05 (two-tailed).

3. Results

3.1. Descriptive analysis

A total of 1682 typhoid fever cases were notified in Yongzhou during study period with a male: female ratio of 1.44: 1. Among all the cases, 21% aged 0–14 years, 69% aged 15–64 years, and 10% aged over 65 years. Figs. 2 and 3 display the distribution of weekly typhoid fever cases and meteorological variables. The mean WAT during the study period was 24.3 °C, the mean WARH was 71.6% and mean WTP was 28.0 mm.

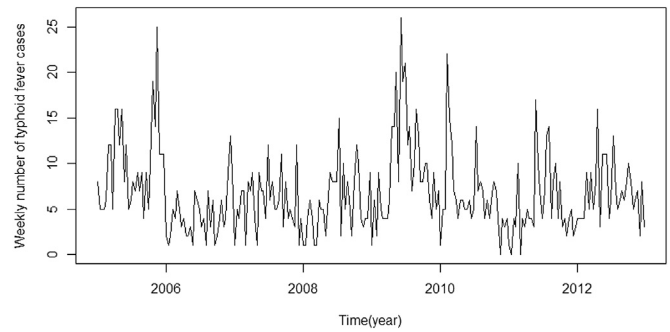

Fig. 2. Weekly typhoid fever cases during study period from 2005 to 2012 in Yongzhou, China.

3.2. Effects of floods on typhoid fever

Fig. 4 (A) illustrated the risk ratios (RRs) of floods on typhoid fever in different lagged period from the DLNM model. The results indicated that, after adjusting for meteorological variables, long-term trend and seasonality, floods significantly increased the risks of typhoid fever at lag 1 week with RR of 1.46 (95% CI: 1.10–1.92). No significant association between typhoid fever and floods was detected in other lagged periods. Fig. 4 (B) displayed cumulative effects of floods on typhoid fever, and significant association was observed at lag 0–1 weeks with RR of 1.76 (95% CI:1.21–2.57).

As shown in Table 1, we list the RRs of floods on weekly typhoid fever cases among various subpopulations. The effects were significant in males at lag 1 week (RR = 1.61, 95% CI: 1.18–2.22), while not in females. An increased risk of typhoid fever was found in 0–4 years old group (lag0, RR = 2.39, 95% CI: 1.02–5.60) and 15–64 years old group (lag1, RR = 1.57, 95% CI: 1.17–2.11). In occupational categories of our study, farmers (lag1, RR = 1.57, 95% CI: 1.12–2.20) and children (lag0, RR = 3.42, 95% CI: 1.78–6.57) were more vulnerable than other occupations. We did not detect any significant difference between risks for 0–4 years old group and 15–64 years old group (95% CI: -0.49–1.32). But children were more vulnerable than farmers (95% CI: 0.04–1.51).

3.3. Residual analysis and sensitivity analysis

Histogram and scatter plot of residuals (Supplementary Material, Fig. S1) showed that model residuals were normally distributed. Autocorrelation function (ACF) and partial auto-correlation function (PACF) plots of residuals (Supplementary Material, Fig. S2) demonstrated that residuals were independent over time. Supplementary Material Fig. S3 indicated that, when using the full-year data, the results were similar with effects obtained from flood season data. The coefficient estimates of floods on typhoid fever at lag 1 week were similar when changing the df (2 − 8) for relative humidity, time and week of year (Supplementary Material, Fig. S4). The results changed little when changing lagged methods (single lag model, unconstrained DLNM model, and constrained DLNM model) (Supplementary Material, Fig. S5). These results suggested that our coefficient estimates were robust.

4. Discussion

In recent years, effects of floods on infectious diseases receive attention in the field of environmental epidemiology (Brown and Murray, 2013; Kouadio et al., 2012). In this study, we have quantified the lagged and cumulative effects of floods on typhoid fever from 2005 to 2012 in Yongzhou, China. Our findings suggest that floods could bring more typhoid fever cases in Yongzhou with a 1-week lagged effect.

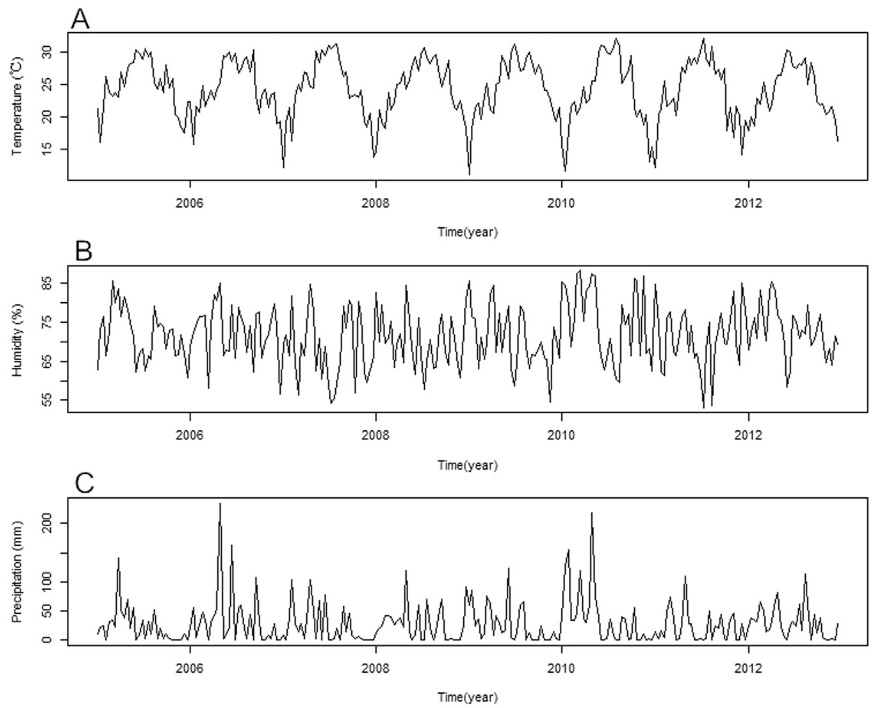

Fig. 3. The distribution of weekly average temperature (A), weekly average relative humidity (B) and weekly total precipitation (C) during study period in Yongzhou, China.

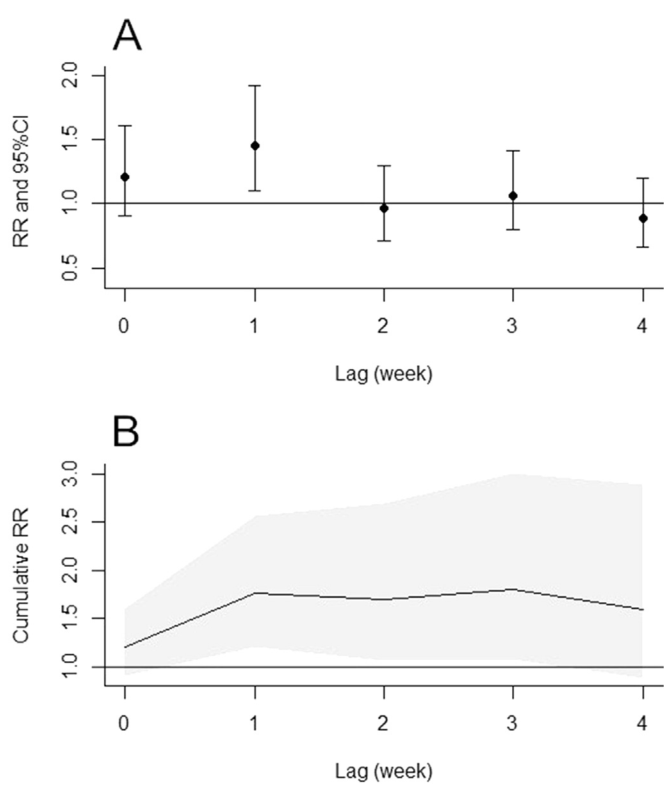

Fig. 4. Lagged effects (A) and cumulative effects (B) of floods on typhoid fever cases in different lagged periods.

An increased risk of gastrointestinal infectious diseases after floods has been reported in previous studies. A study in Bangladesh showed that, during the flood period, the number of cholera and non-cholera diarrhea cases were almost six and two times higher than expected, respectively (Hashizume et al., 2008). A study in Germany discovered that contact with floodwater was a risk factor for diarrhea (OR = 5.8, 95% CI: 1.3–25.1) (Schnitzler et al., 2007). Another study in China showed that floods were positively associated with bacillary dysentery (RR = 1.41, 95% CI: 1.22–1.62) (Zhang et al., 2016). Similar findings are reported in our study. However, our results are different from a community-based case-control study conducted in Indonesia, which showed that floods had no influence on typhoid fever (OR = 1.65, 95% CI: 0.88–3.08) (Vollaard et al., 2004). The difference in sample size and design may be the reason causing the different results.

Epidemic of typhoid fever, most often be resulted from faecal contamination of water and food, tend to occur in the regions without safe water supply and adequate sanitation (Hosoglu et al., 2006). After floods, surface water environment will be contaminated in multiple ways. Firstly, the pollution, which cause by human faeces from rural household toilets, increases pathogens in the water in rural areas without sanitary latrines (Hashizume et al., 2008; Kirsch et al., 2012). Secondly, continuous heavy precipitation will lead to sewage overflows in residential area, which may pollute water supply by domestic pollutant (De Vleeschauwer et al., 2014). Faecal-oral transmission is thought to be major route of typhoid fever transmission, and people suffer from typhoid fever mainly by drinking water contaminated by faeces (Ako et al., 2009; Akullian et al., 2015). Some previous studies have found that *Salmonella* and other pathogens of diarrhea increased in water when floods occurred (Ceuppens et al., 2015; Yard et al., 2014). The result in our study, floods increased the risk of typhoid fever cases in Yongzhou, may cause by water contamination and increase of *Salmonella* during and after floods. In addition, flood water-soaked buildings would be exposed to flood-borne microorganisms (Taylor et al., 2013a), which could lead to infection when victims contact surface of these buildings and pick up food by dirty hands.

We have also discovered lagged effects of floods on typhoid fever. Similar findings appear in previous studies. A study in Massachusetts showed that flood increased the risk of *Clostridium difficile* infection in 7–13 days after the flood (Lin et al., 2015). Another study in China discovered two-weeks' lagged effect of floods on bacillary dysentery (Xu et al., 2017). The reasons for the lag could be complex because of the incubation period and the prolonged increase of pathogens in water

Table 1
The RRs of floods on typhoid fever cases in different demographic categories during study period in Yongzhou, China.

Category	lag0	lag1	lag2	lag3	lag4
Gender					
Males	1.35(0.98,1.87)	1.61(1.18,2.22)[a]	0.97(0.69,1.38)	1.01(0.73,1.40)	1.02(0.73,1.42)
Females	1.09(0.73,1.61)	1.26(0.85,1.85)	0.93(0.62,1.42)	1.14(0.78,1.68)	0.75(0.49,1.14)
Age(years)					
0–4	2.39(1.02,5.60)[a]	1.01(0.39,2.62)	1.53(0.65,3.56)	1.40(0.61,3.23)	1.61(0.66,3.91)
5–14	1.35(0.81,2.25)	1.23(0.71,2.13)	0.67(0.35,1.29)	1.09(0.63,1.89)	1.02(0.57,1.81)
15–64	1.14(0.83,1.55)	1.57(1.17,2.11)[a]	0.99(0.71,1.37)	1.01(0.74,1.38)	0.85(0.61,1.17)
65 +	1.71(0.86,3.41)	1.20(0.58,2.51)	0.90(0.43,1.89)	1.18(0.60,2.33)	0.87(0.41,1.87)
Occupation					
Farmers	0.88(0.59,1.31)	1.57(1.12,2.20)[a]	1.22(0.86,1.74)	1.07(0.75,1.51)	0.80(0.55,1.17)
Students	1.16(0.77,1.77)	1.52(0.98,2.35)	0.61(0.35,1.05)	1.10(0.70,1.73)	1.09(0.68,1.73)
Children	3.42(1.78,6.57)[a]	0.91(0.39,2.14)	1.20(0.55,2.62)	1.39(0.69,2.79)	1.51(0.69,3.31)
Others	1.47(0.85,2.53)	1.47(0.86,2.52)	0.76(0.41,1.41)	0.85(0.47,1.54)	0.87(0.50,1.53)

[a] $p < 0.05$.

and on building surface after floods (Baig et al., 2012; Taylor et al., 2013b).

Increased risks of typhoid fever associated with floods are found in males, 0–4 years old group, 15–64 years old group, farmers, and children. Males and people aged 15–64 years old may undertake more relief work than females and other age groups, which may result in a higher chance of contact with pathogens (Liu et al., 2016). Farmers who live in rural areas may have poor sanitation compared with those people living in urban areas, and farmers' houses are more likely to be destroyed in floods (Christenson et al., 2014; Zhang et al., 2014). High vulnerability of children to typhoid fever during floods may due to their weak physique and poor hygiene awareness (Sarkar, 2013). In addition, child malnutrition during floods can also increase their vulnerability (Goudet et al., 2011).

Underreporting is inevitable in infectious disease surveillance system. In our study, no significant changes of the surveillance system and underreporting rate remain below 15% through the study period (Hu and Chen, 2007; Chen, 2008; Yue et al., 2011). Thus, data quality has a limited impact on the results.

The selection of the most statistically robust and biologically plausible time scales is desirable for time series studies (Imai and Hashizume, 2015). The number of the disease at a time unit should be considered (Wu et al., 2014). In our study, a total of 1682 typhoid fever cases are notified among the study period (1456 days). There are insufficient daily number of typhoid fever cases for the daily time series analysis with too many zero case in the data series. Therefore, the weekly data were analyzed in this study.

Our findings indicate that necessary measures should be taken in order to control the risks of typhoid fever after floods. Clean water and food should be supplied for those affected by flood (Cann et al., 2013). Implementing programs for better sanitation in rural areas also plays important role in gastrointestinal infectious disease prevention. Vulnerable groups identified in this study must be prioritized in responding to floods. In addition, the forecasting ability of floods and early warning of potential health risks should be improved (Janev et al., 2015). Health risk assessment on infectious diseases should be carried out before flood seasons in order to have better public health preparedness (WHO, 2006). Based on the lagged effects detected in this study, preventive measures and public health interventions should sustain for at least two weeks after floods to achieve maximum effectiveness.

There are some strengths of our study. Firstly, the usage of DLNM model allows us to qualify lagged and cumulative effects of floods on typhoid fever. Secondly, multiple methods are used in sensitivity analysis, which provide sufficient evidence for the stability of coefficient estimates. Thirdly, flood season instead of full-year is selected as the study period in our research, which would control confounding effects.

The limitation of our study must be acknowledged. Some influence factors of typhoid fever are not included in the analysis, including different population immune levels, the change of sanitation, socioeconomic status, and demographic change.

Future research could focus on the mechanism of floods on typhoid fever and other gastrointestinal infectious diseases, such as the homology between pathogens in flood water and pathogens in victims' faeces. Other environmental and meteorological factors that could affect the impacts of floods on typhoid fever could also be studied when data are available. In addition, more evidences are required to support local decision-making with considering of various climatic and socioeconomic conditions that could mediate the association between floods and typhoid fever.

5. Conclusion

Our findings indicate that floods can significantly increase the risks of typhoid fever with lagged effects in Yongzhou, China. Males, people aged 0–4 years old, people aged 15–64 years old, farmers, and children appeared to be more vulnerable than the others. Precautionary measures should be implemented after floods, especially for vulnerable groups, to reduce typhoid fever cases.

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Conflict of interest

None.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.envres.2018.08.030.

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