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Association between floods and infectious diarrhea and their effect modifiers in Hunan province, China: A two-stage model

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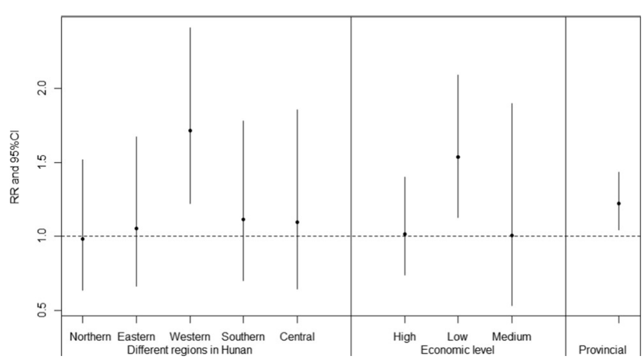
HIGHLIGHTS

- A total of 134,571 cases of infectious diarrhea were included in our study.
- The cumulative and lagged effect of floods in provincial level was reported.
- Our study identified two potential effect modifiers.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: Understanding the potential links between floods and infectious diarrhea is important under the context of climate change. However, little is known about the risk of infectious diarrhea after floods and what factors could modify these effects in China.

Objectives: This study aims to quantitatively examine the relationship between floods and infectious diarrhea and their effect modifiers.

Methods: Weekly number of infectious diarrhea cases from 2004 to 2011 during flood season in Hunan province were supplied by the National Notifiable Disease Surveillance System. Flood and meteorological data over the same period were obtained. A two-stage model was used to estimate a provincial average association and their effect modifiers between floods and infectious diarrhea, accounting for other confounders.

Results: A total of 134,571 cases of infectious diarrhea were notified from 2004 to 2011. After controlling for seasonality, long-term trends, and meteorological factors, floods were significantly associated with infectious diarrhea in the provincial level with a cumulative RR of 1.22 (95% CI: 1.05, 1.43) with a lagged effect of 0–1 week. Geographic locations and economic levels were identified as effect modifiers, with a higher impact of floods on infectious diarrhea in the western and regions with a low economic level of Hunan.

Conclusions: Our study provides strong evidence of a positive association between floods and infectious diarrhea

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in the study area. Local control strategies for public health should be taken in time to prevent and reduce the risk of infectious diarrhea after floods, especially for the vulnerable regions identified.

1. Introduction

Diarrheal diseases are one of the leading mortality causes of children worldwide. In 2010, diarrheal diseases caused about 10.5% (0.801 million) of deaths in children under 5 years old all over the world (Liu et al., 2012). According to the National Notifiable Disease Surveillance System (NDSS), there were 1,086,343 new infectious diarrhea cases reported in 2011 in China (DCFPH, 2011). Hunan province is one of the most seriously affected provinces along the Yangtze River Region of China with millions of people affected each year.

Floods are the most common natural disaster in both developed and developing countries, contributing to 52.1% of the total occurrence of natural disasters in 2011 (Guha-Sapir et al., 2012). Risks of floods are expected to increase due to frequent and heavy precipitation events in future. For example, some heavily-populated mega-deltas in Asia will be at great risks due to increased flooding from the rivers (Parry, 2007). Hunan, located in the Yangtze River Basin, is one of the flood-prone provinces in China. In average, there has been one to three floods occurred in cities of Hunan province each year due to persistent and heavy rainfall (Song, 2012).

Health effects of floods include death, injuries, communicable diseases, water-borne diseases, vector-borne diseases, non-communicable diseases, psychosocial health, and malnutrition (Alderman et al., 2012). In addition, diarrhea is one of the most important after effects of floods especially in areas where the population do not have the access to clean water and sanitation (Ahern et al., 2005). However, the association between infectious diarrhea and floods is far from clear with inconsistent epidemiologic evidences. A survey after the 2002 floods in Germany identifies contacting with floodwater as a risk factor for diarrhea (Schnitzler et al., 2007). Ding et al. found that floods were associated with infectious diarrhea significantly by a study conducted in Anhui, China (Ding et al., 2013). A study from Chennai, India also indicated that extreme precipitation was associated with GI-related hospital admissions (Bush et al., 2014). However, a study developed in Bangladesh found that after controlling for the confounding of seasonality and pre-flood rate differences, there was no clear evidence of increased diarrheal risk during or after floods (Milojevic et al., 2012). Most of these previous studies examining floods and infectious diarrhea were based on one or two cities with very limited research at a provincial level. Effect at a provincial level and effect modifiers of floods on infectious diarrhea have not been explored before. Therefore, the aim of this study was to quantitatively examine the relationship between floods and infectious diarrhea and their effect modifiers based on a time series data. Results will provide more evidences to support decision making and to develop local strategies for preventing and reducing the risks of infectious diarrhea after floods.

2. Materials and methods

2.1. Study location and period

The study was conducted in Hunan province which is located between latitudes 24°38′ and 30°08′N and longitudes 108°47′ and 114°15′E (Fig. 1). It included 14 cities and was divided into southern, northern, eastern, central, and western parts. 13 cities in Hunan province were chosen as our study area except Xiangtan city because there was no weather station for this city. It is characterized by a humid subtropical monsoon climate with an annual mean rainfall between 1200–1700 mm and an annual mean temperature between 15–18 °C. In 2011, Hunan has a population of 71.35 million with an area of 211,829 km^2, and the per capita GDP of 4342 US dollars. Considering the seasonal distribution of floods and infectious diarrhea, the flood seasons (periods between April and September) from 2004 to 2011 were chosen as our study periods.

2.2. Data collection

Weekly number of infectious diarrhea cases from 2004 to 2011 were supplied by the NDSS. The definition of infectious diarrhea, according to the National Health and Family Planning Commission of the People's Republic of China (NHFPC), is a group of infectious diseases which caused by panel of microbes (including bacteria, viruses, and parasites) and have diarrhea as the typical symptom, including dysentery, cholera, paratyphoid, typhoid, and other infectious diarrhea. In our study, all infectious diarrhea cases were defined based on the diagnostic criteria and principles of management for infectious diarrhea (WS 271-2007) (NHFPC, 2007).

Flood data were supplied by the Yearbooks of Meteorological Disasters in China, which recorded the number of deaths, damaged areas, occurrence time, and economic loss due to floods (Song, 2012). Flooding

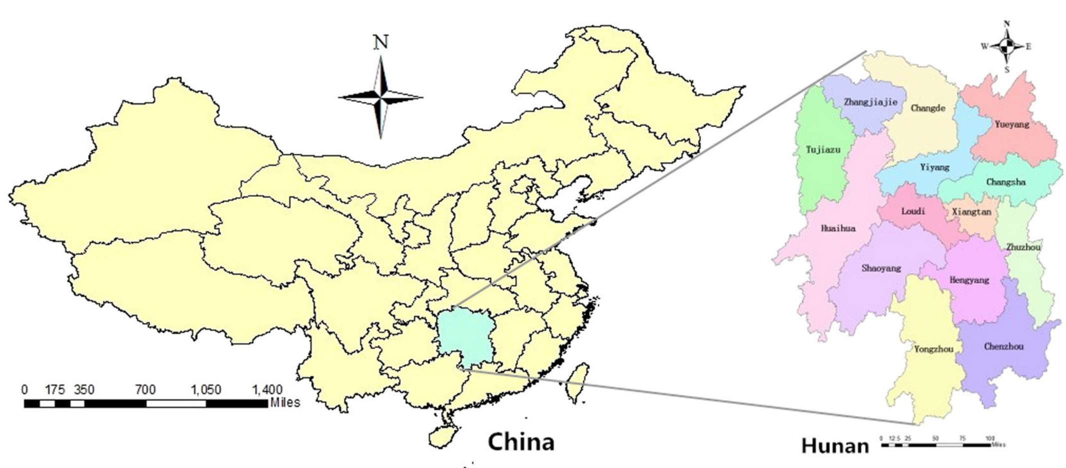

Fig. 1. Location of the study area in China.

event is an extreme climate event with flooding and geological hazards such as debris flow, landslide after local or regional heavy rain process, and the criteria of floods was the same as previously reported (Liu et al., 2016), which was from the Yearbooks of Meteorological Disasters (Song, 2012). Meteorological data over the study period were supplied by the China Meteorological Data Sharing Service System (http://cdc.cma.gov.cn/). Thirteen meteorological stations including Changsha (28°13′N, 112°55′E), Chenzhou (25°48′N, 113°02′E), Changde (29°03′N, 111°41′E), Hengyang (26°54′N, 112°36′E), Zhijiang (27°27′N, 109°41′E), Shuangfeng (27°27′N, 112°22′E), Shaoyang (27°14′N, 111°28′E), Jishou (28°19′N, 109°44′E), Yuanjiang (28°51′N, 114°15′E), Lingling (26°14′N, 111°37′E), Yueyang (29°23′N, 113°05′E), Sangzhi (29°24′N, 110°10′E), and Zhuzhou (27°52′N, 113°10′E) were used for our study. The meteorological factors included mean temperature, mean relative humidity, and cumulative rainfall.

2.3. Statistical analysis

A two-stage statistical model (Bell et al., 2004; Zanobetti et al., 2000; Dominici et al., 2002) was used to estimate the average association between floods and infectious diarrhea at a provincial level, accounting for the confounding of weather factors, long-term trend, and seasonality. At the first stage, a distributed lag non-linear model (DLNM) (Gasparrini et al., 2010) was conducted to quantify the city-specific effects of floods on infectious diarrhea. Weekly counts of infectious diarrhea and floods were chosen as the dependent variable and the independent variable respectively. The DLNM model can estimate the nonlinear and delayed effects and the cumulative effect of floods on infectious diarrhea (model 1). To deal with the over-dispersion, a quasi-Poisson distribution was applied in DLNM models. A time stratified method (by simple indicator variables) was used to control for the long-term trend and seasonality (Bhaskaran et al., 2013). Previous studies have reported that temperature and humidity were associated with diarrheal diseases, and these meteorological factors were usually linked with the replication, persistence, and transmission of pathogens in the environment (Chou et al., 2010; Onozuka et al., 2010). The rainfall has also been taken into account as a confounder for the association between flooding and diarrhea because many studies showed that rainfall was a risk factor of increasing diarrhea (Bush et al., 2014; Carlton et al., 2014; Bhavnani et al., 2014; Mukabutera et al., 2016) and it would obviously cause flooding. Therefore, natural cubic splines with 3 degree of freedom (df) in DLNM for mean temperature, mean relative humidity and cumulative rainfall were used to adjust for potential confounding (Gasparrini, 2014). A 4-week lag association was explored in our model due to the delayed effect in environmental epidemiology (Liu et al., 2015; Imai and Hashizume, 2015; Liu et al., 2016).

Model 1:

$$\log[\mathrm{E}(Y_t)] = \beta + \sum_{p=0}^{4} \alpha_p Floods_{t-p} + ns_1(Hum, df = 3) + ns_2(Tem, df = 3) + ns_3(Rain, df = 3) + strata + Lag(res, 1)$$

In model 1, where Y_t denoted the weekly counts of infectious diarrhea at time *t*. *Floods*, a categorical variable including flooded or non-flooded weeks, was applied with the cross-basis function with a linear relationship (df = 1) for response dimension and a non-linear relationship (df = 4) for lag dimension. The α_p was the effect estimate of the floods *p* days before the day *t*. The $ns_1(Hum, df = 3)$, $ns_2(Tem, df = 3)$, and $ns_3(Rain, df = 3)$ were natural cubic splines of relative humidity and temperature. The *strata* variable was an indicator for the combination of year and month to control the long-term trend and seasonality. To control the autocorrelation, the first-order lagged variable of model residual errors (*Lag (res, 1)*) was included in the model.

At the second stage, the city-specific relative risks were combined to generate a provincial average estimate of the effect of floods on infectious diarrhea by a Hierarchical linear model (Witte et al., 1994). Hierarchical linear model can get not only the provincial effect but also the impact of effect modifiers (Zanobetti et al., 2000). To explore whether the association between floods and infectious diarrhea was modified by some city-specific socio-economic factors, the effect modifications were tested by a weighted second-stage linear regression (Bell et al., 2004) with the city-specific estimate of floods' effect on infectious diarrhea as the dependent variable and the socio-economic factors as the independent variable (model 2).

Model 2:

$$\beta_i = \beta_0 + \delta M_i + \varepsilon$$

In model 2, where β_i was the effect of floods in city *i*, β_0 was provincial average estimate of the effect of floods on infectious diarrhea, M_i was the potential effect modifier to be tested. The variable δ indicated how much the effect of floods changes in different categories of M_i.

We examined the sensitivity of main findings with respect to: (1) using natural cubic splines methods to control the seasonality and long-term trends, including changing the df (2–8) for time and week of year to adjust for seasonality and long-term trend; (2) varying the df (2–8) for relative humidity and temperature. Residual analysis, autocorrelation figure (ACF) and partial autocorrelation figure (PACF) were also conducted to evaluate the fitness of model and autocorrelation of model residual error.

We chose 0.05 (two-tailed) as our statistically significance level. Analyses and figures were conducted using package "dlnm" (Gasparrini, 2011), package "tsModel", and package "mvtsplot" (Peng, 2008) in R v3.1.3 (http://www.r-project.org).

3. Results

3.1. Description of the meteorological and disease data

Fig. S1, S2, and S3 show the time-series distribution of mean temperature, mean relative humidity, and cumulative rainfall from 2004 to 2011 in the cities of Hunan province. The weekly average mean temperature, mean relative humidity, and weekly cumulative rainfall were 24.7 °C (range: 10.2–33.6 °C), 72.5% (range: 44.6–93.9%), and 32.1 mm (range: 0–451 mm). During the study period, the average frequency of floods in the cities of Hunan province was 14 (range: 8–21) (Fig. 2). In total, the floods affected 93.8 million people (17.5%) and killed >455 people from 2004–2011 in Hunan, and the economic damage was estimated at approximately 12.3 billion dollars. A total of 134,571 cases of infectious diarrhea were notified in the study area. Fig. S4 shows the time-series distribution of infectious diarrhea cases from 2004 to 2011 in the cities of Hunan province. Table 1 presents the description for infectious diarrhea in the cities of Hunan province from the flood season of 2004 to 2011. Table 2 shows the social and economic characteristics of the cities in Hunan province, including the level of urbanization, number of health institutions and government expenditure in health.

3.2. Association between floods and infectious diarrhea

Fig. 3 shows the city-specific effect of floods on infectious diarrhea at different lag periods from the DLNM model at the first stage. The cumulative RR at lag 0~1 weeks of floods on infectious diarrhea were significant in four cities including Zhangjiajie, Yongzhou, Tujiazu, and Huaihua (Fig. 4). The provincial average effects of floods on infectious diarrhea at different lag periods from the second stage model are presented in Fig. 5. After controlling for meteorological factors, seasonality and long-term trends, floods were significantly associated with infectious diarrhea in the provincial level with a cumulative RR at lag 0–1 weeks equal to 1.22 (95% CI: 1.05, 1.43). Fig. 6 indicated the combined effects

Fig. 2. The frequency of floods from 2004 to 2011 in Hunan province, China.

of floods on infectious diarrhea at lag 0–1 weeks in different regions and economic levels. The cumulative effects at lag 0–1 weeks are statistically significant in Western Hunan (RR = 1.72, 95% CI: 1.22, 2.41) and regions with low economic level (RR = 1.54, 95% CI: 1.13, 2.09) but not in other regions. Two modifiers, including geographic locations and economic levels, were identified by the weighted second-stage linear regression (Table 3). Effect of floods on infectious diarrhea was significantly higher in western Hunan compared with central Hunan (coefficients = 0.432, *p*-value = .049). Effect of floods on infectious diarrhea was significantly higher in regions with low economic level compared with regions with high economic level (coefficients = 0.416, *p*-value = .002).

Table 1
Description of weekly number of cases of infectious diarrhea in the cities of Hunan, China.

City	Mean ± SD	Min	P25	Median	P75	Max
Chenzhou	81.68 ± 27.89	24	64	77	101	153
Changde	34.13 ± 14.37	10	27	33	40	171
Hengyang	54.81 ± 23.44	18	41	52	65	245
Huaihua	72.38 ± 35.79	13	46	70	95	171
Loudi	22.08 ± 28.18	6	14	19	25	396
Shaoyang	57.69 ± 29.22	10	38	50	75	171
Tujiazu	47.12 ± 24.64	6	30	43	61	174
Yiyang	29.82 ± 31.13	5	20	25	33	330
Yongzhou	47.92 ± 19.80	12	33	45	60	109
Yueyang	36.08 ± 22.49	12	26	34	42	305
Zhangjiajie	12.83 ± 8.78	0	8	11	16	90
Changsha	79.39 ± 52.40	19	57	75	91	483
Zhuzhou	47.08 ± 22.14	6	32	45	58	111

SD: standard deviation; Min: minimum; P_{25}: the 25th percentile; P_{75}: the 75th percentile; Max: maximum;

Table 2
Description of social and economic characteristics of the cities in Hunan province.

City	Economic level	Regions in Hunan	Level of urbanization (%)	Government expenditure in health (billion Yuan)	Number of health institutions
Chenzhou	Medium	Southern	43	1.6	972
Changde	High	Northern	40	2.0	1407
Hengyang	Medium	Southern	46	2.4	632
Huaihua	Low	Western	37	1.6	1123
Loudi	Medium	Central	37	1.3	509
Shaoyang	Low	Central	34	2.3	726
Tujiazu	Low	Western	36	1.2	682
Yiyang	Medium	Central	41	1.6	804
Yongzhou	Low	Southern	37	2.0	923
Yueyang	High	Northern	47	1.8	1304
Zhangjiajie	Low	Western	39	0.56	336
Changsha	High	Eastern	68	2.6	2680
Zhuzhou	High	Eastern	57	1.4	1247

Level of urbanization were estimated by the proportion of population living in cities or towns; Economic levels were defined by the per capita GDP with two cutoffs (4500$, 3000$).

3.3. Sensitivity analysis

We assessed whether the coefficient estimates of DLNM were robust using Tujiazu city as an example. Fig. S6 and Fig. S7 showed that model residuals were randomly distributed and obeying the normal distribution. Fig. S8 and Fig. S9 showed that there were no obvious autocorrelations in model residuals. The effect estimates at lag 0 week of floods on infectious diarrhea were robust when changing df (2–8) for time and week of year (see Fig. S10 and Fig. S11). The similar effects of floods on infectious diarrhea were observed when changing the df (2–8) for relative humidity and temperature (see Fig. S12 and Fig. S13).

4. Discussion

Our multisite time-series study of 13 cities with eight years' data has provided strong evidence of a positive association between floods and infectious diarrhea in Hunan of China. A higher impact of floods on infectious diarrhea has been identified in western Hunan and the cities with a low economic level. The results from our study could contribute to develop local preventive strategies and measures to reduce potential risks of infectious diarrhea after floods. Results might also be applicable to most cities in southern China and other countries where climate conditions are similar with that in Hunan.

Our results indicate that floods are significantly associated with infectious diarrhea in the provincial level at lag 0–1 weeks. Several flood-associated diarrheal epidemics were reported during 1988, 1998, 2004, and 2007 in Dhaka, Bangladesh (Schwartz et al., 2006; Harris et al., 2008). A study conducted in West Bengal, India also showed that 16,590 diarrheal cases were reported with 276 deaths cases after receding of floodwater (Sur et al., 2000). During the floods in the Midwestern United States in 2001, an increase of incidence of gastrointestinal symptoms was observed (Wade et al., 2004). A significant association between flooding and diarrhea was reported in Brazil (Heller et al., 2003). A German study also showed that exposure to floodwater was the major risk factor for diarrhea (OR = 5.8, 95%CI: 1.3, 25.1) (Schnitzler et al., 2007). However, the underlying mechanisms explaining how floods influence the infectious diarrhea have not been clarified by existing studies. Infectious diarrhea, as a waterborne disease, are caused by ingestion of drinking water or food contaminated by *Vibrio cholerae*, *Salmonella*, *Shigella*, and others (Hodge

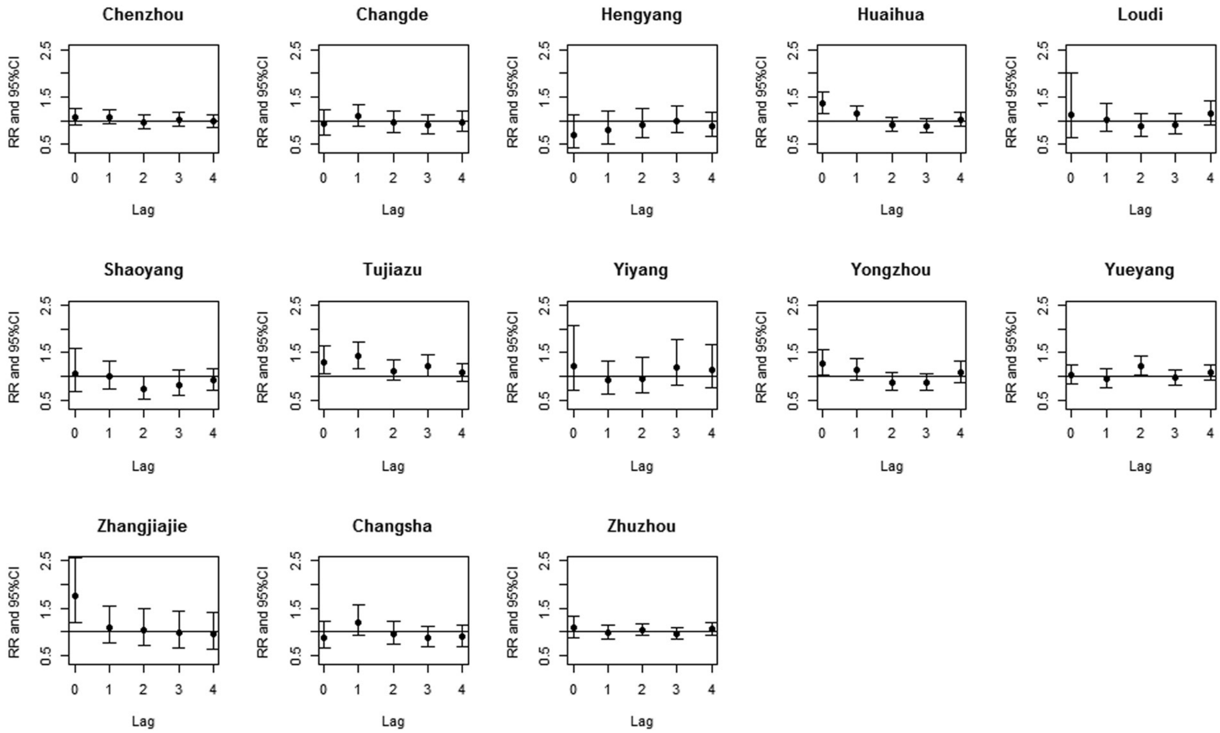

Fig. 3. The city-specific effect of floods on infectious diarrhea at different lag periods in Hunan province, China.

et al., 2016). Floods may flush contaminations into drinking water, deteriorating the quality of local water seriously with considerable diarrheal risk (Wolf et al., 2014). Specific improvements, such as using of water filters and provision of high-quality drinking water are recommended because these measures are associated with greater reductions in diarrhea (Wolf et al., 2014).

The lag pattern reported by previous studies was also different. For example, most of the studies reported a short-term effect of floods with a lag period less than a month (Schwartz et al., 2006; Schnitzler et al., 2007; Liu et al., 2016; Ding et al., 2013), which is consistent with our study. The lagged effect may be associated with the floodwater contaminated by various pathogens. However, other studies have reported longer lag period. For example, the study in Bangladesh reported an increased risk up to 8–20 weeks after the end of the flooding (Hashizume et al., 2008). Differences in lag patterns of the impact of flood could be due to various reasons, including availability of facilities, population vulnerability and adaptive strategies, as well as community resilience. The mechanisms of long-term effect in poor resources countries may be due to the persistence of low hygiene and sanitation status in the flood-affected areas (Hashizume et al., 2008).

Our study also indicates that effect of floods on infectious diarrhea was significantly higher in western Hunan and in regions with a low economic level compared with the other regions. The economic level in western Hunan is also the lowest in Hunan province. Therefore, the

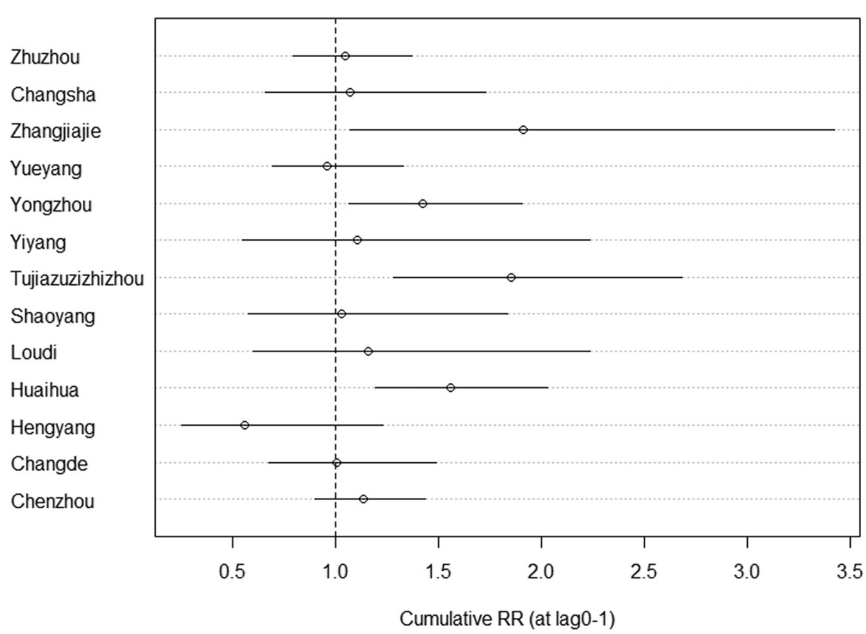

Fig. 4. The cumulative RR and 95%CI at lag0~1 weeks of floods on infectious diarrhea in different cities of Hunan, China.

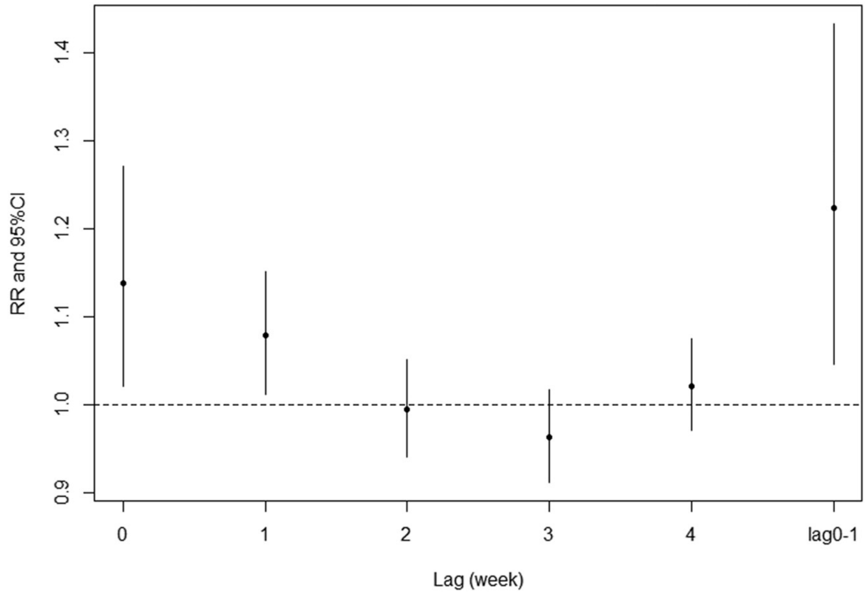

Fig. 5. The provincial average effect of floods on infectious diarrhea at different lag periods in Hunan province, China.

main effect modifier found in Hunan is the poor economic status of the population. A study conducted in German found that compared with non-flood periods, diarrhea cases during flood-associated epidemics were of lower socioeconomic status (Schnitzler et al., 2007). A study from Uttar Pradesh, India indicated that economic condition of the household is associated with the prevalence of diarrhea among under-five children (Joshi et al., 2011). A possible reason is that regions with low economic level usually have poor public health infrastructures and services. Residents with poor social and economic condition probably not have access to clean drinking water after floods, which may increase the risk of infectious diarrhea. A review conducted by Lowe et al. in 2013 also found that factors like low education or socioeconomic status may increase the vulnerability to health effects of floods (Lowe et al., 2013). Thus, regions with low economic level should be paid more attention during or after floods. For people with poor social and economic conditions, some simple, low cost interventions that improve water and latrine infrastructure should be taken to reduce the prevalence of diarrheal diseases during floods (Denslow et al., 2010).

A main strength of our study is the use of distributed lag non-linear model (DLNM), rather than models considering a single day or several days at a particular lag. DLNM is widely used in studies between environment and health, such as meteorological factors, air pollution and health outcomes (Gasparrini and Armstrong, 2011). We constrained model coefficients to fit a polynomial function to reduce collinearity resulting from the correlated independent variable that are close together in time (Bush et al. 2013). DLNM provides an estimate of the cumulative effect and lagged effect simultaneously (Gasparrini, 2014). We choose flood season as our study period to control for some potential confounders in study design (Liu et al., 2016). Results from sensitivity indicated that the estimated effect was relatively robust to adjustment for weather variables, long-term trends, and seasonality. These make our results more credible.

However, our study also has some limitations. Firstly, some confounding factors such as variation of pathogens, different immune levels and intervening measures had not been included in our study. Secondly, the infectious diarrhea cases remain highly under-reported because some people with mild clinical symptoms might not seek help from hospital (Charron et al., 2004).

In the past decades, China has observed rapid urbanization, and its city population is still in steady increase (Seto et al., 2011). Rapid urbanization in China has an adverse impact on urban hydrological processes,

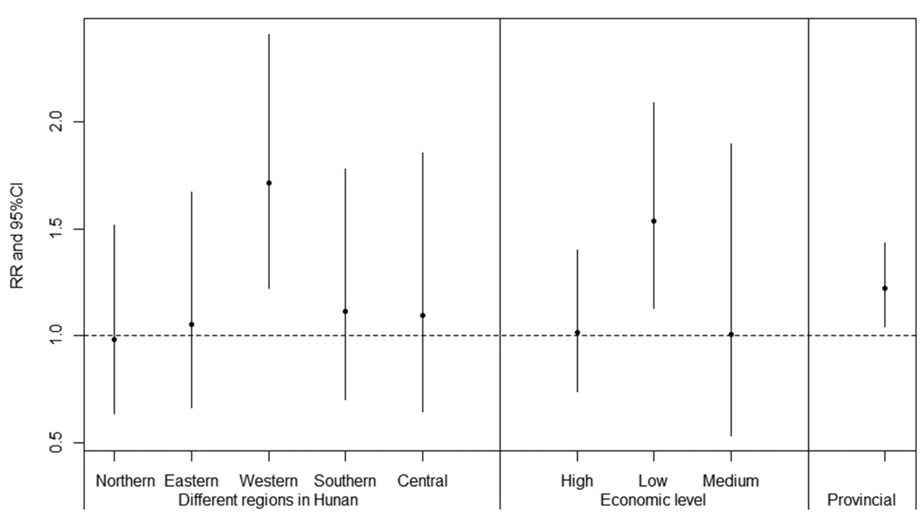

Fig. 6. The combined effects of floods on infectious diarrhea at lag0~1 weeks in different regions and economic levels in Hunan, China.

Table 3
Coefficients from the weighted second-stage linear regression for infectious diarrhea.

Model		Variables	Coefficients	SE	t	p-value
Model 1	Economic level	Intercept	0.017	0.072	0.242	.814
		Low	0.416	0.099	4.220	.002*
		Medium	0.066	0.112	0.587	.570
		High[a]	–	–	–	–
Model 2	Regions	Intercept	0.088	0.163	0.542	.603
		Eastern	−0.038	0.194	−0.194	.851
		Northern	−0.109	0.198	−0.550	.597
		Southern	0.090	0.181	0.494	.634
		Western	0.432	0.186	2.320	.049*
		Central[a]	–	–	–	–

SE: standard error; Adjusted R square was 0.671 for the model1, 0.707 for the model 2.
[a] The reference level.
* $p < .05$.

particularly in increasing the urban flood risks (Chen et al., 2015). Urban flooding increases risks such as polluting drinking water and causing epidemic disease (de Man et al., 2014). Under the context of climate change, people at risk of exposure to excessive floods may increase in future due to urbanization especially in developing countries. Thus, future work should focus on how population density, migration, and sanitation influence the risk of waterborne disease during floods. People in urban slums and shantytowns with a low economic level, recognized as the vulnerable regions should be paid more attention in responding to floods.

5. Conclusion

Our study provides strong evidence of a positive association between floods and infectious diarrhea at a city as well as provincial level in China. The effect last for 2 weeks following floods and can be modified by location and economic levels. People living in west Hunan with a low economic level are identified at higher risk and should be paid more attention to deal with waterborne diseases during flooding season. Our findings can help local CDCs develop public health strategies to prevent and reduce the risks of infectious diarrhea due to floods.

Competing financial interests

The authors declare no competing financial interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2018.01.130.

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