Impacts of Meteorological Factors on the Incidence of Infectious Diarrhea in Urban Shanghai, China

Hemitério Samson da P Zandamela1, Yang Deng1, Xue Han2, Shuo Wang1, Wenbin Liu1, Fan Yang1, Guangwen Cao1*

1Department of Epidemiology, Second Military Medical University, China
2Division of Chronic Diseases, Center for Disease Control and Prevention of Yangpu District, China

*Corresponding author: Guangwen Cao, Department of Epidemiology, Second Military Medical University, China. Tel: +862181871060; Email: gcao@smmu.edu.cn.

Citation: Zandamela HSDP, Deng Y, Han X, Wang S, Liu W, et al. Impacts of Meteorological Factors on the Incidence of Infectious Diarrhea in Urban Shanghai, China. Arch Epidemiol: AEPD -106. DOI: 10.29011/AEPD-106.000006

Received Date: 9 October, 2017; Accepted Date: 23 October, 2017; Published Date: 30 October, 2017

Abstract

Objective: This study aimed to analyze the epidemiology of infectious diarrhea in Yangpu district of Shanghai, from 2006 to 2015, and investigate the associations between meteorological factors and the incidence of infectious diarrhea.

Methods: The epidemiological characteristics were analyzed by descriptive analysis, and the generalized additive model was employed to examine the association between meteorological variables and the incidence of infectious diarrhea.

Results: A total of 3606 infectious diarrhea cases were reported. The average annual crude incidence rate was 33.20/105 and age-standardized incidence rate by world standard population was 63.36/105. Proportion of rotavirus infection accounted for 90.11% of infectious diarrhea cases in 0-4-year-old patients, whereas 56.92% of 5-year-old or older patients were infected with Vibrio. Monthly average maximum temperature below 6.38°C and above 24.59°C, minimum temperature below 5.12°C and above 24.03°C, and precipitation below 1.48 mm and above 7.40 mm had positive effects on the incidence of infectious diarrhea.

Conclusion: High temperature and excess precipitation increase the incidence of infectious diarrhea caused by *Vibrio parahaemolyticus* in 5-year-old or older people. Low temperature and little precipitation increase the incidence of infectious diarrhea caused by rotavirus in 0-4-year-old children. These findings might be references for the prophylaxis and control of infectious diarrhea in urban areas of developing world.

Keywords: Epidemiology; Generalized Additive Model; Incidence; Infectious Diarrhea; Meteorological Factors

Introduction

Approximately 1.7 billion cases of diarrheal disease occur worldwide. Diarrheal disease is the second leading cause of death in 0-4-year-old children, killing around 760,000 children every year [1]. Diarrheal disease accounts for 10.03% of deaths among children aged 1-59 months in the Americas and 31.3% of death among children in South East Asia [2]. Infectious diarrhea is referred to diarrheal disease which is most often caused by infections with viral, bacterial, and parasitic pathogens. According to the web-based real-time disease surveillance system-China Information System for Disease Control and Prevention, infectious diarrhea is grouped into three classes, including class A (cholera), class B (bacillary dysentery, typhoid and paratyphoid) and class C (other infectious diarrhea). In China, a total of 836,591 class C infectious diarrhea cases were reported and the incidence rate was 62.39/105 in 2011 [3]. Among overall diarrheal disease cases, 0-4-year-old children accounted for 52.13%, and the incidence rate was 447.06/105 [3]. Despite remark improvement of public health disease system after the 2003 SARS outbreak, infectious diarrhea poses a great threat to public health, particularly in 0-4-year-old children.

Infectious diarrhea is vulnerable to the influence of meteorological factors, and the occurrence and prevalence of infectious diarrhea are closely related to meteorological factors including temperature, precipitation, relative humidity, and air pressure [4-7]. For example, temperature can directly affect the replication and survival of pathogen and predict the number of...
bacillary dysentery patients. Two time-series analyses reported that 1°C rise of maximum temperature resulted in 11.40% (95% CI: 10.19%-12.69%) and 16% (95% CI: 13%-19%) increase in the number of bacillary dysentery, respectively [8,9]. Precipitation may influence the quality of drinking water via contaminating the supply of drinking water, and there is a positive association between heavy precipitation and risk of infectious diarrhea [8,10]. Moreover, climate changes usually affect the behavior habits of human beings, and increase human exposure to environmental pathogens [8,11,12].

The geographical position of Shanghai is unique, facing the Huangpu River and bordering the East China Sea. Tide level of the Huangpu River is susceptible to many meteorological and hydrological factors such as temperature, ocean tide, upstream flood, local precipitation and runoff. As a city with a subtropical humid monsoon climate, Shanghai is characterized by a mild climate, abundant precipitation, adequate light, and four distinct seasons. It has a sufficient supply of fresh water and reaches the highest temperatures in July and August. Spring in Shanghai is from March to May (recently described as until June). Summer in Shanghai is long, from June to September. There is a particular “Plum Rain Season” (Meiyu Season) from mid-June to early July, and it lasts for nearly one month commencing in early summer. During this period, the precipitation often equals to 25% of the annual total. Autumn of the region comes in October and November, and winter begins from December to the next February. The coldest period starts from the end of January to early February.

In this study, we described the epidemiological and etiological characteristics of infectious diarrhea cases among permanent residents in Yangpu district of Shanghai, China, from 2006 to 2015, and examined the associations between the meteorological factors and the incidence of infectious diarrhea.

**Materials and methods**

**Study area**

Yangpu district is one of the 16 districts of Shanghai, China. It is located at 31°27’ north latitude and 121°52’ east longitude, in northeastern part of downtown Shanghai, bordering the Huangpu River on the east and south. Yangpu district has a total area of 60.61 km² and about a population of 1.1 million [13,14].

**Meteorological and demographic data**

Meteorological data of Yangpu district from 2006 to 2015 were downloaded from China Meteorological Data Network. The meteorological variables included daily wind velocity, daily sunshine time, daily air pressure, daily maximum temperature, daily minimum temperature, daily vapor pressure, daily relative humidity, and daily precipitation. Demographic data during the study period were obtained from the Public Security Bureau of Yangpu Administration.

**Disease surveillance data**

Disease surveillance data used in this study were obtained from the National Notifiable Disease Surveillance System (NDSS), which was approved by Municipal Center for Disease Control and Prevention of Shanghai. Infectious diarrhea cases included cholera, bacillary dysentery, typhoid, paratyphoid, and other infectious diarrhea in NDSS. All infectious diarrhea cases were diagnosed by clinical symptoms and identified by the serological tests and stool specimen tests. Information of reported cases included age, gender, and residential address, type of disease, date of onset, and pathogens. According to the National Communicable Disease Control Act of the People’s Republic of China, physicians in hospitals have the responsibility to report every case of infectious diarrhea to the local center for disease control and prevention within 24 hours.

**Statistical analysis**

The epidemiological characteristics of infectious diarrhea cases in Yangpu district from 2006 to 2015 were analyzed by descriptive analysis. Categorical variables were tested by either χ² test or Poisson approximation. Kruskal-Wallis test was employed to compare the monthly distributions of infectious diarrhea cases among age groups and Nemenyi method was introduced in multiple comparisons. The generalized additive model (GAM) was employed to examine whether these meteorological variables were correlated to the incidence of infectious diarrhea. The GAM method is usually used to perform linear and nonlinear regression analysis in time-series studies with a Poisson regression [15]. GAM has been widely used in studies of association between meteorological variables and incidence of infectious diarrhea, because of its strength in nonparametric adjustment of confounding effects of seasonality and long-term trends [16-18]. In this study, the error distribution and correlation function in GAM were the Poisson distribution and Log correlation, respectively. Smoothing spline method was used in the form of non-linear function, and generalized cross validation was chosen to estimate non-linear function. The GAM regression model was described as follows:

\[ Y = \sum_{i=1}^{q} \beta_i X_i + \sum_{j=1}^{m} f_j(Z_j) + \epsilon + \beta_0 \]

Where \( Y \) represented the monthly number of infectious diarrhea cases. \( \beta_i \) and \( f \) represented linear and non-linear functions based on their regression effects in the model, respectively. \( \epsilon \) was random-error term and \( \beta_0 \) represented the intercept of regression equation. The degree of freedom was specified based on the result of cross validation, and the possible lag effects (up to seven days) of meteorological factors were assessed in GAM. The effects of meteorological factors on the incidence of infectious diarrhea were described by effective value. The effective value above 0 meant...
that meteorological factor had a positive effect on the incidence, whereas the effective value under 0 meant a negative effect. The statistical analyses were conducted using SAS 9.4 (SAS Institute, Inc., Cary, NC), and two-tailed \( P < 0.05 \) was considered statistically significant.

**Results**

**Epidemiological characteristics of infectious diarrhea**

Of 3606 infectious diarrhea cases in Yangpu district from 2006 to 2015, 1843 (51.1%) were male and 1763 (48.9%) were female, with a male-to-female sex ratio 1.05. The annual crude incidence rate ranged from 20.10/10\(^5\) to 57.94/10\(^5\), with an average annual crude incidence rate was 33.20/10\(^5\) and an age-standardized incidence rate by world standard population (ASIRW) of 63.36/10\(^5\) during 2006-2015 period. The average annual crude incidence rate was 366.13/10\(^5\) in 0-4-year-old patients, and this rate was significantly higher than that of 24.13/10\(^5\) in 5-year-old or older patients (\( t = 99.42, P < 0.001 \)). The incidence rates of infectious diarrhea were highest in 2009, and crude incidence rates were 57.04/10\(^5\) in male, 58.86/10\(^5\) in female, 57.94/10\(^5\) in total,

| Year | Male         | Female        | Total         |
|------|--------------|---------------|---------------|
|      | Case | Population | Crude incidence | ASR(W)* | Case | Population | Crude incidence | ASR(W)* | Case | Population | Crude incidence | ASR(W)* |
| 2006 | 118  | 554774 | 21.27 | 34.33 | 99  | 524781 | 18.87 | 24.05 | 217  | 1079555 | 20.10 | 29.42 |
| 2007 | 100  | 552302 | 18.11 | 18.86 | 122  | 525003 | 23.24 | 22.22 | 222  | 1077305 | 20.61 | 20.45 |
| 2008 | 283  | 551412 | 51.32 | 142.29 | 268  | 527962 | 50.76 | 114.97 | 551  | 1079374 | 51.05 | 129.08 |
| 2009 | 315  | 552204 | 57.04 | 195.29 | 313  | 531761 | 58.86 | 156.99 | 628  | 1083965 | 57.94 | 176.73 |
| 2010 | 249  | 553123 | 45.02 | 111.49 | 237  | 535804 | 44.23 | 95.67 | 486  | 1088927 | 44.63 | 103.83 |
| 2011 | 150  | 552502 | 27.15 | 50.10 | 151  | 539420 | 27.99 | 41.02 | 301  | 1091922 | 27.57 | 45.70 |
| 2012 | 129  | 551345 | 23.40 | 49.66 | 112  | 541378 | 20.69 | 41.40 | 241  | 1092723 | 22.05 | 45.62 |
| 2013 | 176  | 549281 | 32.04 | 58.50 | 162  | 542042 | 29.89 | 51.88 | 338  | 1091323 | 30.97 | 55.27 |
| 2014 | 166  | 547036 | 30.35 | 40.24 | 173  | 541979 | 31.92 | 38.61 | 339  | 1089015 | 31.13 | 39.41 |
| 2015 | 157  | 544656 | 28.83 | 33.96 | 126  | 542008 | 23.25 | 24.72 | 283  | 1086664 | 26.04 | 29.44 |
| Total | 1843 | 5508635 | 33.46 | 70.80 | 1763 | 5352138 | 32.94 | 59.56 | 3606 | 33.20 | 63.36 |

* per/100000 person-year; ASR(W): Age-world-standardized incidence rate

Table 1: The incidence of infectious diarrhea cases in Yangpu district of Shanghai, China, from 2006 to 2015.

Occurrence of infectious diarrhea cases in 0-4 year-old patients usually peaked at period from November to next January, while the peak time of 5-year-old or older patients was from July to September (Figure 1).
The age stratification analysis showed that infectious diarrhea cases had statistically different monthly distributions for each age group between 2006 and 2015 ($\chi^2=199.95$, $P<0.001$) (Figure 2). Moreover, a significant difference in the monthly proportion of each age group was found between 0-4-year group and 15-59 year group ($\chi^2=31.37$, $P<0.001$) and between 0-4 year group and >60 years group ($\chi^2=17.24$, $P<0.005$), respectively.

**Pathogen spectrums of infectious diarrhea cases from 0-4-year-old patients and 5-year-old or older patients**

A total of 2809 cases with pathogen information were reported from 3606 infectious diarrhea cases. Due to different types of pathogens causing infectious diarrhea in patients at different age groups, we analyzed the pathogen spectrums from 910 cases of 0-4-year-old patients and 1899 cases of 5-year-old or older patients, respectively. In 0-4-year-old patients, rotavirus accounted for 90.11% (820/910)
and was the dominant pathogen followed by *Salmonella* (8.02%, 73/910), *Shigella* (1.76%, 16/910) and *Campylobacter jejuni* (0.11%, 1/910). The top five pathogens were *Vibrio* (56.92%, 1081/1899), *Salmonella* (15.38%, 292/1899), *Shigella* (15.17%, 288/1899), norovirus (5.11%, 97/1899), and rotavirus (4.11%, 78/1899) in 5-year-old or older patients (Figure 3). Among the 1081 cases of *Vibrio* infected patients, *Vibrio parahaemolyticus* was the predominant bacterial pathogen with a high proportion of 98.43% (1064/1081).

**The association between the incidence of infectious diarrhea and meteorological factors**

The GAM result of 0-4-year-old patients was similar to the result of 5-year-old or older patients, so GAM result was shown in the form of total patients. Monthly average wind velocity, sunshine time, air pressure, vapor pressure, and relative humidity were automatically excluded during the subsequent selection process. Monthly average maximum temperature, minimum temperature and precipitation were introduced into the non-linear part of model. Degrees of freedom (df) for the non-linear functions were set as 3. The lag effects were insignificant and excluded in the final GAM. The final GAM was shown as follows:

$$\log [E(Y)] = f(\text{maximum temperature, } df=3)+f(\text{minimum temperature, } df=3)+f(\text{precipitation, } df=3)+\epsilon+\beta_0$$

As shown in (Figure 4), with the increase of monthly average maximum temperature, minimum temperature and precipitation, the effective value gradually decreased and then increased, which was similar to binary curve. Monthly average maximum temperature below 6.38°C and above 24.59°C had positive effects on the incidence of infectious diarrhea. Monthly average minimum temperature below 5.12°C and above 24.03°C had positive effect on the incidence of infectious diarrhea. Monthly average precipitation below 1.48 mm and above 7.40 mm had positive effects on the incidence of infectious diarrhea.
Our study described the epidemiology of infectious diarrhea cases and analyzed the association between the meteorological factors and incidence of infectious diarrhea cases in Yangpu district from 2006 to 2015. This study revealed that the average annual crude incidence rate was 33.20/10^5 and the ASIRW was 63.36/10^5 during 2006-2015 period, which were relatively low compared with other provinces in China [3]. The average annual crude incidence rate was 366.13/10^5 in 0-4-year-old patients, whereas this rate was 24.13/10^5 in 5-year-old or older patients. Based on this significant difference, we divided overall patients into 0-4-year-old and 5-year-old or older patients for further analyses, such as peak time, pathogen spectrums and the associations between meteorological factors and the incidence of infectious diarrhea.

Our results were consistent with other studies in China showing that infectious diarrhea cases in 0-4-year-old patients usually peaked at period from November to next January, while the peak time of 5-year-old or older patients was from July to September [19,20]. The monthly distributions of infectious diarrhea cases were statistically different among different age groups. For example, the cases of 15-59 years group mainly occurred in June, July and August, but 0-4years group cases occurred in November, December and January. We further investigated the reason why pathogen spectrums might differ among different age groups. Proportion of rotavirus accounted for 90.11% of infectious diarrhea cases and was the dominant pathogen in 0-4-year-old patients, whereas it was only 4.11% in 5-year-old or older patients. Rotavirus is one of the major reasons of diarrhea diseases in 0-4-year-old patients, and about 30%-60% of hospital admissions for diarrhea diseases in young children were infected with rotavirus [21-23]. In order to control the prevalence of rotavirus, several kinds of hygienic measures, such as supplement of clean water and good sanitation, are recommended. We suggest that rotavirus vaccine is the most economical and effective means to prevent rotavirus related infectious diarrhea in 0-4-year-old children. Rotavirus vaccine has been proved to be responsible for a 67% reduction in laboratory-confirmed rotavirus infections for 0-4-year-old children in England [24]. In addition, 56.92% of 5-year-old or older patients were infected with Vibrio, but there were no patients infected with Vibrio in the 0-4-year-old patients. Vibrio parahaemolyticus was the predominant bacterial pathogen among Vibrio infected patients. Vibrio parahaemolyticus has a halophilic characteristic and is often isolated from seawater and seafood. Shanghai is a coastal city and the consumption of contaminated seafood is the main cause of acute diarrhea in adults [25]. To strengthen the supervision of hygiene conditions in the sale, transportation and consumption of seafood may help reduce the occurrence of infectious diarrhea in adults.

The incidence of infectious diarrhea and meteorological factors varied widely in different regions in mainland China [3], the analysis in a certain area can provide more accurate and detailed information. With a population of about 1.1 million, Yangpu district can be a good candidate for the impact of meteorological factors on the incidence of infectious diarrhea. Because of its strengths in the time series analysis, the GAM has been widely used in the studies of the association between climate changes and incidence of infectious diseases [16-18].

We observed that maximum temperature below 6.38°C and above 24.59°C had positive effects on the incidence of infectious diarrhea. The minimum temperature below 5.12°C and above 24.03°C had positive effects on the incidence of infectious diarrhea. Our results suggested that the effects of maximum temperature and minimum temperature were similar. High and low temperatures were associated with an increasing number of infectious diarrhea.
cases. The following are the possible reasons for this phenomenon. Firstly, the possible etiological and meteorological explanations might be that temperature influences the replication and activity of pathogens. For example, the stability of rotavirus is higher under low temperature and it allows rotavirus to survive longer in contaminated environment, providing more opportunities of virus transmission and infection. The highest level of rotavirus was occurred in the colder and drier months, and the rotavirus infectivity was weaker at 37°C than 4°C or 20°C [26]. Moreover, food poisoning which was caused by bacteria such as *Vibrio parahaemolyticus* and *Salmonella*, was common in summer, because food was easy to be rotten in high temperature [27]. A 1°C increase in temperature was associated with a 10.6% increased risk of bacillary dysentery [28]. Secondly, in winter, people usually stay indoors to keep warm and avoid low temperature, providing more chances for person-to-person contacts and rotavirus spread via fecal-oral route and contaminated surfaces in closed environment [29].

We found that precipitation above 7.40 mm had a positive effect on the incidence of infectious diarrhea. More precipitation was associated with an increased risk of infectious diarrhea caused by *Vibrio parahaemolyticus*. Increased precipitation exerts an effect on the survival and transmission of waterborne disease pathogens and leads to a lack of clean water and food supply [30]. Because of contamination of the water distribution systems, more precipitation can trigger higher risk of diarrhea outbreaks [7]. Excess precipitation is positively associated with risk of infectious diarrhea in Beijing [28], Fiji [31], Taiwan [18] and Bangladesh [32]. There are three possible mechanisms in which increased precipitation might influence the quality of water supply and hence the risk of infectious diarrhea outbreaks. Firstly, increased risk of sewer overflows caused by more precipitation might result in water supply contamination [33]. Secondly, excess precipitation will increase the runoff of manure and animal excreta on soil and surface, leading to higher waterborne pathogen concentrations in surface water [34,35]. Thirdly, excess precipitation increases turbulences and sediment resuspension, leading to wide distributions of accumulated pathogens [36,37]. Moreover, precipitation below 1.48 mm also had a positive effect on the incidence of infectious diarrhea. Less precipitation in winter and spring was associated with more infectious diarrhea cases caused by rotavirus. And the infectivity of rotavirus was increased by 0.3% when the precipitation had a decrease of 10 mm [38].

Several limitations should be acknowledged. Firstly, although there have been large improvements in the reporting of NDSS, under-reporting is an inevitable issue in the surveillance of infectious diarrhea [9]. Because of its prosperous economic, yangpu district has a large number of mobile populations, such as tourists or individuals who are on a business trip for a short period of time. Some individuals with mild symptoms might do not go to the hospital or take medicine by themselves. To a certain extent, the NDSS includes the surveillance information of these mobile populations, but it is difficult to avoid the missing data. Under-reporting would weaken the assessment of the association between meteorological factors and infectious diarrhea incidence. Secondly, lack of complete microbiological etiology might limit the evaluation of effect of meteorological variables on each class of infectious diarrhea. Thirdly, the multicollinearity caused by significant correlations among some meteorological variables, such as a positive correlation between temperature and precipitation, might result in the instability of model parameters.

In conclusion, our study suggested that residents in Yangpu district of Shanghai had a relatively low risk of infectious diarrhea. The average annual crude incidence rate, the peak time and the pathogen spectrums of infectious diarrhea cases were distinct between different age groups. In 0-4-year-old patients, rotavirus was the dominant pathogen. And *Vibrio parahemolyticus* was the predominant bacterial pathogen in 5-year-old or older patients. High temperature and excess precipitation had positive effects on the incidence of infectious diarrhea caused by *Vibrio parahemolyticus* in 5-year-old or older people. Low temperature and little precipitation had positive effects on the incidence of infectious diarrhea caused by rotavirus in 0-4-year-old children. Our findings have suggested that meteorological factors can impact the incidence of infectious diarrhea, and might be references for the prophylaxis and control of infectious diarrhea in urban areas of developing world.

**References**

1. World Health Organization (2017) Diarrheal disease. Media center.
2. Walker CL, Aryee MJ, Boschi-Pinto C, Black RE (2012) Estimating diarrhea mortality among young children in low and middle-income countries. PloS One 7: e29151.
3. Liu HX, Zhang J (2013) Analysis of reported infectious diarrhea (other than cholera, dysentery, typhoid and paratyphoid) in China in 2011. (Zhong hua Yu Fang Yi Xue Za Zhi) 47: 328-332.
4. Alexander KA, Carzolli M, Goodin D, Vance E (2013) Climate change is likely to worsen the public health threat of diarrheal disease in Botswana. Int J Environ Res Public Health 10: 1202-1230.
5. Wu J, Yunus M, Streetfield PK, Emch M (2014) Association of climate variability and childhood diarrheal disease in rural Bangladesh, 2000-2006. Epidemiol Infect 142: 1859-1868.
6. Davies GI, McIver L, Kim Y, Hashizume M, Iddings S, et al. (2014) Water-borne diseases and extreme weather events in Cambodia: review of impacts and implications of climate change. Int J Environ Res Public Health 12: 191-213.
7. Lloyd SJ, Kovats RS, Armstrong BG (2007) Global diarrhoea morbidity, weather and climate. Climate Res 34: 119-127.
8. Zhang Y, Bi P, Hiller JE (2008) Weather and the transmission of bacillary dysentery in Jinan, northern China: a time-series analysis. Public Health Rep 123: 61-66.
9. Zhang Y, Bi P, Hiller JE, Sun Y, Ryan P (2007) Climate variations and bacillary dysentery in northern and southern cities of China. J Infect 55: 194-200.

10. Zhou X, Zhou Y, Chen R, Ma W, Deng H (2013) High temperature as a risk factor for infectious diarrhea in Shanghai, China. J Epidemiol 23: 418-423.

11. Jiang FC, Yang F, Chen L, Jia J, Han YL, et al. (2016) Meteorological factors affect the hand, foot, and mouth disease epidemic in Qingdao, China, 2007-2014. Epidemiol Infect 144: 2354-2362.

12. Wang H, Du Z, Wang X, Liu Y, Yuan Z, et al. (2015) Detecting the association between meteorological factors and hand, foot, and mouth disease using spatial panel data models. Int J Infect Dis 34: 66-70.

13. Shanghai Yangpu Government. Shanghai Yangpu: Geographical Location. Retrieved 29 Jul 2011.

14. Shanghai Yangpu Government. 2010 Sixth National population census data Gazette in Shanghai Yangpu. Retrieved 29 Jul 2011.

15. Wood SN (2004) Stable and efficient multiple smoothing parameter estimation for generalized additive models. J Am Stat Assoc 99: 673-686.

16. Ni W, Ding G, Li Y, Li H, Liu Q, et al. (2014) Effects of the floods on dysentery in north central region of Henan Province, China from 2004 to 2009. J Infect 69: 430-439.

17. Gao L, Zhang Y, Ding G, Liu Q, Zhou M, et al. (2014) Meteorological variables and bacillary dysentery cases in Changsha City, China. Am J Trop Med Hyg 90: 697-704.

18. Chou WC, Wu JL, Wang YC, Huang H, Sung FC, et al. (2010) Modeling the impact of climate variability on diarrhea-associated diseases in Taiwan (1996-2007). Sci Total Environ 409: 43-51.

19. Wang X, Wang J, Sun H, Xia S, Duan R, et al. (2015) Etiology of Childhood Infectious Diarrhea in a Developed Region of China: Compared to Childhood Diarrhea in a Developing Region and Adult Diarrhea in a Developed Region. Plos One 10: e0142136.

20. Xu Z, Hu W, Zhang Y, Wang X, Zhou M, et al. Exploration of diarrhoea seasonality and its drivers in China. Sci Rep 5: 8241.

21. Kotloff KL, Nataro JP, Blackwelder WC, Nasrin D, Farag TH, et al. (2013) Burden and aetiology of diarrhoeal disease in infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): a prospective, case-control study. Lancet 382: 209-222.

22. D’Souza RM, Hall G, Becker NG (2008) Climatic factors associated with hospitalizations for rotavirus diarrhoea in children under 5 years of age. Epidemiol Infect 136: 56-64.

23. Anders KL, Thompson CN, Thuy NT, Nguyen NM, Tu Le TP, et al. (2015) The epidemiology and aetiology of diarrhoeal disease in infancy in southern Vietnam: a birth cohort study. Int J Infect Dis 35: 3-10.

24. Atchison C, Collins S, Brown D, Ramsay ME, Ladhani S, et al. (2015) Reduction in rotavirus disease due to the infant immunisation programme in England: evidence from national surveillance. J Infect 71: 128-131.

25. Zhang Y, Zhao Y, Ding K, Wang X, Chen X, et al. (2014) Analysis of bacterial pathogens causing acute diarrhea on the basis of sentinel surveillance in Shanghai, China, 2006-2011. Jpn J Infect Dis 67: 264-268.

26. Moe K, Shirley JA (1982) The effects of relative humidity and temperature on the survival of human rotavirus in faeces. Arch Virol 72: 179-186.

27. Bentham G, Langford IH (2001) Environmental temperatures and the incidence of food poisoning in England and Wales. Int J Biometeorol 45: 22-26.

28. Xiao G, Xu C, Wang J, Yang D, Wang L. (2014) Spatial-temporal pattern and risk factor analysis of bacillary dysentery in the Beijing-Tianjin-Tangshan urban region of China. BMC Public Health 14: 998.

29. Willem L, Van Kerckhove K, Chao DL, Hens N, Beutels P (2012) A nice day for an infection? Weather conditions and social contact patterns relevant to influenza transmission. PloS One 7: e48695.

30. Jofre J, Blanch AR, Lucena F (2010) Water-borne infectious disease outbreaks associated with water scarcity and rainfall events. In: Sabater S, Barcelo D (Eds), Water Scarcity in the Mediterranean: Perspectives Under Global Change. The Handbook of Environmental Chemistry 8: 147-159.

31. Singh RB, Hales S, De Wet N, Raj R, Hearmden M, et al. (2001) The influence of climate variation and change on diarrheal disease in the Pacific Islands. Environ Health Perspect 109: 155-159.

32. Hashizume M, Armstrong B, Hajat S, Wagatsuma Y, Faruque AS, et al. (2007) Association between climate variability and hospital visits for non-cholera diarrhoea in Bangladesh: effects and vulnerable groups. Int J Epidemiol 36: 1030-1037.

33. Hofstra N (2011) Quantifying the impact of climate change on enteric waterborne pathogen concentrations in surface water. Curr Opin Environ Sustain 3: 471-479.

34. Wilby RL, Hedger M, Orr H. (2005) Climate change impacts and adaptation: a science agenda for the Environment Agency and Europe and Wales. Weather 60: 206-211.

35. Moors E, Singh T, Siderius C, Balakrishnan S, Mishra A (2013) Climate change and waterborne diarrhoea in northern India: impacts and adaptation strategies. Sci Total Environ: 468-469.

36. Garzio-Hadzick A, Shelton DR, Hill RL, Pachepsky YA, Guber AK, et al. (2010) Survival of manure-borne E. coli in streambed sediment: effects of temperature and sediment properties. Water Res 44: 2753-2762.

37. Ding G, Zhang Y, Gao L, Ma W, Li X, et al. (2013) Quantitative analysis of burden of infectious diarrhea associated with floods in northwest of anhui province, china: a mixed method evaluation. PloS One 8: e65112.

38. Jagai JS, Sarkar R, Canstronovo D, Kattula D, McEntee J, et al. (2012) Seasonality of rotavirus in South Asia: a meta-analysis approach assessing associations with temperature, precipitation, and vegetation index. PLoS One 7: e38168.