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The Impact of Climate Variability on Infectious Disease Transmission in China: Current Knowledge and Further Directions

Liping Yi [1a], Xin Xu [2a], Wenxin Ge [1a], Haibin Xue [3], Jin Li [4], Daoyuan Li [5], Chunping Wang [1], Haixia Wu [6], Xiaobo Liu [6], Dashan Zheng [1], Zhe Chen [1], Qiyong Liu [6], Peng Bi [7, 8*], Jing Li [1,9*]

Affilications:

1. Division of Environmental Health, School of Public Health and Management, Weifang Medical University, Weifang 261053, Shandong Province, PR China;
2. Department of Dentistry, Affiliated Hospital, Weifang Medical University Weifang 261053, Shandong Province, PR China;
3. Clinical Laboratory, Weifang People's Hospital Weifang 261000. Shandong Province, PR China;
4. Department of Dentistry, Weifang People's Hospital Weifang 261000, Shandong Province, PR China;
5. Department of Emergency, Weifang No.2 People's Hospital 261041, Shandong Province, PR China;
6. State Key Laboratory of Infectious Disease Prevention and Control, National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing 102206, People's Republic of China, Shandong Province, PR China;
7. School of Public Health, the University of Adelaide, Adelaide, SA 5005, Australia;
8. School of Public Health, Anhui Medical University of China
9. "Health Shandong" Major Social Risk Prediction and Governance Collaborative Innovation Center, 261053, Shandong Province, PR China
a Co-first authors

*** Corresponding author:**
Peng Bi, Professor
School of Public Health, the University of Adelaide.
Address: The University of Adelaide, Adelaide, SA 5000
Tel: +61-8- 83133583; Fax: +61-8- 83133583.
Zip code: SA5005. E-mail: Peng.bi@adelaide.edu.au.

Jing Li, Lecturer
Division of Environmental Health, School of Public Health and Management, Weifang Medical University
Address: No. 7166 Baotong Xi Street, Weifang, Shandong Province, PR China
Tel: +86-536-8462238; Fax: +86-536-8462238.
Zip code: 261053. E-mail: lijingsddx@126.com

Abstract:

Background: Climate change may lead to emerging and re-emerging infectious diseases and pose public health challenges to human health and the already overloaded healthcare system. It is therefore important to review current knowledge and identify further directions in China, the largest developing country in the world.

Methods: A comprehensive literature review was conducted to examine the relationship between climate variability and infectious disease transmission in China in the new millennium. Literature was identified using the following MeSH terms and keywords: climatic variables [temperature, precipitation, rainfall, humidity, etc.] and infectious disease [viral, bacterial and parasitic diseases].

Results: Fifty-eight articles published from January 1, 2000 to May 30, 2018 were included in the final analysis, including bacterial diarrhea, dengue, malaria, Japanese encephalitis, HFRS, HFMD, Schistosomiasis. Each 1°C rise may lead to 3.6%-14.8% increase in the incidence of bacillary dysentery disease in south China. A 1 °C rise was corresponded to an increase of 1.8-5.9% in the weekly notified HFMD cases in west China. Each 1°C rise of temperature, 1％ rise in relative humidity and one hour rise in sunshine led to an increase of 0.90%, 3.99% and 0.68% in the monthly malaria cases, respectively. Climate change with the increased temperature and irregular patterns of rainfall may affect the pathogen reproduction rate, their spread and geographical distribution, change human behavior and influence the ecology of vectors, and increase the rate of disease transmission in different regions of China.

Conclusion: Exploring relevant adaptation strategies and the health burden of climate change will assist public health authorities to develop an early warning system and protect China's population health, especially in the new 1.5 degree scenario of the newly released IPCC special report.

Key words: climate change, infectious disease, health burden, China

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1. Introduction:

Climate change, with the changes in temperature and precipitation, and increasing extreme weather events, has and will continue to impact the transmission of infectious diseases via affecting pathogen growth and development, survival of vector and human behavior[1]. World Health Organization (WHO) projected that, 10% of diarrheal diseases will increase by 2030 due to climate change[1,2]. If global temperatures continue to increase by 2–3°C, the population at risk for malaria will increase by 3%–5%[1,2]. With 34 provincial jurisdictions and a total of 1.39 billion populations, China is a major contributor to global infectious disease burden[3,4]. Over the period 2009-2017, there were an average of 6,618,257 infectious disease notifications each year with the mortality rate around 1.25/100,000[5]. Among the notifiable infectious diseases in China, plague, cholera, malaria, dengue fever, Japanese encephalitis, typhoid fever and paratyphoid fever, hand, foot and mouth disease, bacterial dysentery, epidemic hemorrhagic fever and schistosomiasis are climate sensitive. Given the current very low incidence of plague, cholera, typhoid and paratyphoid in China, this paper will focus on the seven infectious diseases with public health significance, examine the impact of climate variability on the transmission of these diseases, discuss the research limitations, and suggest further research directions and government actions to be established in China.

2. Methods:

2.1 Search strategy

Several mainstream databases including the Web of Science, PubMed, CNKI (http://www.cnki.net/) were used to search original literature. To expand the search scope, we used series of key word combinations to conduct the search. More details are listed in **Table 1.**

2.2 Inclusion and exclusion criteria

In this paper, studies published both in English and Chinese about climate change and infectious diseases in China were referenced. **Figure 1** shows the process of search and inclusion/exclusion.

Literatures were included according to following rules:

1. Studies must examine the association between climate variability/ change and infectious disease. Those analyzing the etiology, diagnosis and treatment of communicable disease were excluded.

2. Only the studies published from January 1, 2000 to May 30, 2018 and conducted in China were included.

3. Papers focusing on the seven infectious diseases with public health significance in China (**Table 2**) were included. Those discussing other diseases were excluded.

Among all related literature, fifty-eight articles finally met the inclusion criteria.

3. Results and Discussion

3.1 Infectious diseases under investigation

Climate change affects infectious disease via its impacts on pathogen, host and transmission environment[6]. In this review, we assess its impacts on seven pathogenic diseases with significant public health challenges in China, namely viral infectious diseases, bacterial infectious diseases and parasitic diseases. **Table 2** shows the papers categorized by disease nature[7].

3.2 Research approaches in the literature:

Most of the published studies used ecological study design for the risk assessments. In terms of time-series data analyses, various statistical methods and mathematical models were implemented. The distributed lag non-linear model (DLNM) was used to graphically demonstrate the impact of climate variability on infectious disease transmission[8-17]. The seasonal autoregressive integrated moving average (SARIMA) model was applied to identify and quantify the relationship between the meteorological variables and disease transmission[18-24]. ArcGIS is an effective geographic information system working with mapping and geographic information, which has been utilized together with other statistical approach in this area to explore its temporal-spatial relationship with climate variability.

There are 13 articles exploring the relationship between infectious diseases and climate variability or extreme weather events at the national scale. Three discussed such association at a regional level such as South or North China. Research locations are shown in **Figure 2**, indicating that there are still some regions in which no research was conducted.

3.3 Associations between climatic variables and infectious diseases

3.3.1 Bacterial infectious disease

Bacterial dysentery

Bacterial dysentery, also referred as bacillary dysentery, is an intestinal infectious disease caused by Shigella[25]. It usually occurs in summer and autumn, suggesting that it may be associated with hot, humid weather conditions[18]. Studies in China suggested that bacillary dysentery could be sensitive to precipitation, ambient temperature and flood events[26]. Using time series analysis, the researchers observed that the monthly incidence of dysentery was positively associated with temperature, precipitation and relative humidity, but negatively related to air pressure in Jinan (Eastern China), Shenzhen (South), Shenyang (Northeast) and Beijing (North)[19,27-28]. However, another study conducted in Wuhan, central China, founded that bacillary dysentery occurrence was positively associated with mean temperature while negatively related to relative humidity and precipitation, which may be due to differences in analytical methods, economic development levels, behavioral habits or climatic characteristics[29]. The temperature lag effect in southern cities was found shorter than that in northern cities indicating that baseline temperature is relevant higher in South China and a slight increase in temperature may accelerate the pathogen growth and development[18,27]. A study in Guangzhou found that each 1°C rise of temperature was corresponded to an increase of 3.60% in the monthly notified cases, whereas 1hPa rise in atmospheric pressure corresponded to a decrease in the number of cases by 2.85% [30]. Another study also conducted in South China suggested that 1°C rise in mean temperature, mean maximum temperature (T_{max}), and mean minimum temperature (T_{min}) might lead to 14.8%, 12.9%, and 15.5% increase in the incidence of bacillary dysentery disease, respectively[20], suggesting that climate change will lead to more bacterial dysentery cases in China. It is therefore important to identify the threshold temperature and establish an early warning system **(Table A.1)**.

3.3.2 Parasitic disease

① Malaria

Malaria is a climate-sensitive vector-borne disease caused by *Plasmodium*. With effective interventions, the number of malaria cases had decreased from 24 million cases in the early 1970s to 30,000 in the late 1990s in China[31]. Climatic factors can change the survival and reproduction cycle of Anopheles mosquitoes and accelerate the outer cycle of *Plasmodium* [32]. It is predicted that if there are no preventive measures, the geographical scope of certain malaria vectors such as *Anopheles minimus and Anopheles dirus* will increase by 16-49% by 2030[33], and accordingly, the incidence of malaria may increase by 43-73% in Huaihe River Basin[34]. A series of studies have found that temperature, precipitation, sunshine hours and relative humidity are closely related to the incidence of malaria [8,35], with a certain lag effect[9-10,36-37], which lasts longer in the cool climate zone than that in the warm climate zone[8-10,21,36-37]. A study in Jinan, eastern China, showed that a 1°C rise in T_{max} may be related to a 7.7% to 12.7% increase in the number of malaria cases, while a 1°C rise in T_{min} may result in approximately 11.8% to 15.8% increase in cases[22]. In Tibet, west China, the incidence of malaria is mostly associated with the relative humidity which directly affects the bite and reproductive rate of mosquitoes and when the relative humidity is less than 60%, malaria transmission will be restrained[21,36]. Bi in Yunnan and Gao in Anhui have found that precipitation factors have far more influence on malaria transmission than other weather factors [10.37]. In addition, study in southern China revealed that each 1°C rise of temperature, 1％ rise in relative humidity and one hour rise in sunshine led to an increase of 0.90%, 3.99% and 0.68% in the monthly cases, respectively[35]. During the flood event in 2007 in Anhui, eastern China, the most commonly notified diseases was malaria (incidence rate =17.867/100,000)[26]. Within a certain range, the rainfall provides the *Anopheles* with additional breeding sites [10,37], while heavy rain will wash away the larvae and eggs which would reduce the incidence of malaria[9,36-37]. Given the variations in socioeconomic status, climatic and geographic characteristics, relevant actions could be taken for China's malaria elimination program. In southwestern China, for instance, special attention should be paid to the border regions where the imported malaria cases could play an important role in the disease transmission. An integrated measurement, including vector monitoring and control, disease surveillance and weather watching should be implemented **(Table A.2)**.

② **Schistosomiasis**

In China, the geographical distribution of the snail host *O. hupensis* is restricted to areas where the mean January temperature is above 0 °C [38]. The environmental conditions such as temperature, precipitation and humidity were reported to directly or indirectly influence the living habit of intermediate host snails and schistosome eggs, larvae and adults thus alter the transmission of schistosomiasis[39-41]. Zhou found a temperature threshold of 15.4°C for the development of Schistosoma japonicum within the *Oncomelania hupensis* and a temperature of 5.8°C at which half the snail sample investigated was in hibernation[42-43]. It has been predicted that a northward expansion of transmission area of schistosomiasis may occur due to the climate warming, with an additional 783,883 km^2 area, and 20.7 million people at risk of infection by 2050[42,44-45]. In eastern China, the mean T_{min} -4℃ in January is the boundary line between the epidemic area and the non-endemic area, which suggests that the frozen environment plays a major role in hindering the migration of schistosomiasis to the north[46]. In addition, the differences of the subspecies of *O. hupensis* are worth studying and comparing in a climate change context[47]. The application of geographic information system (GIS) technology and the ecological niche modeling (ENM) may have play a significant role in predicting the prevalence of schistosomiasis in China [47]. **(Table A.3)**

3.3.3 Viral infectious disease

① Dengue

Dengue fever, a viral disease, is the fastest increasing vector-borne disease in the world with only one thousand cases reported in the 1950s to more than 90 million cases in the 2000s[48]. In 2014, a major outbreak occurred in Guangzhou city, southern China, causing significant public health problem, with about 50,000 cases [11]. As the climate gets warmer, there has been a trend of expanded geographical region for dengue infections, from South to North China[49]. Many investigations studied the association between climatic factors and dengue incidence using various analytical approaches controlling for confounders. For example, a study in Guangzhou pointed out that the optimal T_{max} range for dengue transmission was 21.6 – 32.9°C, and 11.2 – 23.7°C for T_{min}[11]. Gu[50] concluded that temperature contributed most to the risk for dengue fever in South China while other research reported that precipitation variables played a more important role than temperature in similar regions[51-52], suggesting more research is needed. Wang[53] found that dengue incidences were positively associated with relative humidity and temperature, and negatively with wind velocity and precipitation in southern China, which was inconsistent with other results[54]. The identification of threshold temperature and lag effects can be helpful for dengue control and prevention in dengue epidemic areas[30,55] **(Table A.4).**

② HFMD

Transmitted by close contact, HFMD is an acute infectious disease caused by a group of enteroviruses, of which *Coxsackie virus A 16* and *Enterovirus 71* are two major agents [56-58]. The incidence of HFMD is one of the major causes of death among children in China[59-60]. Seasonal distribution of HFMD suggested that climatic factors might affect the disease transmission. Average temperature, relative humidity and wind speed were found positively associated, while daily precipitation and sunshine hours were negatively associated with HFMD incidence in Gansu (Northwest), Shanghai (East), Chongqing (Southwest)[12-13,61] while observations in some other areas show contradictory results[62], indicating the local climatic characteristics, socioeconomic status and behavior factors may contribute to the disease transmission. Zhu[14] concluded that within a suitable range, the higher the temperature is, the higher the morbidity is, which is consistent with the findings from Qi[12] and Dong[63]. A research conducted in Gansu Province using generalized linear regression models revealed an increase in weekly HFMD of 1.8-5.9% in association with 1 °C increase in mean temperature[61]. A study in Anhui Province, eastern China, found that extreme precipitation was significantly associated with HFMD[15]. The threshold points for temperature for HFMD transmission in western China ranged from 16℃ to 20℃[61]. Taking the incubation of HFMD (3 – 7 days) into account, the lag effects of temperature, relative humidity, and extreme precipitation were identified, which may provide implications for HFMD early warning system [13,16,23,64] **(Table A.5)**.

③ HFRS

HFRS, also known as epidemic hemorrhagic fever, is a zoonosis caused by different species of Hanta-viruses transmitted by rodents[65]. Widely prevalent in China, a total of 68,069 HFRS cases were reported and 466 people died over the period 2012 to 2017[5]. Climatic factors may influence the crop growth, ecological environment and mice density, as well as human activity, then the incidence rate of HFRS [66]. Given the range of climate zones and geographical and agricultural characteristics, the influences of precipitation, temperature and humidity on HFRS incidence have been found varied. The relative humidity, precipitation, and mean temperature were found to be negatively correlated with the monthly number of HFRS cases, while the effect of wind velocity had a positive correlation in East and North China[66-67]. Other related studies have also demonstrated the average humidity influencing factor shows positive associated with HFRS cases [68]. SOI (Southern Oscillation Index) has been used as an index across a large geographical area[65,69]. Based on 22-years data, an inverse relationship between the SOI and the monthly incidence of HFRS was found in Anhui Province [69], consistent with a study in Heilongjiang Province [65]. Recent years, vaccination programs and rodent control measures have been taken which contributed to the decrease of the disease substantially[70]. However more work is still needed to better quantify the influence of climatic variables, taking into account the impact of landscape, and develop prevention guidelines for high-risk groups **(Table A.6)**.

④ **JE**

Japanese Encephalitis, also known as epidemic encephalitis B, is a major mosquito-borne infectious disease caused by Japanese encephalitis virus with pigs as reservoir host and the source of infection[71]. It can occur throughout the year in tropical regions, but with seasonal distribution in subtropical and temperate regions suggesting that the climatic variables may play a certain role in its transmission. Studies in different regions have indicated that monthly[72-74]or daily[75] climatic variables can affect the epidemiology of JE through affecting the mosquito life cycle, virus ecology, human behavior thus virus-human interaction[72]. Temperature was found to be closely associated with mosquito density and JE incidence[72-73,75]. A study conducted in Chongqing, southwestern China, reported that JE incidence peaked in the years that there was a higher temperature[72]. The Hockey Stick model detected the threshold temperature for JE transmission, with maximum of 25.2℃ and minimum temperature of 21.0℃ in Jinan city, Eastern China[73]. Using the ZIPR model, Bai found a negative association between the precipitation and JE incidence[72]. In addition, Wang[74] found that JE cases were positively associated with relative humidity. A recent study also showed the positive effect of floods on notified cases of Japanese encephalitis[75]. **(Table A.7)**

3.4 Further directions for climate change and infectious disease transmission study in China

① **Lagged effect:** The temperature increase in the southern China is higher than that in the northern part, which seems consistent with the distribution of infectious diseases. Additionally, a series of time-series analyses found the temperature lag effect in southern cities was shorter than that in northern parts indicating that impact of climate change on infectious disease transmission might be more obvious in southern cities of China[18,27]. More studies are needed to confirm this finding, and relevant actions and preventative measurements should be established to protect population health, especially those vulnerable populations.

② **More comprehensive studies are needed:** Most published articles mainly worked at the local level with a limited timeframe. A meta-analysis with multiple-locations with similar climatic characteristics over a long study period will provide a stronger evidence for scientific community[36-37,76-77]. The China National infectious disease surveillance system provides an excellent platform for such initiative. A better data sharing mechanism across sectors and data custodians will promote such collaborations.

③ **Burden of infectious diseases due to climate change:** It is important to understand the burdens of infectious diseases to the health system in

China, especially those could be attributed to climate change in future so relevant health resource planning and allocation can be arranged. Unfortunately, there have been very few studies in this area and more work is needed.

④ **Data analytic approach:** Most of the published studies used an ecological study design for the time-series data. In terms of time-series data analyses, various statistical methods and mathematical models were implemented. The DLNM and SARIMA model were the most commonly used approaches. The Hockey-Stick model might provide a tool for each region to detect its own threshold temperature for early warning purpose. More scientific statistical methods and mathematical models are expected to be explored.

⑤ **Infectious disease adaptation strategy in the context of climate change:** Climate change will continue to impact the transmission of infectious diseases so relevant adaptation strategies are needed. Such initiatives could examine the current capacity in the healthcare system to deal with such challenges, including healthcare workforce, resource and facility, policy and guidelines, as well as the community demands, to reduce the burdens of infectious diseases to the health system.

4. Conclusions：

Many infectious diseases such as malaria, schistosomiasis, dengue fever and other vector-borne diseases are most affected by climate variability and climate change. Exploring the health effects from climatic factors can assist health authorities to develop relevant preventative and adaptive mechanism, implement early warning systems, especially in the context of climate change. More research is needed to further investigate the characterization of climate–infectious diseases associations in different climatic zones; to detect thresholds of meteorological factors for early warning purposes; to identify and to protect vulnerable populations, and to explore adaptation strategies to deal with the various infectious disease challenges that result from climate change.

Highlights:

- Many infectious diseases such as malaria, schistosomiasis, dengue fever and other vector-borne diseases are most affected by climate variability and climate change. The impact of climate change on infectious disease transmission may be more prevalent in southern cities of China.
- More studies with multiple-locations and a long study period as well as relevant adaptation strategies are required to deal with the various infectious disease challenges in the context of climate change in China.

Abbreviations

WHO: World Health Organization; JE: Japanese encephalitis; HFMD: Hand, foot and mouth disease; HFRS: Hemorrhagic fever with renal syndrome; DF: Dengue fever; BD: Bacterial dysentery; DLNM: The distributed lag non-linear model; SARIMA: The seasonal autoregressive integrated moving average model; GEE: Generalized estimating equation models; GAM: Generalized Additive Models; GLM: Generalized Linear Models; GIS: Geographic Information System; ENM: ecological niche modeling; SOI: Southern Oscillation Index; ZIPR model: Zero-Inflated Poisson Regression models; ARIMA: Autoregressive integrated moving average model; PCA: Principle Component Analysis; RR: relative risk; CI: confidence interval; *P. vivax: Plasmodium vivax; O. hupensis: Oncomelania hupensis.*

Conflict of interest

The authors declare that they have no competing interests.

Authors' contributions

JL, PB and QL initiated the study. LY, XX and WG collected the references. HX, JL, DL and CW selected the references. LY, XX and WG drafted the manuscript. HW, XL, DZ and ZC provided significant intellectual advice. JL, PB, QL and XX revised the manuscript. All authors read and approved the final manuscript.

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Table Legends

Table 1. Key terms used for searching

Table 2. Papers categorized by disease topic

Figure legends

Figure 1. Flow chart of literature search strategy

Figure 2. Research locations across China

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Table 1. Key terms used for searching

Infectious disease	Climatic variables
Communicable disease	Climate variability
Infectious disease	Climate change
Viral infectious diseases	Meteorological variables
DF	Global warming
HFRS	Temperature
HFMD	Precipitation
JE	Rainfall
Bacterial infectious diseases	Humidity
Dysentery	Extreme weather
Parasitic diseases	Heat waves
Malaria	Floods
Schistosomiasis	Droughts
	Typhoons

*DF: Dengue fever; HFRS: Hemorrhagic fever with renal syndrome; HFMD: Hand, foot and mouth disease; JE: Japanese encephalitis.

Table 2. Papers categorized by disease topic

Disease nature	**Diseases**	**Numbers of papers**
Viral infection	DF	10
	HFMD	10
	HFRS	5
	JE	5
Bacterial infection	Bacterial dysentery	8
Parasitic infection	Malaria	8
	Schistosomiasis	3
Others		9
Total		58

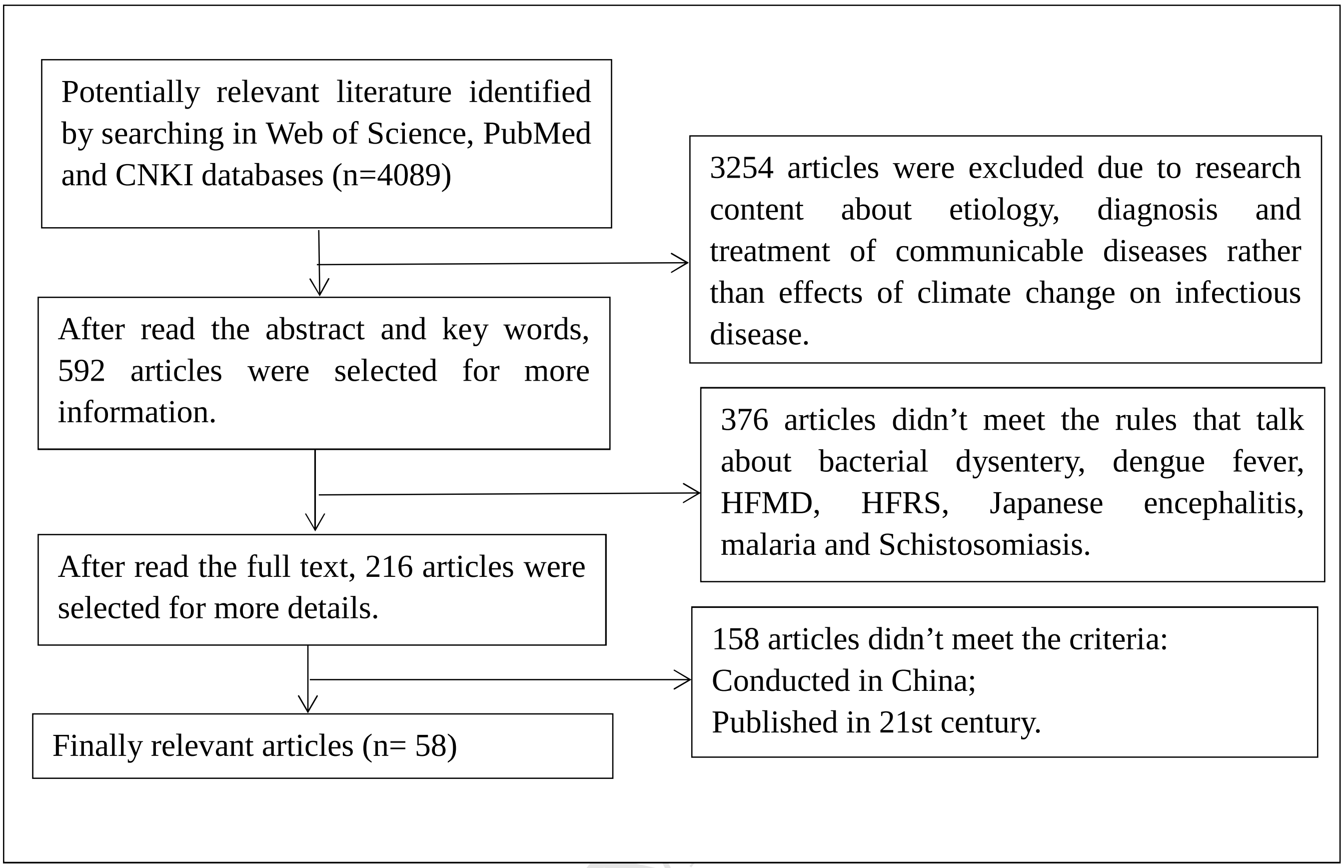

Figure 1. Flow chart of literature search strategy

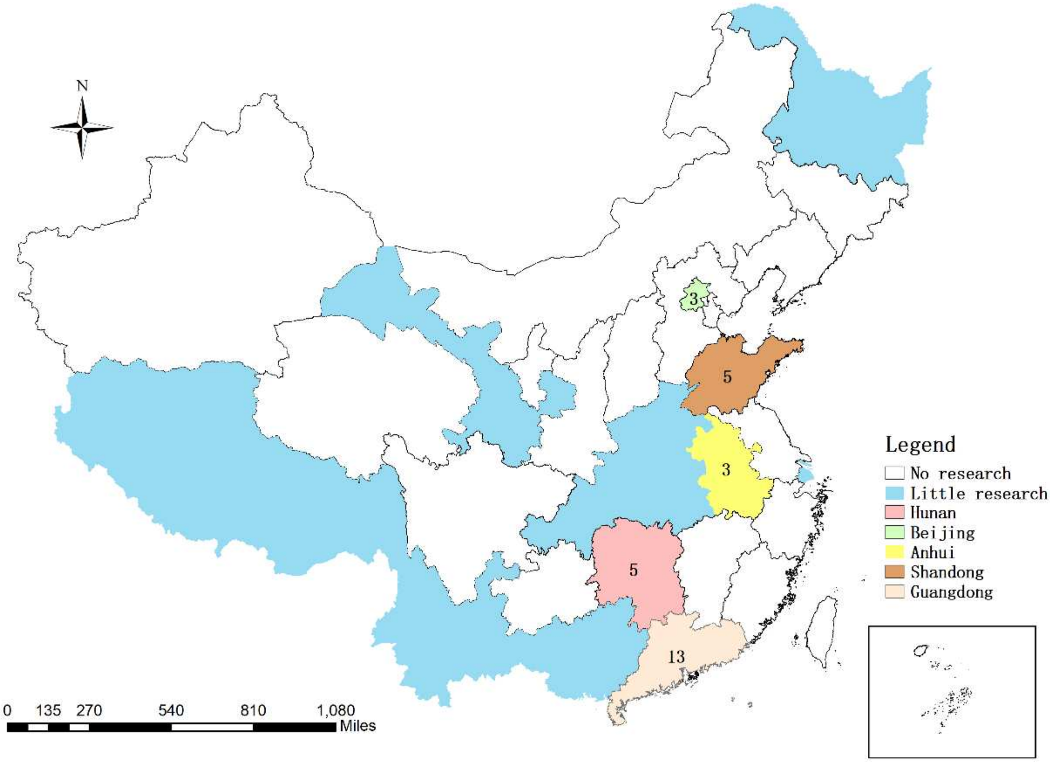

Figure 2. Research locations across China