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Cover Image: The poster for the 49th World Environment Day, designed by Chao Wang, National Institute of Environmental Health, China CDC.

Announcements

The 49th World Environment Day — June 5, 2020

Xiaoming Shi[1,#]; Tiantian Li[1]

World Environment Day, established by the United Nations (UN) at the first Conference on the Human Environment in 1972, is designated each year on June 5 to forge a basic common outlook on how to address the challenge of preserving and enhancing the human environment. World Environment Day is one of the principal vehicles through which the UN stimulates worldwide awareness of the environment and enhances political attention and action, and it is now the most renowned day for environmental action with more than 100 countries joining.

The Ministry of Ecology and Environment announced the theme for the 2020 World Environment Day — "Act towards a Beautiful China", intending to encourage all citizens of the general public to actively contribute to the building of a civilization focused on ecological protection through working together to prevent and control pollution and to develop a beautiful country with blue skies, green lands, and clean waters (*1*).

In the last several decades, environmental pollution has become increasingly prominent in China with several key aspects such as the atmosphere (urban pollution, greenhouse gases, etc.), land (desertification, chemical pollution, etc.), water (pollution including antibiotics/nanopollutants, etc.), oceans (plastic waste, polar melting, etc.), and biodiversity (extinction of genes, species, and ecosystems, etc.). The environmental factors related to health impact have become a significant public health concern in China (*2*). Revised environmental protection law (2015), Healthy China 2030 etc. address the importance of enhancing environmental monitoring, health surveillance, and risk assessment system in the environmental health activities. These policies also stress the importance of carrying out work on environmental health for protecting public health.

In this issue, we invited colleagues from National Institute of Environmental Health, China CDC, Chinese Research Academy of Environmental Sciences, and Fudan University to report their latest research findings on environmental health. Liu et al. assessed the air quality after the implementation of the Clean Air Action in Beijing-Tianjin-Hebei, China. They found significant improvements in air quality and also explored the evolution of air pollution characteristics. Zhong et al. reported the association between high temperature and non-accidental and circulatory mortality in 130 Chinese counties from 2013 to 2018 and found that the daily mean temperature was the optimal indicator for high temperature related mortality risk assessment. Lyu et al. investigated the antibiotics in drinking water and reported the health risks in 6 large river basins, inland river areas, and key lake and reservoir areas of China in 2017, which revealed the potential antibiotic threats for public health in China. Fan et al. conducted a baseline investigation on residential $PM_{2.5}$ pollution in 12 cities in China in 2018 and suggested the necessity for controlling the residential $PM_{2.5}$ pollution in China. Niu et al. found the positive association between short-term exposure to ambient ozone and outpatient visits for respiratory diseases in 5 cities in China, which may further guide policy-making for reducing ozone air pollution and improving public health. We hope these studies in this special issue may encourage readers to better understand environmental and health issues and provide public health policy implications for future environmental health policy-making in China.

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Preplanned Studies

High Temperature and Risk of Cause-Specific Mortality in China, 2013–2018

Yu Zhong[1]; Chen Chen[1]; Qing Wang[1]; Tiantian Li[1,#]

Summary

What is already known about this topic?

High temperature is a well-recognized public health threat and may increase mortality risks, especially mortality risks involving diseases of the circulatory system.

What is added by this report?

Using a six-year time series analysis, the differences of daily mean, maximum, minimum temperature were explored in assessing the health effects of high temperatures in nationwide and at climatic-zone level, and population groups susceptible to high temperatures were identified.

What are the implications for public health practice?

This study suggests that the daily mean temperature is the optimal indicator for high temperature exposure in heat-related health risk assessments and early warnings. The policy measures of heat-related public health protection should be made considering regional distribution, sensitive diseases, and vulnerable populations.

There is no nationally representative conclusion on associations between high temperature and cause-specific mortality, and it is unclear which indicator is applicable for evaluating health risks for high temperature. This study intends to estimate associations between high temperature and cause-specific mortality and to identify suitable indicators for heat-related risk assessment. We applied a time-series study with generalized linear model in 130 Chinese counties to estimate the national and climatic-zone associations between 3 high temperature indicators and cause-specific mortality for summer months of 2013–2018. We also considered estimation for sex and age groups. We found that all 3 high temperature indicators had positive associations with cause-specific mortality, and associations between daily mean temperature and cause-specific mortality were relatively higher than daily maximum and minimum temperature. Female and the elderly aged 75 years old or more were the population groups more susceptible to heat-related mortality. This study provides key information for future heat-related health risk assessments and early warning systems and suggests that public health action plans on high temperatures should be tailored to vulnerable population and climatic zones.

The influence of high temperature on human health has been a worldwide major public concern during the past few decades (*1–4*). During the 2003 heat wave in France, the number of deaths related to high temperature was 3,306, including 3,004 deaths from heat-related circulatory system diseases (*5*). Many studies have found that the mortality rates of ischemic heart disease (IHD) and cerebrovascular disease were associated with high temperature (*4*). The Intergovernmental Panel on Climate Change (IPCC) has predicted that global temperature is likely to increase 1.5 ℃ between the 2030s and 2050s, and global extreme heat events will increase in frequency, duration, and intensity (*6*). Previous studies have predicted that heat-related mortality may increase by 66%, 257%, and 535% by the 2020s, 2050s, and 2080s, respectively (*7*). Along with rising temperature levels under climate change, the effects of high temperature on human health will likely become more serious in the future.

However, as the association between high temperature and mortality may vary by study area, there is no consistent conclusion on the quantitative effect of high-temperature to mortality (*8*). Furthermore, there is currently no agreement on which indicator should be used for high temperature measurements to evaluate health risks (*8–9*). Under the conditions of different climatic zones, it is especially necessary to identify the appropriate indicator to conduct the high temperature related health risk assessment and establish the early warning system in China.

The main purpose of this study is to evaluate the effect of high temperature indicators (daily mean, maximum, and minimum temperature) on mortality and determine the optimal high temperature indicator. Moreover, this study also sought to estimate the mortality effects of high temperature on different population groups and different climatic zones.

We linked three indicators (mean, maximum, and minimum) on daily temperature with daily mortality counts for the summer months (June, July, August, and September) of 2013 to 2018 in 130 Chinese counties. A map of climatic zones was provided by the China Meteorological Administration (*10*) (Supplementary Figure S1 available in http://weekly.chinacdc.cn/). These 130 counties were distributed in different climatic zones with 42 counties in subtropics, 71 counties in warm temperature zone, 15 counties in middle temperate zone, and 2 counties in plateau climatic zone.

Meteorological data were collected from the European Centre for Medium-Range Weather Forecasts. The daily mortality data were obtained from the Disease Surveillance Point System (DSPS) of China CDC. Based on this dataset, the daily counts of non-accidental mortality and circulatory system disease mortality were calculated. The causes of circulatory system mortality, including cerebrovascular disease, ischemic heart disease, myocardial infarction, and stroke, were also analyzed in this study. The International Statistical Classification of Disease Version 10 (ICD-10) of the included diseases was provided in supplementary material (available in http://weekly.chinacdc.cn/). We classified the deaths by age (0–64, 65–74, and ≥75) and sex (female and male). To adjust for the confounding effects of air pollutants, we collected air pollution data, including the concentrations of fine particulate matter ($PM_{2.5}$) and ozone (O_3), and the data sources and cleaning principles of air pollutants had been described in previous study (*11*) .

The associations between high temperature and mortality were investigated in a two-stage analysis. First, we analyzed associations of high temperature and cause-specific mortality in each county by using a generalized liner model (GLM) with quasi-Poisson regression. Second, we pooled estimates nationwide and at climatic-zone scales by a random effects meta-analysis. Considering the lagged effect of high temperature, the moving average exposure of previous 1 day and current day (lag 01) was the largest and used in the core model to assess heat effects (Supplementary Figure S2 available in http://weekly.chinacdc.cn/). We also examined the effects at other lags of high temperature. Furthermore, in order to identify vulnerable populations for heat-related mortality, we performed the subgroup analysis by sex (female and male) and age (0–64, 65–74, and ≥75) groups. We conducted sensitivity analysis to validate the robustness of the core model. The temperature-mortality association was estimated by percent increase in mortality risk and its 95% confidence interval (CI) with 1 ℃ increase of daily high temperature indicators. Detailed information on the statistical model and sensitivity analysis were available in the supplementary materials. All analyses were performed by R statistical software (version 4.0.0; The R Foundation for Statistical Computing).

During the study period, the 24-hour average value of daily mean, maximum, and minimum temperature of all the studying counties was 24 ℃, 29 ℃, and 20 ℃, respectively; the daily mean deaths of non-accidental were 9 ± 6 and circulatory system disease were 4 ± 3 per day (Table 1). For each climatic zone, the descriptive results were shown in supplementary Table S1 (available in http://weekly.chinacdc.cn/).

At the national level, daily mean, maximum temperature, and minimum temperature were all significantly associated with the six causes of mortality. Using Z test, we found that associations between daily mean temperature and the 6 causes of mortality were more significant (Figure 1 and Supplementary Table S2 available in http://weekly.chinacdc.cn/). The 1 ℃ increase of daily mean temperature was estimated to have a 2.71% (95% CI: 2.25%–3.19%) increase of heat effect on IHD mortality, while the heat effect on stroke mortality showed a lower level increase (1.67% with 95% CI: 1.28%–2.07%).

For the climatic zones, the associations between daily mean temperature and the six causes of mortality in all climate zones were consistent with nationwide results, especially in warm temperature zones with 1 ℃ increase in daily mean temperature, the mortality risk for IHD was estimated to increase by 2.95%, (95% CI: 2.31%–3.60%), and the stroke has the lowest mortality risk increase 1.52%, (95% CI: 0.99%–2.05%) (Figure 1).

For subgroup analysis, females and people older than 75 years were more vulnerable to high temperatures. For females, mortality risk of circulatory system disease was estimated to increase by 3.12% (95% CI: 2.67%–3.57%). For the group aged over 75 years old, the mortality risk of circulatory system disease was estimated to increase by 3.00% (95% CI: 2.59%–3.42%) (Table 2).

TABLE 1. Summary statistics of mortality, meteorology, and air pollution of summer months in 2013 to 2018 nationwide

Variable	Mean ± SD	Median (P_{25}, P_{75})
Cause of mortality		
Non-accidental mortality	9 ± 6	7 (4, 12)
Circulatory system disease	4 ± 3	3 (2, 6)
Cerebrovascular disease	2 ± 2	1 (0, 3)
Ischemic heart disease	2 ± 2	1 (0, 3)
Myocardial infarction	1 ± 1	1 (0, 1)
Stroke	1 ± 2	1 (0, 2)
Meteorology		
Temperature (℃)		
Daily mean temperature	24 ± 5	25 (21, 27)
Daily maximum temperature	29 ± 5	29 (26, 32)
Daily minimum temperature	20 ± 5	21 (17, 24)
Relative humidity (%)		
Daily mean relative humidity	72 ± 16	75 (63, 83)
Air pollution		
$PM_{2.5}$ concentration (24-hour average, μg/m^3)	39 ± 28	32 (20, 50)
O_3 concentration (24-hour average, μg/m^3)	73 ± 35	70 (48, 95)

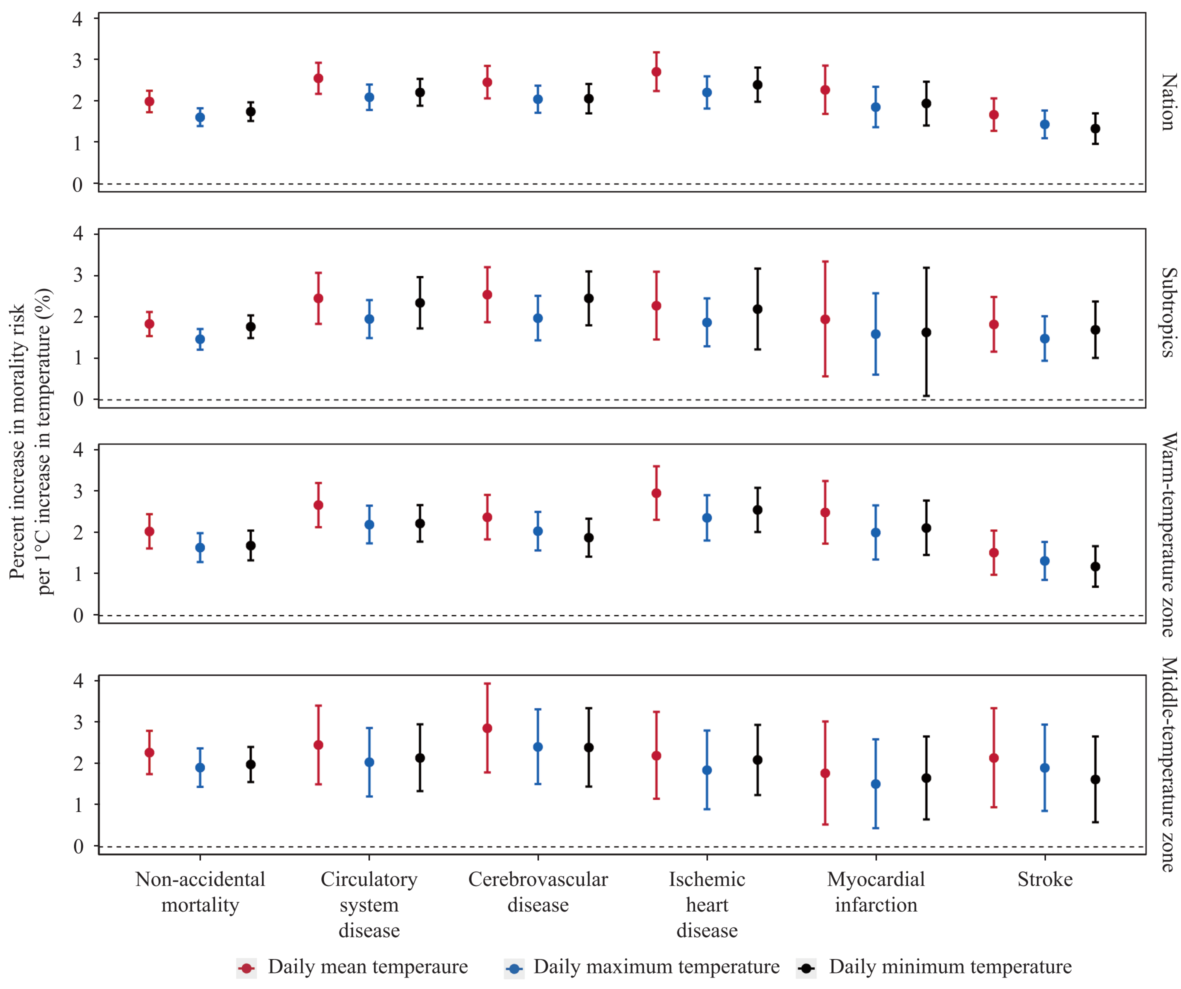

FIGURE 1. Percent increase in mortality risk due to high temperature during summer months of 2013 to 2018 in nation and climate zones.

TABLE 2. Subgroups estimates of high temperature and mortality risk for the summer months in 2013 to 2018 nationwide.

Cause of death	Exposure	Percent increase in mortality risk (%)(95%CI)				
		Female	Male	Age 0–64	Age 65–74	Age ≥75
Non-accidental mortality	Daily mean temperature	2.54 (2.20–2.88)	1.62 (1.39–1.85)	1.06 (0.77–1.34)	1.82 (1.50–2.15)	2.53 (2.21–2.85)
	Daily maximum temperature	2.05 (1.77–2.33)	1.30 (1.10–1.50)	0.86 (0.62–1.10)	1.46 (1.19–1.73)	2.04 (1.78–2.31)
	Daily minimum temperature	2.24 (1.94–2.54)	1.42 (1.22–1.62)	0.90 (0.63–1.17)	1.54 (1.26–1.83)	2.26 (1.97–2.56)
Circulatory system diseases	Daily mean temperature	3.12 (2.67–3.57)	2.08 (1.71–2.46)	1.16 (0.66–1.65)	2.51 (2.06–2.96)	3.00 (2.59, 3.42)
	Daily maximum temperature	2.57 (2.19–2.94)	1.70 (1.38–2.01)	0.94 (0.52–1.37)	2.03 (1.64–2.43)	2.47 (2.13–2.80)
	Daily minimum temperature	2.72 (2.32–3.12)	1.80 (1.46–2.13)	1.00 (0.58–1.42)	2.08 (1.67–2.48)	2.65 (2.26–3.03)

DISCUSSION

In this study, we assessed associations between high temperature indicators and six causes of mortality. We found that high temperature indicators had positive associations with six causes of mortality, and the daily mean temperature was estimated to have higher mortality-effect than daily maximum and minimum temperature. The elderly group (aged 75 years old or more) and female were more vulnerable to heat-related mortality risks.

A study in US showed that a 5 ℃ increase in mean, maximum, and minimum temperature was accompanied by a non-accidental mortality increase of 3.58%, 2.27%, and 3.14%, respectively (*1*). The association between mean temperature and non-accidental mortality was higher than that of the maximum and minimum temperature (*1*), which was consistent with our study. However, a study of nine counties in California found that the daily minimum temperature had a higher association with mortality than daily mean and maximum temperature (*2*). The inconsistency may be due to the differences in geographical characteristics and demographic structure (*8*), as well as the difference in the sensitivity of the population to night temperature changes (*2*). In many countries, daily mean temperature was widely used as the exposure indicator for high temperature monitoring and health risk assessments (*9*). The daily mean temperature represents the average level of exposure and had a good representativeness when applied to estimating health risks due to high temperature. This suggested that we could give priority to daily mean temperature as the exposure measurement indicator when conducting heat-health early warning research.

Previous studies had found that high temperature was associated with deaths due to circulatory system disease (*4*). A worldwide meta-analysis reported that high temperature increased 1 ℃, the mortality risks of circulatory increased by 1.3% (95% CI: 1.1%–1.5%) (*4*), which was consistent with our findings at the national-level and climatic-zone level.

Some previous studies had not found any differences of high-temperature-related mortality risk between genders (*3*). Through subgroup analysis, we observed that females were a high-risk group for high temperature and that the elderly aged over 75 years old were more vulnerable to high temperature. The elderly may be more likely to be in poorer physical health than those in younger groups and may more likely to have basic diseases. In addition, the elderly had a more limited ability to perceive changes in the temperature of the external environment, so their adaptability to high temperatures was reduced (*3*).

This study was subject to at least one limitation. In addition to the single temperature indicator, some studies have constructed composite indicators that included both temperature and humidity variables (*8–9*). Since this model controlled the confounding effects of humidity factors, in order to avoid the variable collinearity, the health impact of the composite indicator had not been estimated in this study and therefore further analysis is needed.

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Preplanned Studies

Antibiotics in Drinking Water and Health Risks — China, 2017

Jia Lyu[1]; Yongyan Chen[1]; Lan Zhang[1,#]

Summary

What is already known about this topic?

Antibiotic contaminations in the environment are understood to pose human health risks including disturbing the microbiome in the human body and producing antibiotic-resistant bacteria, which pose serious public health risks. Antibiotics have been detected in aquatic environments and drinking water worldwide.

What is added by this report?

Contamination levels of antibiotics in raw, finished, and tap water were investigated systematically, to the best of our knowledge, in major Chinese water basins. Multiple antibiotic contaminations in raw water and their incomplete removal during water-treatment processes results in human exposure to antibiotics via drinking water. Human exposure to such antibiotics and its health risks were evaluated in this study.

What are the implications for public health practice?

This study highlights the need to strengthen management of antibiotic exposure from drinking water. A multisectoral action plan at the national level is required to curb the effects of environmental antibiotic pollution.

Antibiotic contamination in the environment has become a global issue attracting substantial attention from the general public. Intake of antibiotics from the environment by food and drinking water may disturb the microbiome, especially the gut microbiota in the human body (*1*). More importantly, antibiotic residues in the environment have the potential to produce antibiotic-resistant bacteria (ARB), which pose serious public health risks (*2*). Antibiotics in aquatic environments and drinking water have been detected in China (*3*), but studies measuring exposure to antibiotics in drinking water and associated health risks are limited. In this study, contamination levels of antibiotics in raw, finished, and tap water were investigated systematically for the first time in major Chinese water basins during the winter and summer of 2017. Human exposure and its health risks were also evaluated. Study results indicated that multiple antibiotics were generally detected in raw water from major Chinese water basins. Concentrations of detected antibiotics were at the nanogram per liter level, which were similar to those in other developed countries (*3*). Based on toxicity data or data on therapeutic approaches in the literature, health risk quotients (HRQs) for water basins from exposure to antibiotics via drinking water ranged from 5.1×10^{-7} to 2.2×10^{-3}, exhibiting spatial and seasonal variations. The HRQs quantified in this study were at an acceptable risk level (HRQs were much lower than 1), but the risks from antibiotic resistance are not well understood and should be researched further. Antibiotic contaminations in environments can induce environmental antibiotic-resistant bacteria (eARB) and horizontal gene transfer (HGT) between eARB and pathogens with antibiotic-resistance (pARB), which has been identified as a major threat to public health. A multisectoral action plan at the national level is required to curb the effects of environmental antibiotic pollution.

Contamination data on antibiotics were extracted from a project investigating emerging contaminants in drinking water in major Chinese river basins. In the project, the levels of contamination of 57 pharmaceuticals in raw, finished, and tap water from representative drinking water treatment plants (DWTPs) located in six large river basins, inland river areas, and key lake and reservoir areas of China during the winter and summer of 2017 were investigated. The water basins and areas investigated in the project included the Yangtze River, Yellow River, Pearl River, Songhua River, Huaihe River, Liaohe River, Northwest Rivers, Taihu Lake, Dianchi Lake, Chaohu Lake, Three Gorges Reservoir, and Danjiangkou Reservoir. Pharmaceuticals were analyzed by an ultra-performance liquid chromatography–tandem mass spectrometer (UPLC–MS/MS), as described in detail in a previous study (*3*). Based on a literature review and preliminary survey results, 21 antibiotics (Table 1) commonly used for human and animals were selected

TABLE 1. Detection rates and concentrations of antibiotics in raw water from major Chinese water basins during the winter and the summer of 2017.

Sub-category	Antibiotic	Usage*	Detection rate in winter(n=54)	Concentration in winter	Detection rate in summer(n=54)	Concentration in summer
			Percentage (%)	Median (P_{25}, P_{75}) (ng/L)	Percentage (%)	Median (P_{25}, P_{75}) (ng/L)
β-lactams (βLs)	Penicillin G	1	0 (0/54)	ND	0 (0/54)	ND
	Cloxacillin	1	1.9 (1/54)	11.0	1.9 (1/54)	1.2
	Cephalecxin	1	38.9 (21/54)	5.1 (2.1, 9.9)	9.3 (5/54)	0.6 (0.5, 0.8)
	Ceftiofur	2	0 (0/54)	ND	0 (0/54)	ND
Macrolides (MLs)	Clarithromycin	1	13.0 (7/54)	1.1 (1.0, 1.5)	68.5 (37/54)	0.3 (0.2, 0.6)
	Roxithromycin	1	77.8 (42/54)	1.0 (0.7,1.8)	83.3 (45/54)	0.8 (0.4, 1.7)
	Tylosin	2	3.7 (2/54)	2.8 (2.7, 2.9)	11.1 (6/54)	10.0 (2.7, 83.0)
Sulfonamides (SAs)	Sulfapyridine	2	33.3 (18/54)	0.8 (0.6, 1.1)	57.4 (31/54)	0.2 (0.1, 0.4)
	Sulfadiazine	1	50.0 (27/54)	2.5 (1.6, 3.2)	88.9 (48/54)	0.7 (0.2, 1.6)
	Sulfamethoxazole	1	88.9 (48/54)	9.1 (6.3, 14.0)	90.7 (49/54)	2.4 (1.5, 4.2)
	Sulfathiazole	1	1.9 (1/54)	98.0	37.0 (20/54)	0.1 (0.1, 0.4)
	Sulfamethazine	1	46.3 (25/54)	2.2 (1.8, 11.0)	53.7 (29/54)	1.0 (0.4, 2.6)
	Sulfaquinoxaline	2	7.4 (4/54)	1.1 (0.8, 1.3)	18.5 (10/54)	0.2 (0.1, 0.4)
	Sulfadoxin	2	0 (0/54)	ND	24.1 (13/54)	0.1 (0.1,0.2)
	Trimethoprim	1	27.8 (15/54)	2.5 (1.9, 2.7)	48.1 (26/54)	0.7 (0.4, 1.0)
Quinolones (QNs)	Norfloxacin	1	0 (0/54)	ND	0 (0/54)	ND
	Ciprofloxacin	1	0 (0/54)	ND	14.8 (8/54)	1.8 (0.8, 2.9)
	Enrofloxacin	2	0 (0/54)	ND	20.4 (11/54)	1.4 (0.9, 7.5)
	Ofloxacin	1	0 (0/54)	ND	5.6 (3/54)	1.3 (1.2, 29.0)
	Clinafloxacin	2	0 (0/54)	ND	0 (0/54)	ND
	Sarafloxacin	2	1.9 (1/54)	1.9	59.3 (32/54)	0.4 (0.2, 0.7)
The number of detected antibiotics			13		17	

* 1=Use for both human and animals; 2=Use for animals only.
Abbreviation: ND=not detected.

for analysis in this study. Removal rates (percent eliminated) of antibiotics in DWTPs were calculated by dividing the removal concentration by the concentration in raw water, and the removal concentration was obtained through subtracting finished water concentration from raw water concentration*.

The HRQ for each water basin was the sum of the HRQs for each antibiotic detected in tap water. An HRQ for each antibiotic was calculated by dividing its average daily potential dose (ADD) by the acceptable daily intake (ADI) or risk-specific dose (RSD)†. The ADI or RSD for each antibiotic was obtained from literature research. When there were more than one ADIs or RSDs for each antibiotic, HRQs were calculated using the most restrictive ADI or RSD (*4*). ADD was the antibiotic exposure dose ingested through drinking and dermal absorption during water consumption, calculated with exposure parameters according to *Chinese Exposure Factor Handbook* and the concentrations of antibiotics in tap water. HRQ above 1 is interpreted as indicating the potential for adverse effects, while HRQ below 1 is interpreted as indicating acceptable risk.

Multiple antibiotics were generally detected in raw water from major Chinese water basins (Table 1), and the detection of antibiotics exhibited seasonal variation. The composition of antibiotic contamination in raw water during the summer was more complex than that during the winter. A total of

* The formula of removal rate of an antibiotic: Removal rate = $(C_{raw}-C_{finished})/C_{raw}\times100\%$, where C_{raw} is the concentration of the antibiotic in raw water (ng/L), $C_{finished}$ is the concentration of the antibiotic in finished water in the same DWTP (ng/L).
† HRQs for antibiotic exposure via drinking water were calculated using the concentration of antibiotics in tap water, exposure parameters, and the ADIs or RSDs from literatures. The formulae are presented in the Supplementary Materials available in http://weekly.chinacdc.cn/.

17 antibiotics were detected in raw water during the summer with median detected concentrations ranging from 0.1 ng/L to 10.0 ng/L. Among which, seven antibiotics had detection rates above 50%, with 2 of these used for animals only, and the others used for both humans and animals. A total of 13 antibiotics were detected in raw water during the winter, and only two antibiotics detected had detection rates above 50%.

The removal efficiency of each antibiotic from DWTPs was shown in Figure 1. A total of 17 antibiotics detected in raw water had average removal rates of above 50%. β-lactams had average removal rates above 98% and were rarely detected in finished and tap water. Although macrolides (MLs), sulfonamides (SAs), and quinolones (QNs) had average removal rates of 51%–97%, incomplete removal of these antibiotics by conventional technologies in drinking-water treatment plants leaves antibiotic residues in finished and tap water. A total of 16 antibiotics were detected in finished water, and similar results were observed in tap water.

HRQs for water basins ranged from 4.79×10^{-6} to 2.15×10^{-3} in the summer and from 5.10×10^{-7} to 1.69×10^{-3} in the winter (Table 2). HRQs of human exposure to antibiotics through drinking water exhibited spatial and seasonal variations. Huaihe River and Chaohu Lake basins had HRQs above 10^{-3} during the summer and the main antibiotic residues in drinking water in these areas were ciprofloxacin and sarafloxacin. Songhua River Basin had HRQs above 10^{-3} during the winter and the main antibiotic residues in drinking water were clarithromycin and roxithromycin. Additionally, among six large Chinese water basins investigated, the contamination risks in the Yangtze River and Yellow River basins were mainly from sarafloxacin and clarithromycin. The contamination risk in the Pearl River Basin was mainly attributable to tylosin.

DISCUSSION

Investigation of antibiotic contaminations in raw, finished, and tap water in major Chinese river basins indicated that the general population had been exposed to multiple antibiotics through drinking water. Concentrations of detected antibiotics were at the nanogram per liter level in raw, finished, and tap water samples. Contamination levels were similar to those in other developed countries (*3*). Among these antibiotics detected in tap water, seven were used for animals only including sarafloxacin and tylosin. Sarafloxacin was one of the main risk components of antibiotic contaminant exposure for people in the Huaihe River, Yellow River, and Yangtze River basins. Tylosin was the main risk component in the Pearl River Basin.

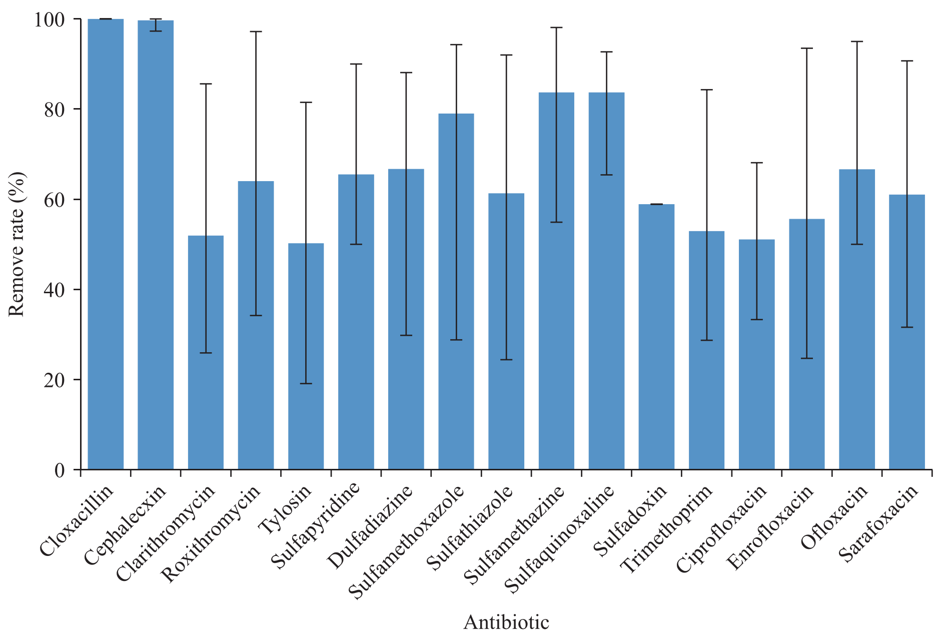

FIGURE 1. Removal efficiency of 17 antibiotics detected in raw water with positive removal rates in the DWTPs. Removal rates (% elimination) were calculated by dividing the removal concentration by the concentration in raw water, and the removal concentration was obtained through subtracting finished water concentration from raw water concentration.

TABLE 2. Health risk quotients of exposures to antibiotics via drinking water for people from major Chinese water basins during the winter and the summer of 2017.

Water Basins	Season	Health risk quotient		
		Minimum	Median	Maximum
Yangtze River (*n*=10)	Winter	$8.62×10^{-6}$	$1.89×10^{-5}$	$2.57×10^{-5}$
	Summer	$3.71×10^{-5}$	$4.19×10^{-5}$	$1.04×10^{-4}$
Yellow River (*n*=10)	Winter	$2.33×10^{-5}$	$4.23×10^{-5}$	$4.40×10^{-5}$
	Summer	$7.17×10^{-5}$	$1.52×10^{-4}$	$9.67×10^{-4}$
Pearl River (*n*=10)	Winter	$5.10×10^{-7}$	$1.33×10^{-6}$	$1.73×10^{-6}$
	Summer	$3.33×10^{-4}$	$5.31×10^{-4}$	$7.67×10^{-4}$
Songhua River (*n*=10)	Winter	$9.63×10^{-5}$	$8.75×10^{-4}$	$1.69×10^{-3}$
	Summer	$3.67×10^{-5}$	$3.08×10^{-4}$	$3.64×10^{-4}$
Huaihe River (*n*=10)	Winter	$7.48×10^{-5}$	$2.83×10^{-4}$	$3.96×10^{-4}$
	Summer	$1.09×10^{-3}$	$1.81×10^{-3}$	$2.15×10^{-3}$
Liaohe River (*n*=10)	Winter	$2.83×10^{-5}$	$3.01×10^{-5}$	$6.35×10^{-5}$
	Summer	$1.16×10^{-4}$	$1.52×10^{-4}$	$1.80×10^{-4}$
Northwest Rivers (*n*=2)	Winter	ND*	ND*	ND*
	Summer	$4.79×10^{-6}$	$4.79×10^{-6}$	$4.79×10^{-6}$
Taihu Lake (*n*=10)	Winter	$1.51×10^{-5}$	$5.73×10^{-5}$	$1.23×10^{-4}$
	Summer	$4.40×10^{-5}$	$7.86×10^{-5}$	$8.22×10^{-5}$
Dianchi Lake (*n*=10)	Winter	$2.03×10^{-5}$	$2.86×10^{-5}$	$3.00×10^{-5}$
	Summer	$3.35×10^{-5}$	$7.16×10^{-5}$	$3.73×10^{-4}$
Chaohu Lake (*n*=10)	Winter	$3.74×10^{-5}$	$6.27×10^{-5}$	$8.02×10^{-5}$
	Summer	$2.95×10^{-4}$	$1.40×10^{-3}$	$1.44×10^{-3}$
Three Gorges Reservoir (*n*=10)	winter	$3.71×10^{-5}$	$9.59×10^{-5}$	$1.78×10^{-4}$
	Summer	$1.67×10^{-5}$	$3.07×10^{-5}$	$4.20×10^{-5}$
Danjiangkou Reservoir (*n*=8)	Winter	$3.92×10^{-5}$	$4.88×10^{-5}$	$4.92×10^{-5}$
	Summer	$2.32×10^{-5}$	$1.62×10^{-4}$	$2.98×10^{-4}$

* No antibiotic was detected in drinking water samples from Northwest Rivers Basin area during the winter.

Antibiotic contaminations in the environment were mainly attributed to the extensive use and emission of antibiotics in livestock farming and aquaculture (*5*–*6*).

The removal rate of each antibiotic in DWTPs investigated in this study showed that conventional purification methods during water treatment cannot remove antibiotics from raw water completely. Similar removal effects of antibiotics were also seen in previous studies (*7*). Incomplete removal during water-treatment processes results in human exposure to antibiotics from contaminated environments via drinking water. Antibiotics can enter an aquatic environment through effluents from sewage treatment plants (STPs) because of the limited removal efficiency from such plants (*8*). In addition to emissions of antibiotics from livestock farming and aquaculture, industrial effluent from drug manufacturing is another major source of antibiotic contamination, contributing high-level contaminations by some antibiotics in surface water and thus in drinking water through water system.

HRQs of antibiotic contaminations in drinking water were less than or equal to 10^{-3} level, which were much lower than 1, indicating an acceptable level of risk from exposure to antibiotics via drinking water. However, these risks from exposure to antibiotics via drinking water varied across water basins and seasons. HRQs above $1×10^{-3}$ were observed in Huaihe River and Chaohu Lake Basins during the summer and in Songhua River Basin during the winter.

There are three limitations in our analysis. First, contamination data used in this study were collected from representative DWTPs in major river basins, which did not cover all river basins and regions in

China. Hence, study results only represented the population in water-supply areas of these DWTPs. Second, ADIs used in this study to calculate HRQs of antibiotics were derived from the data based on the toxicity of experimental animal or microbiological effects in the literature. There is a lack of study on the adverse effects induced by antibiotics exposure from environments among all age groups and sensitive groups such as children and pregnant women. Finally, antibiotic contaminations in environments can induce eARB (*9*). Previous studies have highlighted the potential for environmental HGT between eARB and pARB, which has been identified as a major threat to public health (*10*). However, the risk of antibiotic resistance is not quantified in this study because of the limited research data. A study on the health risks of environmental antibiotic pollution is crucially needed to provide data to support for risk management in China.

From both human and environmental health perspectives, it is a significant task to establish a systematic project for curbing the effects of environmental antibiotic pollution. A multisectoral action plan at the national level is required: (a) to strengthen the control of antibiotic use in livestock farming and aquaculture, taking steps to reduce usage and emissions of antibiotics at national levels; (b) to improve a standard wastewater discharge system for antibiotic industries and to establish an emission standard for antibiotics to strengthen discharge management; (c) to conduct further research on removal mechanisms of antibiotics by water-treatment technology, exploring the applicability of upgrading treatment processes in STPs and DWTPs; (d) to carry out systematic research on environmental antibiotic pollution and antibiotic resistance; and (e) to conduct research on and investigate antibiotic contamination exposure and health risk assessment among all age groups and sensitive groups.

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Recollection

Clean Air Actions and Air Quality Improvements — Beijing-Tianjin-Hebei and Surrounding Areas, China, 2013−2019

Shijie Liu[1]; Yangxi Chu[1]; Jingnan Hu[1,#]

Severe air pollution has brought great challenges to the economic and social development of China, and in response, the Action Plan for the Prevention and Control of Air Pollution was issued and a mix of air pollution prevention and control measures has been released since 2013 such as ultra-low emission retrofitting in thermal power industry, dealing with the small coal-fired boilers, household clean heating programs, and severe pollution mitigation . In addition, the National Research Program for Key Issues in Air Pollution Control was conducted for Beijing-Tianjin-Hebei (BTH) and surrounding areas, which supported significant air quality improvements. This paper reviews the main air pollution prevention and control measures released for BTH and surrounding areas. Moreover, the improvements in air quality and the evolution of air pollution characteristics in this region are also evaluated.

Actions to Prevent and Control Air Pollution

Rapid economic growth based on intensive energy consumption over the past decades has led to serious air pollution across China. At the beginning of 2013, Beijing Municipality, Tianjin Municipality, Hebei Province, and some other regions in China suffered from a persistent haze. Large parts of North and East China were ravaged by haze for more than 20 days, which had a severe effect on human health and economic and social development.

In the same year, the Action Plan for the Prevention and Control of Air Pollution was issued by the State Council, which declared the commencement of intensive air pollution prevention and control. A series of laws, regulations and measures were issued or amended, such as the Environmental Protection Law of the People's Republic of China, the Law of the People's Republic of China on the Prevention and Control of Atmospheric Pollution, etc. The National Ambient Air Quality Standard (GB 3095-2012) was also revised identifing the major air pollutants ($PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and O_3) (*1*). Two additional technical regulations and guidance (HJ 633-2012 and HJ 663-2013) were released to standardize the assessment and management of air quality and provide health guidance to the general public (*2–3*). The so-called "ground-aerial-space" integrated monitoring system was established to comprehensively monitor the atmospheric environment (*4*), including the satellite remote sensing system, the national air quality, regional particulate, and photochemical composition monitoring networks, etc. A mix of emission mitigation measures had been established and implemented since 2013. A seriers of emission standards for key industries have been released or revised. Upgrading and renovation programs for pollution control facilities in key industries have been pushed forward. An ultra-low emission and energy-saving retrofitting of coal-powered venues and pilot programs for clean household heating in northern China were launched. Small coal-fired boilers (below 10 t/h) in urban areas were eliminated. For mobile sources, the standards for gasoline and diesel fuel quality were strengthened twice in five years, and high-emission vehicles, especially heavy-duty diesel trucks, were under strict supervision.

Due to serious air pollution, BTH and surrounding areas were selected as the key region for air pollution prevention and control. In addition to the policies and measures mentioned above, the National Joint Research Center for Tackling Key Problems in Air Pollution Control was established in 2017. More than 2,000 scientists and researchers were organized to investigate the causes of heavy air pollution and provide solutions for 28 cities in BTH and surrounding area (known as "2+26" cities, including Beijing, Tianjin, Shijiazhuang, Tangshan, Baoding, Langfang, Cangzhou, Hengshui, Handan, Xingtai, Taiyuan, Yangquan, Changzhi, Jincheng, Jinan, Zibo, Liaocheng, Dezhou, Binzhou, Jining, Heze, Zhengzhou, Xinxiang, Hebi, Anyang, Jiaozuo, Puyang, and Kaifeng). A total of 28 expert teams were dispatched to "2+26" cities, and investigation on the

"Customized strategy for each city" campaign was conducted. A comprehensive mechanism for responding to heavy pollution was also established for BTH and surrounding areas, including air quality forecast, expert joint-meetings, heavy pollution warnings, instant emission reduction, and supervised enforcement, which significantly improved the capabilities of local governments to tackle the heavy pollution problem.

Trends in Air Quality Improvement

The comprehensive air pollution prevention and control measures have led to sustained improvements in air quality in BTH and surrounding areas (*5–7*). Figure 1 shows the trends of the annual evaluation concentrations for major pollutants, namely the annual average concentrations of $PM_{2.5}$, PM_{10}, SO_2, NO_2, the annual 95th percentile of the daily average concentrations of CO, and the annual 90th percentile of the maximum daily 8-h average (MDA8) concentrations of O_3 (*3*). As some of the cities in Shanxi Province and Henan Province were not included in national air quality monitoring network in 2013 and 2014, the concentrations of CO, O_3 and $PM_{2.5}$ were not measured in those cities. The cities with missing data were listed in Supplementary Table S1. The concentrations of major pollutants, except for O_3, showed continuous decreases from 2013 to 2019. Compared to 2013, the mean annual evaluation concentrations of $PM_{2.5}$, PM_{10}, SO_2, NO_2, and CO in "2+26" cities in 2019 decreased by 50%, 41%, 79%, 20%, and 53%, respectively. SO_2 and CO, with the greatest concentration decrease among basic pollutions in "2+26", showed the remarkable effects of coal consumption control. For Beijing, most notably, the concentration of $PM_{2.5}$ in Beijing dropped from 89.5 μg/m^3 in 2013 to 42 μg/m^3 in 2019.

The Air Quality Index (AQI) also showed similar annual improvements in BTH and surrounding areas as illustrated in Figure 2. From 2013 to 2019, the days of heavy and serious pollution (Grade V and VI according to HJ 633-2012 (2), respectively per year had decreased from 88 days to 20 days on city average. In particular, the days of serious pollution dropped from 31 days in 2013 to 2 days in 2019, reflecting the great progress in emission mitigation efforts in the region. Additionally, days with good and excellent air quality for each year have significantly increased and nearly doubled from 2013 to 2019.

$PM_{2.5}$, PM_{10}, and O_3 are the main pollutants in

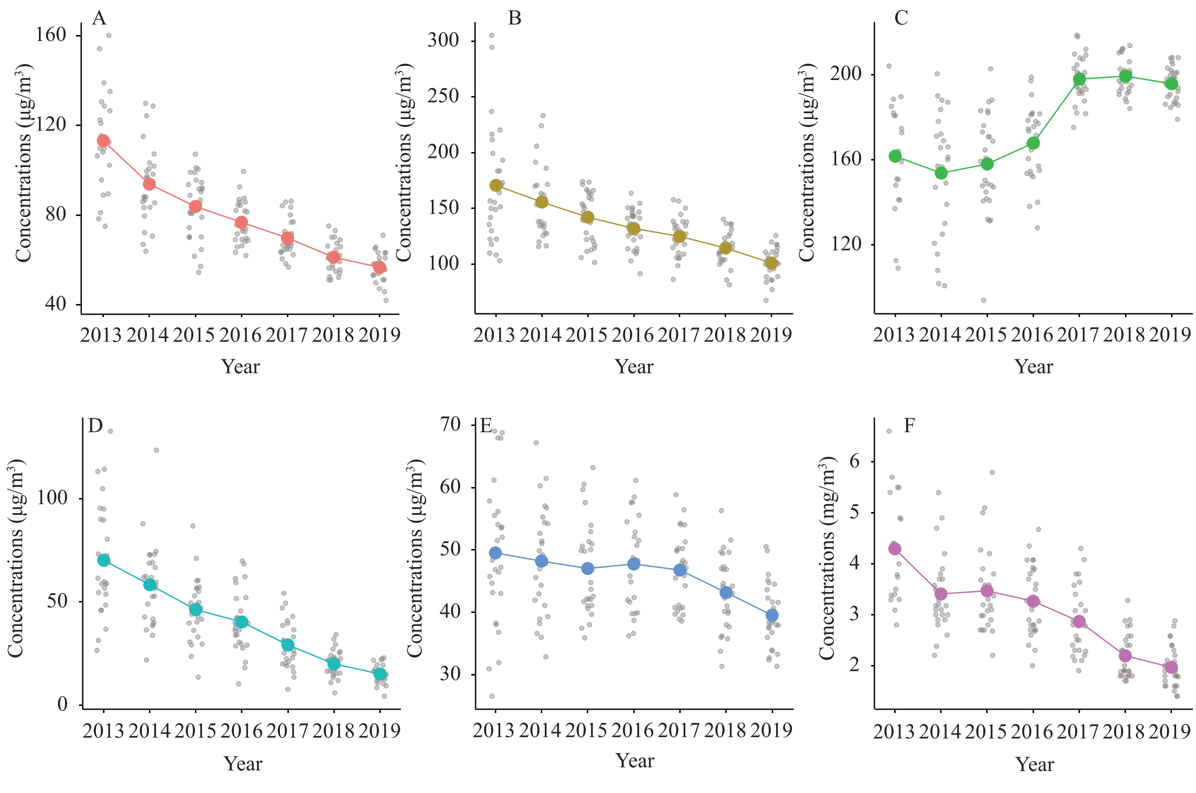

FIGURE 1. Trends of annual evaluations of concentrations of (A) $PM_{2.5}$, (B) PM_{10}, (C) O_3, (D) SO_2, (E) NO_2, and (F) CO in "2+26" cities from 2013 to 2019.

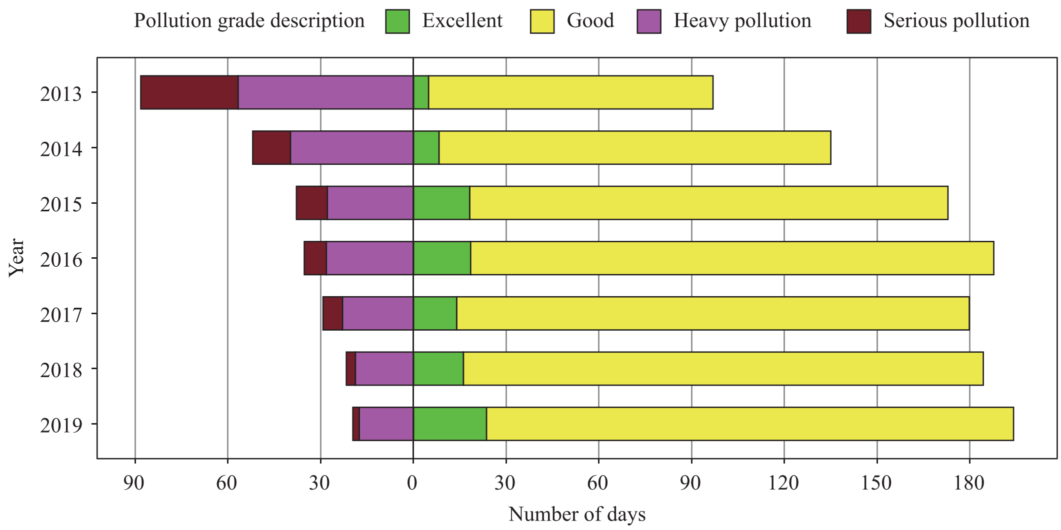

FIGURE 2. Average number of days per year with air quality levels of excellent, good, heavy pollution, and serious pollution in "2+26" cities from 2013 to 2019. The number of days with air quality levels of mild and moderate pollution were not included in the statistics.

polluted days in "2+26" cities. Between 2013 and 2019, the number of polluted days with $PM_{2.5}$ as the chief pollutant decreased continuously (from 189 to 73 days), while the days with O_3 as the chief pollutant increased rapidly from 20 to 80 days. Moreover, O_3 has replaced $PM_{2.5}$ as the most important pollutant in days of chief pollutant from 2018 (Figure 3).

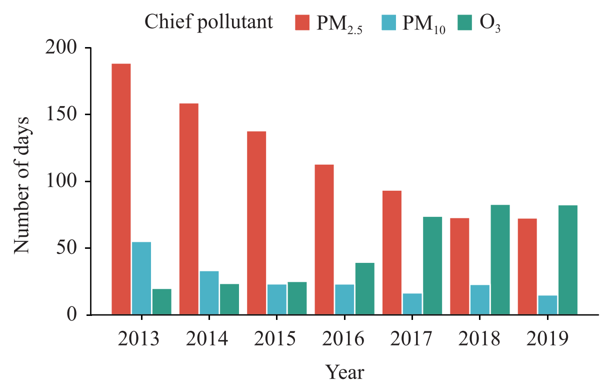

FIGURE 3. The number of air polluted days with different chief pollutants from 2013 to 2019.

Evolution of Air Pollution Characteristics

As the $PM_{2.5}$ concentrations in BTH and surrounding areas decrease, the $PM_{2.5}$ chemical compositions have undergone significant changes over the years. Table 1 shows the changes of major $PM_{2.5}$ components concentrations in the studied region over the years. The most notable change was the reduction in sulfate and organic matter, which decreased by 42% and 31%, respectively, from the 2016–2017 autumn-winter seasons (October 2016–March 2017) to 2018–2019 autumn-winter seasons (October 2018–March 2019). This is due to effective control of coal consumption including household coal replacements, the elimination of small coal-fueled boilers, etc. in BTH and surrounding areas. Emission inventory statistics revealed that households consumed less than 5% of coal in the "2+26" cities but accounted for >20% SO_2 and >30% organic matter emissions. From 2016 to 2018, coal in 8.6 million households were substituted by natural gas and electricity, which reduced emissions of SO_2 and organic matter significantly. On the contrary, the reduction in nitrate concentration (11%) was relatively lower than those of sulfate and organic matter. As a result, the nitrate-to-sulfate mass ratio increased from 1.2 in 2016–2017 autumn-winter seasons to 1.8 in 2018–2019 autumn-winter seasons. Given the decrease in $PM_{2.5}$ concentrations, the mass fraction of nitrate increased to 19.6% in 2018–2019 autumn-winter seasons, and the extent of mass fraction increase (3.4%) is larger than any other species. This highlights the importance of tackling nitrate pollution in the studied region. Ammonium is the major cation in $PM_{2.5}$ to balance the anions charge-wise, and its concentration decreased by 22.4%, which is between the decrease in sulfate and nitrate. Considering the fact that the concentration of ammonia is in excess over those of acidic species (e.g. sulfuric acid and nitric acid gases) in the atmosphere in the studied region, reduction of ammonia emission alone might not lead to substantial air quality improvement without drastic changes (*7*).

TABLE 1. Concentrations and mass fractions of $PM_{2.5}$ components in BTH and surrounding areas in the 2016–2017 and 2018–2019 autumn-winter seasons.

$PM_{2.5}$ component	2016–2017 autumn-winter		2018–2019 autumn-winter	
	Concentration (μg/m^3)	Mass fraction (%)	Concentration (μg/m^3)	Mass fraction (%)
Elemental carbon	4.0	2.6	4.6	4.1
Organic matter	46.3	30.4	31.8	28.3
Nitrate	24.7	16.2	22.1	19.6
Sulfate	21.2	13.9	12.4	11.0
Ammonium	14.5	9.5	11.2	10.0
Chloride	5.9	3.9	4.0	3.6
Crustal matter	4.7	3.1	7.2	6.4
Trace elements	4.2	2.8	2.6	2.3
Others	26.9	17.6	16.5	14.6

Furthermore, studies revealed that the MDA8 surface O_3 concentration during April–September increased in BTH and surrounding areas (*8*). During the seasonal transition period, $PM_{2.5}$ and O_3 complex pollution can occur in the studied region. For instance, on April 30 and May 1, 2020, both daily $PM_{2.5}$ and MDA8 ozone levels exceeded the National Ambient Air Quality Standards (*1–2*) in cities such as Beijing and Tangshan (Supplementary Figure S1 available in http://weekly.chinacdc.cn/). The results show that secondary pollutants such as particulate nitrate, secondary organics, and O_3 had become prominent in recent years, implying the importance and urgency of controlling their precursors such as nitrogen oxides and volatile organic compounds.

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Outbreak Reports

Gastroenteritis Outbreak Caused by *Campylobacter jejuni* — Beijing, China, August, 2019

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Summary

What is already known about this topic?

Campylobacter genus bacteria are recognized as some of the leading causes of the bacterial diarrheal illness in both developing and developed countries. Recent pilot surveillance study revealed *Campylobacter* is the most common pathogen in the diarrheal cases using the enhanced filtration methods in Beijing. One outbreak caused by multi-drug resistant *Campylobacter coli* (*C. coli*) was identified in 2018.

What is added by this report?

This is the first identified gastroenteritis outbreak caused by local *Campylobacter jejuni* (*C. jejuni*) infection in Beijing. A total of 14 patients were identified from August 23 to 26, 2019. The epidemiological investigation indicated that all of the patients worked at the same factory and the diarrhea happened after the same meal supplied from one company which service the meal delivery. Fourteen *C. jejuni* isolates were obtained from 12 patients and 2 food workers. Whole Genome Sequencing (WGS) analysis indicated this outbreak was caused by one highly clonal *C. jejuni*.

What are the implications for public health practice?

Campylobacter is the major foodborne pathogen in the world. Surveillance and risk assessment for *Campylobacter* infection particularly for Guillain-Barré Syndrome (GBS) associated *C. jejuni* infection in China should closely monitored.

BACKGROUND

In the afternoon of August 26, 2019, the Shunyi District CDC of Beijing Municipality was informed that several acute gastroenteritis patients visited the Shunyi District Hospital and the Shunyi Chinese Medicine Hospital. The epidemiological investigation was performed by Shunyi CDC. The time of onset of the first patient and the final patient were the afternoon of August 24, 2019 (26 hours after the meal) and the morning of August 26, 2019 (66 hours after the shared meal), respectively.

Totally, 14 patients were identified. These 14 patients showed similar clinical symptoms, including high fever (over 38.5 ℃), diarrhea, abdominal pain, and headache. All of them had watery stool and diarrhea 2 to 10 times per day. According to the epidemic investigation, these 14 patients were workers at the same factory and the diarrhea happened after lunch supplied from a meal delivery company on August 23. Overall, 14 stool samples (7 fresh stool samples and 7 anal swabs) were collected from 14 individual patients, 7 anal swabs were collected from 7 individual workers of the food supplying company, and 18 suspected food samples and 6 samples from the environment of the kitchen were collected. All samples were screened for 10 major enteric pathogens based on the real-time polymerase chain reaction (PCR) methods published previously (*1*).

INVESTIGATION AND RESULTS

Real-time PCR was performed for 10 specific pathogens: *Vibrio cholerae*, *Vibrio parahaemolyticus*, *C. jejuni*, *C. coli*, *Salmonella*, *Shigella*, diarrheagenic *E. coli*, norovirus, rotavirus, and enteric adenovirus. Fourteen samples were positive for *C. jejuni* including 12 samples from 12 patients and 2 samples from 2 food workers, and the other samples were all negative. All samples were negative for other enteric pathogens except for *C. jejuni*.

Campylobacter isolation was performed for all collected samples and species identification was carried out for suspected colonies as previously described (*2*). In total, 80 colonies were obtained from 14 positive samples including 12 patients' samples and 2 food workers' samples. No isolate was obtained from other samples. For each positive sample, one isolate was selected for further investigation, and 14 isolates were picked in total.

Pulsed-field gel electrophoresis (PFGE) was performed for all 14 selected isolates (one isolate was selected from each positive patient and positive food worker) using *Sma* I as described previously (*3*). All of the selected isolates showed an identical PFGE profile (Figure 1).

Antibiotic susceptibility testing for 11 antimicrobials was performed with the agar dilution method as previous study (*1*). All of the selected isolates had the same susceptibility pattern: they were all resistant to nalidixic acid and ciprofloxacin and sensitive to other 9 drugs.

The draft genomes of 13 outbreak associated isolates (11 isolates from 11 individual patients and 2 isolates from 2 food workers) were sequenced. One isolate SF-18Cj008), which was isolated from a local sporadic diarrheal patient, and another isolate ARI1249, isolated from the diarrheal patients in UK, were selected to be enrolled in this study. The WGS of SF-18Cj008 was obtained from our previous study and the WGS of ARI1249 was obtained from the PubMLST database (https://pubmlst.org/bigsdb?db=pubmlst_campylobacter_isolates&page=seqbin&isolate_id=43065). The Whole Genome Single Nucleotide Polymorphisms (wgSNP) was called among the 15 genomes and the Multilocus Sequence Typing (MLST) of the 15 isolates was determined using the online tool on PubMLST website (http://pubmlst.org/campylobacter). The *ad hoc* whole-genome multilocus sequence typing (wgMLST) analysis was performed for 15 *C. jejuni* isolates with fast-GeP (https://github.com/jizhang-nz/fast-GeP) using the annotated ARI1249 genome as reference (*1*). The Sequence Types (STs) of the entire selected 15 isolates all belong to ST-6959. The difference matrix of the allele loci among 15 *C. jejuni* WGSs were presented in Figure 2 and the neighbor-net phylogeny of 15 isolates using SplitsTree4 based on the shared loci was constructed and presented in Figure 3. The outbreak associated 13 isolates were genetically related (≤9 alleles difference). No mutation in 23S rRNA was found and the *gyrA* C257T mutant was identified in the entire 13 outbreak associated isolates which was consisting with the phenotype of drug resistance of the outbreak associated isolate.

DISCUSSION

In this study, 12 *C. jejuni* isolates were obtained from 12 patients. The real-time PCR screening results were consistent with the bacteria culture results. Unfortunately, no isolates were cultured from the two patients of whom the samples were anal swabs and PCR results were also negative. This might be due to an inadequate number of pathogens in the samples. Bacteria culture is time intensive, rapid multi-targets screening using molecular methods is helpful for pathogen identification during the outbreak investigation. This study confirmed that direct real-

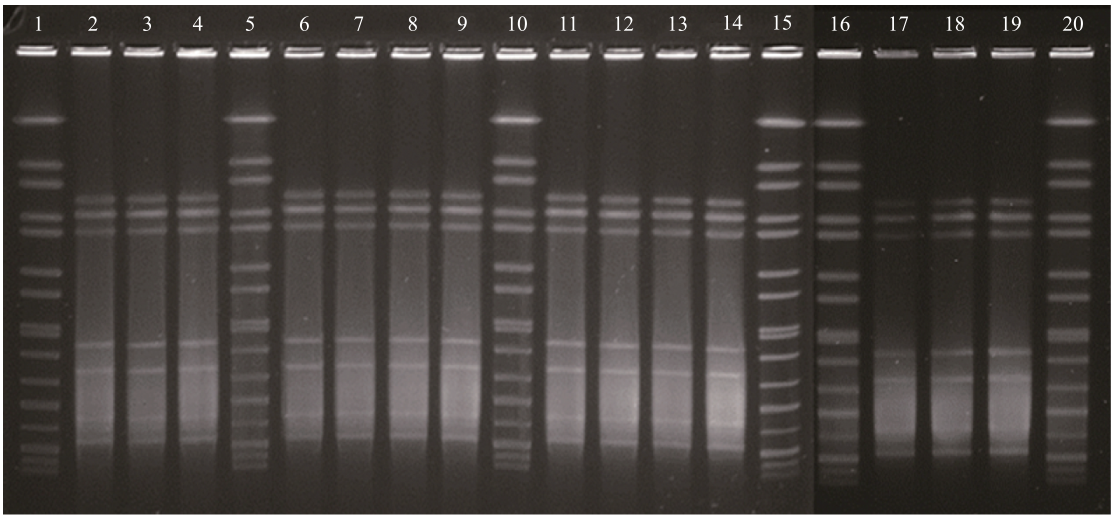

FIGURE 1. Pulsed-field gel electrophoresis (PFGE) analysis with *Sma* I for 14 *Campylobacter jejuni* isolates from 12 patients and 2 food workers. Lanes 1, 5, 10, 15, 16 and 20: refercnce standard H9812; Lanes 2, 3, 4, 6, 7, 8, 9, 11, 12, 13, 14, and 17: *C. jejuni* isolates from 12 patients (isolate 1, 2, 3, 4, 5, 6, 8, 9, 11, 12, 13, and 14); Lanes 18 and 19: *C. jejuni* isolates from 2 food workers (36 and 37). All of the 14 isolates had the same PFGE pattern.

	1.fna	11.fna	12.fna	13.fna	2.fna	3.fna	4.fna	5.fna	6.fna	8.fna	9.fna	36.fna	37.fna	SF-18Cj008.fna	ARI1249.fna
1.fna	0														
11.fna	3	0													
12.fna	4	1	0												
13.fna	2	3	4	0											
2.fna	6	3	4	6	0										
3.fna	5	4	3	5	6	0									
4.fna	6	4	5	4	7	8	0								
5.fna	6	4	5	4	7	8	4	0							
6.fna	6	3	4	6	4	6	7	7	0						
8.fna	5	3	4	6	6	7	7	5	6	0					
9.fna	8	5	6	8	8	8	9	5	8	6	0				
36.fna	8	5	6	8	8	8	9	5	8	6	0	0			
37.fna	8	5	2	4	3	3	5	5	3	4	6	3	0		
SF-18Cj008.fna	59	57	58	58	57	58	56	57	59	57	59	57	56	0	
ARI1249.fna	130	133	134	130	134	135	130	131	136	134	135	135	134	127	0

FIGURE 2. Difference matrix for alleles of the wgMLST with Fast-GeP analysis. Allele sequences were searched with BLAST+ (identity threshold ≥80). ARI1249 was used as the reference genome. The number of the loci in the reference genome was 1,667. The number of loci shared by the 15 genomic sequences was 1,649 and the number of the shared-loci that was found identical was 1,484. The shared-loci that was used to construct distance difference matrix was 1,644 (160 were polymorphic). Five shared-loci were excluded because of hypothetical gene duplication and 18 loci were excluded because of incomplete information (missing, truncation or containing nucleotide ambiguity). The horizontal and vertical columns of the matrix represent the isolates name. The number in the matrix indicated the different alleles numbers between the isolates in the horizontal and vertical. columns. The horizontal and vertical columns of the matrix represent the isolates name. The number in the matrix indicated the different alleles numbers between the isolates in the horizontal and vertical columns.

time PCR examination for *Campylobacter* from the stool sample of diarrheal patients is useful (*4*).

PFGE is useful for bacteria outbreak investigation (*5*). Recently, the WGS for bacterial pathogens become cheaper and faster. The bioinformatics' analysis based on the WGS is crucial for both the epidemic and outbreak investigation (*6*). The ST of the isolate could be reached in real-time with the WGS using the in silico MLST analysis. WgSNP and wgMLST analysis were useful to recognize the genetic distance between the isolates. In this study, the fast-GeP analysis was an effective tool to identify the very closely related *Campylobacter* isolates; it is useful for *Campylobacter* outbreak investigation based on the WGS (*7*). Both the genotyping and antibiotics analysis results indicated this gastroenteritis outbreak was caused by one highly clonal *C. jejuni*.

The isolates from two food workers were of the same genotype as the patients. According to their health history, they did not have significant clinical symptoms. We do not know if they ate the same food as the patients on August 23 or if the bacteria they carried contaminated the foods they cooked. There was a report that *C. jejuni* could colonize in the human gut for extended periods of time (*8*), and there is chance the food workers may contaminate the food during preparation. Unfortunately, we did not get any more samples from any of the food workers for continued bacteria culture.

Recently, the accelerated pace of life may dramatically increase use of meal delivery in major cities and may subsequently increase the risk of infection or food poisoning caused by foodborne pathogens. With an enhanced filtration method, *Campylobacter* was recognized as the leading causes of bacterial diarrhea in Beijing (*1*,*2*,*4*). One gastroenteritis outbreak caused by *C. coli* infection was identified last year (*1*), and this was the first identified

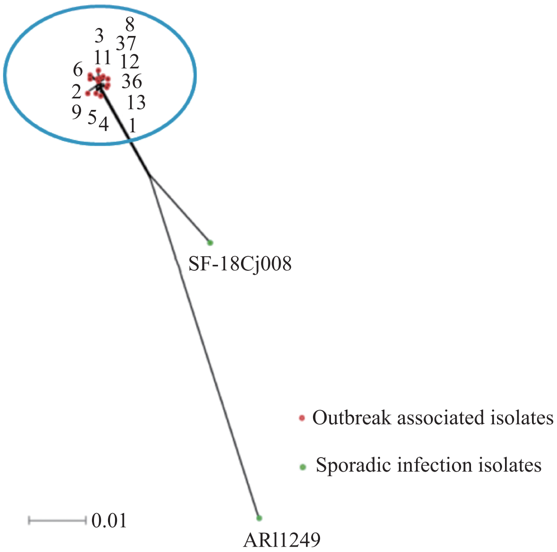

FIGURE 3. Neighbor-net phylogeny for alleles of cgMLST loci of 15 *C. jejuni* isolates. All of these 15 isolates were belonging to ST-6959. Red points representing the outbreak associated 13 isolates (isolate 1, 2, 3, 4, 5, 6, 8, 9, 11, 12, 13, 36 and 37) and green points representing two sporadic isolates (SF-18Cj008 and ARI1249), one from local diarrheal patient, and another one from a diarrheal patient in UK. The blue circle representing the outbreak cluster.

gastroenteritis outbreak caused by local *C. jejuni* infection in Beijing.

In addition to enteritis, *C. jejuni* infection can also cause GBS. Recently, 36 GBS patients outbreak caused by preceding *C. jejuni* infection were reported (*9*–*10*). According to our previous study, the serotype (HS:41) of this GBS outbreak associated *C. jejuni* strain was also identified from the sporadic diarrheal patient in Beijing. Pathogen surveillance and the risk assessment for *Campylobacter* infection particularly for GBS associated *C. jejuni* infection should be closely monitored.

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Perspectives

Urgent Need to Ratify National Legislation Banning Smoking in Public Places

Yuan Jiang[1,#]

China produces 40% of the world's cigarettes (*1*) and has more than 300 million smokers (*2*). How to control smoking is still a serious problem. Smoking damages people's health and increases the burden of medical expenses of the whole society. In order to promote the construction of a healthy China and improve people's health level, the Chinese government issued the outline of "Healthy China 2030" in 2016, which proposed specific measures and objectives for smoking control work: comprehensively promote the implementation of tobacco control, increase the intensity of tobacco control, and use tax and price, law and other means to improve the effectiveness of smoking control. Carry out in-depth tobacco control publicity and education. Actively promote the construction of smoke-free environment and strengthen the supervision and law enforcement of smoke control in public places. We will promote the work of banning smoking in public places and gradually implement a comprehensive ban on smoking in indoor public places. Government leaders should take the lead in banning smoking in public places and build government building into smoke-free one. Strengthen smoking cessation services. By 2030, the adult smoking rate will be reduced to 20% (*3*).

In 2018, China's adult smoking rate was 26.6%, which will be reduced by 6.6 percentage points in 11 years, that is to say, an average annual decrease of 0.6 percentage points. Levy used the SimSmoke model to simulate the implementation of various control policies and their effects (*4*). The results showed that to achieve the Healthy 2030, Framework Convention on Tobacco Control (FCTC) should be fully implemented.

FCTC is the first public health treaty of WHO, it focus on control the prevalence of tobacco from both sides of supply and demand and protect the health of people. Article 8 requires that within five years after ratify, the parties shall adopt legislation to achieve a comprehensive ban on smoking in public places. Although FCTC has been ratified for 14 years in China, there are still no national laws and regulations on tobacco control. By January 2020, more than 20 cities have implemented local regulations on tobacco control, but only 13 cities including Beijing, Shanghai, Shenzhen etc covering about 10% of the national population which meet the requirements of FCTC.

Implement is another important issue after law ratify. Even in Beijing, compared with other cities that have legislation to carry out International Tobacco Control Policy Evaluation projects, the exposure rate of second-hand smoke in indoor workplaces and public places has not decreased to the level of other cities (*5*), but these cities are still very different from the national level (Table 1). After the local laws came into force in Beijing, the adult smoking rate dropped by 1.1 percentage points, and then continued to drop by 2 percentage points in the next two years. It decreased by

TABLE 1. Smoking rate (%) and secondary smoking exposure rate (%) in China, Beijing and Shanghai.

Rate	China			Beijing			Shanghai		
	2010	2015	2018	2014	2016	2019	2016	2017	2018
Adult Smoking Rate	28.1	27.7	26.6	23.4	22.3	20.3	21.0	20.2	19.9
Exposure rate of SHS									
Indoor Working Place	63.3	54.3	50.9	35.7	27.0	27.0	26.1	17.3	17.3
Government Building	54.8	38.1	31.1	19.7	10.8	8.6	11.0	5.3	10.0
Health Facility	37.9	26.9	24.4	12.8	6.2	6.6	11.0	7.5	4.2
Primary and Middle School	36.9	17.2	23.4	32.8	19.1	4.8	17.3	10.9	7.7
Restaurant	88.5	76.3	73.3	65.7	32.5	42.5	44.3	22.8	28.1

3.1 percentage points in four years (*6–7*). The adult smoking rate in Shanghai decreased by 19.9 in 2018 from 21.0% in 2016 before the amendment of the law (*8–10*) while that in China, including these legislative cities, dropped from 28.1% in 2010 to 26.6%, down 1.5 percentage points in eight years. The average annual decline is less than 0.2 percentage points (*2*).

14 years after ratify FCTC, only 13 cities have issued comprehensive ban smoking laws. If we follow this schedule, it will be difficult to achieve the goal of "total ban on smoking in indoor public places" and "reduction of smoking rate to 20% for people over 15 years old" by 2030. At present, there are 334 cities with legislative right in China. Compared with these 13 cities, the basis of tobacco control in cities without legislation is weak, and tobacco control laws and regulations are often not the priority areas of local legislation. Even if we start the legislative process, we will encounter the interests of all parties and difficulties in resistance. Based on the analysis of the law revision process in Hangzhou in 2018, under the various departments conflicts of interests, the new draft law (first review draft) has only two improvements compared with that before the revision, one is the expansion of the legal coverage, including rural areas, the second is the change from a single law enforcement mode to a multi-department law enforcement mode, and the most core "comprehensive smoke-free" was not included (*11*). If these 300 cities legislate one by one, the efficiency is low, the progress is slow, and the cost is huge. It is difficult to achieve the goal by 2030.

In order to achieve the goal of "Healthy China 2030" and protect more people from second-hand smoke, China should pass national smoking ban legislation in public places as soon as possible, and at the same time speed up the implementation of the law in an all-round way to ensure the realization of the goal of healthy China 2030.

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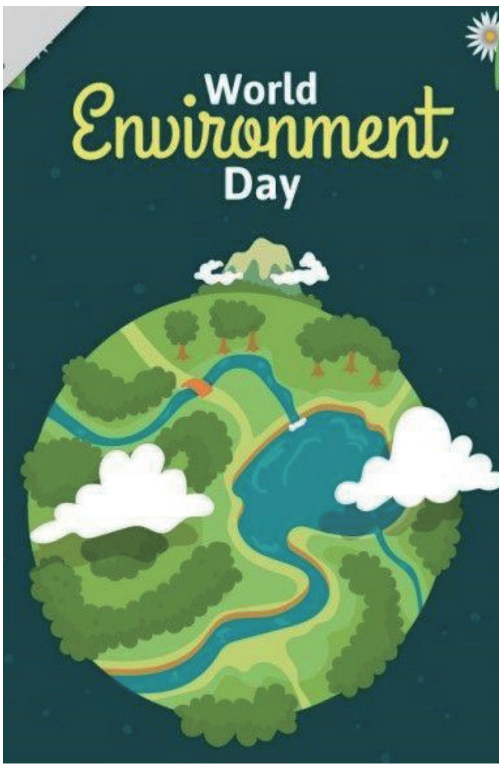

WORLD ENVIRONMENT DAY ISSUE

Foreword

Preplanned Studies

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CLARIVATE ANALYTICS EMERGING SOURCES CITATION INDEX INDEXED

This week's issue was organized by Guest Editor Haidong Kan.

Foreword

Climate Change, Weather Conditions, and Population Health

There is near unanimous consensus that the global climate is warming and most of the warming is attributable to human activities. The world economic expansion has largely been driven by fossil fuels, leading to increasing emissions of greenhouse gases (GHGs). The world's average temperature has risen at a rate of 0.07 ℃ per decade since 1880 and nearly triple that rate since the 1990s. In addition to heat waves and cold spell, climate change may lead to a wide range of extreme weather conditions, including drought, floods, typhoons, windstorms, and landslides. Exposure to non-optimal temperatures and extreme weather conditions has been associated with a range of adverse health outcomes, including excess mortality and morbidity from various causes, and changes in the ecology of infectious diseases. For example, in China, 14.3% of non-accidental mortality during 2013–2015 may be related to non-optimal temperatures, with 11.6% and 2.7% explainable by exposure to cold and heat, respectively (*1*). The recent global burden of diseases study (GBD 2019) shows that non-optimal temperatures are among the ten leading causes of death worldwide (*2*). A projection study showed that under high-emission scenarios, the negative health impacts of climate change would disproportionately affect warmer and poorer regions of the world (*3*). Climate change can also affect climate-sensitive infectious diseases carried by animal hosts or vectors, including malaria, dengue fever, schistosomiasis, Japanese encephalitis, and *Angiostrongylus cantonensis*.

In this special issue, we invited colleagues from Sun Yat-Sen University, China CDC, Peking University, and Shanghai Meteorology Bureau to report their latest findings on climate change, weather conditions, and population health. Qi and coworkers examined the associations between ambient temperature and years of life lost from stroke in 93 Chinese cities (*4*). Zhang et al. assessed the regional distribution of health vulnerability to extreme heat in China (*5*). Using a modelling approach, Huang et al. estimated the $PM_{2.5}$-related health impacts from climate change and air pollution emission control in China (*6*). Finally, Ye et al. evaluated the impact of a health forecasting service on outpatient visits for chronic obstructive pulmonary disease patients in Shanghai (*7*).

In short, the findings from this special issue further confirmed that climate change and extreme weather conditions have posed substantial health risks for population health in China as well as other parts of the world. Future research will need to improve characterization of climate-health relationships, to develop effective and adaptive strategies to help reduce the health risks of climate change, and to promote healthy lifestyles in line with the reduction of greenhouse gas emissions. Finally, GHG emissions need to be controlled. China aims to reach carbon emissions peak before 2030 and achieve carbon neutrality before 2060. Consideration of the health impact of climate change and extreme weather conditions can help decision-makers with appropriate urgency.

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Preplanned Studies

Association Between Ambient Temperature and Years of Life Lost from Stroke — 30 PLADs, China, 2013–2016

Jinlei Qi[1,&]; Fei Tian[2,&]; Siqi Ai[2]; Peng Yin[1]; Maigeng Zhou[1]; Lijun Wang[1,#]; Hualiang Lin[2,#]

Summary

What is already known about this topic?

Previous studies have mainly focused on the relationship between temperature and mortality from stroke, but analysis on the effects on years of life lost (YLL) is limited.

What is added by this report?

YLLs were used as the health outcome, and cold and hot weather were found to be significantly associated with an increase in YLLs from stroke and for different groups, with a stronger effect found to be associated with low temperature.

What are the implications for public health practice?

These findings could help identify vulnerable regions and populations that have a more serious temperature-related burden and to guide the practical and effective measures for stroke control from a YLL perspective.

Although numerous studies suggested non-optimal temperatures may lead to increased stroke mortality, the evidence concerning the effect of ambient temperature on years of life lost (YLLs) due to stroke is still scarce (*1*). Data on daily mortality, years of life lost, meteorological factors, and air pollution from 93 cities within 30 provincial-level administrative divisions (PLADs) between 2013 and 2016 was collected. We applied a two-stage analytic strategy to assess the association between temperature and YLLs. We used a distributed lag non-linear model (DLNM) with a Gaussian link to evaluate the city-specific association between ambient temperature and YLLs from stroke, and then we applied a multivariate meta-analysis to obtain the pooled effects at regional and national levels. Inverse "J" shaped associations between temperature and YLLs from stroke were found. At the national level, we observed 19.77 (95% CI: 11.16, 28.40), 15.34 (95% CI: 7.77, 22.91), 5.47 (95% CI: 2.57, 8.37), and 2.99 (95% CI: 0.49, 5.49) of YLLs were associated with the effects of extreme cold, mild cold, extreme heat, and mild heat relative to the optimum temperature, respectively. In addition, 10.91% (95% CI: 5.67%, 16.15%) of YLLs could be attributed to non-optimum temperatures, and for each deceased person, a national-averaged 1.39 YLLs (95% CI: 0.72, 2.06) were caused by non-optimum temperature. This study suggested both cold and hot weather would lead to significant life lost for stroke patients and regional adaptation policies and interventions should be considered.

We initially obtained the mortality and YLL data for 100 representative cities from the China Cause of Death Reporting System (CDRS) between January 1, 2013 and December 31, 2016. After checking the daily mortality and YLLs distribution in each city, we finally selected 93 cities as our study sites. Based on the climate types and administrative regions (*2*), the study sites were divided into seven regions (Supplementary Figure S1 available in http://weekly.chinacdc.cn/): north, northeast, northwest, east, central, south, and southwest. And according to initial diagnosis coded by 10th International Classification of Diseases (ICD-10), stroke was extracted from the system (I60-I64).

We obtained daily mean temperature (°C) and relative humidity (%) of the selected cities from China Meteorological Data Sharing Service System (http://data.cma.cn/). Also, daily concentrations of fine particulate matter with an aerodynamic diameter ≤ 2.5 μm ($PM_{2.5}$), ozone (O_3), sulfur dioxide (SO_2), nitrogen dioxide (NO_2) was collected from the National Real-time Publishing Platform for Air Quality (http://106.37.208.233:20035).

We conducted a two-stage analysis to assess the associations between ambient temperature and YLL of stroke. At the first stage, we estimated city-specific temperature-YLL associations. Since the daily YLL obeys a normal distribution (*3*), we used a DLNM with a Gaussian link to evaluate the nonlinear and delayed effects of ambient temperature on YLLs due to stroke. To capture the nonlinear relationship between temperature and YLLs, we fitted the exposure-response relationship through a natural cubic B-spline function with three placed knots at 10th, 75th, and 90th percentiles of city-specific temperature distribution. A B-spline with three knots at equally-spaced log scales was applied for the space of lags, with a maximum set of 21 days in according with previous studies (*4*). Some confounding factors, including relative humidity, $PM_{2.5}$, day of the week, public holidays, and long-term trend and seasonality were also controlled in the model. At the second stage, we obtained the regional and national effects within 21 lags between temperature and YLLs by using the best linear unbiased prediction (BLUP) approach. The minimum YLL temperature (MYLLT) corresponds to the minimum risk of YLL across the temperature range, based on the overall temperature-risk curve. On this basis, we further calculated the effects of extreme cold, mild cold, extreme heat, and mild heat on YLL risk and the attributable YLL fraction and attributable life expectancy loss per death. The detailed methods concerning the attributable burden analyses and sensitivity analyses were provided in the Supplementary Material (available in weekly.chinacdc.cn). We used R (Version 3.3.2, R Foundation for Statistical Computing, Vienna, Austria) to conduct all the analyses, "dlnm" package was used to fit DLNM model, and "mvmeta" package was used to conduct meta-analysis. $P<0.05$ (two-tailed) was considered statistically significant.

A total of 1,317,503 deaths due to stroke with 16,793,014 years of life lost were recorded in the 93 cities from January 1, 2013 to December 31, 2016. In Table 1, we observed that the daily death and YLL from stroke varied across study regions, with highest daily deaths and YLL in the northeast. The lowest daily stroke death counts and YLLs were found in the northwest, corresponding to 7 deaths and 97.7 years, respectively. In addition, the daily average temperature

TABLE 1. Summary statistics for daily deaths, years of life lost from stroke and ambient temperature in in seven regions of China, 2013–2016.

Variables	Northwest	North	Northeast	East	Central	Southwest	South	Nationwide
Daily YLL of stroke								
Mean	97.7	158	218	153	145	172	114	155
SD	111	122	160	128	117	230	75	143
Minimum	2.9	2.9	2.4	2.9	2.4	2.4	2.9	2.4
25th percentile	22.4	62.9	108	58.6	71.5	46.8	55	59.1
Median	50.9	119	168	213	121	92.1	102	116
75th percentile	129	230	277	121	184	150	160	202
Maximum	697	736	1,070	1,180	1,530	1,490	540	1,530
Daily mortality of stroke								
Mean	7	14	15	14	12	13.6	9	12
SD	8	11	11	11	9	18.9	6	11
Minimum	1	1	1	1	1	1	1	1
25th percentile	2	5	8	5	6	4	4	5
Median	4	10	12	10	10	7	8	9
75th percentile	9	19	19	19	14	11	13	16
Maximum	91	95	70	95	112	136	37	136
Daily temperature (°C)								
Mean	11.5	12.4	8.6	16.2	17.3	16.9	22.0	15.0
SD	10.7	11.2	13.2	9.4	8.8	7.2	6.6	10.6
Minimum	−22.4	−23.9	−26.4	−20.4	−9.5	−8.1	1.7	−26.4
25th percentile	2.9	2.3	2.5	8.4	9.8	11.7	16.8	7.6
Median	12.7	14	10.4	17.5	18.4	17.5	23.8	16.8
75th percentile	20.3	22.3	20.6	24.0	24.6	22.2	27.5	23.5
Maximum	35.1	33.4	30.8	36.5	35.8	36.2	33.5	36.5

Abbreviations: YLL=years of life lost; SD=standard deviation.

ranged from 8.6 °C in the northeast to 22.0 °C in the south.

We observed the optimum temperature that caused the lowest YLL risk ranged from 16.7 °C in central region to 28.7 °C in the south region in Table 2. In general, the estimated effects of cold weather were stronger than that of high temperature. Specifically, extremely cold weather was significantly associated with YLLs due to stroke, with the strongest magnitude of effects in the northeast, corresponding to 53.73 (95% CI: 8.91, 98.55) years of life lost relative to the reference temperature.

Figure 1 show the BLUP on exposure-response curves of the cumulative effects of temperature on YLLs from stroke at the national level in China, 2013–2016. We observed an inverse “J” shaped association, with increasing YLLs for moving up and down from the minimum YLL temperature. Furthermore, we found consistent curves stratified by sex, regions, and subtypes of stroke (Supplementary Figures S2–S4 available in http://weekly.chinacdc.cn/), particularly in the terms of the general shape.

In attribution burden analysis (Supplementary Table S1 available in http://weekly.chinacdc.cn/), we observed that at the national level, the total fraction of YLLs by non-optimum temperature was 10.91% (95% CI: 5.67, 16.15), in which cold temperature (10.84%, 95% CI: 5.69, 15.99) accounted for a significantly higher contribution. The national-pooled life expectancy loss per death due to non-optimum temperature was 1.39 years (95% CI: 0.72, 2.06), with a significantly higher contribution of cold weather (1.38, 95% CI: 0.72, 2.04) than that of hot weather (0.01, 95% CI: −0.00, 0.02). The life expectancy loss caused by cold temperature was higher than that of hot temperature in all the regions, and the highest estimate occurred in the north region (2.19, 95% CI: 0.31, 4.07).

DISCUSSION

Our present study explored the associations between ambient temperature and daily YLL due to stroke in 93 Chinese cities. We found cold and hot weather were significantly associated with an increase in years of life lost from stroke and for different groups, with stronger effects in low temperature. The present study could provide ample evidence to planning and policy-making in stroke control and climate governance.

A large body of epidemiological studies have documented the link between temperature and mortality due to stroke and its subtypes, however the relevant research about association of temperature with YLL from stroke within China was still scarce. Previous studies have provided similar findings, applying the YLL as the outcome measurement. Luan et al. reported

TABLE 2. Estimated cumulative effects ($lag_{0\text{-}21}$) on YLL under different patterns of temperature relative to the YLL at the reference temperature.

Variables	Overall YLL	OT (°C)	Extreme cold * (years, 95% CI)	Mild cold * (years, 95% CI)	Mild heat * (years, 95% CI)	Extreme heat * (years, 95% CI)
Overall region	16,793,014.0	25.6	19.77 (11.16, 28.40)	15.34 (7.77, 22.91)	2.99 (0.49, 5.49)	5.47 (2.57, 8.37)
Northeast	3,562,080.8	23.2	53.73 (8.91, 98.55)	30.15 (−5.48, 65.77)	23.96 (4.88, 43.04)	21.16 (0.45, 41.88)
Northwest	979,861.7	17.0	12.51 (−22.04, 47.05)	14.57 (−18.83, 47.97)	1.13 (−17.55, 19.80)	10.53 (−5.84, 26.90)
North	1,573,462.6	24.9	41.67 (3.70, 79.64)	46.61 (7.83, 85.39)	11.95 (−4.68, 28.)	11.39 (−0.07, 22.85)
Central	2,380,406.4	16.7	22.28 (−16.52, 61.07)	15.58 (−17.04, 48.20)	0.01 (−0.56, 0.59)	17.09 (−2.79, 36.97)
East	5,413,438.8	25.2	21.80 (8.38, 35.23)	7.38 (−5.65, 20.41)	1.69 (−3.35, 6.72)	18.90 (9.89, 27.90)
Southwest	1,786,702.7	27.7	54.18 (9.90, 29.19)	16.54 (7.86, 25.21)	3.34 (0.01, 6.68)	4.41 (2.31, 6.51)
South	1,097,060.8	28.7	84.98 (22.29, 147.68)	32.24 (−1.88, 66.37)	3.99 (−11.59, 19.57)	2.24 (−8.18, 12.66)
Subtype						
Hemorrhagic stroke	9,852,444.0	28.2	11.62 (4.51, 18.73)	10.53 (4.08, 16.97)	3.13 (0.13, 6.12)	0.36 (−0.60, 1.32)
Ischemic stroke	6,028,666.0	22.4	7.55 (3.50, 11.60)	4.63 (1.18, 8.08)	0.03 (−0.20, 0.25)	6.33 (3.64, 9.01)
Sex						
Male	10,033,788.0	26.0	13.05 (6.87, 19.24)	10.57 (5.32, 15.81)	2.09 (−0.02, 4.21)	2.43 (0.71, 4.17)
Female	6,759,226.0	25.1	5.53 (0.92, 10.15)	4.19 (0.04, 8.34)	0.84 (−0.53, 2.21)	2.45 (0.76, 4.13)

Abbreviations: YLL=years of life lost; OT=optimum temperature. The reference temperature was set at the temperature with lowest YLL.

* Extreme cold, mild cold, extreme hot, and mild hot temperature were defined as 2.5th, 25th, 97.5th and 75th percentile of temperature distribution, respectively, compared with the reference temperature (minimum YLL temperature).

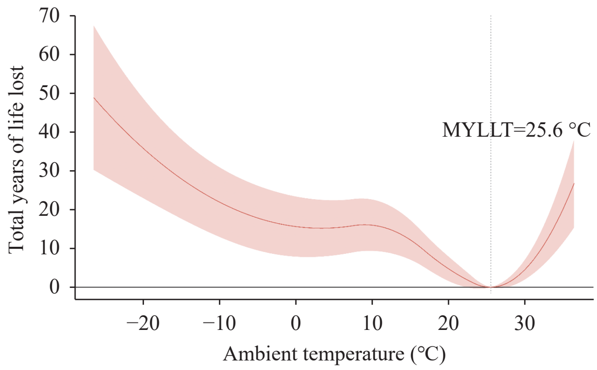

FIGURE 1. Exposure-response curve of the cumulative effects of temperature on years of life lost from stroke at the national level in China (93 cities), 2013–2016.
Abbreviation: MYLLT=The minimum years of life lost temperature.

that both cold and hot temperature were significantly associated with increasing YLL of cardiovascular diseases in which the effects of low temperature took such a large share (*5*). A recent study conducted in three largest English cities found that there was an increased risk in YLL with the increment and decline of the temperature from the thresholds (*6*).

The non-linear relationships between temperature and YLLs from stroke that emphasized the adverse health effects of both low and high temperatures were found in present study. Furthermore, there was biologically plausible evidence for these associations. The effects induced by cold temperature were in association to increasing the level of inflammatory response, and oxidative stress in brain and variation of the blood pressure and autonomic nervous system (*7–8*). In addition, high outdoor temperature was associated with increasing cardiac output and heart rates, dehydration, hypotension, and vasodilatation, which would lead to microvascular thrombosis in brain and elevate the mortality of stroke (*9*). In addition, compared with the heat exposure, the effects from low temperatures on stroke tended to be stronger, which might be explained by the variation in autonomic nervous system and thermogenesis, and fluctuation in blood pressure in cold days (*7*).

We also found that the temperature-related effects could variy across geographical regions. For example, in south region, where the mean temperatures reached 8.4 °C or below (2.5th percentile of the temperature distribution in south region), we observed the strongest YLL (84.98, 95% CI: 22.29, 147.68) for extreme cold temperature, while in northwest region the corresponding number declined to be nonsignificant (12.51, 95% CI: –22.04, 47.05). The observed differences in the estimated effects of temperature across regions might be explained by the discrepancy in climate condition, population susceptibility, and socioeconomic status (*10*). In addition, central heating capacity might be another important region-level characteristic to explain the observed differences across different regions.

We further assess the attributable fraction of YLLs and life expectancy loss per death relative to the reference temperature at the regional and national level. The attributable burden analysis reported that the effects of non-optimum temperature constituted 10.91% of YLLs due to stroke and 1.39 years potential gain in life expectancy per death would achieve by attaining the optimum temperature rom the national perspective. As stroke was the leading cause of death with remarkably high prevalence in China, our study would provide guiding and fundamental advice to improve existing preventive strategies for stroke and reduce the ambient temperature-related burden.

This study was subject to at least some limitations. First, we used monitoring temperature data as the real exposure for the population due to the unavailability of the individual exposure, which may cause exposure misclassification. Second, this study was an ecological study in essence without adjustment for the unmeasurable individual-level covariates. Third, due to mortality data unavailability, the included cities were mainly distributed in the east and central regions but fewer in the northwest, which could lead to a low representativeness of the data and uncertainty to draw a nationwide conclusion. Finally, the coding errors and misclassification may inevitably occur in the nationwide registry-based YLL data, though this process was under strict quality control.

In summary, this nationwide analysis elaborated non-linear associations between ambient temperature and YLLs from stroke in China, with evident adverse health effects due to both cold and hot temperatures. Reducing exposure to ambient non-optimum temperature could lead to a substantial benefit in life expectancy. Our findings could help identify the vulnerable regions and populations that bore more serious temperature-related burdens and to guide the practical and effective measures for stroke control.

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Preplanned Studies

Assessment of Regional Health Vulnerability to Extreme Heat — China, 2019

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Summary

What is already known on this topic?

The health risk caused by high-temperatures depends on the interaction between high temperature exposure and the sensitivity and adaptability of the affected populations.

What is added by this report?

A comprehensive assessment model was established by principal component analysis using the data of 19 cities, 15 provincial-level administrative divisions and used to identify regional characteristics and major influencing factors of health vulnerability to extreme heat in China.

What are the implications for public health practice?

The results of the health vulnerability assessment could effectively identify the regions highly vulnerable to extreme heat in China and provide scientific evidence for the development of adaptive measures and resource allocation plans.

With global warming, the impacts of extremely high temperatures on health have been gradually increasing. Due to the differences in population adaptability, socioeconomic development levels, geographical locations, and climatic conditions, health impacts of extremely heat vary across regions. This study intends to construct an evaluation index system, to evaluate the regional health vulnerability to extreme heat, and to identify the major influencing factors of health vulnerability in China. First, a comprehensive assessment model for health vulnerability to extreme heat was established by principal component analysis with the data from 19 representative cities from a national project, which were distributed in different climatic zones (Supplementary Figure S1 available in http://weekly.chinacdc.cn/), and the results were verified by using the proportion of deaths on extreme heat days in the summer. Then, the extreme heat-health vulnerability index of 31 provincial-level administrative divisions (PLADs) in 2019 were calculated using the established comprehensive assessment model. It was found that regions with high vulnerability were mainly located in the western and central China. The major influencing factors of health vulnerability to extreme heat included indicators of healthcare levels, living environment indicators, socioeconomic level indicators, and air quality. This study could effectively identify areas highly vulnerable to extreme heat in China and provide scientific evidence for the development of adaptive measures and resource allocation plans.

Data on air pollutants (e.g., $PM_{2.5}$, NO_2), meteorological factors (e.g., temperature, precipitation), demographics, and socioeconomic conditions were collected from the China Environment Statistical Yearbook, China Meteorological Administration, China Statistical Yearbook, China Urban Statistical Yearbook, China Health Statistics Yearbook, relevant statistical bulletin, and provincial statistical yearbooks. Data in the 19 representative cities, 15 PLADs were collected from 2014 to 2018 and data in the 31 PLADs were collected in 2019. The mortality data from 2014 to 2018 were obtained from China's Cause of Death Reporting System with assistance by local CDCs. In this study, the 95th percentiles of the temperature range were selected as extreme heat temperatures.

The assessment of health vulnerability to extreme heat was conducted in a three-stage analysis. First, the evaluation indicators for health vulnerability to extreme heat were selected in three dimensions including exposure, sensitivity, and adaptability through literature review, correlation analysis, and principal component analysis (PCA). Second, a comprehensive assessment model of health vulnerability to extreme heat was established by a PCA method using data from 19 representative cities in 15 PLADs in which the death data were collected. The value of health vulnerability index of extreme heat was calculated by the following function: vulnerability index = exposure index score + sensitivity index score - adaptability index score. The results of the vulnerability assessment were verified by correlation analysis between the vulnerability index and the proportion of deaths on extreme heat days. Finally, the extreme heat-health vulnerability indexes of 31 PLADs in 2019 were calculated with the same model in 19 representative cities, 15 PLADs. All analyses were performed using R statistical software (version 4.0.2; The R Foundation for Statistical Computing, Vienna, Austria).

A total of 20 indicators in 3 dimensions were selected for assessment of health vulnerability to extreme heat, including 6 exposure indicators, 7 sensitivity indicators, and 7 adaptability indicators (Table 1). PCA extracted 4 principal components that had a cumulative variance contribution rate of 77% (Table 2). The first principal component mainly represented healthcare indicators including the elderly dependency ratio, maternal mortality rate, perinatal mortality rate, morbidity rate of infectious diseases, etc. The second principal component mainly represented living environment factors including the proportion of households with five or more persons, air temperature, etc. The third principal component represented socioeconomic indicators such as the percentage of people living alone, air temperature, per capita gross domestic product (GDP), and electricity demand. The fourth principal component represented air quality conditions that mainly included concentration of $PM_{2.5}$ and NO_2.

The correlation coefficient between the vulnerability index and the proportion of deaths on hot days in summer in 19 representative cities was 0.518

TABLE 1. The selected evaluation indicators of exposure, sensitivity and adaptability for vulnerability assessment.

Dimension	Indicators	Function relationship
Exposure	Annual average temperature (℃)	+
	Daily maximum temperature≥P_{95}* days	+
	Frequency of heat waves*	+
	Annual average relative humidity (%)	+
	$PM_{2.5}$ (μg/m^3)	+
	NO_2 (mg/m^3)	+
Sensitivity	Elderly dependency ratio (%)*	+
	Poverty population ratio (%)	+
	Living alone (%)	+
	Proportion of households with 5 or more persons* (%)	+
	Maternal mortality rate* (1/100,000)	+
	Perinatal mortality rate* (‰)	+
	Morbidity rate of infectious diseases* (1/100,000)	+
Adaptability	Per capita GDP* (RMB)	−
	Per capita medical care* (RMB)	−
	Green coverage rate of built district* (%)	−
	Air conditioning quantity*	−
	Electricity demand* (100,00/kWh)	−
	Daily water consumption* (L)	−
	Volume of precipitation*	−

* P_{95} is the 95th percentile of the daily maximum temperature; Frequency of heat waves is frequency for 3 consecutive days ≥P_{95} of daily maximum temperature; Elderly dependency ratio is the ratio of the elderly population aged 65 and over to the working-age population aged 15-64; Poverty population ratio is minimum Living Allowances and over to the Total population at year end; Proportion of households with 5 or more persons is the ratio of households with 5 or more persons to the total number of households; Maternal mortality rate is the number of maternal deaths per 100,000 maternal; Perinatal mortality rate is the number of neonatal deaths from 28 weeks of gestation or ≥ 1,000 grams of birth to 7 days after delivery; Morbidity rate of infectious diseases is the number of cases of Class A and B infectious diseases per 100 thousand population in the reference year; Per capita GDP is per capita gross domestic product, the ratio of the GDP by a region to the permanent population; Per capita medical care expenditure is the expenditure on drugs, supplies and services of medical and health care; Green coverage rate of built district is the percentage of green coverage in urban built-up areas to built-up areas; Air conditioning quantity is per 100 households air conditioning quantity; Electricity demand is annual total electricity consumption in urban households; Life-water quantity is the average Daily water consumption per person; Volume of precipitation is the annual precipitation is the summation of 12 months precipitation of a year.

TABLE 2. Factor loadings for extreme heat vulnerability for the four retained varimax-rotated based on data from 19 representative cities, 15 PLADs in China from 2014 to 2018.

Item	Principal component 1	Principal component 2	Principal component 3	Principal component 4
Frequency of heat waves	−0.24	0.70	−0.21	0.23
Annual average temperature (℃)	−0.35	**0.80**	0.29	0.17
Annual average relative humidity (%)	−0.28	0.76	−0.01	−0.29
$PM_{2.5}$ (μg/m^3)	−0.15	−0.11	−0.20	**0.90**
NO_2 (mg/m^3)	0.08	−0.12	0.18	**0.88**
Daily maximum temperature≥P_{95}^{*} days	0.17	0.49	0.04	−0.02
Elderly dependency ratio (%)	**−0.82**	0.02	−0.25	0.31
Poverty population ratio (%)	0.13	−0.35	−0.47	−0.66
living alone (%)	−0.07	0.08	0.85	−0.21
Proportion of households with 5 or more persons (%)	0.23	**0.81**	−0.09	0.09
Maternal mortality rate (1/100,000)	**0.89**	−0.17	−0.28	0.07
Perinatal mortality rate (‰)	**0.91**	−0.07	−0.21	0.05
Morbidity rate of infectious diseases (1/100,000)	**0.90**	0.09	−0.06	−0.01
Per capita GDP (CNY)	−0.21	0.11	**0.83**	0.08
Per capita medical care expenditure (CNY)	0.39	−0.56	0.37	0.17
Green coverage rate of built district (%)	−0.04	0.50	0.45	0.42
Air conditioning quantity	−0.62	0.50	0.45	0.25
Electricity demand (100,00 / kWh)	−0.05	−0.04	**0.84**	0.26
Daily water consumption (L)	0.06	0.77	0.36	−0.10
Volume of precipitation	−0.31	0.78	0.36	−0.20

* P_{95} is the 95th percentile of the daily maximum temperature; Bold font is the greater correlation between the evaluation index and the principal component

(*P*=0.023). We used the same method to evaluate health vulnerability to extreme heat in 31 PLADs (Supplementary Table S1 available in http://weekly.chinacdc.cn/). Results showed that higher vulnerability regions were located in the western and central China (Figure 1). The four highest vulnerability regions were the Tibet (Xizang) Autonomous Region (0.182), Qinghai Province (0.112), Tianjin Municipality (0.076), and Xinjiang Uyghur Autonomous Region (0.075).

DISCUSSION

In this study, an extreme heat-health vulnerability assessment model that included 20 factors in 3 dimensions was created using data from 19 representative cities, and the health vulnerability to extreme heat in 31 PLADs in China was assessed according to the health vulnerability assessment model. It was found that heat vulnerability varied across regions, with generally higher scores of vulnerability in the western and central China, which could be possibly explained by relative lower adaptability in such areas. Healthcare and living environment factors were important influencing factors of regional vulnerability. Regions with poorer healthcare capacities and higher $PM_{2.5}$ or NO_2 concentration tended to have higher extreme heat vulnerability. The findings could provide scientific evidence for local authorities to improve the local adaptability and decrease the health vulnerability to extreme heat.

The distribution of healthcare resources in China demonstrated some inequalities (*1*). The medical and healthcare levels in the western region had relatively lower standards (*2*), where health services were insufficient and access to health information was also limited. In this scenario, people in those regions might be at higher risk when exposed to extreme heat events. For example, western regions of Tibet, Qinghai, and Xinjiang, which had relatively poorer healthcare, had high vulnerability even with their relative mild and temperate climates. Therefore, great efforts should be taken to improve the healthcare conditions in those areas to elevate capability of response to extreme heat

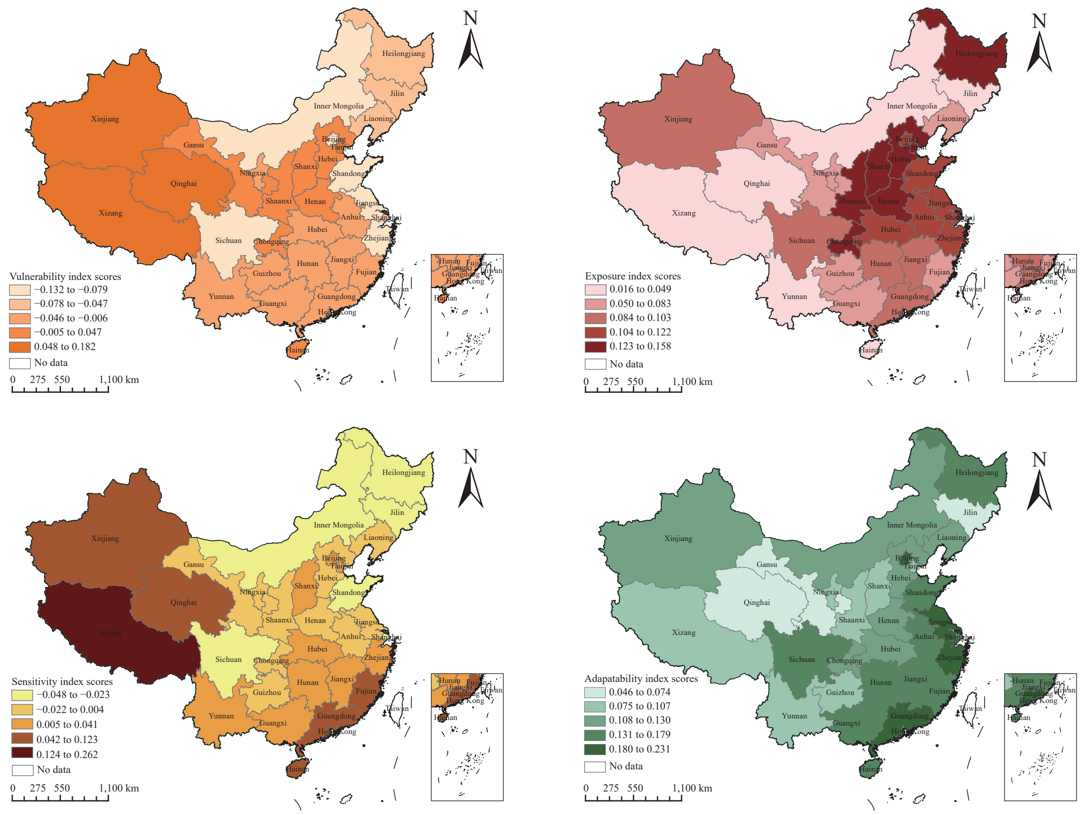

FIGURE 1. National map of extreme heat vulnerability, exposure, sensitivity and adaptability index scores in 31 provincial-level administrative divisions in China, 2019.

Air quality also presented national spatial variability. The annual $PM_{2.5}$ and NO_2 levels in northern China were higher than those in southern China (*3*). In recent years, air pollution had caused more than 1 million deaths per year in China (*4*). Furthermore, a previous study had shown that air pollution could increase the health risks of exposure to heat (*5*). Therefore, regions with higher concentrations of air pollutants tended to have higher extreme heat vulnerability in the central regions, such as Hebei and Shanxi. With rapid urbanization and development of transport infrastructure, it is also important to improve air quality to reduce extreme high temperature vulnerability.

In addition, it was found that eastern PLADs such as Shandong, Jiangsu, and Zhejiang were at low health vulnerability even with usually higher temperatures in summer. This might be due to the higher levels of the per capita GDP, which is highly correlated to the level of local medical services (*6*). In contrast, due to imbalances, western and central regions had lower economic development (*7*), resulting in potentially lower adaptive capacity.

This study was subject to two limitations. First, we excluded some important indicators that were unavailable, such as proportion of population with chronic diseases and high-temperature warnings, which may induce some bias. Second, the lack of provincial health outcome indicators in this study made it impossible to verify the provincial assessment results of health vulnerability to extreme heat. In future studies, we should add a more precise index and optimize the model with more data.

In conclusion, the results of this study showed to some extent that the vulnerability index could reflect comprehensive health effects of extreme heat. Identification of regional health vulnerability to extreme heat can help guide public health authorities to appropriately allocate resources to the more vulnerable regions. A comprehensive adaptation plan should also be developed by local governments to improve local adaptive capacities.

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Preplanned Studies

The Impact of a Health Forecasting Service on the Visits and Costs in Outpatient and Emergency Departments for COPD Patients — Shanghai Municipality, China, October 2019–April 2020

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Summary

What is already known on this topic?

The morbidity and mortality of chronic obstructive pulmonary disease (COPD) is associated with adverse weather and air pollution. However, COPD patients are not able to be alerted in advance of high risk environments.

What is added by this report?

This prospective controlled trial conducted in Pudong New Area of Shanghai from October 2019 to April 2020 provided evidence of COPD risk forecasting service on the reductions in visits and costs of COPD patients in outpatient and emergency departments in China for the first time.

What are the implications for public health practice?

This study suggests that COPD risk forecasting service could be integrated into existing COPD management in public health to improve the health and economic outcomes.

Chronic obstructive pulmonary disease (COPD) is a public health challenge in China because of its high prevalence, related disability and mortality, and heavy economic burden (*1–3*). COPD morbidity and mortality is associated with adverse weather and air pollution (*4–7*). However, it is difficult for both COPD patients and medical staff to be alerted in advance of high-risk periods with existing tools. The Shanghai Meteorological Service (SMS) has developed a health forecasting service for COPD patients based on the weather and air quality forecasts. A prospective controlled trial was conducted in Pudong New Area of Shanghai from October 2019 to April 2020 to examine whether such a forecasting service being available to COPD patients and their general practitioners (GPs) could reduce visits and costs in outpatient and emergency departments (OPED) for COPD. In this study, 1,349 patients in each group were analyzed after balancing the control and intervention groups by using the propensity score matching (PSM) method. Compared with the control group, there was a 17.6% reduction in the proportion of OPED patients and a 13.9% reduction in the OPED visits in the service group. The results of this study suggest that COPD risk forecasting service could be a novel method of COPD management in public health to improve health and economic outcomes.

This study was designed as a prospective intervention study with two groups: the service group (patients receiving COPD risk forecasting service; also known as the intervention group) and the control group (patients not receiving the COPD risk forecasting service). According to previous studies, every 1 °C increase of daily mean temperature was associated with a 7.0% decrease (95% CI: 4.9, 9.0) in the risk of COPD hospitalization in Beijing (*8*) and a 3.0% decrease (95% CI: 2.0, 4.0) in COPD symptoms in Shanghai (*4*). The proportion of COPD patients receiving outpatient treatment, the primary dichotomous endpoint, was usually around 50% (*3*). Assuming that rate ratio of OPED visit for the service group was 0.85 compared with the control group, a total of 1,854 subjects (927 for each group) were required to detect a difference between the two groups at a 90% power with a two-sided significance level of 0.05.

COPD patients in Pudong New Area of Shanghai Municipality were selected as the local CDC had an established routine COPD management system with thousands of clinically diagnosed COPD patients registered to community health service centers. Patients consenting to participate were required to provide following information at baseline: age, sex, number of acute exacerbations of COPD (AECOPD) within the last year. Furthermore, patients selected to receive the COPD risk forecasting service were also asked to provide contact details.

Overall, there were three methods the COPD risk forecast service was provided: 1) a specially designed platform for WeChat displaying daily updated forecast information and chat groups including patients, GPs, CDC staff, and SMS staff; 2) mobile phone text messages; and 3) automated phone calls. Except for the WeChat platform, COPD risk forecast was provided regularly 2 to 3 times per week and before adverse weather events. Patients were sent an information pack that described how future weather could affect COPD and detailed advice on self-management of COPD, such as keeping warm, reducing exposure to cold temperature or air pollution, appropriate exercise, and so on. They were also advised to contact their GP if necessarily. At the end of study, adherence of patients in the service group was self-reported in questionnaire according to whether they adjusted their behavior when they were alerted in high-risk period. Their satisfaction with the forecasting service was also evaluated with answers of satisfied, moderate, or dissatisfied.

In both the service and control groups, patients had died from other diseases during the study period (October 2019–April 2020) and those less than 40 years old were also excluded. As the baseline characteristics of the service and control group were unbalanced (Table 1), the PSM method was used to balance variables and reducing the bias between the control and service groups. The method has been used with increasing frequency in observational studies and clinical trials (*9*), which attempts to adjust post hoc for recognized unbalanced factors at baseline to approximate a randomized data to analyze. Logistic regression was used to calculate the propensity score of each patient. Then the 1∶1 case-control matching was conducted according to the principle of neighboring matching with caliper value of 0.01. The matching variables were the patients' age, gender, and the AECOPD counts within the last year. The service group was also divided into the WeChat group, the text group, the call group, and the mixed group (the group of patients receiving COPD risk forecast in two or more methods). After matching, monthly COPD-related OPED visits and costs of each group during the study period were collected from the information center of Pudong New Area Health Commission. All the COPD-related OPED visits were defined according to clinical diagnosis (J40, J42–J44). OPED costs for COPD were also divided into costs for registration, medication, examination, etc.

A generalized estimation equation (GEE) was used to examine the effects of COPD risk forecasting service on OPED visits and costs for COPD. Monthly visits and costs were used as dependent variables. As the number of OPED visits was approximately Poisson distributed, the Poisson distribution was used in the analysis. OPED visits were also treated into dichotomous variable (yes or no). Patients' age, gender, and AECOPD counts within the last year were adjusted as covariates in the GEE model. All statistical analyses were conducted with R version 4.0.2 (R Development Core Team, Auckland, Nz). The geepack package was used to conduct GEE. The significance level was set at 0.05 (two-tailed).

A total of 4,880 COPD patients participated in this study. After some patients were excluded, 2,204 patients were included in the service group, and 1,631 patients were in the control group (Table 1). Before using PSM, baseline conditions of the two groups were unbalanced. In the service group, the age and proportion of patients having AECOPD in the last year were both smaller than those of the control group. After PSM, 1,349 patients in the service group were

TABLE 1. Characteristics of COPD patients in groups of receiving or not receiving the COPD risk forecast service before and after propensity score matching in Pudong New Area, Shanghai Municipality from October 2019 to April 2020.

Characteristics	Before PSM			After PSM		
	Patients not receiving service (n=1,631)	Patients receiving service (n=2,204)	*P* value	Patients not receiving service (n=1,349)	Patients receiving service (n=1,349)	*P* value
Age, years	71.7±10.3	67.9±9.3	<0.001	69.3±9.1	69.5±9.0	0.522
Male,N (%)	932 (57.1)	1303 (59.1)	0.232	761 (56.4)	774 (57.4)	0.641
AECOPD counts within the last year, N (%)			<0.001			0.010
0	1,307 (80.1)	1,431 (64.9)		1,060 (78.6)	1,002 (74.3)	
1	172 (10.6)	451 (20.5)		143 (10.6)	224 (16.6)	
≥2	152 (9.3)	322 (14.6)		146 (10.8)	123 (9.1)	

Abbreviations: PSM=propensity score matching; COPD=chronic obstructive pulmonary disease; AECOPD=acute exacerbation of COPD.

successfully matched with 1,349 controls. Patients in the control and service group were balanced in age and gender. Compared with the control group, the proportion of patients having AECOPD in the last year increased by 4.3% in the service group, whereas the proportion of patients having more than one time of AECOPD decreased by 1.7%, as shown in Table 1. After a 6-month forecasting service, 85.8% of patients in the service group reported good compliance with advice in the forecasting service. There were 88.7%, 79.6%, and 90.0% of patients satisfied with the service provided by WeChat, text, and call, respectively.

There were 545 COPD patients in the service group that visited OPED at least once for COPD for a total of 1,986 person-times during the study period, while 502 patients in the control group visited for a total of 2,031 person-times. Figure 1 showed the proportion of COPD patients visiting COPD-related OPED in the service and control groups in Pudong New Area, Shanghai, from October 2019 to April 2020. In the service group, 18.1% of patients visited OPED in December 2019, and 12.3% visited OPED in April 2020. Showing a similar time trend in the control group, there were 19.1% and 13.3% of patients visiting OPED in December 2019 and April 2020, respectively. The proportion of patients visiting COPD-related OPED in the service group was consistently lower than that in the control group from December 2019. The monthly person-times of OPED visits also peaked in December 2019 and gradually declined in the following months. In the service group, patients visited OPED for 244 times in December 2019 and 166 times in April 2020. In the control group, the figures were 258 times and 180 times, respectively.

The results of the GEE models in evaluating the effects of COPD risk forecasting service on the proportion of COPD patients visiting OPED and person-times of OPED visits in Pudong New Area of Shanghai from October 2019 to April 2020 were shown in Table 2. When the proportion of patients was analyzed, the relative risk (RR) for patients receiving service relative to those not receiving it was 0.824 (95% CI: 0.686, 0.990), i.e., a 17.6% reduction with a wide 95% CI of 1.0% reduction to 31.4% reduction. When the person-times of OPED visits were used, the corresponding RR was 0.861 (95% CI: 0.744, 0.995), which meant that receiving such service had effect of reducing OPED visits by 13.9%. The RRs for patients receiving service via WeChat, text, or call were mainly less than 1 with wide CIs across 1, suggested less OPED visits although the effects were not significant for patients receiving the service only through a single method. When two or more service methods were used, there was a significant effect of reduction in person-times of OPED visits with a RR of 0.755 (95% CI: 0.597, 0.955).

The total OPED costs of these 2,698 patients were 1.34 million RMB during the study period, in which medicine accounted for 82.9%. The total OPED costs and medicine costs per patient due to COPD were 495.1 RMB and 410.9 RMB, respectively, during the study period. Table 2 also showed the effect of COPD risk forecasting service on the OPED costs for COPD using GEE. In general, patients receiving the COPD risk forecast service seemed to have lower total

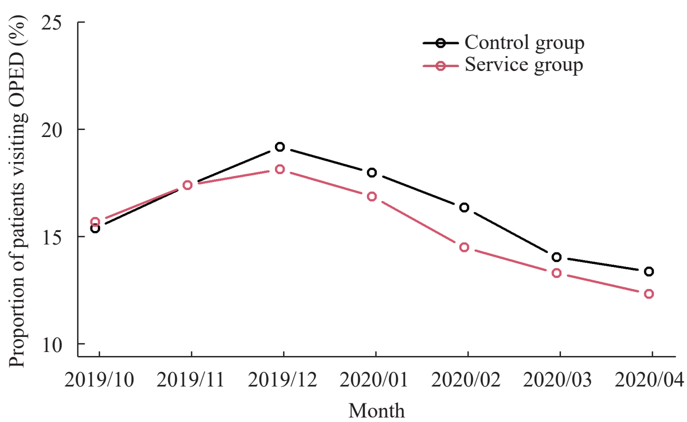

FIGURE 1. The monthly proportion of COPD patients visiting outpatient and emergency departments for COPD in the service group (1,349 patients) and the control group (1,349 patients) in Pudong New Area, Shanghai Municipality from October 2019 to April 2020.
Abbreviation: OPED=outpatient and emergency departments.

TABLE 2. Effects of the COPD risk forecasting service on the visits and costs of outpatient and emergency departments for COPD in Pudong New Area, Shanghai Municipality from October 2019 to April 2020.

Groups	N	Patients visiting OPED		Person-times of OPED visits		OPED costs, RMB		Medicine costs, RMB	
		Persons (%)	RR (95% CI)	Times	RR (95% CI)	Mean	β (95% CI)	Mean	β (95% CI)
Control	1,349	502 (37.2)	Ref	2,031	Ref	511.7	Ref	422.6	Ref
Service	1,349	545 (40.4)	0.824 (0.686, 0.990)*	1,986	0.861 (0.744, 0.995)*	478.4	−11.194 (−24.579, 2.191)	399.1	−9.522 (−21.285, 2.241)
WeChat	204	73 (35.8)	0.945 (0.659, 1.354)	273	1.012 (0.768, 1.335)	455.8	−0.797 (−28.194, 26.600)	394.1	1.727 (−22.287, 25.741)
Text	619	258 (41.7)	0.855 (0.683, 1.071)	919	0.913 (0.764, 1.093)	505.6	−5.389 (−23.368, 12.590)	420.9	−5.120 (−20.985, 10.744)
Call	169	75 (44.4)	0.747 (0.502, 1.112)	294	0.759 (0.532, 1.084)	464.3	−25.900 (−50.865, -0.935)*	370.0	−24.895 (−44.945, −4.845)*
Mixed	357	139 (38.9)	0.756 (0.558, 1.025)	500	0.755 (0.597, 0.955)*	450.9	−20.258 (−39.644, -0.872)*	378.1	−16.172 (−33.425, 1.081)

Abbreviations: OPED=outpatient and emergency departments; Ref=reference group;RR= Relative risk.
* P<0.05.

spending on OPED services and medication than those not receiving the service, although these results were not significant. The cost-reducing effects varied by way of providing the forecasting service, with significantly stronger effects in the call group and mixed group. For example, patients receiving the service via calls and in two or more methods had a decline of 25.90 RMB (95% CI: 0.87, 50.94) and 20.26 RMB (95% CI: 0.87, 39.64), respectively, per patient in OPED costs relative to those not receiving service.

DISCUSSION

This study evaluated the impact of environment-based health forecasting service, a new method of COPD management for the first time in China. Patients receiving the forecasting service had less visits and costs in outpatient and emergency departments due to COPD than those not receiving it between October 2019 and April 2020. It seemed that better effects could be reached by providing services via automated calls or in multiple methods than via WeChat or text messages.

In this study, compared with the control group, there was a 17.6% reduction in the proportion of OPED patients and a 13.9% reduction in the OPED visits in the service group. The effects were similar with those reported in UK (*10–11*), where a COPD forecasting service appeared to reduce the frequency of COPD exacerbation by 18.8% and the severity of exacerbation, but the effects did not reach statistical significance perhaps due to their smaller number of participants (only 79 patients) and lower exacerbation rates. Our study had 2,698 COPD patients participating in and using OPED visits instead of AECOPD hospitalization to enlarge outcome rates.

We used several methods to provide COPD risk forecasting service to patients. However, patients receiving the service via phone calls appeared to have less OPED visits and costs than those receiving the service via WeChat and text. It may be due to different accessibility of these methods. In this study, more than 80% of patients in the call group answered frequently whereas only around 60% of patients registered in the specific WeChat platform. As the most popular social network in China, WeChat has been widely used in chronic disease management (*12*). However, WeChat may be not easy for older patients to use because their education levels, income levels, and physical conditions tend to make app use more challenging. Mobile phone text message is a traditional method to send weather forecast and disease-related information to patients. The use of text messages can be also affected by its higher barrier to engagement (due to being purely text) and the patients' education level, although there was great uncertainty of the proportion of COPD patients in the text group successfully receiving the forecasting service.

The monthly COPD-related OPED patients and visits were both found to peak in December 2019 and declined in the following months. This is possibly caused by there being more COPD morbidity in the cold season than in the warm season. Also, the coronavirus disease 2019 (COVID-19) pandemic occurred in the last 3 months of this study, which might have reduced the OPED visits for COPD to some extent. In a cross-sectional survey in Beijing (*13*), compared with that before the COVID-19 epidemic, fewer COPD patients maintained their pharmacological treatment. It was reported that only 15.6% of COPD patients who experienced respiratory symptoms aggravation sought medical care in hospital as 55.5% were concerned about cross-infection of COVID-19 in the hospital and the remaining 28.8% took more medication by themselves.

This study was subject to some limitations. Patients were not randomly allocated in the control and service groups. However, the PSM method had been adopted to control for selection bias to achieve the goal of balancing. In addition, some potential risk factors (the severity of COPD, respiratory infection, socioeconomic status, and smoking) associated with outpatient visit for COPD might have been missed in the baseline investigation. Moreover, the unexpected emergence of COVID-19 in the late period of the study period changed both patients' and hospitals' practice and resulted in trends such as less hospital visits and better self-management, which thus reduced some OPED visits in both groups during the late period and may limit the effects of the forecasting service.

Despite these limitations, the evaluation shows an association between the delivery of COPD risk forecasting service and the reduction of visits and costs of COPD patients in outpatient and emergency departments. The effectiveness of the service depends on the methods of patients receiving it. More longitudinal research with random allocation of patients and more influencing factors considered on the effectiveness of forecasting service is warranted.

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Preplanned Studies

A Modelling Study on $PM_{2.5}$-Related Health Impacts from Climate Change and Air Pollution Emission Control — China, 2010s and 2040s

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Summary

What is already known about this topic?

Climate change and air pollution are two important environmental issues in China. It is important to investigate particulate matter with aerodynamic diameter less than 2.5 μm ($PM_{2.5}$)-related health impacts from climate change and air pollution emission control.

What is added by this report?

Deaths and years of life lost related to $PM_{2.5}$ would increase in climate change scenario, although emission control would outweigh the influence of climate change.

What are the implications for public health practice?

More targeted actions should be taken to meet challenges of exacerbated $PM_{2.5}$ pollutions and its health impacts related to climate change in the future.

Climate change and air pollution are two important environmental issues in China. The study aimed to model different scenarios to assess the health impacts related to ambient particulate matter with aerodynamic diameter less than 2.5 μm ($PM_{2.5}$) from climate change and air pollution emission control in China. A regional meteorology-climate model was used to simulate the ambient $PM_{2.5}$ concentrations in China in the 2010s and the 2040s under different scenarios (climate change scenario, air pollution emission control scenario, and climate change and emission control scenario). Furthermore, changes in mortality and years of life lost (YLLs), an indicator which considers life expectancy at death, were adopted to estimate $PM_{2.5}$-related health impacts. The concentrations of $PM_{2.5}$ were estimated to slightly increase in climate change scenario but decrease in emission control scenario in 2040s. $PM_{2.5}$-related health impacts would increase in climate change scenario in the 2040s, although emission control would outweigh the influence of climate change. The findings suggest that more targets actions should be taken to confront challenges of exacerbated $PM_{2.5}$ pollutions and its health impacts attributable to climate change in the future.

As the biggest global health threat of the 21st century, tacking climate change could be the greatest global health opportunity (*1–2*). There are multiple linkages connecting climate change and air quality, and climate change is expected to degrade air quality (*3*). Considering $PM_{2.5}$ is one of the leading contributors to global disease burden (*4*), it is of great importance to predict future ambient $PM_{2.5}$ concentrations and its related health impacts by considering both the near-term changes in climate conditions and the changes in anthropogenic pollutant emissions in China on interdecadal timescales. Nevertheless, evidence investigating the health impacts attributable to ambient $PM_{2.5}$ from both climate change and air pollution emission control under different scenarios in China is still lacking.

In order to assess the combined effects of interdecadal climate change and anthropogenic emission reductions on ambient $PM_{2.5}$, the Flexible Global Ocean-Atmosphere-Land System Model, Grid-point Version 2 (FGOALS-g2) decadal climate prediction and a Multi-Resolution Emission Inventory for China (MEIC) were used to drive a Weather Research Forecast Model Coupled with Chemistry (WRF-Chem) model to simulate the ambient $PM_{2.5}$ concentrations in China during the 2010s and the 2040s in the national level and different districts under the Representative Concentration Pathway 4.5 (RCP4.5) scenario. The WRF-Chem model is a flexible and efficient atmospheric simulation model, the chemical module of this model mainly includes the emission, transport, photolysis, gaseous chemical reaction, deposition, aerosol dynamics, and chemical processes of air pollutants. It was used to simulate $PM_{2.5}$ concentrations in the 2010s, which were set as baseline; and $PM_{2.5}$ concentrations with only climate change and emission control, respectively, and under both scenarios in the 2040s in this study (*5*).

The burden attributable to $PM_{2.5}$ under the scenarios above for ischemic heart disease (IHD), stroke, chronic obstructive pulmonary disease (COPD), and lung cancer was estimated using the integrated exposure–response functions (IER) for each cause of death, which have been used in a Global Burden of Disease study (*6*) and are based on studies of ambient air pollution, household air pollution, and second-hand smoke exposure and active smoking (*7*). Data of the annual average population size were collected from the China Statistical Yearbook, and the city-level proportions of different age groups were obtained from the 2010 census. Yearly mortality data in the mainland of China were obtained from the national death surveillance data, which originated from China CDC. The age-specific and cause-specific mortality rates were estimated based on the death surveillance points, and the proportions of cause-specific mortality in different districts and age groups were collected from the China Death Surveillance Data set. The deaths and YLLs attributable to ambient $PM_{2.5}$ were then calculated by applying the year-specific, location-specific, and age-specific population-attributable fractions to the number of deaths and YLLs (*8*). Monte Carlo simulations were used to calculate the 95% confidence interval of death burden of $PM_{2.5}$. Because the data used in the study were collected without any individual identifiers, the study was exempted from the Institutional Review Board of Peking University Health Science Center in Beijing.

The national $PM_{2.5}$ concentrations in the 2010s and the changes of its predicted concentrations under different scenarios in the 2040s in China are presented in Figure 1. Climate change scenarios increased the $PM_{2.5}$ concentrations in most regions, while emission control scenarios would decrease the $PM_{2.5}$ concentrations at the national level. With the impact of both climate change and emission control, the

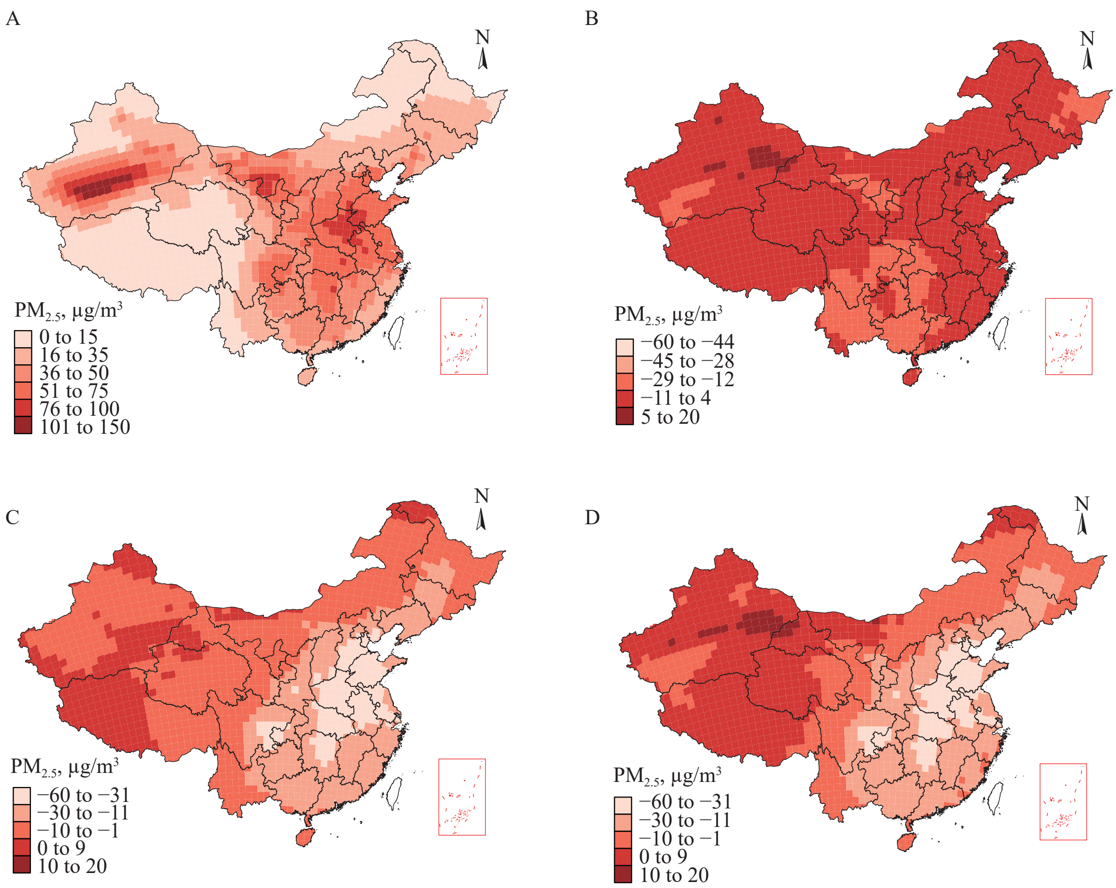

FIGURE 1. Baseline $PM_{2.5}$ concentration in the 2010s and the changes of its predicted concentrations under different scenarios in the 2040s in China. (A) Baseline $PM_{2.5}$ concentrations in the 2010s; (B) Changes of $PM_{2.5}$ concentrations under climate change scenario in the 2040s; (C) Changes of $PM_{2.5}$ concentrations under emission control scenario in the 2040s; (D) Changes of $PM_{2.5}$ concentrations under both climate change and emission control scenarios in the 2040s.

$PM_{2.5}$ concentrations at the national level would decrease from 28.05 μg/m^3 in the 2010s to 18.75 μg/m^3 in the 2040s, with a reduction percentage of 33.16%.

Climate change scenario under RCP4.5 would aggravate the health impacts of $PM_{2.5}$ pollutions on death and YLLs, while the emission control scenario would alleviate the health influence of $PM_{2.5}$ from the 2010s to the 2040s in the national level. The attributable number of deaths related to ambient $PM_{2.5}$ pollutions was estimated to be 1,278,734 in the national level in the 2010s, which comprised of 371,939, 610,694, 177,455, and 118,646 cases from IHD, stroke, COPD, and lung cancer, respectively. In the 2040s, the estimate would increase by 0.96% under the climate change scenario, while it would decrease by 32.20% under the emission control scenario. Considering both the impact of both climate change and emission control, there were an estimated 385,004 fewer deaths, with a reduction percentage of 30.11%. The corresponding YLL would increase by 0.85% under the climate change scenario, while it would decrease by 31.06% under the emission control scenario. The attributable YLLs would decrease from 16,328,977 in the 2010s to 11,577,480 in the 2040s considering both scenarios. There would be 4,751,497 fewer YLL at the national level, with a reduction percentage of 29.10%. The largest reduction number is stroke among the four major diseases (Figure 2).

Table 1 showed the prediction of deaths and YLLs from main types of diseases associated with ambient $PM_{2.5}$ pollutions in different districts of China in the 2040s. Generally, the attributable deaths and YLLs from major diseases would increase in most of the districts in the climate change scenario, with the largest increasing percentage in the east region. While considering both climate change and emission control scenarios, the attributable deaths and YLLs would decrease in the 2040s compared with the 2010s, with the largest percentage change in the Northeast.

DISCUSSION

In this study, the ambient $PM_{2.5}$ in the 2010s and the 2040s in China was simulated. The changes of $PM_{2.5}$ under the scenarios of climate change, emission control, and both climate change and emission control in the 2040s were evaluated. Furthermore, the deaths and YLLs attributable to $PM_{2.5}$ were also assessed. Climate change would aggravate $PM_{2.5}$ pollution and cause adverse health effects, while emission control would reduce $PM_{2.5}$ concentration and alleviate adverse health effects of $PM_{2.5}$ to some degree. The health benefits would be noticeable under the scenario of climate change with emission control. The results were similar to a modelling study conducted in Great Britain which assessed the public health impacts of the air quality changes arising from climate change interventions and indicated that mitigation policies have the potential to generate dramatic improvements in public health through the improvement in air quality (*9*). The findings suggest that emission control may mitigate $PM_{2.5}$-related impacts attributable to climate change and may inform policymaking

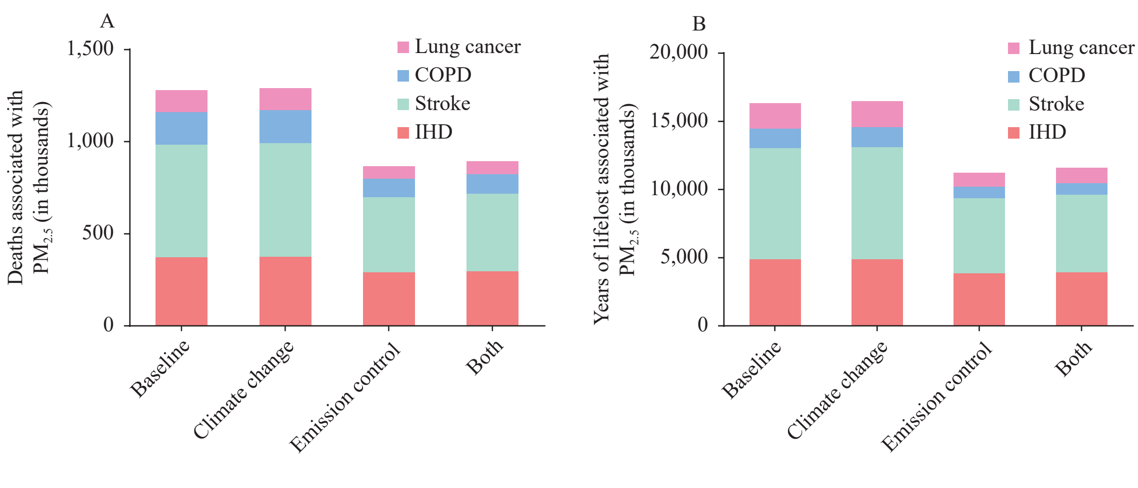

FIGURE 2. Deaths and years of life lost from main types of diseases associated with ambient $PM_{2.5}$ pollution in the national level in the 2010s (baseline) and different scenarios in the 2040s. (A) Deaths associated with $PM_{2.5}$ (in thousands). (B) Years of life lost associated with $PM_{2.5}$ (in thousands).
Abbreviations: COPD=chronic obstructive pulmonary disease; IHD=ischemic heart disease.

TABLE 1. Deaths and years of life lost from main types of diseases associated with ambient $PM_{2.5}$ pollution in different districts in the 2010s and in different scenarios in the 2040s in China.

	Disease	Region	Baseline (2010s)	Emission control (2040s)	Climate change (2040s)	Both scenarios (2040s)
Deaths	Lung cancer	Central	38,961(37,072−40,985)	21,519(20,212−22,825)	39,130(37,309−40,992)	22,109(20,752−23,487)
		East	27,963(25,783−30,140)	16,408(14,688−18,013)	29,371(27,182−31,550)	17,854(16,009−19,647)
		North	26,498(24,619−28,218)	14,537(13,202−15,761)	27,741(25,959−29,476)	16,217(14,873−17,596)
		Northeast	7,446(6,727−8,254)	3,410(2,917−3,866)	7,570(6,724−8,372)	3,325(2,819−3,817)
		Northwest	5,211(4,757−5,652)	3,886(3,509−4,274)	5,283(4,863−5,744)	3,976(3,616−4,353)
		South	12,568(11,544−13,715)	7,352(6,629−8,055)	12,349(11,302−13,432)	7,017(6,294−7,750)
		Subtotal	118,646 (114,756−122,448)	67,112(64,362−69,925)	121,444 (117,581−125,190)	70,498 (67,662−73,192)
	COPD	Central	64,204(61,198−67,190)	35,962(33,880−38,073)	63,973(60,818−67,072)	36,224(34,063−38,449)
		East	36,447(33,740−39,034)	21,779(19,727−23,965)	38,210(35,595−41,120)	23,597(21,496−25,654)
		North	31,488(29,716−33,292)	17,800(16,458−19,084)	32,920(31,243−34,905)	19,710(18,206−21,074)
		Northeast	8,258(7,454−9,026)	3,964(3,460−4,499)	8,393(7,586−9,228)	3,869(3,354−4,396)
		Northwest	11,841(10,900−12,783)	8,919(8,180−9,672)	12,004(11,063−12,987)	9,117(8,342−9,864)
		South	25,217(23,769−26,741)	14,720(13,658−15,827)	24,395(22,823−25,911)	13,894(12,733−14,934)
		Subtotal	177,455(172,588−182,322)	103,144(99,239−106,638)	179,895(175,040−185,082)	106,411(102,670−110,041)
	Stroke	Central	211,289(207,855−214,510)	143,301(140,430−145,945)	211,024(207,658−214,034)	145,453(142,741−148,320)
		East	134,204(130,650−137,631)	94,621(91,183−97,837)	137,556(133,848−141,212)	101,686(98,280−105,428)
		North	114,137(111,590−116,745)	77,724(75,660−80,055)	116,413(113,937−118,848)	85,351(83,266−87,702)
		Northeast	40,158(38,860−41,346)	17,860(17,105−18,580)	40,436(39,159−41,638)	17,379(16,647−18,099)
		Northwest	33,097(32,288−33,905)	26,975(26,238−27,812)	33,454(32,670−34,341)	27,579(26,891−28,303)
		South	77,808(75,814−79,792)	46,743(45,324−48,253)	75,754(73,877−77,502)	44,132(42,768−45,573)
		Subtotal	610,694 (604,864−616,772)	407,224(401,877−412,712)	614,637(608,880−620,705)	421,580(416,769−426,887)
	IHD	Central	122,087(120,667−123,605)	94,903(93,821−95,959)	122,239(120,806−123,808)	96,030(94,922−97,213)
		East	86,372(84,339−88,472)	68,678(67,149−70,229)	88,168(86,186−90,257)	71,379(69,693−73,016)
		North	73,129(71,754−74,462)	56,570(55,614−57,606)	74,447(73,095−75,727)	59,453(58,444−60,418)
		Northeast	28,545(27,984−29,102)	19,549(19,127−19,945)	28,684(28,096−29,275)	19,166(18,780−19,593)
		Northwest	15,877(15,599−16,138)	13,954(13,732−14,182)	16,029(15,778−16,306)	14,209(13,986−14,415)
		South	45,929(44,978−46,852)	35,896(35,282−36,514)	45,404(44,460−46,285)	35,005(34,323−35,639)
		Subtotal	371,939(368,700−375,355)	289,550(287,271−291,731)	374,971(371,754−378,145)	295,242(292,987−297,421)

TABLE 1. (Continued)

	Disease	Region	Baseline (2010s)	Emission control (2040s)	Climate change (2040s)	Both scenarios (2040s)
Years of life lost	Lung cancer	Central	618,254(586,213−649,797)	341,506(319,484−362,722)	621,022(591,164−650,132)	351,005(330,626−373,382)
		East	418,525(382,735−449,965)	245,493(220,072−271,775)	439,634(403,395−473,071)	267,137(241,539−292,445)
		North	420,444(392,967−449,296)	231,199(213,427−249,338)	440,286(411,122−469,785)	257,814(238,033−278,906)
		Northeast	122,896(109,279−136,079)	55,989(48,557−63,878)	124,838(112,378−138,037)	54,451(46,232−62,246)
		Northwest	92,129(83,979−100,523)	68,858(62,224−75,353)	93,412(85,682−102,071)	70,491(64,039−76,854)
		South	195,933(180,046−211,995)	113,982(101,729−125,447)	192,213(176,544−209,435)	108,683(97,777−121,219)
		Subtotal	1,868,180(1,812,549−1,923,629)	1,057,027(1,016,384−1,099,968)	1,911,405(1,853,155−1,968,896)	1,109,581(1,066,029−1,153,705)
	COPD	Central	533,842(508,080−559,411)	298,877(280,884−317,152)	531,693(506,880−555,737)	300,812(283,007−319,205)
		East	264,192(245,779−282,745)	157,595(143,103−171,801)	276,908(258,560−294,864)	170,783(156,431−185,607)
		North	249,773(235,613−264,032)	142,174(132,390−151,925)	261,227(247,682−275,951)	157,236(146,015−168,021)
		Northeast	68,880(62,685−75,530)	32,767(28,474−36,638)	69,885(63,360−76,504)	31,828(27,951−35,856)
		Northwest	115,897(10,6659−125,847)	87,489(80,382−94,952)	117,461(109,153−126,100)	89,434(82,145−96,694)
		South	201,664(190,662−214,335)	116,153(107,836−124,542)	194,344(182,096−205,559)	109,339(101,195−117,871)
		Subtotal	1,434,247(1,396,645−1,473,934)	835,055 (807,109− 862,422)	1,451,518(1,415,206−1,490,994)	859,433 (831,918−888,195)
	Stroke	Central	2,897,759(2,862,356−2,933,572)	1,989,408(1,957,755−2,023,614)	2,894,476(2,857,322−2,928,761)	2,019,695(1,985,656−2,052,569)
		East	1,635,016(1,604,390−1,666,452)	1,166,149(1,135,143−1,192,614)	1,674,562(1,642,650−1,705,592)	1,249,500(1,219,969−1,277,281)
		North	1,512,628(1,488,675−1,536,426)	1,044,102(1,022,670−1,066,083)	1,542,562(1,520,764−1,565,874)	1,141,362(1,118,516−1,164,129)
		Northeast	576,933(562,761−591,702)	264,880(255,562−273,217)	580,051(566,909−594,491)	256,258(247,343−264,957)
		Northwest	524,131(512,919−534,952)	430,440(419,469−440,682)	529,729(517,994−540,703)	440,257(430,930−450,217)
		South	1,024,580(1,006,117−1,041,922)	626,070(613,184−638,980)	995,327(977,612−1,013,550)	591,710(579,543−604,362)
		Subtotal	8,171,047(8,112,361−8,227,274)	5,521,049(5,469,542− 5,570,697)	8,216,707(8,153,930−8,275,064)	5,698,783(5,647,037− 5,751,956)
	IHD	Central	1,615,329(1,601,388−1,629,674)	1,278,244(1,268,105−1,289,128)	1,616,886(1,602,627−1,630,338)	1,291,823(1,280,616−1,303,193)
		East	1,014,773(1,000,467−1,028,710)	820,795(810,026−831,461)	1,034,273(1,020,591−1,048,177)	850,757(839,236−862,970)
		North	951,341(940,914−961,546)	750,993(743,038−759,030)	967,379(955,759−978,445)	786,134(778,072−794,507)
		Northeast	402,678(397,267−408,094)	280,576(276,317−285,381)	404,150(398,385−409,863)	274,587(269,975−278,978)
		Northwest	264,156(260,580−267,665)	234,337(231,380−237,418)	266,697(263,514−269,950)	238,737(235,792−241,603)
		South	607,226(600,696−614,201)	479,783(474,860−485,079)	599,035(592,333−605,730)	467,646(462,523−472,811)
		Subtotal	4,855,503(4,830,782−4,879,767)	3,844,728(3,825,368−3,862,978)	4,888,419(4,862,291−4,914,803)	3,909,683(3,889,792− 3,930,251)

Note: The number in parentheses indicates the 95% confidence interval of the mean death number or years of life lost. Both scenarios indicate considering both climate change and emission control scenarios.

Abbreviations: COPD=chronic obstructive pulmonary disease; IHD=ischemic heart disease.

decisions of emission control to confront climate change.

$PM_{2.5}$ concentrations show an increasing trend with climate change in this study. Climate change is expected to degrade air quality by changing air pollution meteorology, precipitation, and other removal processes and by triggering some amplifying responses in atmospheric chemistry and in anthropogenic and natural sources, which would shape distributions and extreme episodes of particulate matter (*3*). Following higher $PM_{2.5}$ concentrations triggered by climate change, the attributable deaths and YLLs related to $PM_{2.5}$ would increase in most districts. The largest increasing percentage would be in the east region considering high increment in $PM_{2.5}$ concentrations in this region under climate change scenario. Making policies to rival climate change considering the severe health effects and the burden of diseases caused by it is of vital importance. In this modelling study, the measure of emission control could counteract the health impacts attributable to $PM_{2.5}$ generated by climate change due to reduction of $PM_{2.5}$ concentrations. Among the main types of diseases, stroke had the most noticeable health benefits. The evidence emphasizes the necessity of evaluating the effects of mitigation policies such as emission control on health impacts triggered by climate change, which could verify the effectiveness and evaluate the benefits of the policies and, in turn, inform policymaking decisions.

For different districts, the health benefits of avoiding attributable deaths and YLLs from main types of diseases associated with ambient $PM_{2.5}$ pollution varied. The deaths and YLLs from main types of diseases experienced the largest decreasing percentage in the Northeast region under both the climate change and emission control scenarios, which may result from the large reduction percentage of $PM_{2.5}$ concentration in this region.

This study was the first to estimate the health impacts related to ambient $PM_{2.5}$ from both climate change and air pollution emission control under different scenarios in China, and it provided evidence for policymaking related to climate change and emission control. However, the study was subject to some limitations. First, the emission control scenario was designed based on RCP4.5, which only stands for a moderate level of greenhouse gas emissions. Second, accounting for some factors, such as population structure, would affect the climate-related health burden in the future (*10*), and assuming that the $PM_{2.5}$-mortality association, mortality rate, and population structure were constant at the 2010s levels might lead to some deviations. Further exploration should be performed if data are available.

In summary, the findings suggest the ambient $PM_{2.5}$-related health benefits from air pollution emission control outweighed the influence of climate change. The health impacts of $PM_{2.5}$ related to climate change should be prioritized in the future.

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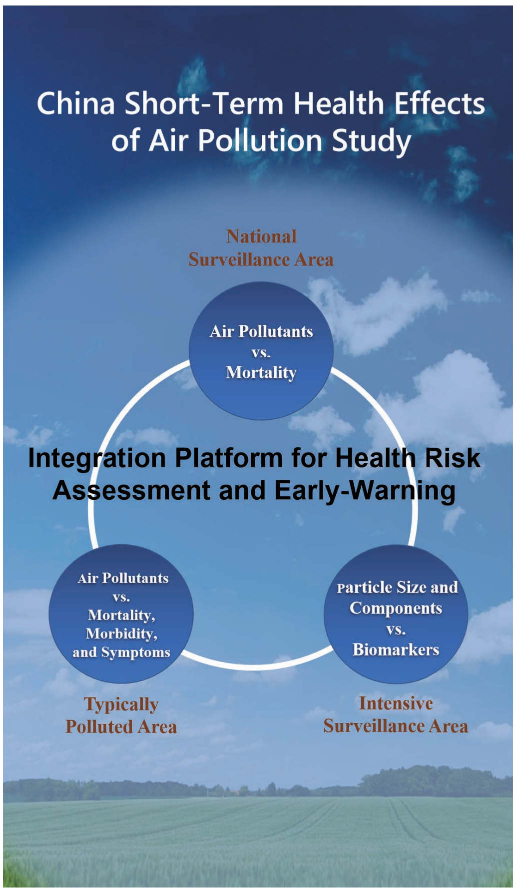

AIR POLLUTION AND HUMAN HEALTH ISSUE

Foreword

Preplanned Studies

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This week's issue was organized by Guest Editor Xiaoming Shi.

Foreword

Acute Effects of Air Pollution on Human Health in China: Evidence and Prospects

The adverse impacts of air pollution on human health have already been a major environmental issue globally, and the challenges are even more severe in China. The World Health Organization (WHO) estimates that 4.2 million deaths annually can be attributed to outdoor air pollution in 2016 (*1*). For example, ambient fine particulate matter ($PM_{2.5}$) has been ranked as the fourth leading risk factor for disease in China (*2*). Atmospheric ozone (O_3) pollution has demonstrated an increasing trend year by year, and the problem of regional compound pollution has become prominent. Therefore, the acute health hazard of air pollution is a major environmental, medical, and public health burden in China. Clarifying the exposure-response relationships between complex air pollution and population-based acute health effects are great strategic demands. With funding from the National Key Research and Development Program of the Ministry of Science and Technology, the "China Short-Term Health Effects of Air Pollution Study" (China SHEAP Study) project was carried out in 2016 and hosted by the National Institute of Environmental Health (NIEH) of China CDC. This project gathered domestic research and development institutions specialized in national public health and clinical medicine to jointly undertake the task. During the four-year implementation period, the project has achieved a series of innovative findings: 1) it clarified the acute impact of short-term exposure of air pollutants on death of residents and their spatiotemporal distribution characteristics in 106 regions nationwide; 2) it systematically evaluated the acute exposure-response relationships between particulate matter (PM) as well as gaseous pollutants and death, morbidities and symptoms of respiratory and cardiovascular diseases in typically polluted cities from three regions and ten urban agglomerations that conducted national air pollution prevention and control; 3) identified acute health effects of differential particle size and chemical component exposures on children, healthy adults, and patients with cardiopulmonary diseases and determined the particles and their components with major toxicity potency; and 4) conducted intervention research to assess the impact of different intervening measures on acute health hazards of air pollution. Through multilevel and multidimension data as well as the integration of key technologies, this project illustrated the distribution characteristics of population-based acute health risks of complex air pollution and established a dataset for complex air pollution and health as well as a data integration platform.

In this special issue, we invited colleagues and collaborators involving in the China SHEAP study project to report their latest findings. For example, Niu et al. examined the associations between air pollutants with daily hospitalizations and outpatient visits of chronic obstructive pulmonary disease (COPD) and asthma within 5 Chinese cities. The results showed that air pollutants were significantly related to the increasing outpatient and hospitalization rates of chronic respiratory diseases (*3*). Liu et al. assessed the associations of short-term $PM_{2.5}$ mass exposure with several ambulatory blood pressure (BP) monitoring indicators from a panel study conducted in Beijing, Shanghai, Wuhan, and Xi'an. The results indicated that short-term $PM_{2.5}$ exposure was significantly associated with BP elevations (*4*). Xia and Niu et al. evaluated the associations between personal O_3 exposure and biomarkers of inflammation, oxidative stress, and mitochondria oxidative damage among 43 college students in Shanghai. They found that short-term exposure to low concentrations of O_3 was significantly associated with vascular inflammation, lipid peroxidation, and mitochondrial oxidative damage (*5*). By conducting a randomized crossover study in Beijing, Zhang et al. found that short-term co-exposure to multiple ambient pollutants could disturb the cardiac autonomic function, and that black carbon (BC) and noise were the two pollutants with the greatest contribution (*6*). Finally, Chen et al. applied two time-series approaches with a two-stage statistical analysis to estimate whether and how temperature-modified acute effects of O_3 affected mortality in Beijing Municipality, Tianjin Municipality, Hebei Province, and surrounding areas. The results suggested that short-term exposure to O_3 was significantly associated with the increased risk of mortality and that the association was positively modified by relative higher (>75th 24 h-average temperature) or extreme cold temperature (<10th 24 h-average temperature) (*7*).

In summary, the above studies employed different epidemiological designs to assess the impact of short-term air pollution exposure on multidimensionally adverse health outcomes. These provocative findings warrant a multiomics approach to comprehensively explore the etiological evidence, the underlying mechanisms, and the causal linkages between air pollution and health effects in China, relying on the available list of biomarkers associated with key toxic components of air pollutants. In view of the compound characteristics of air pollution complex in China, establishing innovative technologies and methods for health risk assessments of multiple exposures simultaneously as well as illustrating their joint effects and mechanisms are highly needed. In addition, the development of early warning techniques for health risks may promote residents to efficiently take actions and protections against air pollution exposures and their health hazards.

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Preplanned Studies

Exposure Response Relationship of Acute Effects of Air Pollution on Respiratory Diseases — China, 2013–2018

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Summary

What is already known about this topic?

Short-term exposure to air pollutants has been associated with chronic obstructive pulmonary disease (COPD) and asthma, which needs continuous observation.

What is added by this report?

This study uses the longest time series data so far from 2013 to 2018 and adds additional data analysis for ozone (O_3) to existing studies.

What are the implications for public health practice?

This study suggests that air pollutants have certain acute effects on outpatient and hospital admission of patients with COPD and asthma, which can be combined with the disease diagnosis and treatment guidelines to guide clinical practice.

Chronic obstructive pulmonary disease (COPD) and asthma are two major chronic airway diseases. Recent studies have focused on the relationship between air pollution and the development of acute exacerbations of COPD and asthma. In 2021, Liu et al. found that fine particulate matter (particles with aerodynamic diameter ≤2.5 μm; $PM_{2.5}$) and nitrogen dioxide (NO_2) increased the risk of COPD and asthma (*1*). Doiron et al. found that $PM_{2.5}$, particles with aerodynamic diameter ≤10 μm (PM_{10}) and NO_2 significantly enhanced the morbidity of COPD (*2*). However, in 2014, a study found that neither NO_2 nor PM levels were associated with COPD morbidity (*3*). It can be concluded that there is no clear conclusion whether short-term exposure to air pollution increases the health risk of COPD and asthma patients. Meanwhile, in China, the available studies about air pollution are based on a three-year time series of data from 2013–2015 (*4*), which may not reflect the health effects of recent air quality improvement initiatives. Therefore, we analyzed daily outpatient and hospitalization data from the China CDC Disease Surveillance Point System (DSPs) from January 1, 2013 to December 31, 2018 to explore the impact of short-term exposure to air pollution on the acute effects of patients with COPD and asthma.

This study collected inpatient and outpatient data for respiratory diseases, concentration of each air pollutant, as well as temperature and relative humidity data from January 1, 2013 to December 31, 2018 in 16 hospitals in China in 5 cities (6 districts and counties). We used the International Classification of Diseases Revision 10 (ICD-10) codes J40–J44 for COPD visits and codes J45–J46 for asthma. Relevant air pollution data was obtained from the National Urban Air Quality Real-Time Release Platform, and temperature and relative humidity was obtained from the National Meteorological Information Center.

Pollutant concentrations were aggregated to daily means [carbon monoxide (CO), sulfur dioxides (SO_2), NO_2, $PM_{2.5}$, and PM_{10}] and daily maximum 8-hour means (O_3).

We used a time-stratified case-crossover design to analyze the associations between air pollution and hospital admissions for respiratory diseases. A time stratum was defined as a combination of year, month, and day-of-week levels. This design allows for the adjustment of long-term and seasonal trends. We then fit a generalized linear model (GLM) with a Poisson distribution. Daily mean temperature and relative humidity were also controlled by the natural spline function in the model. The “stats” package in R software (version 4.0.2, R Foundation for Statistical Computing, Vienna, Austria) was used for analysis. Results were presented as the percentage changes and 95% confidence intervals (CIs) in daily inpatient and outpatient rates associated with a per 10 $\mu g/m^3$ increase in air pollutants (CO is mg/m^3). We also assessed the single-day lag effect (from 0 to 3) and the cumulative lag effect (0–1, 0–2, and 0–3) of air pollutants on daily outpatient and hospitalization rates.

In total, 85,961 outpatient visits and 62,381 hospital admissions were observed for COPD and asthma in 16 hospitals from 2013 to 2018.

Table 1 shows the mean pollutant concentrations,

TABLE 1. Daily counts of hospitalizations and outpatient visit for respiratory diseases and air pollution levels in China, 2013–2018.

Variables	Mean (SD)
Outpatient visit (daily counts per county)	
COPD	38 (18)
Asthma	8 (5)
Hospitalizations (daily counts per county)	
COPD	6 (4)
Asthma	3 (2)
Pollutants	
$PM_{2.5}$ (μg/m^3)	59.1 (43.4)
PM_{10} (μg/m^3)	95.9 (61.9)
O_3 (μg/m^3)	112.8 (59.3)
SO_2 (μg/m^3)	19.8.2 (17.2)
NO_2 (μg/m^3)	47.9 (21.3)
CO (mg/m^3)	1.1 (0.7)

Abbreviations: SD=standard deviation; COPD=chronic obstructive pulmonary disease; $PM_{2.5}$=particulate matter ≤2.5 m in diameter; PM_{10}=particulate matter ≤10 m in diameter; SO_2=sulfur dioxides; NO_2=nitrogen dioxide; CO=carbon monoxide; O_3=ozone.

and the average daily respiratory disease hospitalizations and outpatient visits in the study areas (expressed as mean and standard deviation). The average daily respiratory disease outpatient visits were approximately 38 for COPD and 8 for asthma, 6 for COPD, and 3 for asthma in daily hospital admissions.

Atmospheric pollutants had an acute effect on the risk of hospitalization for COPD (Figure 1A), and the acute effects of $PM_{2.5}$, O_3, and CO on the risk of hospitalization for COPD were most pronounced at lag02, with each 10 μg/m^3 increase in $PM_{2.5}$, O_3, and CO increasing the risk of hospitalization for COPD by 1.1% (95% CI: 0.6%–1.7%), 1.7% (95% CI. 1.3%–2.1%), and 88.2% (95% CI: 6.7%–232%). However, no acute effect of air pollutants on the risk of hospitalization for asthma was seen (Figure 1B).

In patients with COPD, O_3 was negatively associated with an increased risk of outpatient visits for COPD (Figure 2A), and NO_2 was positively associated with increased risk of outpatient visits for COPD, most strongly at lag02, with each 10 μg/m^3 increase in NO_2 associated with a 2.4% (95% CI: 0.4%, 4.4%) increase in risk of outpatient visits for patients with COPD.

Among asthma patients, $PM_{2.5}$ and PM_{10} were negatively associated with the risk of outpatient visits (Figure 2B), with the strongest at lag1, where each 10 μg/m^3 increase in $PM_{2.5}$ and PM_{10} was associated with a 0.6% (95% CI: –0.9%, –0.2%) and 0.4% (95% CI: –0.7%, –0.2%) decrease in the risk of outpatient visits for asthma patients, respectively. O_3, SO_2, and NO_2 were positively associated with increased risk of outpatient asthma visits and were strongest at lag02, with each 10 μg/m^3 increase in O_3 and NO_2 increasing the risk of outpatient asthma visits by 0.9% (95% CI: 0.5%, 1.3%) and 2.9% (95% CI: 2%, 3.8%), respectively. The acute effect of SO_2 on outpatient asthma visits was strongest at lag2, with each 10 μg/m^3 increase in SO_2 increasing the risk of outpatient visits for asthma patients by 1.1% (95% CI: 0.1%, 2.1%).

DISCUSSION

This study showed that air pollutants were related to increasing outpatient and hospitalization rates of chronic respiratory diseases. $PM_{2.5}$, O_3, and CO had an acute effect on the risk of hospitalization, and NO_2 was positively associated with an increased risk of outpatient visits for COPD. In asthma patients, O_3, SO_2, and NO_2 were positively associated with an increased risk of outpatient asthma visits. These results were basically consistent with the results of previous studies. Each 10 μg/m^3 increase in $PM_{2.5}$ was associated with a 1.61% increase in the risk of hospitalization for patients with COPD in the United States and 0.82% in Beijing (*5*–*6*).

The present study showed that CO was positively associated with the risk of hospitalization in patients with COPD, which was inconsistent with the results of previous relevant studies. A few epidemiological studies have found that low levels of CO may have a protective effect in some cases. A time-series study in Hong Kong, China showed that short-term exposure to CO was associated with a reduced risk of hospitalization for COPD (*7*). However, in Spain, a retrospective study found that elevated CO levels were associated with increased hospital admissions in patients with COPD (*8*), which was the same as our results. Therefore, further studies are needed to confirm the direct health effects of CO exposure on patients with COPD. At the same time, our study shows that $PM_{2.5}$ and PM_{10} were negatively associated with the risk of asthma outpatient visits, which was inconsistent with previous research results. A possible reason is that the concentrations of ozone and $PM_{2.5}$ are seasonal and that asthma is affected by many factors. The overall confounders that could affect the association between pollutants and asthma exacerbations also need to be taken into

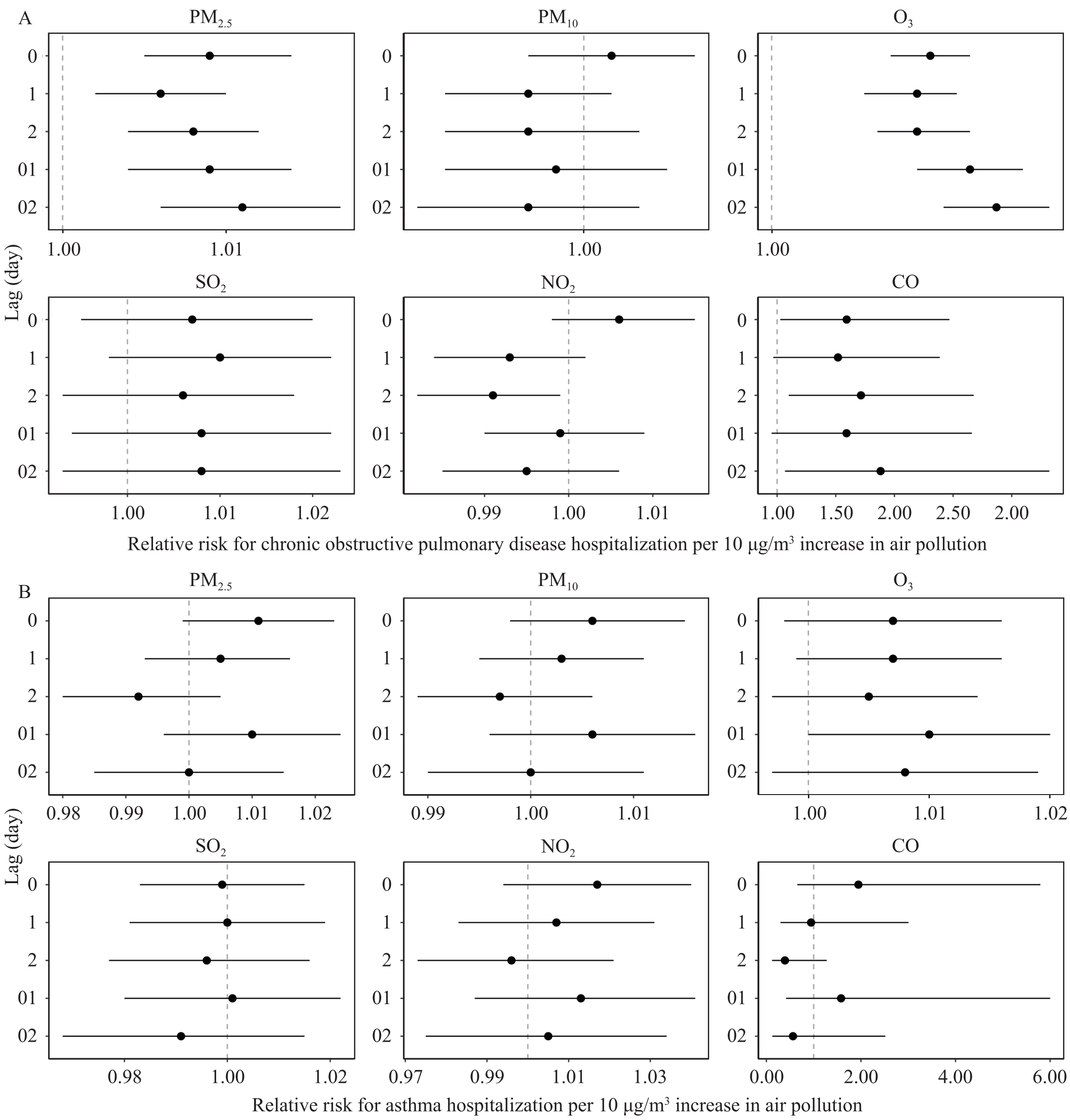

FIGURE 1. Relative risk for chronic obstructive pulmonary disease (A) and asthma (B) daily hospitalization per 10 μg/m^3 increase in concentrations of air pollutants with different lag days in 16 hospitals, 2013–2018.

account and include meteorological factors and data for pollen.

The observed acute effects of particulate matters on respiratory diseases could be explained by inducing an imbalance of systemic inflammation, oxidative stress, autophagy, and apoptosis, and by affecting epigenetic modification. Studies showed that elevated level of blood biomarkers of systemic inflammation (e.g., IL-6, IL-8 and TNF-α), coagulation (e.g., fibrinogen), soluble cluster of differentiation 40 ligands (sCD40L), soluble intercellular adhesion molecule-1 (sICAM-1), and fibrinogen, as well as DNA methylation levels were influenced by exposure to air pollutants (*9–10*).

This study was subject to some limitations. First, the acquisition of air pollution exposure data was from air monitoring stations, which might have some measurement errors. At the same time, the data of the monitoring station cannot fully represent the real exposure of patients, and there will be some exposure errors. Second, we did not obtain data on influenza, seasons and pollen, socioeconomic status, and daily activities, which may be some confounding factors related to outpatient visits and hospitalization. Third, we only analyzed the effects of one air pollutant on disease, but not the effects of exposure to multiple air pollutants. These deficiencies may make our results

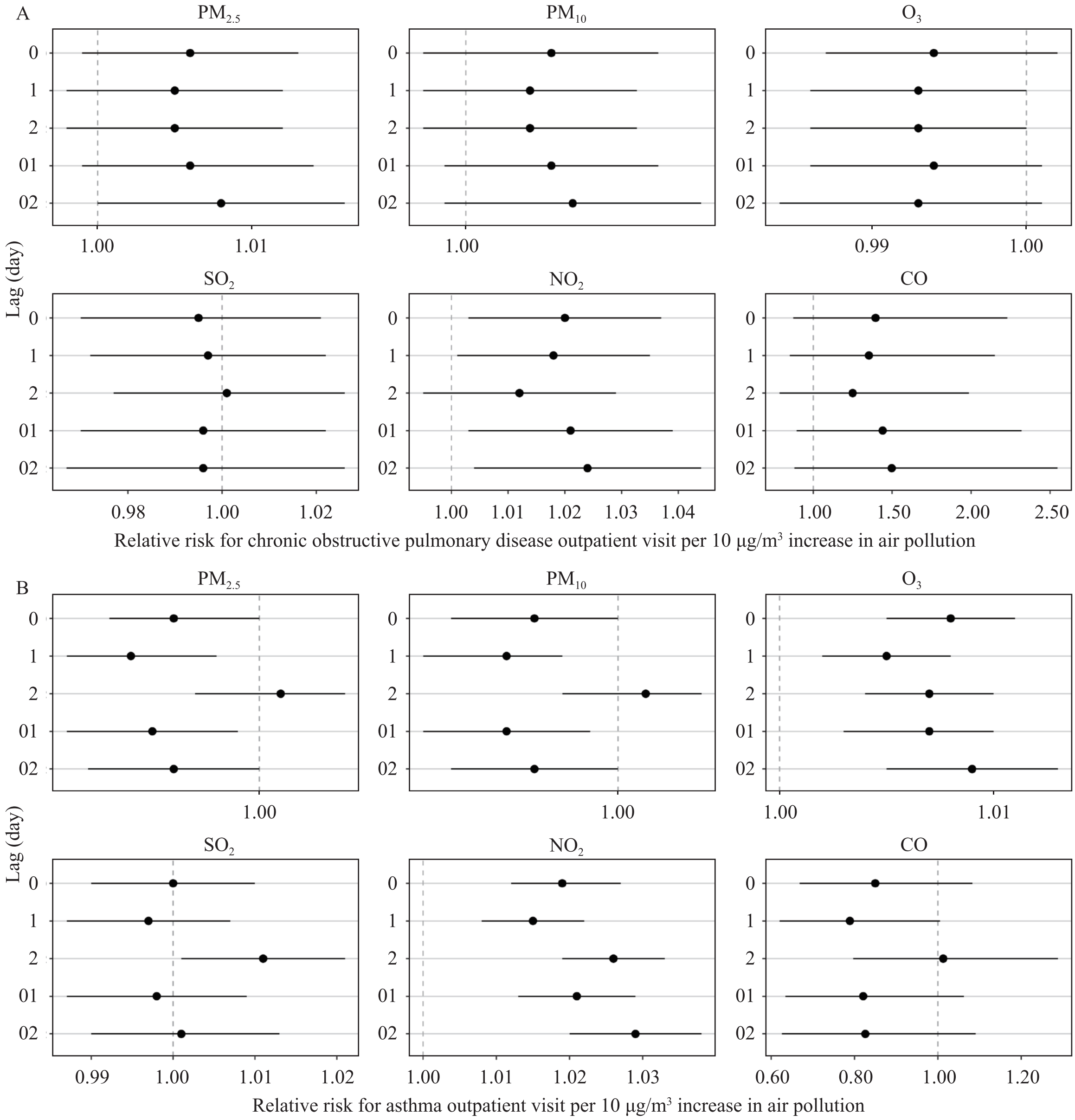

FIGURE 2. Relative risk for chronic obstructive pulmonary disease (A) and asthma (B) outpatient visits per 10 μg/m^3 increase in concentrations of air pollutants with different lag days in 16 hospitals, 2013–2018.

deviate to a certain extent, which needs further exploration.

In conclusion, exposure to $PM_{2.5}$, O_3, SO_2, NO_2, and CO has certain acute effects on outpatient and hospital admission of patients with COPD and asthma. Relevant susceptible people should try to reduce going out under the condition of air pollution to avoid aggravation of the disease. Meanwhile, these findings should be combined with disease diagnosis and treatment guidelines to guide clinical practice. This study not only paid attention to PM, but also emphasized that ozone cannot be ignored, which provides a reference for future research on the impact of PM and ozone coordinated prevention and control and on the effects of carbon neutralization on health.

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Preplanned Studies

Impacts of $PM_{2.5}$ on Ambulatory Blood Pressure Monitoring Indicators Attenuated by Blood Pressure Control Status and Treatment — Two Cities and Two Municipalities, China, 2017−2019

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Summary

What is already known about this topic?

Short-term $PM_{2.5}$ exposure has been associated with hourly, 24-hour, daytime, and nighttime blood pressure (BP) levels, and further studies focusing whether and how the associations with other ambulatory BP monitoring indicators are warranted.

What is added by this report?

This study observed that short-term $PM_{2.5}$ exposure was associated with BP elevations and was the first to report the associations of short-term $PM_{2.5}$ exposure with BP variability. Circadian rhythm of BP and BP load among hypertensive patients were found to be modified by controlled BP status or taking angiotensin receptor blockers (ARBs).

What are the implications for public health practice?

This study suggested that antihypertensive therapy, especially with well-controlled BP status may be potential measurements to attenuate adverse impacts of $PM_{2.5}$ for hypertensive patients with intermediate-to-high risk of cardiovascular disease (CVD).

High blood pressure (BP) is the leading risk factor for cardiovascular disease (CVD) in China. Previous studies from either lowly or highly polluted regions have revealed that increased fine particulate matter (particles with aerodynamic diameter ≤2.5 μm; $PM_{2.5}$) exposure was associated with elevated BP levels and higher risk of hypertension (*1*). In recent years, using personal portable devices to record individual $PM_{2.5}$ exposure and ambulatory BP monitoring (ABPM) to measure BP levels periodically, panel studies also identified the relationship of short-term $PM_{2.5}$ exposure with hourly, 24-hour, daytime, and nighttime average BP levels (*2*–*3*). However, few studies assessed the adverse impacts of $PM_{2.5}$ with other ABPM indicators, such as BP variability, circadian rhythm of BP, and BP load, and the modifying effects of BP control status and antihypertensive therapy were also unclear. To clarify these issues, these associations were assessed using a multicity and municipality panel study conducted from 2017 to 2019 in China. BP levels and BP load elevation were associated with short-term $PM_{2.5}$ exposure. Further stratified analyses demonstrated that the adverse impacts of $PM_{2.5}$ on BP variability, circadian rhythm of BP, and BP load were attenuated among patients with well-controlled BP or taking angiotensin receptor blockers (ARBs), which provided hints about the prevention of $PM_{2.5}$-related adverse outcomes.

This study used data from a three-phase (winter, summer, spring/autumn) panel study conducted in Beijing, Shanghai, Wuhan, and Xi'an from 2017 to 2019. This panel study recruited participants at intermediate-to-high risk of CVD who were defined as having prehypertension or hypertension combined with at least 1 of the 3 conditions (i.e., central obesity, diabetes mellitus, and dyslipidemia) from the community (*2*). Questionnaires were administrated to collect demographic characteristics, lifestyle and risk factors, medication uses, etc. Each participant carried a portable monitor to measure real-time individual $PM_{2.5}$ from the first day to the third day during each phase, and a 24-hour ABPM was scheduled on the third day. This study was approved by the Institutional Review Board of Fuwai Hospital in Beijing, and written informed consent was obtained from all participants before data collection.

This study assessed the association of short-term $PM_{2.5}$ exposure with several ABPM indicators, including 24-hour, daytime, and nighttime average systolic BP (SBP) and diastolic BP (DBP), SBP and

DBP variability (i.e., the standard deviation of BP), SBP and DBP load [i.e. the percentage of the counts for BP readings beyond certain threshold (130/80 mmHg, 135/85 mmHg, and 120/70 mmHg for 24-hour, daytime and nighttime, respectively)], and the percentage of nocturnal BP decline [i.e., (daytime BP-nighttime BP)/daytime BP×100%]. In addition, three methods were used to calculate morning BP surge, including morning BP (i.e., the average BP during the first 2 hours after waking), pre-waking BP surge (i.e., the mean BP during the 2 hours after waking minus the mean BP during the 2 hours before waking), and sleep-trough BP surge (the mean BP during the 2 hours after waking minus the mean BP of the lowest BP and the BP before and after the lowest one during sleeping). The exposure windows of $PM_{2.5}$ included the concurrent day with ABPM (lag0d), lag 1 day (lag1d), lag 2 days (lag2d), and moving average of previous 2 days (MA2d). Estimated changes and 95% confidence intervals (CIs) with per interquartile range (IQR) increment of $PM_{2.5}$ exposure (41.96 $\mu g/m^3$) were calculated using a mixed linear model adjusted for age, gender, current alcohol drinking status, ideal level of physical activity, body mass index (BMI), antihypertensive medication uses, diabetes mellitus, dyslipidemia, and natural splines with 3 degrees of freedom for the daily average of personal environmental temperature and relative humidity at the same exposure windows as $PM_{2.5}$. City-specific and subject-specific random intercepts were used to account for the variations in different cities and within-subjects correlations. Stratified analysis of BP control status (hypertensive patients with SBP/DBP of less than 140/90 mmHg were defined as individuals with controlled BP, otherwise as uncontrolled BP), and for those with uncontrolled BP, a further stratified analysis of ARB uses was conducted. Z tests were conducted to explore the group difference. All analyses were performed using the SAS software (version 9.4; SAS Institute, Cary, NC, USA). A 2-side P of <0.05 was demonstrated statistical significance.

After excluding participants attending only one visit, those missing ABPM data or not fulfilling the valid criteria of ABPM data and prehypertensive patients, a total of 277 hypertensive patients with 802 visits were included for analysis. At baseline, the average age was 59.1±8.5 years and 113 (40.8%) participants were men. The mean office SBP and DBP were 134.5 mmHg and 80.4 mmHg, respectively. Overall, 91.7% patients were taking antihypertensive medications, with 33.2% being taking ARBs (Table 1). Across the three phases, a total of 557 (69.5%) visits reached well-controlled BP status. Among those without controlled BP, 65 (26.5%) visits had been taking ARBs. Generally, short-term $PM_{2.5}$ exposure was associated with BP levels and BP load; for example, the 24-hour, daytime, and nighttime average SBP increased by 0.68 mmHg (95% CI: 0.07–1.29), 0.82 mmHg (95% CI: 0.19–1.45) and 0.93 mmHg (95% CI: 0.17–1.70) per IQR increment of the lag2d $PM_{2.5}$ concentration (Figure 1A). The 24-hour SBP load and DBP load increased by 1.28% (95% CI: 0.01%–2.56%) and 1.38% (95% CI: 0.22%–2.54%), respectively, with per IQR increment of the lag1d $PM_{2.5}$ concentration (Figure 1C). However, short-term $PM_{2.5}$ exposure may not be associated with BP variability, morning BP surge, or the percentage of nocturnal BP decline (Figure 1B, 1D, 1E). When stratified by BP control status, the increment of 24-hour or daytime BP levels associated with $PM_{2.5}$ exposure tended to be higher among those with uncontrolled BP, but the difference was not statistically significant (Figure 2A). Those with uncontrolled BP were more prone to have higher morning BP surges than those with controlled BP. For example, per IQR increment of the lag2d $PM_{2.5}$ concentration was associated with 2.19 mmHg (95% CI: 0.47–3.91), 1.72 mmHg (95% CI: 0.20–3.24) and 1.47 mmHg (95% CI: -0.14–3.07) elevation for morning SBP, pre-waking SBP surge, and sleep-trough SBP surge, respectively, among patients without controlled BP, while no significant changes were noted in patients with controlled BP (all P<0.05) (Figure 2D). Among patients with uncontrolled BP, the association of $PM_{2.5}$ exposure with 24-hour, daytime SBP variability was modified by treatment with ARB. For example, 24-hour SBP variability increased by 0.49 mmHg (95% CI: -0.22–1.20) per IQR increment of lag0d $PM_{2.5}$ exposure among patients taking ARB, which was significantly higher than those not taking ARB (Figure 2G). In addition, patients taking ARB were more likely to have better circadian rhythms for DBP (Figure 2J).

DISCUSSION

This study observed that short-term $PM_{2.5}$ exposure was associated with BP elevations and BP load and was the first to report the associations of short-term $PM_{2.5}$ exposure with BP variability, as well as the circadian rhythm of BP among hypertensive patients being

TABLE 1. Baseline characteristics of study participants in two cities and two municipalities, China, 2017−2019.

Characteristics	Overall (n=277)	Beijing (n=64)	Shanghai (n=68)	Wuhan (n=75)	Xi'an (n=70)
Age, years	59.1±8.5	53.5±8.1	60.3±8.6	62.6±6.0	59.3±8.8
Male, n (%)	113 (40.8)	35 (54.7)	23 (33.8)	23 (30.7)	32 (45.7)
BMI, kg/m^2	26.2±3.2	27.2±2.6	25.0±3.0	26.1±3.5	26.6±3.2
Current alcohol drinking status, n (%)	67 (24.2)	29 (45.3)	11 (16.2)	12 (16.0)	15 (21.4)
Ideal level of physical activity, n (%)	101 (36.5)	23 (35.9)	14 (20.6)	35 (46.7)	29 (41.4)
Central obesity, n (%)	184 (66.4)	53 (82.8)	28 (41.2)	57 (76.0)	46 (65.7)
Office SBP, mmHg	134.5±13.6	134.1±11.4	134.4±12.0	132.6±15.4	137.2±14.7
Office DBP, mmHg	80.4±10.8	83.3±9.4	79.9±13.0	76.7±8.6	82.1±10.7
Diabetes mellitus, n (%)	78 (28.2)	13 (20.3)	29 (42.6)	16 (21.3)	20 (28.6)
Dyslipidemia, n (%)	224 (80.9)	54 (84.4)	55 (80.9)	63 (84.0)	52 (74.3)
Antihypertensive drug use, n (%)	254 (91.7)	54 (84.4)	64 (94.1)	70 (93.3)	66 (94.3)
ACE inhibitor	18 (6.5)	4 (6.3)	2 (2.9)	5 (6.7)	7 (10.0)
ARB	92 (33.2)	15 (23.4)	36 (52.9)	27 (36.0)	14 (20.0)
β-receptor blocker	36 (13.0)	14 (21.9)	6 (8.8)	5 (6.7)	11 (15.7)
CCB	161 (58.1)	42 (65.6)	30 (44.1)	49 (65.3)	40 (57.1)
Diuretics	16 (5.8)	2 (3.1)	6 (8.8)	4 (5.3)	4 (5.7)
Others	13 (4.7)	5 (7.8)	1 (1.5)	2 (2.7)	5 (7.1)
One type of medications	178 (64.3)	32 (50.0)	48 (70.6)	49 (65.3)	49 (70.0)
Two types of medications	61 (22.0)	16 (25.0)	12 (17.6)	18 (24.0)	15 (21.4)
Three or more types of medications	15 (5.4)	6 (9.4)	4 (5.9)	3 (4.0)	2 (2.9)
$PM_{2.5}$, μg/m^3					
Lag0d	50.1±43.9	49.8±45.3	33.6±32.3	57.4±37.8	57.5±52.3
Lag1d	48.5±46.0	48.4±47.9	31.3±26.0	52.4±36.6	60.1±60.4
Lag2d	54.2±50.9	64.6±66.8	34.0±34.6	66.6±45.6	51.8±47.0
MA2d	51.2±44.6	56.5±51.0	32.9±29.0	59.4±38.2	55.8±51.7
PET, ℃					
Lag0d	22.3±5.5	23.8±3.8	20.9±6.1	21.8±7.1	22.5±4.3
Lag1d	22.1±5.7	23.7±4.2	21.1±5.9	21.3±7.3	22.5±4.5
Lag2d	22.2±5.6	23.6±3.8	21.2±5.8	21.2±7.3	22.9±4.2
MA2d	22.1±5.6	23.6±3.9	21.1±5.8	21.2±7.3	22.7±4.3
Relative humidity, %					
Lag0d	53.5±16.2	40.8±17.3	66.1±11.1	59.6±10.8	49.3±12.6
Lag1d	54.7±16.0	41.8±17.3	67.5±10.6	61.1±10.0	49.4±12.0
Lag2d	54.1±15.6	41.6±17.9	64.7±7.9	62.7±8.7	47.2±12.2
MA2d	54.5±15.4	41.7±17.3	65.7±8.6	61.9±9.0	48.3±11.8

Note: Results are presented as mean±SD for continuous variables, and frequency (proportion) for categorical variables.
Abbreviations: SD=standard deviation; BMI=body mass index; SBP=systolic blood pressure; DBP=diastolic blood pressure; ACE=angiotensin-converting enzyme; ARB=angiotensin receptor blockers; CCB=calcium channel blocker; $PM_{2.5}$=particles with aerodynamic diameter ≤2.5 μm; PET=personal environmental temperature; lag0d=current day with BP measurement; lag1d=lag of 1 day; lag2d=lag of 2 days; MA2d=the 2-day moving average of $PM_{2.5}$.

modified by a controlled BP status or by taking ARBs.

BP follows a circadian rhythm with an increase in the morning after waking and a dip during sleep. The existing studies have demonstrated that a disturbed circadian rhythm, including increases of pre-waking BP surges or blunted nocturnal BP declines were associated with increased CVD risk (*4*). In addition, BP variability and BP load were also associated with

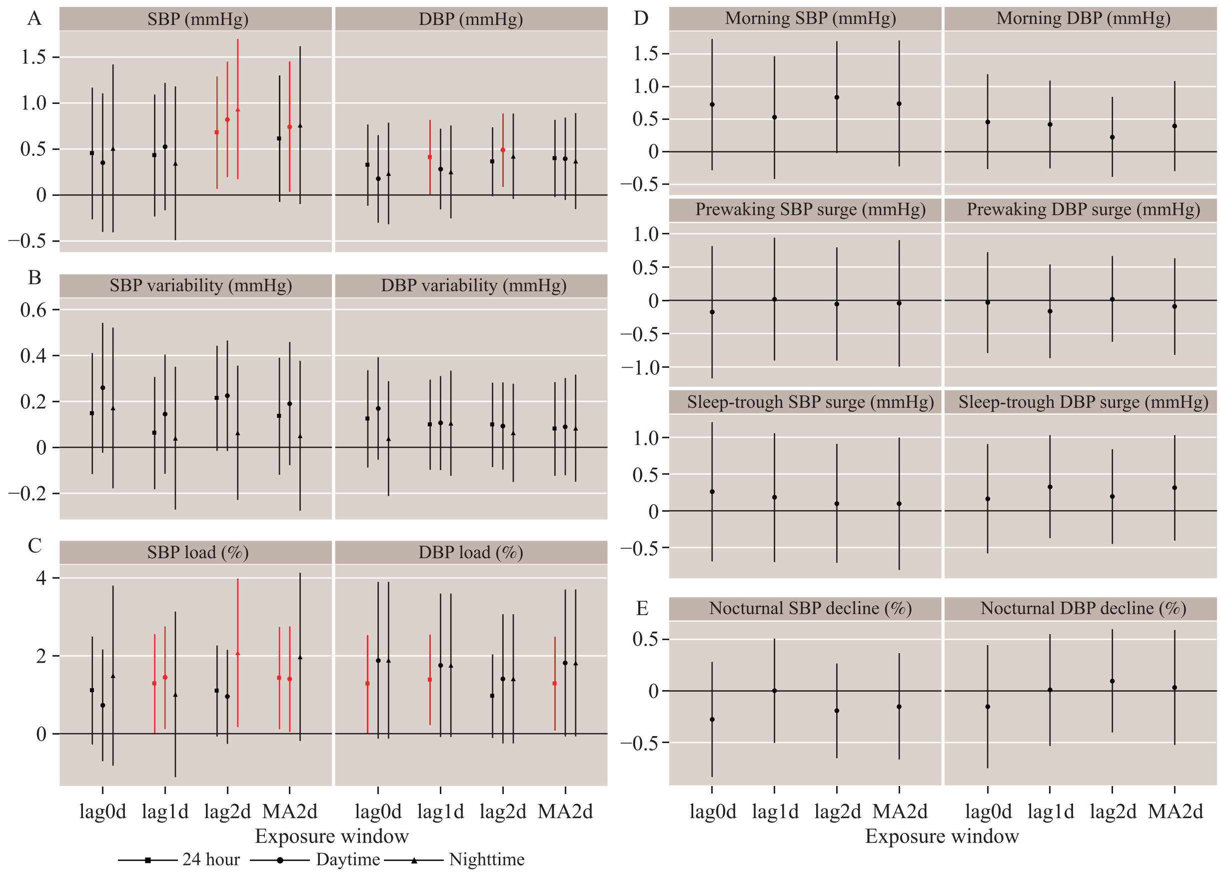

FIGURE 1. Estimated changes and 95% CIs of BP levels (A), BP variability (B), BP load (C), morning BP surge (D) and the percentage of nocturnal BP decline (E) with per IQR (41.96 μg/m^3) of $PM_{2.5}$ exposure among participants in two cities and two municipalities, China, 2017−2019

Note: Statistically significant changes were shown in red.

Abbreviations: CI=confidence interval; BP=blood pressure; IQR=interquartile range; $PM_{2.5}$=particles with aerodynamic diameter ≤2.5 μm; SBP=systolic blood pressure; DBP=diastolic blood pressure; lag0d=current day with BP measurement; lag1d=lag of 1 day; lag2d=lag of 2 days; MA2d=the 2-day moving average of $PM_{2.5}$.

CVD or all-cause mortality (*5–6*). Up to now, only one study has found that increased short-term PM_{10} exposure was associated with blunted SBP dipping, and evidence for $PM_{2.5}$ is still very lacking (*7*). Therefore, findings from the current study may provide evidence on the mechanism linking air pollution to increased CVD risk, and potential preventive measurements, such as a well-controlled BP and taking ARBs, to attenuate the adverse impacts of $PM_{2.5}$.

Sympathetic nerve activation may play a role in the morning BP surge (*8*), and nocturnal BP non-dipping may be associated with endothelial dysfunction (*9*). In accordance with the findings of this study, people reaching well-controlled BP had more stable ANS, hence the adverse impacts of $PM_{2.5}$ on morning BP surges were attenuated. On the other hand, exposure to $PM_{2.5}$ may increase angiotensin II (*10*), which could induce oxidative stress and inflammation and further promote endothelial dysfunction. ARBs could inhibit the effects of angiotensin II. The potential endothelial dysfunction among patients without taking ARBs interfered the dipping of nocturnal BP. Additionally, the different lag effect trends of $PM_{2.5}$ on different BP traits may be due to the various mechanisms of $PM_{2.5}$-mediated BP elevation, which is an issue worth to exploring in future.

This study firstly reported the association of short-term $PM_{2.5}$ exposure with various ABPM indicators, which may provide hints for preventing people from the influences of $PM_{2.5}$. Additionally, this study was a stringent panel study with a multiphase and multicity design, with individual $PM_{2.5}$ monitoring and ABPM, which allowed time-dependent covariates to be adjusted, and was less likely to cause misclassification, making the findings more accurate. However, this study was still subject to some limitations. First, owing

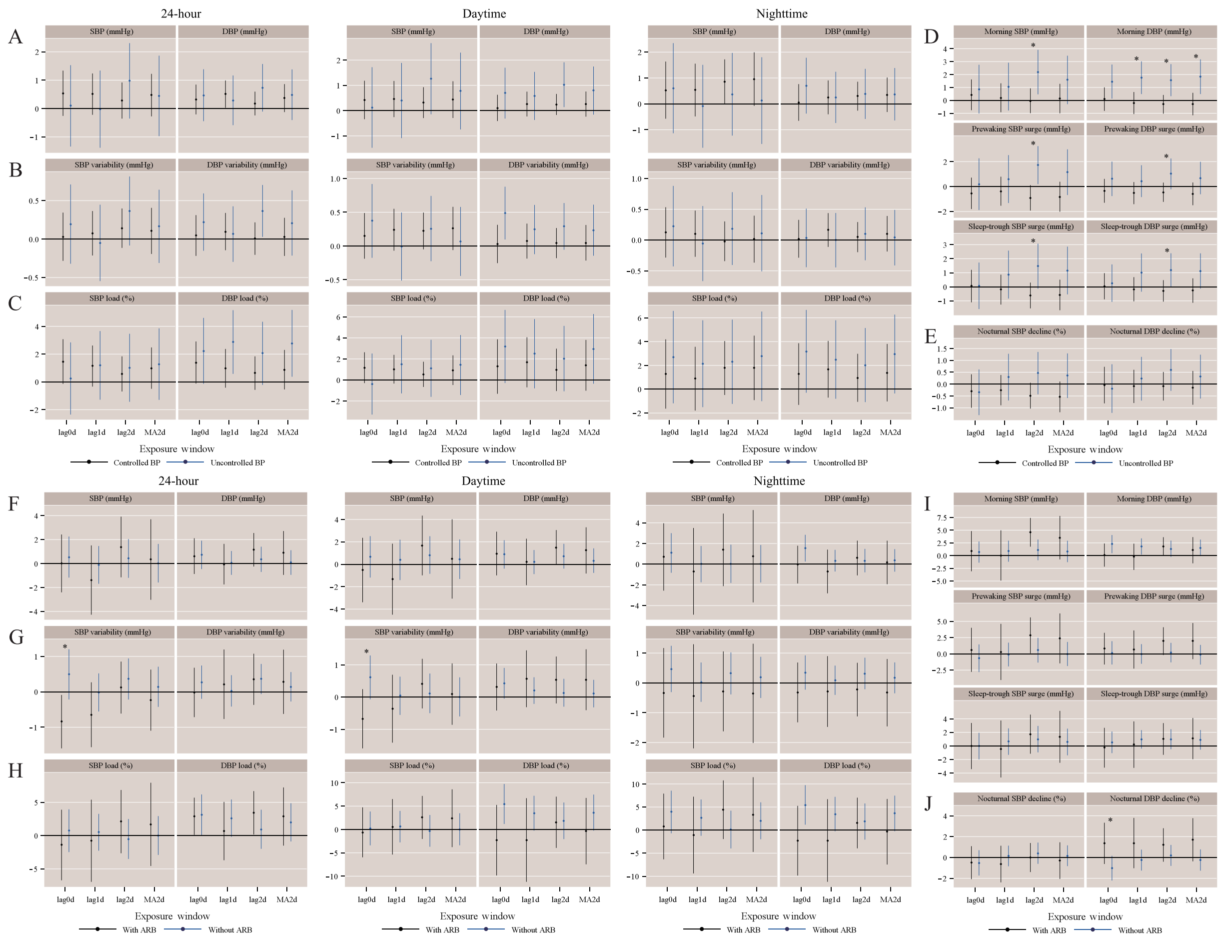

FIGURE 2. Estimated changes and 95% CIs of BP levels (A, F), BP variability (B, G), BP load (C, H), morning BP surge (D, I) and the percentage of nocturnal BP decline (E, J) with per IQR (41.96 μg/m^3) of the $PM_{2.5}$ exposure, stratified by BP control status in overall population and by ARB use in patients without controlled BP in two cities and two municipalities, China, 2017−2019.

* *P*<0.05 for differences between two groups.

Abbreviations: CI=confidence interval; BP=blood pressure; IQR=interquartile range; $PM_{2.5}$=particles with aerodynamic diameter ≤2.5 μm; SBP=systolic blood pressure; DBP=diastolic blood pressure; ARB=angiotensin receptor blockers; lag0d=current day with BP measurement; lag1d=lag of 1 day; lag2d=lag of 2 days; MA2d=the 2-day moving average of $PM_{2.5}$.

to the absence of individual gaseous pollutants, the independent effects of $PM_{2.5}$ have not been assessed. Second, this study used BP measurements from 06:00 to 08:00 instead of BP levels 2 hours after waking to calculate morning surge due to missing information on waking time in this study.

In conclusion, this study added evidence of the associations between short-term $PM_{2.5}$ exposure and ABPM indicators, and further highlighted antihypertensive therapy, especially with well-controlled BP status, which may be a potential measurement to attenuate adverse impacts of $PM_{2.5}$ for patients with intermediate-to-high risk of CVD.

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Preplanned Studies

Acute Effects of Personal Ozone Exposure on Biomarkers of Inflammation, Oxidative Stress, and Mitochondrial Oxidative Damage — Shanghai Municipality, China, May–October 2016

Yongjie Xia[1,&]; Yue Niu[1,&]; Jing Cai[1]; Cong Liu[1]; Xia Meng[1]; Renjie Chen[1,#]; Haidong Kan[1,#]

Summary

What is already known on this topic?

It remains inconclusive whether short-term ozone exposure can cause an inflammatory response and oxidative damage in the circulatory system, particularly at low concentrations.

What is added by this report?

This study made an accurate exposure assessment by conducting personal ozone monitoring, thus minimizing the exposure misclassification commonly found in previous environmental epidemiological studies. Our study found that even short-term exposure to low concentrations of ozone was associated with inflammation, lipid peroxidation, and mitochondrial oxidative damage.

What are the implications for public health practice?

Short-term exposure to low concentrations of ozone can still lead to subclinical cardiovascular effects, suggesting the current air quality standards for ozone need to be further tightened in China.

It remains inconclusive whether short-term ozone exposure can cause an inflammatory response and oxidative damage in the circulatory system. We conducted a longitudinal panel study of 43 non-smoking college students with four rounds of visits in Shanghai Municipality, China, from May to October 2016. Personal real-time ozone exposure was monitored for 3 days per visit, followed by blood sample collection. We measured 10 inflammatory biomarkers, 2 oxidative stress biomarkers, and 2 indicators of mitochondrial oxidative damage in the blood. Linear mixed-effect (LME) models were used to analyze their associations with ozone in R software (V 3.5.2, R Foundation for Statistical Computing, Vienna, Austria) and a *P*-value <0.05 was considered statistically significant. During the study period, mean ozone exposure levels ranged from 18.0 ppb to 22.7 ppb at different lag periods. Each 10-ppb increase in ozone exposure was greatly associated with a 4.86% increase in tumor necrosis factor alpha (TNF-α), 3.14% in soluble intercellular adhesionmolecule-1 (sICAM-1), and 0.89% in malondialdehyde (MDA), as well as a decrease of 0.23 in the average methylation (%5mC) of the mitochondria displacement loop (D-loop) region. Our results suggest that even short-term exposure to low-level ozone may lead to inflammation, lipid peroxidation, and mitochondrial oxidative damage.

For each visit, personal ozone exposure was monitored in real time for 3 days during daytime (from 8∶00 to 18∶00) using Personal Ozone Monitors (POMs, 2B Technologies, US). In addition, we used HOBO data loggers (Onset Computer Corporation, Pocasset, MA, US) to monitor temperature and relative humidity at the individual level. For each individual, we collected blood samples immediately after ozone monitoring. Serum levels of 10 inflammatory biomarkers were measured using the MILLIPLEX MAP Human Cytokine/Chemokine Kit (Millipore Corp., Billerica, MA, US), including interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-10 (IL-10), interleukin-17 alpha (IL-17α), TNF-α, monocyte chemoattractant protein-1 (MCP-1), granulocyte macrophage colony stimulating factor (GM-CSF), sICAM-1, soluble vascular cell adhesion molecule-1 (sVCAM-1), and vascular endothelial growth factor (VEGF). Overall, 2 markers of oxidative stress, including 8-isoprostaglandin F2 alpha (8-iso-PGF2α) and MDA, were measured in serum using enzyme linked immunosorbent assay (Oxford Medical, UK). We also measured the relative mitochondrial DNA copy number (RMtDNAcn) and the methylation of the mitochondria D-loop region in blood to indicate mitochondrial oxidative damage, according to previous methods (*1*). The study was approved by the Institutional Review Board of the School of Public Health, Fudan University (No. 2014-07-0523). All participants signed informed consent at enrollment.

We applied LME models to analyze the associations between personal ozone exposure and these biomarkers, with each participant's identification number incorporated as random intercepts. Data on 10 inflammatory biomarkers, 2 oxidative stress biomarkers, and RMtDNAcn were naturally log-transformed before statistical analyses. To capture the lagged effects of ozone, we considered exposure windows of 0–2 hours, 3–5 hours, 6–8 hours, 0–8 hours, 1 day, and 2 days preceding the blood sample collection. We also included: 1) individual characteristics, including age, sex, body mass index (BMI); 2) two natural cubic smooth functions of temperature and relative humidity with 3 degrees of freedom (dfs) for both; and 3) a natural cubic smooth function of the day within the study period with 3 dfs. We further performed a sensitivity analysis by adjusting for fine particulate matter, sulfur dioxide, nitrogen dioxide, and carbon monoxide, separately.

Three asthmatic patients were excluded, leaving 40 participants (30 females and 10 males) for the current analysis. Their mean age was 24 years, and their mean BMI was 21 kg/m^2. As shown in Supplementary Table S1 (available in http://weekly.chinacdc.cn/), the average personal ozone exposure at different lags ranged from 17.8±20.5 ppb to 22.7±17.4 ppb, which was far below the current ambient air quality standard in China (i.e., 8-hour maximum: 160 μg/m^3, equivalent to 75 ppb). The mean levels of 14 biomarkers varied appreciably, and detailed descriptive data can be found in Table 1.

Among the 10 inflammatory biomarkers, we observed significant increases in TNF-α, sICAM-1, sVCAM-1, and VEGF with ozone exposure (Figure 1). However, we did not find any significant associations of ozone with IL-6, IL-8, IL-10, IL-17α, MCP-1, GM-CSF (Supplementary Figure S1, available in http://weekly.chinacdc.cn/). We also found that ozone exposure showed a positive and statistically significant association with MDA, while the association with 8-iso-PGF2α was insignificant (Figure 2). In addition, we observed a significant increase in RMtDNAcn but a significant decrease in the D-loop methylation with ozone exposure (Figure 2).

The lag patterns of these significant associations were similar, except for the association with MDA. These effects mostly occurred within 2 hours of exposure, then were gradually attenuated over longer

TABLE 1. Summary statistics on biomarkers of inflammation, oxidative stress, and mitochondrial oxidative damage in 40 college students in Shanghai Municipality, China, May–October 2016.

Biomarker	Mean	SD	Min	Median	Max	IQR
Inflammation						
IL-6 (pg/mL)	1.40	1.35	0.41	0.91	10.01	0.90
IL-8 (pg/mL)	9.51	7.18	2.74	6.93	33.22	8.67
IL-10 (pg/mL)	2.05	4.00	0.21	0.70	24.53	0.90
IL-17α (pg/mL)	9.33	16.50	0.82	2.96	122.67	6.86
TNF-α (pg/mL)	7.27	4.21	1.70	6.65	24.57	4.33
MCP-1 (pg/mL)	392.32	156.15	160.24	361.94	1,005.00	181.06
GM-CSF (pg/mL)	6.76	10.36	0.72	1.87	50.88	5.32
sICAM-1 (ng/mL)	133.18	69.43	25.79	112.08	440.74	45.44
sVCAM-1 (ng/mL)	519.97	131.90	34.15	504.76	907.56	178..27
VEGF (pg/mL)	205.32	333.76	7.35	88.17	1,737.00	154.40
Oxidative stress						
8-iso-PGF2α (ng/mL)	0.56	2.46	0.01	0.16	19.80	0.20
MDA (μmol/L)	29.26	2.45	16.81	29.35	35.83	2.76
Mitochondrial oxidative damage						
RMtDNAcn	1.00	2.05	0.00	0.62	20.71	0.42
Methylation (%5mC)*	2.55	2.15	0.00	2.47	8.62	3.99

Abbreviations: SD=standard deviation; Min=minimum; Max=maximum; IQR=interquartile range; pg=picogram; ng=nanogram; IL-6=interleukin-6; IL-8=interleukin-8; IL-10=interleukin-10; IL-17α=interleukin-17 alpha; TNF-α=tumor necrosis factor alpha; MCP-1=monocyte chemoattractant protein-1; GM-CSF=granulocyte macrophage colony stimulating factor; sICAM-1=soluble intercellular adhesionmolecule-1; sVCAM-1=soluble vascular cell adhesion molecule-1; VEGF=vascular endothelial growth factor; 8-iso-PGF2α=8-isoprostaglandin F2 alpha; MDA=malonaldehyde; RMtDNAcn=relative mitochondrial DNA copy number.

* Methylation levels of the D-loop region in mitochondrial DNA.

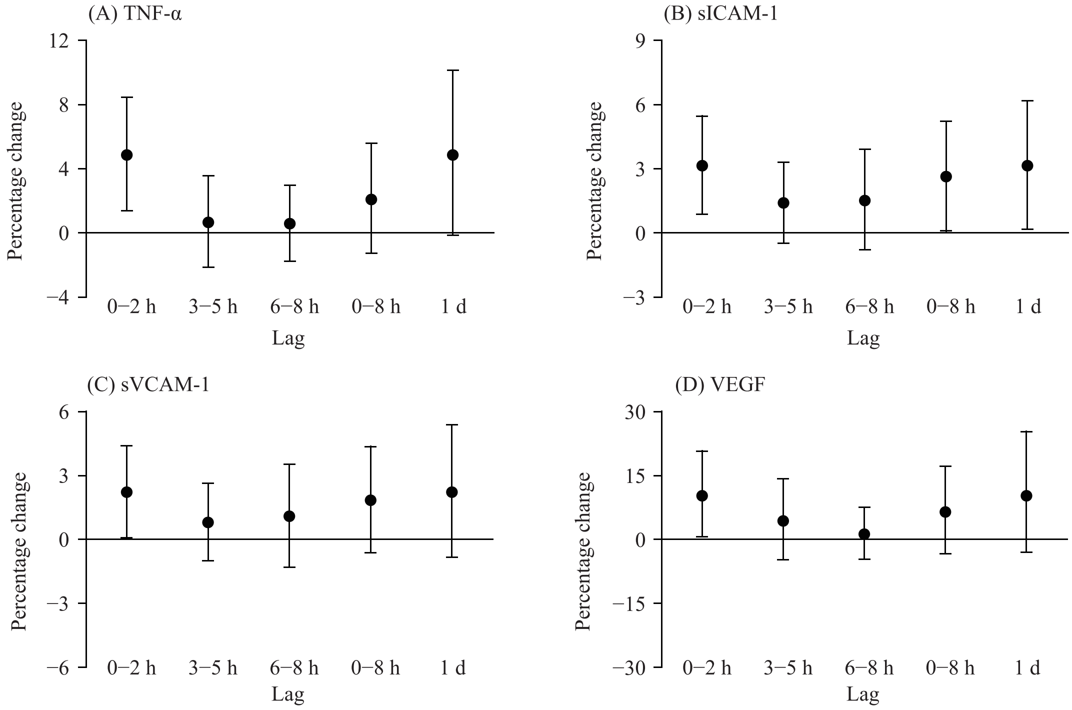

FIGURE 1. Percentage changes in TNF-α (A), sICAM-1 (B), sVCAM-1 (C), and VEGF (D) associated with a 10-ppb increase in personal ozone exposure at different lag periods in 40 college students in Shanghai Municipality, China, May–October 2016.

Note: X-axis denotes to the different lag periods; Y-axis denotes the corresponding percentage change in biomarkers.

Abbreviations: TNF-α=tumor necrosis factor alpha; sICAM-1=soluble intercellular adhesionmolecule-1; sVCAM-1=soluble vascular cell adhesion molecule-1; VEGF=vascular endothelial growth factor.

lags, and lost statistical significance at a lag of 2 days. At lag 0–2 hours, a 10-ppb increase in ozone concentrations was associated with the following increases: 4.86% [95% confidence interval (CI): 1.39%–8.45%] in TNF-α; 3.14% (95% CI: 0.87%–5.46%) in sICAM-1; 2.23% (95% CI: 0.09%–4.40%) in sVCAM-1; 10.26% (95% CI: 0.65%–20.79%) in VEGF; and 30.51% (95% CI: 0.31%–69.81%) in RMtDNAcn. A decrease of 0.23 (95% CI: 0.01%–0.45%) was found in the D-loop methylation (%5mC). The significant association with MDA was observed at lag 3–5 hours only, with a 0.89% (95% CI: 0.14%–1.65%) increase in MDA per 10-ppb increase in ozone exposure at this lag. After adjusting for other air pollutants, the associations of ozone with TNF-α, sICAM-1, MDA, and the D-loop methylation were almost unchanged, while the associations with sVCAM-1, VEGF, and RMtDNAcn were unstable (Supplementary Table S2, available in http://weekly.chinacdc.cn/).

DISCUSSION

In this longitudinal panel study, we found that short-term exposure to low concentrations of ozone may lead to increased biomarkers of inflammation and oxidative stress, including TNF-α, sICAM-1, and MDA. We also observed reduced methylation of the mitochondria D-loop region with ozone exposure.

It remains inconclusive whether ozone exposure could induce an inflammatory response in the circulatory system, although extensive evidence suggested that short-term ozone exposure was associated with respiratory inflammation. Consistent with previous studies (*2–3*), we found ozone exposure was associated with increased sICAM-1 in this study. An increased circulating level of sICAM-1 was relevant to endothelial injury due to inflammation and may be an independent risk factor for atherosclerosis and cardiovascular disease (*4–5*). In addition, we found ozone exposure was associated with elevated TNF-α, a marker of systemic inflammation. However, we did not find any significant associations with other common markers of systemic inflammation (i.e., interleukins, MCP-1, and GM-CSF). Previous studies have also showed mixed results on the inflammatory effects of ozone (*6–7*), and further studies are needed to confirm our findings.

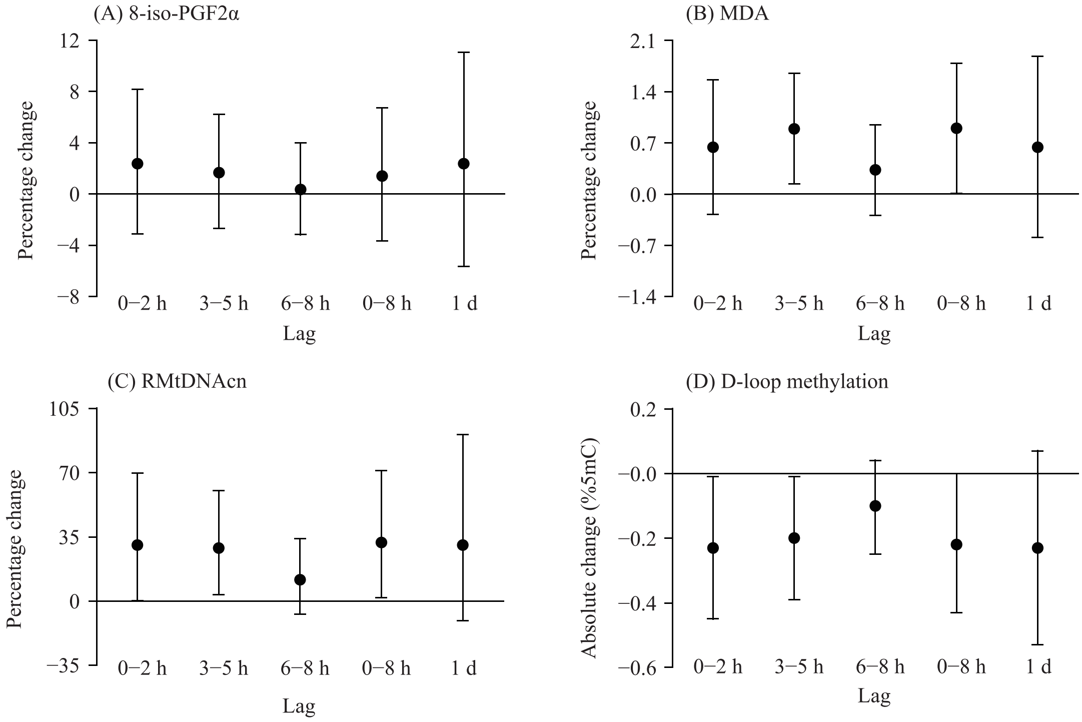

FIGURE 2. Percentage changes in 8-iso-PGF2α (A), MDA (B), and RMtDNAcn (C), and absolute change in mitochondria D-loop methylation levels (D) associated with a 10-ppb increase in personal ozone exposure at different lag periods in 40 college students in Shanghai Municipality, China, May–October 2016.

Note: X-axis denotes to the different lag periods; Y-axis denotes the corresponding percentage/absolute change in biomarkers.

Abbreviations: 8-iso-PGF2α=8-isoprostaglandin F2 alpha; MDA=malonaldehyde; RMtDNAcn=relative mitochondrial DNA copy number.

Mitochondrial DNA is sensitive to reactive oxygen species as it lacks protective histones and DNA repair mechanisms. Mitochondrial DNA methylation is an indicator of mitochondrial oxidative damage (*1*). To the best of our knowledge, this is the first study to find an association between ozone exposure and hypomethylation of the mitochondria D-loop region. This finding suggests that ozone exposure may trigger mitochondrial damage and dysfunction, thereby disrupting cellular homeostasis and leading to metabolic alterations (*8*). We also observed an increase in RMtDNAcn, another indicator of mitochondrial oxidative damage, with ozone exposure. However, the observed increase became statistically insignificant when adjusting for other air pollutants. Notably, these pollutants were measured by fixed-site monitoring rather than personal monitoring, and therefore one should be cautious in interpreting the results of the two-pollutant models. In addition, we found that ozone exposure was associated with increased MDA, which is one of the final products of polyunsaturated fatty acids peroxidation and plays a role in the development of cardiovascular disease (*9*). A previous study found increased 8-iso-PGF after exposure to high levels of ozone (*10*), but the results of this study did not report such an association at low concentrations.

Our study was subject to at least three limitations. First, the statistical power may be restricted due to the small sample size. As a result, the confidence intervals for the effect estimates in this study were wide. Second, the participants were only college students, which may limit the generalizability of our findings to other populations and settings. Third, all health outcomes were measured at the same time, restricting the ability to evaluate the causality between ozone exposure and blood biomarkers.

In conclusion, our study found that even short-term exposure to low concentrations of ozone was associated with inflammation, lipid peroxidation, and mitochondrial oxidative damage. Our results suggest that the current air quality standards for ozone need to be further tightened in China.

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Preplanned Studies

Co-Exposure to Multiple Pollutants and Its Cardiovascular Effects in a Subway System — Beijing Municipality, China, 2017

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Summary

What is already known on this topic?

With rapid urbanization, traffic-related air pollution has become a global concern. However, its association with cardiovascular health has not been fully elucidated.

What is added by this report?

This study provided novel evidence of the joint cardiovascular effect of multiple pollutants in subway cabins, further identified two pollutants that played dominant roles, and validated the effectiveness of targeted interventions.

What are the implications for public health practice?

The findings were helpful to guide the formulation and development of prevention and control strategies for key traffic-related pollutants that endanger the cardiovascular health of commuters.

With rapid global urbanization, air and noise pollution in subway systems (also called metro systems) and the potential cardiovascular hazards they pose have become a global public health issue. However, the joint effect of multiple pollutants, as well as the key pollutants that play a dominant role in cardiovascular health, remain unclear. A randomized crossover study with respirator and/or headphone interventions was conducted among healthy young adults from March 11 to May 28, 2017 in the Beijing subway. This study found that co-exposure to size-fractioned particulate matter (PM), black carbon (BC), and noise was strongly associated with changes in heart rate variability (HRV) indices. BC and noise may be the two dominant pollutants causing the overall impact. Analysis based on data from intervention phases suggested that the impact of BC or noise might be attenuated or even reversed when reducing the level of another pollutant (noise or BC). The findings were helpful in guiding the formulation and development of prevention and control strategies for key traffic-related pollutants that endanger the cardiovascular health of commuters.

Overall, 40 healthy young adults were recruited for this randomized crossover study from March 11 to May 28, 2017, in Beijing. Details of the study implementation could be found in previous publications (*1*–*2*). In brief, participants commuted for about 4 hours between 9∶00–13∶00 in the subway during 4 different periods with/without intervention (wearing respirator and/or headphone). The personal real-time levels of PM_1 (aerodynamic diameters < 1 μm), $PM_{1–2.5}$ (aerodynamic diameter ≥1 μm and < 2.5 μm), $PM_{2.5–10}$ (aerodynamic diameter ≥2.5 μm and <10 μm), BC, and noise were measured. Simultaneously, HRV parameters were obtained using a 12-channel ambulatory ECG monitor. Total power (TP), very-low-frequency power (VLF), low-frequency power (LF), high-frequency power (HF), LF/HF and standard deviation of normal-to-normal intervals (SDNN) were included in this study. Bayesian kernel machine regression (BKMR) was used to further examine the joint health effect of multiple pollutants in the subway cabin. This model allows nonlinear relationships and potential interactions and has been used widely to assess the overall effect of mixed pollutants (*3*). Posterior inclusion probability (PIP) was estimated through variable selection to assess the relative importance of exposure variables. PIP values range from 0 to 1 and a larger PIP value means a higher importance. All exposure and outcome variables were standardized. The covariates included gender, age, body mass index (BMI), temperature, relative humidity and CO_2 level. The number of subjects was used as a random effect term to control the correlation between repeated measurements. The lag effects from 5 min to 2 hours were examined, and the most significant effect was reported at 30 min lag. BKMR analysis was conducted using R software (version 4.0.3; R project for Statistical Computing) with the "bkmr" package. The study protocol was approved by the Institutional Review Board of Peking University Health Science

Center (IRB number: 00001052-16066) and informed consent was obtained from each participant.

In total, 39 participants completed this study, of whom 18 (46.2%) were females. Their mean age and BMI were 21.2 years and 21.6 kg/m^2, respectively. The mean levels of PM_1, $PM_{1–2.5}$, $PM_{2.5–10}$, BC, and noise were 34.1, 51.6, 145.2, 9.5 μg/m^3, and 75.9 dBA, respectively. Increased levels of co-exposure to these pollutants were significantly associated with decreased TP, VLF, SDNN, and increased LF/HF (Figure 1). According to the results of PIPs in Table 1, BC had a higher PIP than other pollutants in most HRV indices, ranging from 0.69 to 1.00. Specifically, BC had the highest PIP value in TP (1.00), VLF (1.00), LF (1.00), and SDNN (0.96), indicating the largest contribution to the overall effect. Noise was the second most important because it had a high PIP in LF (1.00), HF (0.96), and LF/HF (0.72).

To clarify the effectiveness and necessity of BC and noise prevention and control in the subway system, the exposure-response relationships of BC and noise with HRV indices were plotted based on the data from both no-intervention and headphone/respirator intervention phases. As shown in Figure 2, a weaker effect of BC on VLF, LF, HF, and SDNN was observed in the headphone intervention phase (low noise level) than the no-intervention one (high noise level), and the effect on LF/HF was even slightly reversed from a positive to negative association. For the effect of noise on all HRV indices, the relationships significantly differed in the respirator intervention phase (low BC concentration), and positive associations between noise

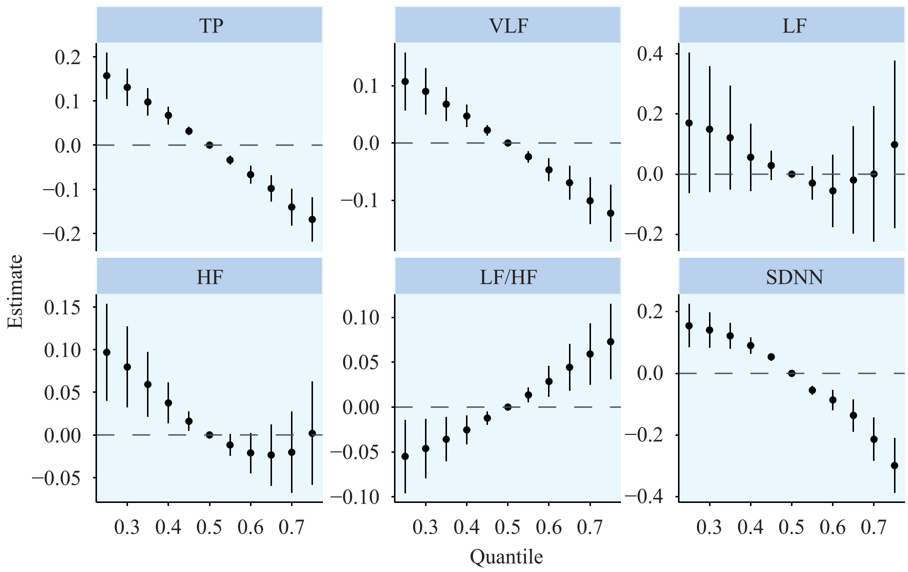

FIGURE 1. The joint effect estimates and 95% confidence interval (CI) of multiple air pollutants (PM_1, $PM_{1–2.5}$, $PM_{2.5–10}$, BC, and noise) in subway cabin on HRV parameters of study participants in Beijing, 2017

Note: The plot compared each HRV index when all exposures were at a particular quantile to when all were at the median (reference).

Abbreviations: TP=total power; VLF=very low frequency power; LF=low frequency power; HF=high frequency power; SDNN=standard deviation of normal-to-normal intervals; HRV=heart rate variability.

TABLE 1. Posterior inclusion probabilities (PIPs) from basyesian kernel machine regression model for heart rate variability parameters of healthy young adults in Beijing, 2017*.

Variable	TP	VLF	LF	HF	LF/HF	SDNN
PM_1	0.51	0.45	1.00	0.80	0.61	0.26
$PM_{1-2.5}$	0.48	0.43	0.76	0.70	0.73	0.27
$PM_{2.5-10}$	0.59	0.63	1.00	0.75	0.76	0.62
Black carbon	1.00	1.00	1.00	0.90	0.69	0.96
Noise	0.60	0.53	1.00	0.96	0.72	0.21

Abbreviations: PM=particulate matter; TP=total power; VLF=very low frequency power; LF=low frequency power; HF=high frequency power; SDNN=standard deviation of normal-to-normal intervals.

* PIP is a measure of the importance of exposure variables, and a larger value means a higher importance.

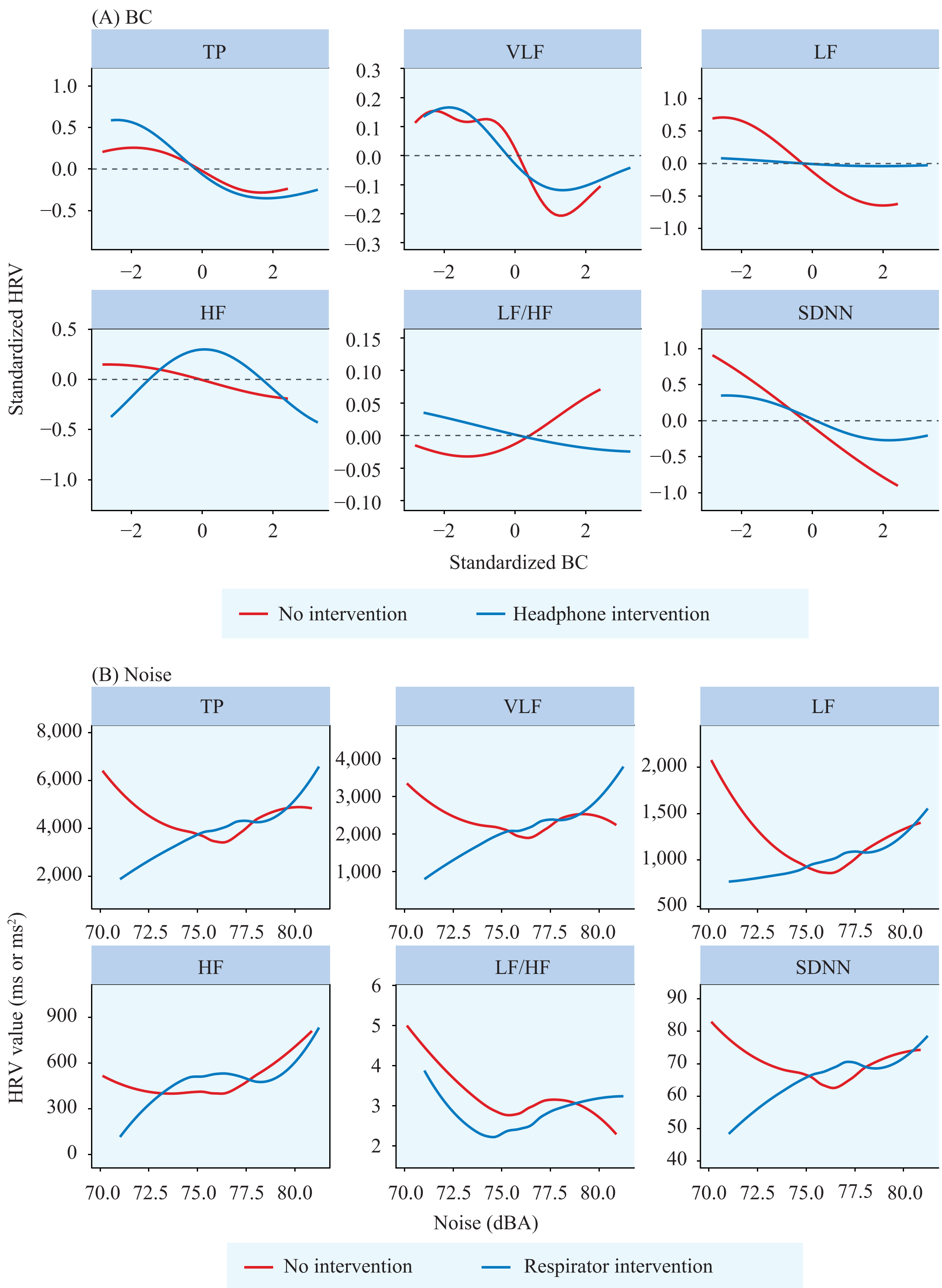

FIGURE 2. The exposure-response relationship of black carbon (BC) and noise in subway cabin with heart rate variability (HRV) indices of participants in Beijing, 2017.

(A) Comparison of the effects of BC on HRV indices between no intervention (high-noise level) and headphone intervention (low-noise level) phase based on basyesian kernel machine regression analysis; (B) Comparison of the effects of noise on HRV indices between no intervention (high-BC concentration) and headphone intervention (low-BC concentration) phase based on LOESS.

Abbreviations: BC=black carbon; HRV=heart rate variability; TP=total power; VLF=very low frequency power; LF=low frequency power; HF=high frequency power; SDNN=standard deviation of normal-to-normal intervals; LOESS=locally weighted regression.

and TP, VLF, LF, HF, and SDNN were found during this phase.

DISCUSSION

The metro system has become an indispensable part of megacities, and its environmental quality and potential health hazards are attracting more and more attention. This study found that short-term (30 min) co-exposure to size-fractioned PM, BC, and noise was strongly associated with changes in HRV indices. HRV can reflect the activities of the sympathetic nervous system (SNS) and the parasympathetic nervous systems (PNS), and its reduction has been related to higher cardiovascular risks (*4*). TP and SDNN are global indicators of HRV, and VLF is thought to be strongly associated with all-cause mortality and other diseases. LF/HF was thought to represent the balance of SNS and PNS and is positively related to SNS activity. In this study, positive association with LF/HF was found, indicating SNS activity increased more than PNS, which was consistent with previous studies (*2*–*3*,*5*–*6*).

To achieve the maximum input-output ratio of pollution prevention and control based on health benefits, it is imperative to identify the pollutants that contribute most to health hazards. The study found that BC mediated most of the cardiovascular health damage, followed by noise. The effects of BC and noise on cardiac autonomic nerve function have also been demonstrated in other studies (*5*–*7*). BC is mainly emitted by traffic transport, where a high level of noise is usually produced simultaneously. They may be two crucial targets for traffic-related air pollution prevention and control, and they seem to deserve more concern in the subway system because of the higher exposure levels compared to other modes of transport, including taxi, bus, cycling, and walking (*8*–*9*).

Our previous study demonstrated the cardiovascular benefits of respirator and headphone interventions (*2*). Considering the potential interaction of BC and noise on cardiovascular health (*6*–*7*), this study further explored the exposure-response relationships between BC or noise and HRV indices, controlling each pollutant at different levels. When reducing the exposure level of BC or noise using respirators or headphones, the adverse effects of another pollutant (noise or BC) on cardiac autonomic nerve function were significantly attenuated and even reversed. The results further validated the effectiveness of the target intervention. In addition, the findings also suggested that healthy adults may develop a protective compensatory response to the adverse effects of single pollutant (BC or noise), though it may be not enough when co-exposed to multiple pollutants. Similarly, a panel study found a weaker association between BC and HRV indices when noise was controlled in the regression model (*6*). Another randomized crossover study also observed the effect of BC on HRV indices of health adults was stronger in a high noise environment (traffic center) than a low noise one (park) (*7*).

This is the first study to explore the joint effect of multiple pollutants in the subway on the cardiac autonomic function and to determine which pollutants deserve particular concern in a near-real exposure scenario. This study further clarified the effectiveness and necessity of targeted interventions for air pollution in the subway system.

This study was still subject to some limitations. First, gaseous pollutants were not included. Second, participants in this study were healthy young adults, which might limit the generalizability of the findings. But it could be expected that similar or even stronger effects might be observed in susceptible populations.

In summary, short-term co-exposure to multiple pollutants could disturb the cardiac autonomic function. BC and noise may be the two pollutants with the greatest contribution. In addition to the direct cardiovascular benefits of wearing a respirators or headphones (*2*), this study further verified that such interventions were also helpful to reduce the susceptibility of the cardiovascular system to other pollutants, possibly because the compensatory response of healthy young people is adequate to cope with short-term high levels of exposure to a single pollutant. Therefore, this study confirmed the potential public health implications of traffic-related air pollution interventions, and highlighted that BC and noise may be key to urban traffic-related air pollution prevention and control to avoid cardiovascular lesions. It is urgent and necessary for individuals and relevant departments to take targeted measures to protect cardiovascular health from air pollution during commuting.

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Preplanned Studies

Temperature-Modified Acute Effects of Ozone on Human Mortality — Beijing Municipality, Tianjin Municipality, Hebei Province, and Surrounding Areas, China, 2013–2018

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Summary

What is already known about this topic?

Ozone (O_3) is a weather-driven photochemical ambient pollutant, and its harm to human health may be affected by meteorological factors such as temperature. However, there is conflicting evidence regarding whether temperature can modify the effects of ozone on health.

What is added by this report?

Short-term exposure to O_3 in the Beijing Municipality, Tianjin Municipality, Hebei Province, and surrounding areas was associated with an increased risk of human mortality and that association was positive modified by relatively higher (>75th 24 h-average temperature) or extreme cold temperature (<10th 24 h-average temperature). Under extreme temperatures (>90th 24 h-average temperature) modification, the associations were further increased. Cardiopulmonary diseases, as vulnerable diseases of air pollution, their mortality risks associated with O_3 were markedly strengthened by uncomfortable temperatures.

What are the implications for public health practice?

This study suggests that policymakers should pay attention to the synergistic effect between ozone and heat or extreme cold on human health, as well as provide evidence for establishing an integrated early-warning system to protect the public against both uncomfortable temperature and air pollution.

Short-term exposure to ambient ozone (O_3), a weather-driven photochemical pollutant, has been found to be associated with increased risk of mortality in previous epidemiological studies (*1–2*). Most of these studies analyzed O_3-mortality associations by controlling for meteorological factors in a model fitting process. Regarding the high correlation between O_3 and temperature, a recent area of interest is whether the observed O_3-mortality associations can be modified by temperature. Jhun et al. found both high and low temperature could strengthen acute effects of O_3 on mortality (*3*), while Chen et al. and Shi et al. reported that O_3-mortality associations were strengthened in high temperature but not in low temperature settings (*4–5*), and Liu et al. and Chen et al. only found modifications by low temperature (*6–7*). In summary, evidence on temperature-modification was inconsistent and needed to be supplemented by regional epidemiological studies involving various meteorological characteristics. Note that in the new air quality guidelines issued by the World Health Organization (WHO), O_3 limits have been distinguished between warm and cold seasons. Beijing Municipality and Tianjin Municipality, along with 26 cities distributed in Hebei, Shandong, Shanxi and Henan Provinces, have formed the regional air pollution transmission channel, and experienced a challenge of regional O_3 pollution increasing steadily. Therefore, additional efforts are needed to better quantify the local health risks of O_3 by considering the influence of temperature in the Beijing, Tianjin, Hebei and surrounding areas.

This study used daily counts of deaths from the Disease Surveillance Point System of China CDC and included 39 counties in the Beijing, Tianjin, Hebei and surrounding areas from January 1, 2013 to December 31, 2018. Three major causes of deaths were classified according to the 10th Revision of the International Statistical Classification of Diseases (ICD-10): non-accidental disease (A00–R99), cardio-cerebrovascular disease (I00–I99), and respiratory disease (J00–J99). Daily ambient O_3 concentrations were collected from the National Urban Air Quality Real-Time Release Platform and calculated to a daily 8-hour moving average maximum (O_3 8 h-average), 1-hour maximum (O_3 1 h-max), and 24 hour-average of O_3 (O_3 24 h-average). Daily average temperature and relative humidity were obtained from the China Meteorological Data Network.

The study applied two time-series approaches with a two-stage statistical analysis to estimate whether and how temperature modified acute effects of O_3 on mortality in the Beijing, Tianjin, Hebei and surrounding areas. The first approach, a temperature-adjusted approach, aimed to control the cumulative temperature impacts with a cross-basis function using a generalized linear model (GLM) and analyze associations between O_3 and death without considering interactions.

The second approach, a temperature-stratified approach by a Pick-A-Point technique centering on changes of the conditional effect of O_3 across the designated levels of the modifier (*8*), aimed to construct interaction terms between O_3 and a stratification variable of temperature in the GLM and analyze differences of associations under three different temperature levels: low, moderate, and high temperature. In this model, we used three cutoffs to categorize daily average temperature, including the 10th and 90th (P_{10}/P_{90}), 20th and 80th (P_{20}/P_{80}), and 25th and 75th (P_{25}/P_{75}) percentiles. The model of the temperature-stratified approach was set up as follows:

$$Log[E(Y_t)] = intercept + \beta O_3 + \beta_1 Tem + \beta_2(O_3 : Temstrata) + ns(RH, df) + dow + ns(time, df)$$

Where was the expected value of death on day t; *Tem* represented the daily value of temperature; $(O_3 : Temstrata)$ was the interaction term between O_3 and temperature, in which temperature was divided into low, moderate, and high levels of the categorical variable by cutoffs. Both approaches estimated effects of the 2-day average of current and previous-day concentrations (lag 01) of O_3 8 h-average and controlled for seasonal and time trends [*time*, natural smoothing function of 8 degrees of freedom (*df*)], day of the week (*dow*), and relative humidity (*RH*, natural smoothing function of 5 *df*). The effect estimate was expressed as a percent increase (PI) in mortality risk per 10 μg/m^3 increase in O_3 exposure.

This study examined the sensitivity of key findings for non-accidental mortality with respect to using the following: 1) the specification of *df* in the smoothing functions of time trend (*df*=6 or 7/year) and relative humidity (*df*=3) in the temperature-adjusted approach to observe model stability; 2) the other two metrics (O_3 1 h-max and O_3 24 h-average) with different lagged exposure [the same day as deaths (lag 0), the previous day (lag 1), and lag 01] in the temperature-adjusted approach to observe impacts from different exposure assessments for the study population; and 3) O_3 1 h-max and O_3 24 h-average with lag 01 exposure in the temperature-stratified approach to observe whether the modification effect of temperature on different ozone metrics was robust. Statistical analyses were conducted in the R Statistical Software (version 4.0.2, the Free Software Foundation's GNU Public License, Vienna, Austria). Statistical significance was considered at a *P*-value <0.05.

From 2013 to 2018, residents in the Beijing, Tianjin, Hebei and surrounding areas were exposed to a concentration of O_3 8 h-average of (95.2±61.4) μg/m^3. Approximately 11 deaths for non-accidental disease, 6 for cardiocerebrovascular disease, and 1 for respiratory disease per day per county were recorded (Table 1).

Based on the temperature-adjusted approach without considering interactions, a per 10 μg/m^3 increase in exposure to O_3 8 h-average would increase daily mortality risks of non-accidental [PI=0.15%, 95% Confidence Interval (CI): 0.06%, 0.24%], cardio-cerebrovascular (PI=0.20%, 95% CI: 0.07%, 0.33%), and respiratory diseases (PI=−0.08%, 95% CI: −0.42%, 0.25%) in the Beijing, Tianjin, Hebei and surrounding areas. Based on temperature-stratified approach, relatively higher temperature (>75th 24 h-average temperature) significantly strengthened O_3-mortality associations, with a 0.57% risk increase of

TABLE 1. Summary for ambient O_3, meteorological factors, and causes of death in the Beijing, Tianjin, Hebei and surrounding areas, 2013 to 2018.

Variable	Mean±SD	P_{25}	P_{50}	P_{75}
O_3 24 h-average (μg/m^3)	56.3±38.7	25.3	49.5	80.2
O_3 8 h-average (μg/m^3)	95.2±61.4	48.2	83.8	135.4
O_3 1 h-max (μg/m^3)	111.0±71.5	59.7	95.0	155.0
Temperature (°C)	13.3±11.1	2.8	14.6	23.4
Humidity (%)	0.6±0.2	0.4	0.6	0.7
Non-accidental diseases	11±8	6	9	14
Cardio-cerebrovascular diseases	6±4	3	5	7
Respiratory diseases	1±1	0	1	2

Abbreviations: SD=standard deviation; P_{25}=25th percentile; P_{50}=50th percentile; P_{75}=75th percentile.

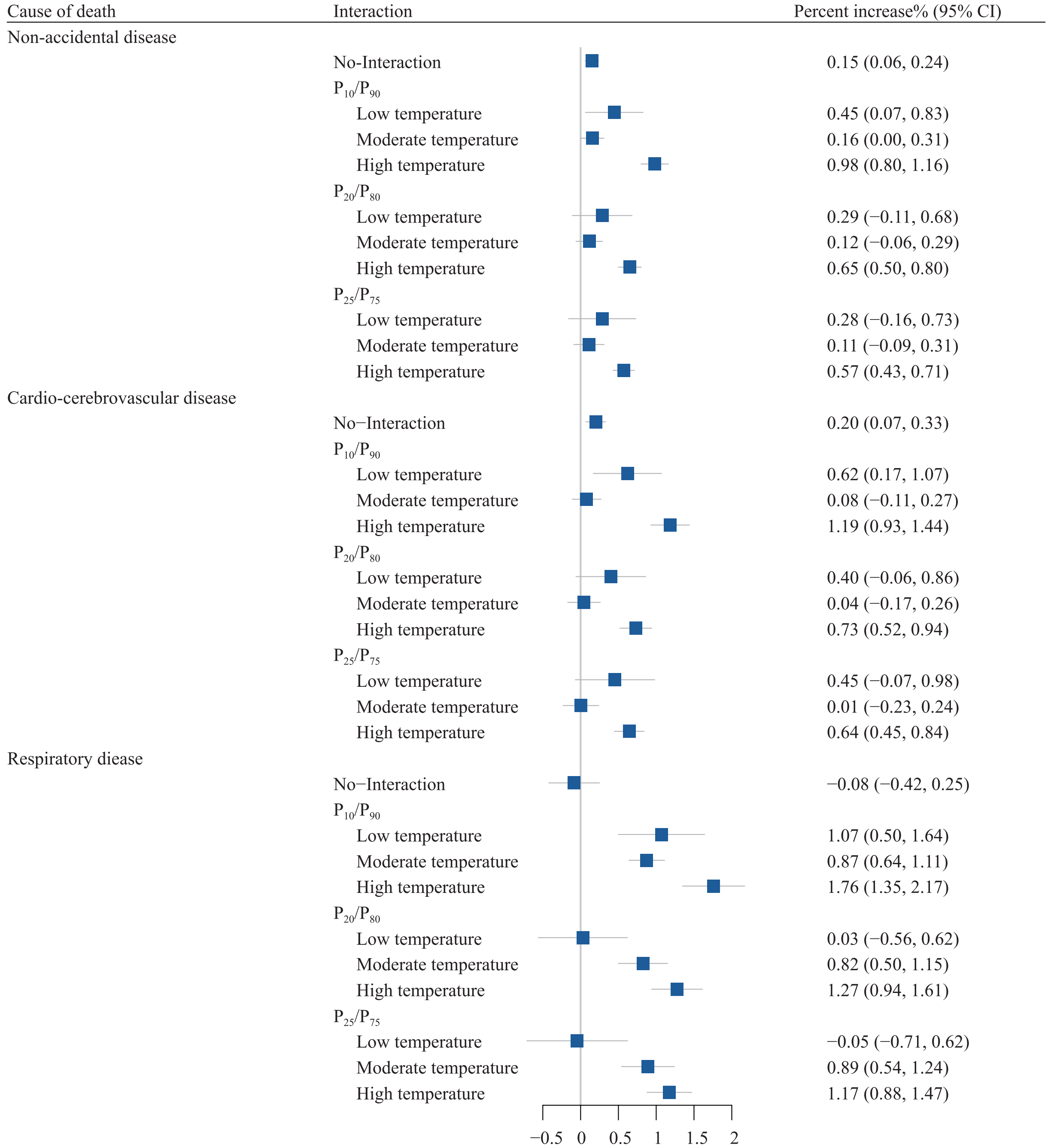

FIGURE 1. Mortality risk estimates associated with Lag 01 exposure of O_3 by using the temperature-adjusted and temperature-stratified approach in the Beijing, Tianjin, Hebei and surrounding areas, 2013–2018.
Abbreviations: P_{10}=10th percentile; P_{90}=90th percentile; P_{20}=20th percentile; P_{80}=80th percentile; P_{25}=25th percentile; P_{75}=75th percentile.

non-accidental disease, 0.64% risk increase of cardio-cerebrovascular disease, and 1.17% risk increase of respiratory disease (Figure 1). Under extreme temperature (>90th 24 h-average temperature) modification, the associations between O_3 and human mortality has further increased: a 0.98% risk increase of non-accidental disease, 1.19% risk increase of cardio-cerebrovascular disease, and 1.76% risk increase of respiratory disease (Figure 1). Moreover, extreme low temperature (<10th 24 h-average temperature) was also found to strengthen the acute effects of O_3 on mortality (Figure 1).

Associations between short-term exposure to O_3 8 h-average and mortality peaked at Lag 01 exposure. Analyses with different metrics of O_3 exposure and more or less stringent time trends and relative

TABLE 2. Percent increase (95% CI) in mortality risks associated with short-term exposure to O_3 for sensitivity analysis by using the temperature-adjusted approach in the Beijing, Tianjin, Hebei and surrounding areas, 2013–2018. (%)

Pollutants	Lag	$df_{tem/rh}$=3, df_{time}=6	$df_{tem/rh}$=5, df_{time}=8	$df_{tem/rh}$=5, df_{time}=7	$df_{tem/rh}$=3	$df_{tem/rh}$=3, df_{time}=7
O_3 8 h-average	Lag 0	0.11 (0.04, 0.19)	0.14 (0.06, 0.22)	0.14 (0.07, 0.22)	0.13 (0.05, 0.21)	0.13 (0.05, 0.20)
	Lag 1	0.03 (−0.05, 0.10)	0.07 (−0.01, 0.14)	0.06 (−0.01, 0.14)	0.05 (−0.02, 0.13)	0.04 (−0.04, 0.11)
	Lag 01	0.09 (−0.00, 0.18)	0.15 (0.06, 0.24)	0.14 (0.04, 0.23)	0.13 (0.04, 0.22)	0.10 (0.01, 0.20)
O_3 1 h-max	Lag 0	0.07 (0.01, 0.13)	0.08 (0.03, 0.14)	0.08 (0.03, 0.14)	0.08 (0.02, 0.14)	0.08 (0.02, 0.13)
	Lag 1	0.06 (−0.00, 0.11)	0.08 (0.02, 0.13)	0.07 (0.01, 0.13)	0.07 (0.01, 0.12)	0.06 (0.00, 0.12)
	Lag 01	0.10 (0.02, 0.17)	0.13 (0.06, 0.21)	0.12 (0.05, 0.20)	0.12 (0.04, 0.19)	0.10 (0.03, 0.18)
O_3 24 h-average	Lag 0	0.13 (0.01, 0.24)	0.14 (0.02, 0.25)	0.17 (0.06, 0.28)	0.13 (0.02, 0.24)	0.15 (0.04, 0.26)
	Lag 1	0.12 (0.01, 0.23)	0.16 (0.05, 0.27)	0.17 (0.06, 0.28)	0.14 (0.03, 0.25)	0.14 (0.03, 0.25)
	Lag 01	0.17 (0.03, 0.30)	0.21 (0.07, 0.35)	0.24 (0.10, 0.38)	0.19 (0.05, 0.32)	0.20 (0.06, 0.34)

Note: $df_{tem/rh}$ is the degree of freedom of natural smoothing function for temperature or relative humidity, df_{time} is the degree of freedom of natural smoothing function for the seasonal and time trends.
Abbreviation: CI=confidence interval.

TABLE 3. Percent increase (95% CI) in mortality risks associated with short-term exposure to O_3 for sensitivity analysis by using the temperature-stratified approach in the Beijing, Tianjin, Hebei and surrounding areas, 2013–2018. (%)

Pollutants	Temperature	P_{10}/P_{90}	P_{20}/P_{80}	P_{25}/P_{75}
O_3 1 h-max	Low	0.30 (−0.01, 0.61)	0.23 (−0.09, 0.54)	0.24 (−0.12, 0.6)
	Moderate	0.14 (0.02, 0.25)	0.13 (−0.01, 0.27)	0.13 (−0.03, 0.28)
	High	0.81 (0.66, 0.97)	0.55 (0.43, 0.68)	0.49 (0.37, 0.61)
O_3 24 h-average	Low	0.61 (0.11, 1.12)	0.31 (−0.24, 0.86)	0.32 (−0.3, 0.94)
	Moderate	0.14 (−0.11, 0.4)	0.08 (−0.22, 0.39)	0.06 (−0.28, 0.41)
	High	1.47 (1.22, 1.73)	1.02 (0.81, 1.24)	0.90 (0.68, 1.12)

Abbreviations: CI=confidence interval; P_{10}=10th percentile; P_{90}=90th percentile; P_{20}=20th percentile; P_{80}=80th percentile; P_{25}=25th percentile; P_{75}=75th percentile.

humidity controlled by varying *df's* did not meaningfully change our findings (Table 2). For the three cutoffs of P_{10}/P_{90}, P_{20}/P_{80}, and P_{25}/P_{75}, the associations between the other two O_3 metrics and morality were both increased under high temperature levels (Table 3). The extreme low temperature was found to only significantly modify the association between O_3 24 h-average and mortality.

DISCUSSION

We used two time-series approaches to explore the effects of short-term exposure to O_3 on mortality across temperature levels in the Beijing, Tianjin, Hebei and surrounding areas throughout a six-year period. Both the temperature-adjusted and temperature-stratified approaches indicated that short-term exposure to O_3 was associated with an increased risk of mortality, and that the association was positive modified by high-temperature levels, especially modified by extreme heat. These findings were consistent with epidemiological evidence from several previous national-level studies *(3,5,9)*. From an exposure standpoint, it may be because ground-level O_3 is usually formed by photochemical reactions of precursor pollutants under the presence of light; as the temperature increases, the formation of O_3 accelerates, and the emission of precursor pollutants increases, resulting in an increase in effect size of O_3 along with increased pollution.

The study also found that the O_3-mortality risks of cardiopulmonary diseases, as vulnerable diseases of air pollution, were further strengthened in the presence of high temperature. However, studies in some southern cities in China *(6–7)* have not observed this modification effect. For example, a study conducted by Chen et al. in Jiangsu showed that O_3 has a higher impact on death from cardiovascular diseases in a low temperature environment. The conflicting results indicated that the modification may vary considerately across different climatic regions. Represented by previous national studies conducted in the United States, Jhun et al. and Ren et al. consistently emphasized that the modification of temperature on the O_3-mortality association varied across different regions (*3*,*9*). In addition to different climates and characteristics of O_3 pollution, various adaptive measures of local residents to mitigate exposure to O_3 and temperature may be another reason for the regional differences (*9*). Residents in the regions of southern China may become less sensitive to the variability of O_3 and temperature due to physical adaptation and higher air conditioning usage rates.

Experimental studies have observed that exposure to O_3 can result in injuries (including cellular response, metabolic activity, and physiological changes in respiratory function) to the nasal cavity, trachea and proximal bronchi, central acinar bronchioles, and alveolar ducts (*9*). O_3 inhaled through respiratory airways can also affect the regulation of the autonomic nervous system and then cause damage to human cardiovascular health. Meanwhile, although the mechanism of low temperature modification is not clear yet, marked changes in temperature can cause physiological stress and make individuals' physiological response vulnerable to toxic pollutants (*10*). This would be the possible reason why we found that the acute effects of a low O_3 exposure on mortality for non-accidental and cardiopulmonary diseases were strengthened by extreme low temperature. What has caught our attention is that when a cold wave hits, even if O_3 is at a low pollution level, it will have an adverse effect on health and should not be underestimated or ignored.

This study was subject to at least three limitations. First, the analytical methods used in our study can semi-quantitatively assess the difference in O_3-related mortality risks across different temperature stratifications, but a more flexible statistical method is needed to quantify nonlinear modifications. Second, due to differences in climate patterns, the modification of temperature on the acute effect of O_3 found here would not be applicable to other regions. We suggest that a more in-depth study of different climate regions in future studies. Finally, our study did not include information regarding the use of air conditioning or heating devices, which could influence the modification of temperature on O_3-related mortality risks.

Our findings suggest that policymakers should pay attention to the synergistic effect between heat or extreme cold and O_3 on human heath, as well as provide evidence for establishing an integrated early-warning system for protecting the public against both unsuitable temperature and air pollution.

Conflicts of interest: No conflicts of interest.

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Recommendations

Recommendations of Controlling and Preventing Acute Health Risks of Fine Particulate Matter Pollution — China, 2021

Expert Consensus Task Force; Xiaoming Shi[1,#]; Guangcai Duan[2,#]

Editorial An expert consensus is the unanimous recognition of experts from multiple disciplines on specific research topics based on scientific evidence and interpretation. This expert consensus on recommendations of controlling and preventing acute health risks of fine particulate matter pollution completes the drafting process that was initiated by selecting several influential experts from different professional fields to form a writing group. After that, the membership of experts was expanded and opinions were obtained from various experts through email, focused discussions, and expert tribunals. Finally, the drafts were revised and feedback was provided until the expert members reach a consensus and formed the final consensus draft. This consensus provides scientific reference for improving and optimizing China's air pollution prevention and control policies, scientific guidance for public health protection, and research directions for carrying out related scientific research. In order to share the recommendation domestically and internationally, the Chinese version is jointly published in the *National Medical Journal of China*.

Summary

The task force has comprehensively reviewed efforts for air pollution prevention and control, the acute health effects of fine particles ($PM_{2.5}$), and the health benefits of air pollution prevention and control in China. It has been found that the overall prevention and control of ambient $PM_{2.5}$ pollution in China has made remarkable progress in recent years. However, it still remains at a relatively high level. Short-term exposure to ambient $PM_{2.5}$ significantly increases the mortality and morbidity risk of Chinese residents, resulting in changes to levels of relevant biological markers. Prolonged $PM_{2.5}$ heavily polluted weather greatly increases the risk of cardiovascular disease morbidity and mortality. Among chemical composition of $PM_{2.5}$, carbon-containing components, some inorganic salts, and heavy metals are linked with the health impacts. The health risks of $PM_{2.5}$ pollution are higher for children, the elderly, and patients with cardiovascular or respiratory diseases than for the general population because the former groups are vulnerable subpopulations. The implementation of air pollution prevention and control policies has significantly improved human health. The implementation of personal protective equipment can significantly reduce the health damage caused by short-term exposure to ambient $PM_{2.5}$ pollution. Based on scientific evidence of $PM_{2.5}$ pollution and acute health risks in China, the following three recommendations are proposed. 1) The policy recommendations for the prevention and control of ambient $PM_{2.5}$ pollution include the following: to continuously strengthen the widespread use and efficient development of clean energy; to further promote industrial upgrading; to focus on the control of transportation pollution; to keep improving the modernization system of air pollution control; to formulate and refine relevant standards for air quality gradually; and to estimate the effects and health benefits after the implementation of clean air actions, and relevant policies. 2) Prevention of ambient $PM_{2.5}$ pollution and protection of public health recommendations include the following: to strengthen the release of air pollution monitoring and relevant information; to strengthen awareness of air pollution hazards; to clarify the guidance and recommendations for protecting population health from air pollution; and to strengthen the health protection of population vulnerable to ambient air pollution. 3) Recommendations for research on health risks of air pollution include the following: to strengthen research on air pollutant monitoring technology and monitoring system based on the promotion of accurate exposure assessment; to systematically carry out full-spectrum identification and correlation studies of air pollutants and health effects; to conduct studies on key toxic components and early biomarker inventory of air pollution health effects; to discover the toxicity mechanisms of the key toxic components of air pollutants; to carry out research on population health risk assessment and early warning of combined exposure to air pollutants; and to execute comprehensive studies on the health and economic benefits of pollution and carbon reduction under the national strategies of carbon neutrality and beautiful China.

INTRODUCTION

The Global Burden of Disease Study 2019 data showed that ambient fine particulate matter ($PM_{2.5}$) is the fourth highest risk factor in the global burden of disease (*1*). In China, about 1,432,633 premature deaths were attributed to $PM_{2.5}$ during 2019 (*1*). It has an important impact on the occurrence, development, and prognosis of cardiovascular and respiratory diseases in the population. It has been a major environmental problem and an important health issue commonly faced by all countries in the world, especially developing countries (*2–4*). China currently experiences high levels of ambient air pollution. With rapid industrialization and urbanization, the prevention and control of air pollution is becoming more difficult. To this end, the State Council issued the "Air Pollution Prevention and Control Action Plan" in September 2013, implementing 10 measures for air pollution prevention and control and releasing and implementing the "Three-Year Action Plan to Win the Blue Sky Defense War" in June 2018. After years of continuous efforts, the overall ambient air quality of China has improved significantly. The average annual concentration of $PM_{2.5}$ has dropped from 72 μg/m^3 in 2013 to 33 μg/m^3 in 2020. Ambient inhalable particulate matter (PM_{10}), sulfur dioxide (SO_2), and carbon monoxide (CO) all showed remarkable downward trends, and the people's sense of the blue sky was significantly enhanced (*5–6*).

As an important measure to implement the "Air Pollution Prevention and Control Action Plan," the Ministry of Science and Technology released the national key research and development plan "Research on Air Pollution Causes and Control Technologies" special project in 2015, which aims to strengthen research and development on several aspects, including (1) the formation mechanism, source analysis, migration law, monitoring and early warning of air pollution; (2) the relationship between air pollution and human health; (3) air pollution control technologies such as desulfurization, denitrification, and high-efficiency dust removal; and (4) the transformation and application of technological achievements, providing scientific and technological support for pollution control. The implementation of this special project has strongly encouraged scholars to conduct extensive, in-depth, and systematic research on the scientific issue of "the relationship between air pollution and population health." The task force conducted a comprehensive review and in-depth discussion on the important innovative achievements in the field of acute health risks of ambient $PM_{2.5}$ pollution in recent years and formed this expert consensus in order to provide scientific evidence for the government and relevant professional institutions to develop relevant policies and/or strategic measures. It also aims to provide scientific information for clinicians, public health and environmental protection professionals to understand the acute health hazards of ambient $PM_{2.5}$ pollution, and to reduce air pollution exposure for the general public, including patients.

THE CURRENT SITUATION OF AMBIENT $PM_{2.5}$ POLLUTION IN CHINA

$PM_{2.5}$ refers to particulate matter with an aerodynamic equivalent diameter of less than or equal to 2.5 μm in ambient air. Its main sources include primary particulates and secondary particulate matter generated from the conversion of SO_2, nitrogen oxides (NO_x), ammonia, and volatile organic compounds emitted from fossil fuels (such as coal, gasoline, and diesel) and biomass combustion, metallurgy and chemical industries, vehicle exhaust, road dust, etc. The chemical composition of ambient $PM_{2.5}$ is very complex, usually consisting of carbon-containing components such as organic carbon and inorganic carbon, inorganic salt ions such as sulfate, nitrate and ammonium salt, and organic matters such as polycyclic aromatic hydrocarbons, metal elements, biological substances, and mineral dust.

Ambient $PM_{2.5}$ Pollution Control has Achieved Remarkable Results in China

The ambient air quality in China was not high a decade ago. In 2012, the first batch of 74 cities that implemented the new air quality standards had an average annual $PM_{2.5}$ concentration of 72 μg/m^3, which exceeded 106% of the secondary standard limit (annual average concentration of 35 μg/m^3) of the "Ambient Air Quality Standard" (GB 3095–2012) (*5*). With the release and implementation of the "Air Pollution Prevention and Control Action Plan," ambient $PM_{2.5}$ pollution has been effectively controlled. As of 2017, the annual average concentration of ambient $PM_{2.5}$ in 74 cities dropped to 47 μg/m^3, a decrease of 34.7% compared to 2013. The average number of days with air quality reaching the standard increased from 60.5% to 72.7%; the average concentration of ambient $PM_{2.5}$ in key regions such as Beijing-Tianjin-Hebei, the Yangtze River Delta, and the Pearl River Delta decreased by 39.6%, 34.3% and 27.7%, respectively (*7*). Due to the effective implementation of 6 important measures from 2013 to 2017, including upgrading the industrial sector, upgrading industrial boilers, eliminating outdated industrial production capacity, promoting the use of clean fuels in residents' lives, shutting down small polluting factories, and strengthening vehicle emission control, SO_2, NO_x, and primary $PM_{2.5}$ emissions in China decreased by 16.4 million, 8 million and 3.5 million tons, respectively (*8*). In 2020, the national ambient $PM_{2.5}$ pollution situation was further improved, and 87% of the 337 prefecture-level or higher cities met the air quality standard on average. The average annual concentration of $PM_{2.5}$ was 33 μg/m^3, lower than the secondary standard limit of "Ambient Air Quality Standards" (GB 3095–2012) (*6*).

Ambient $PM_{2.5}$ Pollution Is Still at a High Level in China

Currently, ambient $PM_{2.5}$ pollution levels in China are still relatively high, which is higher than the population-weighted annual $PM_{2.5}$ concentration in the United Kingdom, the United States, and other countries in the same time period (about 10 μg/m^3) (*9*), and far exceeding the air quality guidelines (5 μg/m^3) issued by the World Health Organization (WHO) in 2021. In 2020, 37.1% of the 337 cities (involved prefecture-level and municipality city) nationwide still have an average annual $PM_{2.5}$ concentration that does not meet the secondary standard limit of the "Ambient Air Quality Standards" (GB 3095–2012). At the same time, heavy pollution weather still occurs on a large scale across the country. In 2017, 2,311 days of heavy pollution occurred in those cities, and the number of days with heavy $PM_{2.5}$ pollution (daily average $PM_{2.5}$ concentrations higher than 150 μg/m^3) accounted for 74.2% of the days with heavy pollution and above (*7*). In 2020, the frequency of heavy pollution in the 337 cities was the same as in 2017, and the number of days with heavy $PM_{2.5}$ pollution accounted for 77.7% of the days with heavy pollution and above (*6*). From January to February 2020, the number of days with heavy $PM_{2.5}$ pollution in prefecture-level cities across the country was the lowest in the same period in record, which was reduced by 39.2% in the same period since 2015, and the number of hours with hourly $PM_{2.5}$ concentration exceeding 300 μg/m^3 has decreased by 47.8% compared to 2015. Among them, regional pollution was at a consistently high level in key polluted areas represented by Beijing-Tianjin-Hebei and the Fenwei Plain. In 2020, the average annual $PM_{2.5}$ concentration in Beijing-Tianjin-Hebei region was up to 51 μg/m^3, the average number of days exceeding the standard was 36.5%, and the number of days with $PM_{2.5}$ as the primary pollutant accounted for 48.0% of the total number of pollution days; the average annual concentration of $PM_{2.5}$ in the Fenwei Plain was up to 48 μg/m^3, the average number of days exceeding the standard was 29.4%, and the number of days with $PM_{2.5}$ as the primary pollutant accounted for 56.4% of the total number of days with pollution (*6*).

ACUTE HEALTH RISKS OF AMBIENT $PM_{2.5}$ POLLUTION IN CHINA

The acute health risk of ambient $PM_{2.5}$ pollution usually means that short-term exposure to $PM_{2.5}$ (exposure duration usually at the level of hours to days) may cause acute damage to the body, trigger the onset of symptoms or diseases (mainly cardiovascular or respiratory disease), and lead to premature death and a series of adverse health effects.

Short-term Exposure to Ambient $PM_{2.5}$ Significantly Increases the Mortality Risk of Residents in China

$PM_{2.5}$ is the primary air pollutant in China. Short-term exposure to $PM_{2.5}$ will significantly increase the risk of non-accidental death of residents in China, especially the risks of death from cardiovascular and respiratory diseases (*10*–*12*). A time series study of 272 cities in China found that from 2013 to 2015, the annual average concentration of $PM_{2.5}$ across all cities was 56 μg/m^3. At this concentration level, the percentage increase in the risk of mortality due to non-accidental causes, cardiovascular diseases, and respiratory diseases per 10 μg/m^3 increase in $PM_{2.5}$ from lag0 to lag1 was 0.22%, 0.27%, and 0.29%, respectively (*10*). Compared to similar studies conducted in China and abroad, the relative risk of acute death of people exposed to short-term ambient $PM_{2.5}$ in China was lower than that in European and North American countries (*2–4*,*13*). A study investigating the association between ambient $PM_{2.5}$ and daily population death in 652 cities around the world found that per 10 μg/m^3 increase in $PM_{2.5}$ from lag0 to lag1, the risk of non-accidental death in the United States, Canada, Spain, and Greece increased by 1.58%, 1.70%, 1.96%, and 2.54%, respectively (*13*). The reason for the difference in effect estimates may be that the exposure-response relationship between $PM_{2.5}$ and death showed a nonlinear trend. The slope of the exposure-response relationship curve was larger at low concentration levels, thus the population death observed was more seriously affected by exposure to unit $PM_{2.5}$ concentration. With the increase of exposure level, the slope of the curve gradually decreases, and the curve becomes stable at higher exposure levels, indicating that the relative risk of acute death caused by $PM_{2.5}$ increases in a smaller magnitude (*13–14*). Currently, China is at a high exposure level of global $PM_{2.5}$ pollution concentration. For each unit level increase in $PM_{2.5}$ concentration, the relative risk of acute death in the Chinese population is relatively lower. In addition, the differences in effects may also be related to the chemical composition of $PM_{2.5}$ in different regions, climate characteristics, the health status of the study population, and the degree of socioeconomic development.

Short-term Exposure to Ambient $PM_{2.5}$ Significantly Increases the Incidence of Cardiovascular and Respiratory Diseases

Due to the small particle size and large specific surface area of ambient $PM_{2.5}$, it can enter the respiratory tract or be deposited in the alveoli, causing respiratory system damage and increasing the incidence of disease (*15–17*). Each 10 μg/m^3 increase in $PM_{2.5}$ (lag0 day) was associated with a 0.34% increase in the risk of hospitalization for respiratory diseases (including pneumonia, acute bronchitis, upper respiratory tract infection, chronic obstructive pulmonary disease, and bronchiectasis) in 252 cities in China (*15*); and each 10 μg/m^3 increase in moving average $PM_{2.5}$ (lag0–2 days) was associated with a 0.31% increase in the risk of hospitalization for pneumonia (*16*). Inhaled $PM_{2.5}$ enters the blood through macrophage phagocytosis and pulmonary capillaries and acts on the body's circulatory system, increasing the risk of cardiovascular diseases such as ischemic heart disease, stroke, and heart failure (*18–20*). A time series study of 184 cities in China from 2014 to 2017 found that a 10 μg/m^3 increase in the same-day $PM_{2.5}$ exposure was significantly associated with 0.26%, 0.31%, 0.27%, and 0.29% increases of hospital admissions for cardiovascular disease, ischemic heart disease, heart failure, and arrhythmia, respectively (*18*). A time series study of 248 cities in China from 2013 to 2017 found that a 10 μg/m^3 increase in $PM_{2.5}$ concentration was significantly associated with a 0.26% increase in same-day hospital admissions for ischemic stroke and transient ischemic attack (TIA) (*19*).

Prolonged Heavily $PM_{2.5}$ Polluted Weather Greatly Increases the Risk of Morbidity and Mortality

Heavy air pollution weather in China is usually characterized by persistent high concentrations of $PM_{2.5}$. Existing epidemiological evidence shows that prolonged heavily $PM_{2.5}$-polluted weather will greatly increase the risk of morbidity and mortality and cause more serious health problems (*21–23*). A study based on the continuous heavily polluted weather of ambient $PM_{2.5}$ occurred in Beijing from January 10 to 17, 2013, the average daily concentration of $PM_{2.5}$ was 231 μg/m^3, showed that compared with other periods in winter in 2013, emergency and outpatient risk of respiratory illness increased by 74% and 16%, respectively, during prolonged heavily polluted weather, indicating that continuous exposure to high concentrations of $PM_{2.5}$ has caused a substantial increase in the number of patients with respiratory diseases (*21*). Another time-stratified case-crossover study observed that persistent heavily or extremely heavily $PM_{2.5}$-polluted weather was associated with increased risk of cardiovascular disease hospitalization among Beijing residents. The odds ratios (ORs) associated with extremely heavy PM pollution events (PM concentration ≥150 μg/m^3 for 3 days or more) were 1.085, 1.112, 1.068, 1.071, and 1.060 for total cardiovascular disease, angina, myocardial infarction, ischemic stroke, and heart failure, respectively (*22*). The study also showed that the higher the concentration and the longer the duration of heavy pollution events, the greater the impact was on hospitalizations for various cardiovascular diseases (*22*). Among them, the risks of angina pectoris and ischemic stroke were more pronounced. However, existing research has not yet formed a unified standard for the definition of prolonged heavily $PM_{2.5}$ polluted weather (*21–23*), and the specific role of pollution concentration and duration in the health impacts of heavily polluted weather requires more researches.

The Chemical Composition of Ambient $PM_{2.5}$ is Related to the Degree of Health Hazards

Ambient $PM_{2.5}$ has a very complex chemical composition. Affected by factors such as local industrial pollution sources and energy structure, there are significant spatiotemporal differences in the chemical compositions of $PM_{2.5}$ across China. Current epidemiological studies believe that carbon-containing components (including organic carbon and elemental carbon or black carbon), some inorganic salts (mainly sulfates and nitrates), and metal elements [such as nickel (Ni), zinc, chromium, and lead] are closely related to health hazards caused by $PM_{2.5}$ (*24–28*). For example, a study on the acute effects of $PM_{2.5}$ chemical components on mortality in Xi'an found that organic carbon, elemental carbon, sulfate, and nitrate increased by an interquartile range (IQR) for 1-day lag, which were 19.3 μg/m^3, 8.8 μg/m^3, 27.8 μg/m^3, and 15.4 μg/m^3, respectively, will increase the risk of non-accidental, cardiovascular, and respiratory deaths in the population by more than 1%. An IQR increase of 0.01 μg/m^3 in 1-day lagged Ni was associated with 0.4%, 0.6%, and 0.9% increases in the risk of non-accidental death, cardiovascular, and respiratory mortality, respectively (*24*). A study on the acute effects of $PM_{2.5}$ chemical components on mortality in Beijing found that for a 0-day lag, an IQR (10.11 μg/m^3) increase in organic carbon was associated with 2.65% increase in respiratory mortality and an IQR (20.10 μg/m^3) increase in sulfate was associated with a 1.57% increase in cardiovascular disease mortality, and the acute death effect in the cold season was strengthened (*25*). The above chemical components mainly come from fossil fuel combustion (including coal combustion and vehicle emissions) and secondary particulate matters formed by ambient SO_2/NO_x. Their toxic effects are mainly produced by inducing oxidative stress and inflammatory responses. Greater $PM_{2.5}$-related acute health hazards could be observed when the content of these toxic chemical components was high (*24–28*).

Short-term Exposure to Ambient $PM_{2.5}$ Can Cause Changes in the Level of Biological Effect Markers Reflecting Early Health Damage in the Population

Epidemiological studies of the Chinese population have shown that ambient $PM_{2.5}$ mainly produces damage by causing oxidative stress and inflammatory responses in the body, as well as autonomic dysfunction. After $PM_{2.5}$ is inhaled through the respiratory tract, changes in biomarkers of lung inflammation could be observed in a short period of time, followed by systemic inflammatory response and oxidative stress, resulting in changes in the levels of biomarkers related to cardiovascular effects such as coagulation, vasoconstriction, and vascular endothelial function (*27–33*). Short-term exposure to $PM_{2.5}$ could also activate the human "hypothalamus-pituitary-adrenal axis," affecting cardiovascular health through the neuro-endocrine pathway (*31*). In a fixed panel study of healthy and prediabetic people (50–65 years old), increased $PM_{2.5}$ exposure was associated with an increment in exhaled nitric oxide (FeNO) (*34*). In a randomized double-blind controlled intervention trial of healthy college students, the reduction of $PM_{2.5}$ exposure significantly reduced the level of exhaled FeNO (*35*). The possible mechanism of cardiovascular system damage caused by short-term exposure to ambient $PM_{2.5}$ is relatively complex. In addition to triggering a systemic inflammatory response and oxidative stress, it can also cause autonomic dysfunction and changes in coagulation function, destroy vascular endothelial structure, and damage endothelial function (*35–38*). A randomized double-blind controlled intervention trial found that high $PM_{2.5}$ exposure can cause an increase in inflammatory markers such as soluble CD40 ligand (sCD40L), interleukin-1β (IL-1β), and C-reactive protein (CRP), as well as blood pressure in healthy college students (*31*). With the decrease of $PM_{2.5}$ exposure, soluble sCD40L, IL-1β, and blood pressure of healthy college students were significantly reduced (*35*). Another randomized double-blind cross-over controlled trial conducted during a typical haze event found that a 10 μg/m^3 increase in time-weighted individual $PM_{2.5}$ exposure concentration was significantly associated with an increment of 1.31%–5.33% in cytokine concentrations of IFN-α 2, GM-CSF, IL-1RA, sCD40L, IL-4, MIP-1α, MCP-1, Eotaxin, and FGF-2, respectively, in circulatory system (*39*). A study on air pollution and cardiovascular dysfunction in healthy adults in Beijing found that short-term $PM_{2.5}$ exposure was associated with increased levels of atherosclerotic plaque damage or thrombosis-related markers such as fibrinogen, CRP, and IL-1β (*33*). Due to the wide range of health effects of $PM_{2.5}$ exposure, in addition to the cardiovascular and respiratory systems, it may also act on the genitourinary system, causing a decrease in glomerular filtration rate (*40*) and the total number and concentration of sperm (*41*).

Children, the Elderly, and Patients with Cardiovascular and Respiratory Diseases are Groups Vulnerable to Ambient $PM_{2.5}$ Pollution

Several studies have confirmed that children, the elderly, and patients with cardiovascular and respiratory diseases are vulnerable groups for ambient $PM_{2.5}$ pollution (*10–11*,*42–43*). The respiratory system of children was more susceptible to the harm of ambient $PM_{2.5}$ than that of adults, and short-term exposure to $PM_{2.5}$ could result in an increase of FeNO exhaled by children (*30*,*43–46*) and increased airway resistance, causing asthma attacks (*44*). The reduction of $PM_{2.5}$ exposure would greatly reduce the level of exhaled FeNO (*30*). Short-term exposure to $PM_{2.5}$ can also cause an increase in heart rate and norepinephrine in preschool children, resulting in damage to the sympathetic-adrenal medulla (*44*). Both time series studies conducted in 272 cities and 130 districts and counties in China found that short-term exposure to $PM_{2.5}$ significantly increased the risk of non-accidental deaths and cardiovascular disease deaths in the elderly over 75 years old, and its increased risk of death exceeded the acute effect of $PM_{2.5}$ on death in the general population (*10–11*). In addition, patients with cardiovascular and respiratory diseases are particularly sensitive to $PM_{2.5}$ exposure, and short-term exposure will cause oxidative stress damage to their cardiovascular and respiratory systems, causing dysfunction and reduction, and subsequently increasing their incidence rates. In patients with chronic obstructive pulmonary diseases, a 10 μg/m^3 increase in daily average $PM_{2.5}$ concentrations was associated with a 26 mL decrease in forced vital capacity (FVC), a 26 mL decrease in forced expiratory volume in 1 second (FEV_1), and a 0.96% decrease in FEV_1% (*46*). $PM_{2.5}$ exposure for 0–6 hours significantly increased the levels of serum fibrinogen, CRP, tumor necrosis factor-α (TNF-α), and other biomarkers in patients with chronic obstructive pulmonary disease (*32*). The results of a cohort study of 4 cities (Beijing, Shanghai, Wuhan, and Xi'an) in high-risk groups of cardiovascular disease showed that an increase of 1- to 9-hour moving average $PM_{2.5}$ concentration was associated with 0.22 to 0.39 mmHg increase in systolic pressure, while the effect of $PM_{2.5}$ was attenuated in patients with controlled blood pressure (*47*).

HEALTH BENEFITS OF $PM_{2.5}$ POLLUTION PREVENTION AND CONTROL IN CHINA

The Implementation of Air Pollution Prevention and Control Policies has Significantly Improved the Public Health

During the implementation of the "Air Pollution Prevention and Control Action Plan," air pollution represented by $PM_{2.5}$ was effectively controlled, and the health benefits of the population were significant (*48–52*). A study on the health benefits of emission reduction scenarios based on short-term exposure-response relationships estimated that if the average daily concentration of ambient $PM_{2.5}$ reached the current ambient air quality secondary standard (75 μg/m^3), a total of 69,000 years of life lost could be avoided and increase life expectancy by 0.06 years among residents of 72 cities in China. Reaching the WHO-recommended transitional target 2 (25 μg/m^3) could avoid a total of 168,000 years of life lost each year and increase life expectancy by 0.14 years (*48*). A study simulating the annual ambient $PM_{2.5}$ concentration via chemical transport model and estimating the health benefits under emission reduction policy scenarios during 2013–2017, considering the chronic exposure-response relationship, demonstrated that the deaths due to the $PM_{2.5}$ were reduced from 1.389 million in 2013 to 1.102 million in 2017 in China, of which, 88.7% of contributions were from emission reductions (*49*). A long-term health benefits study focusing on emissions reduction policies in 74 cities across the country estimated that the $PM_{2.5}$ pollution was reduced by 33.3%, the death number of people due to the $PM_{2.5}$ pollution was reduced by 47,000, and the years of life lost were avoided by 710,000 years. The number of the deaths attributable to $PM_{2.5}$ pollution decreased by 26,000 premature deaths, and the years of life lost attributable to $PM_{2.5}$ were avoided by 390,000 years in Beijing-Tianjin-Hebei, the Yangtze River Delta, and the Pearl River Delta regions (*50*). Other studies have pointed out that measures such as civilian clean energy replacement will reduce indoor and outdoor $PM_{2.5}$ pollution levels simultaneously and further improve human health (*51*). For example, the integrated population-weighted exposure to $PM_{2.5}$ (IPWE) in China decreased by 47% from 2005 to 2015; 90% of the reduction was attributed to the reduction in the use of household solid-fuel, and the resulting health benefits were the avoidance of around 0.40 million premature deaths annually. If we replaced the remaining household solid fuels with clean fuels, an additional 0.51 million premature deaths would be avoided (*51*). It is worth noting that the potential benefits of emissions reduction with end-of-pipe control will be exhausted by 2030. In order to reduce the air pollution level in China to the value recommended by the WHO and effectively protect public health from pollution effects, a deep transformation of low-carbon energy under the goal of the carbon neutrality is crucial (*52*).

The short-term implementation of air pollution control policies has greatly improved air quality and brought certain population health benefits. During the 2008 Beijing Olympic Games, a series of measures to control industrial emissions and traffic pollution were implemented, and the concentration of ambient particulate matter was significantly reduced. Consequently, the economic costs associated with human health decreased by 38% and 16% before and after the Beijing Olympic Games, respectively (*53*). During the meeting of Asia-Pacific Economic Cooperation (APEC) held in November 2014 (12 days) and the military parade to commemorate the 70th anniversary of the victory of the Chinese People's War of Resistance against Japanese Aggression in September 2015 (15 days), the short-term air pollution control policies have also been carried out in Beijing. During the 2 events, the ambient $PM_{2.5}$ concentration was decreased by more than 40% compared with that before the event in Beijing. According to estimates, 39–63 and 41–65 deaths were avoided due to the decrease in $PM_{2.5}$ concentration during the APEC meeting and the military parade, respectively (*54*).

Implementation of Individual Protective Interventions Can Significantly Reduce Health Damage from Short-Term Exposure to Ambient $PM_{2.5}$

With the deepening of awareness of the health hazards of the $PM_{2.5}$ pollution, the utilization rate and popularization range of personal protective measures such as air purification devices and wearing masks have increased and expanded significantly. A number of current intervention studies have shown that the proper wearing of masks or using air purifiers can reduce individual $PM_{2.5}$ exposure effectively, thereby reducing their health hazards to varying degrees (*30–31,37,55–57*). A randomized double-blind controlled intervention trial using N95 masks as an intervention measure showed that the use of masks for protection in heavily polluted weather could reduce the levels of serum inflammatory markers and $PM_{2.5}$-related airway inflammatory responses in healthy young people (*55*). Another randomized crossover study of healthy young adults observed that the wearing particulate-filtering respirators in a short-term might reduce cardiovascular risks through enhancing the function of autonomic nervous and decreasing blood pressure (*56*).

A randomized double-blind crossover study which took healthy college students as the research object found that the $PM_{2.5}$ average concentration in the environment with air purifiers was much lower than that in the environment without air purifiers, and higher $PM_{2.5}$ environmental exposure might induce metabolic alterations associated with the hypothalamus-pituitary-adrenal and sympathetic-adrenal-medullary axes activations, indicating that air purification measures could effectively reduce the health damage caused by $PM_{2.5}$. A randomized double-blind crossover experiment on school-aged children also observed that air purifiers had a good removal effect on indoor particles of different sizes and could protect the respiratory health of children by increasing energy production and anti-inflammatory and antioxidant capacities (*30,57*).

MAIN RECOMMENDATIONS ON PREVENTION AND CONTROL OF AMBIENT $PM_{2.5}$ POLLUTION IN CHINA

Recommendations on Policy Development for Prevention and Control of Ambient $PM_{2.5}$ Pollution

At present, the situation of air pollution in China is still severe, the ambient $PM_{2.5}$ concentration is still relatively high, and the ozone (O_3) pollution has not been effectively controlled and even has an upward trend in some areas. Exposure to various air pollutants together threatens the health of local residents. Air pollution is a clear hazard to human health, and when measures are taken to reduce air pollution, it can bring significant health benefits. This complies with the primary prevention requirements of the three categories of the prevention strategy. Therefore, the task force recommends that the policies for preventing and controlling air pollution should be formulated by reducing source emissions and strengthening regional control to further reduce the level of air pollution and promote the continuous improvement of the health of residents by focusing on the national strategic goals of beautiful China and healthy China in combination of the mission requirements of carbon peaking and carbon neutrality.

First, the widespread use and efficient development of clean energy should be continuously strengthened. It is necessary to strengthen source control through energy structure reform, reduce the proportion of fossil energy consumption, and build a new energy system with hydropower, nuclear power, solar power, and wind power as the main components. Energy coupling technology should be vigorously developed to increase energy efficiency, and at the same time, the application of clean energy for civilian use should be promoted. As a result, a green and efficient energy system should be ultimately formed, which will control source emissions of air pollution and improve the health benefits brought by energy structure improvement.

Second, the promotion of industrial upgrading should be continued. Measures should be taken to strictly limit high energy consumption and high emission enterprises and accelerate the development of low energy consumption and low emission enterprises. The research and promotion of cleaner production technology should be increased to provide assistance for industrial upgrading. Rational industrial structure composition should be planned to enhance regional pollution control benefits.

Third, pollution in the transportation sector should be effectively controlled. According to the development characteristics of large cities, the number of vehicles should be controlled and the proportion of energy-saving and environmentally-friendly vehicles should be expanded via planning. It is necessary to gradually improve the fuel quality and emission standards of vehicles, vigorously develop urban green transportation, and increase the proportion of clean transportation. The health benefits of urban populations would be increased by comprehensively improving the level of cleanliness in the transportation field through multiple measures and reducing the proportion and level of pollution from transportation sources.

Fourth, the modernization of the air pollution control system should be continuously enhanced. Regular capacity building such as laws and regulations, policy mechanisms, monitoring, and supervision should be further deepened from a scientific perspective. Combined with carbon peaking and carbon neutral policy situations to optimize the construction framework of the system, carbon emission control and related contents should be included in the current air pollution control chain. The coordinated management should be strengthened to realize the dual reduction goal of carbon emission and air pollution. In the meantime, it is necessary to guide and encourage the public to adopt a green and low-carbon lifestyle and increase the participation of the whole society in pollution reduction and carbon reduction policies.

Fifth, the formulation and revision of relevant air quality standards need to be carried out gradually. Compared with the air quality guidelines issued by the WHO, combined with the latest research evidence on the health impacts of air pollution, and according to the actual situation in China, the current standards for air quality should be revised. Air pollution prevention and control should be ensured by gradually tightening the standard limits of air pollutants and increasing the protection of human health from a legal perspective.

Sixth, effects after the implementation of clean air actions and policies should be estimated, including the health benefits assessment after the implementation of relevant policies. The policies formulated and implemented by various localities for the prevention and control of air pollution should be evaluated regularly. The prevention and control policy can be optimized by screening the level of pollution concentration reduction and the degree of health benefits. Local governments are encouraged to prioritize measures that maximize population health benefits when formulating air pollution control programs.

Recommendations on Public Health Protection Linked with the Prevention and Control of Ambient $PM_{2.5}$ Pollution

Combined with the existing evidence of the impact of air pollution on human health, the research advances of human health protection, and the new air quality guideline value issued by the WHO, multiple measures should be taken to improve the public's awareness of the health hazards of $PM_{2.5}$ pollution, strengthen scientific protection capabilities, improve the overall health literacy of the public, and reduce health damage caused by $PM_{2.5}$ exposure.

First, the release of air pollution monitoring and relevant information should be strengthened and the formulation of protection policies should be promoted to ensure that the public is informed. Accurately and promptly release pollution and health-related information to ensure that the public could grasp information on changes in pollution and can take timely health protection measures and change outdoor activities. Based on the continuously strengthened air pollution monitoring network, more valid data can be obtained. By comprehensively analyzing these environmental data and health impact data, it is possible to formulate effective pollution control and health protection policies in China.

Second, the propagation of air pollution health hazards should be enhanced to help the public to understand the health hazards of air pollution and the benefits of prevention and control, and improve their relevant knowledge base. Knowledge of air pollution health hazards should be widely publicized through health education via new media dissemination, communities, healthcare institutions, primary medical staff and other channels and forms. In addition, scientific measures of health protection against air pollution should be demonstrated to promote the public to understand relevant information and strengthen risk awareness. Improve the public's awareness of the health hazards of air pollution, and improve their knowledge reserve for taking timely and effective health protection behaviors.

Third, air pollution health protection guidance and recommendations should be clarified and the operability should be improved to ensure the effectiveness of public health protection. According to the air quality forecast or warning information released by relevant agencies and combined with the results of some pollution prevention studies, different air pollution health protection guidance and suggestions could be given. These suggestions include formulating reasonable outdoor travel arrangements, correctly wearing masks that filter $PM_{2.5}$ when going out, opening windows for indoor ventilation in a timely and appropriate manner according to air quality conditions, and using purification equipment to reduce indoor $PM_{2.5}$ concentrations when the air pollution is heavy. Through the above practical guidance and suggestions, the protection skills of the public against air pollution can be effectively improved.

Fourth, it is necessary to strengthen the health protection of sensitive groups who are vulnerable to air pollution and reduce the exposure risk of the $PM_{2.5}$ for sensitive groups. For vulnerable groups such as children, the elderly, and patients with cardiovascular and respiratory diseases, the guidance and recommendations for individual protection should be targeted. The risk prevention awareness and self-protection ability of vulnerable groups should be improved through continuous health education and information dissemination in specific locations (such as hospitals, communities, kindergartens, nursing homes, and schools). This will enable these vulnerable groups to take correct protective measures based on air quality forecasts and their own characteristics to reduce health hazards caused by air pollution.

Recommendations on Research for Assessing Population Health Risks of Air Pollution

At this stage, studies focusing on acute health risks of the $PM_{2.5}$ pollution in China have basically clarified the impact of short-term exposure to $PM_{2.5}$ on local residents' health. Since the air pollution level in China is much higher than the air quality guidelines recommended by the WHO, and the health consequences of air pollution are a long-term and complex process, it is of great social and economic benefits to continue to carry out in-depth scientific research in this field. Based on the current research hotspots and technical difficulties, the task force recommends that the related research on air pollution and population health should be strengthened from the following six aspects during "the Fourteenth Five-Year Plan" period.

First, strengthen the research on air pollutant monitoring technology and monitoring system based on the promotion of accurate exposure assessment. Combined with new technologies and methods, high-density, high-precision, and real-time air pollution monitoring stations should be established; research on population and individual exposure assessment and monitoring methods should be strengthened, and the research and development of exposure model simulation and source apportionment technologies should be promoted. Based on the current monitoring system, the refined exposure data should be gradually included, and the types of air pollutants that can be monitored could be expanded. This enables monitoring systems to include both large-scale regional data and nationally mandated pollutant data, as well as small-scale individual exposure data and key pollutant data. The monitoring system can provide data support for subsequent identification and traceability of key toxic components of different types of air pollutants, as well as carrying out research on air pollution-related health effects.

Second, a full-spectrum identification and correlation study of air pollutants and health effects should be systematically carried out. Through targeted and non-targeted high-throughput screening technologies, the analysis of the $PM_{2.5}$ pollution spectrum should be carried out in-depth, and the identification of gaseous pollutants including volatile organic compounds (VOCs) should be gradually carried out. The acute and chronic health effects of air pollution in China on different human systems and the joint effects of the $PM_{2.5}$ and the O_3 should be further explored. It should be concentrated on sorting out the full health effect spectrum of $PM_{2.5}$ and gaseous pollutants and carrying out correlation research to support further identification of typical health hazards and degrees of specific substances in the pollution spectrum.

Third, studies on key toxic components and early biomarker inventory of air pollution health effects should be carried out. Based on the obtained full spectrum of the association between air pollution and health, systematic evaluation and toxicological verification studies of key components and effect biomarkers should be carried out via population epidemiological survey methods. Health impact assessment indicators should be established to dynamically monitor the health effects of the $PM_{2.5}$ and its components. And stepwise and cross validation needs to be carried out potential key components and biomarkers through research methods at different levels of evidence. Key components and early health effect biomarkers with high sensitivity and specificity that have been consistently validated in the cell, animal, and human studies could be included in the inventory. It can provide a scientific basis for the early detection and early intervention of the health effects of air pollution in China.

Fourth, the toxicity mechanism of key toxic components of air pollutants should be explored. Based on multi-omics technologies such as genome, epigenome, transcriptome, metabolome, proteome, and gut microbiome, research on the molecular mechanism of the impact of air pollution on human health should be systematically carried out. It can also explain the relationship between key toxic components of air pollutants and related diseases, key toxic pathways, and molecular mechanisms, in order to provide a possible toxicological mechanism basis for explaining the causal relationship between air pollution and health effects in China.

Fifth, research on health risk assessment and early warning of combined exposure to air pollutants should be carried out. In view of the characteristics of complex ambient pollution in China, combined with high-precision exposure assessment, the health risk characteristics of regional air pollution should be accurately quantified to reveal regional risk levels for different types of air pollutants. It is necessary to actively carry out research on air pollution health risk early warning, further promote health risk intervention research after the early warning is released, provide the public with risk warning according to local conditions, improve public health service capabilities, and reduce health risks caused by air pollution. Research on disease prevention and control closely related to air pollution should be strengthened to accurately assess and estimate the health benefits of the population under air pollution reduction measures, and to promote the formulation of air pollution and health prevention and control strategies focusing on "health risk control."

Sixth, research on the health and economic benefits of pollution reduction and carbon reduction under the carbon neutrality and beautiful China strategies should be carried out. Economy, energy, and emissions scenarios for China to achieve carbon neutrality and beautiful China strategies should be established. At the same time, by coupling the global change assessment model, global climate model, and regional meteorological-chemical model, the regional air pollution and climate change trends in China under different scenarios could be predicted. The acute health impacts of air pollution from various emergencies, including the COVID-19 pandemic and policy responses, should be assessed. Combined with the latest epidemiological evidence, the health benefits from improved air quality and climate change mitigation could be quantified, and the comprehensive economic costs of pollution and carbon reduction and health co-benefits could be estimated.

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Preplanned Studies

Effects of Cold Spells on Mortality — Ningbo City, Zhejiang Province, China, 2014–2018

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Summary

What is already known about this topic?

In recent years, climate change may lead to an increase in cold spells in the middle latitudes, and there is a positive correlation between cold spells and population mortality.

What is added by this report?

The acute response period and the vulnerable population were identified under the optimal definition of cold spells, and the mortality burden caused by cold spells was estimated.

What are the implications for public health practice?

This research would provide evidence on the acute mortality effects of cold spells in southern China. Therefore, vulnerable populations, especially the elderly, should take timely measures to reduce the health damage caused by cold spells, especially in the first week after cold waves.

The frequency of extremely cold events has gradually decreased due to globing warming around the world, but there are cold spells caused by the continuous transfer of the Arctic polar vortex in the mid-latitude regions (*1–2*). As most cities in China are located in mid-latitude areas, the frequency of cold waves is expected to increase, especially in southern China. A study showed that the cold spells in 2008 swept through south-central China, resulting in a sharp mortality increase with estimated losses exceeding US $22.3 billion (*3*). Additionally, the varying tolerance and adaptability of populations in different regions led to inconsistencies on the definition of cold spells and its health effects in different regions (*4*). This study applied time-stratified case-crossover analysis to explore the associations between cold spells and mortality during different lag periods and among different population groups during cold months of 2014–2018 in Ningbo City, China. The mortality burden attributed to cold spells was also estimated. It was found that an acute effective response period appeared within about a week. Circulatory and respiratory system diseases were sensitive diseases and the elderly over 65 years old were more vulnerable. About 21.6% deaths could be attributed to cold spells.

The daily death data, meteorological data (e.g., temperature), and air pollution data (eg. $PM_{2.5}$, O_3) during 2014–2018 came from Ningbo CDC, China Meteorological Administration, and Ningbo Environmental Protection Bureau. The research period was defined as the November–March of each year from 2014 to 2018 to exclude the impact of heatwave events. We defined cold spells as days when the daily mean temperature was at or below the P_{10} (5.5 ℃) or P_5 (3.9 ℃) percentile for at least 2, 3, or 4 consecutive days of the study period (1=cold spell days, 2=non-cold spell days). We compared the results of different definitions and selected the optimal one for stratified analysis to identify potential vulnerable populations and sensitive diseases.

The associations between cold spells and mortality were investigated in a two-stage analysis. First, the associations between cold spells and mortality were estimated by using a time-stratified case-crossover design combined with a distributed lag non-linear model (DLNM) (*5*), controlling for relative humidity and air pollutants. In order to identify the temporal characteristics of cold spells, we assessed the associations during different lag periods. Stratified analysis by sex, age, and cause of mortality was also conducted to identify sensitive diseases and vulnerable populations. Second, the attributable fractions (AFs) were estimated according to the associations between cold spells and mortality to evaluate the attributable mortality burden of cold spells (*6*). In addition, the stability of the model was validated by conducting sensitivity analysis (Supplementary Table S1, available in http://weekly.chinacdc.cn/). All analyses were implemented by using R statistical software (version 4.0.2, The R Foundation for Statistical Computing, Vienna, Austria).

During the study period, the total number of deaths was 83,532. The average daily mean temperature was 9.1 ℃ and the daily mean deaths of all causes were 120±19 per day (Table 1). This study shows the summary information of cold spells under different definitions (Supplementary Table S2, available in http://weekly.chinacdc.cn/). Under the same temperature threshold, the shorter the duration, the more cold spells and days would occur.

Figure 1 depicted the lag responses of associations between cold spells under 6 different definitions and the mortality. All cold spells had a non-linear effect on the risk of total death. The death risk showed a trend of decreasing first and then increasing, and it was the largest on the day of exposure (lag0).

According to the lag effects, the cumulative relative risks (CRR) of total mortality associated to cold spells under different definitions were obtained for different lag periods (lag0, lag0–7, lag0–14, and lag0–21) (Supplementary Table S3, available in http://weekly.chinacdc.cn/). Based on the value of CRR, we selected "cold spell A" (temperature threshold $\leq P_5$, duration ≥2d) as the best cold spell definition to conduct the stratified analysis by sex, age, and cause of death. Under the "cold spell A", the value of CRR increased with the increasing of lag periods. While a sharp increment of CRR value on lag0–7 was detected (Table 2), which indicated that there was an acute effect period about 7 days after the cold spell appeared.

The CRR for males and females were 1.322 [95% confidence interval (CI): 1.171, 1.493] and 1.220 (95% CI: 1.068, 1.394), respectively, within 21 days after cold spell happened compared with non-cold spell periods. The people above 65 years old increased the most when cold spell appeared, the CRR was 1.325 (95% CI: 1.186, 1.481). No statistically significant association was found for the people of 0–14 years, and the CRR was 1.772 (95% CI: 0.613, 5.120).

The CRR of death from respiratory diseases and circulatory diseases were 1.444 (95% CI: 1.173, 1.777) and 1.465 (95% CI: 1.261, 1.702) on lag0–21,

TABLE 1. Summary statistics of meteorology, air pollution, and mortality of cold season in 2014 to 2018 in Ningbo City, China.

Variable	N	`X (SD)	M (P_{25}, P_{75})
Meteorology			
Daily mean temperature (℃)	/	9.1 (4.8)	8.6 (5.6, 12.4)
Relative humidity (%)	/	79.4 (12.5)	81 (71.3, 89)
Average pressure (hPa)	/	1,023.9 (5.5)	1,024 (1,020, 1,027.8)
Air pollution			
$PM_{2.5}$ (μg/m³)	/	52.4 (29.9)	46 (31, 66)
O_3 (μg/m³)	/	73.1 (29.9)	73 (53, 92)
PM_{10} (μg/m³)	/	80.2 (42.1)	71 (49, 101)
CO (mg/m³)	/	1.0 (0.3)	0.9 (0.8, 1.1)
Death data			
All causes of death	83,532	120 (19)	119 (107, 132)
Sex			
Female	37,006	53 (11)	53 (46, 60)
Male	46,526	67 (12)	66 (59, 74)
Age (years old)			
15–65	16,291	23 (5)	23 (20, 27)
>65	66,771	96 (18)	94 (84, 106)
Cause of mortality			
Respiratory diseases	13,101	19 (6)	18 (14, 23)
Circulatory system diseases	26,550	38 (9)	38 (32, 44)
Genitourinary system diseases	933	1 (1)	1 (0, 2)
Endocrine system diseases	2,724	4 (2)	4 (2, 5)

Note: "/" means not applicable.

Abbreviations: N=total deaths; `X=mean; SD=standard deviation; M=median; P_{25}=the 25th percentile; P_{75}=the 75th percentile.

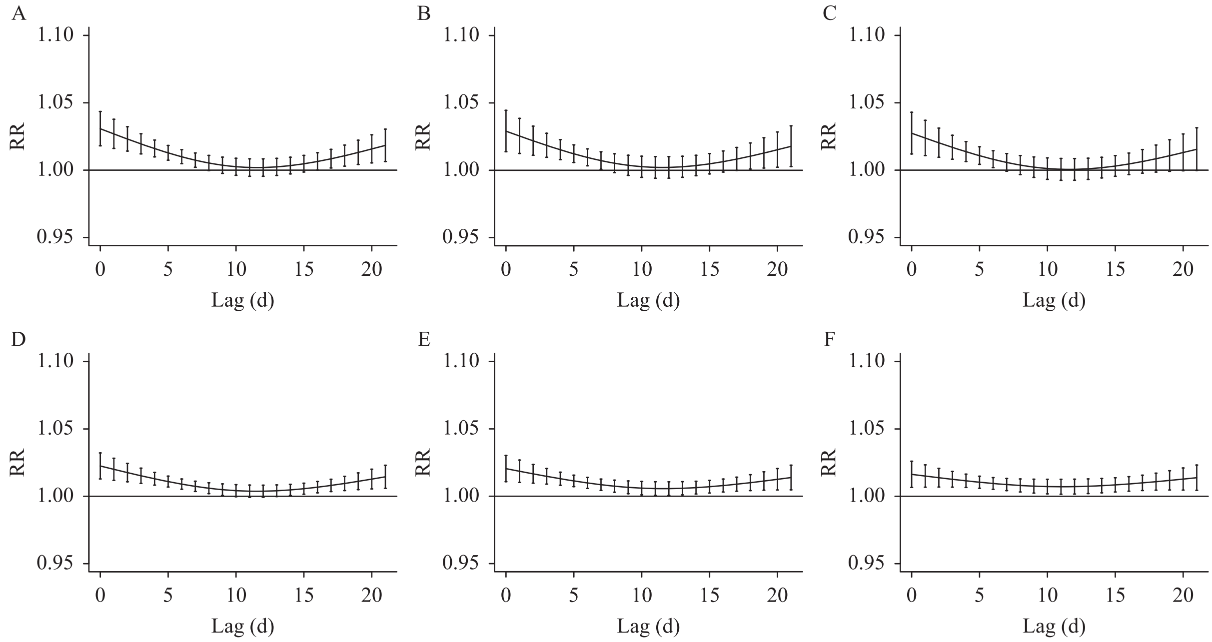

FIGURE 1. Lag-response associations between cold spells and total death under 6 different definitions in cold seasons of Ningbo, China, 2014–2018.

Note: "A–F" refers to 6 different definitions of cold spells, which were defined as days when the daily mean temperature was at or below the P_{10} (5.5℃) or P_5 (3.9℃) percentile for at least 2, 3, or 4 consecutive days during the study period. (A) P_5, ≥2 consecutive days; (B) P_5, ≥3 consecutive days; (C) P_5, ≥4 consecutive days; (D) P_{10}, ≥2 consecutive days; (E) P_{10}, ≥3 consecutive days; (F) P_{10}, ≥4 consecutive days.

Abbreviations: P_5=the 5th percentile; P_{10}=the 10th percentile; RR=relative risk.

TABLE 2. The cumulative relative risks and attributable fractions of mortality caused by cold spell for different populations.

Variables	CRR (95% CI)				AF, %(95% CI)
	Lag0	Lag0–7	Lag0–14	Lag0–21	Lag0−21
Total death	1.031 (1.018, 1.044)*	1.156 (1.095, 1.221)*	1.181 (1.099, 1.268)*	1.276 (1.153, 1.411)*	21.6 (13.3, 29.1)*
Sex					
Male	1.035 (1.020, 1.051)*	1.174 (1.100, 1.254)*	1.198 (1.099, 1.305)*	1.322 (1.171, 1.493)*	24.4 (14.6, 33.0)*
Female	1.025 (1.009, 1.042)*	1.133 (1.054, 1.219)*	1.160 (1.056, 1.274)*	1.220 (1.068, 1.394)*	18.0 (6.4, 28.3)*
Age (years old)					
14–65	1.030 (1.006, 1.055)*	1.110 (1.000, 1.232)*	1.050 (0.916, 1.204)	1.072 (0.884, 1.299)	6.7 (−13.1, 23.0)
>65	1.031 (1.017, 1.045)*	1.168 (1.100, 1.241)*	1.213 (1.122, 1.312)*	1.325 (1.186, 1.481)*	24.5 (15.7, 32.5)*
Causes					
Respiratory system	1.027 (1.001, 1.053)*	1.168 (1.044, 1.307)*	1.266 (1.094, 1.464)*	1.444 (1.173, 1.777)*	30.7 (14.7, 43.7)*
Circulatory system	1.037 (1.018, 1.056)*	1.203 (1.108, 1.305)*	1.270 (1.142, 1.412)*	1.465 (1.261, 1.702)*	31.7 (20.7, 41.2)*
Genitourinary system	1.058 (0.970, 1.153)	1.326 (0.906, 1.941)	1.284 (0.777, 2.120)	1.021 (0.495, 2.109)	1.4 (−50.6, 35.4)
Endocrine system	0.993 (0.942, 1.047)	0.976 (0.773, 1.232)	0.996 (0.738, 1.344)	1.014 (0.664, 1.549)	2.1 (−10.2, 52.6)

* P<0.05.

Abbreviations: CRR=cumulative relative risk; CI=confidence interval; AF= attributable fraction.

respectively. No statistically significant associations were found between cold spell and mortality of genitourinary and endocrine system diseases.

It was shown in Table 2 that 21.6% (95% CI: 13.3%, 29.1%) of deaths could be attributed to cold spells during cold season in Ningbo. The attributable fraction (AF) for males and females was 24.4% (95% CI: 14.6%, 33.0%) and 18.0% (95% CI: 6.4%, 28.3%), respectively. Among different age groups, the population over 65 years old had the highest death burden ascribed to cold spell, with the AF of 24.5% (95% CI: 15.7%, 32.5%). The AF value of respiratory system diseases and circulatory system diseases was 30.7% (95% CI: 14.7%, 43.7%) and 31.7% (95% CI: 20.7%, 41.2%), respectively.

DISCUSSION

Our study assessed the relationship between cold spells and mortality in Ningbo. One week after cold spells appeared, there was an acute high-effect period. And 21.6% of total mortality could be attributed to cold spells during cold season. In the first week after the cold spells, decision-makers in relevant department should consider adaptive measures in time to decrease the death risk and disease burden.

In this study, it was shown that CRR of population deaths was greater under the definition of cold wave with lower temperature threshold and shorter duration compared with higher temperature threshold. This is consistent with the research of Liang et al., that is, the optimal cold wave was defined as temperature threshold $\leq P_5$ and duration ≥2 days (*4*). However, Liu et al. found that the optimal cold wave was defined as the days with temperature threshold $\leq P_{10}$ and duration ≥4 days for COPD hospitalized population in Beijing (*7*). This suggested that different definitions may apply to different regions, climates, and health outcomes. In general, more effective cold spell definitions and early warning systems should be explored in the future to adapt to changes in the regional economy, climate, disease, and population mobility.

Within 7 days of lag, there was an acute high-effect period of the cold spell on the death risk. However, the current studies lack more evidence for the acute effect of the cold spell, especially in the southern regions in China. These findings may provide evidence for the optimal time for the prevention and control of sensitive diseases after cold waves. Additionally, the results discovered that the elderly aged above 65 years were the most vulnerable population, and circulatory and respiratory system diseases were sensitive diseases to cold spells, which were mirror with other studies (*8–10*).

For example, a study in Wuhan found that cold wave weather could increase the death risk of residents, and patients with cardiovascular disease and the elderly were the sensitive groups. But they found higher CRR values on sensitive groups (1.960 and 1.670) than our research, with the CRR of 1.465 and 1.325 for cardiovascular disease and the population of over 65 years (*8*). Moreover, the results of this study showed that the risk of death in the age group of 14–65 years also increased significantly within a short lag period (lag0–7). It is speculated that young people, especially outdoor workers, spend more time outdoors and have more opportunities to be exposed to cold waves.

This research also evaluated the mortality burden attributed to cold spells and found that 21.6% of mortality could be ascribed to cold spells during cold season in Ningbo. It was of great significance for the health risk early warning, the formulation of health preventive measures against cold waves, and the evaluation of potential benefits of public health intervention.

The study was subject to at least two limitations. First, the research area only involved one city, and the generalizability of results was limited. Second, the sample size of the group of <14 years and the group of genitourinary system diseases was too small, which may cause certain deviations in the results. However, the study will provide important evidence for evaluating the impact of cold wave on population health in southern regions in China. At the same time, health departments and medical institutions should strengthen cooperation and take active actions to do their best in providing monitoring, forecasting, and early warning services. It is suggested that vulnerable groups, especially the elderly and patients with circulatory and respiratory diseases, should take timely measures to keep warm to reduce the health damage caused by extremely cold weather events.

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Methods and Applications

Preliminary Study of Pulsed Ultraviolet Technology for Low-Temperature Disinfection

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ABSTRACT

Introduction: To explore the feasibility of pulsed ultraviolet (UV) light technology for low-temperature disinfection, a series of experiments were conducted.

Methods: Pulsed UV technology's effectiveness in disinfecting Gram-positive *Staphylococcus aureus* and Gram-negative *Escherichia coli* on different carriers were studied under varying temperatures.

Results: Under different temperatures and constant radiation illumination (i.e., distance), the disinfection effect was correlated with irradiation time; among the three carriers, the disinfection effect of cloth sheets was the best, followed by stainless steel sheets, and corrugated paper sheet. The disinfection effect on Gram-negative bacteria *Escherichia coli* was better than that on Gram-positive bacteria *Staphylococcus aureus* overall.

Discussion: Temperature has a limited effect on pulsed UV disinfection. Irradiation times and carrier types are influencing factors.

INTRODUCTION

Disinfection is an effective measure to cut off the transmission of infectious diseases which is important in the prevention and control of infectious diseases. Temperature is one of the most important factors affecting the effectiveness of disinfection, and all commonly used disinfection techniques, whether chemical or physical, have a range of applicable temperatures. There are sometimes problems with disinfection in cold environments, especially as transmission of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from contaminated cold-chain shipments to humans has been listed as one of the possible transmission routes for the epidemic (*1–2*). Not only is it difficult to apply most physical disinfection methods at this time, but the commonly used chemical disinfectants freeze and are ineffective.

Therefore, in order to cope with the cold chain and the low temperature environment in alpine regions, there is an urgent need for research into low temperature disinfection technology. Some initial progress has been made in the field of cryogenic disinfection. In terms of chemical disinfection, several studies have shown that some disinfectants suitable for ambient temperatures can maintain their disinfection performance at low temperatures when certain conditions are met, such as the addition of antifreeze agents and increased doses of disinfectant, or thermal fogging with custom optimized thermal foggers (*3–6*). In terms of physical disinfection, research is directed towards ultraviolet (UV) light, γ-rays, X-rays, electron beams, microwaves, and high-voltage pulsed electric fields (*7–10*). But there are no clear and feasible disinfection methods or evaluation criteria yet.

This study used pulsed UV technology. The experiment was designed and the disinfection effect was determined in accordance with Technical Standard For Disinfection (2002 version) to investigate the disinfection effect of pulsed UV technology on two microbial indicator bacteria at different temperatures and on different carriers. The study was carried out to verify whether there was an effect of temperature on the disinfection effect of pulsed UV technology. The cloth sheet in the carriers is a conventional carrier for disinfection experiments. The stainless steel sheet was selected to take into account the possible need for disinfection in cold chain environments such as van walls and shelves. And the corrugated paper sheet was selected considering the outer packaging of common goods. Because the resistibility of coronavirus to ultraviolet light is weaker than that of bacterial propagules, a gram-positive bacterium Staphylococcus aureus and a gram-negative bacterium Escherichia coli were selected as indicator microorganisms.

METHODS

The two bacterial species selected in this study were

Staphylococcus aureus (ATCC 6538) and *Escherichia coli* (8099). Staphylococcus aureus (ATCC 6538) was from American Type Culture Collection (ATCC), *Escherichia coli* (8099) was from China General Microbiological Culture Collection Center (CGMCC).

The three selected carriers were cloth sheet (10 mm × 10 mm in size), stainless steel sheet (12 mm in diameter and 0.5 mm in thickness) and corrugated paper sheet (10 mm × 10 mm in size). All carriers were sterilized by pressure steam before use. Among them, the production method of the corrugated paper sheet was to peel off the outer layer of the common corrugated cardboard box in daily life, and cut into square pieces of 10 mm × 10 mm. In this study, tryptone soy agar (TSA) was used as the medium, tryptone soy broth (TSB) was used as the organic interferent, and 0.03 mol/L phosphate-buffered saline (PBS) containing 0.1% tween 80 was used as a diluent.

The instruments required for this experiment include a heating and cooling circulator (the temperature is set to −20.0 °C, 0.0 °C, 20.0 °C, and the temperature difference is ±0.05 °C), a pulsed UV xenon lamp (model GZU7280, with a pulse flicker frequency of 20 Hz and an instantaneous irradiation intensity of 332.87 mW/cm^2 at a distance of 1 meter), a hand-held infrared thermometer (the measurement range is −38 ℃ to 520 ℃, and the temperature difference is ±2 ℃). Other required equipment were 37 ℃ constant temperature incubator, electric mixer, graduated straws (1.0 mL, 5.0 mL), disposable sterile petri dishes, autoclaved spare glass petri dishes, and pipette (10 μL) and matching plastic pipette tips, etc.

Bacteria freshly cultured from 18 h to 24 h were diluted with TSB to the desired concentration. 10 μL of fresh bacterial propagule suspension was applied on the vector separately, and 16–19 pieces of each bacteria carrier were prepared, of which 12–15 pieces were used for the test, 2 pieces were used as positive control, and 2 pieces were set aside. The amount of recovered bacteria for positive control should be $1×10^6$–$5×10^6$ CFU/tablet.

The stainless steel tablets were placed in a constant temperature incubator at 37 ℃ for 20 minutes to dry and ready for use. The corrugated paper tablets were set at room temperature (25 ℃) for 15 minutes to dry and reserve, and the cloth tablets for 5 minutes to dry and reserve.

The heating and cooling circulator was adjusted to −20.0 ℃ and the temperature was stabilized for the test. For each test, one piece of each of the three bacteria carrier was placed flat in a disposable sterile Petri dish with a glass Petri dish over it and put into the water bath of the heating and cooling circulator (Figure 1). The actual temperature of the carriers was measured and recorded with a hand-held infrared thermometer 5 minutes later. A pulsed UV lamp was placed above the water bath and fix the lamp height 10 centimeters away from the bacteria piece. The waiting time was set to 5 seconds, and the experiment was conducted in 4 groups respectively, with each group disinfecting for 15 seconds, 30 seconds, 1 minute, and 2 minutes. After disinfection, the bacteria piece was inoculated in an aseptic manner with appropriate dilution as the test group sample. The heating and cooling circulator was set to 0.0 ℃ and 20.0 ℃, and the experimental method to −20.0 ℃. Two pieces of each contaminated vector without disinfection by pulsed UV light were taken as positive control. The medium from the same test batch was used as the negative control.

The test group samples, positive control and negative control were incubated in a constant temperature incubator at 37 °C for 48 hours to observe the results. The test was repeated three times. The results were observed and the killing log value were calculated. On the basis of this, *Escherichia coli* was tested again with three sets of disinfection times of 5, 10, and 20 seconds. This experiment is a quantitative carrier kill test, killing log value ≥3.00 can be judged as disinfection qualified, otherwise judged as disinfection failed.

Statistical Product Service Solutions (26.0, International Business Machines Corporation, Armonk, America) was applied to statistically analyse the data, comparing the differences in the disinfection effect of each influencing factor including temperature, irradiation time, carrier type, and test strain.

RESULTS

The test was repeated with a total sample size of 297. The disinfection effect of the pulsed UV technology on two microbial indicator bacteria on different carriers at different temperatures, expressed as the average killing log value (Tables 1–2). When the set temperature was 20.0 ℃, the average carrier temperature was 20.4 ℃, ranging from 20.1 ℃ to 20.7 ℃; when the set temperature was 0.0 ℃, the average carrier temperature was 1.3 ℃, ranging from −0.8 ℃ to 2.0 ℃; when the set temperature was −20.0 ℃, the average carrier temperature was

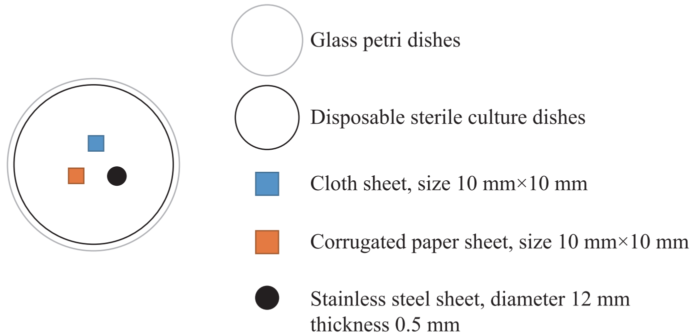

FIGURE 1. Schematic diagram of the placement of the contaminated vector in the water bath of the heating and cooling circulator during the test.

TABLE 1. Killing effect of pulsed UV light on *Staphylococcus aureus* under different temperature conditions.

Test strain	Bacterial vector	Setting temperature (℃)	Pulsed UV irradiation disinfection average elimination killing log value			
			15 s	30 s	1 min	2 min
Staphylococcus aureus	Paper sheets	20.0	1.42	2.81	6.40	>6.32
		0.0	1.30	2.36	6.40	>6.32
		−20.0	1.27	1.86	5.80	5.29
	Stainless steel sheet	20.0	2.60	5.08	>6.32	>6.32
		0.0	2.41	3.27	>6.32	>6.32
		−20.0	1.51	3.38	>6.32	>6.32
	Cloth sheet	20.0	>6.32	>6.32	>6.32	>6.32
		0.0	>6.32	>6.32	>6.32	>6.32
		−20.0	5.50	>6.32	>6.32	>6.32

Notes: Negative control sterile growth. Positive control number: $1.00×10^6$–$4.20×10^6$ CFU/sheet. The mean logarithmic value of the positive control was 6.32. >6.32 indicates sterile growth in the test group.
Abbreviations: UV=ultraviolet; CFU=colony forming units.

TABLE 2. Killing effect of pulsed UV light on *Escherichia coli* under different temperature conditions.

Test strain	Bacterial vector	Setting temperature (℃)	Pulsed UV irradiation disinfection average elimination killing log value						
			5 s	10 s	15 s	20 s	30 s	1 min	2 min
Escherichia coli	Paper sheets	20.0	1.61	2.86	3.63	4.42	5.84	>6.31	>6.31
		0.0	2.04	2.38	3.14	3.23	4.02	>6.31	>6.31
		−20.0	1.82	2.01	2.45	3.37	3.77	>6.31	>6.31
	Stainless steel sheet	20.0	2.65	4.41	4.37	>6.31	>6.31	>6.31	>6.31
		0.0	1.98	3.60	3.62	>6.31	>6.31	>6.31	>6.31
		−20.0	1.70	2.98	3.92	>6.31	4.35	>6.31	>6.31
	Cloth sheet	20.0	2.75	4.28	>6.31	>6.31	>6.31	>6.31	>6.31
		0.0	1.55	4.37	6.69	>6.31	>6.31	>6.31	>6.31
		−20.0	1.37	4.88	6.21	>6.31	>6.31	>6.31	>6.31

Notes: Negative control sterile growth. Positive control number: $1.00×10^6$–$3.83×10^6$ CFU/sheet. The mean logarithmic value of the positive control was 6.31. >6.31 indicates sterile growth in the test group.
Abbreviations: UV=ultraviolet; CFU=colony forming units.

−16.7 ℃, ranging from −18.7 ℃ to −15.0 ℃.

To enhance the comparability of the analysis, the same irradiation time as the *Staphylococcus aureus* was selected in the experimental results of *Escherichia coli*. That is, four sets of data with irradiation times of 15 seconds, 30 seconds, 1 minute, and 2 minutes. The four influencing factors of temperature, irradiation time, carrier type and test species were used as groups, respectively, and the mean killing log values were calculated for each group. The differences in the disinfection effect of each influencing factor were compared using a non-parametric test for independent samples. The value of *P* less than 0.05 indicates that the difference is statistically significant (Table 3).

The effect of temperature on the disinfection effect of pulsed UV light is limited. A non-parametric test of disinfection effectiveness for independent samples with temperature as a group at $P>0.05$, which was not significant, concluded that the difference in disinfection effectiveness at each temperature was not statistically significant. No significant effect of temperature on the disinfection effect of pulsed UV was found (Table 3).

The irradiation time is the influencing factor of pulse UV disinfection effect. A non-parametric test of disinfection effect for independent samples with irradiation time as a group found a significant *P*-value, $P<0.05$. Further comparisons between groups, the *P*-values were less than 0.05 between all other groups except between the 1-minute and the 2-minute groups. This means that the differences in disinfection effectiveness between the groups were considered statistically significant within the irradiation time of 15 seconds to 1 minute. The longer the irradiation time, the better the disinfection effectiveness was.

The carrier type is an influential factor in the effectiveness of pulsed UV disinfection. A non-parametric test of disinfection effectiveness was performed on independent samples using carriers as groups and found $P<0.05$. Further comparisons between groups, the *P*-values were less than 0.05 between any two groups, which means that the differences in disinfection effect of each carrier were considered statistically significant.

The test strain is an influential factor in the effectiveness of pulsed UV disinfection. A non-parametric test of disinfection effect for independent samples with test strains as groups found $P<0.05$, which concluded that the difference in disinfection effectiveness between the two test strains was statistically significant.

DISCUSSION

There are a number of environmental and safety issues that may arise from the use of low temperature disinfectants. These include the safety risks associated with the high concentrations required for disinfection, the pollution of the environment caused by excessive use of disinfectants, the corrosion of metals and the potential for bacteria to acquire antimicrobial resistance, the short-term and long-term effects of disinfection by-products on human health, and the safety of storage and transport of disinfectants and raw materials. It is necessary to explore physical cryogenic disinfection techniques.

Conventional UV germicidal lamps are generally low-pressure mercury vapor discharge lamps, microwave induction lamps or UV light-emitting diode (UV-LED) (*11–12*), which is far less irradiating than pulsed UV. *Ultraviolet germicidal lamp* (GB/T 19258-2012) states that, for the nominal power of 36W double-ended lamps and single-ended lamps, measured at a distance of 1 m, the initial UV radiation

TABLE 3. Comparison of the effect of different influencing factors on the effectiveness of pulsed UV disinfection.

Influencing Factors	Median (Q1, Q3)	Statistics	*P*
Setting temperature			
20.0 ℃	6.31 (5.27, 6.32)	1.792	0.408
0.0 ℃	6.31 (3.72, 6.32)		
20.0 ℃	6.26 (3.81, 6.31)		
Irradiation time			
15 s	3.63 (2.41, 6.21)	28.667	0.000
30 s	5.46 (3.38, 6.31)		
1 min	6.31 (6.31, 6.32)		
2 min	6.31 (6.31, 6.32)		
Bacterial vector			
Paper sheets	5.55 (2.54, 6.31)	23.292	0.000
Stainless steel sheet	6.31 (3.70, 6.32)		
Cloth sheet	6.32 (6.31, 6.32)		
Test strain			
Staphylococcus aureus	6.32 (2.93, 6.32)	5.465	0.000
Escherichia coli	6.31 (4.74, 6.31)		

Abbreviation: UV=ultraviolet.

illumination should be no less than 125.55 μW/cm^2 and 139.5 μW/cm^2 (*13*). And UV germicidal lamps are susceptible to environmental conditions and have poor applicability in complex environments. Continuous UV-LED is also susceptible to ambient temperatures and drive currents leading to higher solder temperatures, which ultimately affects disinfection efficiency (*14*).

Compared to this, pulsed UV technology has great advantages. Pulsed UV technology is a pulsed engineering technique using instantaneous discharge and special inert gas lamps to excite xenon gas in a pulsed form, emitting ultraviolet to near-infrared light. Its spectrum is very similar to that of sunlight, but thousands to tens of thousands of times more intense (*15*). It kills bacteria through the interplay of photochemical, photothermal and continuous pulse effects. Not only is the irradiation intensity high, the irradiation time short and no ozone or other harmful by-products have been detected, making it safer *(16)*. Therefore, the pulsed UV technique was chosen for experimental exploration in this study. The GZU7280 UV xenon lamp used in this study has a pulsed flicker frequency of 20Hz. The instantaneous radiation illumination at an experimental distance of 10 cm was calculated by laboratory measurements and formula simulations to be approximately 11,845–13,000 mW/cm^2.

This study intended to explore the initial application of pulsed UV technology in the field of low-temperature disinfection, and the influencing factors studied are mainly carrier temperature, test strains, carrier type and irradiation time. It was experimentally confirmed that the carrier temperature has a limited effect on the disinfection effect of pulsed UV. It was found that corrugated paper sheets were slightly less effective in disinfection than cloth and stainless steel sheets, suggesting that the type of carrier may have a greater effect on the disinfection effect at low temperatures. The disinfection effect of pulsed UV was also related to the irradiation time, the longer the irradiation time, the more desirable the disinfection effect. The disinfection effect of the Gram-negative bacterium *Escherichia coli* was found to be better than that of the Gram-positive bacterium *Staphylococcus aureus* overall.

This experiment verified that temperature has limited effects on the disinfection effect of pulsed UV, and irradiation time and carrier type are the influencing factors of pulsed UV disinfection effect. It suggests the feasibility of the application of pulsed UV technology in the field of low-temperature disinfection, and the preliminary application may be possible after an in-depth study.

However, there were some limitations in this study. In this experiment, only the contaminated carriers were controlled in low-temperature conditions, and the complete disinfection equipment was not put into the same environment. It was not clear whether there was an effect of ambient temperature on the irradiation intensity of the pulsed UV-Xenon lamp. Therefore, subsequent studies should be conducted in a simulated low-temperature environment to further verify the applicable temperature range of pulsed UV. The carrier type has a large effect on the disinfection effect of pulsed UV. Later tests should pay attention to the use of other common commodity outer packaging to make carriers, refine the experimental conditions, and verify the disinfection effect of pulsed UV.

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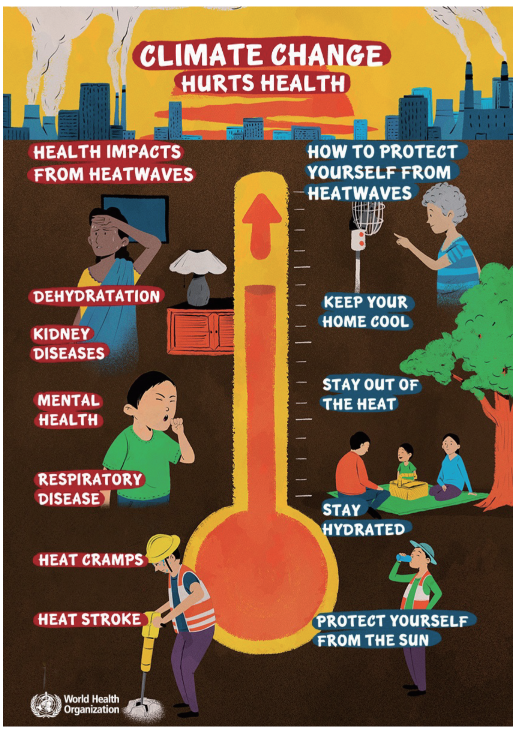

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Preplanned Studies

Long-Term Temperature Variability and Risk of Dyslipidemia Among Middle-Aged and Elderly Adults: A Prospective Cohort Study — China, 2011–2018

Jianbo Jin[1]; Yuxin Wang[1]; Zhihu Xu[1]; Ru Cao[1]; Hanbin Zhang[3]; Qiang Zeng[2]; Xiaochuan Pan[1]; Jing Huang[1,4,#]; Guoxing Li[1,3,#]

Summary

What is already known about this topic?

Long-term temperature variability (TV) has been examined to be associated with cardiovascular disease (CVD). TV-related dyslipidemia helps us understand the mechanism of how climate change affects CVD.

What is added by this report?

Based on the China Health and Retirement Longitudinal Study (CHARLS) from 2011 to 2018, this study estimated the long-term effect of TV on dyslipidemia in middle-aged and elderly adults.

What are the implications for public health practice?

This study suggested that long-term TV may increase the risk of dyslipidemia. With the threat of climate change, these findings have great significance for making policies and adaptive strategies to reduce relevant risk of CVD.

Dyslipidemia is a vital risk factor for cardiovascular disease (CVD) and has increased considerably in recent years. Temperature was convinced to be a major climate factor that affected plasma lipid levels (*1*). In 2021, Kang et al. suggested long-term temperature variability (TV), an indicator of extreme temperatures, increased the risk of CVD; furthermore, dyslipidemia can modify the long-term TV-related risk of CVD (*2*). Lao et al. also found that the variation of dyslipidemia prevalence showed seasonal features in China (*3*). However, as an indicator of climate change, TV was rarely included in exploring its impacts on dyslipidemia. Therefore, we evaluated the long-term effect of TV on dyslipidemia in middle-aged and older adults based on the China Health and Retirement Longitudinal Study (CHARLS) from 2011 to 2018.

The study data were collected from 17,596 individual participants in 150 county-level units sampled from 450 communities in 125 cities among 28 provincial-level administrative divisions (PLADs) of China selecting by the multi-stage probability sampling method. We excluded 1,615 participants with dyslipidemia, 5,753 participants without dyslipidemia reports, and 609 participants for the lack of key covariate information. The final analysis sample included 9,619 individuals without dyslipidemia at baseline with key variables in 2011–2018 (Supplementary Figure S1, available in http://weekly.chinacdc.cn/). In CHARLS, all participants provided written informed consent.

This study defined the dependent variable as being diagnosed with dyslipidemia or not at baseline. Diagnosed dyslipidemia was defined as participants' self-reports of ever having been diagnosed with dyslipidemia by doctors. The daily meteorological information of all selected cities in the same period (2011–2018) was obtained from the China Meteorological Science Data Sharing Service Network. Nearest-neighbour interpolation was applied to estimate the daily data across the mainland of China at a spatial resolution of a regular grid of 10 km × 10 km (ten-fold cross validation: R^2=0.95; root mean square error=2.34 ℃). We calculated the annual standard deviation (SD) of the daily average temperature as the TV index, and TV of the year before each survey was considered as the long-term TV exposure. TV data were assigned to each participant by their residential cities and survey year. Annual average concentrations of fine particles with a diameter ≤2.5 μm ($PM_{2.5}$) from 2011 to 2018 were calculated from a combination of satellite observations, chemical transport modeling, and ground-based monitoring (R^2=0.81; slope=0.90) (*4*). We assigned the annual average city-level $PM_{2.5}$ concentration of the year before each survey to each participant.

Recorded demographic characteristics (age, sex) in CHARLS were included in covariates. We also collated three lifestyle covariates (smoking, alcohol drinking, social interactions) and three socioeconomic status covariates (education attainment, residence, and household income per capita). Household income status was divided into binaries by average. Educational attainment was divided by whether junior school education was attained. Gross domestic product (GDP) at the city level was also collected from the National Bureau of Statistics and China's National Knowledge Infrastructure. By the Kunlun-Qinling-Huaihe line, the cities were divided into southern cities and northern cities. Environmental variables and dependent variables were time-varying for each survey, and other covariables were the values at baseline.

We assessed the association between long-term TV and the incidence of dyslipidemia using time-varying Cox proportional hazards model on a year-based time scale. We first evaluated the effects of TV on a continuous scale and reported the association with per 1 ℃ increase in TV. According to a previous study about long-term TV (*2*), TV was also divided into three categories (low<8.03 ℃, medium=8.03–10.23 ℃, high>10.23 ℃), with the low TV as the reference group. We tested the statistical significance of the linear trend between each category of TV and dyslipidemia.

We fitted three models with different categories of covariates, and TV was included as a continuous variable or categorical variable in the models. Punitive spline regression (df=3) was used to analyse the exposure-response curve of TV and dyslipidemia. Furthermore, we evaluated the modification in the association between long-term TV and dyslipidemia, stratifying by age, sex, residency, household income status, education attainment, and geographical location.

Data arrangement, cleaning, and all statistical analyses were conducted using R (version 4.0.2, R Foundation for Statistical Computing, Vienna, Austria) with packages dplyr, survival, smoothHR, and coxme. Statistical significance was defined as $P<0.05$, two sides. We included 9,619 participants without dyslipidemia and found 1,848 of them with dyslipidemia during the follow-up period. The median follow-up time was 4 years [interquartile range (IQR): 2–7 years]. In cities of CHARLS, the average annual TV between 2011 and 2018 ranged from 4.18 ℃ to 17.75 ℃. Participants living with high TV were more likely to have higher education attainment, live in urban areas, smoke more, drink less, and have higher $PM_{2.5}$ exposure and higher incidence of dyslipidemia (Supplementary Table S1, available in http://weekly.chinacdc.cn/).

We observed a positive association between dyslipidemia and long-term exposure to TV in three models (details about the models can be found in Table 1). In model 3, we observed 8.3% [95% confidence interval (CI): 4.2%–12.6%] increase in dyslipidemia for each 1 ℃ increase in TV (Table 1). Compared with low TV levels, the increase in medium and high TV levels was associated with 34.0% (95% CI: 15.6%–55.3%) and 57.9% (95% CI: 30.3%–91.3%) higher risks of dyslipidemia in a significant positive trend (Table 1). We also did a sensitivity analysis using the interval years of TV between surveys as long-term exposure and found that hazard ratio (HR) was 1.079 (95% CI: 1.036–1.123) (Table 1). Punitive spline regression with 3 degrees of freedom showed that exposure-response curve of long-term TV exposure and dyslipidemia was almost linear (Figure 1).

Marginal significant difference was found in the long-term TV-related risk between participants with low education attainment (HR: 1.093; 95% CI: 1.011–1.181) and high education attainment (HR: 1.084; 95% CI: 1.036–1.134) (Interaction *P* value=0.053) (Supplementary Table S2, available in http://weekly.chinacdc.cn/). No significant difference

TABLE 1. Cox regression models of TV and dyslipidemia among middle-aged and elderly adults, 2011–2018.

Models	TV per 1 ℃ increment [Hazard ratio (95%CI)]	TV levels [Hazard ratio (95%CI)]			*P*
		Low	Medium	High	
Model 1*	1.089 (1.071–1.107)	1.00 (Ref)	1.346 (1.167–1.553)	1.566 (1.301–1.885)	<0.001
Model 2†	1.093 (1.052–1.136)	1.00 (Ref)	1.340 (1.156–1.553)	1.579 (1.303–1.913)	<0.001
Model 3§	1.083 (1.042–1.126)	1.00 (Ref)	1.338 (1.153–1.553)	1.583 (1.303–1.924)	<0.001
Model 4¶	1.079 (1.036–1.123)	1.00 (Ref)	1.279 (1.106–1.478)	1.389 (1.148–1.681)	<0.001

Abbreviations: CI=confidence interval; $PM_{2.5}$=particulate matter of diameter ≤2.5 μm; TV=temperature variability.

* Crude model.

† Adjusted for model 1 criteria and age, sex, whether having lifestyle of smoking, drinking, annual average temperature, $PM_{2.5}$, GDP.

§ Adjusted for model 2 criteria and residency, household income per capita, educational attainment.

¶ Adjusted for model 3 criteria, using the interval years of TV between surveys as long-term exposure.

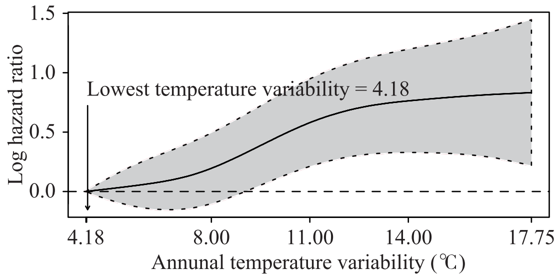

FIGURE 1. The exposure-response curve of long-term TV and dyslipidemia among middle-aged and elderly adults — China, 2011–2018.

Notes: Age, sex, marriage status, having disability, smoking, drinking, having accident injury, and having social interactions were adjusted. The solid line represents log hazard ratio, and the gray zone indicates 95% confidence interval.

Abbreviation: TV=temperature variability.

was found in the long-term TV effects in age, sex, residence, household income status, and living in different geographical regions.

DISCUSSION

In this study, we found a positive near-linear association between TV and risk the of dyslipidemia in middle-aged and elderly people. TV might affect the incidence of dyslipidemia, the risk factor of CVD.

Previous studies focused more on TV-related mortality or the incidence of CVD. A study analysed the effects of short-term TV among 31 cities in China, and observed a 1 ℃ rise of TV would increase 0.98 of CVD mortality (*5*). Shi et al. study in the USA found that for each 1 ℃ increase in TV, mortality in summer and winter increased by 0.80 and 0.41, respectively (*6*). A study in China with 35,000 participants over 35 years found that per 1 ℃ increase of long-term TV was associated with 6 increased incidence of CVD, and dyslipidemia was possibly a modifying factor (*2*). In this current study, we observed that higher TV would increase the incidence of dyslipidemia, which helps to understand the effects of long-term TV on CVD, especially among middle-aged and elderly populations. However, further studies were needed to examine the cause-and-effect relationship among long-term TV, dyslipidemia, and CVD.

Limited researches had been carried out to explore the underlying mechanism. Several studies suggested that extreme ambient temperature might affect the levels of high-density lipoprotein (HDL) and low-density lipoprotein (LDL), possibly by disturbing the absorbing of lipid (*7*–*8*). Some mechanistic studies showed that the unstable temperature would affect other blood biomarkers, such as blood cholesterol levels and plasma fibrinogen concentrations (*5*). The fluctuation in ambient temperature due to climate change would result in an imbalance between energy intake and energy expenditure, which contributes to the prevalence of metabolic syndrome (*9*–*10*). The mechanism of how TV affects plasma lipid levels needs further investigation.

The study was subject to some limitations. First, because of the limitation of geographical information, exposure of TV was assessed at the city level, which might have induced exposure misclassification. Second, since the research object was the middle-aged and elderly people over 45 years old, the results could not represent the impact of long-term TV on dyslipidemia in younger people. Third, the long-term exposure could be affected by other potential unknown confounding factors, such as indoor air-conditioner use, which might have led to inaccurate estimation.

In conclusion, we observed that long-term exposure to TV may increase the risk of dyslipidemia. Under the challenges of climate change and aging of population, these findings provided implications for making policies and adaptive strategies, such as providing extreme temperature warnings and plans to protect people working outdoors. Further studies are needed to investigate the underlying mechanisms for the reported association.

Conflicts of interest: No conflicts of interest.

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Preplanned Studies

Independent and Interactive Effects of Environmental Conditions on Aerosolized Surrogate SARS-CoV-2 — Beijing, China, June to September 2020

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Summary

What is already known about this topic?

Environmental factors such as temperature and humidity play important roles in the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) via droplets/aerosols.

What is added by this report?

Higher relative humidity (61%–80%), longer spreading time (120 min), and greater dispersal distance (1 m) significantly reduced SARS-CoV-2 pseudovirus loads. There was an interaction effect between relative humidity and spreading time.

What are the implications for public health practice?

The findings contribute to our understanding of the impact of environmental factors on the transmission of SARS-CoV-2 via airborne droplets/aerosols.

Coronavirus disease 2019 (COVID-19) has led to a global pandemic and has highlighted the role of environmental factors in the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) via droplets/aerosols. By altering the size distribution and evaporation rate of aerosols, temperature and relative humidity (RH) affect the shape and length of airborne trajectories (*1*). However, few studies have considered the interactions between multiple environmental factors and their combined impact on virus-laden droplets and aerosols.

Between June and September 2020, an orthogonal design was used to conduct suspension experiments in a 1.5 m × 1.0 m × 1.2 m laboratory exposure chamber. Independent and interactive impacts of temperature, RH, and distance on suspension time of droplets/aerosols with varying diameters and rates of size reduction of virus-laden droplets/aerosols size were explored. The numbers of droplets/aerosols with different diameters and reductions in viral load were measured in suspension and residual assays. We varied exposure chamber temperature from 16 ℃–28 ℃, RH from 30%–80%, and spreading distances of 0.5 m and 1 m to obtain data during 120 min after spreading sneeze-generated droplets/aerosols containing SARS-CoV-2 pseudovirus.

Droplets/aerosols settlement velocities increased over time under each temperature, RH, and distance range (Figure 1). With increasing time, larger aerosol particles (>1 μm) settled faster than smaller particles (<0.5 μm). After 120 min, approximately 50% of small particles (<0.5 μm) remained in suspension. Aerosol particles with diameters of >3 μm settled faster at lower RH (30%–45%), and there was a stepwise effect on aerosol particles with diameters of <0.5 μm with higher RH values (Figure 1). Aerosols remained in suspension in air currents longer than larger particles, but the numbers of suspended smaller particles decreased fastest at the highest RH range of 61%–80%.

Despite many studies on RH, few have investigated the relationship between temperature and stability of SARS-CoV-2 in aerosols. We found little difference between settling velocities of aerosols <0.5 μm in diameter under different temperature conditions compared with differences under varying RH values (Figure 1). However, particles >1 μm settled faster at higher temperatures (24 ℃–28 ℃) than at lower temperatures. Unlike variation in settling velocity from RH and temperature differences, settling velocities varied little by distances of 0.5 m and 1 m — a finding that might have been due to the relatively short (1 m) maximal dispersal distance we studied.

At the temperatures and distances studied, the lowest residual viral loads in droplets and aerosols at high RHs (61%–80%) were observed after 120 min (Table 1), suggesting that the highest RH range reduced viral loads (Figure 2A). Based on multiple

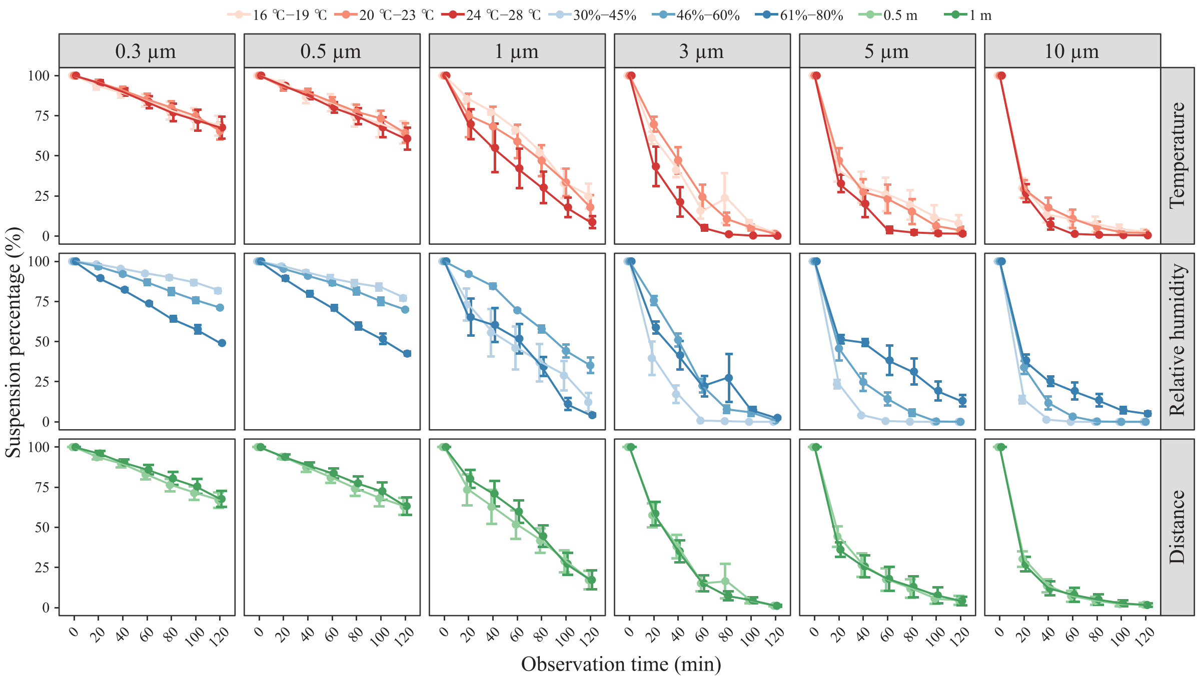

FIGURE 1. Suspension percentages of virus-laden droplet and aerosol particles with different diameters (0.3 μm, 0.5 μm, 1 μm, 3 μm, 5 μm, and 10 μm) under different conditions as a function of observation time.
Note: Environmental conditions include temperatures of 16 ℃–19 ℃, 20 ℃–23 ℃, and 24 ℃–48 ℃; relative humidity ranges of 30%–45%, 46%–60%, and 61%–80%; and spreading distances of 0.5 m and 1 m. Means and standard errors (mean±SE) are shown for three experimental replicates.

TABLE 1. Percentage of residual viral load in virus-laden droplets/aerosols under different environmental conditions at different observation time.

Experiment	T (℃)	RH (%)	Viral load (Log_{10} copies)				Percentage of residual viral load after 120 min (%)	
			0.5 m		1 m		0.5 m	1 m
			0 min	120 min	0 min	120 min	120 min *vs.* 0 min	120 min *vs.* 0 min
1	16–19	30–45	6.83	4.80	6.46	4.45	70.28	68.89
2	16–19	46–60	6.75	4.74	5.86	4.68	66.22	79.86
3	16–19	61–80	6.86	3.91	5.97	3.56	60.00	59.63
4	20–23	30–45	6.57	4.57	6.81	4.61	69.96	67.69
5	20–23	46–60	6.73	4.70	6.80	4.70	69.84	68.93
6	20–23	61–80	6.88	4.13	6.80	4.04	60.03	59.41
7	24–28	30–45	6.78	4.57	6.46	4.72	67.40	73.07
8	24–28	46–60	6.71	4.56	6.37	4.53	67.96	70.64
9	24–28	61–80	6.81	4.46	6.54	3.91	65.49	59.79

Notes: Environmental conditions include temperatures of 16 ℃–19 ℃, 20 ℃–23 ℃, and 24 ℃–48 ℃; RH ranges of 30%–45%, 46%–60%, and 61%–80%; and spreading distances of 0.5 m and 1 m.
Abbreviations: T=temperature, RH=relative humidity.

linear regression analysis, a time of 120 min and a spreading distance of 1 m significantly reduced droplet/aerosol viral loads (Figure 2A), with the most significant reduction factor being time. Mean viral loads after 120 min at distances of 0.5 m and 1 m were 66.33% and 67.81% of the mean viral loads at 0 min (Table 1).

We observed a significant interaction effect of time (120 min) and RH (61%–80%) on viral load (Figure 2C). There were no other statistically significant two-way or three-way interactions (Figure 2B, 2D, and 2E). According to modeling results, residual viral load decreased at high RH (61%–80%), while an increase in time (120 min)

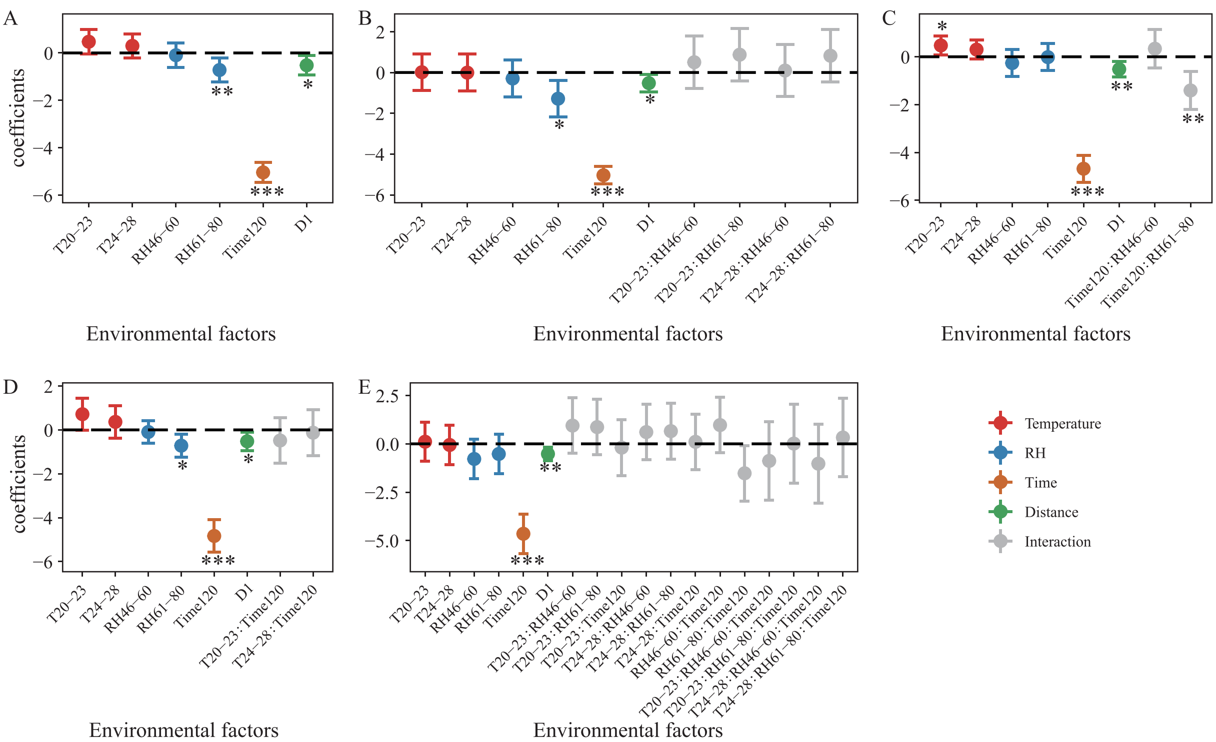

FIGURE 2. Modeled viral loads of virus-laden droplets/aerosols based on multiple interaction combinations of different environmental factors. (A) Multiple linear regression for independent factors; (B) two-way interaction between temperature and RH; (C) two-way interaction between time and RH; (D) two-way interaction between temperature and time; (E) three-way interaction among time, temperature, and RH.
Notes: Correlation refers to correlation coefficients and has no unit; T20–23 indicates the temperature was 20 ℃–23 ℃, and T24–28 indicates the temperature was 24 ℃–28 ℃; RH46–60 indicates relative humidity was 46%–60%, and RH61–80 indicates relative humidity was 61%–80%; Time120 indicates the interaction time was 120 min; and D1 indicates the spreading distance was 1 m.
Abbreviations: T=temperature, RH=relative humidity.
*: significance levels of $P<0.05$;
**: significance levels of $P<0.01$;
***: significance levels of $P<0.001$.

significantly affected the impact of RH on the viral load. Our results also showed that viral load was also significantly correlated with large particle size (≥3 μm) (Supplementary Figure S1, available in https://weekly.chinacdc.cn/), indicating that SARS-CoV-2 was mostly suspended within particles of this size class during sneezing.

DISCUSSION

The results showed that larger aerosol particles settled faster than smaller particles. The amount of small particles dicreased faster with higher relative hmidity. At high RHs, small droplets can uptake water vapor (*2*) and/or cohere to each other to form larger droplets, thus increasing their weight and size (*3*) and, therefore, increasing their settling rate. In contrast, aerosol particles with greater diameters (>3 μm) settled out faster at lower RHs (30%–45%). Higher RHs (61%–80%) significantly increased the settling velocity of aerosols with smaller diameters (<0.5 μm) and simultaneously reduced the viral load at any temperature or distance, implying that RH plays a significant role in the spread of SARS-CoV-2. The risk of transmitting SARS-CoV-2 via aerosols is higher in dry indoor environments. Therefore, this risk might be reduced by regulating the RH of indoor environments.

We also found that particles larger than 1 μm settled more rapidly at higher temperatures (24 ℃–28 ℃). High temperatures increased the evaporation of water and the conversion of respiratory droplets into aerosols. Hence, relatively high temperatures may affect large particles in a similar way that low RH values do. In addition, the mean viral loads after 120 min at different distances (0.5 m or 1 m) remained high. Time had a significant effect on viral loads, so this finding may indicate a long suspension time and potentially long-range infection through the air (*4*). But the distances we studied (0.5 m or 1 m) had little effect on aerosol particle settlement. Thus, further studies involving larger distances are required to clarify the importance of distance on aerosol transmission.

Our findings are consistent with conclusions from other studies. Larger aerosol particles (>1 μm) settled faster, consistent with a study by Lindsley and colleagues (*5*). Approximately half of the small particles (<0.5 μm) remained suspended after 120 min. Respirable viral aerosols can linger and remain viable in air for relatively long periods (<16 h) owing to their smaller size (*6*). The number of smaller particles decreased fastest at the highest RHs. Similarly, a study of influenza virus found that exhaled respiratory droplets contributed to the propagation of influenza virus at a high RH (80%) (*7*). However, our maximum observation distance was small, and the difference in viral loads at different distances was not apparent. A previous study in hospital wards in Wuhan found that SARS-CoV-2-laden aerosols could spread over a distance of up to 4 m (*8*). A modeling simulation study reported that the maximum spreading distance of droplets could reach 6 m in an extremely cold and humid environment (*1*).

The study was subject to some limitations. First, due to bio-safety concerns, the study used a SARS-CoV-2 pseudovirus instead of SARS-CoV-2 to generate droplets and aerosols. Therefore, infectivity of the virus under different environmental conditions could not be determined. Second, the experiments were performed in a laboratory exposure chamber within a quiescent indoor environment, which was not necessarily representative of real exposure scenarios. Third, high viral loads were reported for the Delta and Omicron variants of SARS-CoV-2 (*9*), and these variants of concern (VOCs) were prone to spreading quickly in enclosed spaces (*10*). However, we did not consider the potential differences in the stabilities and transmission of these VOCs and/or variants of interest under different environmental conditions.

This study found that temperature, RH, spreading time, and dispersal distance, as well as the interaction between RH and spreading time, significantly affect the transmission of SARS-CoV-2 pseudovirus via droplets/aerosols. These findings highlighted the independent and interactive effects of environmental factors on virus-laden droplets and aerosols. By elucidating the effects of different environmental conditions on the trajectory of airborne viral transmission, adaptive public health strategies for preventing and controlling COVID-19 could incorporate seasonal weather variations and local environments. In order to reduce viral load and duration in the air, the following targeted preventive control measures might be adopted: 1) appropriately increase air humidity in residential and confined public places (e.g., using humidifiers); 2) appropriately increase ambient temperature; 3) increase the frequency of air disinfection; and 4) expand the scope of disinfection. Our study provided useful information for policymakers and guidance for the general public in the global combat against COVID-19.

Conflicts of Interest: No conflict of interest.

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Vital Surveillances

Interactive Effects Between Temperature and $PM_{2.5}$ on Mortality: A Study of Varying Coefficient Distributed Lag Model — Guangzhou, Guangdong Province, China, 2013–2020

Sujuan Chen[1,&]; Hang Dong[2,&]; Mengmeng Li[3]; Lin Huang[1]; Guozhen Lin[2,#]; Qiyong Liu[4]; Boguang Wang[1]; Jun Yang[5,#]

ABSTRACT

Introduction: There is a large body of epidemiological evidence showing significantly increased mortality risks from air pollution and temperature. However, findings on the modification of the association between air pollution and mortality by temperature are mixed.

Methods: We used a varying coefficient distributed lag model to assess the complex interplay between air temperature and $PM_{2.5}$ on daily mortality in Guangzhou City from 2013 to 2020, with the aim of establishing the $PM_{2.5}$-mortality association at different temperatures and exploring synergetic mortality risks from $PM_{2.5}$ and temperature on vulnerable populations.

Results: We observed near-linear concentration-response associations between $PM_{2.5}$ and mortality across different temperature levels. Each 10 μg/m³ increase of $PM_{2.5}$ in low, medium, and high temperature strata was associated with increments of 0.73% [95% confidence interval (CI): 0.38%, 1.09%], 0.12% (95% CI: −0.27%, 0.52%), and 0.46% (95% CI: 0.11%, 0.81%) in non-accidental mortality, with a statistically significant difference between low and medium temperatures (P=0.02). There were significant modification effects of $PM_{2.5}$ by low temperature for cardiovascular mortality and among individuals 75 years or older.

Conclusions: Low temperatures may exacerbate physiological responses to short-term $PM_{2.5}$ exposure in Guangzhou, China.

INTRODUCTION

Ambient air pollution and temperature are leading environmental challenges to global public health. In 2019, $PM_{2.5}$ was responsible for an estimated 4.14 million deaths and 118 million disability-adjusted life years (DALYs) (*1*). Temperature is an important predictor of many diseases and has been perceived as a key environmental factor in climate change scenarios (*2*). Air pollution was identified as the fourth leading risk factor for death worldwide (*3*). Short-term exposure to $PM_{2.5}$ can increase the risk of death from chronic diseases (*4*).

In the context of climate change, health risk assessment of the joint effect of air pollution and temperature has attracted growing public concern (*5*). In Chengdu, China for example, stronger associations between air pollution and hospital admission for chronic obstructive pulmonary disease (COPD) were found at low-temperatures than at moderate temperatures (*6*). However, other studies have failed to identify synergetic health effects of air pollution and temperature. For example, Jhun and co-authors found that the interaction between ozone and temperature was not statistically significant in 97 US cities (*7*). In addition, potential variations of exposure-response patterns under various temperature levels have been less well documented. As an extension of distributed lag models, the varying-coefficient distributed lag model has been flexibly applied to explore interactive and time-lagged effects between different exposure hazards (*8*).

We aimed to establish the exposure-response association between $PM_{2.5}$ and mortality at different temperature strata using the varying coefficient distributed lag model in Guangzhou, China, and to explore synergetic mortality risks from $PM_{2.5}$ and temperature on vulnerable populations.

METHODS

The study period was 2013–2020. We obtained daily mortality data in Guangzhou from Guangzhou Center for Disease Control and Prevention. Causes of death were classified according to International

Classification of Diseases, Tenth Revision: non-accidental causes (A00–R99), cardiovascular disease (I00–I99), ischemic heart disease (IHD, I20–I25), stroke (I60–I69), respiratory disease (J00–J98), and COPD (J40–J47). Daily counts of non-accidental deaths were stratified by age (<75 and ≥75 years), gender, and educational level (≤9 and >9 years). We obtained daily concentrations of air pollutants (O_3, $PM_{2.5}$, PM_{10}, NO_2, SO_2, and CO) from Guangzhou monitoring stations and daily meteorological data from basic weather stations in Guangzhou from the China Meteorological Data Service Center (http://data.cma.cn/).

The varying coefficient distributed lag model, based on generalized linear models with a quasi-Poisson family (*9*), was used to estimate the modifying effect of temperature on the association between $PM_{2.5}$ and mortality. We incorporated several covariates in the model: a natural cubic spline with 7 degrees of freedom (df) per year for a time variable; a natural cubic spline with 3 df for relative humidity, air pressure, and moving average temperature (with time lags of 0–10 days); and holidays and day of the week as indicator variables. The cross-product of categorical temperature levels [low (<25th percentile), medium (25th–75th), and high (>75th percentile)] and $PM_{2.5}$ was used to examine the interaction between air pollution and temperature. In addition, stratified analyses were conducted by gender, age group, and education. Relative differences of RRs across strata [relative risk ratios (*RRR*)] were calculated to detect potential effect modifications by temperature. To verify the robustness of our results, we performed a series of sensitivity analyses. Details of the model are provided in the Supplementary Material (available in https://weekly.chinacdc.cn/). All statistical analyses were conducted in the R language environment (R Core Team 2021, Vienna, Austria) using the "dlnm", "mgcv", and "splines" packages.

RESULTS

Table 1 depicts summary statistics on daily air pollution, weather conditions, and mortality. The average $PM_{2.5}$ value was 35.1 μg/m^3 during 2013–2020. During the study period, there were 403,492 deaths registered in Guangzhou, among which cardiovascular diseases, IHD, stroke, respiratory disease, and COPD accounted for 39.5%, 16.7%, 10.3%, 14.4%, and 6.1%, respectively.

Supplementary Figure S1 (available in https://weekly.chinacdc.cn/) shows Spearman's correlations between air pollution and weather conditions. There were negative correlations between temperature and relative humidity and air pollutants (except for O_3) and positive correlations among air pollutants.

Figure 1 shows lag patterns of $PM_{2.5}$ on cause-specific mortality at different temperature levels. Effect

TABLE 1. Summary statistics for daily weather conditions, air pollution, and mortality in Guangzhou, 2013–2018.

Variable	Mean	Minimum	Percentiles			Maximum
			25th	50th	75th	
Temperature (℃)	22.2	3.4	17.4	23.3	27.3	32.0
Low (<25th)	13.6	4.6	11.8	14.0	15.8	17.7
Medium (25th–75th)	23.1	17.8	20.7	23.3	25.7	27.3
High (>75th)	28.9	27.4	27.9	28.8	29 .6	31.9
Mean humidity (%)	80.4	31.0	75.0	81.5	88.0	100.0
Mean pressure (hPa)	1,007.1	985.7	1,000.3	1,005.4	1,010.8	3,276.6
$PM_{2.5}$ (μg/m³)	35.1	3.5	20.0	30.0	45.0	150.0
Cause (Number of deaths per day)						
Non-accidental	131	79	115	128	143	238
Cardiovascular disease	55	21	45	53	62	115
Ischemic heart disease	23	6	18	22	27	51
Stroke	14	0	11	14	17	34
Respiratory disease	20	6	15	19	24	48
COPD	8	0	6	8	11	30

Abbreviation: COPD=chronic obstructive pulmonary disease.

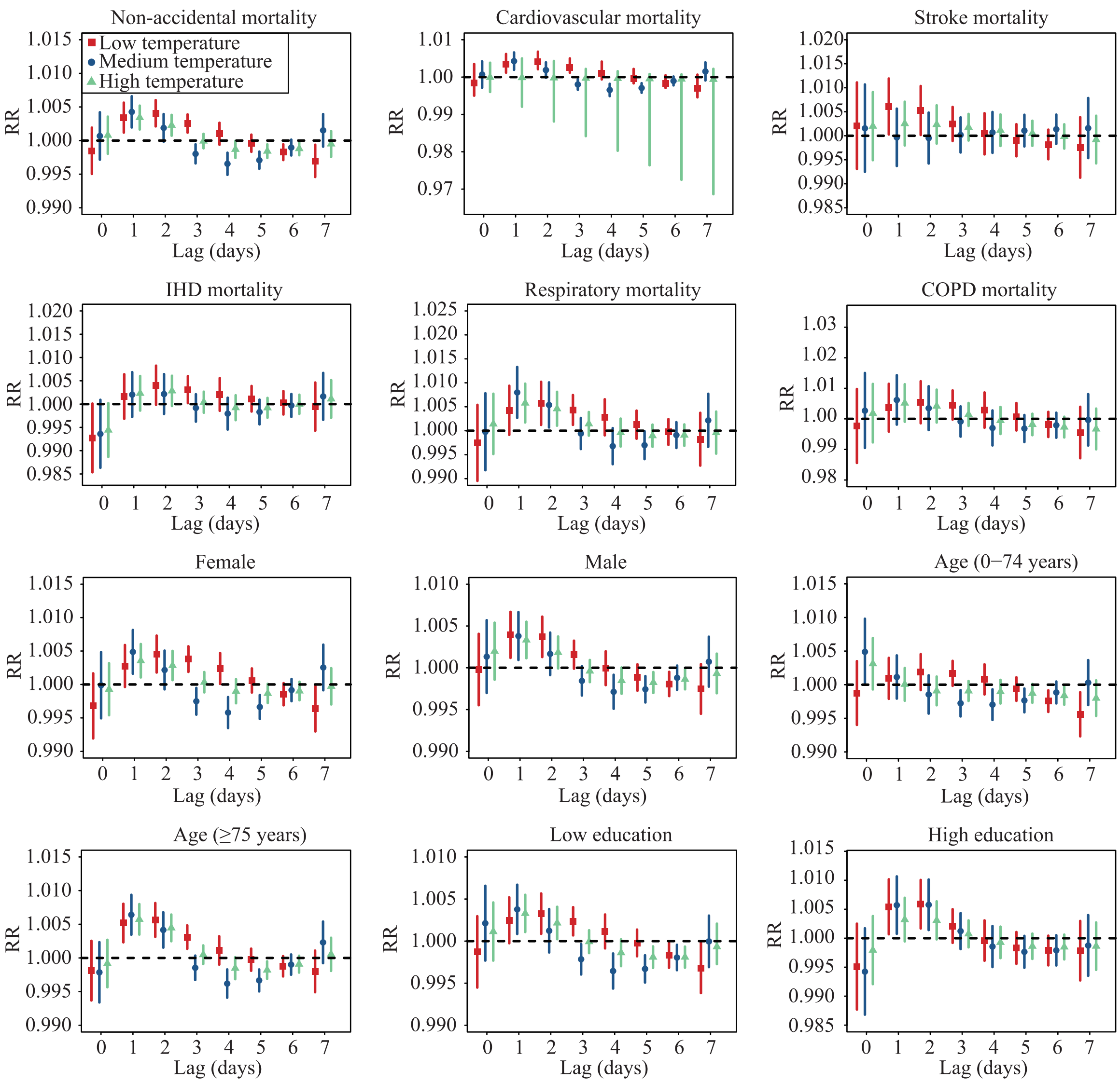

FIGURE 1. RR (95% CI) of mortality associated with 10 μg/m³ increase of $PM_{2.5}$ by a time lag of 0–7 days.
Note: dots and vertical lines represent point estimates and 95% confidence intervals of $PM_{2.5}$ at individual lag days.
Abbreviations: RR=relative risk; IHD=ischemic heart disease; COPD=chronic obstructive pulmonary disease; CI=confidence interval.

of $PM_{2.5}$ on the daily death toll of different diseases had consistent and evident trends in which mortality risks reached maximum within 1–2 lag days of exposure, then leveled off, and disappeared within 4–5 days.

Figure 2 shows the estimates of exposure-response relationships between $PM_{2.5}$ and mortality at different temperature levels. We found approximately linear associations between $PM_{2.5}$ and mortality. The highest effect estimates of $PM_{2.5}$ on mortality were consistently observed at the lower temperatures, while lower effect estimates were seen at the higher temperatures. Each 10 μg/m³ increase of $PM_{2.5}$ in low, medium, and high temperature strata was associated with respective increments of 0.73% [95% confidence interval (CI): 0.38%, 1.09%], 0.12% (95% CI: −0.27%, 0.52%), and 0.46% (95% CI: 0.11%, 0.81%) in non-accidental mortality (Table 2). There was an *RRR* of 1.01 (95% CI: 1.00, 1.01) between low and medium temperatures (P=0.02) (Supplementary Table S1, available in https://weekly.chinacdc.cn/). For cause-specific mortality, statistically significant differences between the risk of $PM_{2.5}$ across temperature levels were only observed for cardiovascular mortality, with effect estimates of 0.88% (95% CI: 0.37%, 1.39%), 0.04% (95% CI: −0.52%, 0.60%) and 0.50% (95% CI: 0.00%, 0.99%) at low, medium and high temperature levels (Table 2),

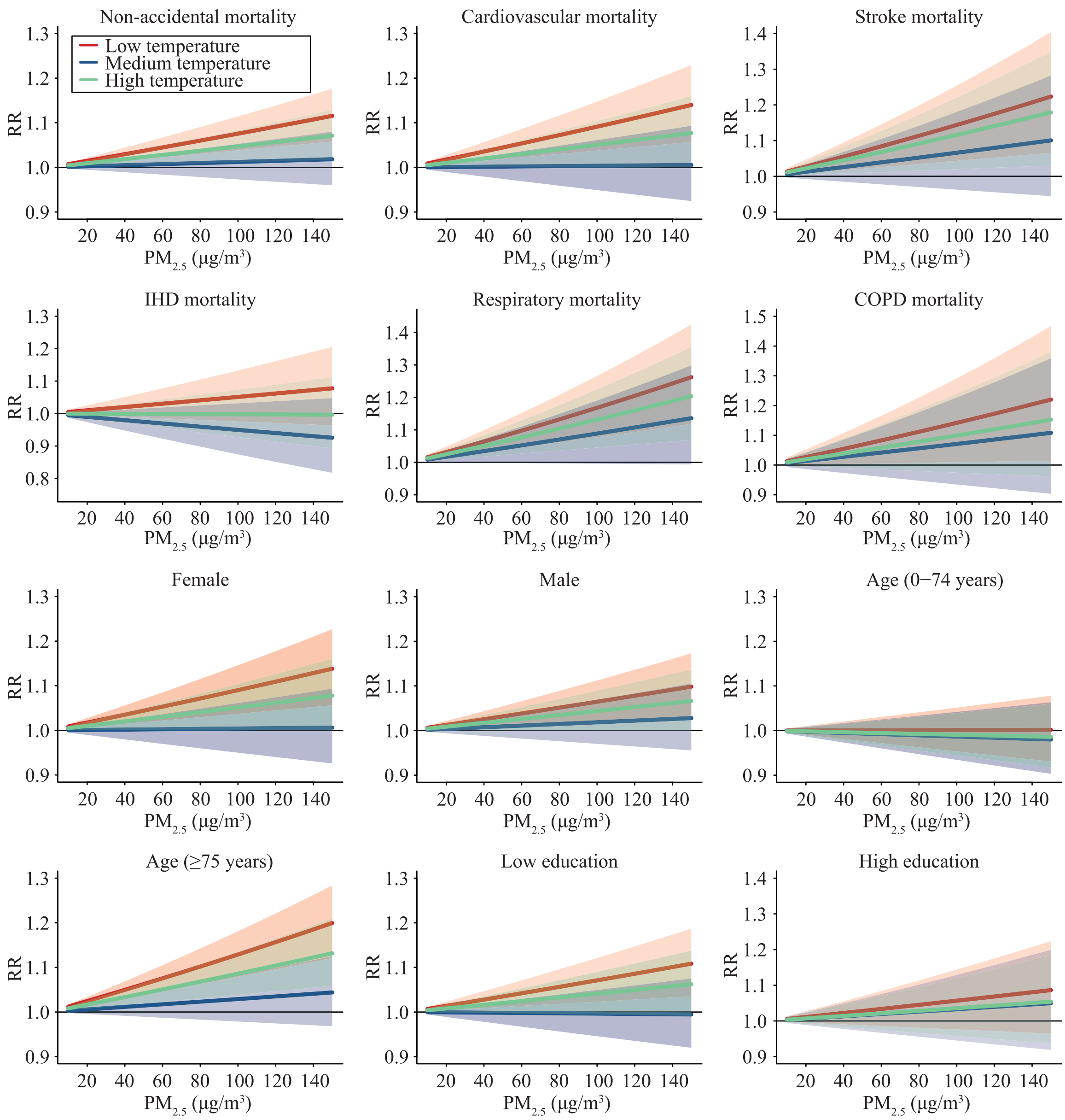

FIGURE 2. Concentration-response associations between $PM_{2.5}$ and mortality under different temperature conditions.
Abbreviations: RR=relative risk; IHD=ischemic heart disease; COPD=chronic obstructive pulmonary disease.

and an *RRR* of 1.01 (95% CI: 1.00, 1.02) between low temperature and medium temperature (*P*=0.03). The highest effect of $PM_{2.5}$ was found in respiratory mortality at low temperatures, with an effect estimate of 1.57% (95% CI: 0.75%, 2.39%); however, difference by temperature was not statistically significant.

In analyses stratified by personal characteristics, we found consistently higher effects of $PM_{2.5}$ at low temperatures compared with medium temperatures, but the only statistically significant difference was among individuals of 75 years or older. Each 10 μg/m³ increase of $PM_{2.5}$ in the low, medium, and high temperature strata was associated with increments of 1.22% (95% CI: 0.76%, 1.68%), 0.29% (95% CI: −0.22%, 0.79%), and 0.83% (95% CI: 0.38%, 1.28%) in mortality of the elderly, respectively, with *RRR* of 1.01 (95% CI: 1.00, 1.02) between low and medium temperature strata (*P*=0.01). The elderly were more susceptible to $PM_{2.5}$ compared with younger age groups under both low and high temperature conditions.

Using different degrees of freedom for time trend analyses adjusting for co-pollutants changed the effect estimates only slightly (Supplementary Tables S2–S3, available in https://weekly.chinacdc.cn/), indicating

TABLE 2. Cumulative (lag 0–4 days) mortality risk of each 10 μg/m³ increase in $PM_{2.5}$ at different temperature strata (ER, 95% CI).

Variable	Low temperature		Medium temperature		High temperature	
	ER%	95% CI	ER%	95% CI	ER%	95% CI
Non-accidental mortality	0.73*	(0.38, 1.09)*	0.12	(−0.27, 0.52)	0.46*	(0.11, 0.81)*
Cardiovascular mortality	0.88*	(0.37, 1.39)*	0.04	(−0.52, 0.60)	0.50*	(0.00, 0.99)*
Stroke mortality	1.35*	(0.43, 2.29)*	0.64	(−0.38, 1.67)	1.10*	(0.20, 2.02)*
Ischemic heart mortality	0.50	(−0.25, 1.25)	−0.52	(−1.33, 0.31)	−0.02	(−0.64, 0.77)
Respiratory mortality	1.57*	(0.75, 2.39)*	0.85	(−0.04, 1.76)	1.24*	(0.45, 2.05)*
COPD mortality	1.34*	(0.10, 2.59)*	0.69	(−0.67, 2.07)	0.95	(−0.26, 2.17)
Gender						
Female	0.87*	(0.37, 1.37)*	0.04	(−0.51, 0.60)	0.50*	(0.01, 1.00)*
Male	0.63*	(0.19, 1.07)*	0.18	(−0.30, 0.67)	0.43*	(0.00, 0.86)*
Age (years)						
0–74	0.01	(−0.48, 0.50)	−0.13	(−0.68, 0.41)	−0.09	(−0.57, 0.39)
≥75	1.22*	(0.76, 1.68)*	0.29	(−0.22, 0.79)	0.83*	(0.38, 1.28)*
Education						
Low education	0.69*	(0.23, 1.15)*	−0.04	(−0.56, 0.48)	0.40	(−0.05, 0.86)
High education	0.55	(−0.24, 1.35)	0.32	(−0.56, 1.22)	0.32	(−0.43, 1.14)

Abbreviations: ER=excess risk; CI=confidence interval; COPD=chronic obstructive pulmonary disease.
* indicates statistically significant results.

robustness of our main results. Using different temperature cutoffs (Supplementary Table S4, available in https://weekly.chinacdc.cn/) and different $PM_{2.5}$ time-lags (Supplementary Table S5, available in https://weekly.chinacdc.cn/) did not remarkably change the estimates of temperature-stratified air pollution effects on mortality.

CONCLUSIONS

To the best of our knowledge, this is one of the few studies exploring exposure-response associations between air pollution and mortality under different temperature conditions. Our study consistently observed greater mortality risks from $PM_{2.5}$ in lower temperatures than in moderate temperatures across different causes of death. Interaction effects between $PM_{2.5}$ and low temperatures were more pronounced in the elderly than in younger people.

We observed the highest effect of $PM_{2.5}$ on mortality in low temperature strata compared with high and medium temperature strata. Low temperatures have consistently been found to enhance the effect of $PM_{2.5}$ on cardiovascular mortality in Beijing (*10*), natural and respiratory mortality in Hong Kong (*11*), and COPD mortality in Chengdu (*6*). For instance, Li and coauthors found that each 10 μg/m³ increment of $PM_{2.5}$ during the lowest temperature range was associated with a 1.27% (95% CI: 0.38%, 2.17%) increase in cardiovascular mortality, compared with 0.59% (95% CI: 0.22%, 1.16%) across the whole temperature range (*10*). Likewise, the association between $PM_{2.5}$ and mortality in Hong Kong was stronger at low temperatures than at higher temperatures, with corresponding effect estimates of 0.94% (0.95% CI: 0.65%, 1.24%) and 0.47% (95% CI: 0.65%, 1.24%) for each 10 μg/m³ increment in $PM_{2.5}$ (*11*). The reduced beat frequency of nose and trachea cilia on cold days, which affects the clearance rate of particulate matter and makes people more susceptible to $PM_{2.5}$, is suspected as an underlying mechanism for the greater effect of $PM_{2.5}$ on mortality at low temperatures in Guangzhou (*12*). Some studies found that people living in warm regions probably experience a higher mortality risk during cold weather than do people living in cold regions (*13*). In addition, low temperatures may exacerbate airway inflammation and increase the burden on respiratory functions (*14*).

We also found relatively higher effect estimates of $PM_{2.5}$ on mortality in high temperatures compared to moderate temperatures, although the difference was not statistically significant, consistent with previous studies (*6*,*10*). However, another study reported a statistically significant higher health effect of $PM_{2.5}$ in high temperature strata (*15*). The discrepant results may be explained by differences in population structure and air pollution exposure patterns.

In this study, we observed a significant modification of the effect of $PM_{2.5}$ on cardiovascular mortality by low temperatures. As ambient temperature decreases, cold receptors in the skin are stimulated, the sympathetic nervous system increases catecholamine levels, blood vessels near the skin constrict to reduce heat loss, and blood pressure suddenly increases (*10*). High blood pressure can lead to oxygen deficiency, myocardial ischemia, or arrhythmia, and become a risk factor for vascular spasms and ruptures of atherosclerotic plaque that cause thromboses (*12*). Such marked changes make people more susceptible to adverse cardiovascular outcomes caused by $PM_{2.5}$. The findings are important from a public health perspective, as 39.5% of all non-accidental deaths in Guangzhou were cardiovascular deaths.

Our analysis also found significant interaction effects of $PM_{2.5}$ and low temperature among the elderly but not among young people, which is consistent with a previous study (*6*). The body's homeostasis and thermoregulatory functions, and the capacity to eliminate chemicals from the body decrease with age (*16*), which may contribute to the combined health hazards of $PM_{2.5}$ and temperature change. The elderly also suffer from higher rates of comorbidities, which may further enhance their vulnerability to environmental exposure.

The study was subject to some limitations. First, we substituted measured air pollution and air temperature at fixed outdoor monitoring stations for personal exposures, which will lead to some exposure measurement errors. Second, only adverse associations of $PM_{2.5}$ were examined in this study, leaving confounding by other factors unexplored. Last, our results may not generalize to areas with different population structures and air pollution compositions.

In summary, we observed an interaction between $PM_{2.5}$ and low temperature on mortality, especially for non-accidental and cardiovascular mortality and among the elderly. Considering the synergetic health risks of air pollution and temperature, cooperation from multiple sectors with the aim of protecting vulnerable populations may mitigate health challenges from climate change and air pollution.

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Review

Air Pollution Health Impact Monitoring and Health Risk Assessment Technology and Its Application — China, 2006–2019

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ABSTRACT

Air pollution is a significant risk factor contributing to the burden of disease in China. Health risk assessment and management are important to reduce the impact of air pollution on public health. To help formulate standardized health risk assessment techniques, a series of studies were conducted from 2006 to 2019. Through systematic review, study of molecular mechanisms, epidemiological investigation, and health effect monitoring, the overall project established a monitoring and evaluation indicator system, a comprehensive information platform, software for automatic data cleaning, and standardized health risk assessment techniques. Technical specifications have been issued by the National Health Commission for promoting health risk assessments across China. This paper introduces the project, the research approach, its main research accomplishments, innovations, and public health significance, and describes directions for further research.

BACKGROUND

Air pollution is one of the most important public health problems in China. The Global Burden of Disease Study found that ambient and household air pollution were the fourth and fifth most significant risk factors contributing to the nation's age-standardized disability-adjusted life-years rating (*1*). To reduce the impact of air pollution on health, China enacted laws requiring the establishment and improvement of environment and health monitoring, investigations, and risk assessment systems. Establishing a comprehensive air pollution and health monitoring system and health risk assessment technology involved three major technical problems. First, a population-wide indicator system for monitoring and evaluating the health effects of air pollution that spanned the life cycle and range of severity, from sub-clinical health effects to death, needed to be established. Second, a comprehensive information platform that incorporated multi-source data integration and data quality control was required. Third, a health risk assessment technology needed to be established based on the mechanisms of action of air pollution on health.

After 14 years of hard work, a multi-disciplinary collaborative research program was finished ,which was funded by the National Health Commission (NHC), the Ministry of Science and Technology, and the National Natural Science Foundation of China. Through a series of studies (systematic reviews, molecular mechanisms studies, epidemiological investigations, and health effect monitoring), the three major technical problems were solved, and specifications were formulated. The project identified the major health impacts and potential health risks of urban air pollution and is working to reduce disease burden by integrating health into air pollution prevention and control policies.

OVERALL RESEARCH APPROACH

Figure 1 shows the studies used to establish a monitoring and evaluation indicator system (MEIS), a comprehensive information platform, and health risk assessment technology. First, MEIS indicators (i.e., air pollution, and health influencing factors) were established through systematic literature review, mechanistic studies of respiratory system damage and cardiovascular disease, and analyses of existing air pollution and health monitoring systems.

Second, air quality, meteorological, toxicological, and health data were collected in selected cities with smog. After analyzing the data, evaluating data quality, and defining a data dictionary, an information

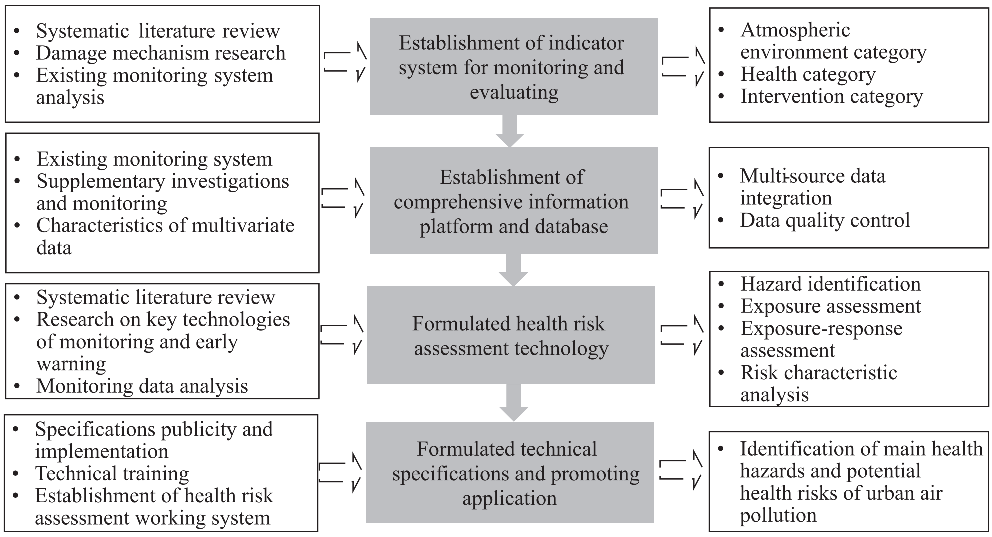

FIGURE 1. Overall research approach of air pollution health impact monitoring and health risk assessment technology and its application.

platform and database for integrated monitoring of air pollution on health was established.

Third, data application rules were clarified by studying relevant technologies, after which accurate exposure assessment models, exposure-response assessment models, public health risk assessment models, and health risk assessment techniques for air pollution were established. Finally, the indicator system, a comprehensive information platform, and health risk assessment technology were promoted to provide technical support for establishing and improving the health risk assessment system and implementing health risk management.

RESEARCH ACCOMPLISHMENTS

Figure 2 shows the research milestones leading to the indicator system, the information platforms and database, and health risk assessment technology.

Indicator System

In accordance with the World Health Organization (WHO) Driving Force-Pressure-State-Exposure-Effect-Action (DPSEEA) framework and the American hazard, exposure, health effects, and intervention (HEHI) framework, air pollution and health indicators were divided into basic, atmospheric environment, health, and intervention categories (*2*). Indicators with clear and probable causal evidence for health effects were stratified into core indicators. Research clarified the health impact of indicators that are closely related to or possibly have causal effects on health.

A guiding principle was that the indicator set should make full use of existing monitoring data in China. Studies were conducted in eight cities to determine the relationship between smog pollutant characteristics and health. Disease and death data were obtained from existing monitoring or registration systems, and data characteristics, quality, accessibility, and availability were evaluated. Ultimately, an atmospheric pollution environmental health indicator system was established based on existing literature, mechanism studies, and data from existing monitoring systems (*2*).

Information Platform and Database

Data from existing monitoring systems and supplementary investigations were used to establish a comprehensive information platform and database in selected cities with smog. Relevant data included air pollutant and fine particulate matter ($PM_{2.5}$) composition, meteorological factors, and multi-sourced data on physiological and functional indicators for entire populations and sub-groups — morbidity and symptoms, hospital outpatient services, emergencies, and hospitalizations, and causes of death. Multivariate analyses were conducted, and a data dictionary was defined. A basic database on health impact of smog was established, and data rules were defined. Data quality was evaluated by assessing repeatability, completeness, validity, and standardization. An object-oriented methodology was used to design the software, and the resulting Comprehensive Information Platform for Health Impact of Smog (HIS platform) was developed in Java with middleware technology and centralized

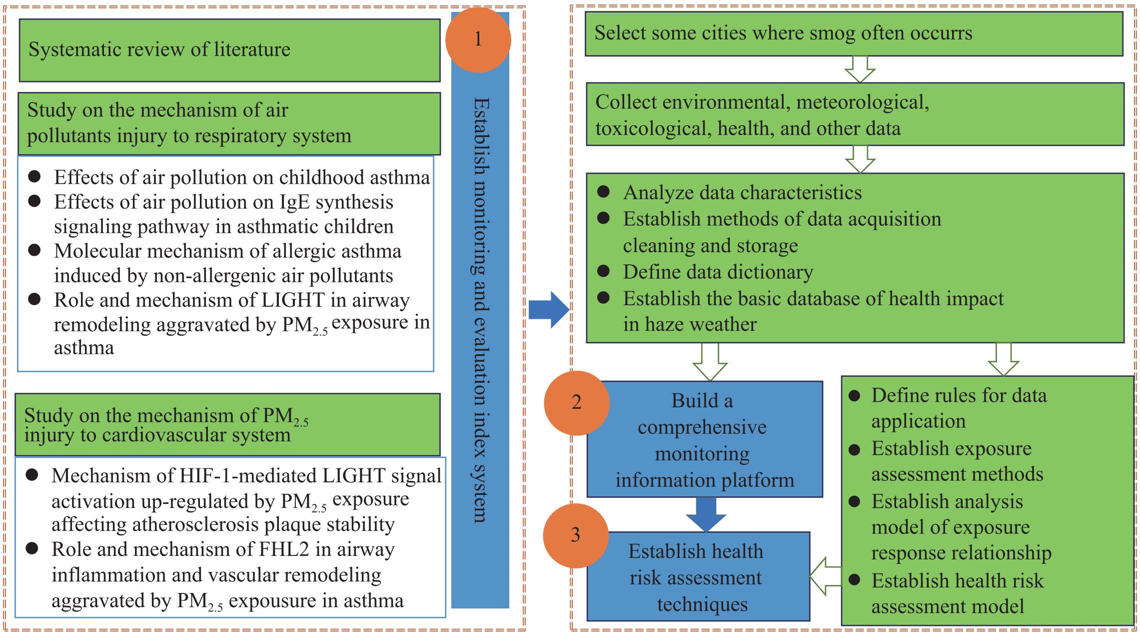

FIGURE 2. Research milestones of air pollution health impact monitoring and health risk assessment technology and its application.

Abbreviation: LIGHT=Tumor necrosis factor ligand superfamily member 14, a tumor necrosis factor (TNF) superfamily ligand; IgE=Immunoglobulin E; HIF-1= hypoxia inducible factor-1; FHL2=four and a half LIM domain protein 2.

data management. This approach allowed for multi-source data collection, data quality assessment, statistical analyses, data management, and visual display of analytic results.

Automated Data Cleaning Tools

Java was used to develop the Toolkit Software for Cleaning Monitoring Data of Air Pollutants and Health (CMDAPH software) in a structured query language database. The resulting software is a secure tool without requiring installation. It is easy to operate, allowing for intuitive data import, automatic auditing, cleaning, export, and visual display. A professional book was published: "*Methods for Data Cleaning and Public Health Impact Evaluation of Air Pollutant.*"

Health Risk Assessment and Technical Specifications

Health hazards were identified through a systematic literature review and the findings of molecular mechanism studies of airway and blood vessel damage due to typical air pollutants. An accurate assessment model of individual exposure to $PM_{2.5}$ was established by integrating air pollution data, building characteristics, permeability coefficients, 24-hour population activity patterns, and concentrations of air pollutants in microenvironments. Exposure-response evaluation models suitable for long-term or short-term exposure were formulated using public health, air pollution, and meteorological data. Based on sensitivity analyses, the influence of other air pollutants, meteorological factors, day of the week, time, and seasonal trends were adjusted to evaluate the relation between smog exposure and outcomes in several pilot cities in China. This model became a key method for population-based and toxicity-based health risk assessments. These technologies were integrated to develop comprehensive, mechanistic health risk assessments. Major project outputs included the publication of the *Methods and Application for Health Risk Assessment of Air Pollution*, and formulation of *Technical Specifications for Health Risk Assessment of Ambient Air Pollution* (HRAAAP specification, WS/T 666–2019).

INNOVATIONS

This project brought about several technical innovations in systems integration. Based on molecular mechanism study results, monitoring data analyses, and DPSEEA and HEHI frameworks, an end-to-end technology system was established. This system, in turn, led to the establishment of a monitoring and evaluation indicator system, a comprehensive information platform with multi-source data integration and data quality control, and comprehensive health risk assessment technology.

The molecular mechanism studies yielded six major findings or outputs. First, non-allergenic air pollutants such as formaldehyde, phthalate, and $PM_{2.5}$ may cause allergies and asthma. Second, two phthalates (i.e., diisononyl phthalate, Di 2-Ethyl Hexyl Phthalate (DEHP)] increase blood pressure by activating angiotensin converting enzyme and inhibiting the nitric oxide (NO) pathway. DEHP with high molecular weight and dibutyl phthalate with low molecular weight had different effects on blood pressure due to their differential effects on the renin-angiotensin-aldosterone system or estrogen levels (*3–6*). Third, $PM_{2.5}$ exposure can induce the expression of nitric oxide synthase 2 (NOS2) and production of NO to cause high levels of autophagy. Conversely, blocking the NOS2 signaling pathway can inhibit autophagosome formation and subsequent cell death. NO plays a key role in the lung oxidative stress response earlier than in inflammatory responses (*7*). Fourth, four and a half LIM domain protein 2 (FHL2) and autophagy play an important role in the vascular inflammatory response and vascular remodeling induced by $PM_{2.5}$ exposure (*8*). Fifth and sixth, two markers and primers developed in this project were converted to patents — a marker for the detection of asthma in children (Grant No. ZL 201110060515.7) and a marker and primer for the detection of asthma in children (Grant No. ZL 201310299330.0).

Another innovative development is obtaining software copyrights by the project's HIS platform and CMDAPH software.

The $PM_{2.5}$ individual exposure assessment model became more accurate and comprehensive, as it considered building characteristics, indoor and outdoor $PM_{2.5}$ concentrations, permeability coefficients, 24-hour population activity characteristics, and the concentrations of air pollutants in residential, office, supermarket, outdoor exercise, or transportation settings (*9–10*).

Finally, the HRAAAP specification represented the first health risk assessment standard of environmental exposure for China's health industry (*11*).

PUBLIC HEALTH SIGNIFICANCE

The key air pollution health risk assessment technologies established by the project expanded the understanding of health impacts and health risks caused by typical air pollutants and provided technical support for establishing an environmental health risk assessment and risk management system.

Promoting Monitoring and Health Risk Assessment Across the Country

Due to severe smog and concerns about its health impact, NHC launched the national air pollution (smog) health impact monitoring program in 2013. The establishment of a timely indicator system provided a top-level design and monitoring scheme. The HIS platform and CMDAPH software have also been widely used in monitoring projects since 2017, including in applications in all 31 provincial-level administrative divisions (PLADs), 87 monitoring cities, and 167 monitoring sites by 2021.

The HRAAAP specification was promulgated by NHC in 2019 and officially implemented on January 1, 2020. By implementing standardized technical training in the monitoring program, monitoring staff in the 31 PLADs improved their skills in data review, clearing, statistical analysis, and health risk assessment. Air pollution health risk assessment has been widely implemented in monitoring cities. Identification of major health impacts and potential health risks of urban air pollution based on local conditions provides evidence and a scientific basis for the formulation of air pollution prevention and control policies and the development of targeted health protection measures.

Decision-making Basis for National Environmental Health Actions

Promulgation and implementation of the HRAAAP specification enabled the establishment of relevant standards for environmental and health risk assessment and laid a foundation for establishing a risk assessment system. It also supported decision-making related to air pollution health risk management and public health protection in China. Relevant results provided a scientific basis for formulating the Three-year Action Plan for Resolutely Fighting the Battle Against Pollution, Comprehensively Strengthening Environmental and Health Work, and the Healthy China Action (2019–2030): Action to Promote a Healthy Environment.

Enhancing Public Health Protection Awareness

The popular science books *Smog and Health Knowledge Q&A* and *Abnormal Weather and*

Environmental Pollution Events Cognition and Response were published as part of this project. The content was translated into various publicity materials including web pages, posters, and leaflets. Targeted health protection suggestions were promoted through display boards, websites, and news media. In a national survey, 430,000 parents received information about the prevention and control of childhood asthma. These efforts enhance the public's awareness of the health impact of air pollution and protective behaviours that can be adopted, thus playing an important role in reducing the health impact of air pollution.

NEXT RESEARCH DIRECTIONS

The atmosphere has a complex composition, and with the widespread application of new chemicals, people are exposed to an increasing number of novel air pollutants. Many studies have shown that health effects differ by air pollutant composition. It is still not clear how to accurately assess the health impact and health risk of single pollutants in mixed pollutant exposures. With the progress of science and the emergence of new air pollutants, future research should focus on several topics. First, health impact and mechanisms of action of new air pollutants and key components of particulate matter should be investigated to provide more evidence for causal health effects of air pollutants. Second, exposure characteristics and quantitative evaluation methods should be established for new air pollutants and air pollutant mixtures. This will provide accurate exposure data for the assessment of the health impact of pollutants. Third, a quantitative health risk assessment technology needs to be established to improve health protection intervention measures by assessing combined exposures of various air pollutants and the comprehensive influence of geographical, meteorological, population, and economic factors. Finally, the impact of continuous air quality improvement or deterioration on public health requires further investigation to support the establishment of a sustainable development path between economic development and ecological balance.

Conflicts of interest: No conflicts of interest.

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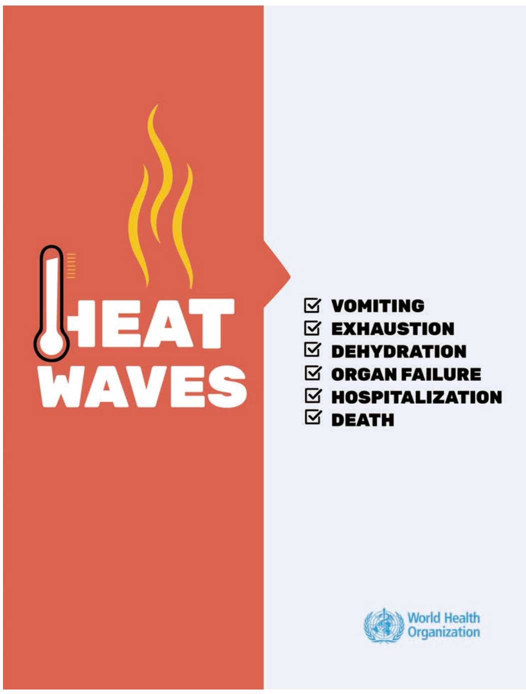

HEAT HEALTH RISK EARLY WARNING ISSUE

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Cover Image: adapted from the World Health Organization, https://www.who.int/multi-media/details/heat-waves.
This week's issue was organized by Guest Editor Tiantian Li.

Foreword

A Public Health Initiative for Action on Early Warning of Heat Health Risks

Tiantian Li[1,#]

Heatwaves, also known as extreme heat events, represent periods of excessively hot weather and rank among the most perilous natural hazards worldwide due to their increased mortality risk, especially among vulnerable populations. The frequency, intensity, and geographical spread of heatwaves are noticeably increasing in the setting of climate change (*1*). In 2019, there were a reported 475 million heatwave events worldwide, an increase of 160 million per capita days in comparison to 2016 (*2*). Disturbingly, in 2003 there were approximately 25,000–70,000 premature heat-related deaths in Western Europe (*3*), and in the summer of 2010 around 55,000 excess deaths in Russia were linked to heatwaves (*4*). A similar pattern was observed in 2019 with approximately 26,800 deaths in China being attributed to heatwaves (*5*). Furthermore, in the same year, nearly half (46.2%) of the total global heat-related deaths were elderly individuals, with the majority of these deaths occurring in Japan, Eastern China, Northern India, and Central Europe (*6*). Given the relentless trends in population aging and urbanization, heatwaves could pose a significantly bigger health hazard in future years. Projections from the World Health Organization (WHO) predict over 92,000 premature deaths from high temperatures globally by 2030, with over 19,000 premature deaths expected in Eastern Asia (inclusive of China and the Republic of Korea) alone (*7*). Hence, the development and implementation of effective strategies to combat heatwaves, as well as improving public safeguards, are and will continue to be pivotal challenges across the intersecting fields of climate change and public health.

In an effort to mitigate the health consequences of heat, the United States pioneered the establishment of the Hot Weather-Health Watch/Warning System during the 1990s. This was not only based on traditional high-temperature forecast warnings, but also focused on the premature mortality risk (*8*). The devastating heatwave of 2003 spurred many European countries into active research about health risks associated with such heatwaves. This resulted in the development of a more comprehensive heat health warning system (*9*). In 2015, to further global public health protection, the World Meteorological Organization and WHO collaboratively published the guidance document “Heatwaves and Health: Guidance on Warning-System Development”. This aimed to influence the development of similar early warning systems worldwide (*10*).

In China, the reaction to heatwaves primarily depends on the early heat wave warnings disseminated by the China Meteorological Administration, which consist of three classifications: yellow, orange, and red. However, this system exclusively considers temperature intensity, neglecting the correlation between heatwaves and health ramifications. Consequently, its effectiveness in safeguarding public health remains limited. Over the past two decades, Chinese researchers have endeavored to develop a more efficient heatwave health risk early warning system. Despite pieces of related research, the full-scale implementation of this system across the country has not yet materialized.

In 2001, the Shanghai Meteorological Bureau, in conjunction with the Shanghai Health Commission, launched the pioneering “Heatwave/Health Warning System” in Shanghai Municipality (*11*). Subsequently, in 2013, led by the National Institute of Environmental Health, Chinese Center for Disease Control and Prevention (NIEH, China CDC), a heatwave health early warning system was set up in Shenzhen, Nanjing, Chongqing, and Harbin, which are located in various climatic zones with different climatic characteristics (*12–14*). Researchers gathered historical data related to meteorology, air quality, mortality, and morbidity, and established models to identify the relationships between heatwaves and mortality and morbidity rates for various diseases in each city. The warning levels encompass red, orange, yellow, and blue. Depending on the risk reaching the corresponding warning level, the system generates an alert indicating the disease risk level, appropriate response measures, and recommendations for mitigation for diverse population groups. However, this system only operated on a trial basis and was not expanded nationwide.

In response to the prevailing global heatwaves and the inadequate public health protective measures in many countries, we recently proposed a comprehensive prevention and control framework. This framework incorporates a full spectrum coverage of heat health risk management into heat health early warning systems. It includes identifying warning signals based on the attributes of health issues caused by heat, and undertaking proactive and targeted measures on the basis of early warning information concerning heat-related health risks throughout the summer season (*15*). Under this framework, researchers from the NIEH, China CDC, developed a heat health risk early warning model that includes China's various climatic zones. The model, which relies on heat or heatwave-related mortality risks, recognizes the threshold levels for health risk surveillance, watch, and warnings (consisting of three warning levels) applicable for the entire summer season. This innovative model, which provides heat health risk alerts throughout the summer, allows for a more comprehensive public management of heat health risks compared to previous models that focused solely on warnings for extreme heat or health risks associated with extreme heat.

This innovative model has been successfully translated to local CDCs for application. For example, in collaboration with the NIEH, China CDC, the Jinan CDC leveraged this model to develop a heat health risk early warning announcement platform that issued its first cautionary message about heat or heatwave-related health risks on August 2, 2021. The platform provides a three-day forecast on potential heat or heatwave-related health risk surveillance, watch and warning information for Jinan City, which is disseminated via WeChat Official Account of the Jinan CDC. In addition to covering all local counties, the platform also provides health protection recommendations. The public can therefore access early warning information from the platform to understand their health risk from the heat or heatwaves predicted for the next three days, facilitating proactive protection against the impending high temperatures. According to the estimation, the implementation of this heatwave health risk early warning in Jinan resulted in a reduction of 10.9 deaths per million people during the 2022 warm season's warning stage. Furthermore, it helped to prevent economic losses of approximately 227 million Chinese Yuan (CNY). If this early warning system had been implemented nationally during the warm season of 2022, it could have yielded significant health benefits, potentially saving 15,115 lives and averting economic losses of approximately 62.0 billion CNY (*16*). In conclusion, the successful adoption of this system in Jinan represents a solid foundation for its further promotion among other local CDCs in China.

This edition centers on the subject of heat health risk early warning, incorporating two "Preplanned Studies" articles and one "Recollections" piece. An analysis by Chen et al. appraised the benefits of utilizing the heat health risk warning model in Jinan, and the potential for its nationwide promotion in the future (*16*). To tackle the deficiency in extended-term heatwave forecasts, Zhang et al. launched an innovative early warning system with the goal of predicting heatwave-related health hazards, within China, at sub-seasonal to seasonal intervals. The results from the evaluation indicated substantial potential for this system (*17*). Sun et al. conducted a review of NIEH, China CDC's experience in promoting environmental health risk early warning intervention, and suggested upcoming challenges and prospects (*18*). This special issue methodically encapsulates nationwide experiences of pioneering efforts in heat health risk early warning, thus providing a robust foundation for China CDC to further advance health risk early warning for environmental risk factors such as heat throughout the country.

One of the functions of the newly established National Bureau of Disease Control and Prevention is surveillance and early warning. There is an immediate need to develop early health risk warnings for environmental risk factors such as heatwaves. We propose the following steps. First, a standard technical system for early health risk warnings stemming from environmental risk factors must be designed in advance. Second, creating and publicly disseminating an information platform that can forecast and provide early warnings about health risks from environmental hazards is essential, with a focus on protecting vulnerable populations. Third, efforts should be accelerated to establish working and emergency consultation mechanisms for early health risk warnings related to heatwaves and other hazardous environmental factors. Additionally, the development of a coordinated mechanism between the national CDC and local CDCs is crucial. Finally, we recommend the gradual establishment of a collaborative working mechanism for early health risk warnings, with the China CDC serving as the primary issuer and multiple departments collaborating.

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Preplanned Studies

Evaluating the Applicability and Health Benefits of the Graded Heat Health Risk Early Warning Model — Jinan City, Shandong Province, China, 2022

Chen Chen[1,&]; Jing Liu[2,&]; Menghan Wang[1]; Liangliang Cui[3]; Tiantian Li[1,#]

Summary

What is already known about this topic?

The heat health early warning model serves as an effective strategy for reducing health risks related to heatwaves and improving population adaptability. Several high-income countries have taken the lead in conducting research and implementing measures aimed at safeguarding their populations.

What is added by this report?

The graded heat health risk early warning model (GHREWM) in Jinan City has demonstrated efficacy in safeguarding males, females, individuals aged above 75 years, and those with cardiopulmonary diseases. During the summer of 2022, the warning stage of GHREWM contributed to the prevention of 10.9 deaths per million individuals, concurrently averting health-related economic losses estimated at approximately 227 million Chinese Yuan (CNY).

What are the implications for public health practice?

The GHREWM has the potential to enhance cities' adaptability to climate change. It is crucial to incorporate additional adverse health endpoint data in the development of early warning models, as this will improve their applicability and protective efficacy.

In the summer of 2022, the world experienced unprecedented heatwaves, which broke previous records and led to severe droughts and wildfires. Due to global warming, heatwaves are expected to become more frequent and intense (*1*). Some high-income countries have implemented heat health early warning models to mitigate the impacts of heatwaves and have reported initial positive health outcomes (*2*). The World Health Organization (WHO) and the World Meteorological Organization (WMO) jointly endorsed heat health early warning models as proactive adaptation measures to reduce heat-related mortality and prevent the onset of heat-sensitive diseases during summer months (*3*). However, research on heat health early warning models in China began relatively late, and a national model has yet to be established (*2*).

In 2021, Jinan City, Shandong Province implemented a graded heat health risk early warning model (GHREWM) focused on population-health-oriented management (*4*). Further investigations are necessary to assess the utility and effectiveness of this novel heat health early warning model in safeguarding the health of residents. In the current study, an episode-based approach was employed to evaluate the applicability of Jinan's GHREWM for heat-sensitive diseases and mortality across various populations. Additionally, this study aimed to quantify the health benefits associated with the reduction of mortality risks. These findings can serve as a critical foundation for the scientific establishment of a national GHREWM in China.

In order to evaluate GHREWM's capacity to identify health risks, daily mortality data from 8 urban areas in Jinan City, Shandong Province, China, during the warm seasons (May to October) between 2013 and 2018 were collected utilizing the Disease Surveillance Point System of the China CDC. Three categories of mortality causes were considered: non-accidental, circulatory diseases, and respiratory diseases, further stratified by age (<65 years, 65–74 years, and >74 years) and gender (female and male). Daily 24-hour average temperature, relative humidity, and ozone (O_3) concentrations were obtained from the National Climate Centre, the European Centre for Medium-range Weather Forecasts, and the National Urban Air Quality Real-time Release Platform, respectively.

In calculating health benefits, we gathered data from the GHREWM, including daily 24-hour average temperatures for the 2022 warm season, number of resident populations, and gross domestic product (GDP)-adjusted provincial value of a statistical life (VSL). The GHREWM, organized by heatwave mortality risks, encompasses surveillance, watch, and warning stages. The warning stage consists of warning levels 1, 2, and 3 (Supplementary Figure S1, available in https://weekly.chinacdc.cn). The GHREWM's structure and warning grading thresholds for different climate-architecture regions are depicted in Supplementary Figure S1 and Supplementary Table S1 (available in https://weekly.chinacdc.cn). Additional information regarding the sources and contents of the data can be found in the Supplementary Materials (available in https://weekly.chinacdc.cn).

This study utilized an episode-based approach and a two-stage statistical model to examine associations between warning levels and daily mortality risks for three sensitive diseases and sub-populations, determining if mortality risks varied with increasing warning levels. In the first stage, a generalized linear model employing quasi-Poisson regression was applied to fit county-specific associations, adjusting for relative humidity, time trends, and days of the week. In the second stage, a random-effects meta-analysis was conducted to pool the associations. The settings for the primary model and sensitivity analysis can be found in Supplementary Materials. Associations were expressed as percentage increases in mortality associated with a one-rank increase in warning levels, using the surveillance stage as the reference level.

We calculated the number of deaths prevented per million individuals and the economic losses averted during the warm season of 2022, as a result of the warning stage, in order to assess the health benefits provided by GHREWM in Jinan (*5*–*6*).

$$\Delta Lives = \sum(\Delta Mortality \times days_i \times pop_i)$$

$$VSL_{total} = \sum(\Delta Mortality \times days_i \times pop_i \times VSL_i)$$

In this formula, $\Delta Lives$ and VSL_{total} represent the number of lives saved and the economic loss avoided by the warning stage, respectively. $\Delta Mortality$ [0.69 persons/(million people·day)] refers to the number of deaths prevented per million people per day and is derived from the estimated number of deaths per million population per day saved by the warning stage in Benmarhnia's study, as described in detail in Supplementary Materials and adjusted for population size (*5*). $days_i$ represents the number of days in the warning stage for area i; pop_i denotes the local population for area i; and VSL_i is the VSL at the provincial level for area i (*6*).

Assuming the nationwide implementation of the GHREWM model in 2022, health benefits were estimated for six climatic-architecture regions (covering 366 cities), utilizing the number of lives saved and adjusting for the local population in Jinan.

The R Statistical software (version 4.0.2; Kurt Hornik and the R Core Team, Vienna, Austria) was used to perform all analyses. Statistical significance was set at P<0.05. ArcGIS (version 10.7; Esri Inc., RedLands, California, USA) was used to draw the map of China.

Between 2013 and 2018, during the warm seasons, a total of 104,346 non-accidental disease-related deaths were reported in Jinan. Of these, 55.8% were males, and 44.2% were females. The majority of the deceased were aged 75 years and older (Table 1).

As illustrated in Figure 1, the watch level demonstrated a substantial rise in the risk of non-accidental and circulatory disease-related deaths in comparison with the surveillance stage. This increase amounted to 8.20% [95% confidence interval (*CI*): 5.37%, 11.11%] and 9.34% (95% *CI*: 5.43%, 13.40%), respectively. During the warning stage, the augmentation in mortality risks associated with non-accidental, circulatory, and respiratory diseases in the general population correlated with an escalation in the warning level. The most significant increase was observed at warning level 3, with risks of 31.81% (95% *CI*: 17.41%, 47.97%), 39.94% (95% *CI*: 19.12%, 64.41%), and 49.24% (95% *CI*: 22.03%, 82.51%), respectively. These findings suggest that the GHREWM model possesses a robust capacity for identifying health risks based on their ranking.

There was a positive correlation between the increasing mortality risks and warning levels observed for both sexes and individuals aged over 75 years (Figure 1 and Supplementary Table S3 available in https://weekly.chinacdc.cn). However, this trend was not observed in the other two age groups.

Following the implementation of GHREWM in Jinan during the warm seasons of 2022, the warning stage resulted in a reduction of 10.9 deaths per million individuals and averted economic losses of approximately 227 million CNY. If applied on a nationwide scale, this strategy could have led to significant health benefits, with a potential savings of 15,115 deaths and a prevention of economic losses amounting to 62.0 billion CNY.

DISCUSSION

Jinan's GHREWM utilizes population mortality risk as a foundation for establishing warning ranks and adopts the three-stage risk management concept of risk surveillance, watch, and warning to address heat-related health risks during summer (*4*). Existing heat

TABLE 1. Overview of daily mortality causes, meteorological factors, and ozone (O_3) levels in Jinan City, Shandong Province during warm seasons (May–October) from 2013 to 2018.

Variable	Total	Mean±SD	P_{50} (P_{25}, P_{75})
Cause of Mortality			
Non-accidental disease	104,346	12±6	11 (7, 15)
Female	46,130	5±3	5 (3, 7)
Male	58,212	7±4	6 (4, 9)
Age <65 years	26,877	3±2	3 (1, 4)
Age 65–74 years	22,377	3±2	2 (1, 4)
Age >74 years	55,082	6±4	6 (4, 8)
Circulatory disease	54,809	6±4	6 (4, 8)
Respiratory disease	8,864	1±1	1 (0, 2)
Environmental Factors			
Temperature (°C)		22.7±5.1	23.6 (19.7, 26.5)
Relative humidity (%)		66.2±14.6	67.4 (55.7, 77.4)
O_3 8 h-average (μg/m^3)		133.5±58.8	135.9 (91.1, 175.8)

Note: Mean represents the daily average of a variable during the warm seasons from 2013 to 2018.
Abbreviation: SD=standard deviation; P_{25}=the 25th percentile; P_{50}=the 50th percentile; P_{75}=the 75th percentile.

health early warning models in high-income countries, such as the United Kingdom and France, primarily focus on identifying heatwaves associated with elevated health risks (*2*). In contrast, Jinan's GHREWM refines the classification of early warning levels, which our findings suggest effectively represents the increasing tendency of heat health risks, particularly for individuals over 75 years of age and those with cardiopulmonary diseases.

This study demonstrates that early warning grading based on mortality risk is more sensitive to populations with death as the primary effect endpoint (e.g., adults over 65 years of age). However, it also indicates that constructing a health early warning model solely based on death data may not capture the full range of heat-related effects on all populations. For instance, children tend to spend more time outdoors, exposing themselves to higher temperatures for extended periods, and their limited self-protection abilities (*7*) increase their susceptibility to high-temperature-induced diseases, such as heat stroke. Consequently, future heat health warning research should consider incorporating various sensitive effect endpoints.

The United Nations Intergovernmental Panel on Climate Change's Sixth Assessment Report highlights the positive effects of 24 representative adaptation measures on human well-being, with the benefits of disaster early warning systems on human health being particularly notable (*8*). Successful implementations in high-income countries have shown significant health benefits from population-based risk approaches for early disaster warnings. Benmarhnia et al. estimated that heat action plans in Montreal, Quebec, reduced mortality by 2.52 deaths per day during heatwaves (*5*). Additionally, the nationwide heatwave plan for England saved 1,189 lives over a 20-day heatwave in 2013 (*9*). Philadelphia's Hot Weather-Health Watch/Early Warning System resulted in 117 lives saved between 1995 and 1998, generating 468 million USD in revenue (*10*). Our study also illustrates the benefits of implementing Jinan's GHREWM in the summer of 2022. As the negative effects of climate change are irreversible, effective adaptation measures (such as GHREWM) provide a practical and timely means of preventing further losses.

Rapid urbanization has led to increased population density, which, when combined with the urban heat island effect and severe air pollution, negatively impacts urban living conditions. Addressing the growing health needs of the population and enhancing urban resilience and adaptability to climate change have become critical challenges. Our study indicates that implementing the Jinan's health warning model nationwide in 2022 could have yielded significant health benefits for residents. Consequently, we recommend the immediate establishment of a national heat health early warning system to better adapt to the escalating trend of extreme heat events, accompanied by the execution of a multi-sectoral heat health collaboration action plan.

This study was subject to several limitations. First, due to the inability to accurately measure personal

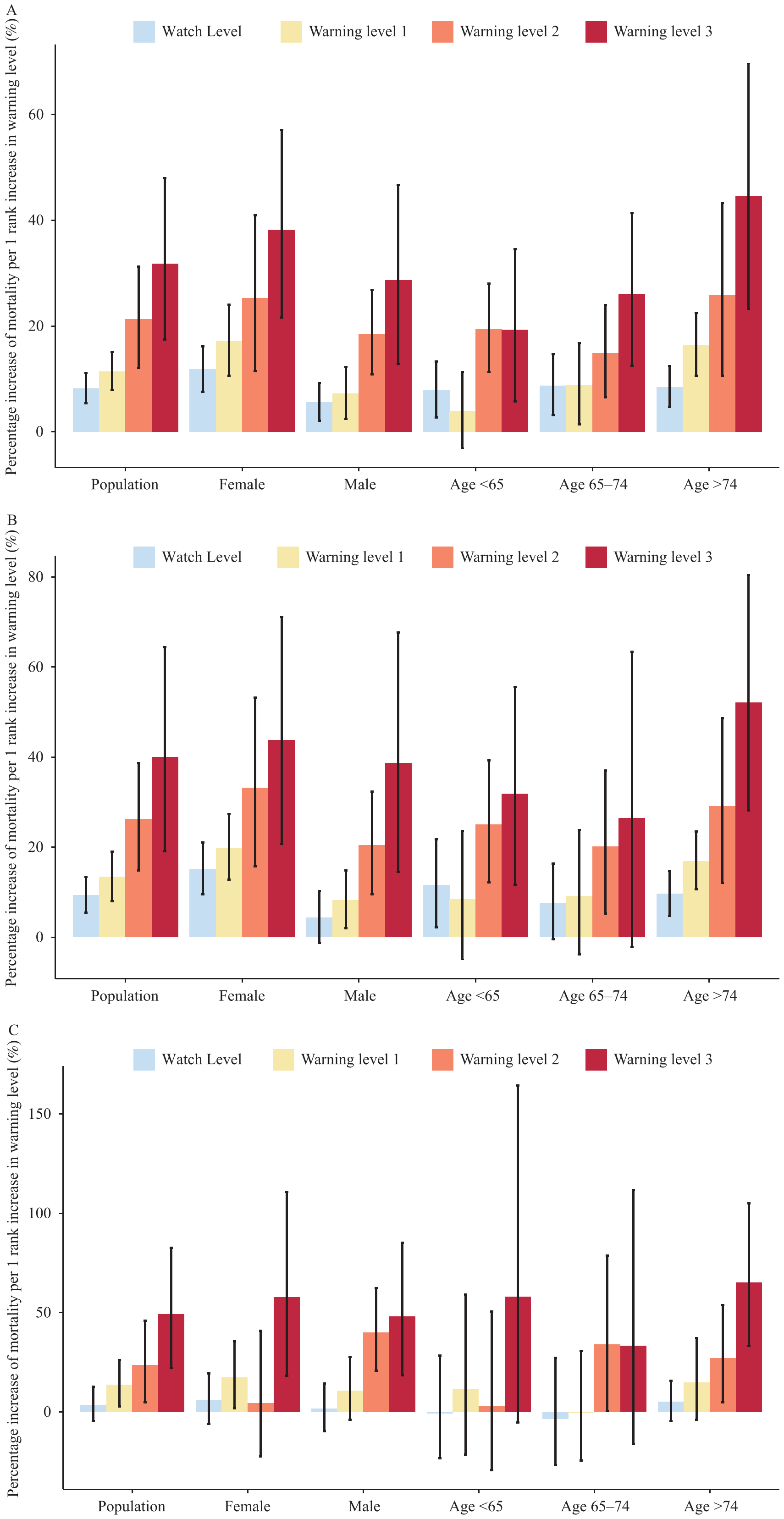

FIGURE 1. Percentage increase in non-accidental mortality (A), circulatory mortality (B), and respiratory mortality (C) per 1 rank increase in warning level during warm seasons in Jinan from 2013 to 2018, with population and sub-population estimates displayed.

temperature exposure, we utilized ambient temperature as a proxy for individual exposure, potentially introducing exposure uncertainty. Second, the assessment of national health benefits relied on scenario assumptions, serving as a reference for the nationwide value derived from the application of GHREWM. Furthermore, the establishment of GHREWM did not encompass certain western regions; hence, these areas were excluded from the estimation of nationwide health benefits.

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Preplanned Studies

An Early Warning System for Heatwave-Induced Health Risks in China: A Sub-Seasonal to Seasonal Perspective — China, 2022

Baichao Zhang[1]; Huiqi Chen[2]; Bo Lu[1,#]

Summary

What is already known about this topic?

Climate change has had a detrimental impact on global health, particularly through the rise of extreme heatwaves. Presently, the early warning system for heatwave-related health risks can forecast potential dangers several days in advance; however, long-term warnings fall short.

What is added by this report?

This report introduces a novel early warning system aimed at predicting heatwave-induced health risks in China at sub-seasonal to seasonal timescales. The outcomes of the assessment suggest this system holds significant potential.

What are the implications for public health practices?

The system facilitates advanced assessment of both the scale and dispersal of risk among various demographic groups. This allows for the proactive management of potential risks with extended lead times.

Global climate change has had a negative impact on the physical health of populations worldwide, with heatwave events causing significant human mortality and morbidity (*1*). The formation of an early warning system for health risks induced by heatwaves is vital, as it facilitates proactive measures by public health practitioners and public individuals. Current methodologies have developed various systems that provide advance warning several days ahead, effectively lessening heat-related dangers (*2*–*6*). The adoption of long-term pre-warning measures aids in preparing individuals and policymakers to take informed actions to reduce potential risks.

Despite the initial success of these long-term heatwave predictions, there remains a notable deficit in the provision of a health-risk warning system that covers the sub-seasonal to the seasonal scales (spanning two weeks to two months). The aim of this paper is to present a system that successfully addresses this gap.

By incorporating the China heatwave-attributable mortality model (*7*–*8*) with real-time temperature forecasts from the China Meteorological Administration-Climate Prediction System (CMA-CPSv3), this system provides up-to-date estimates of mortality rates and burdens for the forthcoming two months. As such, this system is poised to serve as a valuable tool for public health practitioners, enabling them to better plan personnel deployments and effectively allocate resources.

This study aims to combine heatwave events and health-risk assessment tools by using real-time, rolling temperature data projected for the subsequent 60 days from the advanced CMA-CPSv3 prediction system. Notably, the CMA-CPSv3 applies the enhanced resolution version of the Beijing Climate Center Climate System Model (BCC-CSM2-HR), recognized for its accuracy in predicting high temperatures within China (*9*). Initially, we commenced by systematically rectifying the temperature components produced by the CMA-CPSv3. A series of at least 3 days during the summer months (May to September) when the daily peak temperature surpasses the 92.5th percentile of the reference period (1961–2020) is characterized as a heatwave.

We utilized the nationwide heatwave-attributable mortality model established by Chen et al. (*7*–*8*) to analyze the health risks associated with heatwaves, including related mortality burden and death rate. This model investigates the specific exposure-response functional relationships between heatwaves and ensuing deaths across different climate zones using generalized linear models and meta-analysis. Estimations of mortality burden ascribed to heatwaves employ risk appraisals applicable to respective gridded heatwave series and nationwide mortality. The model considers factors such as population size, mortality rate, heatwave frequency, and exposure-response dynamics. By integrating the computed heatwave day data into the model, we ascertained the death burden and death rate due to heatwave-induced fatalities (depicted as gridded mortality burden per million population). A representation of this approach is illustrated in Figure 1.

Table 1, issued on July 1, 2022, provides estimates for the number of heatwave days expected in China over the subsequent two months. Data indicate a higher projection of heatwave days for July in regions like Western Sichuan, Chongqing, and other areas of Central China, with more than 20 heatwave days predicted per month. Similarly, nearly 20 days of heatwave occurrences were estimated for Northwest China, inclusive of areas such as Ningxia and Xinjiang. Moving into August, the northern reaches of Northeast

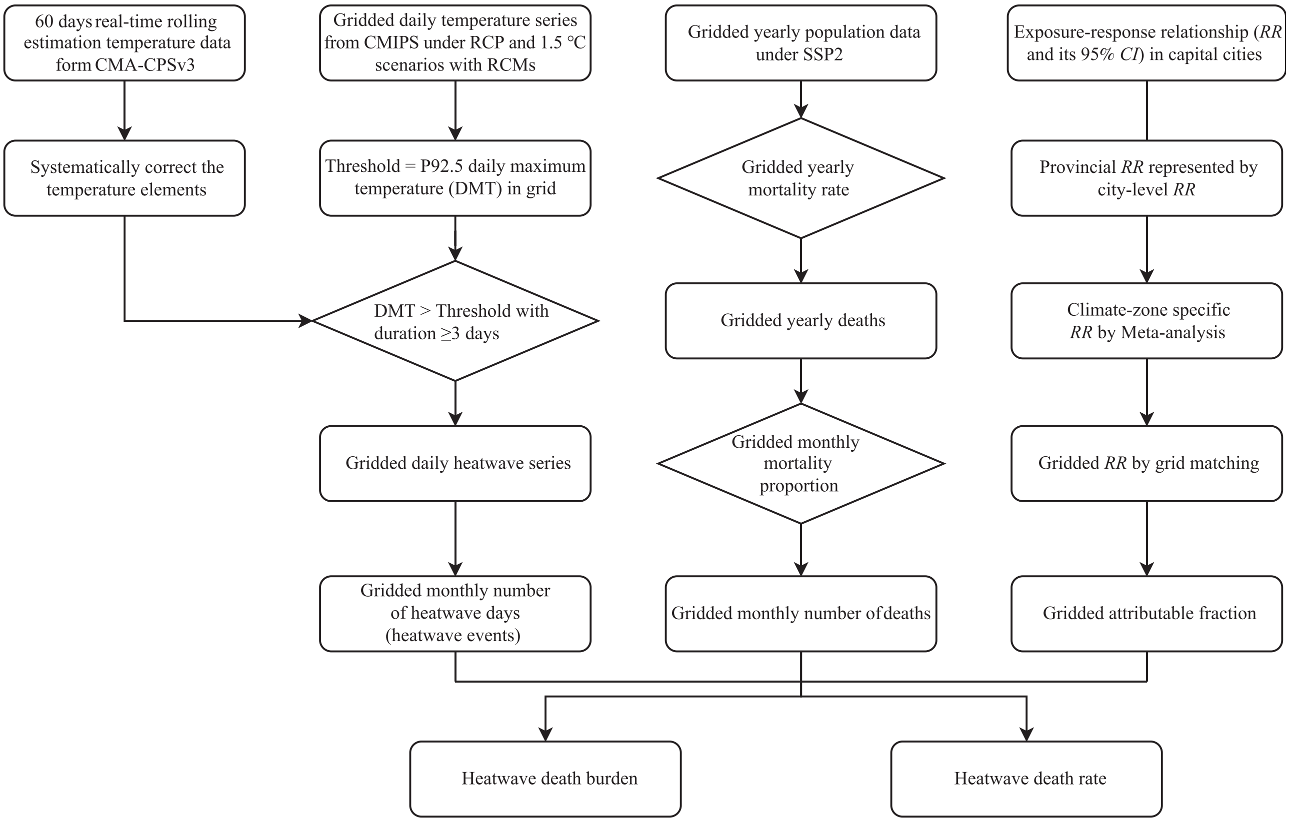

FIGURE 1. Flow diagram illustrating the operational process of the early warning system.
Abbreviation: RCMs=regional climate models; RCP=representative concentration pathways; SSP=shared socio-economic pathway; CMIP=coupled model intercomparison project; *RR*=relative risk; AF=attributable fraction; DMT=daily maximum temperature.

TABLE 1. Top 10 provincial-level administrative divisions (PLADs) by number of heatwave days, resulting death burden, and death rate.

Heatwave days				Heatwave-induced death burden				Heatwave-induced death rate			
0–30 days		31–60 days		0–30 days		31–60 days		0–30 days		31–60 days	
PLAD	Value	PLAD	Value	PLAD	Value	PLAD	Value	PLAD	Value	PLAD	Value
Chongqing	20.63	Anhui	20.01	Henan	3,530	Henan	3,402	Xinjiang	17,318	Xinjiang	21,003
Ningxia	19.25	Xinjiang	19.72	Shaanxi	1,817	Sichuan	1,750	Inner Mongolia	9,119	Inner Mongolia	12,471
Shaanxi	19.10	Chongqing	16.26	Sichuan	1,809	Anhui	1,666	Gansu	6,498	Gansu	4,418
Gansu	18.48	Hebei	15.61	Hubei	1,498	Hubei	1,663	Qinghai	4,588	Heilongjiang	4,060
Qinghai	18.44	Henan	14.79	Shandong	1,050	Jiangsu	1,331	Shaanxi	3,682	Henan	2,412
Hebei	18.00	Guizhou	14.76	Gansu	959	Shandong	1,316	Xizang	3,199	Qinghai	2,335
Xinjiang	17.00	Hunan	12.94	Anhui	941	Shaanxi	893	Sichuan	2,851	Sichuan	2,113
Sichuan	15.63	Inner Mongolia	12.85	Shanxi	736	Xinjiang	804	Henan	2,571	Hubei	1,837
Henan	15.45	Jiangsu	12.30	Xinjiang	608	Inner Mongolia	642	Heilongjiang	2,268	Shaanxi	1,751
Anhui	12.14	Gansu	12.09	Inner Mongolia	525	Heilongjiang	603	Hubei	2,085	Anhui	1,452

China forecast an increased frequency of heatwave days, with most regions predicted to experience over 20 such days per month on average. Of particular note is the Yangtze River Basin, which endured the most intense heatwave event ever recorded in the late summer of 2022 (*10*). As outlined in Table 1, this model accurately predicted this distinct pattern a month in advance.

The projected results were released on July 1, supplemented by real-time daily forecasts for one-month duration heatwave days in the summer of 2022. Figure 2 compares estimated and actual data, with solid lines reflecting observed data and dashed lines illustrating CMA-CPSv3 predictions. The figure demonstrates CMA-CPSv3's effective prediction of heatwave events during the summer of 2022. Accurate forecasting of heatwave days forms the basis for dependable subsequent estimations of heatwave health risks.

The study provided an analysis of the mortality rate due to heatwaves in July and August 2022, as depicted in Table 1. When contrasted with heatwave occurrences, the distribution of heatwave-related mortality correlates strongly with heatwave patterns in central China. Henan and Sichuan, both populous provinces, recorded the highest mortality rates due to heatwaves, with approximately 3,400 and 2,000 deaths respectively. Upon conducting a subgroup analysis, cardiovascular diseases (CVD) emerged as the leading cause of heatwave-induced mortality, contributing to an estimated 80% of the cases. Further, seniors and females were found to be at a relatively higher risk, accounting for around 75% and 70% of cases respectively.

The mortality burden indicator can enable policymakers and public health practitioners to allocate resources effectively. Nonetheless, it is crucial to acknowledge that the impact of the mortality burden during heatwaves is related to the local population size, which may limit its relevance on an individual basis. Therefore, this indicator also includes a heatwave-related mortality rate, derived from the mortality burden per million people during heatwaves. Over a span of two months, the highest risk was observed in Xinjiang, with an estimated heatwave-related mortality risk of about 20,000 per million individuals monthly. This was closely followed by Inner Mongolia, which had a risk estimated at 10,000 individuals per million monthly. Notably, the risk in August surpassed that of July.

DISCUSSION

This study presents two results within the sub-seasonal to a seasonal early warning system for heatwave-related health risks: death burden and death rate. These results can be beneficial for a variety of users. For policymakers and public healthcare practitioners, the distribution of heatwave incidents and a ranking system for province-wide mortality burden due to heatwaves can help inform the scope of heatwave impacts, prioritize critical areas, and effectively allocate resources. For individual users, the mortality rate due to heatwaves gives a more precise understanding of an individual's risk during a heatwave event, assisting in making well-informed travel plans and activity scheduling.

The two outputs show variations in detail when compared with the prediction of heatwave days. For instance, while the northeastern and northwestern regions of China experience more heatwave days, they

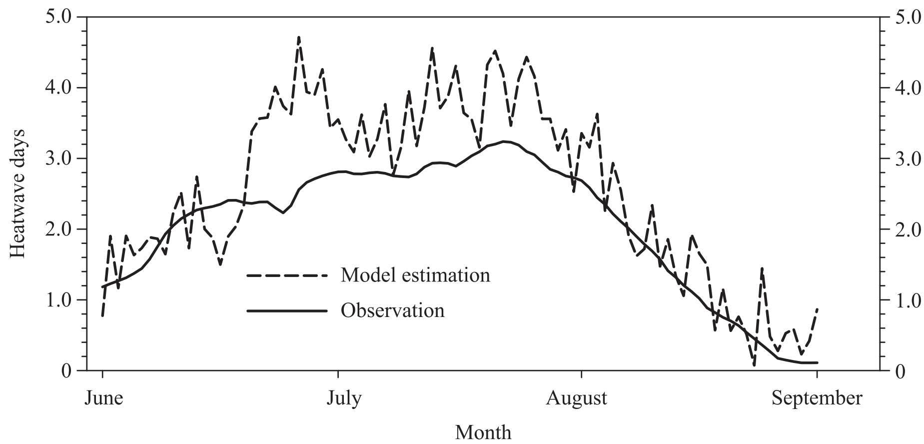

FIGURE 2. Comparison of the average heatwave days predicted over the next 30 days in China (dashed curve) with actual observations (solid curve).

show a lower heatwave-induced mortality burden due to their lower population densities. The heatwave-induced mortality rate provides a more accurate representation of the effect of heatwave duration on individuals. As expected, higher heatwave mortality rates align with the predicted heatwave days in the northeastern and northwestern regions. However, despite the high number of heatwave days in Sichuan-Chongqing, there is no significant increase in heatwave-induced mortality rate. This is likely due to the region's higher adaptive capacity to high temperatures, as its population has been exposed to such conditions for a long period of time. Consequently, despite experiencing the same number of heatwave days as in other regions, the risk in Sichuan-Chongqing is lower than in the northeastern and northwestern regions of China.

This study possesses numerous limitations. Predominantly, the CMA-CPSv3 data estimation appeared to slightly exaggerate the quantity of heatwave days in July. Further, the all-encompassing model for heatwave-related mortality utilized in this study does not accommodate prospective shifts in population exposure and vulnerability. Additionally, the hypothesized burden of heatwave deaths lacks substantiation through real-time mortality data. To address these limitations, the following remedies are suggested. 1) The improvement of climate model predictive capabilities is imperative. The enhancements presented with the development of the BCC-CSM2-HR model will allow for greater accuracy in the data derived from CMA-CPSv3. 2) The usage of multi-year estimation results for adjustments is advocated. The CMA-CPSv3 system, applied in this study, underwent certain modifications. Nonetheless, its efficacy is limited during months of extremely high temperatures due to the inadequate representation of such extreme conditions in the correction dataset. However, the performance of the modification is projected to improve as more estimated data from CMA-CPSv3 becomes available. 3) It is crucial to frequently update the nationwide model of mortality attributable to regional heatwaves to accurately depict the changing exposure and vulnerability of the population. 4) The enhancement of cross-disciplinary collaboration is of the utmost importance. This includes promoting a closer cooperation with the China CDC for the exchange of real-time mortality data and the validation of the system's outputs. Such collaboration will significantly contribute to the improvement of the system's performance.

In conclusion, the early warning system for health risks induced by sub-seasonal to seasonal heatwaves offers timely and quantitative assessments of both the impact magnitude and risk levels linked to heatwaves in China. This tool accommodates a broad spectrum of users and delivers crucial insights.

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Recollections

Early Warning Interventions for Environmental Risk Factors at China CDC

Qinghua Sun[1]; Chen Chen[1]; Qing Wang[1]; Tiantian Li[1,#]

BACKGROUND

President Xi Jinping emphasized the paramount importance of bolstering early surveillance and early warning capacities within a robust public health system (*1*). These elements constitute one of the five major functionalities of the National Bureau of Disease Control and Prevention (*2*). As an integral division of the National Bureau of Disease Control and Prevention, the Center for Disease Control and Prevention (CDC) is responsible for executing early surveillance and warning procedures in the realm of public health. Nonetheless, a deficiency persists concerning the early warning of public health risk factors.

In 2019, the National Bureau of Disease Control and Prevention initiated nationwide pilots for environmental health risk assessment. Building upon these pilot studies, the National Institute of Environmental Health (NIEH) of China CDC embarked on research and development for early warning technology in environmental health risk. Utilizing factors such as air quality, heatwave, and cold-spell health risks as key areas of intervention, the NIEH undertook extensive research and development of suitable adaptive technologies. This was done through a systematic coordination of resources among all stakeholders, and exploration of effective mechanisms for health risk early warning interventions in public health.

The NIEH has successfully integrated public health considerations into early warning systems for environmental risk factors, developing intricate, health risk-based warning and intervention technologies. These encompass air quality, heatwaves, and cold spell-related health risk warnings. Building on this achievement, the NIEH has fervently promoted the early warning intervention through a pilot program on three fundamental aspects: technology research and development, platform construction, and mechanism development. Table 1 outlines the pilot program for health risk early warning initiatives related to air quality, heatwaves, and cold spells.

In recognizing the significance of integrating early warning technology into health services, the NIEH facilitated early risk intervention strategies. This resulted in the pioneering fusion of medical and disease prevention sectors, giving birth to an innovative model for preventative disease control through early health warnings. Moreover, these developments offer a distinctively Chinese solution to global practices of early warning intervention.

WORK CONTENT

NIEH conducted the following tasks.

Technology research and development: In our investigation of the primary environmental risk factors and their associated health risks in China, we focused on air pollution, heatwaves, and cold spells. We developed an early warning intervention system for health risks, grounded on localized data, parameters, and unique innovative technology (*3*–*5*). This system aims to forecast health-risk interventions within the next 3–7 days.

The construction of the platform: Building upon the comprehensive environmental health monitoring program by NIEH, we developed a health risk early warning platform for environmental risk factors. This

TABLE 1. Early warning pilots for environmental health risks.

Environmental risk factors	Pilots of early warning
Air quality	Hebei Province, Jiangsu Province, Shandong Province, Henan Province, Sichuan Province, Jinan City, Qingdao City, Ningbo City, Shenzhen City, Hefei City
Heatwaves	Jinan City, Shenzhen City, Qingdao City
Cold spells	Jinan City, Qingdao City

platform is designed to access real-time and predictive data on environmental factor exposure, automatically cleanse and compute the data, match it with health information, and share it with local CDCs for dissemination via a data interface. Figure 1 presents the architecture diagram for the data processing of this early warning system platform. A massive amount of professional real-time and forecasted environmental factor data is processed within the computing platform. This data is then cleansed, aligned and integrated in real time, following which it is paired with the graded warning model. The model is utilized to automatically compute the warning level and associate it with health recommendations. Ultimately, it produces a graded warning index that is readily comprehensible to the general public.

Mechanism development: Since 2019, in cooperation with local CDCs, a pilot program was implemented for demonstrating the application of early warning public health services. The method of data sharing between NIEH and the pilot programs is depicted in Figure 2. NIEH is tasked with the computation of the warning index, which is subsequently relayed to the local CDCs via an interface program. The local CDCs then access the data and disseminate it through their respective visualization platforms. Through this initiative, a synergistic working mechanism for early warning dissemination between national and local CDCs was gradually developed, thus advancing the technical approach to convert scientific research findings into public health services.

ACCOMPLISHMENTS AND EXPERIENCES

Development of an Early Warning Technology for Environmental Health Risks in China

Reflecting on the unique aspects of local environmental pollution in China, we developed methods for warning of health risks associated with air quality, heatwaves, and cold spells. In formulating

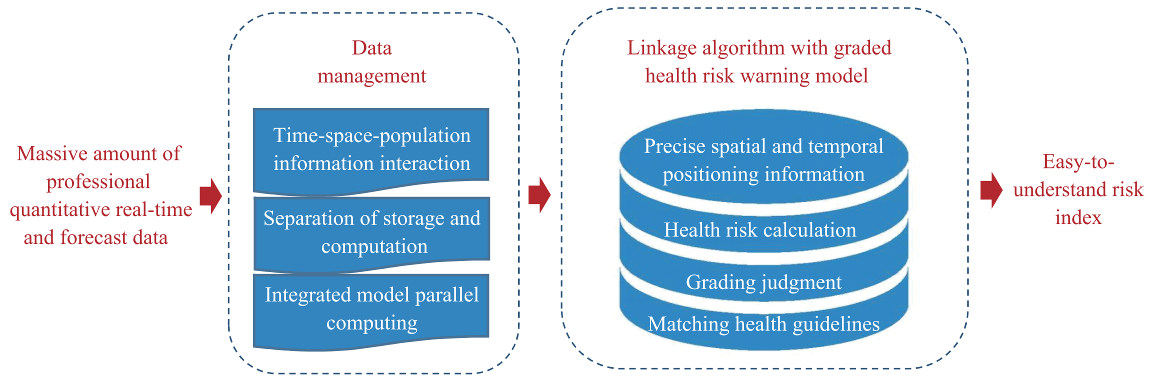

FIGURE 1. Diagram illustrating the data processing architecture of the early warning system platform.

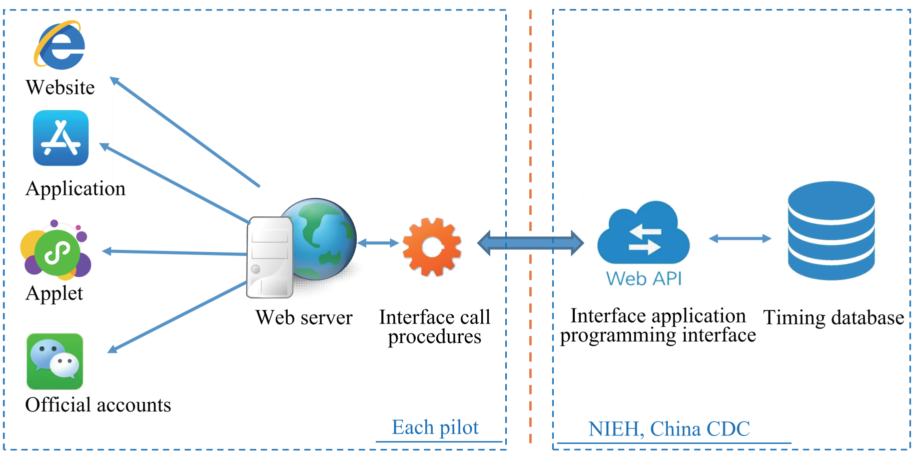

FIGURE 2. Method of data sharing between China CDC and pilot studies.

these approaches, we incorporated considerations of China's varied geographical and climatic characteristics and the adaptability of the populace among other factors. Also, a comprehensive evaluation procedure for warning validation was established, which incorporated the capability of the warning methods to highlight health risks, their synergy with the preexisting warning methods in China, and public acceptability.

Developing a Novel Public Health Service Model for Environmental Risk Factors and Health Risk Alerting

Supported public health services within the CDC: We initiated a pilot program for environmental health risk assessment in ten local CDCs. This program included the regular release of early warning intervention information. To date, the AQHI(air quality health index) has been consistently released in real-time and forecasted for over three years across two provinces and ten cities. This coverage spans a population of approximately 180 million individuals. Additionally, a health risk early warning system for heatwaves has been successfully operational in Jinan for a period of two years. Furthermore, we have implemented health risk early warning systems for cold spells in two cities.

Supported public health services in the meteorological sector: Our approach integrated health factors into the forecasting of extreme weather events through collaboration with other governmental departments. An example of this is our technical support to the Public Meteorological Service Center of the China Meteorological Administration during national extreme weather forecast gatherings. This allowed the inclusion of public health factors into predictions and warnings.

Supported public health services in medical institutions: Supported public health services in medical institutions played crucial roles in providing early warning intervention services for susceptible populations. For example, in partnership with the Chinese Cardiovascular Association, a health-risk warning linked to cold spells was disseminated to over 1,000 hospitals across the country. This notice, targeting vulnerable cardiovascular populations, provided health guidelines ahead of extreme weather events. This novel approach to risk prevention and management for individuals with high cardiovascular risk has shifted the health protection paradigm forward. Thus, it encourages the integration and synchronization of medical prevention.

Rationalizing the Collaborative Mechanism for Health Risk Warnings Related to Environmental Risk Factors

Construction of a national-provincial-municipal CDC joint working mechanism: The China CDC, the primary entity responsible for intervening early with environmental risk factors, has developed a collaborative model involving national, provincial, and municipal CDC branches. This model leverages the technical and data resources of the national CDC and utilizes local CDCs' accessibility to the general public. The initial work has rationalized a data information sharing mechanism and work content collaboration within the CDC, laying the groundwork for the subsequent implementation of operational tasks.

Construction of a joint working mechanism with the meteorological department: A collaborative mechanism has been developed in conjunction with the meteorological department, leveraging its established public service channel to create a joint early warning system. This system enhances the integration of health considerations into governmental early warning decisions while also broadening the demographic reach of these early warning interventions.

Construction of a joint working mechanism with medical institutions: This framework was designed with the aim of specifically identifying populations at risk from environmental factors. This targeted approach seeks to enhance the effectiveness and precision of risk warnings and interventions.

CHALLENGES AND PROSPECTS

Challenges

The work encountered two primary obstacles. First, the current early warning technology system lacked effective standardization. Previous health risk early warning effort did not possess consistent documentation, like guidelines for early warning technology or specifications for the release of early warning information. This significantly impeded the progress towards achieving systematic, scalable, and standardized early warning procedures.

Second, an operational mechanism for the prediction and alerting of health risks associated with environmental factors has yet to be established. Although early warnings for health risks attributed to environmental factors are crucial tools for public health services, they have not been integrated into the routine operations of environmental health work. The lack of an established mechanism for conducting early warning work leaves the respective responsibilities of all involved parties unclear, impeding the orderly initiation and seamless execution of these crucial tasks.

Outlook

The optimization and advancement of health-risk early warning and intervention systems for environmental risk factors are necessitated. Building on existing progress, the NIEH aims to enhance the early warning intervention model and compile technical specification documents that expand and refine mature health-risk early warning intervention technologies for air pollution, heatwaves, and cold spells. Concurrently, researches on other significant environmental risk factors, such as those related to water pollution, should be emphasized in order to establish health-risk early warning intervention technologies. Following the verification and evaluation of the intervention effects of the primary environmental risk factors' health risk early warning intervention technology, there is a clear need for further enhancement of the early warning model technology, health protection recommendations, and the early warning dissemination methods.

Second, there is a need for enhanced collaborative efforts across multiple departments. Agencies such as health, environmental protection, and data management should collaboratively strategize and establish a mechanism for sharing environmental risk factor monitoring and forecasting data, as well as early warning intervention information. There should also be well-defined communication channels established for the systematic dissemination of health risk early warnings to medical and health institutions. This would facilitate efficient early warnings for populations vulnerable to environmental risk factors and bolster the role of environmental health risk early-warning interventions in the precise management and control of sensitive diseases.

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Notifiable Infectious Diseases Reports

Reported Cases and Deaths of National Notifiable Infectious Diseases — China, December 2022*

Diseases	Cases	Deaths
Plague	0	0
Cholera	0	0
SARS-CoV	0	0
Acquired immune deficiency syndrome†	5,264	1,987
Hepatitis	72,630	51
Hepatitis A	532	0
Hepatitis B	59,498	24
Hepatitis C	11,050	26
Hepatitis D	16	0
Hepatitis E	1,187	1
Other hepatitis	347	0
Poliomyelitis	0	0
Human infection with H5N1 virus	0	0
Measles	79	0
Epidemic hemorrhagic fever	512	4
Rabies	6	20
Japanese encephalitis	3	0
Dengue	11	0
Anthrax	11	0
Dysentery	1,215	0
Tuberculosis	33,951	316
Typhoid fever and paratyphoid fever	234	0
Meningococcal meningitis	2	0
Pertussis	1,293	0
Diphtheria	0	0
Neonatal tetanus	3	0
Scarlet fever	1,026	0
Brucellosis	1,820	0
Gonorrhea	6,027	0
Syphilis	24,367	4
Leptospirosis	12	0
Schistosomiasis	28	0
Malaria	79	2
Human infection with H7N9 virus	0	0
Influenza	67,888	0
Mumps	3,839	0
Rubella	72	0

Continued

Diseases	Cases	Deaths
Acute hemorrhagic conjunctivitis	1,569	0
Leprosy	20	0
Typhus	36	0
Kala azar	9	0
Echinococcosis	144	0
Filariasis	0	0
Infectious diarrhea[§]	29,010	0
Hand, foot and mouth disease	27,747	0
Total	278,907	2,384

* According to the National Bureau of Disease Control and Prevention, not included coronavirus disease 2019 (COVID-19).

† The number of deaths of acquired immune deficiency syndrome (AIDS) is the number of all-cause deaths reported in the month by cumulative reported AIDS patients.

§ Infectious diarrhea excludes cholera, dysentery, typhoid fever and paratyphoid fever.

The number of cases and cause-specific deaths refer to data recorded in National Notifiable Disease Reporting System in China, which includes both clinically-diagnosed cases and laboratory-confirmed cases. Only reported cases of the 31 provincial-level administrative divisions in Chinese mainland are included in the table, whereas data of Hong Kong Special Administrative Region, Macau Special Administrative Region, and Taiwan, China are not included. Monthly statistics are calculated without annual verification, which were usually conducted in February of the next year for de-duplication and verification of reported cases in annual statistics. Therefore, 12-month cases could not be added together directly to calculate the cumulative cases because the individual information might be verified via National Notifiable Disease Reporting System according to information verification or field investigations by local CDCs.

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