


BMJ Open Air pollution and cancer daily mortality in Hangzhou, China: an ecological research

Zongxue Cheng , Kang Qin, Yan Zhang, Zhecong Yu, Biao Li, Caixia Jiang, Jue Xu

To cite: Cheng Z, Qin K, Zhang Y, *et al.* Air pollution and cancer daily mortality in Hangzhou, China: an ecological research. *BMJ Open* 2024;**14**:e084804. doi:10.1136/bmjopen-2024-084804

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<https://doi.org/10.1136/bmjopen-2024-084804>).

ZC and KQ contributed equally.

Received 29 January 2024
Accepted 14 May 2024



© Author(s) (or their employer(s)) 2024. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

Department of Chronic and Non-Communicable Disease, Hangzhou Center for Disease Control and Prevention, Hangzhou, China

Correspondence to
Professor Jue Xu;
xu.jue@outlook.com

ABSTRACT

Background Long-term exposure to air pollution has been linked to cancer incidence. However, the evidence is limited regarding the effect of short-term exposure to air pollution on cancer mortality.

Objectives This study aimed to investigate associations between short-term exposure to air pollutants (sulfur dioxide (SO₂), nitrogen dioxide (NO₂), particulate matter with an aerodynamic diameter <10 μm (PM₁₀) and PM_{2.5}) and cancer daily mortality.

Methods This study used air quality, meteorological and daily cancer death data from 2014 to 2019 in Hangzhou, China. Generalised additive models (GAM) with quasi-Poisson regression were used to analyse the associations between air pollutants and cancer mortality with adjustment for confounding factors including time trends, day of week, temperature and humidity. Then, we conducted stratified analyses by sex, age, season and education. In addition, stratified analyses of age, season and education were performed within each sex to determine whether sex difference was modified by such factors.

Results After adjusting for potential confounders, the GAM results indicated a statistically significant relationship between increased cancer mortality and elevated air pollution concentrations, but only in the female population. For every 10 μg/m³ rise in pollutant concentration, the increased risk of cancer death in females was 6.82% (95% CI 3.63% to 10.10%) for SO₂ on lag 03, and 2.02% (95% CI 1.12% to 2.93%) for NO₂ on lag 01 and 0.89% (95% CI 0.46% to 1.33%) for PM₁₀ on lag 03 and 1.29% (95% CI 0.64% to 1.95%) for PM_{2.5} on lag 03. However, no statistically significant association was found among males. Moreover, the differences in effect sizes between males and females were more pronounced during the cold season, among the elderly and among subjects with low levels of education.

Conclusions Increased cancer mortality was only observed in females with rising concentrations of air pollutants. Further research is required to confirm this sex difference. Advocate for the reduction of air pollutant emissions to protect vulnerable groups.

INTRODUCTION

Cancer has been the leading cause of death in the Chinese population. According to Global Cancer Observatory 2020 data, nearly

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study is the first to investigate the relationship between air pollution and all cancer daily mortality in a developing country.
- ⇒ We explored whether male and female cancer mortality is modified by different seasons, different ages or with different levels of education.
- ⇒ Surveillance of cancer deaths for this study was derived from one of the national cancer registries, which submits data to the International Agency for Research on Cancer regularly. The sample size is considerable and the data are of excellent quality.
- ⇒ Individual air exposure doses were not available in our method and the use of averaged exposures as a proxy may have resulted in misclassification bias.
- ⇒ Ecological studies merely reveal associations and cannot draw causal conclusions.

10 million people die from cancer each year worldwide, with China accounting for 30% of all cancer deaths worldwide.¹ The cancer mortality rate in China has been increasing over time due to the increasing ageing of the population, from 74.2 per 100 000 in 1973 to 170.1 per 100 000 in 2015.² Cancer brings a huge heavy chronic disease burden in China. Therefore, early identification of risk factors for cancer mortality is a crucial way to prolong survival and alleviate a burden. According to the Global Disease Study, 25.8% of disability-adjusted life-years for cancer in China are attributable to air pollution.³

With the rapid development of industrialisation, large cities in China have been suffering from severe air pollution.⁴ Over the past few decades, air pollution has been proven to be linked with various chronic diseases such as cardiovascular disease, stroke, diabetes, hypertension and respiratory diseases.^{5–10} Many cohort studies from developed countries have found relationships between long-term exposure to air pollution and the incidence and mortality of cancer. A handful of studies from Europe reported

that long-term exposure to low levels of air pollution is associated with lung cancer incidence and mortality.^{11–13} Another multiethnic cohort from the US summarised adverse effects of nitrogen dioxide (NO₂) on breast cancer mortality and the HR was 1.45 (95% CI 1.02 to 2.07) with per 20 ppb rise during 8 years follow-up.¹⁴

However, the short-term effects of air pollution on all cancer mortality remain to be investigated. Although the acute effects of air pollution do not cause cancer, air pollution can accelerate cancer deaths through damage to the respiratory or other systems. Many studies have shown that inhalation of air pollutants in the respiratory tract causes an inflammatory response and adverse systemic effects.^{15 16} Air pollutants that enter the circulatory system through the respiratory system generate reactive oxygen species and activate proinflammatory pathways, leading to cardiovascular toxicity. Patients with cancer generally have cardiovascular and respiratory comorbidities. Moreover, patients with cancer, who are generally weakened by disease and side effects of treatment, are more susceptible to the toxic effects of air pollutants, thereby increasing the risk of death. Current research evidence on air pollution and short-term exposure to cancer deaths is sparse and inconsistent. Several studies have found a higher lung cancer mortality rate with short-term exposure to air pollution.^{17 18} However, more studies have not found a significant acute effect of air pollution on cancer deaths.^{19–21}

Most studies on air pollution and cancer deaths have focused on long-term exposures, with the study areas mainly in high-income, low-pollution European and American countries. Air pollutant emissions in China greatly exceed those of developed countries. Hangzhou is one of the largest cities in the eastern region of China, with a developed economy and a large population. In order to ensure economic development, the city's air quality has been suffering from pollution. The main source of air pollutants in Hangzhou is motor vehicle exhaust, followed by coal combustion and dust. In this study, we used data from Hangzhou to investigate the relationship between short-term exposure to air pollutants and cancer mortality and to further explore sex differences.

MATERIALS AND METHODS

Daily mortality data

Daily cancer mortality data from 2014 to 2019 were collected from the Disease Surveillance Points System (DSPS) in Hangzhou, which is managed by the Centers for Disease Control and Prevention (CDC). The surveillance system covers all household residents of Hangzhou. A detailed description of the sampling and development of DSPS was issued.^{22 23} Hangzhou is one of the national cancer registries with a large population. Cancer mortality data are regularly submitted to the International Agency for Research on Cancer and checked by them to ensure data quality. All facilities conducting surveillance were

subject to strict quality control by the CDC system to ensure the accuracy and integrity of cancer mortality data.

This study extracted daily cancer deaths from the DSPTS database based on underlying causes of death as defined by the International Classification of Diseases-10th Revision (ICD-10), with the ICD-10 codes for cancer being C00–C97.

Daily air quality and meteorological data

Daily air pollutant data for the same period, including sulfur dioxide (SO₂), NO₂, particulate matter with an aerodynamic diameter <10 μm (PM₁₀) and PM with an aerodynamic diameter <2.5 μm (PM_{2.5}) were obtained from 11 air monitoring stations of the Hangzhou Environmental Protection Bureau. These air monitoring stations continuously monitor pollutants daily. The average daily air pollutant concentration was calculated using the median level recorded across 11 monitoring points. In addition, meteorological data were sourced from the China Meteorological Data Sharing Service (<http://data.cma.cn/>), comprising daily mean temperature and mean relative humidity.

Statistical analysis

In this study, the association between air pollutant concentrations and cancer mortality was estimated using time series analysis combined with a generalised additive model (GAM) of quasi-Poisson regression. To evaluate the lagged effects of air pollutants on cancer deaths, the study calculated single-day lagged and multiday average lag effects separately. lags 0–4 represent single-day lags of 0–4 days, respectively. lags 01–04 refer to the multiday average lag of 2–5 days, respectively. In the preliminary analysis, we constructed GAM models for all different lag days, up to lag of 7 days. The maximum effect values for the pollutions were at lag 03 or 04 days and decreased thereafter. The results of previous studies also found that the short-term effects of air pollution on disease reach their maximum at shorter times.^{24 25} Therefore, we used a maximum lag of 4 days for the final presentation of the main results. The model adjusted for the following confounding factors: (1) Dates were fitted using a natural cubic spline smoothing function with 7 df per year to reduce the effect of time trends; (2) Days of the week to avoid the day of the week effect; (3) Daily average temperature (6 df) and daily average relative humidity (3 df) were fitted using a natural cubic spline smoothing function to reduce the effects of potential non-linearity and lagged confounding of weather conditions.²⁶ The dfs of the model were determined according to the criterion of minimum Akaike information criterion (AIC) and previous literature of previous large-scale studies was considered.

To explore the effects of air pollution on cancer deaths in different participants and seasons, we conducted stratified analyses by sex, age, season and education. The study divided participants into subgroups based on sexes (male and female), ages (≥ 65 years and <65 years), seasons

(cold season and warm season) and education levels (low-edu and high-edu). The cool season was defined as October–May while the warm season was defined as April–September. Low-edu was defined as having education levels of junior high school and below, and high-edu was defined as senior high school and above. Furthermore, we performed hierarchical analyses by seasons, ages and education for each sex to examine whether these factors modify sex differences. Z-scores were calculated to test for statistical differences between effect values for different subgroups.

Several sensitivity analyses were conducted to determine the robustness of the results. We used two new sets of dfs to test the robustness of the results. One set was 6 df per year, 3 df for daily average temperature and 3 df for relative humidity. The other was 6 df for long-term trends, 3 df for temperature and 4 df for humidity. In addition, we used a two-pollutant model to additionally adjust the daily concentrations of other air pollutants. In constructing the two-pollution model, due to the high correlation between PM₁₀ and PM_{2.5} (Pearson's correlation coefficients=0.930), we found that when they were added to the model at the same time, the variance inflation factors were greater than 2. Therefore, we do not adjust PM₁₀ and PM_{2.5} for each other in the model.

All analyses were conducted through R (V.4.0.2) software. The GAM model was fitted using the R package 'mgcv', while 'splines' were implemented for parameter smoothing in the model. Two-sided p values <0.05 were considered to be statistically significant.

Patient and public involvement

There was no patient or public involvement.

RESULTS

Descriptive statistics

As shown in [table 1](#), there were 77 891 cancer deaths in Hangzhou from 2014 to 2019, averaging 35.55 deaths per day. A total of 50 515 (64.9%) males and 27 376 (35.1%) females were among all cancer deaths. The number of deaths per day attributed to cancer was 23.06 for males and 12.49 for females. The daily average concentrations of SO₂, NO₂, PM₁₀ and PM_{2.5} in Hangzhou were 11.98 µg/m³, 45.68 µg/m³, 77.26 µg/m³ and 48.46 µg/m³, respectively. During the study time, the daily mean temperature was 17.98 °C, and the relative humidity was 73.68%. [Table 2](#) summarises the Pearson's correlation coefficients between air pollutants. There was a statistically significant positive correlation between SO₂, NO₂, PM₁₀ and PM_{2.5}, with p<0.05.

Air pollutant concentrations and cancer deaths

[Table 3](#) shows the air pollutant concentrations and the excess risk (ER) of daily cancer mortality for different lag days, up to lag 4 and 04 days. Effect values and CIs for lags up to 7 days are presented in online supplemental table 1. After adjusting for day of the week, time trend, daily average temperature and daily average relative humidity, this study detected a significant positive association between short-term exposure to air pollutants (SO₂,

Table 1 Summary statistics for air pollutants, meteorological parameters and cancer daily deaths from January 2014 to December 2019 in Hangzhou, China

Variables	Mean	SD	Min	P ₂₅	Median	P ₇₅	Max	Total
Daily air pollutants								
SO ₂ , µg/m ³	11.98	6.85	3.00	7.25	10.00	14.00	79.00	–
NO ₂ , µg/m ³	45.68	18.12	7.00	32.00	44.00	57.00	121.00	–
PM ₁₀ , µg/m ³	77.26	41.88	8.00	46.00	69.00	99.00	302.00	–
PM _{2.5} , µg/m ³	48.46	29.01	3.00	28.00	42.00	62.00	233.50	–
Meteorological factors								
Temperature, °C	17.98	8.65	–5.00	10.40	19.10	24.90	35.60	–
Relative humidity, %	73.68	13.88	27.00	64.00	75.00	85.00	98.00	–
Cancer daily deaths								
Total daily deaths	35.55	6.43	14	31	35	40	58	77 891
Male	23.06	5.02	7	20	23	26	41	50 515
Female	12.49	3.57	3	10	12	15	26	27 376
Cold season	36.09	6.55	14	31	36	40.5	58	39 231
Warm season	35.02	6.27	16	31	35	39	58	38 660
≥65 years	24.48	5.37	8	21	24	28	42	53 646
<65 years	11.07	3.39	1	9	11	13	25	24 245
Low-edu	30.53	5.87	11	26	30	34	52	66 902
High-edu	5.02	2.39	0	3	5	7	15	10 989

Low-edu=junior high school and below; High-edu=senior high school and above.
 NO₂, nitrogen dioxide; PM₁₀, particulate matter with an aerodynamic diameter <10 µm; SO₂, sulfur dioxide.

Table 2 Pearson's correlation coefficients between air pollutants in Hangzhou, China, during 2014–2019

Air pollutants	SO ₂	NO ₂	PM ₁₀	PM _{2.5}
SO ₂	1	0.569	0.640	0.649
NO ₂		1	0.736	0.687
PM ₁₀			1	0.930
PM _{2.5}				1

The bold number indicates the p<0.05.

NO₂, nitrogen dioxide; PM₁₀, particulate matter with an aerodynamic diameter <10 mm; SO₂, sulfur dioxide.

NO₂ and PM₁₀) and cancer deaths. For single-day lags, the ER of cancer death for each 10 µg/m³ increment in SO₂ concentration peaked at 2.17% (95% CI 0.58% to 3.78%) for SO₂ on lag 2, NO₂ peaked to 0.60% (95% CI 0.06% to 1.14%) at lag 1 and PM₁₀ peaked to 0.26% (95% CI 0.04% to 0.47%) on lag 2.

For multiday average lags, greater effect estimates were observed for the cumulative effect of multiday lag than the individual effect of single-day lag. Specifically, the ER in cancer mortality linked to an increase of 10 µg/m³ in pollutant concentrations had the highest value after lag 03 days, up to 2.98% (95% CI 0.63% to 5.39%) for SO₂ and 0.37% (95% CI 0.07% to 0.67%) for PM₁₀ while the highest estimates for NO₂ were discovered at lag 02 and the ER was 0.74% (95% CI 0.06% to 1.41%). The relationship between PM_{2.5} and cancer mortality approached statistical significance at lag 03, with p=0.07. And the maximum effect value was 0.41% (95% CI -0.04% to 0.87%) per 10 µg/m³ increment of PM_{2.5}.

Air pollutant concentrations and cancer deaths in different sexes, ages, seasons and education

Due to the more significant effect values for all air pollutants at multiday average lags, the ERs of stratification for lag 01–04 are shown in table 4, and the complete tables of all lag days in different sexes are shown in online supplemental tables 2 and 3. All air pollutants (SO₂, NO₂, PM₁₀

and PM_{2.5}) were associated with cancer deaths in the female subjects. In the female population, for every 10 µg/m³ rise in pollutant concentration, the ER of cancer death was 6.82% (95% CI 3.63% to 10.10%) for SO₂ on lag 03, and 2.02% (95% CI 1.12% to 2.93%) for NO₂ on lag 01 and 0.89% (95% CI 0.46% to 1.33%) for PM₁₀ on lag 03 and 1.29% (95% CI 0.64% to 1.95%) for PM_{2.5} on lag 03. However, no statistically significant association was found between air pollutant concentrations and cancer mortality in the male subjects.

In other stratified results, SO₂ and NO₂ had a statistically significant effect on cancer deaths in individuals aged 65 years and older, the association of increased SO₂ concentrations with increased cancer deaths was a statistically significant in the cold season, and SO₂ and PM₁₀ demonstrated an association with increased cancer deaths in the low education level study population. The associations of all four pollutants with daily cancer deaths were not statistically significant in the <65 years, warm season and high education stratification.

Air pollutant concentrations and cancer deaths in different sexes stratified by seasons, ages and education

As the differences in effect sizes between males and females were obvious in previous stratified analyses, we further explored the air pollutant concentrations and cancer deaths stratified by seasons, ages and education in each sex. We selected the lag days with the largest effect values to calculate the stratified results for season, age and education, which were the lag 03 for SO₂, PM₁₀ and PM_{2.5}, and the lag 02 for NO₂, respectively. For SO₂, the association between air pollutants and cancer deaths in stratified analyses of seasons was a statistically significant only for females in the cold season. The ER was significantly greater for females than males in the cold season, with a value of 9.43% (95% CI 5.32% to 13.70%). Age-stratified results indicated that this association was a statistically significant only in females ≥65 years, with a 10 µg/m³ rise in SO₂ increasing cancer deaths by 8.05% (95% CI 4.15% to 12.09%). In addition, the stratified results for

Table 3 Increased air pollutant concentrations and excess risk (ER) of cancer daily mortality with different lag days

Lag days	SO ₂		NO ₂		PM ₁₀		PM _{2.5}	
	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI
0	0.18	(-1.59 to 1.97)	0.54	(0.00 to 1.08)	0.00	(-0.23 to 0.23)	0.11	(-0.22 to 0.45)
1	1.97	(0.36 to 3.61)	0.60	(0.06 to 1.14)	0.20	(-0.01 to 0.42)	0.23	(-0.08 to 0.55)
2	2.17	(0.58 to 3.78)	0.27	(-0.26 to 0.80)	0.26	(0.04 to 0.47)	0.26	(-0.06 to 0.57)
3	1.26	(-0.33 to 2.86)	0.05	(-0.47 to 0.58)	0.25	(0.04 to 0.46)	0.19	(-0.13 to 0.50)
4	0.18	(-1.39 to 1.77)	-0.07	(-0.60 to 0.45)	0.00	(-0.21 to 0.21)	-0.18	(-0.49 to 0.14)
01	1.70	(-0.30 to 3.74)	0.72	(0.11 to 1.34)	0.14	(-0.11 to 0.40)	0.24	(-0.13 to 0.62)
02	2.74	(0.55 to 4.99)	0.74	(0.06 to 1.41)	0.27	(-0.01 to 0.55)	0.35	(-0.06 to 0.77)
03	2.98	(0.63 to 5.39)	0.63	(-0.09 to 1.36)	0.37	(0.07 to 0.67)	0.41	(-0.04 to 0.87)
04	2.86	(0.36 to 5.43)	0.54	(-0.23 to 1.31)	0.34	(0.02 to 0.67)	0.30	(-0.19 to 0.80)

The bold number indicates the p<0.05.

NO₂, nitrogen dioxide; PM₁₀, particulate matter with an aerodynamic diameter <10 mm; SO₂, sulfur dioxide.

Table 4 Increased air pollutant concentrations and excess risk (ER) of cancer daily mortality stratified by sex, season, age and education for different lag days

Lag days	SO ₂		NO ₂		PM ₁₀		PM _{2.5}	
	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI
Male								
01	-0.78	(-3.13 to 1.62)	0.17	(-0.55 to 0.90)	-0.04	(-0.35 to 0.26)	-0.04	(-0.48 to 0.41)
02	0.47	(-2.11 to 3.11)	0.24	(-0.55 to 1.05)	0.10	(-0.24 to 0.43)	0.06	(-0.44 to 0.55)
03	0.37	(-2.37 to 3.20)	0.13	(-0.73 to 0.99)	0.16	(-0.19 to 0.52)	0.11	(-0.43 to 0.65)
04	0.40	(-2.51 to 3.40)	0.07	(-0.84 to 0.98)	0.18	(-0.20 to 0.57)	0.05	(-0.53 to 0.64)
Female								
01	5.94	(3.09 to 8.88)	2.02	(1.12 to 2.93)	0.67	(0.30 to 1.04)	1.06	(0.50 to 1.61)
02	6.40	(3.36 to 9.52)	2.00	(1.02 to 2.98)	0.77	(0.37 to 1.18)	1.21	(0.60 to 1.82)
03	6.82	(3.63 to 10.10)	1.94	(0.90 to 2.99)	0.89	(0.46 to 1.33)	1.29	(0.64 to 1.95)
04	6.45	(3.13 to 9.88)	1.84	(0.75 to 2.94)	0.83	(0.37 to 1.29)	1.17	(0.47 to 1.88)
Cold season								
01	1.83	(-0.50 to 4.22)	0.66	(-0.09 to 1.41)	0.14	(-0.17 to 0.45)	0.24	(-0.20 to 0.68)
02	2.82	(0.23 to 5.47)	0.62	(-0.21 to 1.45)	0.21	(-0.12 to 0.55)	0.30	(-0.18 to 0.79)
03	3.25	(0.42 to 6.16)	0.49	(-0.40 to 1.39)	0.27	(-0.09 to 0.64)	0.36	(-0.18 to 0.89)
04	3.16	(0.15 to 6.26)	0.30	(-0.64 to 1.25)	0.18	(-0.21 to 0.57)	0.20	(-0.39 to 0.78)
Warm season								
01	1.03	(-3.24 to 5.49)	-0.03	(-1.22 to 1.19)	-0.24	(-0.75 to 0.27)	-0.24	(-1.03 to 0.56)
02	2.42	(-2.46 to 7.54)	-0.13	(-1.47 to 1.23)	-0.05	(-0.62 to 0.52)	-0.05	(-0.93 to 0.84)
03	2.31	(-2.98 to 7.88)	-0.40	(-1.88 to 1.10)	0.07	(-0.56 to 0.71)	-0.04	(-1.02 to 0.95)
04	1.43	(-4.23 to 7.42)	-0.40	(-2.00 to 1.22)	0.15	(-0.55 to 0.86)	-0.12	(-1.18 to 0.96)
≥65 years								
01	2.01	(-0.40 to 4.47)	0.71	(-0.01 to 1.45)	0.10	(-0.21 to 0.40)	0.18	(-0.27 to 0.63)
02	3.09	(0.45 to 5.81)	0.81	(0.01 to 1.62)	0.23	(-0.10 to 0.56)	0.33	(-0.17 to 0.83)
03	3.80	(0.95 to 6.73)	0.89	(0.03 to 1.75)	0.35	(-0.01 to 0.71)	0.40	(-0.14 to 0.94)
04	3.85	(0.83 to 6.97)	0.81	(-0.10 to 1.73)	0.33	(-0.06 to 0.71)	0.26	(-0.33 to 0.85)
<65 years								
01	1.05	(-1.82 to 4.02)	0.75	(-0.17 to 1.68)	0.19	(-0.20 to 0.57)	0.32	(-0.26 to 0.89)
02	1.79	(-1.28 to 4.96)	0.63	(-0.36 to 1.63)	0.28	(-0.14 to 0.70)	0.34	(-0.29 to 0.98)
03	1.21	(-1.99 to 4.52)	0.23	(-0.80 to 1.27)	0.32	(-0.13 to 0.77)	0.37	(-0.31 to 1.06)
04	0.88	(-2.45 to 4.33)	0.14	(-0.94 to 1.22)	0.29	(-0.19 to 0.77)	0.32	(-0.41 to 1.06)
Low-edu								
01	1.79	(-0.32 to 3.94)	0.56	(-0.08 to 1.21)	0.12	(-0.15 to 0.39)	0.22	(-0.17 to 0.62)
02	2.94	(0.62 to 5.31)	0.59	(-0.12 to 1.30)	0.22	(-0.07 to 0.52)	0.28	(-0.16 to 0.72)
03	3.37	(0.88 to 5.92)	0.53	(-0.23 to 1.30)	0.35	(0.03 to 0.67)	0.36	(-0.12 to 0.84)
04	3.19	(0.55 to 5.89)	0.47	(-0.33 to 1.28)	0.36	(0.02 to 0.70)	0.28	(-0.24 to 0.81)
High-edu								
01	0.04	(-5.47 to 5.88)	1.52	(-0.15 to 3.23)	0.23	(-0.46 to 0.93)	0.29	(-0.74 to 1.33)
02	-0.07	(-6.13 to 6.38)	1.45	(-0.41 to 3.35)	0.50	(-0.27 to 1.28)	0.77	(-0.39 to 1.93)
03	-1.47	(-7.92 to 5.42)	1.03	(-0.96 to 3.07)	0.47	(-0.37 to 1.31)	0.74	(-0.53 to 2.01)
04	-1.38	(-8.27 to 6.03)	0.73	(-1.39 to 2.89)	0.23	(-0.67 to 1.13)	0.40	(-0.97 to 1.79)

The bold number indicates the p<0.05.

NO₂, nitrogen dioxide; PM₁₀, particulate matter with an aerodynamic diameter <10 μm; SO₂, sulfur dioxide.

education suggested that the association on lag 03 was a statistically significant only among females with a low level of education, with an 8.49% (95% CI 4.37% to 12.78%)

increase in cancer mortality (figure 1A). For the other pollutants (NO₂, PM₁₀ and PM_{2.5}), stratified analyses likewise found stronger associations for females in the cold

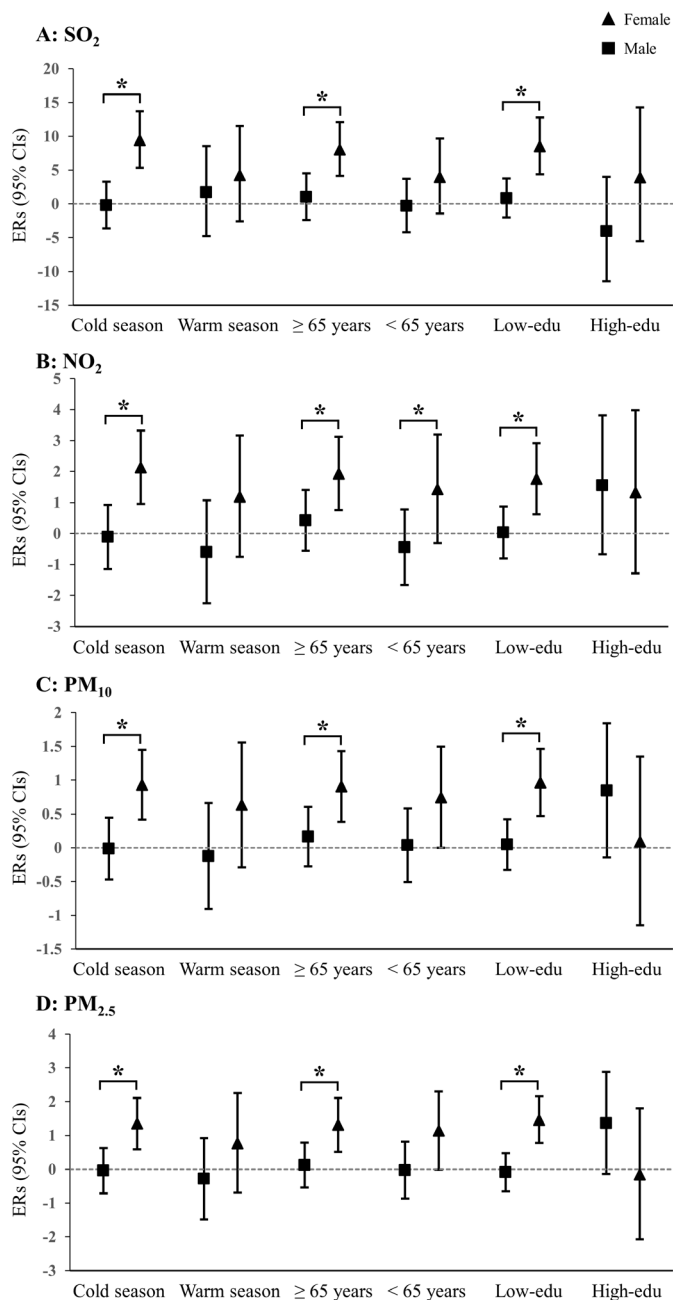


Figure 1 Excess risk (ER) of cancer mortality associated with each 10 $\mu\text{g}/\text{m}^3$ increase of four air pollutant (SO_2 , NO_2 , PM_{10} and $\text{PM}_{2.5}$) in each sex, stratified by seasons, ages and education levels. *Indicates a statistically significant difference between sexes, the $p < 0.05$. NO_2 , nitrogen dioxide; PM_{10} , particulate matter with an aerodynamic diameter < 10 mm; SO_2 , sulfur dioxide.

season, ≥ 65 years and low education levels (figure 1B–D). Detailed numerical results are presented in online supplemental table 4. Overall, sex differences were more pronounced in the cold season, among the elderly and at lower levels of education.

Sensitivity analysis

The results of the model with varying the dfs construct are presented in online supplemental tables 5 and 6. The results for the different dfs are similar to the main results.

In the results of the two-pollutant model, the effect values increased marginally than those of the one-pollutant model in all subjects and the male while they slightly dropped in females. Although the effect values for SO_2 and PM_{10} decreased slightly to become non-significant after adjusting NO_2 in all subjects, they were still close to being statistically significant, with $p = 0.059$ for SO_2 and $p = 0.072$ for PM_{10} . Moreover, the results were still statistically significant in the female study subjects (online supplemental table 7). The results of the sensitivity analyses demonstrated the stability and robustness of the results of the primary model.

DISCUSSION

This study used data from 2014 to 2019 to explore the short-term effects of air pollutants in developed cities of eastern China. The result demonstrated a significant positive association between air pollutant (SO_2 , NO_2 , PM_{10} and $\text{PM}_{2.5}$) concentrations and cancer mortality only in the female population. This association was more pronounced during the cold season, among older adults, and among those with low levels of education. Our study provided evidence for the effect of short-term exposure to air pollution on cancer deaths in China.

Previous short-term effects studies on mortality have focused solely on respiratory, cardiovascular and all-cause death.^{26–28} A few literature have investigated lung cancer mortality and found adverse effects of air pollution on lung cancer survival.^{17 18 29} Published research evidence focusing on all cancer mortality is limited. We used cancer mortality data to further explore the acute effects of air pollution on all cancer mortality. The adverse effects of air pollution extend beyond the realm of lung cancer. A prospective cohort study found that long-term exposure to air pollution was associated with death from several non-lung cancers.³⁰ Another US study similarly found a significant effect between $\text{PM}_{2.5}$ and liver cancer survival.³¹ As for the acute effects, a survey of low-pollution areas in Canada indicated that the association between air pollution and all cancer deaths among the elderly was a statistically significant only during the warm season.³² These studies suggested the risk of elevated air pollutant concentrations for non-respiratory cancer deaths. Our short-term exposure results similarly supported the finding. Yet, some studies did not draw a statistical association between short-term exposure to air pollution and cancer deaths.^{19–21} Air pollution concentrations, sources and composition are not the same between cities as well as different climatic and population characteristics in the various study areas. These factors may lead to different results.

The number of cancer deaths in females was considerably smaller than in males during the study period (male=50 515, female=27 376). However, in our study, a statistically significant association of air pollution with cancer deaths was found only in the female participants. Sex differences have inconsistent results across different

research. Some studies have found that air pollution contributes more significantly to lung cancer deaths in men than in women.^{17 33} Conversely, studies have also found that females are more sensitive to air pollution.^{29 34} Anatomically, females have smaller airways than males, resulting in easier deposition of PM and more severe airway reactivity. Second, females breathe in a thoracic pattern differently than males. More research is needed to confirm this sex difference and elucidate the underlying mechanisms.

Sex differences were more pronounced in the elderly population (≥ 65 years) compared with the younger group (< 65 years). This could be attributed to the fact that many elderly individuals suffer from worse health conditions, a decreased physical fitness, immunity and ability to repair themselves, in comparison to younger individuals. These findings align with prior research on the correlation between air pollution and various illnesses.³⁵ Similarly, the level of education has a noticeable effect on the sex difference in this study. Populations with lower levels of education were more susceptible to the adverse effects of air pollution. One possible explanation might be that they received less health education and lacked protective awareness leading to less protective measures in case of air pollution. Because of the low socioeconomic status associated with low levels of education, they are more frequently exposed to outdoor air pollution to make a living and have less access to healthcare resources.³⁶ This result is also consistent with other studies.^{26 37} In addition, our study found that seasons modify the short-term effects of air pollutants on cancer deaths. Stronger sex difference associations were detected in the cold season instead of the warm season. This can be explained that the concentration of pollutants is higher in the cold season, which is more likely to cause adverse reactions. These studies on other outcomes confirm our findings.³⁷

The exact pathophysiological mechanisms of air pollution promoting cancer mortality remain unclear. Harmful substances contained in air pollutants can directly trigger cancer and promote cancer progression through oxidative stress, chromosomal damage, DNA damage and mutations.^{38–40} It has been suggested that mRNA and microRNA biomarkers linked to the risk of cancer were significantly expressed even at low exposure levels over short periods of time.⁴¹ A cohort study from Europe found that short-term exposure to PM₁₀ was associated with increased inflammation and tumour necrosis factor.⁴² Another experimental study in mice similarly found an increase in inflammatory activity with exposure to airborne PM.⁴³ It is likely that these same factors that promote cancer incidence and progression can diminish the survival of patients with cancer. A long-term study of PM_{2.5} found that patients who received radiochemotherapy had a greater risk of cardiorespiratory death than those who did not.⁴⁴ The weakness of patients with cancer and the side effects of treatment make them more sensitive to air pollution.

To our knowledge, we are the first study to explore sex differences in short-term air pollution and all cancer mortality. Nevertheless, there are some limitations of our study. First, we were unable to obtain individual air pollution exposure measures data and instead used the average concentration at the 11 monitoring stations as the exposure concentration for the entire study population. This exposure misclassification may lead to an underestimation of pollutant effects. Second, the study could not control for confounding factors such as occupation, income, physical activity and family history of cancer. Third, as dietary information is not included in the surveillance data of cancer deaths, it could not stratify analyses for diet and explore the role that dietary factors play. Finally, as an ecological study, we could merely suggest an association between air pollution and cancer daily mortality but could not derive a causal relation inference. Therefore, more research is needed to confirm this finding.

CONCLUSION

In summary, this epidemiological study showed a positive association between the short-term effects of air pollutant concentrations and all cancer deaths, particularly in the female population. Our results provide evidence for the acute effects of air pollution on cancer mortality and sex differences therein. Future studies need to continue to validate this finding and focus on the underlying pathological mechanisms. Vulnerable populations need more concern and protection in the face of air pollution.

Acknowledgements The authors thank all the investigators and staff of the cancer deaths, air quality and meteorological data for their valuable contributions.

Contributors JX, CJ and ZC designed the research. YZ, KQ and BL supported the data collection. ZC, KQ and ZY performed the data analysis. ZC wrote the manuscript. JX and CJ provided revision of the manuscript. JX is the guarantor of this study, accepting full responsibility for the work and the conduct of the study, having access to the data, and controlling the decision to publish. All authors read and approved the final manuscript.

Funding This work was supported by the Hangzhou General Research Project on Agriculture and Social Development (20201203B207).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and the protocol of this study was approved by the Ethics Review Committee of Hangzhou Center for Disease Control and Prevention. The ID is 2020-54. Informed consent was not required in this study because we used data for the number of people on death surveillance in the whole area.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iD

Zongxue Cheng <http://orcid.org/0000-0002-4687-0920>

REFERENCES

- Qi J, Li M, Wang L, *et al*. National and Subnational trends in cancer burden in China, 2005–20: an analysis of national mortality surveillance data. *Lancet Public Health* 2023;8:e943–55.
- Wei W, Zeng H, Zheng R, *et al*. Cancer registration in China and its role in cancer prevention and control. *Lancet Oncol* 2020;21:e342–9.
- Yin P, Brauer M, Cohen AJ, *et al*. The effect of air pollution on deaths, disease burden, and life expectancy across China and its provinces, 1990–2017: an analysis for the global burden of disease study 2017. *Lancet Planet Health* 2020;4:e386–98.
- Kan H, Chen R, Tong S. Ambient air pollution, climate change, and population health in China. *Environ Int* 2012;42:10–9.
- Guan W-J, Zheng X-Y, Chung KF, *et al*. Impact of air pollution on the burden of chronic respiratory diseases in China: time for urgent action. *Lancet* 2016;388:1939–51.
- Chen Q, Wang Q, Xu B, *et al*. Air pollution and cardiovascular mortality in Nanjing, China: evidence highlighting the roles of cumulative exposure and mortality displacement. *Chemosphere* 2021;265:129035.
- Shah ASV, Lee KK, McAllister DA, *et al*. Short term exposure to air pollution and stroke: systematic review and meta-analysis [BMJ (Clinical research ed) 2015;350:h1295]. *BMJ* 2015;350:h1295.
- Rajagopalan S, Al-Kindi SG, Brook RD. Air pollution and cardiovascular disease: JACC state-of-the-art review. *J Am Coll Cardiol* 2018;72:2054–70.
- Eze IC, Hemkens LG, Bucher HC, *et al*. Association between ambient air pollution and diabetes mellitus in Europe and North America: systematic review and meta-analysis. *Environ Health Perspect* 2015;123:381–9.
- Qin P, Luo X, Zeng Y, *et al*. Long-term Association of ambient air pollution and hypertension in adults and in children: A systematic review and meta-analysis. *Sci Total Environ* 2021;796:S0048-9697(21)03692-5.
- Stafoggia M, Oftedal B, Chen J, *et al*. Long-term exposure to low ambient air pollution concentrations and mortality among 28 million people: results from seven large European cohorts within the ELAPSE project. *Lancet Planet Health* 2022;6:e9–18.
- So R, Andersen ZJ, Chen J, *et al*. Long-term exposure to air pollution and mortality in a Danish nationwide administrative cohort study: beyond mortality from cardiopulmonary disease and lung cancer. *Environ Int* 2022;164:S0160-4120(22)00167-2.
- Huang Y, Zhu M, Ji M, *et al*. Air pollution, genetic factors, and the risk of lung cancer: A prospective study in the UK Biobank. *Am J Respir Crit Care Med* 2021;204:817–25.
- Cheng I, Yang J, Tseng C, *et al*. Outdoor ambient air pollution and breast cancer survival among California participants of the Multiethnic cohort study. *Environ Int* 2022;161:S0160-4120(22)00013-7.
- Pope CA III, Bhatnagar A, McCracken JP, *et al*. Exposure to fine particulate air pollution is associated with endothelial injury and systemic inflammation. *Circulation Research* 2016;119:1204–14.
- He S, Klevebro S, Baldanzi G, *et al*. Ambient air pollution and inflammation-related proteins during early childhood. *Environ Res* 2022;215:S0013-9351(22)01691-7.
- Wang N, Mengersen K, Tong S, *et al*. Short-term association between ambient air pollution and lung cancer mortality. *Environ Res* 2019;179:S0013-9351(19)30545-6.
- Ma C, Jung C-R, Nakayama SF, *et al*. Short-term Association of air pollution with lung cancer mortality in Osaka, Japan. *Environ Res* 2023;224:115503.
- Xia S-Y, Huang D-S, Jia H, *et al*. Relationship between atmospheric Pollutants and risk of death caused by cardiovascular and respiratory diseases and malignant tumors in Shenyang, China, from 2013 to 2016: an ecological research. *Chin Med J (Engl)* 2019;132:2269–77.
- Sui X, Zhang J, Zhang Q, *et al*. The short-term effect of PM_{2.5}/O₃ on daily mortality from 2013 to 2018 in Hefei, China. *Environ Geochem Health* 2021;43:153–69.
- Costa AF, Hoek G, Brunekreef B, *et al*. Air pollution and deaths among elderly residents of São Paulo, Brazil: an analysis of mortality displacement. *Environ Health Perspect* 2017;125:349–54.
- Liu S, Wu X, Lopez AD, *et al*. An integrated national mortality surveillance system for death registration and mortality surveillance, China. *Bull World Health Organ* 2016;94:46–57.
- Yang G, Hu J, Rao KQ, *et al*. Mortality registration and surveillance in China: history, current situation and challenges. *Popul Health Metr* 2005;3:3.
- Phosri A, Ueda K, Phung VLH, *et al*. Effects of ambient air pollution on daily hospital admissions for respiratory and cardiovascular diseases in Bangkok, Thailand. *Sci Total Environ* 2019;651:1144–53.
- Cheng MH, Chiu HF, Yang CY. Coarse particulate air pollution associated with increased risk of hospital admissions for respiratory diseases in a tropical city, Kaohsiung, Taiwan. *Int J Environ Res Public Health* 2015;12:13053–68.
- Chen R, Yin P, Meng X, *et al*. Fine particulate air pollution and daily mortality. A nationwide analysis in 272 Chinese cities. *Am J Respir Crit Care Med* 2017;196:73–81.
- Shang Y, Sun Z, Cao J, *et al*. Systematic review of Chinese studies of short-term exposure to air pollution and daily mortality. *Environ Int* 2013;54:100–11.
- Liu C, Chen R, Sera F, *et al*. Ambient particulate air pollution and daily mortality in 652 cities. *N Engl J Med* 2019;381:705–15.
- Zhu F, Ding R, Lei R, *et al*. The short-term effects of air pollution on respiratory diseases and lung cancer mortality in Hefei: A time-series analysis. *Resp Med* 2019;146:57–65.
- Turner MC, Krewski D, Diver WR, *et al*. Ambient air pollution and cancer mortality in the cancer prevention study II. *Environ Health Perspect* 2017;125:087013.
- Deng H, Eckel SP, Liu L, *et al*. Particulate matter air pollution and liver cancer survival. *Int J Cancer* 2017;141:744–9.
- Goldberg MS, Burnett RT, Stieb DM, *et al*. Associations between ambient air pollution and daily mortality among elderly persons in Montreal, Quebec. *Sci Total Environ* 2013;463–464:931–42.
- Xue X, Chen J, Sun B, *et al*. Temporal trends in respiratory mortality and short-term effects of air Pollutants in Shenyang. *Environ Sci Pollut Res* 2018;25:11468–79.
- Wu C, Yan Y, Chen X, *et al*. Short-term exposure to ambient air pollution and type 2 diabetes mortality: A population-based time series study. *Environmental Pollution* 2021;289:117886.
- Ma Y, Zhao Y, Yang S, *et al*. Short-term effects of ambient air pollution on emergency room admissions due to cardiovascular causes in. *Environmental Pollution* 2017;230:974–80.
- Pratt GC, Vadali ML, Kvale DL, *et al*. Traffic, air pollution, minority and socio-economic status: addressing inequities in exposure and risk. *Int J Environ Res Public Health* 2015;12:5355–72.
- Kan H, London SJ, Chen G, *et al*. Season, sex, age, and education as modifiers of the effects of outdoor air pollution on daily mortality in Shanghai, China: the public health and air pollution in Asia (PAPA) study. *Environ Health Perspect* 2008;116:1183–8.
- Xu J, Zhang Q, Su Z, *et al*. Genetic damage and potential mechanism exploration under different air pollution patterns by multi-Omics. *Environ Int* 2022;170:S0160-4120(22)00563-3.
- Møller P, Loft S. Oxidative damage to DNA and lipids as biomarkers of exposure to air pollution. *Environ Health Perspect* 2010;118:1126–36.
- Vineis P, Husgafvel-Pursiainen K. Air pollution and cancer: biomarker studies in human populations. *Carcinogenesis* 2005;26:1846–55.
- Espín-Pérez A, Krauskopf J, Chadeau-Hyam M, *et al*. Short-term Transcriptome and microRNAs responses to exposure to different air Pollutants in two population studies. *Environ Pollut* 2018;242:182–90.
- Tsai D-H, Amyai N, Marques-Vidal P, *et al*. Effects of particulate matter on inflammatory markers in the general adult population. *Part Fibre Toxicol* 2012;9:24.
- Happo MS, Salonen RO, Hälinen AI, *et al*. Dose and time dependency of inflammatory responses in the Mouse lung to urban air coarse, fine, and Ultrafine particles from six European cities. *Inhal Toxicol* 2007;19:227–46.
- Coleman NC, Ezzati M, Marshall JD, *et al*. Fine particulate matter air pollution and mortality risk among US cancer patients and survivors. *JNCI Cancer Spectr* 2021;5:pkab001.