Urban Climate 58 (2024) 102163

Contents lists available at ScienceDirect

Urban Climate

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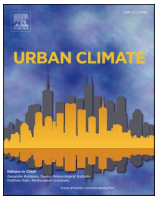

Effects of ambient temperature on chronic obstructive pulmonary disease (COPD) mortality in highly polluted region

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ARTICLE INFO

Keywords:
Ambient temperature
Climate change
COPD
DLNM
Extreme weather

ABSTRACT

The Global Burden of Disease (GBD) studies have established a clear connection between ambient air pollution, extreme temperatures, and an increased risk of mortality from chronic obstructive pulmonary disease (COPD). However, limited research has been conducted on the relationship between ambient temperature and COPD mortality in heavily polluted regions in China. This particular study examines the above effect using weekly data from the Yangtze River Delta area from 2013 to 2017. A Poisson generalized linear regression model with a distributed lag non-linear model (DLNM) was employed to assess the risk of COPD mortality associated with temperature and lag effects on a weekly basis. The analysis showed that colder temperatures posed a higher risk, with extreme cold temperatures (3 °C) having a significant impact on COPD mortality. On the other hand, extreme hot temperatures (32 °C) did not demonstrate significant short-term effects. The study also revealed that females and individuals already suffering from COPD were more susceptible to the adverse effects of extreme temperatures. These findings provide valuable insights into the association between ambient temperature and cause-specific mortality risk in highly polluted regions, which can help in managing the disease burden related to climate change, including extreme weather events such as heat waves and cold waves.

1. Introduction

The adverse health impacts resulting from the dramatic changes in ambient temperature caused by climate change have become a pressing concern (Costello et al., 2009). Extreme weather events, such as heat waves and cold waves, have been closely associated with extreme ambient temperatures. While the effect of ambient temperature on disease burden has been studied over the past few decades, the focus has primarily been on cardiovascular diseases (Rocklöv and Forsberg, 2008; Kysely et al., 2009; Cheng and Su, 2010). Previous studies have examined the impact of ambient temperature on mortality in various regions, including North America (Anderson and Bell, 2009; Barnett, 2007; Martin et al., 2012), Europe (Iniguez et al., 2010; Sartor et al., 1995), and Asia (Onozuka and

Abbreviations: CI, Confidence interval; COPD, Chronic obstructive pulmonary disease; DLNM, Distributed non-linear lag model; GLM, Generalized linear model; GBD, Global Burden of Disease; O_3, Ozone; $PM_{2.5}$, Particles with an aerodynamic diameter of equal to or less than 2.5 μm; PM_{10}, Particles with an aerodynamic diameter of equal to or less than 10 μm; RH, Relative humidity; Temp, Temperature.

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https://doi.org/10.1016/j.uclim.2024.102163
Received 29 October 2023; Received in revised form 6 July 2024; Accepted 7 October 2024

Hagihara, 2015; Son et al., 2012; Chung et al., 2009). However, most of these studies were conducted in regions with relatively low levels of pollution. Therefore, it is crucial to investigate this association in highly polluted regions, providing quantitative insights into the link between ambient temperature and cause-specific mortality, such as chronic obstructive pulmonary disease (COPD).

As the global population continues to grow, rapid urbanization and industrialization are leading to significant variations in ambient temperature and an increase in air pollution levels. Both extreme temperatures and high levels of pollution have been associated with an elevated risk of mortality. The Global Burden of Disease (GBD) studies have highlighted the clear link between exposure to ambient air pollution, including fine particulate matter ($PM_{2.5}$) and ozone (O_3), and an increased risk of COPD mortality (Lim et al., 2012; Forouzanfar et al., 2016; Murray et al., 2020), particularly in regions with high $PM_{2.5}$ levels, such as China and India (Apte et al., 2015). The GBD study in 2017 estimated that in China, there were approximately 227.8 thousand COPD deaths attributable to ambient $PM_{2.5}$ pollution and 178.2 thousand deaths attributable to ambient O_3 pollution (Yin et al., 2020). Moreover, global risk assessments have incorporated the risk factors of high and low non-optimal temperatures, contributing to nearly 2 million deaths worldwide (Murray et al., 2020). In the GBD study in 2019, 2.3 thousand COPD deaths in China were attributed to high non-optimal temperatures, while 175.0 thousand deaths were attributed to low non-optimal temperatures (Murray et al., 2020).

While tobacco smoking is a major contributing factor to COPD mortality (Soriano et al., 2020), other environmental factors, including exposure to air pollution and extreme ambient temperatures, are significantly associated with an increased risk of mortality. In recent years, several Asian countries, such as Bangladesh, China, India, and Pakistan, have been recognized as highly polluted regions due to high observed $PM_{2.5}$ levels. In eastern China, high $PM_{2.5}$ emissions were identified in the sectors of household, industry, and transportation (Brauer et al., 2016). However, research exploring the effects of ambient temperature on mortality in these areas remains limited (Guo et al., 2011; Wang et al., 2014; Zhang et al., 2017; Liu et al., 2011), especially regarding cause-specific mortality such as COPD. Furthermore, this study employs a distributed lag non-linear model (DLNM) to assess the effects of ambient temperature exposure on a weekly basis on the risk of COPD mortality in the Yangtze River Delta region, eastern China. The objectives of this study are as follows: (1) to determine the effects of temperature and lag on COPD mortality on a weekly basis, (2) to examine the impact of extreme hot and cold ambient temperatures on COPD mortality, and (3) to evaluate the effect of extreme temperatures on COPD mortality in specific subpopulations, stratified by gender.

2. Materials and methods

2.1. Data

Ningbo, a city of 9.62 million population in the southern part of Yangtze River Delta region in China, was selected in this study due to high pollutant levels, especially ambient $PM_{2.5}$. The daily average $PM_{2.5}$ in Ningbo exceeded the minimum threshold of 35 $\mu g/m^3$, which might pose a potential risk to public health (Chung et al., 2021). Daily COPD mortality data for the residents in Ningbo were obtained from the Ningbo Centre for Disease Control and Prevention (Ningbo CDC) and classified as J44 according to the Tenth Revision of the International Classification of Diseases (ICD-10). Additionally, daily meteorological data including temperature and relative humidity, as well as air pollutant data ($PM_{2.5}$ and O_3), were collected from the Ningbo Environmental Monitoring Centre (Ningbo EMC). Data were collected over the study period from 2013 to 2017. To facilitate further analysis, the weekly average values of mortality, meteorological data, and air pollutant data were calculated based on the raw data.

2.2. Statistical analysis

A generalized linear model (GLM) with Poisson regression was used to study the association between ambient temperature and mortality on a weekly basis as follows:

$$ln[E(m_t)] = \alpha + \beta T_{t,l} + ns(PM_{2.5,t}, df) + ns(O_{3,t}, df) + ns(RH_t, df) + ns(Time_t, df) \quad (1)$$

where t represents the week of observations ($t = 1, 2, 3 \ldots 260$), $E(m_t)$ is the expected number of average COPD mortality on week t, and α is the model intercept. The $T_{t,l}$ term represents a matrix measured by employing the cross-basis function of DLNM to temperature, where β is the vector of coefficients for $T_{t,l}$ on week t and lag week l. Weekly average values of fine particulate matter ($PM_{2.5,t}$), ozone ($O_{3,t}$), and relative humidity (RH_t) were also included in the model fitting process with the adjustment made using a natural cubic spline (ns) and 5 degrees of freedom (df) for each variable. $Time_t$ is the sequential number of weeks in the study ranging from 1 to 260. A natural cubic spline for time with 1 degree of freedom (df) per year was employed in the model fitting to explain the long-term trends and seasonality.

The DLNM framework used in this study has been extensively discussed in previous studies (Gasparrini et al., 2010; Gasparrini, 2011). This methodology relies on a cross-basis, which characterizes the relationship between temperature and its lag effects using a two-dimensional space of functions. In our model fitting process, a natural cubic spline DLNM was employed to estimate the non-linear temperature effect and lag effect on COPD mortality on a weekly basis. The weekly average temperatures were calculated based on the daily average temperatures collected, with Monday marking the beginning of a week and Sunday marking the end. To capture a more detailed view of the lag effect on COPD mortality, a maximum lag of 8 weeks was utilized in this analysis. The spline knots for the temperature effect were evenly spaced within the temperature range, while the spline knots for the lag effect were evenly spaced in the logarithmic scale of lags. This approach allows for a high level of flexibility in modeling both the temperature and lag effects (Guo et al., 2011). The degrees of freedom (df) for both the temperature and lag effects were selected by minimizing the Akaike Information

Criteria (AIC) and residuals (Peng et al., 2006).

In this analysis, the reference temperature (also known asthreshold temperature or minimum mortality temperature) was defined as the average temperature corresponding to the study period when the number of COPD mortality was below the 5th percentile of the mortality distribution. This implies that the relative risk of COPD mortality due to ambient temperature was estimated to be 1 at the reference temperature. Relative risks were then calculated at different ambient temperatures relative to the reference temperature. To illustrate the variation of the relative risk of COPD mortality over the lag period, the single lag effect and cumulative effect of ambient temperature were plotted. Additionally, the impact of extreme cold and hot temperatures on COPD mortality was examined based on the 1st and 99th percentiles of the temperature distribution during the study period, respectively (Wang et al., 2014). Stratification analyses were conducted to investigate the effect of extreme temperatures on COPD mortality in different subpopulations by gender (male and female). Sensitivity analyses were performed by varying the maximum lag period from 4 to 6 weeks and adjusting the degree of freedom for $PM_{2.5}$, O_3, and relative humidity from 4 to 6.

All the analyses were conducted using the dlnm and splines package of R statistical software (version 3.6.1). Results were considered statistically significant when the measured *p*-value was less than 0.05 ($P < 0.05$).

3. Results

3.1. Data description

During the study period from January 1, 2013 to December 31, 2017, a total of 16,468 deaths due to COPD were recorded in Ningbo. On average, there were 9.2 deaths related to COPD per week. The average weekly temperature was 17.6 °C, with the lowest temperature of 1.5 °C observed in week 1 of 2013 and the highest temperature of 33.1 °C observed in week 32 of 2013. The weekly average values of relative humidity, $PM_{2.5}$, and O_3 were reported as 74.5 %, 43.8 μg/m^3, and 94.4 μg/m^3, respectively. Table 1 provides an overview of the collected data during the study period (2013–2017) in Ningbo, China. Additionally, it was observed that the COPD mortality rate for males was relatively higher than that for females, accounting for 56.8 % of the total COPD mortality.

The correlation matrix between key variables in the model, including $PM_{2.5}$, O_3, temperature, and COPD mortality, is presented in Fig. 1. The matrix reveals several notable findings. Firstly, $PM_{2.5}$ is negatively correlated with temperature, indicating that lower ambient temperatures during the winter period are associated with higher concentrations of ambient $PM_{2.5}$. Secondly, O_3 is positively correlated with ambient temperature, which may account for the higher incidence of O_3 pollution attributed to the stronger atmospheric photochemical reactions during periods of elevated temperature, such as in the summer. Additionally, there is consistently a negative correlation between ambient temperature and COPD mortality, as well as a positive correlation between $PM_{2.5}$ and COPD mortality. The absolute correlation coefficients for COPD mortality were notably higher, with values of −0.73 for temperature and 0.63 for $PM_{2.5}$. These findings suggest significant effects of ambient temperature and air pollution on COPD mortality.

The association between ambient temperature and COPD mortality was further analyzed under different seasons. Fig. 2 and Fig. 3 show the trends of ambient temperature and COPD mortality in winter and summer, respectively, throughout the study period. A noteworthy finding is the significant increase in average winter temperatures from 2013 to 2017, as well as in average summer temperatures from 2014 to 2017. These findings provide strong evidence of ongoing climate change. Furthermore, the negative relationship between ambient temperature and COPD mortality in winter suggests that extremely cold temperatures may increase the risk of COPD mortality. Similarly, the positive relationship between ambient temperature and COPD mortality in summer indicates that extremely hot temperatures potentially contribute to an elevated risk of COPD mortality. The impact of extreme weather, encompassing both extreme cold and hot temperatures, on COPD mortality was particularly observed in the Yangtze River Delta in 2013, as demonstrated by the highest levels of COPD mortality during both winter and summer across the study years.

3.2. Effect of ambient temperature on COPD mortality

The final DLNM model was selected based on the principles of minimum AIC and residuals. This model utilized a natural cubic spline with 5 degrees of freedom for the temperature effect, and a natural cubic spline with 4 degrees of freedom for the lag effect. The results of AIC and residuals are presented in Table S1. To visualize the relationship between mean temperatures, lag weeks, and the relative risk of COPD mortality, a three-dimensional plot is shown in Fig. 4. In this study, the reference temperature for COPD mortality was determined to be 25 °C, as it corresponded to the weekly average temperatures during periods with COPD mortality recorded below the 5th percentile of the distribution. Fig. 4 illustrates a non-flat surface, which represents the combined effect of temperature and lag on the relative risk of COPD mortality. As an example, the highest relative risk of 1.45 for COPD mortality was observed at a

Table 1
Characteristics of weekly mortality, weather conditions, and air pollution in Ningbo, China, 2013–2017.

Variable	Mean ± SD	Minimum	25 %	Median	75 %	Maximum
COPD mortality	9.2 ± 2.9	4.6	7.0	8.3	11.1	19.4
Temperature (°C)	17.6 ± 8.1	1.5	10.1	18.0	24.2	33.1
Relative humidity (%)	74.5 ± 8.2	43.6	69.7	74.9	80.4	92.4
$PM_{2.5}$ (μg/m^3)	43.8 ± 23.3	9.8	29.0	39.1	52.6	230.9
O_3 (μg/m^3)	94.4 ± 30.7	28.8	71.8	95.4	116.3	166.4

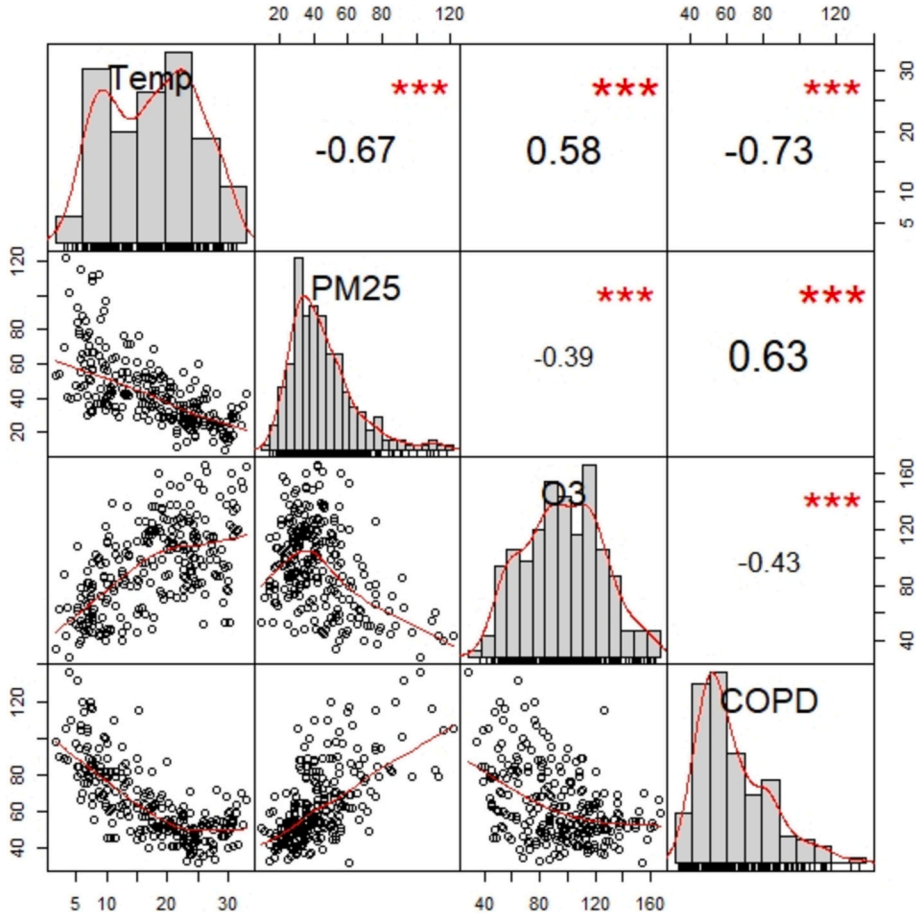

Fig. 1. Chart of correlation matrix.

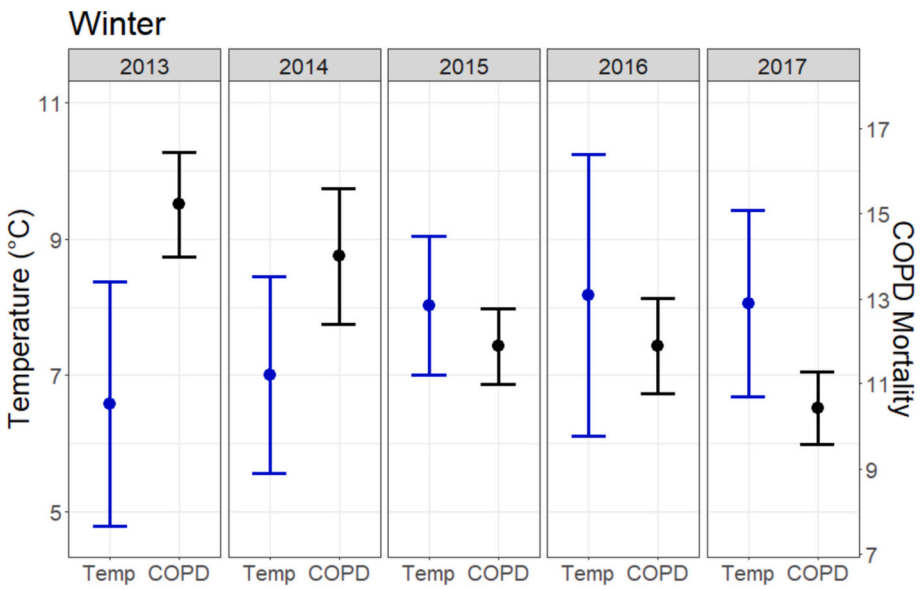

Fig. 2. Weekly average values and their 95 % CIs of ambient temperature and COPD mortality in winter in Ningbo.

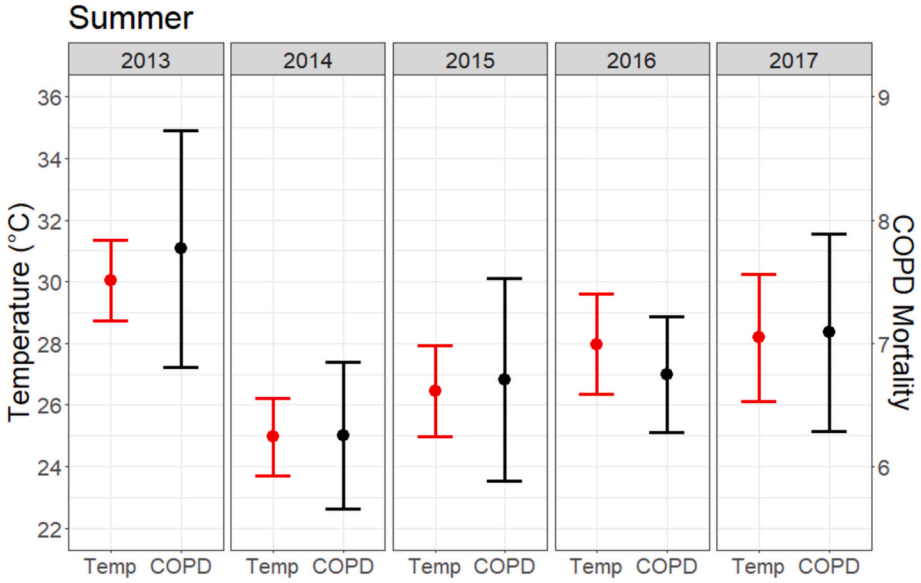

Fig. 3. Weekly average values and their 95 % CIs of ambient temperature and COPD mortality in summer in Ningbo.

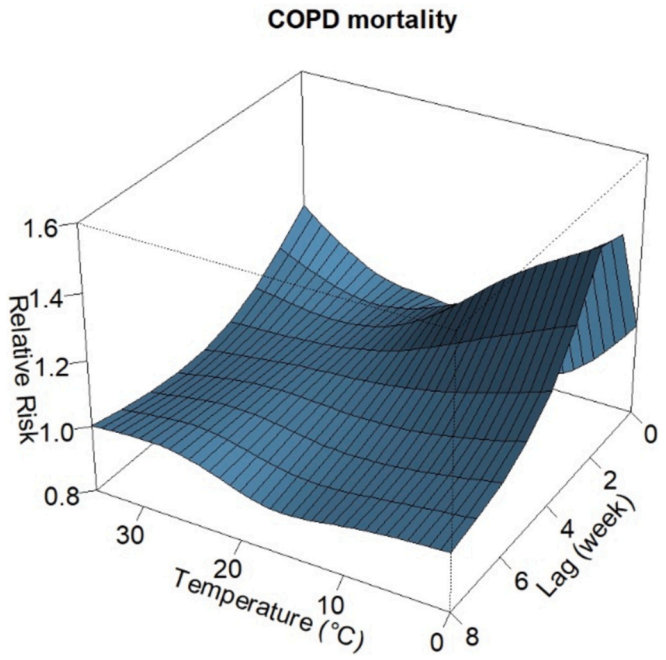

Fig. 4. Relative risks of COPD mortality attributable to the effect of weekly average ambient temperature and lag.

temperature of 0 °C with a 2-week lag.

Fig. 5 displays the cumulative impact of ambient temperature over an 8-week lag on mortality related to COPD. The relationship between ambient temperature and COPD mortality demonstrates nonlinearity, with higher relative risks observed at lower temperatures. Specifically, a J-shaped association was identified between relative risk and temperature, indicating a greater cumulative relative risk at colder temperatures compared to hotter temperatures. The current study reveals a moderate exponential growth in the relative risk of COPD mortality as ambient temperatures decrease. However, at higher temperatures, the estimated cumulative relative risk slightly increases, ranging from 1.0 to 1.1.

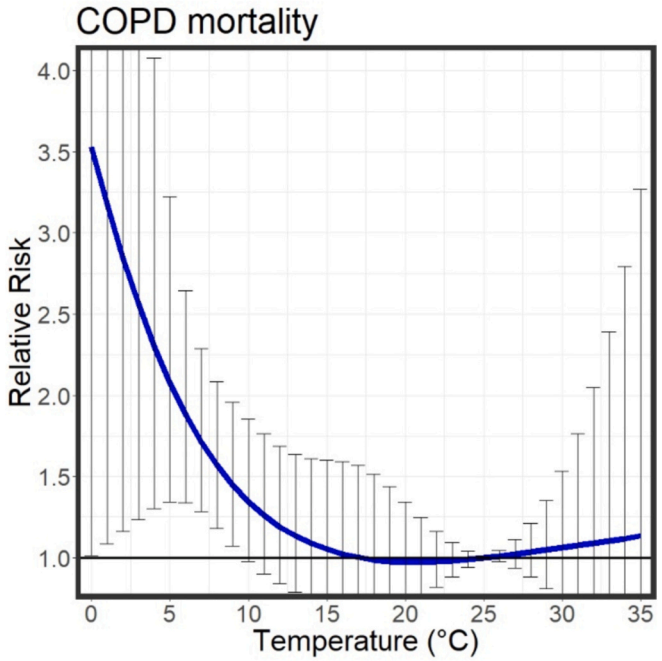

Fig. 5. Relative risks of COPD mortality attributable to the estimated cumulative effect of ambient temperature over lag 0–8 week (The blue line gives the mean value of relative risk with the bars representing the 95 % CIs). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

3.3. Effect of extreme cold and hot ambient temperatures on COPD mortality

In the present study, we considered extreme cold temperatures (3 °C) and hot ambient temperatures (32 °C) as the 1st and 99th percentiles, respectively, of the temperature distribution during the investigation period. Fig. 6 displays the relative risks of mortality from COPD associated with extreme temperatures, taking into account the lag time in relation to the reference temperature of 25 °C. The impact of extreme cold temperatures on COPD mortality was found to be significantly stronger with a lag of 1 to 2 weeks, gradually decreasing after the second week. On the contrary, the impact of extreme hot temperatures was highest with no lag. To provide further

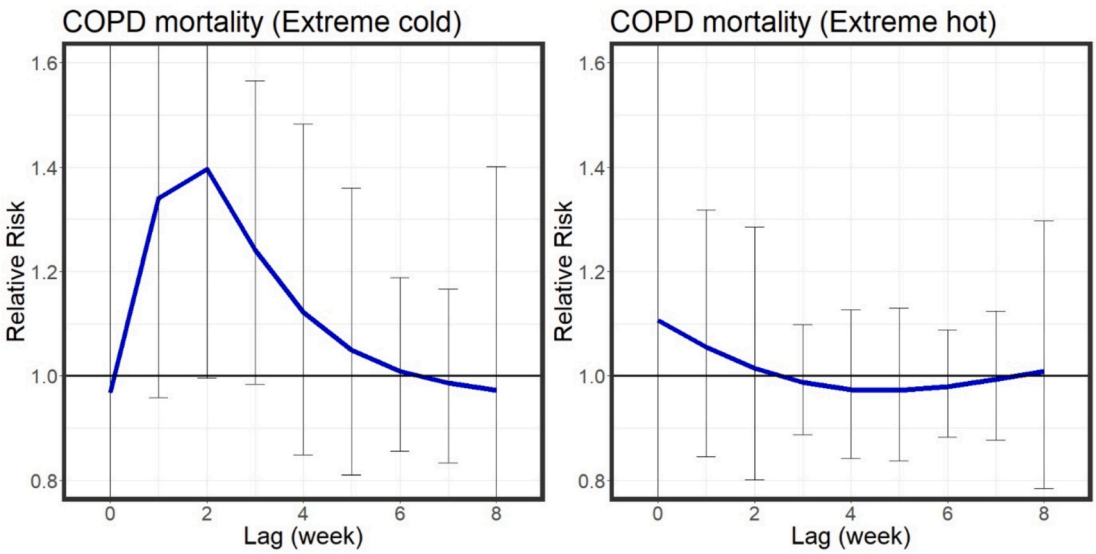

Fig. 6. Relative risks of COPD mortality attributable to the effect of lag week under the extreme cold (3 °C; *left*) and hot (32 °C; *right*) ambient temperatures, respectively (The blue line gives the mean value of relative risk with the bars representing the 95 % CIs). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

insight, Table 2 presents the cumulative relative risks of COPD mortality under extreme cold and hot temperatures across various lag weeks. Notably, the highest cumulative relative risk for COPD mortality was 2.67 (95 % CI: 1.15–6.17) at a lag of 0–6 weeks under extreme cold temperature (3 °C), while for extreme hot temperature (32 °C) the risk was 1.19 (95 % CI: 0.80–1.76) at a lag of 0–2 weeks, all with reference to a temperature of 25 °C.

3.4. Subpopulation analysis stratified by gender

The stratified analysis by gender involved the creation of three-dimensional plots, as shown in Fig. 7, to illustrate the relative risk of COPD mortality based on mean temperatures and lag weeks. It was observed that the influence of gender modified the surface plot of relative risk of COPD mortality, resulting in slightly different patterns on the surfaces. Specifically, females exhibited a higher risk of COPD mortality at both extreme cold and hot temperatures. To further examine this relationship, Fig. 8 displays the plots of relative risk of COPD mortality, considering the estimated cumulative effect of ambient temperature over a lag of 0–8 weeks for the stratified analysis by gender. Consistently, it was found that females had a greater cumulative risk of COPD mortality at both cold and hot temperatures. Table 3 provides a summary of the cumulative relative risks of COPD mortality associated with extreme cold and hot temperatures based on gender. Interestingly, the most pronounced cumulative effect of extreme cold temperature (3 °C) occurred at the same lag week for both genders, specifically at a lag of 0–6 weeks. However, distinct lag weeks were observed for the strongest cumulative effect of extreme hot temperature (32 °C) based on gender. For males, the strongest hot effect was observed at a lag of 0–2 weeks, whereas for females, it occurred at a lag of 0–8 weeks.

3.5. Sensitivity analysis

A sensitivity analysis was performed to evaluate the impact of altering the number of maximum lag weeks from 4 to 6, as well as the degree of freedom of $PM_{2.5}$, O_3, and relative humidity from 4 to 6. The results demonstrated that the relative risk of COPD mortality associated with extreme temperatures did not undergo significant changes. This finding suggests that the estimated effect of ambient temperature on COPD mortality, as reported in this study, provides robust evidence of an association between ambient temperature and COPD mortality. Detailed results of the sensitivity analysis are provided in Table S2 and Table S3.

4. Discussion

The current study employed a Poisson generalized linear model (GLM) with the DLNM to assess the impact of ambient temperature and lag time on mortality due to COPD. Weekly data from Ningbo, China, spanning the years of 2013 to 2017, were utilized for analysis. The model incorporated a maximum lag of 8 weeks and controlled for confounding factors such as air pollutants ($PM_{2.5}$ and O_3), relative humidity, and temporal effects. The findings revealed a significant association between ambient temperature and an increased risk of COPD mortality, indicating that temperature effects were dependent on the lag time. Specifically, a non-linear relationship characterized by a J-shaped curve was observed between relative risk and ambient temperature, suggesting higher mortality risks in colder temperatures. Regarding the lag week effect, extreme cold temperatures (3 °C) exhibited a pronounced impact on COPD mortality at lag 1 and 2 weeks, while extreme hot temperatures (32 °C) were found to have an acute effect. The relative risks associated with extreme cold and hot temperatures for COPD mortality were 2.67 (95 % CI: 1.15–6.17) and 1.19 (95 % CI: 0.80–1.76) within a lag time of 0–6 weeks and 0–2 weeks, respectively.

Comparisons with previous studies investigating the relationship between ambient temperature and COPD mortality are limited, as most of these studies focused on all-cause, cardiovascular, and respiratory mortality, using a daily lag basis (Guo et al., 2011; Wang et al., 2014; Ding et al., 2015). However, our findings are consistent with those of similar studies examining temperature-related mortality (Liu et al., 2020; Yang et al., 2015; Chen et al., 2018). Specifically, our study observed a non-linear inverse J-shaped relationship between ambient temperature and COPD mortality, indicating that colder temperatures were associated with higher risks of COPD mortality compared to hotter temperatures. These results align with the Global Burden of Disease (GBD) study of 2019, which reported a 2.2 times greater mortality due to cold-related effects, although this balance may vary across specific locations or regions (Murray et al., 2020). Most previous studies conducted in China on temperature-related mortality utilized a daily lag basis, with maximum lags ranging between 21 and 28 days (Wang et al., 2014; Yang et al., 2015; Ma et al., 2015). However, it should be noted that employing shorter lags may underestimate the impact of cold temperatures and overestimate the effect of hot temperatures (Guo et al., 2011). In our study, we adopted a weekly basis with a maximum lag of 8 weeks to shed new light on the association between ambient temperature and COPD mortality in a more heavily polluted region. By analyzing the effect of temperature on a weekly scale, this study

Table 2
Cumulative lag week effect of ambient temperature on COPD mortality under the extreme cold and hot temperatures.

Extreme temperature	Relative risk				
	Lag 0	Lag 0–2	Lag 0–4	Lag 0–6	Lag 0–8
Cold	0.97 (0.57–1.65)	1.81 (0.93–3.53)	2.52 (1.22–5.19)	2.67 (1.15–6.17)	2.56 (1.24–5.30)
Hot	1.11 (0.74–1.64)	1.19 (0.80–1.76)	1.14 (0.78–1.66)	1.09 (0.68–1.75)	1.09 (0.58–2.05)

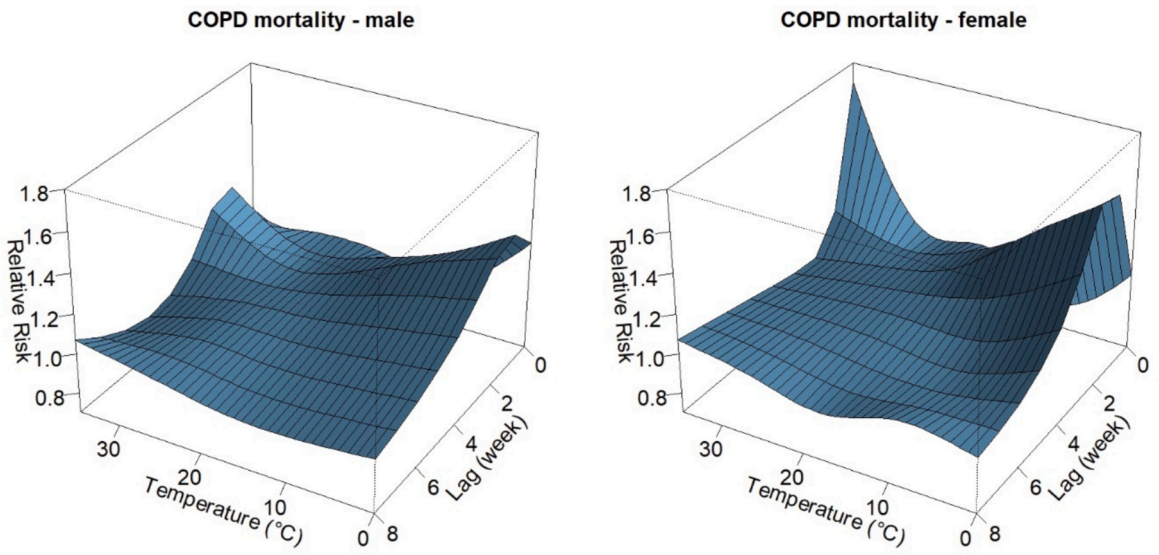

Fig. 7. Relative risks of COPD mortality attributable to the effect of weekly average ambient temperature and lag for stratified analysis of gender.

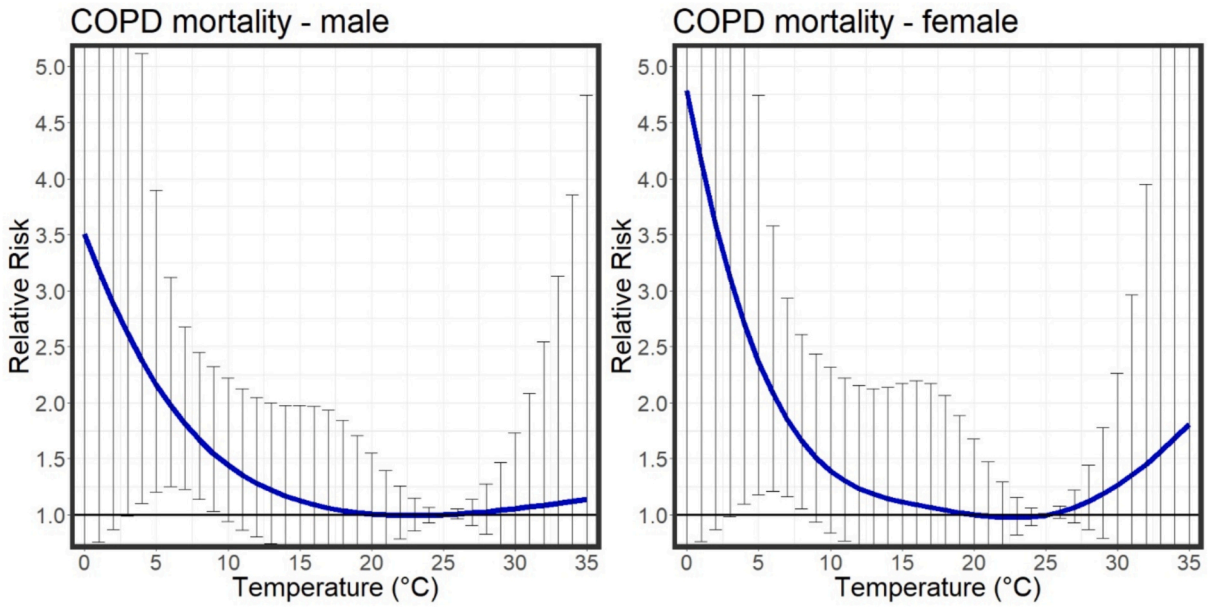

Fig. 8. Relative risks of COPD mortality attributable to the estimated cumulative effect of ambient temperature over lag 0–8 week for stratified analysis of gender (The blue line gives the mean value of relative risk with the bars representing the 95 % CIs). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

offered a different perspective on the temperature-related cause-specific mortality, allowing us to capture subtle variations and temporal patterns that might not be obvious on a daily scale. Our results revealed a significant cold effect from lag 1 to 2 weeks, lasting until lag 5 weeks, while the significant hot effect was immediate, with no lag observed. These findings align with previous studies investigating the relationship between daily mortality and temperature (Wang et al., 2014; Ma et al., 2015; Liu et al., 2015; Son et al., 2011; Guo et al., 2014).

In our study, the relative risks we reported were generally higher compared to previous studies, particularly for colder temperatures. For instance, a study conducted in Taiwan found a 0.8 % increase in the exacerbation rate among COPD patients for each 1 °C decrease in daily mean temperature (Tseng et al., 2013). Similarly, a study in Jiangsu Province, China, reported significant effects of extreme temperatures on COPD, with relative risks of 1.92 (95 % CI: 1.41–2.62) for cold temperatures and 1.57 (95 % CI: 1.36–1.81) for hot temperatures (Ma et al., 2020). These findings align with our study, suggesting a stronger cold effect compared to a hot effect on

Table 3
Cumulative lag week effect of ambient temperature on COPD mortality under the extreme cold and hot temperatures in different genders.

Extreme temperatures	Relative risk				
	Lag 0	Lag 0–2	Lag 0–4	Lag 0–6	Lag 0–8
Male					
Cold	1.12	1.90	2.57	2.78	2.62
	(0.55–2.29)	(0.77–4.67)	(0.97–6.81)	(0.90–8.61)	(0.99–6.94)
Hot	0.96	1.22	1.17	1.04	1.09
	(0.56–1.65)	(0.71–2.09)	(0.70–1.95)	(0.55–1.97)	(0.46–2.54)
Female					
Cold	0.95	2.14	3.04	3.12	3.11
	(0.41–2.20)	(0.75–6.14)	(0.98–9.49)	(0.83–11.7)	(0.98–9.85)
Hot	1.39	1.40	1.31	1.33	1.45
	(0.74–2.59)	(0.75–2.62)	(0.72–2.39)	(0.63–2.81)	(0.53–3.95)

COPD mortality. Furthermore, as depicted in Fig. 5 and Fig. 6, the curves of the generated relative risk plots in our study show consistency with a previous study that analyzed the association between temperature and COPD mortality in 272 Chinese cities, using a maximum lag of 21 days (Chen et al., 2018). However, it is worth noting that comparing relative risk values with other studies may be less conclusive due to variations in study designs, different types of attributable mortality, and the selection of reference temperature in those studies. For example, Guo et al. (2011) used a reference temperature of 28 °C and a maximum lag period of 27 days to examine the effect of temperature on nonaccidental, cardiopulmonary, cardiovascular, and respiratory mortality in Tianjin. Wang et al. (2014) and Yang et al. (2015) used a reference temperature of 26 °C and a maximum lag period of 28 days to assess temperature-related mortality in Suzhou and Shanghai, respectively. Moreover, previous studies often selected approximately the 75th percentile of the mean temperature distribution as the reference temperature for measuring relative risks at different temperatures (Ma et al., 2015; Gasparrini et al., 2012; Martin et al., 2012; Guo et al., 2014). For instance, Ma et al. (2015) reported relative risks by comparing them with the 75th percentiles of the pooled temperature distribution (23.8 °C) across 66 communities in China. In our study, we selected a reference temperature of 25 °C, which approximated the 81st percentile of the temperature distribution. This value represented the mean temperature during a period that corresponded to less than the 5th percentile of the mortality distribution over the study period. It is important to note that the reference temperature, also known as the threshold temperature or minimum mortality temperature in other studies, can vary significantly across regions due to different socioeconomic and geographical factors (Curriero et al., 2002; Ma et al., 2015). Additionally, the reference temperature should be applied specifically for each cause-specific mortality, as the effect of temperature may vary for different mortality types, such as cardiovascular and respiratory mortality.

The association between extreme ambient temperature and COPD mortality has been extensively studied and considered in the Global Burden of Disease (GBD) study of 2019, which provides insight into the direct effect of ambient temperature on COPD. Several possible mechanisms have been proposed to explain this association. Notably, the effects of cold temperatures on mortality are believed to be more indirect compared to the effects of heat (Anderson and Bell, 2009). Exposure to extreme cold temperatures can lead to enhanced sympathetic reactivity and activation of the renin-angiotensin system, both of which are often linked to elevated blood pressure (Liu et al., 2015). Sympathetic activation and increased blood pressure are thought to have an adverse impact on COPD patients (Andreas et al., 2014; Byrd et al., 2018). One potential mechanism is the bronchoconstriction and inflammation caused by cold temperatures (Hansel et al., 2016; Koskela et al., 1996), which may affect the prognosis of COPD. On the other hand, extreme heat can disrupt the body's heat dissipation mechanism through the circulatory system, particularly in the elderly population and COPD patients (Liu et al., 2011). The effects of extreme heat may include a systemic inflammatory response due to heat stroke, leading to multiple organ damage and exacerbation of existing COPD conditions (Liu et al., 2015). Additionally, elevated temperatures are associated with a higher risk of exposure to allergens such as moulds, mites, and pollen (Song et al., 2017).

Outdoor air pollutants have been frequently associated with the exacerbation and mortality of COPD (Hansel et al., 2016). Notably, pollutants like $PM_{2.5}$ and O_3 demonstrate distinct associations with ambient temperature, with higher levels of $PM_{2.5}$ observed during cold seasons and increased O_3 concentration during warm seasons (Chung et al., 2021). The combined impact of extreme ambient temperature and air pollutants may contribute to the exacerbation of COPD. This study addresses limitations of previous research by considering the effects of air pollutants such as $PM_{2.5}$, O_3, and relative humidity during the model fitting process (Guo et al., 2011; Wang et al., 2014; Ma et al., 2014). Adjusting the models to include O_3 and PM_{10} results in slightly lower heat effects (Anderson and Bell, 2009), suggesting a potential relationship between ambient temperature and air pollutants. Analitis et al. (2014) report that higher concentrations of O_3 and PM_{10} are associated with an increased heat wave effect on total mortality, indicating that pollutants like O_3 and PM_{10} may modify the estimated effects in the model. Another possible explanation for the indirect effect of extreme ambient temperature on air pollution-related COPD mortality is the atmospheric transport and dispersion of pollutants during the winter. Air pollution is often exacerbated by temperature inversions, which occur when the temperature profile in the atmosphere is inverted (Xu et al., 2015; He et al., 2009). In normal atmospheric conditions, temperature typically decreases with increasing altitude. However, during a temperature inversion episode, temperature increases with altitude. A study conducted in Beijing found that 93 % of severely polluted days are associated with temperature inversions, most of which occurred during the winter season (Xu et al., 2019). As depicted in Fig. 1, higher concentrations of $PM_{2.5}$ are often observed during periods of lower temperatures. Because air does not efficiently conduct heat, a warmer thermal inversion layer forms above the cooler surface air, which hinders convection. This warm

layer acts as a cap, impeding the turbulent mixing and atmospheric transport of pollutants and leading to the accumulation of particulate matter in the atmosphere (Li et al., 2015). This accumulation of pollutants may result in increased outdoor exposure to $PM_{2.5}$ during the winter, particularly during extreme weather events like cold waves, which suggests a plausible interaction between ambient temperature and air pollution-related diseases. In the present study, the impact of extreme weather on COPD mortality in the Yangtze River Delta region was clearly observed, especially in 2013, as depicted in Figs. 2 and 3. Both extremely cold and hot temperatures were associated with increased COPD mortality during the winter and summer, respectively, in 2013.

Subpopulation analysis was conducted by stratifying the data based on gender, revealing a significant modifying effect. Females exhibited higher vulnerability to both colder and hotter temperatures compared to males in relation to COPD mortality. Additionally, distinct patterns were observed in the effect of extreme hot temperatures on both genders. A stronger cumulative effect of extreme hot temperatures was observed at a lag of 0–8 weeks for females, providing a possible explanation for their greater susceptibility. Similar findings were reported in a study conducted in Korea, which highlighted that females are more susceptible to both heat and cold effects on temperature-related mortality (Son et al., 2011). The variation in susceptibility between genders may be attributed to differences in their ability to regulate body temperature in response to extreme ambient temperatures (Barnett, 2007). Another important factor that contributes to the gender difference in susceptibility to cold-related mortality may be the use of protective measures such as clothing.

This study has several significant implications. Firstly, it offers new insights into the impact of ambient temperature on COPD mortality related to air pollution in highly polluted regions, using weekly data. Secondly, these findings underscore the need for heightened public awareness and the implementation of policies, particularly in healthcare facilities, to address the substantial burden of disease stemming from extreme ambient temperatures in heavily polluted regions worldwide. Vulnerable populations should be encouraged to minimize their outdoor exposure during extreme weather events such as heatwaves and cold waves. Thirdly, this study specifically evaluates the lagged effect of ambient temperature and emphasizes the importance of future research that examines the combined impact of ambient temperature and air pollution on cause-specific mortality, specifically in the development of a novel risk model for global risk assessment. However, there are certain limitations in this study and recommendations for future research. Firstly, the analysis only focused on one region in China, which limits the generalizability of the findings. It is recommended to replicate the study in other cities with similar meteorological conditions to validate the results. Secondly, the model did not incorporate data on influenza epidemics and smoking habits due to their unavailability. Thirdly, demographic and socioeconomic variables were not included in the analysis due to limited data. It is suggested that future studies should carefully control for population effects in the model by including demographic and socioeconomic factors such as educational level or income of the study population, as these factors may influence self-protective measures against extreme hot and cold temperatures. For instance, the presence of air conditioning in living areas could potentially play a role in protecting individuals against hot temperatures, particularly during heatwaves.

5. Conclusion

In summary, this study identifies a clear association between ambient temperature and an increased risk of mortality from COPD in the highly polluted Yangtze River Delta region of China. The analysis reveals an inverse J-shaped relationship, indicating that the effect of cold temperature on COPD mortality is more pronounced than that of hot temperature. Specifically, the study finds a significant impact of extreme cold temperatures (3 °C) with a lag of 1 to 2 weeks, while the effect of extreme hot temperatures (32 °C) is acute. In order to reduce COPD mortality related to the combined influence of air pollution and extreme ambient temperatures, it is recommended that individuals minimize their time spent outdoors during periods of high pollution levels and extreme temperatures, particularly during heat waves and cold waves. The findings of this study provide a quantitative understanding of the relationship between ambient temperature and COPD mortality risk, which can be valuable in estimating the disease burden associated with extreme weather events in global risk assessments.

CRediT authorship contribution statement

Chee Yap Chung: Writing – original draft, Investigation, Conceptualization. **Jie Yang:** Supervision, Funding acquisition, Formal analysis, Data curation. **Xiaogang Yang:** Writing – review & editing, Supervision. **Jun He:** Writing – review & editing, Supervision, Resources, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Jun He reports financial support was provided by Ningbo Science and Technology Bureau. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgements

This study was financially supported by the National Natural Science Foundation of China (21750110446) and Ningbo Commonweal Key Research Program (2023S038). The authors would like to thank Ningbo Environmental Monitoring Centre (Ningbo EMC) and Ningbo Centre for Disease Control and Prevention (Ningbo CDC) for sharing the data. Chung C. Y. was supported by the Faculty of Science and Engineering PhD scholarship (Ref No. 19073FOSE) at University of Nottingham Ningbo China (UNNC).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.uclim.2024.102163.

References

Analitis, A., Michelozzi, P., D'ippoliti, D., De'donato, F., Menne, B., Matthies, F., Atkinson, R.W., Iniguez, C., Basagana, X., Schneider, A., Lefranc, A., Paldy, A., Bisanti, L., Katsouyanni, K., 2014. Effects of heat waves on mortality: effect modification and confounding by air pollutants. Epidemiology 25 (1), 15–22.

Anderson, B.G., Bell, M.L., 2009. Weather-related mortality: how heat, cold, and heat waves affect mortality in the United States. Epidemiology 20, 205–213.

Andreas, S., Haarmann, H., Klarner, S., Hasenfuss, G., Raupach, T., 2014. Increased sympathetic nerve activity in COPD is associated with morbidity and mortality. Lung 192, 235–241.

Apte, J.S., Marshall, J.D., Cohen, A.J., Brauer, M., 2015. Addressing global mortality from ambient $PM_{2.5}$. Environ. Sci. Technol. 49, 8057–8066.

Barnett, A.G., 2007. Temperature and cardiovascular deaths in the US elderly: changes over time. Epidemiology 18, 369–372.

Brauer, M., Freedman, G., Frostad, J., van Donkelaar, A., Martin, R.V., Dentener, F., van Dingenen, R., Estep, K., Amini, H., Apte, J.S., Balakrishnan, K., et al., 2016. Ambient air pollution exposure estimation for the global burden of disease 2013. Environ. Sci. Technol. 50, 79–88.

Byrd, J.B., Newby, D.E., Anderson, J.A., Calverley, P.M.A., Celli, B.R., Cowans, N.J., Crim, C., Martinez, F.J., Vestbo, J., yates, J, Brook, R.D., 2018. Blood pressure, heart rate, and mortality in chronic obstructive pulmonary disease: the SUMMIT trial. Eur. Heart J. 39, 3128–3134.

Chen, R., Yin, P., Wang, L., Liu, C., Niu, Y., Wang, W., Jiang, Y., Liu, Y., Liu, J., Qi, J., You, J., Kan, H., Zhou, M., 2018. Association between ambient temperature and mortality risk and burden: time series study in 272 main Chinese cities. BMJ 363, k4306.

Cheng, X., Su, H., 2010. Effects of climatic temperature stress on cardiovascular diseases. Eur. J. Intern. Med. 21, 164–167.

Chung, J.Y., Honda, Y., Hong, Y.C., Pan, X.C., Guo, Y.L., Kim, H., 2009. Ambient temperature and mortality: an international study in four capital cities of East Asia. Sci. Total Environ. 408, 390–396.

Chung, C.Y., Yang, J., He, J., Yang, X., Hubbard, R., Ji, D., 2021. An investigation into the impact of variations of ambient air pollution and meteorological factors on lung cancer mortality in Yangtze River Delta. Sci. Total Environ. 779, 146427.

Costello, A., Abbas, M., Allen, A., Ball, S., Bell, S., Bellamy, R., Friel, S., Groce, N., Johnson, A., Kett, M., Lee, M., Levey, C., Maslin, M., McCoy, D., McGuire, B., Montgomery, H., Napier, D., Pagel, C., Pael, J., de Oliveria, J.A.P., Redclift, N., Rees, H., Rogger, D., Scott, J., Stephenson, J., Twigg, J., Wolff, J., Patterson, C., 2009. Managing the health effects of climate change: lancet and University College London Institute for Global Health Commission. Lancet 373, 1693–1733.

Curriero, F.C., Heiner, K.S., Samet, J.M., Zeger, S.L., Strug, L., Patz, J.A., 2002. Temperature and mortality in 11 cities of the eastern United States. Am. J. Epidemiol. 155, 80–87.

Ding, Z., Guo, P., Xie, F., Chu, H., Li, K., Pu, J., Pang, S., Dong, H., Liu, Y., Pi, F., Zhang, Q., 2015. Impact of diurnal temperature range on mortality in a high plateau area in Southwest China: A time series analysis. Sci. Total Environ. 526, 358–365.

Forouzanfar, M.H., Afshin, A., Alexander, L.T., Anderson, H.R., Bhutta, Z.A., Biryukov, S., et al., 2016. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the global burden of disease study 2015. Lancet 388, 1659–1724.

Gasparrini, A., 2011. Distributed lag linear and non-linear models in R: the package dlnm. J. Stat. Softw. 43, 1–20.

Gasparrini, A., Armstrong, B., Kenward, M.G., 2010. Distributed lag non-linear models. Stat. Med. 29, 2224–2234.

Gasparrini, A., Armstrong, B., Kenward, M.G., 2012. Multivariate meta-analysis for non-linear and other multi-parameter associations. Stat. Med. 31, 3821–3839.

Guo, Y., Barnett, A.G., Pan, X., Yu, W., Tong, S., 2011. The impact of temperature on mortality in Tianjin, China: a case-crossover design with a distributed lag nonlinear model. Environ. Health Perspect. 119, 1719–1725.

Guo, Y., Gasparrini, A., Armstrong, B., Li, S., Tawatsupa, B., Tobias, A., et al., 2014. Global variation in the effects of ambient temperature on mortality: a systematic evaluation. Epidemiology 25, 781–789.

Hansel, N. N., Mccormack, M. C. & Kim, V. 2016. The effects of air pollution and temperature on COPD. *COPD,* 13, 372–9.

He, J., Balasubramanian, R., Karthikeyan, S., Joshi, U.M., 2009. Determination of semi-volatile organochlorine compounds in the atmosphere of Singapore using accelerated solvent extraction. Chemosphere 75 (5), 640–648.

Iniguez, C., Ballester, F., Ferrandiz, J., Perez-Hoyos, S., Saez, M., Lopez, A., Tempro, E., 2010. Relation between temperature and mortality in thirteen Spanish cities. Int. J. Environ. Res. Public Health 7, 3196–3210.

Koskela, H.O., Koskela, A.K., Tukiaineu, H.O., 1996. Bronchoconstriction due to cold weather in COPD. The roles of direct airway effects and cutaneous reflex mechanisms. Chest 110, 632–636.

Kysely, J., Pokorna, L., Kyncl, J., Kriz, B., 2009. Excess cardiovascular mortality associated with cold spells in the Czech Republic. BMC Public Health 9, 19.

Li, Y., Chen, Q., Zhao, H., Wang, L., Tao, R., 2015. Variations in PM10, PM2.5 and PM1.0 in an urban area of the Sichuan Basin and their relation to meteorological factors. Atmosphere 6, 150–163.

Lim, S.S., Vos, T., Flaxman, A.D., Danaei, G., Shibuya, K., Adair-Rohani, H., et al., 2012. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the global burden of disease study 2010. Lancet 380, 2224–2260.

Liu, L., Breitner, S., Pan, X., Franck, U., Leitte, A.M., Wiedensohler, A., Klot, S., Wichmann, H., Peters, A., Schneider, A., 2011. Associations between air temperature and cardio-respiratory mortality in the urban area of Beijing, China: a time-series analysis. Environ. Health 10, 51.

Liu, C., Yavar, Z., Sun, Q., 2015. Cardiovascular response to thermoregulatory challenges. Am. J. Physiol. Heart Circ. Physiol. 309, H1793–H1812.

Liu, J., Hansen, A., Varghese, B., Liu, Z., Tong, M., Qiu, H., Tian, L., Lau, K., Ng, E., Ren, C., Bi, P., 2020. Cause-specific mortality attributable to cold and hot ambient temperatures in Hong Kong: a time-series study, 2006–2016. Sustain. Cities Soc. 57, 102131.

Ma, W., Chen, R., Kan, H., 2014. Temperature-related mortality in 17 large Chinese cities: how heat and cold affect mortality in China. Environ. Res. 134, 127–133.

Ma, W., Wang, L., Lin, H., Liu, T., Zhang, Y., Rutherford, S., Luo, Y., Zeng, W., Zhang, Y., Wang, X., Gu, X., Chu, C., Xiao, J., Zhou, M., 2015. The temperature-mortality relationship in China: an analysis from 66 Chinese communities. Environ. Res. 137, 72–77.

Ma, Y., Zhou, L., Chen, K., 2020. Burden of cause-specific mortality attributable to heat and cold: A multicity time-series study in Jiangsu Province, China. Environ. Int. 144, 105994.

Martin, S.L., Cakmak, S., Hebbern, C.A., Avramescu, M.L., Tremblay, N., 2012. Climate change and future temperature-related mortality in 15 Canadian cities. Int. J. Biometeorol. 56, 605–619.

Murray, C.J.L., Aravkin, A.Y., Zheng, P., Abbafati, C., Abbas, K.M., Abbasi-Kangevari, M., et al., 2020. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the global burden of disease study 2019. Lancet 396, 1223–1249.
Onozuka, D., Hagihara, A., 2015. Variation in vulnerability to extreme-temperature-related mortality in Japan: A 40-year time-series analysis. Environ. Res. 140, 177–184.
Peng, R.D., Dominici, F., Louis, T.A., 2006. Model choice in time series studies of air pollution and mortality. J. R. Stat. Soc. 169, 179–203.
Rocklöv, J., Forsberg, B., 2008. The effect of temperature on mortality in Stockholm 1998—2003: A study of lag structures and heatwave effects. Scand. J. Public Health 36, 516–523.
Sartor, F., Snacken, R., Walckiers, D., Demuth, C., 1995. Temperature, ambient ozone levels, and mortality during summer, 1994, Belgium. Environ. Res. 70 (2), 105–113.
Son, J.Y., Lee, J.T., Anderson, G.B., Bell, M.L., 2011. Vulnerability to Temperature-Related Mortality in Seoul. Korea, Environ Res Lett, p. 6.
Son, J.Y., Lee, J.T., Anderson, G.B., Bell, M.L., 2012. The impact of heat waves on mortality in seven major cities in Korea. Environ. Health Perspect. 120, 566–571.
Song, X., Wang, S., Hu, Y., Yue, M., Zhang, T., Liu, Y., Tian, J., Shang, K., 2017. Impact of ambient temperature on morbidity and mortality: an overview of reviews. Sci. Total Environ. 586, 241–254.
Soriano, J.B., Kendrick, P.J., Paulson, K.R., Gupta, V., Abrams, E.M., Adedoyin, R.A., et al., 2020. Prevalence and attributable health burden of chronic respiratory diseases, 1990–2017: a systematic analysis for the global burden of disease study 2017. Lancet Respir. Med. 8, 585–596.
Tseng, C.M., Chen, Y.T., Ou, S.M., Hsiao, Y.H., Li, S.Y., Wang, S.J., Yang, A.C., Chen, T.J., Perng, D.W., 2013. The effect of cold temperature on increased exacerbation of chronic obstructive pulmonary disease: a nationwide study. PLoS One 8, e57066.
Wang, C., Chen, R., Kuang, X., Duan, X., Kan, H., 2014. Temperature and daily mortality in Suzhou, China: a time series analysis. Sci. Total Environ. 466-467, 985–990.
Xu, T., Song, Y., Liu, M., Cai, X., Zhang, H., Guo, J., Zhu, T., 2019. Temperature inversions in severe polluted days derived from radiosonde data in North China from 2011 to 2016. Sci. Total Environ. 647, 1011–1020.
Xu, J.S., Tai, X.H., Betha, R., He, J., Balasubramanian, R., 2015. Comparison of physical and chemical properties of ambient aerosols during the 2009 haze and non-haze periods in Southeast Asia. Environ. Geochem. HlTH. 37 (5), 831–841.
Yang, C., Meng, X., Chen, R., Cai, J., Zhao, Z., Wan, Y., Kan, H., 2015. Long-term variations in the association between ambient temperature and daily cardiovascular mortality in Shanghai, China. Sci. Total Environ. 538, 524–530.
Yin, P., Brauer, M., Cohen, A.J., Wang, H., Li, J., Burnett, R.T., Stanaway, J.D., Causey, K., Larson, S., Godwin, w., Frostad, J., Marks, A., Wang, L., Zhou, M., Murray, C., 2020. 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 4, e386–e398.
Zhang, Y., Yu, C., Bao, J., Li, X., 2017. Impact of temperature variation on mortality: an observational study from 12 counties across Hubei Province in China. Sci. Total Environ. 587-588, 196–203.