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Short-term effects of fine particulate matter on non-accidental and circulatory diseases mortality: A time series study among the elder in Changchun

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Abstract

Background and objectives

Fine particulate matter ($PM_{2.5}$, particulate matter with an aerodynamic diameter less than or equal to 2.5 µm) has multiple adverse effects on human health, especially on the respiratory and circulatory system. The purpose of this study was to evaluate the short-term effect of $PM_{2.5}$ on the mortality risk of non-accidental and circulatory diseases, and to explore the potential effect modification by sex, education and death location.

Methods

We collected daily mortality counts of Changchun (China) residents, daily meteorology and air pollution data, from January 1, 2014, to January 1, 2017. We focused on the elderly (\geq 65 years old) population who died from non-accidental causes and circulatory diseases, and stratified them by sex, education, and death location. A generalized additive Poisson regression model (GAM) was used to analyse the impact of air pollutants on mortality. We fit single pollutant models to examine PM_{2.5} effects with different lag structures of single-day (distributed lag:lag0-lag3) and multi-day (moving average lag: lag01-lag03). To test the sensitivity of the model, a multi-pollutant model was established when the PM_{2.5} effect was strongest.

Results

In the single pollutant models, an increment of $PM_{2.5}$ by 10 µg/m³ at lag0-3 was associated with a 0.385% (95% CI: 0.069% to 0.702%) increase in daily non-accidental mortality and a 0.442% (95% CI: 0.038% to 0.848%) increase in daily circulatory disease mortality. NO₂ (lag1) and O₃ (lag0, lag1, lag2, lag01, lag02, lag03) were associated with daily non-accidental death and NO₂ (lag1, lag3, lag03) and O₃ (lag0, lag1, lag01, lag02, lag03) were associated with daily circulatory disease mortality. In the co-pollutant models, the risk estimates for



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PM_{2.5} changed slightly. The excess mortality risk of non-accidental and circulatory diseases was higher for women, people with low education, and died outside hospital.

Conclusions

We found that short-term exposure to $PM_{2.5}$ increased the mortality risk of non-accidental and circulatory diseases among the elderly in Changchun. Women, people with low education and died outside hospital are more susceptible to $PM_{2.5}$. NO₂ and O₃ were also associated with an increase in mortality from non-accidental and circulatory diseases and the O₃ is a high effect.

1.Introduction

Ambient air pollution (AAP), which has a substantial impact on human health, has become a global public health risk[1]. Data from the World Health Organization (WHO) show that 98% of cities in the world's low- and middle-income countries experience high levels of air pollution [2]. Fine particulate matter (PM_{2.5}, particulate matter with an aerodynamic diameter less than or equal to 2.5 μ m) is a principal air pollutant [3]. PM_{2.5} is a mixture of various compounds that can enter major organ systems through the lungs, and it has multiple adverse effects on human health, especially on the respiratory and circulatory systems[4–8]. Numerous epidemiologic studies have reported the short-term effects of PM_{2.5}[9–12]. However, short-term effects varied by exposure levels, air pollutant, population characteristics, and geographic location[13].

The WHO air quality guidelines (AQGs) set an annual mean of 10 μ g/m³ and a 24-hour mean of 25 μ g/m³ for PM_{2.5}, and the risks of short-term and long-term mortality can be significantly reduced at below-mean concentrations[14]. Globally, the population-weighted average concentration of PM_{2.5} continues to increase, and 87% of people worldwide were exposed to PM_{2.5} levels greater than 10 μ g/m³ in 2013[15].

In China, $PM_{2.5}$ pollution is more severe. Only 4% of Chinese people live in areas that meet the WHO AQGs[15]. In 2013, 760,000 people in China died from exposure to $PM_{2.5}$ [16]. As the capital city of Jilin Province (China), Changchun is the largest automobile industrial city in China and the birthplace of China's automobile, film, optical, bio-pharmaceutical, and track bus industries. In 2017, the total area was 20,565 square kilometres, with a total registered population of 7.489 million and an urban population of 4.383 million. The energy source of Changchun mainly consists of coal, making it a soot polluted city. In recent years, with the increase in car ownership, there is a trend towards mixed pollution. Due to the long heating period, the air pollution in Changchun is more serious in the winter. No study on the relationship between short-term exposure to $PM_{2.5}$ and mortality risk has been conducted in Changchun. Since the elderly are more vulnerable to air pollution[17,18], we therefore conducted a time-series study of the elderly in Changchun to evaluate the short-term effect of $PM_{2.5}$ on non-accidental and circulatory disease mortality, and explored the potential effect modification by sex, education and death location.

2. Materials and methods

2.1. Data

2.1.1. Mortality data. Daily mortality data for residents in Changchun from January 1, 2014, to January 1, 2017, was obtained from the Jilin Provincial Center for Disease Control and Prevention. The anonymous records included age, sex, date of death, and the underlying

cause of death. The underlying causes of death are classified by the International Classification of Diseases (ICD-10), in which non-accidental mortality are A00-R99 and circulatory system diseases are I00~I99. To determine the daily death toll, we selected all the elderly (\geq 65 years old) who 'died of non-accidental causes and those who died of circulatory diseases and stratified them by sex, education and death location.

2.1.2. Air pollution and meteorology data. Daily air pollution data were obtained from ten national environmental monitoring stations in Changchun, including $PM_{2.5}$, particulate matter with an aerodynamic diameter of equal or less than 10 µm (PM_{10}), sulphur dioxide (SO_2), nitrogen dioxide (NO_2) and ozone (O_3) (average concentration over 8 hours). Each indicator has at least 27 daily averages per month (at least 25 daily averages in February), and at least 324 daily averages per year. Daily meteorology data were obtained from the Changchun meteorological bureau, including average relative humidity and mean temperature. The annual data loss rate is less than 5%, and each index has at least 347 daily mean values per year. Audits of the validity, accuracy, normalization of the data, and of data quality can be used for analysis.

2.2. Statistical analysis

Spearman's rank correlation test was used to evaluate the correlation between air pollutants and meteorological conditions. The generalized additive Poisson regression model (GAM) was used to analyse the impact of air pollutants on the mortality of people. We applied smoothing spline functions to control the effects of confounding factors such as daily mean temperature, relative humidity, secular trend and seasonality on population mortality. The day of the week (DOW) was included in the multiple regression model as a dummy variable. The basic model was as follows:

$$log[E(Yi)] = \beta Zi + s(time, v) + s(temp, v) + s(RH, v) + dow + o$$

where:

- -- $E(Y_i)$ is the expected daily death toll;
- -- *s*(.) is the smoothing spline function for nonlinear variables;
- -- β is the regression coefficient;
- -- *v* is the degree of freedom. The degree of freedom was selected according to minimum Akaike information criterion (AIC). We applied the following degrees of freedom (df): 7/ year for the time trend and 3 for mean temperature and average relative humidity;
- -- *dow* is the day of the week;
- -- α is the intercept

We fit single pollutant models to examine $PM_{2.5}$ effects with different lag structures of single-day (distributed lag: lag0-lag3) and multi-day (moving average lag: lag01-lag03). In singleday models, lag0 and lag1 for example correspond to the pollution concentration on the day and the day before. In multi-day lag models, lag03 for example corresponds to a 4-day moving average pollutant concentration of the current and previous 3 days. To test the sensitivity of the model, a multi-pollutant model was established when the $PM_{2.5}$ effect was strongest. Considering that there may be collinearity among air pollutants, other pollutants (PM_{10} , SO₂, NO₂, O₃) are entered in the multi- pollutant model step-by-step. The excess risk (*ER*) was used to evaluate the increased death risk of non-accidental and circulatory diseases with each increase of $10\mu g/m^3$ of air pollutants (*ER* = (*RR*-1)×100%; RR, relative risk). We also stratified the association of daily mortality with PM_{2.5} by sex, education, and death location (died in hospital versus outside of hospital).

SPSS(Version 17.0; IBM Corp, Armonk, New York, USA) was used for descriptive analysis and Spearman correlation analysis, and R software (version 3.5.0; http://www.r-project.org) was used for time series analysis, with test degree $\alpha = 0.05$.

3. Results

3.1. Descriptive statistics

From January 2014 to January 2017, a total of 46,780 non-accidental deaths were reported among the elderly (\geq 65 years old) in Changchun, of which 26,498 died of circulatory diseases. The mean daily deaths from non-accidental and circulatory diseases were 32.0 and 18.1, respectively. The daily average temperature was 7.0 °C, and the daily average relative humidity was 60.1%. The daily mean concentration of PM_{2.5} was 55.9 µg/m³, with a Standard deviation (SD) of 49.5 µg/m³. For the other air pollutants, the daily mean concentrations of PM₁₀, SO₂, NO₂ and O₃ were 93.3 µg/m³, 30.7 µg/m³, 40.8 µg/m³ and 89.1 µg/m³, respectively (Table 1).

3.2. Spearman correlation between air pollutants and weather conditions

 $PM_{2.5}$ was positively correlated with PM_{10} (r = 0.83), SO_2 (r = 0.52) and NO_2 (r = 0.72). O_3 , mean temperature and relative humidity were negatively correlated with $PM_{2.5}$ (Table 2).

3.3. Single pollutant model

Table 3 shows the excess mortality risk of non-accidental and circulatory diseases for the elderly due to $PM_{2.5}$ for each 10 µg/m³ increase on different lag days in single pollutant models. $PM_{2.5}$ was associated with daily non-accidental mortality on lag1 and lag2 days, and the largest risk estimates were found with lag03; $PM_{2.5}$ was associated with daily circulatory disease mortality on lag1, the largest risk estimates were also found with lag03.

Fig 1 shows the excess mortality risk to the elderly population caused by per 10 μ g/m³ increase in air pollutions. NO₂ (lag1) and O₃ (lag0, lag1, lag2, lag01, lag02, lag03) were associated with daily non-accidental death; Fig 2 shows the excess mortality risk to the elderly who die of circulatory diseases caused by per 10 μ g/m³ increase in air pollution. NO₂ (lag1, lag3, lag03) and O₃ (lag0, lag1, lag01, lag02, lag03) were associated with daily circulatory disease mortality.

3.4. Co-pollutant model

In the single pollutant models, an increment of $PM_{2.5}$ by 10 µg/m³ at lag0-3 was associated with a 0.386% (95% CI: 0.07% to 0.70%) increase in daily non-accidental mortality and a 0.44% (95% CI: 0.04% to 0.85%) increase in daily circulatory disease mortality; NO₂ was associated with increased daily circulatory disease mortality, and O₃ was associated with increased daily non-accidental mortality and daily circulatory disease mortality. In the co-pollutant models, the risk estimates for PM_{2.5} changed slightly (Table 4).

3.5. Subgroup analysis

The excess mortality risk of non-accidental and circulatory diseases was higher for women, people with low education and died outside hospital than it was for men, poeple with high education and died in hospital (Table 5).

Table 1. Descriptive statistics.

PLOS

Index	Mean	Standard deviation	25% quartile	Median	75% quartile	Range
Pollution concentration						
PM _{2.5} (μg/m ³)	55.9	49.5	25.0	41.0	71.0	481.0
PM ₁₀ (µg/m ³)	93.3	66.2	53.0	77.0	114.0	12.0
$SO_2 (\mu g/m^3)$	30.7	28.9	8.0	16.0	48.0	148.0
$NO_2 (\mu g/m^3)$	40.8	14.0	30.0	39.0	48.0	98.0
O _{3 (} µg/m ³)	89.1	38.1	58.0	82.0	113.0	212.0
Meteorology measures						
Mean temperature (°C)	7.0	13.8	-5.8	9.2	19.5	52.6
Average relative humidity (%)	60.1	16.8	48.0	61.0	73.0	86.0
Daily non-accidental death counts ¹						
Total	32.0	6.5	27.0	32.0	36.0	39.0
Women	15.2	4.3	12.0	15.0	18.0	26.0
Men	16.8	4.4	14.0	17.0	20.0	28.0
Junior high school and below	24.1	5.6	20.0	24.0	28.0	35.0
High school degree or above	8.0	3.1	6.0	8.0	10.0	26.0
Died in the hospital	15.8	4.3	13.0	15.0	19.0	28.0
Died outside the hospital	16.2	4.5	13.0	16.0	19.0	28.0
Daily circulatory diseases death counts ² (I00-I99)						
Total	18.1	4.7	15.0	18.0	21.0	33.0
Women	9.0	3.3	7.0	9.0	11.0	21.0
Men	9.1	3.1	7.0	9.0	11.0	21.0
Junior high school and below	14.2	4.2	11.0	14.0	17.0	29.0
High school degree or above	3.9	2.2	2.0	4.0	5.0	16.0
Died in the hospital	6.7	2.7	5.0	6.0	9.0	17.0
Died outside the hospital	11.4	3.7	9.0	11.0	14.0	24.0

¹ people who died of all-nonaccidental causes

² people who died of circulatory diseases.

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4. Discussion

Our study analysed the short-term effects of $PM_{2.5}$ on the elderly in Changchun. This study is the first study to examine the relationship between $PM_{2.5}$ and population mortality in Jilin Province. We found that $PM_{2.5}$ was associated with an increase in mortality from non-

Table 2. Spearman correlation between air pollutants and weather conditions.

Index	PM _{2.5}	PM ₁₀	SO ₂	NO ₂	03	СО
PM _{2.5}	-	-	-	-	-	-
PM ₁₀	0.83**	-	-	-	-	-
SO ₂	0.52**	0.37**	-	-	-	-
NO ₂	0.72**	0.57**	0.49**	-	-	-
0 ₃	-0.17**	-0.03*	-0.50**	-0.11**	-	-
Mean temperature	-0.34**	-0.21**	-0.81**	-0.25**	0.70**	-
Average relative humidity	-0.02**	-0.22**	-0.05**	-0.09**	-0.23**	0.09*

*P<0.05

***P*<0.01.

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Lag days	ER of daily non-accidental death count (%)	ER of daily circulatory diseases death count (%)
lag0	0.21 (-0.02, 0.44)	0.27 (-0.03, 0.57)
lag1	0.33 (0.10, 0.57)*	0.38 (0.08, 0.68)*
lag2	0.23 (0.01, 0.46)*	0.16 (-0.13, 0.45)
lag3	0.05 (-0.18, 0.28)	0.14 (-0.15, 0.43)
lag01	0.35 (0.09, 0.62)*	0.42 (0.08, 0.76)*
lag02	0.42 (0.12, 0.71)*	0.44 (0.06, 0.81)*
lag03	0.39 (0.07, 0.70)*	0.442 (0.04, 0.85)*

Table 3. Association between 10 μ g/m³ increase in PM_{2.5} and increase in deaths by lags.

*P<0.05

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accidental and circulatory diseases. There appears to be a greater impact of $PM_{2.5}$ on mortality from non-accidental and circulatory diseases on women, poeple with low education and died



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Fig 2. The excess mortality risk of Circulatory diseases death per 10 μ g/m³ increase in air pollutants.

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outside hospital. NO_2 and O_3 were also associated with an increase in mortality from non-accidental and circulatory diseases. The effect of O_3 is higher than other pollutants.

The estimated effects in our study of $PM_{2.5}$ on non-accidental mortality risk were lower than effects observed in a worldwide meta-analysis of a 1.04% (0.52%-1.56%) per 10 µg/m³ increase in $PM_{2.5}$ [19]. This discrepancy could be due to differences in population composition, geographical location and $PM_{2.5}$ sources. However, compared with studies of Chinese populations, the estimated effects in our study are higher. For example, a recent Chinese multicity study found that the risk of non-accidental death increased by 0.22% for every 10 µg/m³ increase in $PM_{2.5}$ (lag01)[20]. In another study, mortality risks for non-accidental deaths increased by 0.25% at lag days 0–1 for every 10 µg/m³ increase in $PM_{2.5}$ [21]. The larger effect estimates observed in our study may be due to the age of the subject. We studied the elderly and the elderly make up a high-risk group[22,23]. The short-term association of $PM_{2.5}$ with mortality from circulatory diseases was consistent with previous epidemiological studies[17]. $PM_{2.5}$ may reduce cardiac parasympathetic input leading to decreased heart rate variability

Pollutant model	ER of daily non-accidental death count (%)	ER of daily circulatory diseases death count (%)		
Single pollutant model				
PM _{2.5}	0.36 (0.07, 0.70)*	0.44 (0.04, 0.85)*		
PM ₁₀	0.21 (-0.03, 0.46)	0.25 (-0.06, 0.57)		
SO ₂	0.65 (-0.96, 2.02)	0.85 (-0.84, 2.57)		
NO ₂	1.08 (-0.03, 2.20)	1.48 (0.05, 2.92)*		
O ₃	1.13 (0.50, 1.77)*	1.34 (0.54, 2.15)*		
Co-pollutant model				
PM _{2.5} +PM ₁₀	0.63 (-0.03, 1.30)	0.68 (-0.18, 1.54)		
PM _{2.5} +SO ₂	0.39 (0.04, 0.73)*	0.43 (-0.01, 0.86)		
PM _{2.5} +NO ₂	0.33 (-0.08, 0.75)	0.30 (-0.23, 0.83)		
PM _{2.5} +O ₃	0.24 (-0.09, 0.57)	0.28 (-0.14, 0.70)		
PM _{2.5} +PM ₁₀ +SO ₂	0.64 (-0.06, 1.34)	0.66 (-0.24, 1.56)		
PM _{2.5} +PM ₁₀ +NO ₂	0.58 (-0.16, 1.33)	0.50 (-0.46, 1.47)		
PM _{2.5} +PM ₁₀ +O ₃	0.62 (-0.05, 1.28)	0.65 (-0.20, 1.51)		
PM _{2.5} +SO ₂ +NO ₂	0.33 (-0.08, 0.75)	0.30 (-0.23, 0.83)		
PM _{2.5} +SO ₂ +O ₃	0.22 (-0.14, 0.57)	0.23 (-0.23, 0.68)		
PM _{2.5} +NO ₂ +O ₃	0.18 (-0.24, 0.60)	0.11 (-0.43, 0.66)		

Table 4. Association between a 10 $\mu g/m^3$ increase in $PM_{2.5}$ (lag 03 day) and an increase in deaths using the co-pollutant model.

*P<0.05

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(HRV)[24,25]. Additionally, the direct translocation of $PM_{2.5}$ into the circulatory system can lead to an acute cardiovascular response[26–28].

For the metric of mortality from non-accidental and circulatory diseases, women, people with low education and died outside hospital were found to have increased susceptibility to $PM_{2.5}$. Previous studies on the gender-specific health effects of air pollution are lacking, and the patterns are not conclusive. For example, Franklin et al. studied over 1.3 million deaths in 27 US communities and found that women were more susceptible than men to the mortality effects of $PM_{2.5}[29]$. Hong et al. also found that elderly woman were more susceptible than elderly men to the mortality effects of $PM_{10}[30]$. Similarly, a statement from the American

Table 5. Association between a 10 μ g/m³ increase in PM_{2.5} (lag 03 day) and an increase in deaths using the single pollutant model, according to sex, education and death location.

Index	ER of daily non-accidental death count (%)	ER of daily circulatory diseases death count (%)
Sex		
Women	0.52 (0.10, 0.94)*	0.65 (0.11, 1.19)*
Men	0.38 (-0.04, 0.80)	0.40 (-0.16, 0.96)
Education		
Junior high school and below	0.45 (0.09, 0.82)*	0.54 (0.08, 0.99)*
High school degree or above	0.24 (-0.36, 0.84)	0.21 (-0.61, 1.04)
Death location		
In the hospital	0.24 (-0.36, 0.84)	0.12 (-0.56, 0.79)
Outside the hospital	0.52 (0.10, 0.95)*	0.65 (0.15,1.15)*

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Heart Association (AHA) concluded that particulate matter exposure may contribute to higher cardiovascular mortality in women[31]. There are some reasons that may explain the increased vulnerability of women. Inhaled particles could deposit regionally in women.[32]; women have fewer red blood cells than men, so women are more vulnerable to the toxic effects of air pollution[33]; in addition, the high reactivity of the airway to oxidants, hormonal status, smoking rates, and even a relatively low socioeconomic status are also possible causes[34]. However, the exact reasons for the gender-specific effects of air pollution on health are unclear and deserve further investigation.

Our study found that the impact on non-accidental and circulatory disease mortality from PM_{2.5} is higher for those at a lower education level than for those with a higher education level, which is consistent with previous observations on individual education level[35]. In epidemio-logical studies, education has been used as a surrogate indicator of socioeconomic status (SES) [36]. It is well known that SES can affect health indicators such as mortality[37]. People with a lower SES are more likely to be exposed to air pollutants and are more likely to suffer from diseases linked to air pollution that confer a greater risk of dying[38–40]. People of a lower SES may also receive inferior medical treatment and less health care, making them more susceptible to the effects of air pollution[18]. In addition, people with a lower SES may have more limited access to fish, fresh fruits and vegetables, resulting in a reduced intake of protective fatty acids and vitamins[41].

Our results showed that the impact of $PM_{2.5}$ on mortality from non-accidental and circulatory diseases appears to be greater among people that die outside of a hospital. People outside hospital are less likely to acquire knowledge about $PM_{2.5}$ prevention and have more exposure risks. In addition, it is more difficult for people outside hospital to receive timely treatment to alleviate a condition in the event of an outbreak.

Changchun is located in northeast China and has significant seasonal differences. Although the annual average concentration of gaseous pollutants such as SO_2 , NO_2 and O_3 is not high, both SO_2 and NO_2 maintain relatively high levels during heating periods in the winter, while O_3 is relatively high in the summer, which exposes residents to persistent hazards from different air pollutants in different seasons. Our results showed that NO_2 and O_3 can increase the risk of non-accidental death in the elderly, and there was also a lag effect. Previous studies have also reached the same conclusion[42]. With co-pollutant adjustment in multi-pollutant models, the effect of $PM_{2.5}$ on mortality changed slightly. This result suggests that our model is relatively stable.

The findings support public policy-related activities focused on the reduction of $PM_{2.5}$ levels and the improvement of target daily $PM_{2.5}$ standards. The estimation of the short-term mortality risk due to short-term exposure to $PM_{2.5}$ can also help in planning appropriate medical interventions. Some limitations exist in our study: (1) Our study was based in a single city, Changchun, and generalizations need to be made in conjunction with other evidence. (2) Although it is considered reasonable to use the ambient pollutant concentration of $PM_{2.5}$ to represent individual exposure[43], there may be errors in the $PM_{2.5}$ exposure of different subgroups[44]. Further studies of the relationship between $PM_{2.5}$ and mortality are needed.

5. Conclusions

We found that short-term exposure to $PM_{2.5}$ increased the mortality risk of non-accidental and circulatory diseases among the elderly in Changchun. Women, people with low education and died outside hospital are more susceptible to $PM_{2.5}$. NO₂ and O₃ were also associated with an increase in mortality from non-accidental and circulatory diseases and the O₃ is a high effect.

Supporting information

S1 Table. Site coordinates. (XLSX)

Author Contributions

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References

- Ren M, Fang X (2017) Concentration-Response Relationship between PM2.5 and Daily Respiratory Deaths in China: A Systematic Review and Metaregression Analysis of Time-Series Studies. 2017: 5806185. https://doi.org/10.1155/2017/5806185 PMID: 29124065
- Li P, Xin J, Wang Y, Li G, Pan X, Wang S, et al. (2015) Association between particulate matter and its chemical constituents of urban air pollution and daily mortality or morbidity in Beijing City. Environ Sci Pollut Res Int 22: 358–368. https://doi.org/10.1007/s11356-014-3301-1 PMID: 25074829
- **3.** (1973) Electric heating versus oil heating in the service territory of Long Island Lighting Company. II. An analysis of air pollution effects associated with electric heating and oil-fired on site heating.
- Kim KH, Kabir E, Kabir S (2015) A review on the human health impact of airborne particulate matter. Environment International 74: 136–143. https://doi.org/10.1016/j.envint.2014.10.005 PMID: 25454230
- Evangelia S, Massimo S, Sophia R, Bart O, Christophe D, Ester A, et al. (2013) Associations between Fine and Coarse Particles and Mortality in Mediterranean Cities: Results from the MED-PARTICLES Project. Environmental Health Perspectives 121: 932–938. https://doi.org/10.1289/ehp.1206124 PMID: 23687008
- Lepeule J, Laden F, Dockery D, Schwartz J (2012) Chronic exposure to fine particles and mortality: an extended follow-up of the Harvard Six Cities study from 1974 to 2009. Environ Health Perspect 120: 965–970. https://doi.org/10.1289/ehp.1104660 PMID: 22456598
- Krewski D, Jerrett M, Burnett RT, Ma R, Hughes E, Shi Y, et al. (2009) Extended follow-up and spatial analysis of the American Cancer Society study linking particulate air pollution and mortality. Res Rep Health Eff Inst: 5–114; discussion 115–136.
- Kloog I, Nordio F, Zanobetti A, Coull BA, Koutrakis P, Schwartz JD. (2014) Short term effects of particle exposure on hospital admissions in the Mid-Atlantic states: a population estimate. PLoS One 9: e88578. https://doi.org/10.1371/journal.pone.0088578 PMID: 24516670
- Kloog I, Ridgway B, Koutrakis P, Coull BA, Schwartz JD (2013) Long- and short-term exposure to PM2.5 and mortality: using novel exposure models. Epidemiology 24: 555–561. <u>https://doi.org/10.1097/EDE.0b013e318294beaa</u> PMID: 23676266
- Janssen NA, Fischer P, Marra M, Ameling C, Cassee FR (2013) Short-term effects of PM2.5, PM10 and PM2.5–10 on daily mortality in The Netherlands. Sci Total Environ 463–464: 20–26. https://doi.org/ 10.1016/j.scitotenv.2013.05.062 PMID: 23787105
- Apte JS, Marshall JD, Cohen AJ, Brauer M (2015) Addressing Global Mortality from Ambient PM2.5. Environ Sci Technol 49: 8057–8066. https://doi.org/10.1021/acs.est.5b01236 PMID: 26077815
- Baxter LK, Duvall RM, Sacks J (2013) Examining the effects of air pollution composition on within region differences in PM2.5 mortality risk estimates. J Expo Sci Environ Epidemiol 23: 457–465. <u>https://doi.org/10.1038/jes.2012.114</u> PMID: 23250195
- Petronella SA, Conboy-Ellis K (2003) Asthma epidemiology: risk factors, case finding, and the role of asthma coalitions. Nurs Clin North Am 38: 725–735. PMID: 14763373
- Organization WH (2007) Air quality guidelines: Global update 2005. Particulate matter, ozone, nitrogen dioxide and sulfur dioxide. Indian Journal of Medical Research 4: 492–493.

- Brauer M, Freedman G, Frostad J, van Donkelaar A, Martin RV, Dentener F, et al. (2016) Ambient Air Pollution Exposure Estimation for the Global Burden of Disease 2013. Environ Sci Technol 50: 79–88. https://doi.org/10.1021/acs.est.5b03709 PMID: 26595236
- Song Y, Wang X, Maher BA, Li F, Xu C, Liu X, et al. (2016) The spatial-temporal characteristics and health impacts of ambient fine particulate matter in China. Journal of Cleaner Production 112: 1312– 1318.
- Liang H, Qiu H, Tian L (2018) Short-term effects of fine particulate matter on acute myocardial infraction mortality and years of life lost: A time series study in Hong Kong. Sci Total Environ 615: 558–563. https://doi.org/10.1016/j.scitotenv.2017.09.266 PMID: 28988091
- Yang C, Peng X, Huang W, Chen R, Xu Z, Chen B, et al. (2012) A time-stratified case-crossover study of fine particulate matter air pollution and mortality in Guangzhou, China. Int Arch Occup Environ Health 85: 579–585. https://doi.org/10.1007/s00420-011-0707-7 PMID: 21960028
- Atkinson RW, Kang S, Anderson HR, Mills IC, Walton HA (2015) Epidemiological time series studies of PM2.5 and daily mortality and hospital admissions: a systematic review and meta-analysis. Journal of Exposure Science & Environmental Epidemiology 25: 208–214.
- Chen R, Yin P, Meng X, Liu C, Wang L, Xu X, et al. (2017) Fine Particulate Air Pollution and Daily Mortality. A Nationwide Analysis in 272 Chinese Cities. Am J Respir Crit Care Med 196: 73–81. https://doi. org/10.1164/rccm.201609-1862OC PMID: 28248546
- Li T, Yan M, Sun Q, Anderson GB (2018) Mortality risks from a spectrum of causes associated with wide-ranging exposure to fine particulate matter: A case-crossover study in Beijing, China. Environ Int 111: 52–59. https://doi.org/10.1016/j.envint.2017.10.023 PMID: 29174689
- Cox LA Jr., Popken DA, Ricci PF (2013) Warmer is healthier: effects on mortality rates of changes in average fine particulate matter (PM2.5) concentrations and temperatures in 100 U.S. cities. Regul Toxicol Pharmacol 66: 336–346. https://doi.org/10.1016/j.yrtph.2013.05.006 PMID: 23707535
- Wang Y, Shi L, Lee M, Liu P, Di Q, Zanobetti A, et al. (2017) Long-term Exposure to PM2.5 and Mortality Among Older Adults in the Southeastern US. Epidemiology 28: 207–214. <u>https://doi.org/10.1097/EDE.</u> 00000000000614 PMID: 28005571
- Devlin RB, Ghio AJ, Kehrl H, Sanders G, Cascio W (2003) Elderly humans exposed to concentrated air pollution particles have decreased heart rate variability. Eur Respir J Suppl 40: 76s–80s. PMID: 12762579
- 25. Gong H Jr., Linn WS, Terrell SL, Clark KW, Geller MD, Anderson KR, et al. (2004) Altered heart-rate variability in asthmatic and healthy volunteers exposed to concentrated ambient coarse particles. Inhal Toxicol 16: 335–343. https://doi.org/10.1080/08958370490439470 PMID: 15204749
- Fiordelisi A, Piscitelli P, Trimarco B, Coscioni E, Iaccarino G, Sorriento D. (2017) The mechanisms of air pollution and particulate matter in cardiovascular diseases. 22: 337–347. https://doi.org/10.1007/ s10741-017-9606-7 PMID: 28303426
- Niu J, Liberda EN, Qu S, Guo X, Li X, Zhang J, et al. (2013) The role of metal components in the cardiovascular effects of PM2.5. PLoS One 8: e83782. <u>https://doi.org/10.1371/journal.pone.0083782</u> PMID: 24386277
- Zuo L, Youtz DJ, Wold LE (2011) Particulate matter exposure exacerbates high glucose-induced cardionyocyte dysfunction through ROS generation. PLoS One 6: e23116. https://doi.org/10.1371/journal.pone.0023116 PMID: 21850256
- Franklin M, Zeka A, Schwartz J (2007) Association between PM2.5 and all-cause and specific-cause mortality in 27 US communities. Journal of Exposure Science & Environmental Epidemiology 17: 279.
- Hong YC, Lee JT, Kim H, Ha EH, Schwartz J, Christiani DC. (2002) Effects of air pollutants on acute stroke mortality. Environ Health Perspect 110: 187–191. https://doi.org/10.1289/ehp.02110187 PMID: 11836148
- Brook RD, Rajagopalan S, Pope CA 3rd, Brook JR, Bhatnagar A, Diez-Roux AV, et al. (2010) Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. Circulation 121: 2331–2378. <u>https://doi.org/10.1161/CIR.0b013e3181dbece1 PMID: 20458016</u>
- Kim CS, Hu SC (1998) Regional deposition of inhaled particles in human lungs: comparison between men and women. J Appl Physiol (1985) 84: 1834–1844. https://doi.org/10.1152/jappl.1998.84.6.1834 PMID: 9609774
- Sorensen M, Daneshvar B, Hansen M, Dragsted LO, Hertel O, Knudsen L, et al. (2003) Personal PM2.5 exposure and markers of oxidative stress in blood. Environ Health Perspect 111: 161–166. https://doi.org/10.1289/ehp.111-1241344 PMID: 12573899
- Clougherty JE (2010) A growing role for gender analysis in air pollution epidemiology. Environ Health Perspect 118: 167–176. https://doi.org/10.1289/ehp.0900994 PMID: 20123621

- 35. Kan H, London SJ, Chen G, Zhang Y, Song G, et al. (2008) 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 116: 1183–1188. <u>https://doi.org/10.1289/ehp.10851</u> PMID: 18795161
- Zeka A, Zanobetti A, Schwartz J (2006) Individual-level modifiers of the effects of particulate matter on daily mortality. Am J Epidemiol 163: 849–859. https://doi.org/10.1093/aje/kwj116 PMID: 16554348
- Wilkinson RG (1997) Socioeconomic inequalities in morbidity and mortality in western Europe. Lancet 350: 516–517; author reply 517–518.
- **38.** Sexton K, Gong H Jr., Bailar JC 3rd, Ford JG, Gold DR, Lambert WE, et al. (1993) Air pollution health risks: do class and race matter? Toxicol Ind Health 9: 843–878. PMID: 8184446
- Rotko T, Kousa A, Alm S, Jantunen M (2001) Exposures to nitrogen dioxide in EXPOLIS-Helsinki: microenvironment, behavioral and sociodemographic factors. J Expo Anal Environ Epidemiol 11: 216– 223. https://doi.org/10.1038/sj.jea.7500162 PMID: 11477519
- 40. Pellizzari ED, Perritt RL, Clayton CA (1999) National human exposure assessment survey (NHEXAS): exploratory survey of exposure among population subgroups in EPA Region V. J Expo Anal Environ Epidemiol 9: 49–55. PMID: 10189626
- Romieu I, Téllez-Rojo MM, Lazo M, Manzano-Patiño A, Cortez-Lugo M, Julien P, et al. (2005) Omega-3 fatty acid prevents heart rate variability reductions associated with particulate matter. American Journal of Respiratory & Critical Care Medicine 172: 1534.
- 42. Chen R, Pan G, Zhang Y, Xu Q, Zeng G, Xu X, et al. (2011) Ambient carbon monoxide and daily mortality in three Chinese cities: the China Air Pollution and Health Effects Study (CAPES). Sci Total Environ 409: 4923–4928. https://doi.org/10.1016/j.scitotenv.2011.08.029 PMID: 21908017
- 43. Schwartz J, Sarnat JA, Coull BA, Wilson WE (2007) Effects of exposure measurement error on particle matter epidemiology: a simulation using data from a panel study in Baltimore, MD. J Expo Sci Environ Epidemiol 17 Suppl 2: S2–10.
- Zeger SL, Thomas D, Dominici F, Samet JM, Schwartz J, Dockery D, et al. (2000) Exposure measurement error in time-series studies of air pollution: concepts and consequences. Environ Health Perspect 108: 419–426. https://doi.org/10.1289/ehp.00108419 PMID: 10811568