Am J Transl Res 2023;15(8):5495-5507
www.ajtr.org /ISSN:1943-8141/AJTR0151053

Original Article

The mortality trends analysis of ischemic heart disease attributed to (PM) 2.5 exposure in China from 1990 to 2019 in APC model

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Received May 4, 2023; Accepted July 12, 2023; Epub August 15, 2023; Published August 30, 2023

Abstract: Objective: To analyze the mortality trend of ischemic heart disease (IHD) attributed to particulate matter (PM) 2.5 exposure among Chinese populations from 1990 to 2019. To evaluate the influences of cohort, period, and age on long-term of IHD mortality trends. Methods: Global burden of disease (GBD) data in 2019 regarding IHD death rate attributed to exposure to (PM) 2.5 in China from 1990 to 2019 were adopted. The age-period-cohort (APC) model based on the R language produced by the National Cancer Institute of the United States was used for statistical analysis to investigate the influences of different ages, periods, and cohorts on IHD death rate attributed to exposure to (PM) 2.5. Results: The age-standardized death rate of IHD attributed to exposure to ambient (PM) 2.5 in China revealed an uptrend from 1990 to 2019. This increased from 8.63/100,000 in 1990 to 21.31/100,000 in 2019. This was an increase of 1.47%. The age-standardized IHD death rate attributed to exposure to household (PM) 2.5 showed a decreasing trend. This decreased from 19.61/100,000 in 1990 to 8.72/100,000 in 2019. This was a decrease of 0.74%. The results of the APC model indicated that the annual net drift of IHD mortality attributed to exposure to (PM) 2.5 was -0.10%. The annual net drifts of exposure to household and ambient (PM) 2.5 were -4.54% and 3.44%, respectively. The IHD death rate attributed to ambient and household (PM) 2.5 exposure in the same birth cohort enhanced with age. With time, the rate ration (RR) of period effects of IHD mortality attributed to ambient (PM) 2.5 exposure for both male and female showed an upward trend. The RR of period effects of IHD death rate attributed to household (PM) 2.5 exposure suggested a downtrend. In the consecutive birth cohorts, the population in China with a later birth cohort presented a higher risk of IHD death attributed to exposure to ambient (PM) 2.5 and a lower risk of IHD death attributed to household (PM) 2.5 exposure. Conclusions: In China for the burden of IHD attributed to exposure to (PM) 2.5, the primary environmental risk was ambient (PM) 2.5 exposure compared to exposure to household PM2.5. IHD exposure to environmental air pollution posed a greater risk to young people.

Keywords: Age-period-cohort model, ambient exposure, household exposure, (PM) 2.5, ischemic heart disease

Introduction

Cardiovascular disease is the largest factor contributing to the global burden of diseases and has been considered as the world's largest death cause. Statistics in 2019, showed that there were approximately 56.5 million deaths worldwide. A total of 16.8 million deaths were caused by cardiovascular disease [1]. Among all cardiovascular diseases, ischemic heart disease (IHD) is recognized as one of the primary causes of premature mortality [2]. IHD is considered a chronic disease featured by coronary ischemia and secondary myocardial injuries [3]. The ranking of death causes has increased from fourth in 1990 to second in 2017. IHD has become a global public health issue with a significant burden of diseases [4, 5]. It was reported that deaths caused by IHD were gradually shifting from developed countries to developing countries, posing a huge challenge to the prevention of IHD in developing countries [6]. As the most populous developing country, China accounts for 36% of the global population. The death rate caused by IHD in China rose from 1,100,000 in 1990 to 1,377,000 in 2016 [7].

There are numerous risk factors for IHD, most are attributed to variable risk factors, with particulate matter (PM) 2.5 exposure being a significant risk factor for IHD [8, 9].

In the past two decades, with the expansion of China's economic system, industrialization process, and urbanization scale, the problem of air pollution is increasingly serious. Its severity has attracted worldwide attention. It is facing the dual challenges of environmental and indoor air pollution exposure [10, 11]. Epidemiological investigation results indicated that the long-term solid fuels exposure in environmental and household air pollution was positively correlated with various chronic diseases, including IHD [12]. In China, the death numbers of ischemic heart disease related with (PM) 2.5 has risen from 800,000 in 2004 to over 1,200,000 in 2012 [13].

This study utilized the latest data from the global burden of disease (GBD) in 2019, adopting the Age-Period-Queue (APC) model to divide age, period, and cohort by gender. This helped us to explore the potential trends of IHD death rates attributed to exposure to (PM) 2.5 from 1990 to 2019 in China. The results of this study will lay the foundation for promoting the IHD control strategies development and environmental improvement.

Materials and methods

Sources of data

The GBD 2019 database published on the official website of the Institute for Health Metrics and Evaluation (IHME) were adopted. GDB 2019 evaluated the burden of diseases attributable to 87 risk factors and 369 diseases in 204 countries (regions) worldwide [14, 15]. GBD 2019 estimates the burden of disease in China using data from multiple sources. Death data were from the Chinese Center for Disease Control and Prevention Death Cause Network Reporting System, the China Maternal and Child Health Monitoring System, the National Disease Monitoring System, China Cancer Registration Data, and Hong Kong and Macao death cause data [16]. The age-standardized death rate was obtained based on the average age structure of the world population from 2010 to 2035. GBD 2019 used the data integration model for air quality 2 (DIMAQ2) and the weighted sampling method to extract the annual average mass concentration data of (PM) 2.5 with less than 2.5 μm aerodynamic diameter. It estimated the population weighted annual average concentration of (PM) 2.5 (μg/m^3), with the minimum risk exposure level between 2.4 μg/m^3-5.9 μg/m^3. According to the disease classification rules "International Statistical Classification of Diseases and Related Health Issues (10th Revision)" (ICD-10), the classification codes of IHD were I20-I25 [17].

There are two primary forms of (PM) 2.5 exposure in the GBD trials, including ambient and household (PM) 2.5 exposure. The former referred to the population-weighted annual average mass concentration of (PM) 2.5 in a cubic meter of air. Ambient (PM) 2.5 exposure was examined through annual average. It referred to the integration of satellite observations of aerosols in the atmosphere plus with surface measurements, chemical transport model simulations and geographical data at a 0.1 × 0.1 resolution. It aggregated to population-weighted means to generate an exposure estimate. Solid fuels were composed of coal, agricultural residues, charcoal, wood, and dung. The concentrations of atmospheric particulate matter (APM) estimated the standard multi-country survey series including living standards measurement surveys (LSMS), demographic and health surveys (DHS), world health surveys (WHS), multiple indicator cluster surveys (MICS), and censuses and country-specific survey series. Age-standardized IHD death rate due to exposure to (PM) 2.5 was calculated according to the world standard population [18].

Statistical methods

APC model is currently a commonly used statistical method for independently assessing the impact of cohort, period, and age on disease death and incidence rate in the fields of demography, sociology, and epidemiology [19]. This study used an R-based web tool produced by the National Cancer Institute of the United States (https://Analysis sis tools.nci.nih.gov/apc/) for APC model analysis. In this research, the intrinsic estimator (IE) method was used for calculation and analysis, to overcome the high collinearity of cohort, period, and age [20].

In the analysis of APC model, the attributable death rate and population data from this study were converted to consecutive 5-year periods. The periods were divided into the following two consecutive 5-year periods: 1990-1994 period and 2015-2019 period. Populations with younger than 25 years were excluded from this study because of the rare mortality for this age of individuals. The collected data were arranged into the following 15 age groups: 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90-94, and more than 95. The central age group, period, and birth cohort within each interval were defined as the control group in all APC model analysis. In the case of an even number of categories, the two lower central values were set as the control group. The main estimating functions used in the analysis process were as follows: Net drift was defined as the trend of overall annual percentage changes in the observation period of the entire study. Local drift was defined as the annual percentage change in death rate over time within every age group. The curve of longitudinal age was defined as the longitudinal age specific ratio regulated by periodic bias in the reference queue, representing the trend of disease changes related to age (i.e., age effect). The rate ratio (RR) for each period (or queue) referred to the ratio of mortality in a specific age group to the reference period (or queue) within each period (or queue) [18]. Using a general linear model to test the difference in RR slopes between periods and queues, the estimable function was conducted by Wald χ^2 tests (Bilateral), with a test level of $\alpha=0.05$. All analyses were performed in R-based web tool (version 4.2.0).

Results

Trends in IHD death rate due to (PM) 2.5 exposure

As seen in **Figure 1**, the trend of age-standardized death rate of IHD due to exposure to ambient (PM) 2.5 from 1990 to 2019 in China was increased. The number of IHD deaths due to exposure to ambient (PM) 2.5 from 1990 to 2019 rose by 1.47%, from 8.63/100 thousand to 21.31/100 thousand. The change rate of age-standardized mortality ranked among the top five in the world. The trend of age-standardized death rate of IHD due to exposure to household (PM) 2.5 in China was reduced. The number of IHD mortality attributable to exposure to household (PM) 2.5 from 1990 to 2019 decreased by 0.74%, from 19.61/100 thousand to 8.72/100 thousand.

Local drift and net drift

As described in **Figure 2**, in all age groups, the values for local drift of IHD death rate due to (PM) 2.5 exposure was above 0 between the age group of 65-69 to more than 90. The values for local drift of IHD death rate due to exposure to household (PM) 2.5 were below 0 for both sexes in all age groups, suggesting a significant downtrend in IHD death rate. The most significant decline was observed in males aged 65-69 and females aged 25-29. The values for local drift of IHD death rate due to exposure to ambient (PM) 2.5 were above 0 for both sexes, being initially decreased, and then increased in males with all ages, and slowly increased in females. From 1990 to 2019, the annual net drift of IHD attributable to (PM) 2.5 exposure, ambient (PM) 2.5 exposure and household (PM) 2.5 exposure for male and female are listed in **Table 1**. It indicates that the annual net drift of IHD attributable to (PM) 2.5 exposure was more pronounced in male than female.

Age impacts on IHD death rate due to (PM) 2.5 exposure

As shown in **Figure 3**, age impacts on IHD death rate due to exposure to (PM) 2.5 revealed an exponential distribution with a rapidly rising rate in the elderly. It was like that due to ambient PM2.5 exposure. The death rate of IHD due to exposure to household (PM) 2.5 in males and females from all age groups was kept at a low level, showing a slight increased trend. The significant upward trend was shown in the groups aged 65-69 and 90-94, with increasing from 85.64/100 thousand and 49.68/100 thousand in group aged 65-69 to 1298.66/100 thousand and 2083.83/100 thousand in group aged more than 95, respectively. For the causes of the ambient and household (PM) 2.5 exposure, among them IHD mortality rate of males increased from 10.399/100 thousand and 63.95/100 thousand to 1457.70/100 thousand and 2341.2/100 thousand, respec-

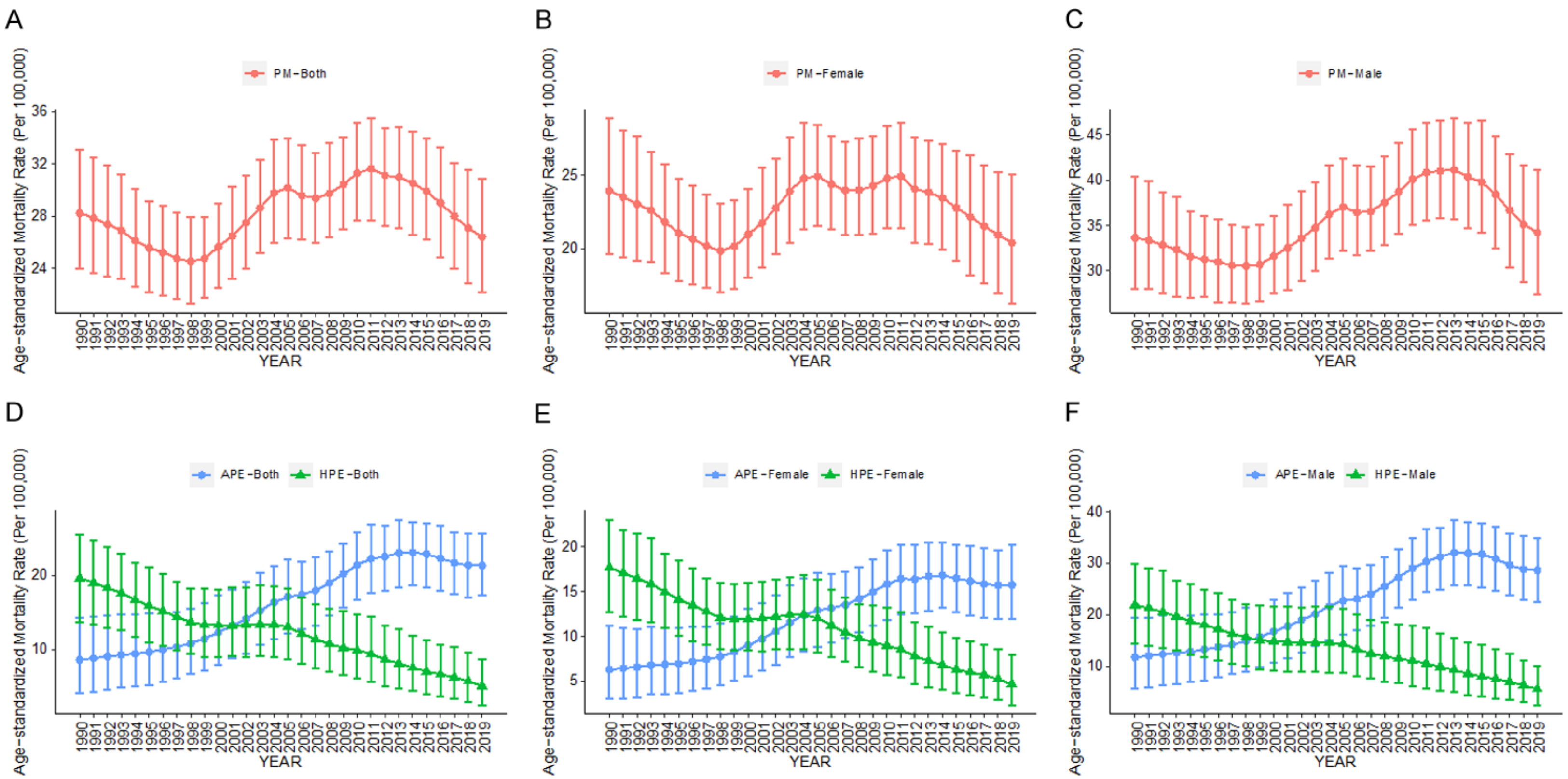

Figure 1. The change trend of age-standardized mortality rate of ischemic heart disease (IHD) attributed to particulate matter (PM) 2.5 exposure in China from 1990 to 2019. A: Corresponding to both sexes for the mortality of IHD attributed to (PM) 2.5. B: Corresponding to female for the mortality of IHD attributed to (PM) 2.5. C: Corresponding to male for the mortality of IHD attributed to (PM) 2.5. D: Corresponding to both sexes for the mortality of IHD attributed to ambient and household (PM) 2.5, respectively. E: Corresponding to female for the mortality of IHD attributed to ambient and household (PM) 2.5, respectively. F: Corresponding to male for the mortality of IHD attributed to ambient and household (PM) 2.5, respectively.

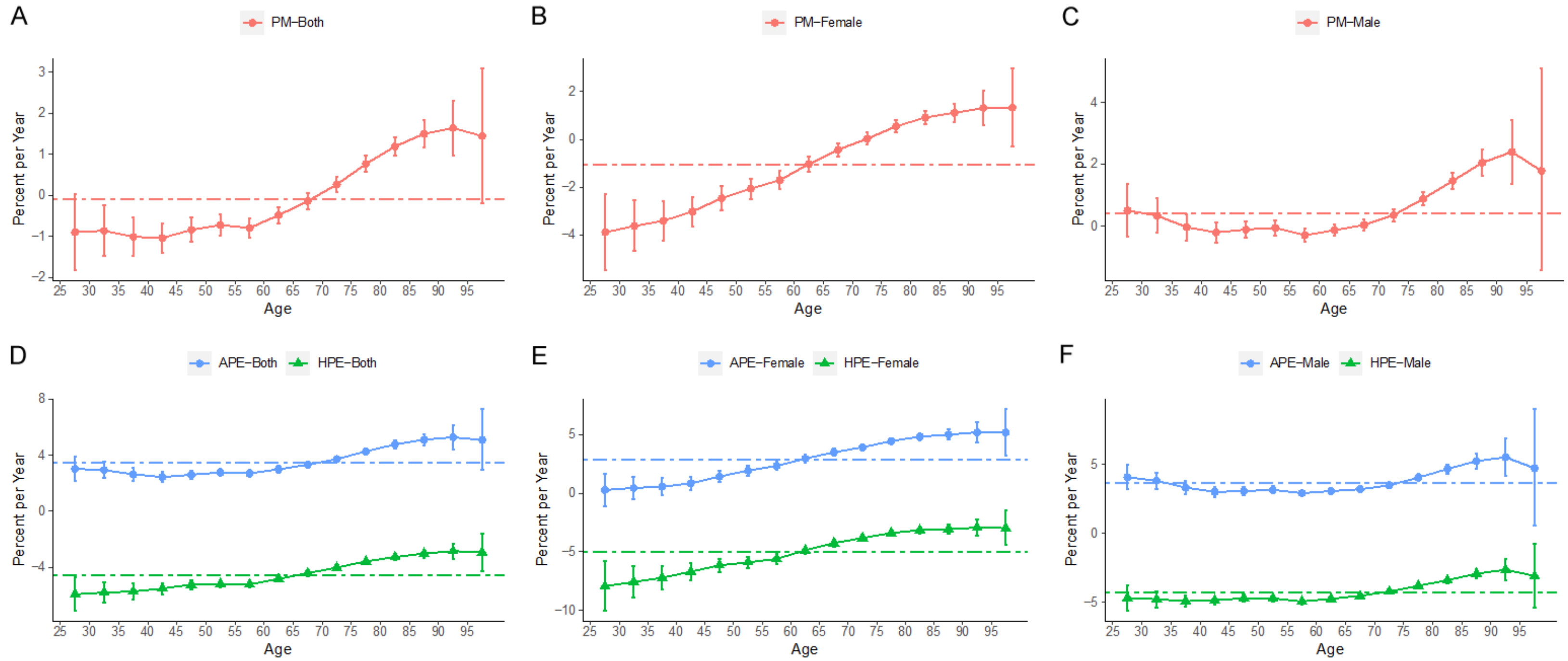

Figure 2. Local drifts with net drift values of the ischemic heart disease (IHD) mortality attributed to particulate matter (PM) 2.5 in China from 1990 to 2019. A: Corresponding to both sexes for the mortality of IHD attributed to (PM) 2.5. B: Corresponding to female for the mortality of IHD attributed to (PM) 2.5. C: Corresponding to male for the mortality of IHD attributed to (PM) 2.5. D: Corresponding to both sexes for the mortality of IHD attributed to ambient and household (PM) 2.5, respectively. E: Corresponding to female for the mortality of IHD attributed to ambient and household (PM) 2.5, respectively. F: Corresponding to male for the mortality of IHD attributed to ambient and household (PM) 2.5, respectively.

Table 1. The annual net drift of IHD attributed to (PM) 2.5 exposure for males and females from 1990 to 2019

Gender	(PM) 2.5 exposure		Ambient (PM) 2.5 exposure		Household (PM) 2.5 exposure	
	Values	95% CI	Values	95% CI	Values	95% CI
Both sexes	-0.10%	-0.24%~0.04%	3.44%	3.27%~3.6%	-4.54%	-4.68%~-4.40%
Male	0.42%	0.31%~0.50%	3.66%	3.41%~3.84%	-4.30%	-4.44%~-4.16%
Female	-1.07%	1.29%~-0.86%	2.87%	2.65%~3.10%	-4.98%	-5.22%~-4.74%

Note: IHD: Ischemic heart disease; CI: Confidence interval; PM: Particulate matter.

tively. Results showed that females increased from 66.68/100 thousand and 34.75/100 thousand to 1216.00/100 thousand and 2127.01/100 thousand.

Period impacts on IHD death rate due to (PM) 2.5 exposure

As shown in **Figure 4**, period impacts due to exposure to (PM) 2.5 revealed no great change in trend. The improvement was more significant in females than males between 2005 and 2019, with the corresponding RR of less than 1 in females. RR of period impacts attributed to ambient (PM) 2.5 exposure was gradually raised, with increasing from 0.7 (95% *CI*: 0.67~0.74) in 1990-1994 group to 1.47 (95% *CI*: 1.42~1.52) in 2015-2019 group. This indicated a progressive rise in risk of IHD death in the whole population. It showed that the negative effects of period on the whole population was gradually being regulated after 2012. Period effects due to household (PM) 2.5 exposure significantly reduced during the whole study period, with increasing from 1.53 (95% *CI*: 1.48~1.59) in 1990-1994 group to 0.45 (95% *CI*: 0.44~0.47) in 2015-2019 group. This suggested in the whole population a significant decrease in the risk of IHD death due to exposure to household (PM) 2.5.

Cohort impacts on IHD death due to (PM) 2.5 exposure

As described in **Figure 5**, after adjusting for age and period impacts, the RR of cohort impacts due to exposure to ambient and household (PM) 2.5 showed different trends. The RR of cohort impacts due to ambient (PM) 2.5 exposure was slowly increased, with enhancing from 0.17 (95% *CI*: 0.04~0.67) in 1900-1904 birth cohort to 5.73 (95% *CI*: 4.40~7.46) in 1995-1999 birth cohort for male, and from 0.13 (95% *CI*: 0.07~0.24) in 1900-1904 birth cohort to 1.77 (95% *CI*: 1.14~2.74) in 1995-1999 birth cohort for female, suggesting the risk of male for the mortality of IHD was more than that of female. The rate ratio (RR) of cohort effects due to household (PM) 2.5 exposure was gradually decreased for male and female.

Discussion

Previous studies revealed that from 2018 to 2050, China was expected to increase an additional 25,000,000 urban residents, and by 2050, more than 80% of these individuals would reside in urban areas [21]. The attributed diseases caused by the rapid development of China's economy and rapid urbanization were a heavy burden. Studies reported that long-term environmental air pollution exposure may lead to the oxidative damage and increase the formation of vascular plaques through inflammatory responses, developing the incidence of IHD [22, 23]. The results of this study found that from 1990 to 2019, the standardized death rate attributed to APE in China showed an upward trend. The age-standardized mortality rate attributed to HPE presented a downtrend. The trend of household air pollution exposure caused by solid fuels decreased, but 32% of Chinese people continued to cook or heat using solid fuels [24]. This suggested that in China the burden of IHD disease because of exposure to (PM) 2.5 was not optimistic. The disease continued to increase. This study focused on the impact of IHD due to exposure to (PM) 2.5 in the term of demography characteristics. This fit the age-period-cohort model to understand the driving factors behind it. This study provided scientific evidence for developing the effective measures of prevention and control for IHD.

In the age period-cohort model, the age impacts results reported that the mortality rate of IHD attributed to APE and HPE showed an upward

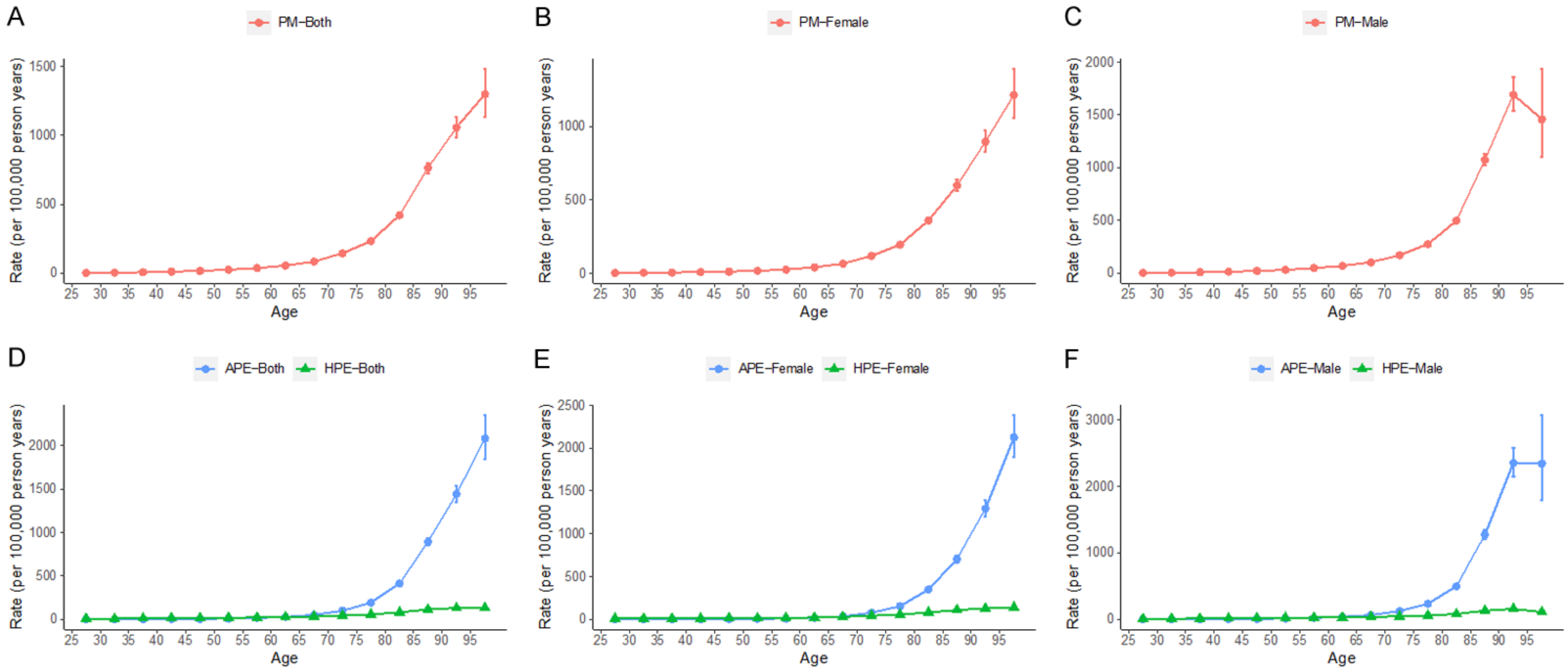

Figure 3. The fitted longitudinal age curves of the ischemic heart disease (IHD) mortality attributed to particulate matter (PM) 2.5 exposure. A: Corresponding to both sexes for the mortality of IHD attributed to (PM) 2.5. B: Corresponding to female for the mortality of IHD attributed to (PM) 2.5. C: Corresponding to male for the mortality of IHD attributed to (PM) 2.5. D: Corresponding to both sexes for the mortality of IHD attributed to ambient and household (PM) 2.5, respectively. E: Corresponding to female for the mortality of IHD attributed to ambient and household (PM) 2.5, respectively. F: Corresponding to male for the mortality of IHD attributed to ambient and household (PM) 2.5, respectively.

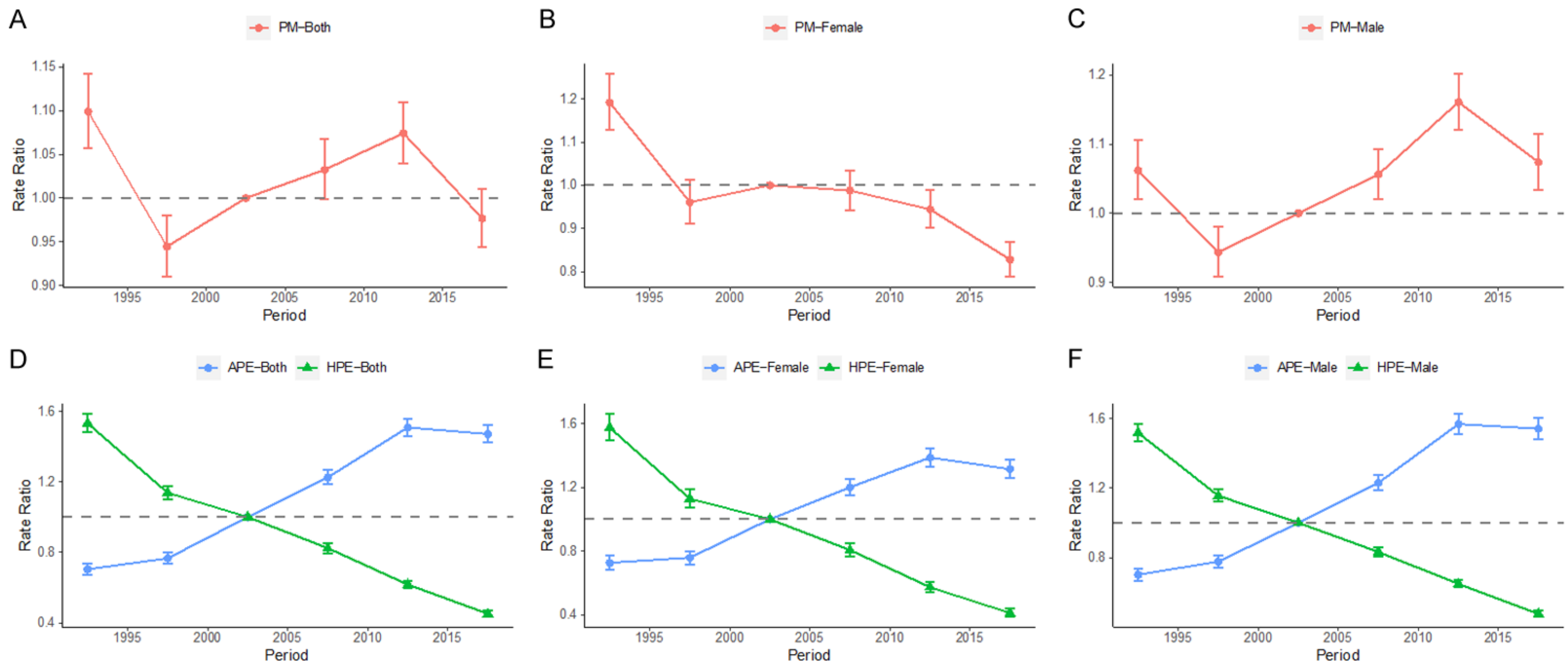

Figure 4. The rate ration (RR) of each period for the ischemic heart disease (IHD) mortality attributed to particulate matter (PM) 2.5 exposure. A: Corresponding to both sexes for the mortality of IHD attributed to(PM) 2.5. B: Corresponding to female for the mortality of IHD attributed to (PM) 2.5. C: Corresponding to male for the mortality of IHD attributed to (PM) 2.5. D: Corresponding to both sexes for the mortality of IHD attributed to ambient and household (PM) 2.5, respectively. E: Corresponding to female for the mortality of IHD attributed to ambient and household (PM) 2.5, respectively. F: Corresponding to male for the mortality of IHD attributed to ambient and household (PM) 2.5, respectively.

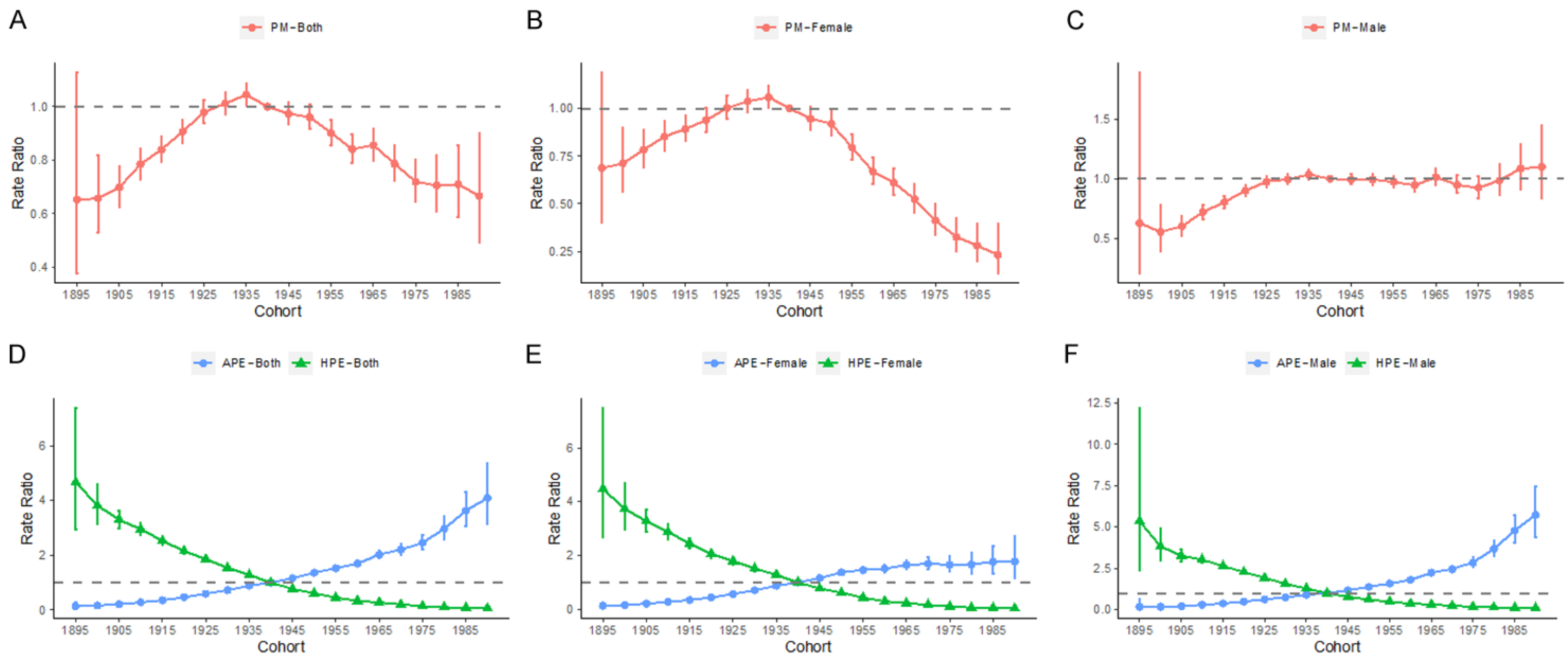

Figure 5. Rate ratio of each cohort for the ischemic heart disease (IHD) mortality attributed to particulate matter (PM) 2.5 exposure. A: Corresponding to both sexes for the mortality of IHD attributed to (PM) 2.5. B: Corresponding to female for the mortality of IHD attributed to (PM) 2.5. C: Corresponding to male for the mortality of IHD attributed to (PM) 2.5. D: Corresponding to both sexes for the mortality of IHD attributed to ambient and household (PM) 2.5, respectively. E: Corresponding to female for the mortality of IHD attributed to ambient and household (PM) 2.5, respectively. F: Corresponding to male for the mortality of IHD attributed to ambient and household (PM) 2.5, respectively.

trend with the increased age, especially significantly increasing after 65-69 years group. This may be due to the gradual decline of physical function, decreased metabolism, and reduced arterial compliance with increased age in the elderly population, leading to be more sensitive to (PM) 2.5 exposure and more susceptible to the impact of air pollution [25-27]. It was attributed to the high proportion of elderly people suffering from chronic diseases including cardiovascular diseases. The (PM) 2.5 exposure had a cumulative adverse impact on health outcomes in these people [28]. With the fast development of China's economy, the improvement of healthcare services has prolonged the health of the Chinese population, leading to population growth and aging. The elderly population is gradually increasing. It is expected that by 2050, the elderly population in China would reach 500 million [29]. Research revealed that aging may exacerbate air pollution by enhancing fossil fuel consumption and medical product consumption. For every 1% rising in the proportion of individuals aged 65 and above, the air quality index would increase by 0.121%. The air pollution degree would worsen with the increasing population of the aging [30, 31]. This suggested that with the accelerated aging of the population in China the future would have a significant effect on the burden of IHD diseases attributed to APE and HPE. Considering the acceleration of aging, it is recommended to conduct health education and promote the use of masks outdoors and the application of air purifiers at home to reduce the exposure to air pollution. Increasing energy-saving products related to elderly consumption would reduce the carbon emissions. This may be a necessary measure to alleviate the burden of IHD diseases attributed to APE and HPE caused by China's aging population.

In this study, the period effect results revealed that with the passage of time, the rate ratio of period effects attributed to APE for male and female showed an upward trend. The rate ratio of period effects attributed to HPE for male and female showed a downward trend. These differences may be attributed to the rapid development of economy in China and rapid urbanization progression. The fast development of economy in China and the recent acceleration of urbanization has led to a continuous increase in air pollution emissions. This phenomenon promoted the improvement of living conditions for Chinese residents, such as the popularization of electrical appliances and natural gas stoves. It reduced the solid fuels consumption including coal, carbon, and woods. This may be the main reason for the reduction of household (PM) 2.5 in China [32]. Research suggested that the proportion of solid fuels for cooking in Chinese households has decreased from 61% in 2005 to 32% in 2017. This greatly reduces the occurrence of household air pollution, alleviating the burden of IHD diseases attributed to HPE. According to statistics, most of the population (81.1%) lived in areas that exceed 35 UM/m^3. This was the temporary air quality target of World Health Organization [12]. This suggested that environmental air pollution remained an important challenge for China and should become a priority issue that the government urgently needs to address.

In this study, the cohort effects suggested that the RR of cohort effects in IHD attributed to APE showed an opposite pattern to that attributed to HPE. The younger population exposure to environmental (PM) 2.5 had the higher risk of IHD mortality. The risk of IHD mortality in the younger population with household (PM) 2.5 exposure was lower. The mortality risk of males was higher than that in females. This may be associated with the fact that younger people, especially males, spent more time exposed to environmental air pollution, increasing the negative impact of environmental air pollution. Proper physical activities were beneficial to health. The exposure level of air pollution may increase with the acceleration of respiratory rate during exercises [33]. These results suggested that we should pay attention to the susceptible populations and remind them to take personal protective measures.

This research had limitations. The data of this study was collected from the GBD in 2019. The data was limited in terms of elimination bias and the insufficient information on non-fatal consequences of IHD. This could influence the accuracy and reliability of the results. Using a model to estimate (PM) 2.5 concentration instead of the actual human exposure level may result in exposure concentration errors. This study assumed that (PM) 2.5 pollution had independent effects and did not consider possible interactions with other risk factors, such as the combined effect and antagonistic effect. The age-period-cohort model only explored the impacts of age, period, and cohort. More risks need to be investigated in the future.

The mortality of IHD due to exposure to ambient (PM) 2.5 is the heavy health burden in China, and the impact is significantly severe for the populations aged over 65 years. The health policies, strategies, and interventions in the future need to be performed to relieve the ambient air pollution, decreasing the ambient (PM) 2.5 exposure effects on the mortality of IHD.

Disclosure of conflict of interest

None.

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