Chemosphere 263 (2021) 128134

Contents lists available at ScienceDirect

Chemosphere

journal homepage: www.elsevier.com/locate/chemosphere

# Global burden of ischemic heart disease attributable to ambient $PM_{2.5}$ pollution from 1990 to 2017

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## HIGHLIGHTS

- We estimate the spatial and temporal variations in global $PM_{2.5}$ associated IHD burden between 1990 and 2017.
- We decomposed total attributable IHD deaths to population growth, aging, and mortality changes.
- $PM_{2.5}$ associated IHD burden decreased at a global scale but increased in low SDI regions.
- $PM_{2.5}$ still accounted for a large fraction of IHD burden in 2017 globally.

## ARTICLE INFO

*Article history:*
Received 2 July 2020
Received in revised form
20 August 2020
Accepted 24 August 2020
Available online 27 August 2020

Handling Editor: A. Gies

*Keywords:*
Ischemic heart disease
Air pollution
Mortality
Global disease burden

## ABSTRACT

*Objectives:* We aimed to estimate the spatial and temporal variation in the $PM_{2.5}$ associated ischemic heart disease (IHD) burden on a global scale between 1990 and 2017.
*Methods:* We obtained data on IHD attributable to $PM_{2.5}$ from the Global Burden of Disease Study (GBD) 2017. We used the numbers and age-standardized mortality rate (ASMR) and disability-adjusted life years (DALYs) rate (ASDR) of IHD attributable to $PM_{2.5}$ by sex, socio-demographic index (SDI), and countries. We calculated the estimated annual percentage changes (EAPCs) to assess the trends of ASMR and ASDR between 1990 and 2017. We further calculated the contribution of population growth, population aging, and mortality or DALYs changes to the total IHD deaths and DALYs attributable to $PM_{2.5}$ between 1990 and 2017.
*Results:* In 2017, IHD attributable to $PM_{2.5}$ resulted in 977,140 (95% UI: 838,900–1123,240) deaths and 21.93 million (95% UI: 18.88–25.37) DALYs globally. There has been a significant change of attributable IHD burden, from being a common burden to one that mainly affects low and middle-SDI countries in Asia, Oceania and sub-Saharan Africa. This global change has occurred as a consequence of opposing trends in high-SDI countries and in Asia, Oceania and sub-Saharan Africa, which has led to some Asian countries having the highest IHD burden attributable to $PM_{2.5}$ in 2017.
*Conclusions:* Although the global age-standardized burden of IHD attributable to $PM_{2.5}$ has decreased from 1990 to 2017, there has been an unpleasant increase in some low and middle-income countries, mainly in Asia, Oceania, and Africa.



## 1. Introduction

Ischemic heart disease (IHD), also called coronary heart disease, is the leading cause of morbidity and mortality worldwide, accounting for 16% (8.9 million) of total deaths and 7% (170 million) of all disability-adjusted life years (DALYs) in 2017 (Dicker et al., 2018). The lifetime risk of developing IHD at age 40 is one in two for men and one in three for women (Lloyd-Jones et al., 1999), which has led to substantial medical burden and economic loss. For example, the estimated direct and indirect cost of heart disease from 2014 to 2015 was $218.7 billion in the US alone (Virani et al., 2020).

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https://doi.org/10.1016/j.chemosphere.2020.128134

A variety of risk factors may play a role in developing IHD. Some of the risk factors are modifiable, such as smoking, lack of exercise, and obesity (Virani et al., 2020). Long-term exposure to ambient air pollution may plausibly develop IHD through multiple pathways, such as through triggering inflammatory responses (Shrey et al., 2011), causing oxidative damage (Dockery and Stone, 2007), and increased plaque formation in the blood vessels (Sun et al., 2005). Regional epidemiologic studies also provide evidence that exposure to particulate matter (PM) air pollution is associated with a higher risk of IHD deaths and hospitalizations (Guan et al., 2016; Mannucci et al., 2019; Pope, 2015; Siponen et al., 2015; Xie et al., 2015). However, few studies have estimated and compared the $PM_{2.5}$ associated IHD burden at the global and national levels. Understanding the $PM_{2.5}$ associated IHD burden and its temporal changes worldwide are of great significance for prioritizing action for the global prevention of IHD.

Accordingly, we sought to estimate the global burden of IHD attributable to $PM_{2.5}$ and to examine whether there were spatial and temporal variations in the $PM_{2.5}$ associated IHD burden between 1990 and 2017. We used the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) (Bisanzio et al., 2018; Gakidou et al., 2017), an ongoing global effort to measure death and disability attributable to diseases, injuries, and risk factors in 195 countries and territories worldwide. We used data of GBD 2017, which is the most recent release of the study, providing a valuable opportunity to evaluate the global patterns and trends of IHD burden associated with $PM_{2.5}$.

## 2. Material and methods

### 2.1. Study data

We obtained data on IHD and $PM_{2.5}$ from GBD 2017 through the Global Health Data Exchange (GHDx) query tool (http://ghdx.healthdata.org/gbd-results-tool), which is an online query tool of GBD 2017. We obtained data on age-standardized rates of deaths and DALYs of IHD attributable to $PM_{2.5}$ between 1990 and 2017 for 195 countries and territories worldwide. Data of cases and the rates are reported as numbers with 95% uncertainty intervals (UIs).

GBD 2017 divided countries and regions into five super regions based on the socio-demographic index (SDI): low SDI, low-middle SDI, middle SDI, high-middle SDI, and high SDI. SDI is a summary measure of the level of social development of a country or territory, and was defined by GBD 2017 based on the combination of total fertility rate for women younger than 25 years, educational attainment in people age 15 years or older, and lag-distributed per capita income (Bisanzio et al., 2018; James et al., 2018). GBD 2017 also divided the world into 21 geographic regions according to epidemiological similarity and geographical proximity, such as East Asia, Australasia, Central Europe.

### 2.2. IHD mortality rates and DALYs

We used age-standardized rates of deaths and DALYs (per 100,000 population) to quantify the burden of IHD attributable to $PM_{2.5}$. The methods for estimating the IHD burden have been detailed elsewhere (Bisanzio et al., 2018; James et al., 2018). Briefly, IHD was defined based on the World Health Organization clinical criteria and the International Statistical Classification of Diseases, Ninth and Tenth revisions. GBD 2017 used the comparative risk assessment framework to estimate exposure levels of $PM_{2.5}$, attributable deaths and DALYs, and location for each risk from 1990 to 2017, by age group, sex, and calendar year. The portion of deaths and DALYs that could be attributed to $PM_{2.5}$ were estimated by using the counterfactual scenario of theoretical minimum risk exposure level (TMREL). GBD 2017 calculated DALYs as the sum of years lost due to premature death (YLLs) and years lived with disability (YLDs), where YLLs were the multiplication of deaths and a standard life expectancy at the age of death, and YLDs were the years lived with any short-term or long-term health loss weighted for severity by the disability weights. Deaths were defined as the number of deaths occurring in a population during a specific period.

### 2.3. Ambient air pollution assessment

Ambient particulate matter pollution in GBD 2017 was defined as the annual average daily exposure to outdoor air concentrations of $PM_{2.5}$, measured in $\mu g/m^3$, at a spatial resolution of a $0.1° \times 0.1°$ grid cell over the globe, from a combination of satellite-based and ground level data (Bisanzio et al., 2018).

### 2.4. Statistical analysis

The differences in population age structures may lead to the heterogeneity in IHD burden and mortality quantified by death rates and DALYs. To eliminate the influence of population structure differences, we used the age-standardized mortality rate (ASMR) and age-standardized DALYs rate (ASDR). We used estimated annual percentage changes (EAPCs) to assess the trends of ASMR and ASDR attributable to $PM_{2.5}$ . EAPC is a measure of the trend of age-standardized rates (ASR) over a time interval (Hankey et al., 2000). The ASR could be fitted in a regression model: $\ln(ASR) = \alpha + \beta x + \varepsilon$, where x is the calendar year, while EAPCs was calculated as $100 \times (\exp(\beta) - 1)$ (Hankey et al., 2000). The ASR (i.e., ASMR and ASDR) was considered to be increased if the lower boundary of its 95% CIs is higher than zero. In contrast, if the higher boundary of its 95% CIs is lower than zero, then there is a decreasing trend for ASR. Otherwise, the ASR was considered to be stable.

We used Pearson's test to evaluate the correlation of the SDI with the ASR for 21 GBD regions. The expected relation between SDI and ASRs was determined by fitting a Gaussian process regression on estimates for 21 GBD regions from 1990 to 2017, and a Loess smoother was fitted between SDI and ASR (Bisanzio et al., 2018; Kyu et al., 2018) to examine the correlation between development status and IHD burden attributable to $PM_{2.5}$.

Additionally, we used a recently developed decomposition method to attribute changes in $PM_{2.5}$ associated total IHD deaths and DALYs to population growth, population aging, and mortality or DALYs changes from 1990 to 2017 in 21 GBD regions. Additional methodologic details are described elsewhere (Cheng et al., 2019). All statistics were performed using the R software (Version 3.5.3, R core team). A 2-sided $p$-value <0.05 was considered as statistically significant.

## 3. Results

### 3.1. Global burden of IHD attributable to $PM_{2.5}$ in 2017 and trends from 1990 to 2017

In 2017, global ASMR of IHD attributable to $PM_{2.5}$ was 16.56 (95% UI: 14.19−19.20) for males and 8.81 (95% UI: 7.43−10.24) for females per 100,000 population (Table S1), the corresponding risk estimate for ASDR was 376.76 (95% UI: 322.96−437.42) and 170.04 (95% UI: 145.78−197.74) per 100,000 population (Table S2). There was a decreasing trend in global ASR from 1990 to 2017 (Table S1 & S2). For example, the global ASMR of IHD attributable to $PM_{2.5}$ decreased by an average 0.42% (95% CI: 0.35, 0.50) per year for males and 0.78% (95% CI: 0.72, 0.84) per year for females. In terms

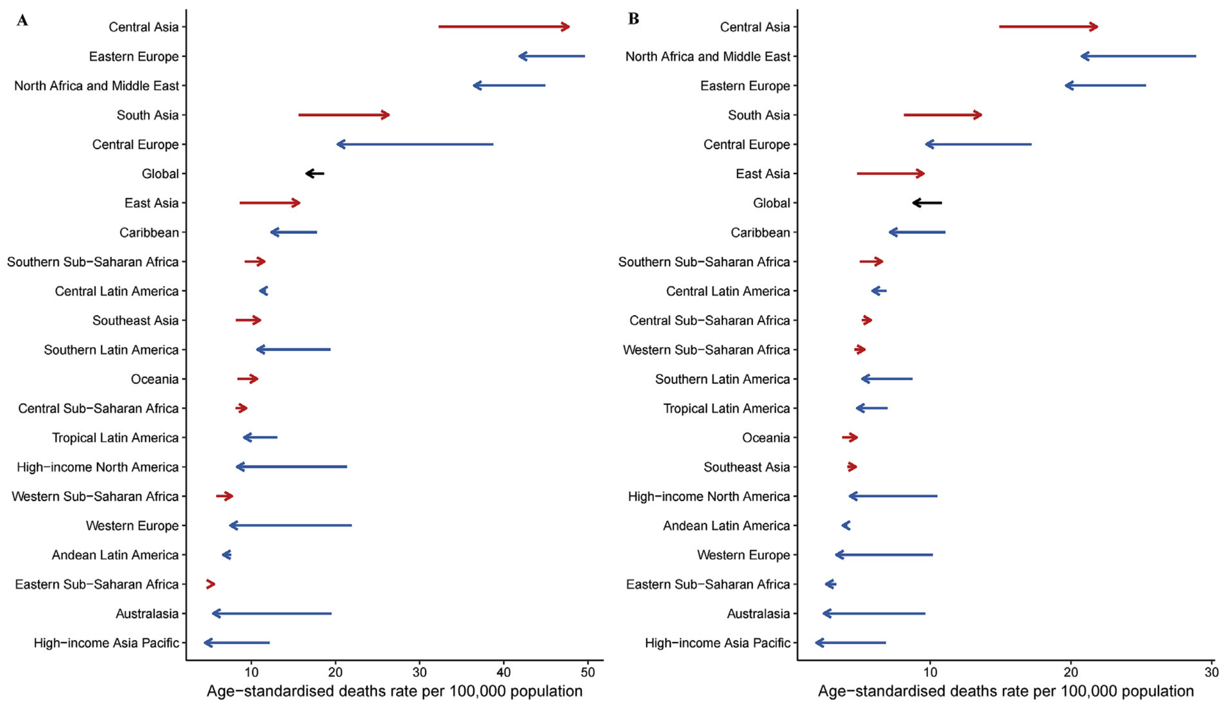


**Fig. 1.** Change in age-standardized deaths rate of ischemic heart disease (IHD) attributable to ambient $PM_{2.5}$ between 1990 and 2017. A, age-standardized IHD deaths rate attributable to ambient $PM_{2.5}$ in males. **B**, age-standardized IHD deaths rate attributable to ambient $PM_{2.5}$ in females. The start of the arrow shows the age-standardized deaths rate of IHD attributable to ambient $PM_{2.5}$ in 1990, and the head indicates the value in 2017.

of air pollution, $PM_{2.5}$ levels increased in most countries in 2017 compared to 1990 levels, with the exception of those countries with high SDI that showed a decreasing trend in $PM_{2.5}$ levels.

Regionally, the ASMR and ASDR of IHD attributable to $PM_{2.5}$ decreased in most regions (Fig. 1 & Fig. S1), especially in Europe, Australasia, High-income North America. The most substantial decrease was observed in Central Europe for males, followed by Western Europe and Australasia. By contrast, the ASMR and ASDR of IHD attributable to $PM_{2.5}$ were increased in Central Asia, South Asia, East Asia, Oceania, and sub-Saharan Africa, with the most massive increase in Central Asia (except for females in ASDR).

In 2017, $PM_{2.5}$ claimed 977,140 (95% UI: 838,900–1123,240) deaths (Table S1) and 21.93 million (95% UI: 18.88–25.37) DALYs (Table S2) among IHD patients globally. From 1990 to 2017, the global number of IHD deaths and DALYs attributable to $PM_{2.5}$ increased by ~430,000 and ~9.6 million, respectively. These net increases in $PM_{2.5}$ associated IHD deaths and DALYs resulted from significant decreases in high-income western countries, but considerable increases throughout Asia and Oceania (Fig. 2, Fig. S2, Table S1, and Table S2). The number and DALYs of IHD deaths attributable to $PM_{2.5}$ increased by two to four times from 1990 to 2017 in East Asia, Southeast Asia, South Asia, Central Asia, North Africa and Middle East countries. As a result, the above countries accounted for more than two-thirds of IHD deaths and DALYs attributable to $PM_{2.5}$ in 2017, whereas the proportion was only less than half in 1990.

### 3.2. Demographic change on IHD burden attributable to $PM_{2.5}$

We used a newly developed decomposition method to attribute changes in total number of IHD deaths and DALYs attributable to $PM_{2.5}$ to population growth, population aging, and mortality or DALY rate changes from 1990 to 2017 in 21 GBD regions (Fig. 4 & Fig. S3). Deaths and DALY rates are mostly declined in Europe, the Americas and Latin America but increased in Asia and Africa regions. The contributions of population aging and population growth on the total number of IHD deaths and DALYs attributable to $PM_{2.5}$ generally increased globally, and the increases are more pronounced among Europe, the Americas and Latin America for population aging but Asia and Africa regions for population growth. As a result, countries in Europe and the Americas experienced a net decrease in IHD burden attributable to $PM_{2.5}$. Conversely, for countries in Asia, Africa and Oceania, there was a net increase in IHD burden due to $PM_{2.5}$.

### 3.3. Global IHD burden attributable to $PM_{2.5}$ by SDI

In general, the IHD burden attributable to $PM_{2.5}$ was higher in lower SDI quintiles in 2017 (Table S1 & Table S2). Countries in the upper SDI quintile saw the most significant decreases in ASMR and ASDR from 1990 to 2017, changing by an average −3.74% (95% CI: −3.79, −3.69) per year for ASMR and −3.77% (95% CI: −3.81, −3.73) per year for ASDR. The most substantial increase of ASMR and ASDR were observed in low SDI quintile, increasing by an average 1.75% (95% CI: 1.49, 2.00) per year for ASMR and 1.63% (95% CI: 1.38, 1.88) per year for ASDR (Table S1 & Table S2). In terms of total IHD deaths and DALYs, all SDI quintiles but high SDI showed a net increase from 1990 to 2017, driven by population growth and aging.

We used Pearson's test to evaluate the correlation between SDI and ASR for 21 GBD regions. The relationship between SDI and expected ASMR and ASDR of IHD attributable to $PM_{2.5}$ was positive when SDI was lower than 0.52, but negative when SDI was above 0.52 (Fig. 3).

### 3.4. IHD burden attributable to $PM_{2.5}$ by countries

Considerable variation in the IHD burden attributable to

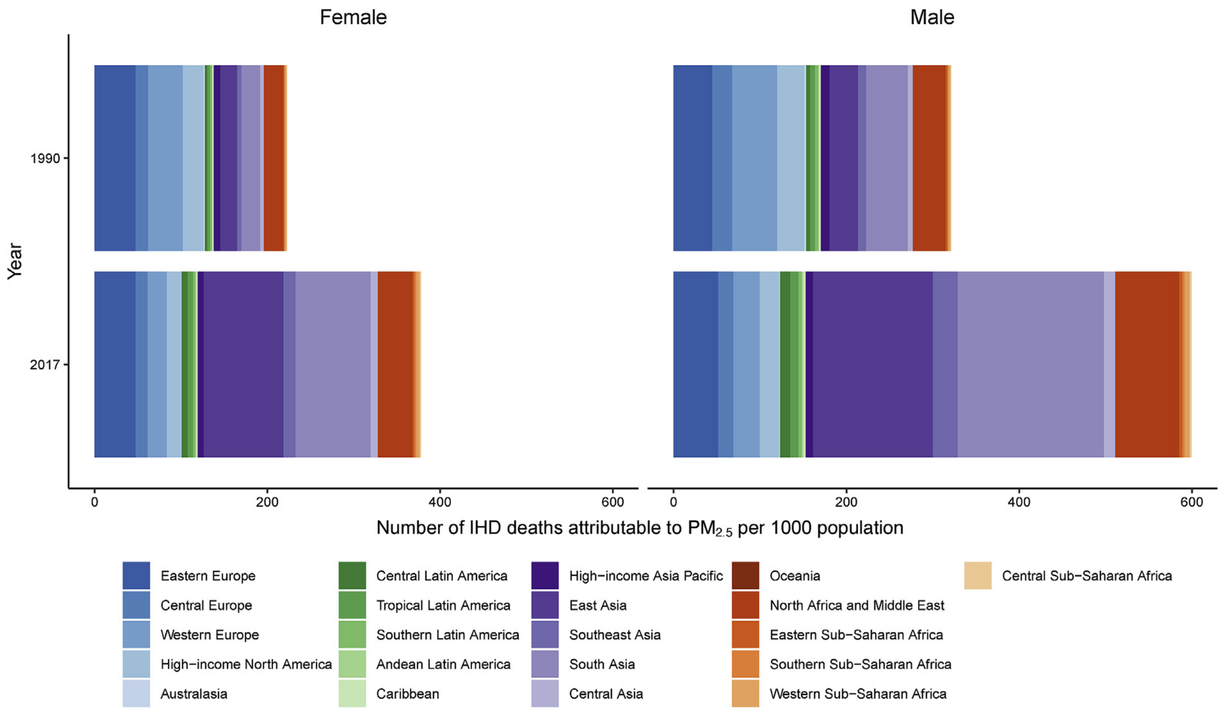


**Fig. 2.** Ischemic heart disease (IHD) deaths attributable to ambient $PM_{2.5}$ by region in 1990 and 2017 for females and males.

$PM_{2.5}$was noted among different countries in both 1990 and 2017. In 2017, the ASMR of IHD burden attributable to $PM_{2.5}$ varying more than 25-fold between countries (Fig. 5), ranging from 3.25 (95% UI: 1.51, 6.32) in Liberia to 86.03 (95% UI: 65.80, 107.53) in Egypt for males per 100,000 population, and from 1.68 (95% UI: 0.65, 3.45) in Malawi to 43.10 (95% UI: 31.07, 55.79) in Egypt for females per 100,000 population.

In 2017, the highest ASMRs of IHD burden attributable to $PM_{2.5}$ were observed in males in Egypt, Uzbekistan, and Ukraine. In general, countries in North Africa and the Middle East, East Asia, Southeast Asia, South Asia, and Central Asia had a higher burden of IHD attributable to $PM_{2.5}$. In contrast, countries in Europe, the Americas, Australia, and part of Africa had a relatively lower burden of IHD attributable to $PM_{2.5}$.

Australia, Bahrain, Denmark, Ireland, Isreal, and South Korea had some of the highest ASMR of IHD burden attributable to $PM_{2.5}$ in 1990 (ranked in the top one-third). However, they experienced some of the most significant declines thereafter (Figs. 5 and 6). At the extreme, ASMR of IHD burden attributable to $PM_{2.5}$ declined by more than an average of 6.0% per year for Bahrain females, changing its rank from first place in 1990 to being ranked 35th place in 2017. The most substantial increases were found in Asia countries (e.g., Bhutan, Bangladesh, China, India, Pakistan, and Uzbekistan) and African countries (e.g., Swaziland, Lesotho, and Uganda). In these countries, the ASMR of IHD burden attributable to $PM_{2.5}$ increased by an average of 5.86% per year. Although the ASMR is not the highest, China had the largest numbers of IHD deaths attributable to $PM_{2.5}$ because of a large population, followed by India, the Russian Federation, and the US. India had the most significant numbers of IHD DALYs attributable to $PM_{2.5}$, followed by China, the Russian Federation, and the US. The trends in ASDR of IHD due to $PM_{2.5}$ among countries were similar to those of ASMR (Fig. S4 & Fig. S5).

## 4. Discussion

In this study, we performed a comprehensive estimation of the global spatial patterns and temporal trends of IHD mortality and DALYs attributable to $PM_{2.5}$ from 1990 to 2017. Our results show that there has been a significant global change of IHD burden attributable to $PM_{2.5,}$ from being a common global burden to one that mainly affects low and middle-SDI countries in Central Asia, South Asia, East Asia, as well as some countries in Oceania and sub-Saharan Africa. This global change has occurred as a consequence of opposing trends in high-SDI countries and in Asia, Oceania and sub-Saharan Africa, which has led to some Asian countries (e.g., China, India, Pakistan, and Bangladesh) having the highest IHD burden attributable to $PM_{2.5}$ in 2017.

A growing body of literature shows that $PM_{2.5}$ is a well-defined risk factor for IHD. Previous studies have shown that long-term and acute exposure to $PM_{2.5}$ are associated with higher risks of IHD morbidity and mortality (Brown et al., 2015; Chang et al., 2015; Faustini et al., 2015; Li et al., 2015; Sun et al., 2019, Sun, 2020; Thurston et al., 2016; Xie et al., 2015; Yu et al., 2020). Several potential mechanisms might be involved in the pathophysiological process of IHD attributable to $PM_{2.5}$ (Hayes et al., 2020; Ljungman et al., 2019; Thurston et al., 2016; Xie et al., 2015). $PM_{2.5}$ can be directly translocated to the bloodstream and remote target organs (Furuyama et al., 2009), or mediated by lung oxidative stress and inflammatory response (Dockery and Stone, 2007).

The IHD burden attributed to $PM_{2.5}$ were higher in males than females, as a result of higher all-cause mortality rates in males (Cohen et al., 2017). The gaps between IHD burden attributable to $PM_{2.5}$ in low, low-middle, and middle SDI quintiles compared with high-middle and high and SDI quintiles reflect inequities in access to preventive care of IHD and air pollution control. The IHD burden attributed to $PM_{2.5}$ in high SDI countries has been gradually decreasing since the 1990s. This reduction may be a combined effect of several factors. First, $PM_{2.5}$ exposure levels in these countries have been relatively low and stable (Cohen et al., 2017), followed by the widespread use of statins (Walley et al., 2005) and low-dose aspirin (Willard et al., 1992) for primary and secondary prevention for IHD in high SDI countries. On the contrast, $PM_{2.5}$ exposure levels in low- and middle-income countries were either increasing

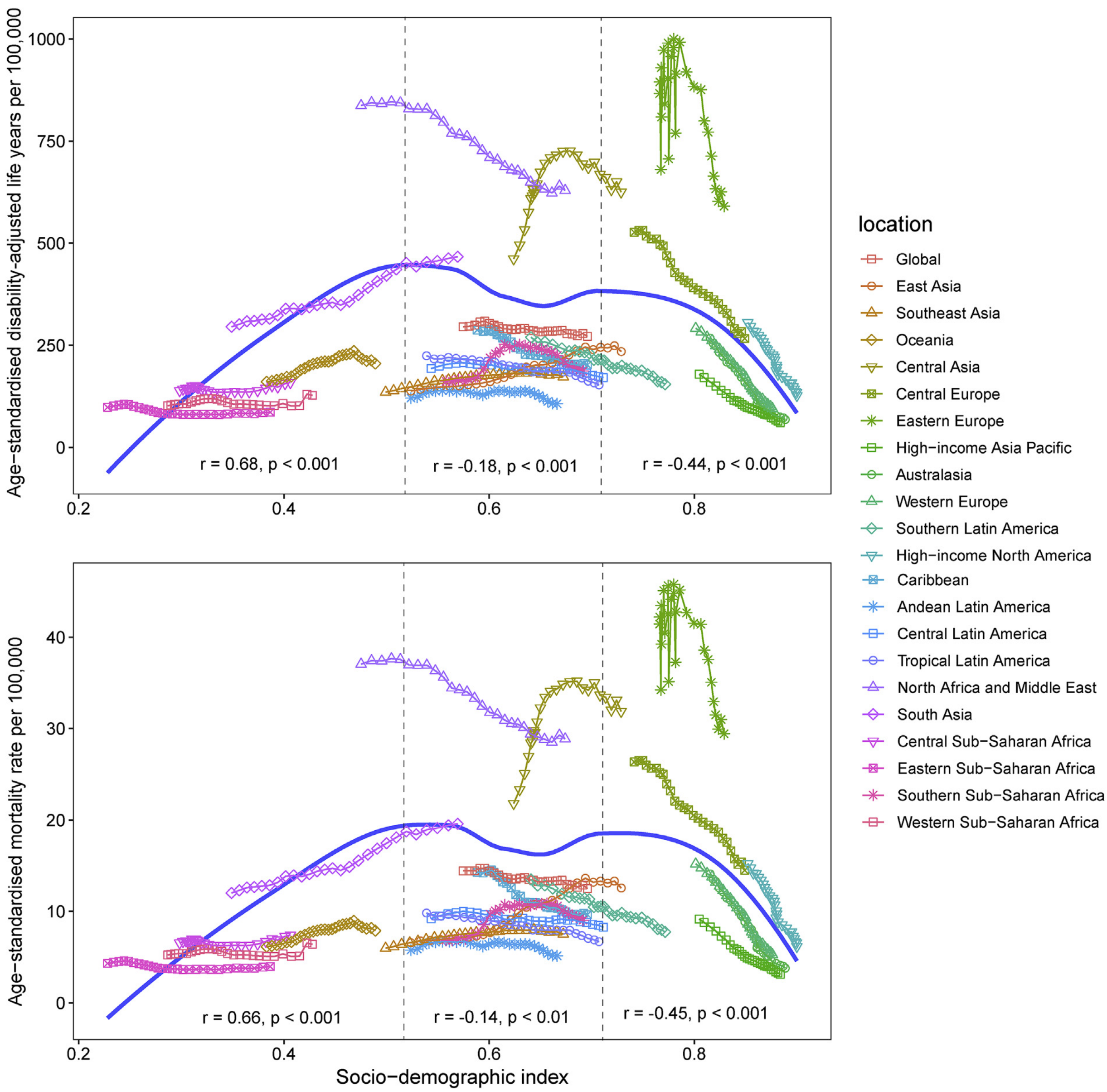


**Fig. 3.** Age-standardized rate of deaths and DALYs of ischemic heart disease (IHD) attributable to ambient $PM_{2.5}$ by region from 1990 to 2017. The solid blue line shows expected values across the spectrum of the socio-demographic index. The Pearson correlation coefficient and its p-value were denoted. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

or maintaining a high level despite the decline (Cohen et al., 2017; India State-Level Disease Burden Initiative Air Pollution Collaborators, 2019), and statins and low-dose aspirin use remain low (Roth et al., 2011), which may be the major contributors to the increase of IHD burden attributed to $PM_{2.5}$ in low- and middle-income countries. Second, population growth and population aging also play an essential role in the trend of IHD burden attributed to $PM_{2.5}$. For example, in China, India, and Bangladesh, increases in $PM_{2.5}$ exposure levels combined with increases in population growth and population aging resulted in net increases in IHD deaths and DALYs attributable to $PM_{2.5}$. While Brazil, Indonesia, and Pakistan experienced decreases in $PM_{2.5}$ exposure levels, population growth, as well as population aging led to a net increase in IHD deaths and DALYs attributable to $PM_{2.5}$ (Cohen et al., 2017). In particular, Eastern Europe and Central Asia have the highest burden of IHD attributable to $PM_{2.5}$. The main reason for this result is that these regions have the highest IHD mortality in the world, for example, eastern Europe has more than twice than the global level of IHD mortality, and central Asia has almost three times than the global level of IHD mortality (Finegold et al., 2013; Nowbar et al., 2019). Therefore, the burden of IHD attributable to $PM_{2.5}$ is also higher in these regions than in other regions.

We show here that in the past three decades, the global pattern of IHD burden attributable to $PM_{2.5}$ has changed from a global health problem to a health problem mainly affecting low- and middle-income countries in Asia and Africa. Actions are needed to reduce the burden of IHD by adopting multiple approaches to air pollution management, and promoting the use of statins and low-dose aspirin for primary and secondary prevention for IHD. Take China as an example. China had the most massive numbers of IHD deaths attributable to $PM_{2.5}$ in 2017, $PM_{2.5}$ exposure level also remained high. In recent years, China has been striving to move to cleaner energy options, improve the application of emission control technologies, promote public transportation systems, promulgate

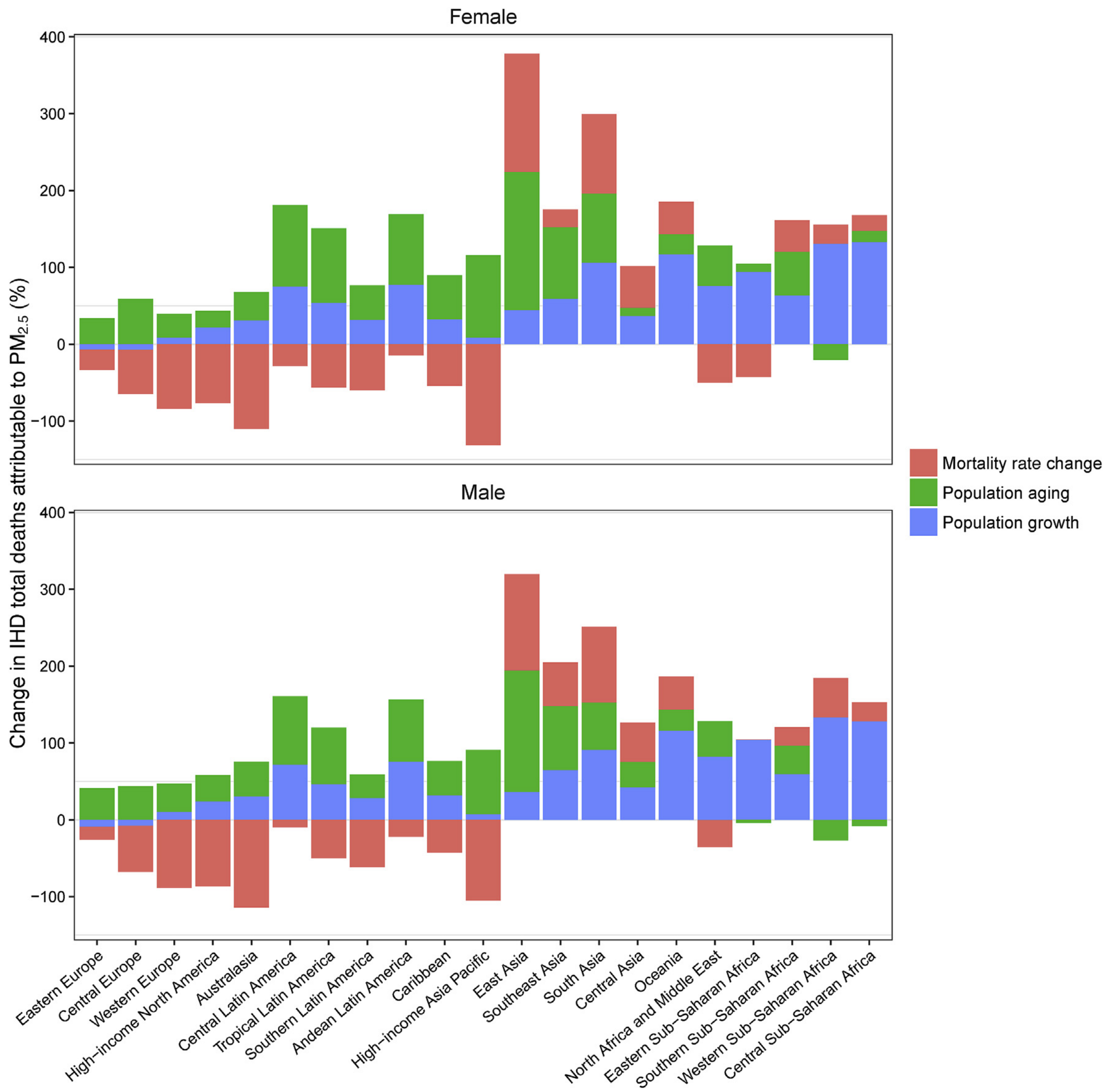


**Fig. 4.** Changes in deaths of ischemic heart disease (IHD) attributable to ambient $PM_{2.5}$ according to population-level determinants in 21 GBD regions between 1990 and 2017. The decomposition was performed using the number of deaths in 1990 as the reference.

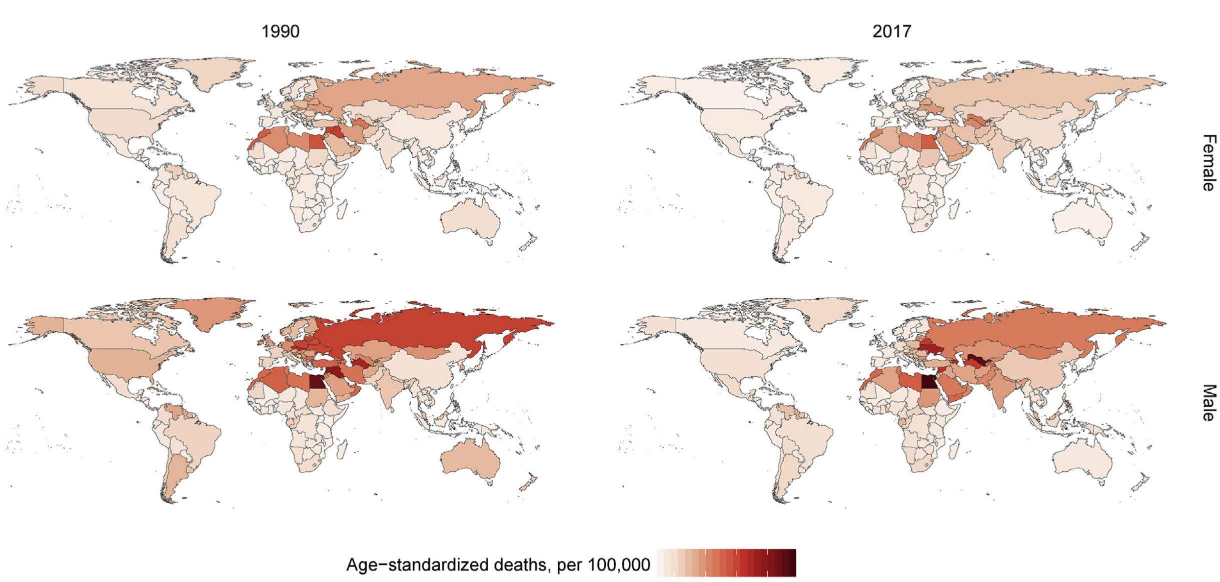


**Fig. 5.** Age-standardized deaths rate of ischemic heart disease (IHD) attributable to ambient $PM_{2.5}$ by country in 1990 and 2017 for females and males.

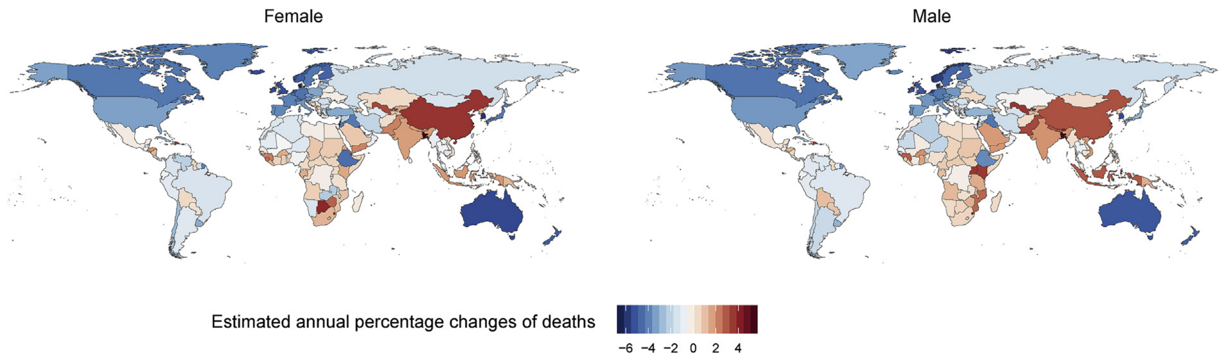


**Fig. 6.** Estimated annual percentage changes in age-standardized deaths rate of ischemic heart disease (IHD) attributable to ambient $PM_{2.5}$ by country between 1990 and 2017 for females and males.

policies to reduce total energy consumption, and promote environmental education and research to address all significant sources of air pollution (Jin et al., 2016). Therefore, the burden of IHD caused by $PM_{2.5}$ in China has remained stable or even started to decline since 2012 (Cohen et al., 2017; Huang et al., 2018).

This study has several limitations. First, some degrees of exposure misclassification cannot be avoided due to less monitoring stations or lack of IHD data in some low-income countries. Second, although prior studies have reported that the toxicity of ambient $PM_{2.5}$ may vary by source (e.g., diesel combustion, biomass burning) (Perrone et al., 2013; Sun et al., 2019). Due to the unavailability of information regarding $PM_{2.5}$ source, in this study, we assume that the toxicity of ambient $PM_{2.5}$ depends only on the magnitude of concentration.

## 5. Conclusion

In summary, our study assessed global temporal and spatial changes in IHD burden attributable to $PM_{2.5}$. Although the global age-standardized burden of IHD attributable to $PM_{2.5}$ has decreased from 1990 to 2017, there has been an unpleasant increase in some low- and middle-income countries, mainly in Asia, Oceania, and Africa. In these countries, there is an urgent need to strengthen the prevention of IHD, as well as air quality management programs, to reduce the burden of IHD attributable to $PM_{2.5}$. Our findings will contribute to developing targeted plans and policies for future IHD prevention and air management in different regions.

## Authorship Contribution Statement

Lina Wang: Conceptualization, Writing – original draft, Methodology, data analysis, Writing – review & editing. Xiaoming Wu: Conceptualization, Writing – review & editing. Jianqiang Du: Conceptualization, Writing – original draft, Methodology, data analysis, Writing – review & editing. Wangnan Cao: Writing – review & editing. Shengzhi Sun: Conceptualization, Writing – original draft, Data curation, Investigation, Writing – review & editing.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgments

This study was funded by Natural Science Research Program of Shaanxi Province of China (No.: 2019JM-478).

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chemosphere.2020.128134.

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