The Analysis in the Burden of Lung Cancer Attributable to PM2.5 Exposure in China

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Research article

Keywords: PM2.5, ambient exposure, Household exposure, Lung cancer, Age-Period-Cohort Analysis

Posted Date: August 11th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-48956/v1

Abstract

Objective Air pollution is the major contributor of lung cancer mortality, we want to analyze the long-term trends and the differences in lung cancer burden attributable to PM2.5 exposure between ambient air pollution and household air pollution.

Methods The indicators (mortality rate, disability-adjusted life years rate, years lived with disability rate, and years of life lost rate) of lung cancer burden were obtained from GBD 2017. The joinpoint regression analysis was used to assess the magnitude and direction of trends from 1990 to 2017, and the age-period-cohort method was used to analyze the temporal trends of the indicators of lung cancer by age, period, and cohort.

Results The age-standardized indicators showed an upward trend in ambient PM2.5 exposure (APE) and a downward trend in household PM2.5 exposure (HPE). The overall net drifts per year were above zero for APE and below zero for HPE, and the local drift values in APE and HPE increased by age groups. For the longitudinal age curves, the indicators of lung cancer burden for younger in APE or HPE were in a low level, and significantly increased from 45-49 age group to 90-94 age group. For the period RRs, the indicators of lung cancer burden in APE increased from 1990 to 2017, but decreased in HPE from 1990 to 2017. For the cohort RRs, the indicators of lung cancer burden in APE was on the upward trend before 1965, and fluctuated after from 1970 to 1990. The indicators of lung cancer burden in HPE was on the downward trend.

Conclusions For lung cancer attributable to air pollution, China had changed from household air pollution to ambient air pollution. PM2.5 exposure had more harmful in male and older people. Ambient air pollution should be emphasized, China should strengthen implementation of effective public policies and other interventions.

Introduction

Air pollution is an important global health problem, and the severity of air pollution in China has attracted attention all over the world[1]. Air pollution contains ambient and household air pollution. Ambient air pollution mainly came from traffic, factories and household fuel, and household air pollution mainly comes from cooking and heating biomass and coal fuel[2]. As the most widely studied air pollutant, PM2.5 is increasingly used as an indicator pollutant, with annual average concentrations ranging from less than 10 to more than 100 μg/m^3 globally, was associated with risk of many non-communicable diseases, such as cardiovascular disease[3], chronic obstructive pulmonary disease (COPD)[4] and diabetes[5], and led to 8.3 million premature deaths in 2017. International Agency for Research on Cancer (IARC) unanimously agreed that PM2.5 is carcinogenic to humans (Group 1) after evaluating this component of air pollution[2].

A growing number of studies show that PM2.5 exposure was closely related to the risk of lung cancer. In ambient PM2.5 exposure (APE), a large cohort study on long-term exposures to ambient PM2.5 in

Canada, Bai et al. found that each 5 μg/m^3 increased in ambient PM2.5 concentration was associated with a 2% (95% CI: 1%–5%) increased risk of lung cancer after adjusting for a series of individual and area-level risk factors[6]. In the AHSMOG-2 Study, Gharibvand L et al. also found each 10-μg/m3 increment in ambient PM2.5 concentration was associated with a 43% (95% CI: 11%–84%) increased risk of lung cancer[7]. In the European Study of Cohorts for Air Pollution effects used data from 17 cohort studies based in nine European countries, the results also showed a statistically significant association between risk for adenocarcinomas of the lung and ambient PM2.5[8]. Household PM2.5 exposure (HPE) is an important component of household air pollution. Approximately 17% of lung cancer deaths in adults are attributable to exposure to carcinogens from household air pollution caused by cooking with kerosene or solid fuels like wood, charcoal or coal. The estimated number of lung cancer deaths attributable to HPE in China was 271,089 in 2017, and China had the largest number in the world[9].

In China, lung cancer had grown from 14th in 1990 to 4th in 2017 in the cause of human death, was the leading cause of cancer death among both men and women, and more than one-third of all newly diagnosed lung cancers occurred in China[10]. It brought enormous health and economic burdens to patients, families and the whole country. At present, air pollution in China has become a serious environmental problem, which had attracted more and more attention. Therefore, it was very important to evaluate the disease burden of lung cancer caused by air pollution, especially in PM2.5. Therefore, in our study, we wanted to analyze the changes of ambient/household PM2.5 exposure on lung cancer from 1990 to 2017. There was few studies on the comprehensive analysis of the possible reasons underlying the long-term trends of lung cancer burden attributable to PM2.5 exposure. We performed the age-period-cohort model (APCM) to analyze the independent effects of chronological age, time period, and birth cohort and the temporal trends, and provided the theoretical basis for the public health policy on $PM_{2.5}$-induced health effects.

Materials And Methods

Data Source

The indicators of disease burden contained mortality rate, disability-adjusted life years (DALY) rate, years lived with disability (YLD) rate, and years of life lost (YLL) rate. Data on burden of lung cancer (C33–C34) from 1990 to 2017 in China were extracted from Global Burden of Disease (GBD) 2017 in terms of the International Classification of Diseases (ICD) version 10 (ICD-10), which are available at the GBD Data Tool repository and can be accessed at http://ghdx.healthdata.org/gbd-results-tool. GBD 2017 is the most comprehensive effort to date to measure epidemiological levels and trends worldwide, and contained the data on 84 behavioral, environmental and occupational, and metabolic risks or clusters of risks, 282 causes of death, 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, and quantifies the impact of hundreds of diseases, injuries, and risk factors in countries around the world. To analyze the status on burden of lung cancer attributable to Ambient/Household PM2.5 exposure in China, we extract the related indicators of disease burden on lung cancer. Ambient PM2.5 exposure was defined as annual average daily exposure to outdoor air concentrations of PM2.5, and Household PM2.5 exposure was defined as Individual exposure to PM2.5 due to use of solid cooking fuel. The rates were age-standardized by the GBD 2017 global age-standardized population.

Statistical Analyses

The age-standardized mortality rate (ASMR) was used to estimate the trend. Because the age structure of Chinese and American population is different, it is necessary to perform standardization when comparing the trend of mortality. The ASMR (per 100,000 population) is calculated by the direct method, which is the sum of the age-specific rates (a_i, where i denotes the i^{th} age class) and the number of persons (or weight) (w_i) in the same age subgroup i of the chosen reference standard population, divided by the sum of standard population weights, i.e.,

$$\mathrm{ASR} = \frac{\sum_{i=1}^{A} a_i w_i}{\sum_{i=1}^{A} w_i} \times 100{,}000$$

In order to assess the magnitude and direction of trends over time for the related indicators of disease burden, we used JoinPoint software (Version 4.7.0.0) to calculate the average annual percentage change (AAPC) and the corresponding 95% CIs by joinpoint regression analysis. JoinPoint software took trend data and fitted the simplest joinpoint model by the data, with the natural logarithm of age-standardized rates as dependent variable and calendar year as independent variable. The tests of significance used a Monte Carlo Permutation method, and the overall asymptotic significance level is maintained through a Bonferroni correction.

In order to assess the related indicators of disease burden experienced by the population in a particular year and the accumulation of health risks since birth, we used APCM to analyze the temporal trends of the related indicators of disease burden by age, period, and cohort and after adjustment for age, period, and cohort on PM2.5-attributable lung cancer mortality. The APCM could provide a useful parametric framework that complements standard nonparametric descriptive methods. In our APCM, we needed to convert the collected data to successive 5-year age groups and consecutive 5-year periods. Because the GBD dataset did not provide successive 5-year age groups under 24 or over 95 years in PM2.5 exposure, the related indicators of disease burden on lung cancer attributable to PM2.5 exposure were recoded into successive 5-year age groups (25-29 years to 90-94 years) and consecutive 5-year periods (1990 to 2017). The general linear model was used to analyze the slope of the period/cohort RRs. The statistical analysis was performed by R statistical software (R version 3.5.1), and $p<0.05$ was considered significant.

Results

(1) The temporal trend in the related age-standardized indicators of disease burden on lung cancer attributable to PM2.5 exposure from 1990 to 2017

Figure 1 showed the temporal trend in the related age-standardized indicators of disease burden on lung cancer attributable to PM2.5 exposure from 1990 to 2017. Table 1 showed the results by joinpoint regression analysis on the related age-standardized indicators of disease burden on lung cancer attributable to PM2.5 exposure from 1990 to 2017. For APE, in our study, there were 2317497 Chinese lung cancer deaths (1657372 males and 660124 females) aged 25 to 94 years from 1990 to 2017. The age-standardized mortality rate (ASMR) of lung cancer attributable to APE increased significantly in both sexes (AAPC: 1.8%; 95% CI: 1.6%, 2.1%), so was in male and female. The ASMR of lung cancer attributable to APE in male was higher than that in female. For HPE, there were 1340022 Chinese lung cancer deaths (806630 males and 533390 females) aged 25 to 94 years from 1990 to 2017. The ASMR of lung cancer attributable to HPE decreased significantly in both sexes (AAPC: -4.6%; 95% CI: -4.9%, -4.4%), so was in male and female. The ASMR of lung cancer attributable to HPE in male was also higher than that in female. The ASMR in APE was higher than that in HPE after 1998. For male, the ASMR in APE was higher than that in HPE after 1996, and for female, the ASMR in APE was higher than that in HPE after 2003. The results of DALY rate, YLD rate and YLL rate were similar to those of mortality rate.

(2) The APCM analysis in the related indicators of disease burden on lung cancer attributable to PM2.5 exposure from 1990 to 2017

Figure 2 showed the net drifts and local drifts for APE and HPE. In mortality rate, the overall net drifts per year were 1.46% (95% CI, 1.22% to 1.70%) for APE and −5.14% (95% CI, −5.34% to −4.93%) for HPE, and the local drift values in APE and HPE increased by age groups. So were the results of the male and female. The results of DALY rate, YLD rate and YLL rate were also similar to those of mortality rate.

Figure 3 showed the longitudinal age curves for APE and HPE. In the same birth cohort, before <55 age groups, the mortality rate in APE was low, and then increased significantly, reached the peak in the 90-94 age group. However, the mortality rate in HPE was always in a low level, and reached the peak in the 75-79 age group and then decline. So were the results of the male and female. The changes of the longitudinal age curves on YLD rate were similar to those on mortality rate. In DALY and YLL rate, before <40 age groups, the DALY rate in APE was low, and then increased significantly, reached the peak in the 75-79 age group and then decline, and the DALY rate in HPE reached the peak in the 65-69 age group and then decline. At 50-54 age group, the DALY rate in APE exceed that in HPE. So were the results of the male and female. The changes of the longitudinal age curves on YLL rate were similar to those on DALY rate.

Figure 4 showed the trend of the estimated period RRs in APE and HPE. In mortality rate, the period RRs in APE increased from 1990 to 2017, but the period RRs in HPE decreased from 1990 to 2017. So were the results of the male and female. The changes of the estimated period RRs on DALY rate, YLD rate and YLL rate were similar to those results of mortality rate. Figure 5 showed the trend of the estimated cohort RRs in APE and HPE. In mortality rate, the cohort RRs in APE was on the upward trend before 1965, and after from 1970 to 1990, the cohort RRs fluctuated. The cohort RRs in HPE was on the downward trend. So were the results of the male and female. The changes of the estimated period RRs on DALY rate, YLD rate and YLL rate were similar to those results of mortality rate.

Discussion

In the past 20 years, China has experienced rapid industrialization, urbanization and urban transport development, industrial emissions, urban construction and vehicle exhaust caused serious air pollution. In recent years, the studies on air pollution increased, and found that PM2.5 exposure associated with all-cause, lung cancer, and cardiopulmonary mortality. Fine particulate air pollution was associated with approximately a 4%, 6%, and 8% increased risk of all-cause, cardiopulmonary, and lung cancer mortality, respectively[11], the study areas involved Beijing[12], Shanghai[12], Guangzhou[13], Taiyuan[14], Shenyang[15] and other large cities in China. Compared with developed countries, the type of air pollution in Chinese cities changed from traditional soot type to hybrid soot/vehicle exhaust type, which made the source of PM more complicated and diversified[16]. As PM2.5 level increased, health effects and diseases burden had more attention. An increase of 10 μg/m^3 of PM2.5 was associated with 12% increases in the risk of mortality from lung cancer, and the concentration response curve suggested a nonlinear relationship between PM2.5 and mortality in China, where the exposure is higher than exposure in developed countries[17]. Therefore, research on the association between PM2.5 and lung cancer is very important and necessary, this is helpful to understand the impact of PM2.5 on lung cancer in China and formulate targeted measures.

In our study, from 1990 to 2017, for the lung cancer case attributable to PM2.5, the number of APE was 1.5 times that of HPE. In mortality rate, the ASMRs in APE increased significantly between 1990 and 2017, while that in the HPE decreased significantly, after 2006, the ASMRs in APE were significant higher than those in HPE. Both in APE and HPE, the ASMRs in male were higher than those in female, and after 2004, the ASMRs of APE in male were highest. At the same time, we also analyzed the other three indicators of disease burden, and found the similar changes. In the APCM, net drift represented the average annual percentage change of the indicators over the study period[18]. For all the indicators of burden disease, the overall net drift were above zero in APE, while below zero in HPE. This suggested that the burden of lung cancer had shown a significant upward trend in APE, and a significant downward trend in HPE from 1990 to 2017. With the urbanization of China, it had gradually shifted from household air pollution to ambient air pollution, this is consistent with our results[19]. Previous studies in China also showed a significant effect of outdoor $PM_{2.5}$ exposure on lung-cancer mortality[20, 21].We further analyzed the local drifts of four indicators in each age group, which represented the average annual percentage changes in indicators over time across different age groups[18]. We found that local drift values in APE and HPE increased by age groups, but the local drifts values in APE were above zero after 45-49 age group, all the local drifts values in HPE were below zero. In the longitudinal age curves, the indicators of lung cancer burden for younger in APE or HPE were in a low level, and significantly increased from 45-49 age group to 90-94 age group. So were the results of the male and female. It suggested that the Lung cancer burden attributable to APE or HPE for younger was low, and for older, the burden was high. It may be mainly related to immune system decline in older people. In China, policy action to reduce PM2.5 concentrations could have a large potential to reduce lung cancer cases, especially in outdoor and elders.

In our results, period effects showed an opposite effect on four indicators of disease burden for APE and HPE; an elevated trend for APE, but a declined trend for HPE. China has always attached great importance to indoor and outdoor air pollution. Since the early 1980s, China introduced more than 180 million improved stoves to improve household energy use. All introduced stoves had chimneys and some had manual or electric blowers to promote more efficient combustion for reducing the concentration of indoor pollutants[22].Since the 20th century, with the serious ambient air pollution in China, the government had implemented emission-control policies that have been continuously tightened since 2005, and the overarching goal was to cut down the total emissions of air pollutants. In 2013, the government issued the “Air Pollution Prevention and Control Action Plan”, which was the most stringent policy on air pollution in Chinese history [23]. In 2018, the government also issued the three-year action plan to win the blue sky defense war, proposing to effectively promote clean heating in the northern region, accelerate the upgrading and transformation of "coal to electricity" in rural area, carry out comprehensive renovation of coal-fired boilers, and strengthen the elimination of small coal-fired boilers. The related studies also found that the decrease in household solid-fuel consumption was mostly responsible for the reduced indoor PM2.5 pollution in China, and the whole society solid-fuel consumption, which mainly came from power, industrial, and transportation sources was responsible for the ambient PM2.5 pollution [23].In the cohort RRs, compared to the 1945 reference cohort, the related indicators of lung cancer in APE indicated an upward trend before 1965, and after from 1970 to 1990, the related indicators of lung cancer fluctuated, while the related indicators of lung cancer in HPE indicated a downward trend. The results were also similar to those of local drifts. The cohort RRs also indicated that lung cancer burden of younger generations in APE was higher than that in HPE. Compared with adults, due to small airway size, immature detoxification and metabolic system, children are more sensitive to ambient PM2.5 exposure[24].In order to prevent children from being affected by PM2.5 for a long time, we should pay attention to protection for them. For male, the APE levels of the related indicators exceed the HPE levels at earlier age (45-49). However, for female, the APE levels of the related indicators exceed the HPE levels at earlier age (55-59). The results showed that PM2.5 exposure had more harmful in male. Both the period and cohort RRs also confirmed that China had changed from household air pollution to ambient air pollution. Meanwhile, our study found that the changes of DALY rate was mainly dominated by YLL rate, due to the low 5-year survival rate of lung cancer [25].

Our study was the first to analyze the effects of age-period-cohort on the temporal trends of lung cancer mortality attributable to PM2.5 exposure and focus on a comprehensive comparison between APE and HPE. GBD 2017 could provide sufficient data, which contained age- and sex-specific all-cause and cause-specific indicators, to reduce the possibility of misclassification of outcomes. Our study found that the effect of APE on the related indicators of lung cancer burden were higher than those of HPE, and PM2.5 exposure had more harmful in male and older people. WHO recommended that public policies and interventions can improve air quality with consequently wide-ranging health benefits. Our study contributed to the importance of reducing PM2.5 exposure in the population. Based on the above findings, China should try our best to implement public policies and interventions to reduce the effect of

PM2.5 exposure on lung cancer burden in the next few years, to achieve the goal of reducing the burden of lung cancer.

Declarations

Ethics approval and consent to participate

GBD 2017 was publicly available for free use, the protocol was approved by the Medical Research Ethics Committee of the First Hospital of China Medical University.

Consent for publication

Not applicable

Availability of data and materials

All our research data are obtained from GBD 2017, the website was http://ghdx.healthdata.org/ gbd-results-tool.

Conflict of interest

The authors declare that they have no competing interests.

Funding

The present study was partially supported by the National Key Research and Development Program of China (grant no. 2016YFC1302501).

Author Contributions

XMW and B Z designed the whole research, J Z and Y L conducted the data collection, B Z and XMW analyzed the data. YF B, S X and XM W wrote the manuscript. XM W and BS Z discussed the relevant results. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

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Tables

Table 1: The results by joinpoint regression analysis on the the related age-standardized indicators of disease burden on lung cancer attributable to PM2.5 exposure from 1990 to 2017.

		APE		HPE	
		AAPC(%)	**95%CI(%)**	**AAPC(%)**	**95%CI(%)**
Mortality Rate	**Both sexes**	2.3*	(1.8,2.7)	-4.2*	(-4.5,-3.9)
	Male	2.1*	(1.7,2.4)	-4.3*	(-4.6,-3.9)
	Female	2.5*	(2.2,2.8)	-4.1*	(-4.3,-3.9)
DALY rate	**Both sexes**	1.8*	(1.6,2.1)	-4.6*	(-4.9,-4.4)
	Male	1.7*	(1.3,2.1)	-4.7*	(-4.9,-4.4)
	Female	2.0*	(1.8,2.3)	-4.6*	(-4.8,-4.4)
YLD rate	**Both sexes**	3.2*	(2.7,3.6)	-3.5*	(-3.8,-3.1)
	Male	3.2*	(2.7,3.6)	-3.5*	(-3.9,-3.0)
	Female	3.5*	(3.2,3.7)	-3.5*	(-3.7,-3.2)
YLL rate	**Both sexes**	1.8*	(1.5,2.1)	-4.6*	(-4.9,-4.4)
	Male	1.7*	(1.2,2.1)	-4.7*	(-5,-4.4)
	Female	2.0*	(1.8,2.2)	-4.6*	(-4.8,-4.4)

*: statistically significant (p<0.05); AAPC: average annual percent change.

Figures

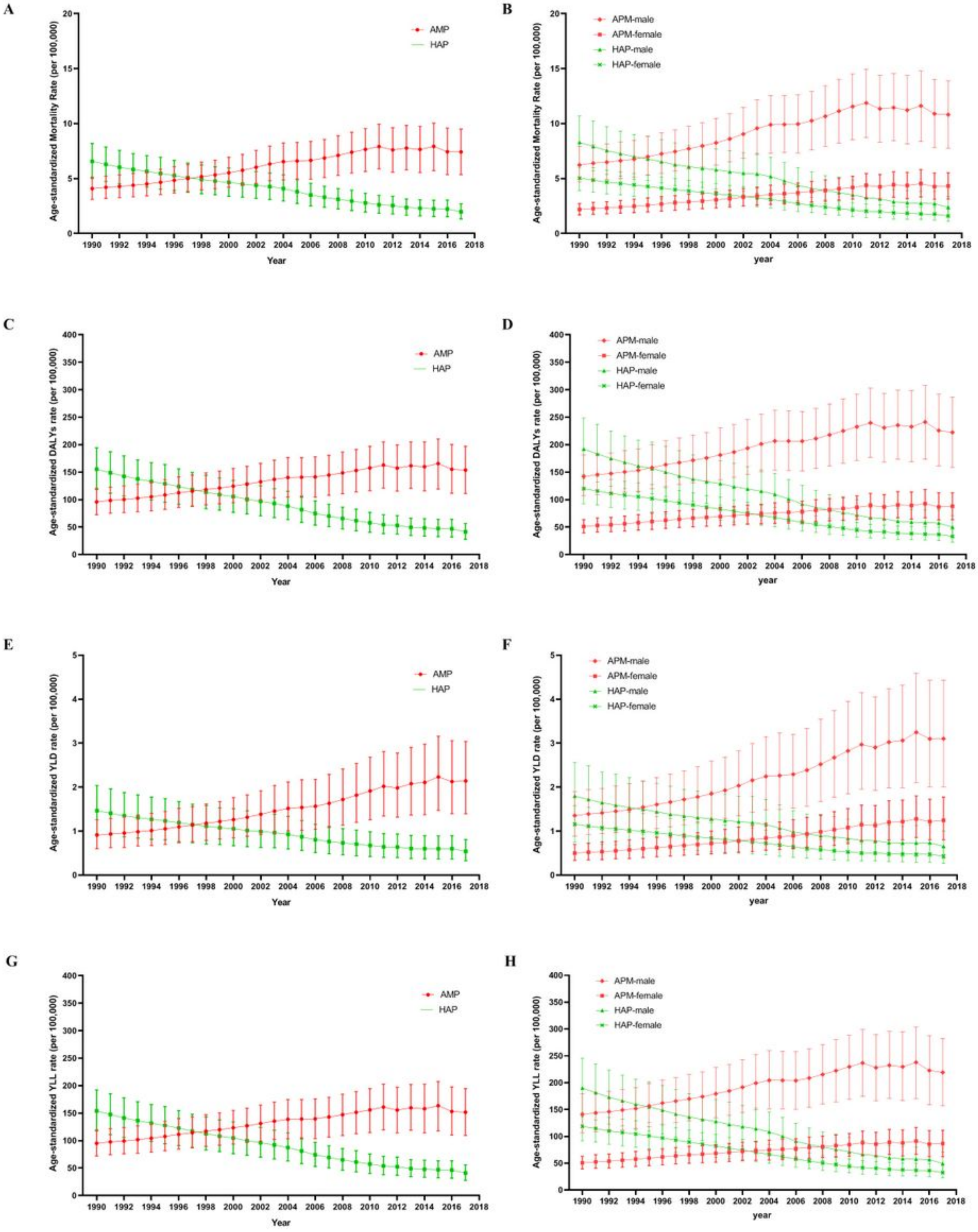

Figure 1

The temporal trend in the related age-standardized indicators of disease burden on lung cancer attributable to PM2.5 exposure from 1990 to 2017. (A) the mortality rate for both sexes in APE and HPE. (B) the mortality rate by sex in APE and HPE. (C) the DALY rate for both sexes in APE and HPE. (D) the DALY rate by sex in APE and HPE. (E) the YLD rate for both sexes in APE and HPE. (F) the YLD rate by sex in APE and HPE. (G) the YLL rate for both sexes in APE and HPE. (H) the YLL rate by sex in APE and HPE.

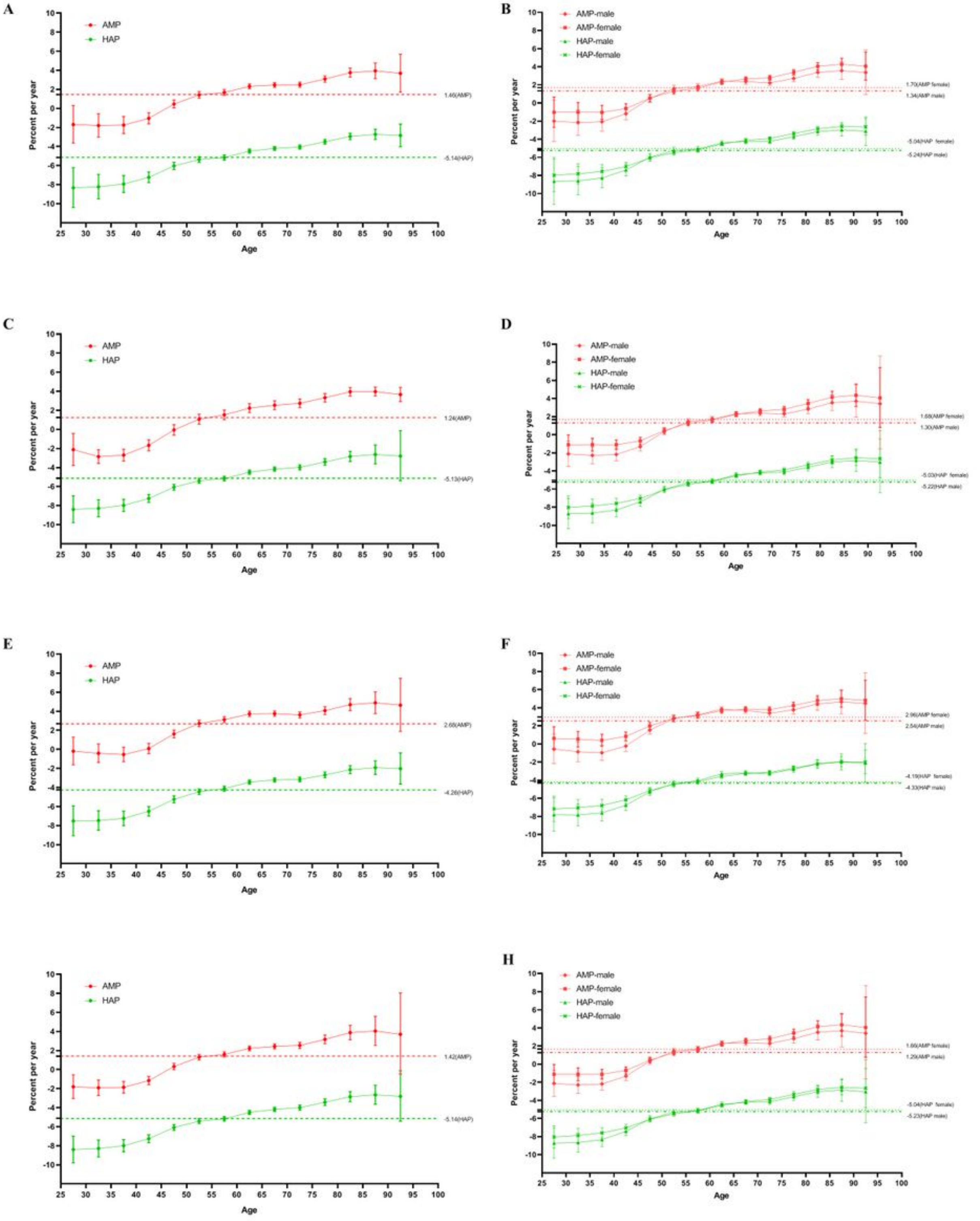

Figure 2

The net drifts and local drifts of the related indicators of disease burden on lung cancer attributable to PM2.5 exposure from 1990 to 2017. (A) the mortality rate for both sexes in APE and HPE. (B) the mortality rate by sex in APE and HPE. (C) the DALY rate for both sexes in APE and HPE. (D) the DALY rate by sex in APE and HPE. (E) the YLD rate for both sexes in APE and HPE. (F) the YLD rate by sex in APE and HPE. (G) the YLL rate for both sexes in APE and HPE. (H) the YLL rate by sex in APE and HPE.

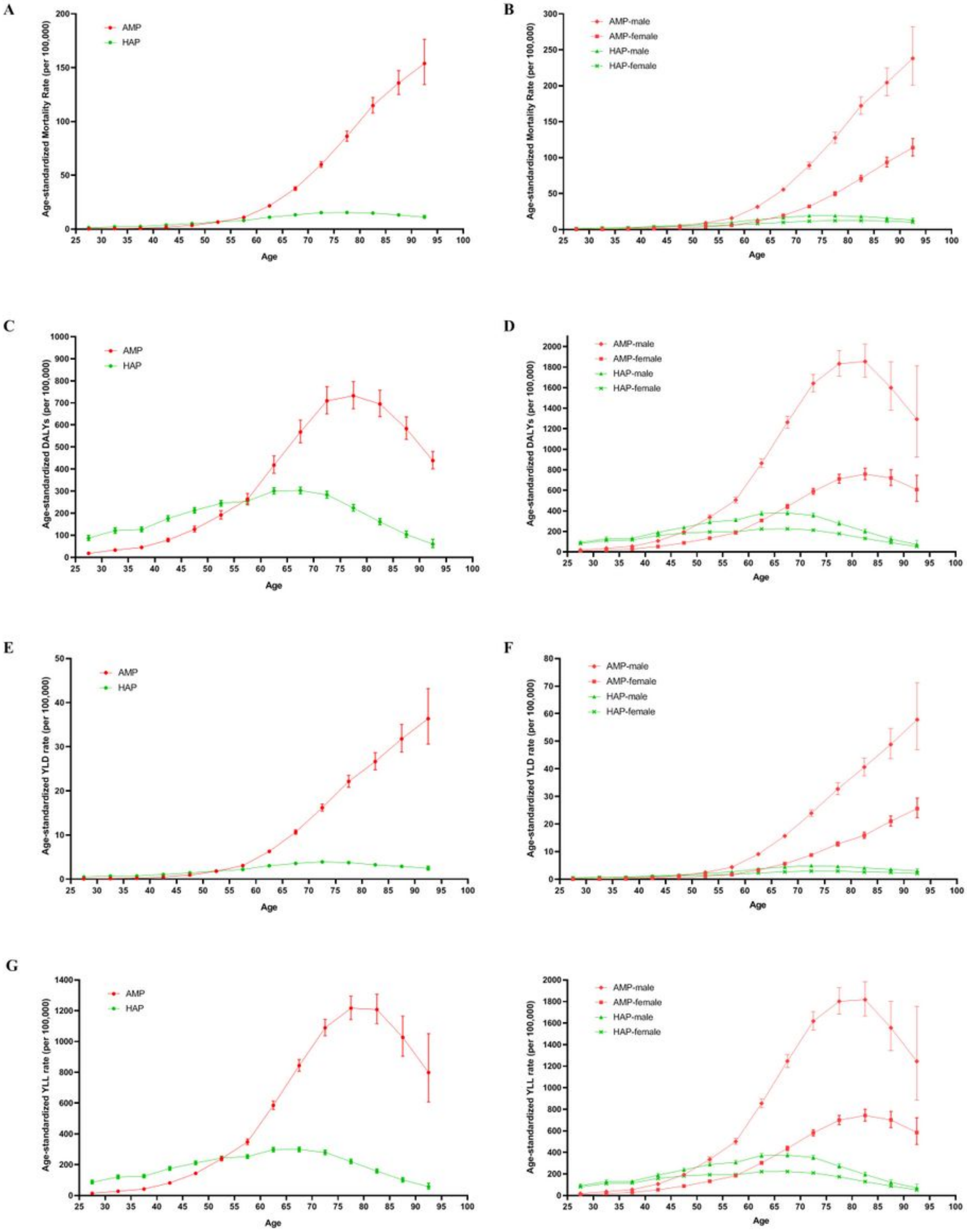

Figure 3

The longitudinal age curves of the related indicators of disease burden on lung cancer attributable to PM2.5 exposure from 1990 to 2017. (A) the mortality rate for both sexes in APE and HPE. (B) the mortality rate by sex in APE and HPE. (C) the DALY rate for both sexes in APE and HPE. (D) the DALY rate by sex in APE and HPE. (E) the YLD rate for both sexes in APE and HPE. (F) the YLD rate by sex in APE and HPE. (G) the YLL rate for both sexes in APE and HPE. (H) the YLL rate by sex in APE and HPE.

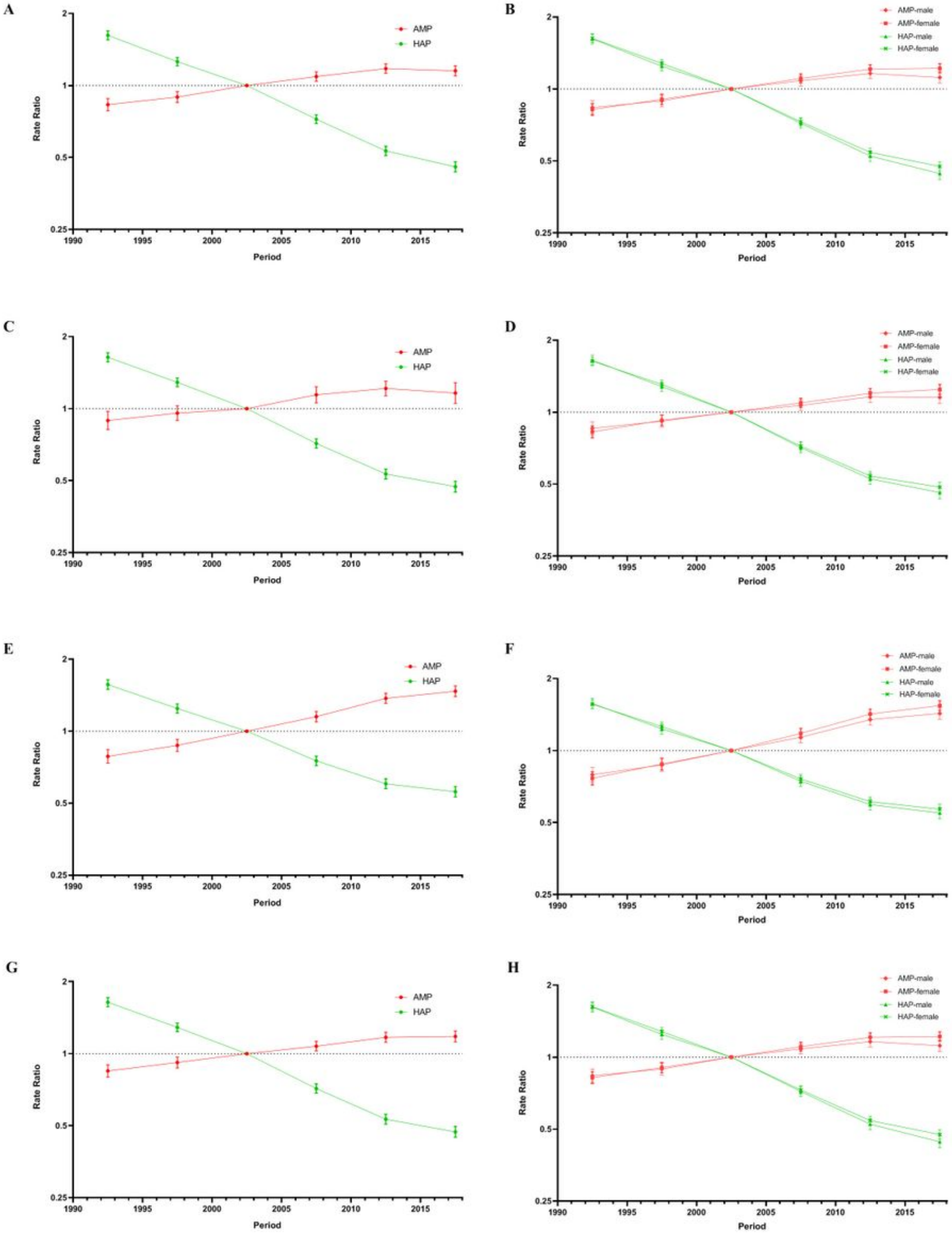

Figure 4

The estimated period RRs of the related indicators of disease burden on lung cancer attributable to PM2.5 exposure from 1990 to 2017. (A) the mortality rate for both sexes in APE and HPE. (B) the mortality rate by sex in APE and HPE. (C) the DALY rate for both sexes in APE and HPE. (D) the DALY rate by sex in APE and HPE. (E) the YLD rate for both sexes in APE and HPE. (F) the YLD rate by sex in APE and HPE. (G) the YLL rate for both sexes in APE and HPE. (H) the YLL rate by sex in APE and HPE.

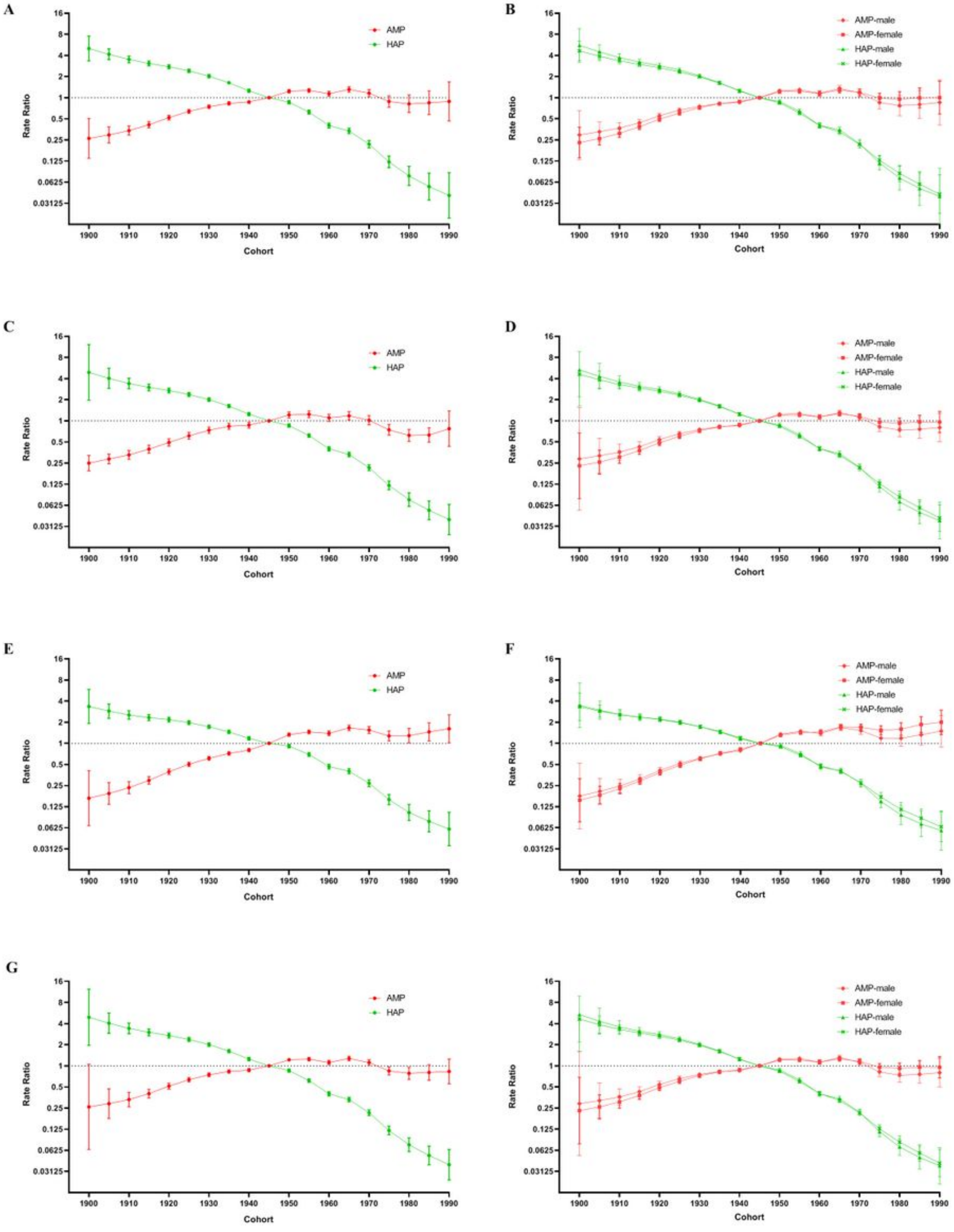

Figure 5

The estimated cohort RRs of the related indicators of disease burden on lung cancer attributable to PM2.5 exposure from 1990 to 2017. (A) the mortality rate for both sexes in APE and HPE. (B) the mortality rate by sex in APE and HPE. (C) the DALY rate for both sexes in APE and HPE. (D) the DALY rate by sex in APE and HPE. (E) the YLD rate for both sexes in APE and HPE. (F) the YLD rate by sex in APE and HPE. (G) the YLL rate for both sexes in APE and HPE. (H) the YLL rate by sex in APE and HPE.