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# Landscape fire PM<sub>2.5</sub> and hospital admissions for cause-specific cardiovascular disease in urban China

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There is a growing interest in the health impacts of PM<sub>2.5</sub> originating from landscape fires. We conducted a time-series study to investigate the association between daily exposure to landscape fire PM<sub>2.5</sub> and hospital admissions for cardiovascular events in 184 major Chinese cities. We developed a machine learning model combining outputs from chemical transport models, meteorological information and observed air pollution data to determine daily concentrations of landscape fire PM<sub>2.5</sub>. Furthermore, we fitted quasi-Poisson regression to evaluate the link between landscape fire PM<sub>2.5</sub> concentrations and cardiovascular hospitalizations in each city, and conducted randomeffects meta-analysis to pool the city-specific estimates. Here we show that, on a national scale, a rise of 1-µg/m<sup>3</sup> in landscape fire PM<sub>2.5</sub> concentrations is positively related to a same-day 0.16% (95% confidence interval: 0.01%-0.32%) increase in hospital admissions for cardiovascular disease, 0.28% (0.12%-0.44%) for ischemic heart disease, and 0.25% (0.02%-0.47%) for ischemic stroke. The associations remain significant even after adjusting for other sources of PM<sub>2.5</sub>. Our findings indicate that transient elevation in landscape fire PM<sub>2.5</sub> levels may increase risk of cardiovascular diseases.

Landscape fires have emerged as a growingly conspicuous and formidable menace worldwide. In recent years, a number of large-scale landscape fires have erupted across the globe<sup>1</sup>. For example, the 2019/ 20 Australian wildfires have burned millions of acres, causing significant social, economic, and environmental impacts that are still being felt by many Australians today<sup>2</sup>. Toxic smoke emitted by wildfires can spread over vast distances<sup>2,3</sup>, and cause direct and indirect impacts on human health that may have long-term consequences<sup>1,4</sup>. Robust projections suggest that as climate change worsens, the occurrence and severity of landscape fires will keep rising in the vast majority of world<sup>5,6</sup>, and that the fires are expected to result in excess morbidity and mortality<sup>1,4,7</sup>. According to the projections of the UN Environment Programme (UNEP), the world is set to witness a gradual escalation in catastrophic wildfires, with anticipated increases of 14% by 2030, 30% by 2050, and a substantial 50% by 2100.

Landscape fire smoke is a complex combination of small particles and harmful gases. Of the diverse pollutants originating from land-scape fires, fine particulate matter ( $PM_{2.5}$ ) is a major threat. The size of these particles allows them to penetrate the lungs and enter the alveoli, where they can pass through the alveolar epithelium and enter the bloodstream<sup>8</sup>. In addition, landscape fire smoke particles can interact with pulmonary neuroreceptors, activate neural pathways, and initiate inflammatory responses that could precipitate cardiovascular responses and thrombosis<sup>9</sup>.  $PM_{2.5}$  from landscape fire is considered to

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be more toxic than that from urban sources, as it exhibits unique chemical properties and is characterized by smaller particle size<sup>1,10</sup>. Additionally, it is frequently accompanied by concurrent exposure to other detrimental environmental factors, including elevated temperatures, which may exacerbate its health effects<sup>1</sup>. Compared with the extensive research on total PM<sub>2.5</sub>, there is significantly less research specifically focused on landscape fire PM<sub>2.5</sub>, especially concerning China. Recent studies from the North America, Europe, Australia, and Brazil have shown that exposures to landscape fire PM<sub>2.5</sub> were related to various health outcomes, including reduced lung function, asthma, and premature mortality<sup>11–16</sup>. PM<sub>2.5</sub> emitted by landscape fire smoke is associated with an estimated more than 675,000 deaths annually worldwide, primarily linked to cardiovascular issues<sup>17</sup>. Landscape fire smoke is recognized as an emerging and fast-growing threat to cardiovascular health worldwide<sup>18,19</sup>.

In China, since the devastating forest fire that occurred in the Greater Xing'an Mountains of Northeast China in 1987, there has been a growing focus on the study of landscape fires. In the past few decades, China has experienced one of the largest increases in the number of person-days affected by landscape fires<sup>20</sup>. Although the Chinese Government has regarded forest fires as a significant threat in recent decades, comprehensive studies investigating the features, causes, and environmental impacts of landscape fires at the national scale have remained scarce. As a result, there is still a significant lack of information available for effective landscape fire management. Studies reported that the ratio of particulate matter from landscape fires to total dust, as well as the ratio of its concentration to ambient PM<sub>2.5</sub>, has both shown an increasing trend, indicating a potential increase in the environmental influence caused by landscape fire PM<sub>2.5</sub> pollution<sup>21</sup>. Despite growing concern, there has been a lack of studies on the health impacts of landscape fire PM<sub>2.5</sub>, and to date, no study has assessed the effects of landscape fire PM<sub>2.5</sub> on cardiovascular morbidity in China.

In this study, we utilized a nationwide hospitalization dataset and sought to explore the links between landscape fire PM<sub>2.5</sub> and daily admissions for cardiovascular disease (CVD) in China.

# Results

#### Characteristics of study participants and exposures

Table 1 displays the characteristics of individuals enrolled in the UEBMI program. The study population consisted of 54.4% male individuals and 4.9% individuals aged ≥75. Table 2 summarizes the admission counts and environmental data in the 184 cities. The annual-average landscape fire PM<sub>2.5</sub> concentrations varied considerably, with an average of 1.7 μg/m³ (standard deviation 1.3 μg/m³) across the 184 cities. The daily landscape fire PM<sub>2.5</sub> concentrations ranged from 0 to 108.16 μg/m<sup>3</sup>. Figure S1 presents the landscape fire PM<sub>2.5</sub> probability density curve. Figure S2 illustrates the distribution of landscape fire PM<sub>2.5</sub>. During the study period, there were 1,815 days of exposure to substantial fire-sourced air pollution (SFAP). A day with SFAP is defined as a day when the daily PM<sub>2.5</sub> exceeds the WHO's 2021 daily guideline value (15  $\mu$ g/m<sup>3</sup>), and the landscape fire PM<sub>2.5</sub> accounts for at least 50% of the daily PM2.5. The annual-average landscape fire PM2.5 concentrations exhibited significant variations across study locations (Fig. 1). Over the study period, the average daily hospital admissions for CVD, IHD, and stroke were 47, 26, and 14 per city, respectively. Cities in the north had higher landscape fire PM<sub>2.5</sub> concentrations, and lower relative humidity and air temperature.

# Associations between landscape fire PM<sub>2.5</sub> and CVD

The associations of landscape fire  $PM_{2.5}$  with CVD, IHD, and ischemic stroke were almost linear (P for non-linearity > 0.05, Figs. S3–S5). Figure 2 presents the national estimates of the relations between landscape fire  $PM_{2.5}$  levels and cardiovascular outcomes at differing lags. The lag structures were similar for all outcomes. The most robust correlations were observed on the same day (lag 0) for the three health

conditions. Each 1- $\mu$ g/m³ increase of same-day landscape fire PM<sub>2.5</sub> concentrations corresponded to a 0.16% (95% CI: 0.01%–0.32%) increase in CVD admissions, 0.28% (0.12%–0.44%) increase in IHD, and 0.25% (0.02%–0.47%) increase in ischemic stroke. We also evaluated the relationships of PM<sub>2.5</sub> from other sources and CVD hospitalizations (Fig. 2). The CVD, IHD, and ischemic stroke admissions increased by 0.06% (95% CI: 0.04%–0.07%), 0.06% (95% CI: 0.05%–0.08%), and 0.06% (95% CI: 0.03%–0.09%), respectively.

# Stratified and meta-regression analyses

Figure 3 illustrates the stratified analyses results. We observed similar estimates for males and females (all P > 0.05). The associations by age varied by outcomes. The estimates for CVD were greater for patients aged 75 years and older compared to those aged 18 to 64 years but the difference did not reach statistical significance (P = 0.323). For ischemic stroke, the estimate was higher in the elderly, but this difference fell just slightly below the cutoff value for statistical significance (P = 0.048). For IHD, the largest estimate was observed in patients aged 18-64 years, but the difference between age groups was insignificant (P > 0.05). We observed higher effect estimates for all health outcomes in the northern region than in the southern region, although the differences were not always statistically significant (P > 0.05 for IHD). We also conducted stratified analysis by city GDP per capita, and did not observe significant modifications (Table S1). Table 3 presents the meta-regression results. The associations were more pronounced in cities with decreased relative humidity (P = 0.024). City GDP per capita and annual-average temperature did not modify the association (P = 0.677 and P = 0.302, respectively).

## Results of sensitivity analyses

The estimates were relatively unchanged after additional adjustment of other-source  $PM_{2.5}$  (Table S2). A 1-µg/m³ increment of landscape fire  $PM_{2.5}$  corresponded to a 0.16% (95% CI: 0–0.33%), 0.27% (95% CI: 0.10%–0.43%), and 0.25% (0–0.49%) increase in CVD, IHD and ischemic stroke admissions, respectively. Table S3 displays the results of sensitivity analyses. The substitution of different  $\it df$  for calendar day (6–8 per year) and temperature (5–7) did not affect the estimates. The negative control exposure showed a negative and insignificant association with admission for landscape fire  $PM_{2.5}$  (-0.08% (95% CI: -0.19%–0.03%)). The association remained when using landscape fire  $PM_{2.5}$  data from GEOS-Chem (percentage change, 0.14%; 95% CI: 0.01%–0.28%).

# **Discussion**

To our knowledge, this is the first and largest study to examine the associations between landscape fire PM<sub>2.5</sub> and cardiovascular risk in China. Transient increase in landscape fire PM<sub>2.5</sub> concentrations was consistently associated with increased admissions for CVD, IHD, and ischemic stroke. The strength of the associations differed across cities with varying annual average relative humidity levels.

The PM<sub>2.5</sub>-related disease burden primarily falls on CVD, which accounts for 60-80% of PM<sub>2.5</sub>-related deaths<sup>22</sup>. Previous studies consistently reported the respiratory health of landscape fire, but epidemiological research from around the world has yielded inconsistent findings on the relationship between landscape fire exposure and CVD<sup>4</sup>. Many studies investigating the effects of landscape fire PM<sub>2.5</sub> reported no associations with cardiovascular outcomes<sup>23–25</sup>, potentially due to their limited sample size. For example, a study performed in the United States reported that acute wildfire-specific PM<sub>2.5</sub> exposure increased the risk of respiratory diseases in the elderly population, but failed to observe a significant association of PM<sub>2.5</sub> with cardiovascular admissions<sup>12</sup>. Recently, a growing number of large studies demonstrated the hazardous effects of short-term landscape fire PM<sub>2.5</sub> exposures on cardiovascular hospitalizations in the U.S., Europe, and Brazil<sup>14,26–28</sup>, in line with our findings based on over 8.8

Table 1 | Demographic characteristics of individuals enrolled in the UEBMI program

Variables	Overall	Southern China <sup>a</sup>	Northern China <sup>a</sup>
Number of cities	184	94	90
Number of individuals	197 230 556	127 263 223	69 967 333
Age (years)			
18-64 (%)	172 616 807 (87.5)	113 036 386 (88.8)	59 580 421 (85.2)
65-74 (%)	14 553 516 (7.4)	8 376 202 (6.6)	6 177 314 (8.8)
≥75 (%)	9 645 159 (4.9)	5 448 893 (4.3)	4 196 266 (6.0)
Sex			
Male (%)	107 209 773 (54.4)	68 600 413 (53.9)	38 609 360 (55.2)
Female (%)	90 020 783(45.6)	58 662 810 (46.1)	31 357 973 (44.8)

<sup>&</sup>lt;sup>a</sup> Southern and northern regions separated by the Huai River-Qinling Mountains line. *UEBMI* urban employee basic medical insurance.

Table 2 | Summary statistics on daily hospital admissions for cardiovascular diseases, landscape fire  $PM_{2.5}$  levels, and meteorological conditions in 184 Chinese cities, 2014-17, by geographical region

Variable	Nationwide	South	North		
Number of cities	184	94	90		
Annual-average landscape fire PM <sub>2.5</sub> (mean (SD), µg/m³)	1.7 (1.3)	1.4 (0.7)	1.9 (1.6)		
Daily landscape fire $PM_{2.5}$ , range $(\mu g/m^3)$	0.00-108.16	0.00-66.26	0.00-108.16		
Annual-average temperature (mean (SD), °C)	14 (5)	18 (3)	10 (4)		
Annual-average relative humidity (mean (SD), %)	68 (12)	77 (5)	57 (8)		
Daily hospital admissions per city (mean (SD))					
Cardiovascular disease	47 (74)	33 (56)	51 (87)		
Ischemic heart disease	26 (53)	20 (35)	33 (66)		
Ischemic stroke	14 (28)	12 (26)	17 (29)		

SD standard deviation.

million CVD hospitalization records. It should be noted that landscape fire in this study encompasses not only wildfires but also other components, such as agricultural waste burning. We also explored the effects of landscape fire  $PM_{2.5}$  on two major cardiovascular outcomes, i.e., IHD and ischemic stroke, which is rarely reported in previous studies. Examining the cause-specific associations of cardiovascular outcomes with landscape fire  $PM_{2.5}$  has crucial implications for assessing the health impacts of landscape fire and its management.

Our previous nationwide study analyzed the effect of acute ambient PM25 exposure on daily CVD admissions in China and observed that an increase of 10-μg/m3 in concurrent day PM<sub>2.5</sub> concentrations was related to a 0.26% (95% CI 0.17%-0.36%) increase in hospitalizations for all CVD, 0.31% (0.22%-0.40%) for IHD, and 0.29% (0.18%-0.40%) for ischemic stroke<sup>29</sup>. A recent meta-analysis reported that cardiovascular morbidity increased by 0.38% for every 10-µg/m<sup>3</sup> increase in acute PM<sub>2.5</sub> exposure in China<sup>30</sup>. Studying the differences in the health effects of landscape fire PM<sub>2.5</sub> and PM<sub>2.5</sub> from other sources is meaningful. Aguilera et al. 31 discovered that the estimates for respiratory hospitalizations associated with PM<sub>2.5</sub> from wildfires were higher than those for PM<sub>2.5</sub> originating from other sources. In addition, Deflorio-Barker et al. also showed that wildfire PM<sub>2.5</sub> has a stronger effect on the respiratory system than PM<sub>2.5</sub> from other sources, but observed similar increased risk for cardiovascular outcomes<sup>26</sup>. An invitro study indicated that exposure to coarse PM from a peat fire led to greater lung inflammation in association with endotoxin and reactive oxygen species, whereas ultrafine PM had a more pronounced effect on cardiac responses<sup>32</sup>. The higher toxicity of PM<sub>2.5</sub> from landscape fire might be due to the difference in the chemical composition. Landscape fire PM<sub>2.5</sub> has higher content of small particles, including submicrometer and ultrafine particles. It is also characterized by a higher proportion of oxidative and proinflammatory constituents, including aldehydes and polycyclic aromatic hydrocarbon<sup>33</sup>. However, we did not observe clear evidence that the estimates for PM<sub>2.5</sub> from landscape fires were higher than those for PM<sub>2.5</sub> from other sources. Additionally, the evidence for IHD was marginal and could be due to chance, given the wide CI. Therefore, the interpretation of the results should be cautious, and future studies are needed to confirm these findings.

Despite the relatively low risk of cardiovascular outcomes attributed to landscape fire PM<sub>2.5</sub> for a single individual, the impact of widespread exposures affecting large populations results in a considerable disease burden. Identifying and educating vulnerable populations is a crucial intervention to mitigate the risk and safeguard cardiovascular health from PM<sub>2.5</sub> emissions from landscape fire<sup>18</sup>. Our analysis revealed no significant disparities in health outcomes between sexes. Notably, our results suggested that the effect of exposure appeared to be more pronounced in older adults, while statistical significance was not always achieved, which is largely in line with the findings of previous studies<sup>14,18,28,34</sup>. High susceptibility may be related to declining biological function and a high prevalence of chronic diseases in the elderly.

Few studies have examined modifying effects of city-level characteristics on the health impact induced by landscape fire PM<sub>2.5</sub>, likely due to a small number of study sites in previous studies. Our national analysis revealed that the impact of exposure was more pronounced in cities with lower levels of relative humidity. This observation is consistent with the fact that droughts are the most typical abnormal weather conditions for landscape fires<sup>35</sup>. Additionally, we examined the risk variation between southern and northern regions and found that the estimates were higher in the northern region. This is contrary to the findings of previous studies on total PM<sub>2.5</sub>. Two previous national studies conducted in China that examined the health effect of ambient PM2.5 reported greater impacts on CVD morbidity or mortality in the south than in the north<sup>29,36</sup>. There are multiple potential explanations for the regional discrepancies in effect size estimates. First, the higher landscape fire PM<sub>2.5</sub> levels in the north may partly explain the higher estimate in northern China. The exposure-response curve showed that the risk of CVD admissions increased monotonically across landscape fire PM<sub>2.5</sub> concentrations. Second, another possible factor contributing to regional heterogeneity in estimates is variations in the characteristics of enrolled individuals. The northern region of China has a higher percentage of individuals aged 75 years and older, who were more vulnerable to the detrimental effects of exposure. Third, the significant disparities in meteorological conditions may also contribute to the regional variation in effect estimates. The northern region has lower relative humidity, which could amplify the CVD effects, as shown in the meta-regression analysis.

Climate change is exacerbating the frequency and intensity of landscape fires worldwide, representing a perilous consequence of our warming planet<sup>1</sup>. Rising temperatures and prolonged droughts create ideal conditions for the ignition and rapid spread of fires<sup>6</sup>. The prolonged fire seasons, coupled with changing precipitation patterns, have altered the landscapes, making them more susceptible to ignition and prolonging the fire's duration. The resulting destruction not only devastates forests and wildlife habitats but also releases substantial amounts of carbon dioxide into the atmosphere, further fueling the vicious cycle of climate change<sup>1,5</sup>. Urgent global action to mitigate greenhouse gas emissions, coupled with effective land management strategies, is imperative to mitigate the devastating impacts of climate change-driven landscape fires. In urban China, the

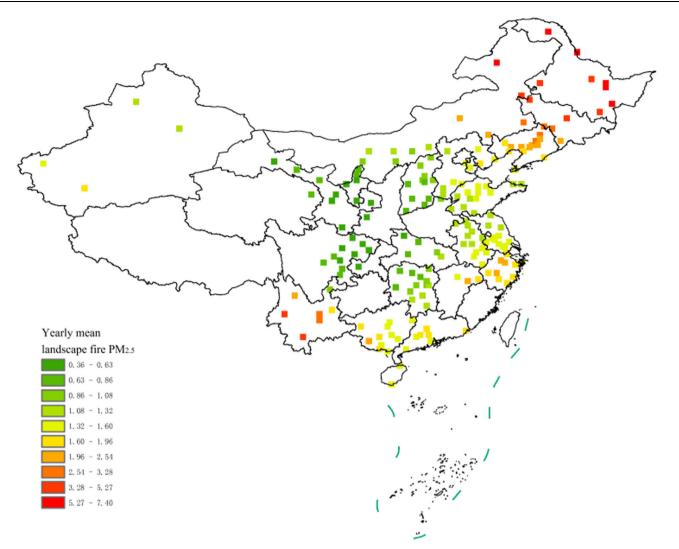


Fig. 1 | Yearly mean landscape fire PM<sub>2.5</sub> concentrations across China during 2014–2017. Squares represent study cities. The colors of the squares represent the yearly mean landscape fire PM<sub>2.5</sub> concentrations for each city.

proportion of landscape fire  $PM_{2.5}$  in total  $PM_{2.5}$  is indeed quite limited. However, considering the relatively significant impact of landscape fire  $PM_{2.5}$  on CVD, and the rising occurrence and severity of landscape fires, the health hazards caused by landscape fire  $PM_{2.5}$  cannot be ignored.

Our large epidemiological study included more than 8.8 million cardiovascular admissions in 184 cities across China. Given the large sample and wide geographical coverage, we were able to obtain consistent evidence of relationships between landscape fire PM<sub>2.5</sub> concentrations and hospitalizations for multiple cardiovascular causes. We used the same statistical method across the cities, enhancing the internal comparison of findings across these cities and the external comparison with the results of other studies. Therefore, our study should provide more generalized evidence supporting the effects of landscape fire PM<sub>2.5</sub> on the circulatory system. However, it should be noted that the confidence intervals of the results were wide. Furthermore, it is important to acknowledge that air pollution in urban China was very high, while the levels of PM<sub>2.5</sub> from landscape fires were low during the study period, making the selected study area less than ideal for investigating the impact of landscape fires. Moreover, the model's accuracy may not be sufficient to effectively differentiate the impacts of landscape fires from other sources. Consequently, caution should be exercised in interpreting the results, and further studies are necessary to validate our findings.

A significant limitation of this study was that the results rely heavily on the models utilized to estimate landscape fire PM<sub>2.5</sub> exposure. Although the overall accuracy of the machine learning model in capturing the major characteristics of landscape fire PM<sub>2.5</sub> distribution has been validated in our previous studies 10,14,34,37, exposure error may occur when using pollution data at a coarse resolution. Nevertheless, this error is mainly of the Berkson type, which means it is statistically uncorrelated with the observed variable. This bias does not significantly affect the estimates of the association between exposure and response, but it does decrease precision, resulting in wider confidence intervals<sup>38,39</sup>. Second, diagnostic errors may have introduced misclassification bias. However, such errors are unlikely to be related to PM<sub>2.5</sub> exposure and thus may result in a downward bias in the estimates. Third, the lack of data on city-specific characteristics, such as lifestyles and chronic disease burden, hindered further study of factors modifying the correlation between landscape fire PM2.5 and cardiovascular disease. Fourth, the impacts of landscape fire PM<sub>2.5</sub> on other CVD conditions, such as deep venous thrombosis, pulmonary embolism, myocardial infraction, and unstable angina, were not assessed due to the unavailability of health data. Fifth, this analysis only encompassed urban employees, leaving the associations in urban residents without any formal employment or rural residents unclear. Since landscape fires predominantly occur in suburban or uninhabited regions, urban employees may not accurately represent

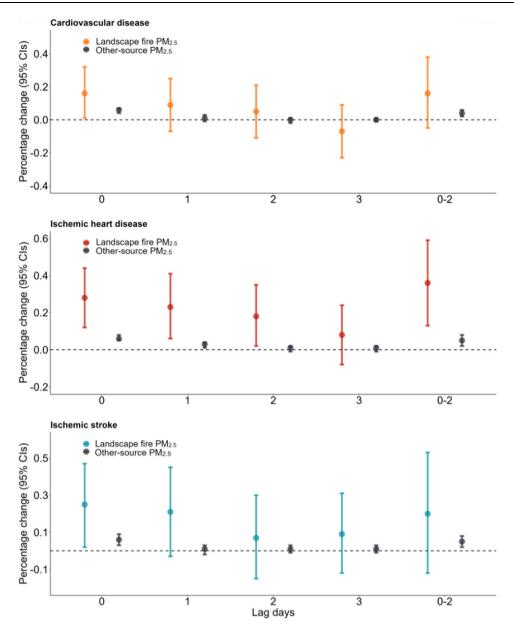


Fig. 2 | National estimates of the relations between landscape fire and other-source  $PM_{2.5}$  levels (per 1- $\mu$ g/m³) and cardiovascular outcomes at differing lags. Points represent the estimated change in cardiovascular admissions. Vertical lines

represent the 95% confidence interval. The sample size used to estimate these changes consisted of 8834533 hospital admissions for cardiovascular causes across 184 Chinese cities. Source data are provided as a Source Data file.

the population most affected by such events. This study may have unintentionally overlooked the full extent of landscape fire impacts, specifically on rural populations. Given the variations in socio-demographic characteristics and levels of landscape fire  $PM_{2.5}$  between rural and urban areas, the generalizability of our findings should be approached with caution. Future studies should aim to include more representative samples to better understand these dynamics. Sixth, this study focused on the impacts of landscape fire  $PM_{2.5}$  and may have overlooked the complex interplay of various pollutants, including the absence of landscape fire  $PM_{10}$ , which is known to have significant health effects.

This national study in China found associations between transient increases in landscape fire  $PM_{2.5}$  levels and hospitalizations for total cardiovascular diseases, ischemic heart disease, and ischemic stroke. Our study also provided evidence that the acute effects of landscape fire  $PM_{2.5}$  on cardiovascular health were modified by certain individual-and city-level characteristics.

## Methods

# Health and socioenvironmental data

In this nationwide time-series analysis, we collected admission records between 2014 and 2017 from the Urban Employee Basic Medical Insurance (UEBMI) database, as described in our previous publications<sup>29,40</sup>. The UEBMI is one of the three primary healthcare insurance plans in China, offering health insurance to both current and former urban employees, and covering 280 million individuals in 2016. More information have been previously published<sup>29,40</sup>. Typically, each billable medical service requires a claim, and it includes data on individual's fundamental demographics, admission dates, and main diagnosis upon discharge (International Classification of Diseases [ICD] code and text). We extracted daily city-specific counts of hospital admissions for CVD (I00–I99) as well as its two main subtypes (ischemic heart disease (IHD, ICD-10 codes I20–I25) and ischemic stroke (I63)) based on the primary diagnoses using ICD code or text of disease diagnosis. We stratified daily admissions based on sex and age

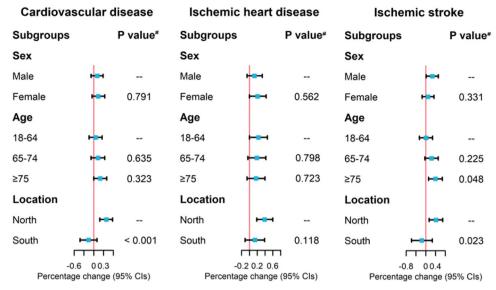


Fig. 3 | National estimates of the relations between landscape fire PM $_{2.5}$  levels (lag 0, per 1- $\mu$ g/m $^3$ ) and cardiovascular outcomes stratified by sex, age, and geographical region. \* P value (two-sided) obtained from Z-test for the difference between the two risk estimates derived from subgroup analysis. The P value in the figure, indicated as <0.001, is specifically 0.0007. Points represent the estimated

change of cardiovascular admissions. Vertical lines represent the 95% confidence interval. The sample size used to estimate these changes consisted of 8834533 hospital admissions for cardiovascular causes across 184 Chinese cities. Source data are provided as a Source Data file.

ranges (18–64, 65–74, and ≥75 years). In addition, we gathered city-specific meteorological data, including daily mean relative humidity and temperature, from the China Meteorological Data Sharing Service System<sup>40</sup>. We also collected data on gross domestic product (GDP) per capita for each city. Due to the city-specific nature of the health information, which consisted of daily counts of CVD admissions without any individual identifiers, the data were anonymised and analyzed at aggregate level and no participants were contacted. This study was granted an exemption from the requirement for Institutional Review Board approval by the Ethics Committee of Peking University Health Science Center, Beijing, China. The need for informed consent was also waived by the Institutional Review Board.

# Estimation of landscape fire and all-source PM<sub>2.5</sub>

Daily landscape fire  $PM_{2.5}$  at  $0.25^{\circ} \times 0.25^{\circ}$  (-28 km  $\times$  28 km) spatial resolution during the study period were estimated by machine learning model, combining information from chemical transport model, observed air pollution data and meteorological conditions<sup>41</sup>. This dataset is an improved version compared with the one described by our previous studies<sup>10,14,37,42</sup>. For each day, city-level daily landscape fire  $PM_{2.5}$  exposures were calculated by averaging the daily exposure of all  $0.25^{\circ} \times 0.25^{\circ}$  grids within the city boundary weighted by population size of each grid. Additional information regarding data estimation,

Table 3 | Multivariable meta-regression results of the modification effects of city-level characteristics on the associations between landscape fire  $PM_{2.5}$  (lag 0) and daily hospital admissions for cardiovascular disease in 184 cities in China, 2014–2017

Variables	Percentage change	95% CI	P value*
Relative humidity (%)	-0.210	-0.392 - 0.028	0.024
Temperature (°C)	-0.186	-0.539 - 0.169	0.302
GDP per capita (¥10,000)	-0.182	-1.037 - 0.681	0.677

<sup>¥10,000 (£1169; \$1456; €1377)</sup> 

CI confidence interval, GDP gross domestic product.

validation, and adjustment can be found elsewhere<sup>41</sup>. Briefly, the model was developed using 9,528,180 valid daily average PM<sub>2.5</sub> observations of 5,661 stations from 73 countries and territories during 2000-2019, and reached a high accuracy in estimating all-source daily average  $PM_{2.5}$  (10-fold CV:  $R^2 = 0.91$ , root mean squared error [RMSE] = 8.47 µg/ m<sup>3</sup>). Our machine learning models also demonstrated a high level of accuracy in estimating all-source daily average PM<sub>2.5</sub> in the 184 urban cities (10-fold CV:  $R^2 = 0.87$ , RMSE = 14.27  $\mu$ g/m<sup>3</sup>). The estimation of daily all-source PM<sub>2.5</sub> and landscape fire PM<sub>2.5</sub> were both based on the data obtained from the China National Environmental Monitoring Centre (http://www.cnemc.cn/en/). Daily landscape fire PM<sub>2.5</sub> concentrations were estimated as the differences between model simulations with and those without fire emissions. The data on fire emissions was sourced from the Global Fire Emissions Database (version 4.1 including small fires, GFED4.1s). This database recorded aerosol releases from six types of fires: boreal forests, tropical forests, savannas, grasslands, shrublands, temperate forests, peatlands, and agricultural waste burning. The data collection relied on satellite analysis of burned areas and active fire monitoring<sup>41</sup>.

# Statistical analysis

We adopted a two-stage time-series approach to derive the relationships between landscape fire PM<sub>2.5</sub> and CVD morbidity<sup>10,14</sup>. In the first stage, we employed a quasi-Poisson regression to investigate the city-specific association of daily landscape fire PM<sub>2.5</sub> concentrations with admissions. We included several covariates in our model to align with the methods employed in prior studies 10,14,34: (1) A natural cubic spline of calendar day with 7 degrees of freedom (df) per year to control seasonality and long-term trends; (2) natural cubic splines of 21-day moving average temperature with 6 df and 7-day moving average relative humidity with 3 df; (3) two categorical variables for public holidays and day of week. Based on prior studies 10,14,34, we estimated the effects of landscape fire PM<sub>2.5</sub> for the same day (lag 0) and its lagged effects up to 3 days (lag 1, lag 2, and lag 3 days), as well as for cumulative exposure over the same and previous 2 days (lag 0-2). In the second stage, we combined the city-specific estimates at the national and regional level by random-effects meta-analyses. To assess potential non-linear associations, we utilized a cubic spline

<sup>\*</sup>P-value (two-sided) obtained from meta-regression analysis, and no adjustments were made for multiple comparisons.

with two knots at the 25th and 75th percentiles of  $PM_{2.5}$  concentrations across all cities. Next, we combined the concentration-response associations between landscape fire  $PM_{2.5}$  and CVD morbidity at the national level.

We performed subgroup analyses by sex, age, GDP per capita, and geographical region (south and north regions, defined using the Huai River-Qinling Mountains line). The difference in estimates between strata was assessed via Z-test<sup>29,43</sup>. We also evaluated effect modification of the association of landscape fire PM2.5 levels with cardiovascular admissions by city characteristics, including annual-average temperature, relative humidity, and GDP per capita using meta-regression models<sup>29</sup>. To test the robustness of the association, we changed the df of calendar day and meteorological variables. We also included othersource PM<sub>2.5</sub> in the model to test its potential confounding effects. We also employed a negative exposure control to address the influence of unmeasured confounding variables<sup>44,45</sup>. We included exposures occurring after admission (lead) as negative exposure controls. Furthermore, we examined the impacts of landscape fire PM2.5 on cardiovascular admissions using landscape fire PM2.5 data from GEOS-Chem.

We conducted the first-stage analyses using R program and the second-stage analyses using Stata 12, and a two-sided P < 0.05 was considered statistically significant. The mgcv package was used to fit a quasi-Poisson regression, and the"metareg" function to fit meta-regression. The effects of landscape fire PM<sub>2.5</sub> on CVD admissions were presented as percentage changes and 95% confidence intervals in daily admissions per 1- $\mu$ g/m³ increase in PM<sub>2.5</sub> concentrations.

## Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

# Data availability

All data supporting the findings of this study are available within this manuscript and its Supplementary Information files. Publicly available data is found here: meteorological data can be downloaded from the China Meteorological Data Sharing Service System (http://data.cma.cn/). modern-Era Retrospective analysis for Research and Applications version 2 (MERRA-2) data, biomass burning emissions inventory of Global Fire Emissions Database version 4.1 (GFED V4.1) data, and anthropogenic emissions inventory of EDGAR version 4.2 data that support the GEOS-Chem model development and landscape fire PM<sub>2.5</sub> simulation in this study are available from https://gmao.gsfc. nasa.gov/reanalysis/MERRA-2/, https://daac.ornl.gov/VEGETATION/ guides/fire\_emissions\_v4\_R1.html, and http://edgar.jrc. ec.europa.eu/, respectively. Health data from the Urban Employee Basic Medical Insurance database used in this study are available under restricted access for the identifiable nature of the data and data use agreements. Access can be obtained by contacting the National Insurance Claims for Epidemiological Research (NICER) Group, School of Public Health, Peking University; contact email, 0016156078@bjmu.edu.cn. The request will be answered within 12 weeks. The data can be used through collaborative research with authors. The duration of data availability is set for a period of two years following publication. Source data are provided with this paper. Source data are provided with this paper.

# **Code availability**

Codes utilized for analyses have been made available through the GitHub repository: https://github.com/DonnaWang21/Tian-Wildfire-related-PM2.5-code.

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# **Author contributions**

Y.H.T., Y.M.G, and Y.H.H. contributed to the study concept. Y.M.G. and Y.H.H. had full access to all the data in the study and take responsibility for the integrity of the data. Y.H.T., Y.D.Y.M., and R.B.X. contributed to the statistical analysis and tables' development of this article. Y.H.T., Y.D.Y.M., R.B.X., S.S.L, Y.W., Y.M.G., and Y.H.H. interpreted the findings and drafted the article. All the authors contributed to the critical revision of the article for important intellectual content.

# **Competing interests**

The authors declare no competing interests.

# **Additional information**

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