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# Long-term impacts of wildfire smoke on human health

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## Copyright notice

# Contents

## List of abbreviations

| | |
|---|---|
| WFS | Wildfire smoke |
| LFS | Landscape fire smoke |
| $PM_{2.5}$ | Particulate matter with a diameter of ≤2.5μm |
| $O_3$ | Ozone |
| NOx | Nitrogen oxides |
| VOCs | Volatile organic compounds |
| US | United States |
| UK | United Kingdom |
| RESP | Respiratory |
| CVD | Cardiovascular disease |
| COPD | Chronic obstructive pulmonary disease |
| RCP | Representative concentration pathway |
| HAs | Hospital admissions |
| EDVs | Emergency department visits |
| LOCP | Lung, and lip, oral cavity and pharynx |
| HR | Hazard ratio |
| RR | Relative risk |
| CI | Confidence interval |
| IBGE | Brazilian National Institute of Statistics |
| AD | Alzheimer's disease |
| VAD | Vascular dementia |

## Abstract

Although the short-term health risks of wildfire smoke have been widely assessed, the long-term health risks remain underexplored. Using national data from the UK and Brazil, this thesis aims to investigate the long-term health risks associated with exposure to wildfire smoke. The global daily wildfire smoke $PM_{2.5}$ data during 2000-2019 were estimated by a 3-D chemical transport model (GEOS-Chem), and calibrated by a machine learning method, achieving high accuracy.

This thesis begins with a systematic review that incorporates 36 original studies, providing a comprehensive and up-to-date synthesis of the existing literature. Through a systematic search, detailed synthesis, and rigorous assessment of literature quality, I found that existing literature primarily focused on the prevalence of mental health issues, lacked high-quality risk estimates, insufficiently explored vulnerable populations, was overrepresented by studies from high-fire developed countries, and suffered from poor quality and high heterogeneity across studies. Based on these findings, potential research directions were proposed, such as expanding the geographical scope to include regions with varying levels of economic development and wildfire exposure, broadening the range of wildfire-related pollutants studied, expanding the scope of health outcomes assessed, improving the quality of quantitative research designs, and enhancing the control of confounding variables.

Using national cohort data from the UK during 2004-2019, I employed time-varying Cox regression methods to explore the association of long-term wildfire smoke $PM_{2.5}$ exposure with a variety of mortality outcomes (including all-cause, nonaccidental, neoplasm, cardiovascular, respiratory, mental, cancer-specific), and dementia incidence (including all-cause, Alzheimer's disease, vascular dementia). A wide range of covariates were adjusted for, including socio-demographic factors (age, sex, ethnic group, educational attainment, employment, income, Townsend deprivation index), environmental factors (non-fire $PM_{2.5}$), and health risk factors (body mass index, smoking, alcohol consumption). I also conducted a series of sensitivity analyses and subgroup analyses to check the robustness of the findings and identify potential high-risk groups.

Using national cardiovascular mortality data from Brazil during 2010-2018, I employed a variant of the difference-in-differences model to explore the long-term impacts of wildfire smoke $PM_{2.5}$ exposure on cardiovascular mortality, with adjustments for a range of time-space varying confounders, including temperature, population density, and gross domestic product. I also examined the modifying effects of age and sex, and estimated the mortality burden of wildfire smoke $PM_{2.5}$ exposure during 2010-2018 in Brazil.

Through a systematic review and several original studies, this thesis provides a scientific framework for understanding the long-term health risks associated with wildfire smoke $PM_{2.5}$ exposure. These findings offer valuable guidance for public health by highlighting the need for preventive measures and targeted interventions to mitigate wildfire smoke exposure, especially in vulnerable regions and populations. Additionally, this research underscores critical gaps and suggests directions for future studies, such as improving quantitative research quality, expanding geographical diversity, and enhancing control of confounding variables. This foundation is essential for advancing policies and research aimed at reducing the long-term impacts of wildfire smoke exposure in a warming climate.

## Declaration

This thesis is an original work of my research and contains no materials which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

Signature:

Print Name: YUAN GAO

Date: 6/11/2024

## Publications during enrolment

Publications included in the thesis:

1. **Gao Y**, Huang W, Yu P, Xu R, Yang Z, Gasevic D, Ye T, Guo Y, Li S. Long-term impacts of non-occupational wildfire exposure on human health: A systematic review. *Environmental Pollution* 2023; 320: 121041.
2. **Gao Y**, Huang W, Xu R, Gasevic D, Liu Y, Yu W, Yu P, Yue X, Zhou G, Zhang Y, Liu H, Song J, Guo Y, Li S. Association between long-term exposure to wildfire-related $PM_{2.5}$ and mortality: A longitudinal analysis of the UK Biobank. *Journal of Hazardous Materials* 2023; 457: 131779.
3. **Gao Y**, Huang W, Yu P, Xu R, Gasevic D, Yue X, Coelho M, Saldiva PHN, Guo Y, Li S. Wildfire-related $PM_{2.5}$ and cardiovascular mortality: A difference-in-differences analysis in Brazil. *Environmental Pollution* 2024; 347: 123810.
4. **Gao Y**, Huang W, Yu P, Xu Z, Xu R, Gasevic D, Liu Y, Yue X, Zhou G, Zhang Y, Song J, Liu H, Guo Y, Li S. Wildfire-related $PM_{2.5}$ and cause-specific cancer mortality. *Ecotoxicology and Environmental Safety* 2024; 285: 117023.
5. **Gao Y**, Huang W, Wu Y, Xu Z, Ye T, Xu R, Gasevic D, Yue X, Zhou G, Zhang Y, Song J, Liu H, Guo Y, Li S. Long-term exposure to low-level wildfire-sourced $PM_{2.5}$ and dementia incidence in the UK (Submitted).

**Other related publications during enrolment:**

1. **Gao Y**, Huang W, Zhao Q, et al. Global, regional, and national burden of mortality associated with cold spells during 2000-19: a three-stage modelling study. *The Lancet Planetary Health* 2024; 8(2): e108-e16.
2. Huang W, **Gao Y**, Xu R, Yang Z, Yu P, Ye T, Ritchie EA, Li S, Guo Y. Health effects of cyclones: A systematic review and meta-analysis of epidemiological studies. *Environmental Health Perspectives* 2023;131 (8): 086001.
3. Wang J, Li W, Huang W, **Gao Y**, Liu Y, Teng Q, Zhao Q, Chen M, Guo Y, Ma W. The associations of ambient fine particles with tuberculosis incidence and the modification effects of ambient temperature: A nationwide time-series study in China. *Journal of Hazardous Materials* 2023; 460: 132448.
4. Zhao Q, Yu P, Mahendran R, Huang W, **Gao Y**, Yang Z, Ye T, Wen B, Wu Y, Li S, Guo Y. Global climate change and human health: Pathways and possible solutions. *Eco-Environment & Health* 2022; 1(2): 53-62.
5. Guo Y, Wu Y, Wen B, Huang W, Ku K, **Gao Y**, Li S. Floods in China, COVID-19, and climate change. *The Lancet Planetary Health* 2020; 4(10): e443-e4.

## Thesis including published works declaration

I hereby declare that this thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

This thesis includes four original papers published in peer reviewed journals and one submitted publication. The core theme of the thesis is long-term impacts of wildfire on human health. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the student, working within the School of Public Health and Preventive Medicine under the supervision of Professor Shanshan Li.

The inclusion of co-authors reflects the fact that the work came from active collaboration between researchers and acknowledges input into team-based research.

In the case of chapters 2-6, my contribution to the work involved the following:

| Thesis Chapter | Publication Title | Status | Nature and % of student contribution | Co-author name(s) Nature and % of Co-author's contribution* | Co-author(s), Monash student Y/N* |
|---|---|---|---|---|---|
| 2 | Long-term impacts of non-occupational wildfire | Published | 80%, conceptualization, literature search and screening, data analysis, results | 1) Wenzhong Huang, 5%, data extraction, supervision, results | No for all but Wenzhong Huang, Pei |

| | | | | | |
|---|---|---|---|---|---|
| | exposure on human health: A systematic review | | interpretation, writing first draft, submitting and revising | interpretation, manuscript editing.<br>2) Pei Yu, 1%, results interpretation, manuscript editing.<br>3) Rongbin Xu, 1%, manuscript editing.<br>4) Zhengyu Yang, 1%, manuscript editing.<br>5) Danijela Gasevic, 1%, results interpretation, supervision and manuscript editing.<br>6) Tingting Ye, 1%, results interpretation, supervision and manuscript editing.<br>7) Yuming Guo, 5%, conceptualization, results interpretation, supervision, project Administration, funding acquisition, manuscript editing.<br>8) Shanshan Li, 5%, conceptualization, results interpretation, supervision, project Administration, funding acquisition, manuscript editing. | Yu, Rongbin Xu, Zhengyu Yang, Tingting Ye |
| 3 | Association between long-term exposure to wildfire-related $PM_{2.5}$ and mortality: A longitudinal analysis of the UK Biobank | Published | 73%, conceptualization, data analysis, results interpretation, writing first draft, submitting and revising manuscript. | 1) Wenzhong Huang, 5%, data linkage, supervision, results interpretation, manuscript editing.<br>2) Rongbin Xu, 2%, supervision, results interpretation, manuscript editing.<br>3) Danijela Gasevic, 2%, supervision, results interpretation, manuscript editing.<br>4) Yanming Liu, 1%, manuscript editing.<br>5) Wenhua Yu, 1%, manuscript editing.<br>6) Pei Yu, 1%, manuscript editing.<br>7) Xu Yue, 1%, manuscript editing.<br>8) Guowei Zhou, 1%, data management, manuscript editing.<br>9) Yan Zhang, 1%, data management, manuscript editing. | No for all but Wenzhong Huang, Wenhua Yu, Pei Yu |

| | | | | | |
|---|---|---|---|---|---|
| | | | | 10) Hong Liu, 1%, data management, manuscript editing. 11) Jiangning Song, 1%, data management, manuscript editing. 12) Yuming Guo, 5%, conceptualization, results interpretation, supervision, project Administration, funding acquisition, manuscript editing. 13) Shanshan Li, 5%, conceptualization, results interpretation, supervision, project Administration, funding acquisition, manuscript editing. | |
| 4 | Wildfire-related $PM_{2.5}$ and cause-specific cancer mortality | Published | 75%, conceptualization, data analysis, results interpretation, writing first draft, submitting and revising manuscript. | 1) Wenzhong Huang, 3%, data linkage, supervision, results interpretation, manuscript editing. 2) Zhihu Xu, 2%, supervision, results interpretation, manuscript editing. 3) Rongbin Xu, 2%, supervision, results interpretation, manuscript editing. 4) Danijela Gasevic, 2%, supervision, results interpretation, manuscript editing. 5) Yanming Liu, 1%, manuscript editing. 6) Xu Yue, 1%, manuscript editing. 7) Guowei Zhou, 1%, data management, manuscript editing. 8) Yan Zhang, 1%, data management, manuscript editing. 9) Jiangning Song, 1%, data management, manuscript editing. 10) Hong Liu, 1%, data management, manuscript editing. 11) Yuming Guo, 5%, conceptualization, | No for all but Wenzhong Huang, Zhihu Xu |

| | | | | | |
|---|---|---|---|---|---|
| | | | | results interpretation, supervision, project Administration, funding acquisition, manuscript editing. 12) Shanshan Li, 5%, conceptualization, results interpretation, supervision, project Administration, funding acquisition, manuscript editing. | |
| 5 | Wildfire-related $PM_{2.5}$ and cardiovascular mortality: A difference-in-differences analysis in Brazil | Published | 75%, conceptualization, data analysis, results interpretation, writing first draft, submitting and revising manuscript. | 1) Wenzhong Huang, 6%, supervision, results interpretation, manuscript editing. 2) Pei Yu, 2%, supervision, results interpretation, manuscript editing. 3) Rongbin Xu, 2%, supervision, manuscript editing. 4) Danijela Gasevic, 2%, supervision, results interpretation, supervision and manuscript editing. 5) Xu Yue, 1%, results interpretation, supervision and manuscript editing. 6) Micheline de Sousa Zanotti Stagliorio Coˆelho, 1%, results interpretation, manuscript editing. 7) Paulo Hilario Nascimento Saldiva, 1%, results interpretation, manuscript editing. 8) Yuming Guo, 5%, conceptualization, results interpretation, supervision, project Administration, funding acquisition, manuscript editing. 9) Shanshan Li, 5%, conceptualization, results interpretation, supervision, project Administration, funding acquisition, manuscript editing. | No for all but Wenzhong Huang |

| | | | | | |
|---|---|---|---|---|---|
| 6 | Long-term exposure to low-level wildfire-sourced $PM_{2.5}$ and dementia incidence in the UK | Submitted | 76%. Conceptualization, data cleaning, analysis and interpretation, writing first draft, submitting and revising manuscript. | 1) Wenzhong Huang, 3%, data linkage, supervision, results interpretation, manuscript editing. 2) Yao Wu, 2%, data management, results interpretation, manuscript editing. 3) Zhihu Xu, 1%, supervision, results interpretation, manuscript editing. 4) Tingting Ye, 1%, supervision, manuscript editing. 5) Rongbin Xu, 1%, supervision, results interpretation, manuscript editing. 6) Danijela Gasevic, 1%, supervision, results interpretation, manuscript editing. 7) Xu Yue, 1%, manuscript editing. 8) Guowei Zhou, 1%, data management, manuscript editing. 9) Yan Zhang, 1%, data management, manuscript editing. 10) Jiangning Song, 1%, data management, manuscript editing. 11) Hong Liu, 1%, data management, manuscript editing. 12) Yuming Guo, 5%, conceptualization, results interpretation, supervision, project Administration, funding acquisition, manuscript editing. 13) Shanshan Li, 5%, conceptualization, results interpretation, supervision, project Administration, funding acquisition, manuscript editing. | No for all but Wenzhong Huang, Yao Wu, Zhihu Xu, Tingting Ye |

I have renumbered sections of published papers in order to generate a consistent presentation within the thesis.

**Student name:** YUAN GAO

**Student signature:**

**Date:** 6/11/2024

I hereby certify that the above declaration correctly reflects the nature and extent of the student's and co-authors' contributions to this work. In instances where I am not the responsible author I have consulted with the responsible author to agree on the respective contributions of the authors.

**Main Supervisor name:** Shanshan Li

**Main Supervisor signature:**

**Date:** 15/11/2024

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# Chapter 1. Introduction

## 1.1 Background and rationale

### 1.1.1 Wildfire introduction

Landscape fires are fires occurring in natural and cultural landscapes, including unplanned wildfires and planned fires (e.g., prescribed fires, agricultural fires)[1,2]. Wildfires are unplanned fires characterized by uncontrollability and unexpectedness that typically occur in vegetated ecosystems[2]. Various similar terms are used to describe wildfires based on the type of ecosystem they occur in, such as bushfires, forest fires, grassland fires and vegetation fires[3]. Wildfires in this thesis specifically refer to a broad category of landscape fires originating from boreal forests, tropical forests, savannas, grasslands, shrublands, temperate forests, peatlands, and agricultural waste[2]. The initiation and development of wildfires are influenced and determined by the interaction of ecological, climatic, and human factors, requiring three essential conditions: fuels, oxygen, and ignition[4]. Specifically, the availability and flammability of fuels are mainly influenced by ecological and climatic factors such as ecological composition, vegetation species, vegetation density, vegetation structure, soil moisture, temperature, humidity, and rainfall[5-7]. Dryer, hotter, and windier climate conditions are more conducive to the initiation and spread of wildfires[3,5]. Wind serves as the main transporter of oxygen, while lightning acts as the main natural source of ignition[3,5], while human activities influence wildfire risks primarily through ignition creation, land alteration, and human-induced climate

change[3]. Accidental and deliberate ignitions resulting from human activities contribute to the occurrence of wildfires, such as those ignited by discarded cigarettes, campfires, and sparks from power lines[8]. Anthropogenic land alteration and management contribute to the increased probability of wildfires, such as production-related deforestation (e.g., agricultural lands, pastures)[9], and expanded built environment (e.g., settlements, infrastructure)[10]. For example, global wildland-urban interface areas expanded by 12.56% during 1985-2020, with the majority from the United States (US), Brazil, China, India, and Australia[10].

### 1.1.2 Climate change and wildfire

The intensity, frequency and severity of wildfires have been increasing regionally during the past decades, driven by climate change and human activities[5]. With global warming, climate change has created more favorable conditions for wildfires, such as higher temperatures and evaporation contributing to fuel desiccation, increased winds facilitating oxygen transport, and variant lightning potentially increasing regional ignition[5,11]. Global temperature during 2001-2020 was 0.99°C above that during 1850-1900, with a more rapid increase observed since 1970[12]. In 2023, the global average temperature reached the highest recorded level during 1850-2023, exceeding the 20$^{th}$ century average (13.9°C) by 1.18°C[13]. Rising temperatures lengthen wildfire seasons and increase wildfire potential in specific regions by increasing

water evaporation, altering vegetation structure and weather patterns, which makes ice melt earlier and fuel (e.g., soil, vegetation) be drier and more flammable[14,15]. A positive feedback pathway was suggested between fire-weather interaction, where radiative impacts of wildfire smoke enhanced particulate matter with a diameter of $\leqslant$2.5μm ($PM_{2.5}$) exposure and increased extreme wildfire potential by altering meteorological conditions, such as reduced humidity and rainfall[16].

Wildfire risks and threats are rising around the world. Globally, although the burned area was estimated to decrease by 27% during 2001-2019, the length of fire-prone season and the extremity of fire conditions (measured by the frequency of 95$^{th}$ fire weather index, which is an comprehensive index of fire intensity with the consideration of fuel aridity and weather variables) increased by 27% and 54% annually during 1979-2019, respectively[17]. During 2003-2023, the frequency and magnitude of global extreme wildfires (defined as >99.99$^{th}$ of daily summed fire radiative power) rose by a 2.2- and a 2.3- fold, respectively[18].

Wildfires are projected to be more frequent, extensive, and intense. Globally, compared with 2010-2020, catastrophic wildfires will increase by 36% to 57% under the representative concentration pathway (RCP) 6.0 emission scenario during 2090-2100, according to a projection from the UN Environment

Programme[19]. Compared with 1996-2016, global warming will lead to a 29% expansion in areas frequently susceptible to wildfires during 2070-2099 under the RCP 8.5 emission scenario, with the most significant increase occurring in areas with Boreal (e.g., Canada, Russia, Alaska) and Temperate (e.g., China, Europe) climate classified by Köppen–Geiger climate criteria[20].

### 1.1.3 Wildfire impacts

Since 2020, several catastrophic wildfires have been witnessed around the world, such as 2019-2020 Australia bushfires, 2020-2021 California megafires, 2020-2021 Brazil Amazon wildfires, 2021 Russia wildfires, and 2023 Canada wildfires. As an integral part of the ecosystem, the impacts of wildfires on the ecological environment are bidirectional. Beneficial impacts of wildfires on the ecological environment include promoting species, habitat and ecosystem regeneration, while harmful impacts include biodiversity threats (e.g., extinction risks, habitat destruction), soil contamination and erosion, water and air degradation, and climate change via greenhouse gas (e.g., carbon dioxide, methane) emission[21-23]. However, the impacts of wildfires on social economy and public health are negative, such as casualties and disabilities of people and animals, burning and destroying of properties and buildings, destruction and disruption of infrastructure (e.g., road, communication) and services (e.g., water, electricity), and health hazards from wildfire flames, smoke and associated health stressors[3]. For example, the 2023 record-breaking wildfires, with the

burning of 15.0 million hectares and the duration of six months in Canada, caused extensive environmental impacts and substantial social impacts, such as emitting 763 teragrams of carbon, deteriorating air quality with record-high $PM_{2.5}$ levels, evacuating >232,000 people, destroying hundreds of homes, and causing eight firefighter fatalities[24].

### 1.1.4 Wildfire smoke

Wildfire smoke (WFS) is a chemical mixture rich in gases and aerosols, the composition and content of which varies depending on fuel conditions, weather factors, and combustion efficiency[25]. WFS contains various health-hazardous gaseous and aerosol emissions, such as hydrocarbons, ozone ($O_3$), carbon monoxide, sulfur dioxide, nitrogen oxides (NOx), volatile organic compounds (VOCs), PM, organic/inorganic carbon, and metal particles[26]. WFS is capable of long persistence and spatiotemporal spread, which is associated with smoke plume dynamics, meteorological factors, and geographic topography[27]. For example, during the Canadian wildfires, monitored concentrations of multiple air pollutants in Maryland, US, increased significantly, such as $O_3$, VOCs, NOx, and $PM_{2.5}$[28]. Globally, during 2000-2019, an increasing trend was observed for the population-weighted WFS $PM_{2.5}$, but not for WFS $O_3$[2]. Distribution of WFS $PM_{2.5}$ and $O_3$ varies geographically, with higher contributions from Central Africa, South America, northern Australia, and Southeast Asia[2].

The large release of hazardous and irritating emissions from wildfires poses short-term health risks (e.g., asthma). These emissions can also disperse with the wind over vast distances and linger in the atmosphere for extended periods, exposing populations both near and far from the fire source to long-lasting, chronic, and cumulative health impacts[29]. In recent years, as global attention to wildfires has increased, research on the health hazards associated with WFS PM has grown significantly. Compared with urban PM, WFS PM was reported to be finer and more spherical, with higher levels of icons ($SO_4^{2-}$, $NO_3^-$, $F^-$), and metal particles (Mn, Co, Sb)[30]. WFS $PM_{2.5}$ is considered a major health threat due to its toxic impacts, as its smaller particle size allows it enter the bloodstream[3]. Higher toxicity of WFS $PM_{2.5}$ than non-WFS $PM_{2.5}$ has been proposed by several epidemiological studies[31,32]. Specifically, observational findings from Southern California[32] and Brazil[31] reported that WFS $PM_{2.5}$ had a greater impact on respiratory hospitalizations and cancer mortality than non-WFS $PM_{2.5}$. Twin and family findings reported that long-term exposure to WFS $PM_{2.5}$ was associated with distinct DNA methylation patterns in Australian women, with significant findings in genes related to inflammation and disease pathways, which showed non-overlap with those linked to non-WFS $PM_{2.5}$[33].

### 1.1.5 Health impacts of wildfires

Wildfires are detrimental to physical and mental health by wildfire flames, smoke, and associated health stressors. In general, wildfire health impacts can

be summarized as short-term, sub-chronic, and long-term, despite no standardized definition. Typically categorized according to the thresholds of impact occurrence and duration, with short-term impacts referring to impacts within 1-month, sub-chronic impacts referring to impacts between 1-12 months, and long-term impacts referring to impacts over 12 months.

#### 1.1.5.1 Short-term impacts of wildfires

Short-term impacts of wildfires include casualties and burns from direct flame/radiant heat exposure, mortality and morbidity from indirect WFS exposure, mental disorders (e.g., trauma, fear) resulting from indirect stressors (e.g., experience, witness, evacuation) exposure[5]. Recently, short-term impacts of WFS have been increasingly explored, revealing positive associations with diverse mortality and morbidity outcomes[4].

Previous evidence with risk estimation at the global and regional levels has observed a positive association between WFS and mortality, including all-cause, respiratory (RESP, including all-, chronic obstructive pulmonary disease [COPD]), and all-cardiovascular disease (CVD) mortality. Concretely, for 749 locations worldwide, during 2000-2016, WFS $PM_{2.5}$ (3-day moving average [exposure on the current day and the previous 2 days, lag 0-2]) annually accounted for 0.62% (95% confidence interval [95% CI]: 0.48, 0.75) of all-cause, 0.55% (0.43, 0.67) of all-CVD, and 0.64% (0.50, 0.78) of all-RESP mortality,

while WFS $O_3$ (3-day moving average of lag 0-2) accounted for 0.58% (0.31, 0.85), 0.41% (-0.10, 0.91), and 0.86% (0.18 to 1.51) to these respective mortality[34,35]. For 55 low- and middle-income countries worldwide, during 2000-2014, each 1μg/$m^3$ increase in $PM_{2.5}$ from landscape fire smoke (LFS) was associated with a 2.31% (1.50, 3.13) increase in children (<18 years) mortality[36]. Regionally, in Brazil, during 2000-2016, each 10μg/$m^3$ increase in WFS $PM_{2.5}$ (average of lag 0-14) was associated with increases of 3.1% (2.4, 3.9) in all-cause, 2.6% (1.5, 3.8) in all-CVD, 7.7% (5.9, 9.5) in all-RESP mortality, respectively[37]. During 2017 Portugal wildfires, each 10μg/$m^3$ increase in WFS $PM_{10}$ was associated with increases of 0.89% (0, 1.77) in natural and 2.34% (0.99, 3.66) in cardiorespiratory mortality, respectively[38]. In Sydney Australia, during 2010-2020, each 10μg/$m^3$ increase in WFS $PM_{2.5}$ (cumulative of lag 0-2) was associated with a 3.2% (0.3, 6.2) increase in all-cause mortality[39]. In Washington US, during 2006-2017, WFS $PM_{2.5}$ was associated with increases of 1.0% (-1.0, 4.0%) in non-traumatic, 9.0% (0.0, 18.0) in all-RESP, and 14.0% (2.0, 26.0) in COPD mortality, respectively, during 2006-2017[40]. Among hemodialysis patients in US, during 2008-2012, each 10μg/$m^3$ increase in WFS $PM_{2.5}$ was associated with increases of 4% (1.0, 7.0) for lag0 and 7% (1.0, 12.0) for lag 0-30 in all-cause mortality[41]. Modifications of age and gender have been observed in the short-term mortality impacts of WFS. Females and older adults (≥ 60 years) showed higher vulnerability to all-cause mortality associated with WFS $PM_{2.5}$ at lag 0-14[37]. Older adults (≥ 65 years) showed higher vulnerability

to all-cause mortality at cumulative lag 0-3[39], while adults aged 45-64 years showed higher vulnerability to all-RESP mortality at lag0[40].

Acute WFS exposure is linked to elevated risks of diverse morbidity (as measured by morbidity surveillance, medications, hospital admissions [HAs], emergency department visits [EDVs], out hospital visits, ambulance dispatches, self-reported investigations), primarily RESP (all-[42-50], asthma[43,48,50-53], chronic lower RESP disease[48], COPD[52], upper RESP infection[54], breathing problems[55], chest pain[55]) and CVD (all-[43,44,47-49], cardiac arrests[55-57]) events, as well as all-cause morbidity[42,47], circulatory disease[46], skin disease (atopic dermatitis, itch)[54,58], cerebrovascular disease (stroke)[59,60], mental disorders (reduced attention[61], schizophrenia[48]). A meta-analysis published in 2019 summarized that each 10μg/m$^3$ increase in LFS $PM_{2.5}$ was associated with a 6% (2.0, 9.0), and a 7% (4.0, 9.0) increase in asthma HAs and EDVs, respectively. Another latest meta-analysis published in 2024 summarized that, each 1μg/m$^3$ increase in WFS $PM_{2.5}$ at lag0 was associated with a 25% (9, 42) increase in all-RESP HAs, and a 36% (19, 53) increase in all-RESP EDVs[4]. However, the pooled risk estimation for CVD morbidity was not statistically significant[4]. Modifications of age, gender, and race have been observed in the short-term morbidity impacts of WFS. Female[53] and African Americans[44] showed higher vulnerability to asthma associated with WFS $PM_{2.5}$. Older adults (≥65 years) showed higher vulnerability to EDVs from all-RESP, asthma, all-CVD, hypertension, and

dysrhythmia associated with WFS $PM_{2.5}$ at lag 0-3[49,53]. Middle-aged adults (19-64 years) showed higher vulnerability to all-RESP disease associated with WFS $PM_{2.5}$, and those aged 5-64 years were more vulnerable to asthma EDVs[43]. While children (≤9 years) and older adults (≥80 years) showed higher vulnerability to all-cause HAs associated with WFS $PM_{2.5}$ at lag 0-1[47]. Adults (>55 years) showed higher vulnerability to heart disease EDVs associated with WFS $PM_{2.5}$ at lag3[44].

#### 1.1.5.2 Sub-chronic impacts of wildfires

Previous evidence suggested that wildfires have sub-chronic impacts on birth abnormalities (e.g., reduced weight and defects at birth, premature birth, stillbirth, non-normal gestation length)[54,62-64], mental disorders (e.g., suicide mortality, anxiety and post-traumatic stress disorder prevalence)[65,66], and coccidioidomycosis morbidity[67]. For example, a meta-analysis summarized that each 10μg/$m^3$ increase in gestational WFS $PM_{2.5}$ exposure was associated with a -21.71g (-32.92, -10.50) decrease in birth weight[54]. WFS $PM_{2.5}$ exposure in rural counties of US, during 2007-2019, each 1μg/$m^3$ increase in monthly WFS $PM_{2.5}$ was associated with a 2.0% increase in suicide mortality[68]. Coccidioidomycosis hospitalizations increased by 20% (5, 38) and 1% (1, 2) in the first and third months after any WFS exposure, respectively[67].

#### 1.1.5.3 Long-term impacts of wildfires

Long-term impacts of wildfires are inconclusive, focusing primarily on mental and psychological prevalance[66,69]. For example, a meta-analysis summarized that, in Australia, psychological distress was prevalent in 14% of the general populations in the 2-4 years after bushfires, while psychological problems were prevalent in 28%-47.6% of firefighters in the 2-7 years after bushfires[69].

## 1.2 Knowledge gaps

As summarized above, wildfires are well-established health hazards. Despite the growing number of studies on the impacts of wildfires, most of them have focused on short-term impacts. There are relatively fewer studies focusing on long-term impacts of wildfires on humans. Short-term and sub-chronic studies, while valuable, may overlook delayed, cumulative, and long-lasting effects. Addressing this research gap will provide critical insights for understanding long-term health impacts, informing public health interventions and developing effective risk adaptation and mitigation strategies associated with wildfires. Furthermore, there is a lack of systematic summaries of the available long-term findings, recognition of research gaps, as well as indications of possible research directions. Therefore, in Chapter 2, a systematic review was provided to fill this research gap.

This review incorporated 36 original epidemiological studies exploring long-term impacts (>1 year) of wildfires. Through a systematic summary, the following research gaps were recognized. First, most evidence came from developed countries with higher exposure, including Australia, USA, and Canada[2]. Evidence from developed countries with lower exposure, developing countries, and multi-regions is needed. Second, most evidence focused on the prevalence of negative mental and psychological issues. Original quantification of the extensive health risks posed by wildfires is urgently needed. Third, most study designs were cohort and cross-sectional surveys with certain biases. Evidence of high-quality and low-bias research design is expected. Fourth, existing evidence showed high heterogeneity in analytical methods, confounder control, and exposure assessment. Evidence with more precise methods of exposure assessment and analysis, as well as more comprehensive and uniform control of confounders, is necessary. Fifth, high-vulnerability populations need further exploration.

### 1.3 Thesis aims

This thesis aimed to provide a systematic overview of available evidence, research gaps, and future directions for the long-term impacts of wildfires. Then, based on these gaps, given that WFS $PM_{2.5}$ is a major component of WFS and poses a significant health threat to human beings due to the inflammatory response and oxidative stress it triggers upon entering the bloodstream[3], a set

of studies was scientifically designed to understand long-term WFS $PM_{2.5}$ risks of mortality and morbidity, with the results guiding health protection and promotion efforts. Specifically, this thesis aimed to:

(1) provide a systematic summary to summarize previous findings, identify research gaps, and discover possible directions;

(2) explore the association between WFS $PM_{2.5}$ and mortality;

(3) explore the association between WFS $PM_{2.5}$ and cause-specific cancer mortality;

(4) explore the association between WFS $PM_{2.5}$ and cause-specific cardiovascular mortality;

(5) explore the association between WFS $PM_{2.5}$ and dementia incidence.

### 1.4 Thesis overview

In this thesis, I first conducted a systematic review of the long-term impacts of wildfires by summarizing previous findings, identifying potential gaps, and guiding potential directions. Then, I added existing knowledge from the following two dimensions using UK Biobank (UKB) and Brazil data: mortality and morbidity. Subgroup analyses were also provided to detect potentially vulnerable groups.

This thesis is presented by publication, including four peer-reviewed publications, one submitted study, and seven chapters:

(1) Chapter 1: Introduction to the thesis background, rationale, aims, structure, and significance.

(2) Chapter 2: A systematic review of long-term impacts of non-occupational wildfire exposure on human health. This study has been published in *Environmental Pollution*.

(3) Chapter 3: Exploring the association between long-term exposure to WFS $PM_{2.5}$ and mortality using the UKB data. This study has been published in *Journal of Hazardous Materials*.

(4) Chapter 4: Exploring the association between long-term exposure to WFS $PM_{2.5}$ and cause-specific cancer mortality using the UKB data. This study has been published in *Ecotoxicology and Environmental Safety*.

(5) Chapter 5: Exploring the association between WFS $PM_{2.5}$ and cause-specific cardiovascular mortality using the Brazil data. This study has been published in *Environmental Pollution*.

(6) Chapter 6: Exploring the association between long-term exposure to WFS $PM_{2.5}$ and dementia incidence using the UKB data.

(7) Chapter 7: Thesis summary of the main findings, comparisons, strengths, limitations, significance, future directions, and conclusions.

### 1.5 Significance

Considering the destructiveness and impairments of wildfires and the long-persistence and long-transport of WFS, this thesis has important implications

for understanding and communicating the long-term health risks of wildfires, as well as formulating targeted mitigation and adaptation strategies such as health education, early warning and allocation of medical resources.

The significant threats and impacts of wildfires to human health are evident. However, to date, the long-term risks of wildfires and vulnerable populations remain greatly unexplored, resulting in potential knowledge gaps, inadequate responses, and poor resilience. This thesis explored the long-term impacts of WFS $PM_{2.5}$ on various mortality outcomes and dementia incidence, which filled knowledge gaps by adding risk and vulnerability knowledge.

Understanding the long-term health risks of wildfires and the vulnerable populations also help develop targeted strategies and preventions to reduce risks and protect health. Targeted and effective mitigation and adaptation strategies can minimize costs and maximize benefits. For example, at the national level, it can help in developing targeted mitigation and adaptation measures, such as fire source and prescribed burning management, and fire early detection and response. At the government and public health sector levels, it allows for the formulation of targeted policies and strategies to protect public health, such as long-term health surveillance and management, and targeted medical resource allocation. At the community level, it can enhance adaptation and strengthen resilience through health education and targeted psychological

support. At the individual level, it helps to perceive health risks, raise protection awareness, and take personalized measures to protect their health.

## Chapter 2. Long-term impacts of non-occupational wildfire exposure on human health: A systematic review

In Chapter 1, I have introduced the hazards of wildfires, the current state and gaps of existing research, and the aims and significance of my thesis. To address the research gap in the lack of a systematic review summarizing previous large body of findings on the long-term impacts of wildfires, I conducted this systematic review, which incorporated 36 original studies and provided the most up-to-date and systematic synthesis of the previous findings. Compared with the existing scoping review on the same topic restricted to literature from 2011-2021[70], our review conducted a more comprehensive search, a more detailed synthesis, and a more rigorous literature quality assessment. This systematic review has been published and cited as follows: **Gao Y**, Huang W, Yu P, Xu R, Yang Z, Gasevic D, Ye T, Guo Y, Li S. Long-term impacts of non-occupational wildfire exposure on human health: A systematic review. *Environmental Pollution* 2023; 320: 121041. Full contents are presented in Chapter 2 and Appendix 1.

Several research gaps were found through the systematic summary, including main focus on the prevalence of mental issues, lack of high-quality risk estimates, insufficient exploration of vulnerable populations, main concentration in high-exposure developed countries, poor quality of literature, and high heterogeneity of studies. Potential research directions were proposed,

such as broadening the geographical scope to include regions with varying levels of economic development and wildfire exposure, expanding the scope of wildfire-related pollutants studied and the range of health outcomes assessed, improving the quality of quantitative research designs and enhancing the control of confounding variables. This chapter provides the theoretical foundation and scientific basis for the original research in the following chapters 3-6.

## Chapter 3. Association between long-term exposure to wildfire-related $PM_{2.5}$ and mortality: A longitudinal analysis of the UK Biobank

In Chapter 2, I presented a systematic review on the long-term impacts of wildfires and identified potential gaps in this field. To partially address certain research gaps, I conducted this original study in the UK, a developed country with low-fire exposure, to explore associations and vulnerabilities of WFS $PM_{2.5}$ with mortality. The mortality data during 2004-2019 were obtained from the national UK cohort collected by the UK Biobank, and the WFS $PM_{2.5}$ data (spatial resolution: 0.1° × 0.1°) during 2000-2019 were estimated by a 3-D chemical transport model (GEOS-Chem), and calibrated by a machine learning method. The association of WFS $PM_{2.5}$ with mortality was investigated by a time-varying Cox Regression model, with adjustments for individual- and area-level confounders, such as age, sex, income, and area-level economic development. Several sensitivity and subgroup analyses were also conducted. The results found higher long-term risks associated with WFS $PM_{2.5}$ (3-year cumulative) for all-cause, non-accidental, and neoplasm mortality. This study has been published and cited as follows: **Gao Y**, Huang W, Xu R, Gasevic D, Liu Y, Yu W, Yu P, Yue X, Zhou G, Zhang Y, Liu H, Song J, Guo Y, Li S. Association between long-term exposure to wildfire-related $PM_{2.5}$ and mortality: A longitudinal analysis of the UK Biobank. *Journal of Hazardous Materials* 2023; 457: 131779. Full contents are presented in Chapter 3 and Appendix 2.

## Chapter 4. Association between wildfire-related $PM_{2.5}$ and cause-specific cancer mortality

Long-term exposure to wildfire-related $PM_{2.5}$ has been linked to cancer mortality. However, prospective evidence is limited for investigating the association between long-term WFS $PM_{2.5}$ exposure and cancer-specific mortality, as well as identifying the potentially vulnerable population. Chapter 3 found a higher neoplasm mortality risk associated with WFS $PM_{2.5}$. However, little is known about the more sensitive cancer subtypes and more vulnerable populations. To address this research gap, on the basis of the findings of Chapter 3, I conducted a more in-depth exploration of the associations between WFS $PM_{2.5}$ and cancer-specific mortality, using the same data and statistical method. The results found higher long-term risks of cancer mortality from total, lung, and lip, oral cavity and pharynx (LOCP) associated with WFS $PM_{2.5}$. Participants being retired showed a more pronounced risk of lung cancer mortality. These findings revealed sensitive cancer subtypes and vulnerable populations of WFS $PM_{2.5}$, underscoring the critical need for targeted prevention and intervention strategies to mitigate the risks and protect these high-risk groups.

This study has been published and cited as follows: **Gao Y**, Huang W, Yu P, Xu Z, Xu R, Gasevic D, Liu Y, Yue X, Zhou G, Zhang Y, Song J, Liu H, Guo Y, Li S. Wildfire-related $PM_{2.5}$ and cause-specific cancer mortality. *Ecotoxicology*

*and Environmental Safety* 2024; 285: 117023. Full contents are presented in Chapter 4 and Appendix 3.

## Chapter 5. Wildfire-related $PM_{2.5}$ and cardiovascular mortality: A difference-in-differences analysis in Brazil

Chapters 3-4 contributed to the understanding of long-term mortality risks associated with WFS $PM_{2.5}$ using prospective designs from the UK. Although a non-statistically significant risk of cardiovascular mortality was found, this potential risk cannot be excluded due to study limitations and heterogeneities (e.g., study design, population characteristics). Therefore, in Chapter 5, I conducted this original study using national mortality data from Brazil, a developing country with high-fire exposure, to explore the associations and vulnerabilities between WFS $PM_{2.5}$ and CVD-specific mortality, as well as to estimate the attributable mortality burden during 2010-2018. The CVD mortality data during 2010-2018 were obtained from the Brazil Mortality Information System, and the WFS $PM_{2.5}$ data (0.25° × 0.25°) during 2002-2018 were estimated by a 3-D chemical transport model (GEOS-Chem), and calibrated by a random forest model.

This study adopted a variant of the difference-in-differences model and adjusted for time-space varying confounders, including temperature, population, and gross domestic product (GDP). Statistically significant concentration-response associations were found between WFS $PM_{2.5}$ and total-CVD, ischaemic heart disease, and stroke. The modification effects of age and gender were not identified. During 2010-2018, WFS $PM_{2.5}$ was estimated to

account for 35,847 CVD deaths, equivalent to 17.77 per 100,000 populations. A higher mortality burden was observed in the Central-West and Southeast regions of Brazil. These findings highlight the significant cardiovascular mortality risks and burdens associated with WFS $PM_{2.5}$, emphasizing the urgent need for implementing targeted protective measures, particularly in the central-west and southeast regions of Brazil.

This study has been published and cited as follows: **Gao Y**, Huang W, Yu P, Xu R, Gasevic, D, Yue X, Coelho M, Saldiva PHN, Guo Y, Li S. Wildfire-related $PM_{2.5}$ and cardiovascular mortality: A difference-in-differences analysis in Brazil. *Environmental Pollution* 2024; 347: 123810. Full contents are presented in Chapter 5 and Appendix 4.

## Chapter 6. Wildfire-related $PM_{2.5}$ and dementia incidence

In Chapters 3-5, I examined the associations and vulnerabilities of WFS $PM_{2.5}$ with all-cause, cause-specific, cancer-specific, and CVD-specific mortality. However, limited evidence exists regarding the association and vulnerability of WFS $PM_{2.5}$ with morbidity. To partially address this research gap, Chapter 6 presents an original study conducted in the UK to explore the associations and vulnerabilities of WFS $PM_{2.5}$ with dementia incidence. The dementia data during 2004-2019 were obtained from the UK Biobank, and the WFS $PM_{2.5}$ data (0.1° × 0.1°) during 2000-2019 were estimated by a 3-D chemical transport model (GEOS-Chem), and calibrated by a machine learning method. The association of WFS $PM_{2.5}$ with dementia incidence was investigated by a time-varying Cox Regression model, with adjustments for individual- and area- level confounders, such as age, sex, income, and area-level economic development. The results found statistically significant associations between WFS $PM_{2.5}$ (1-year cumulative) and all-cause, Alzheimer's disease (AD), and vascular dementia (VAD). More pronounced effects were found among low-educated individuals. Longer-term effects were observed for Alzheimer's disease (4-year), and vascular dementia (5-year). These findings contributed to understanding the potential neurological impacts of WFS $PM_{2.5}$, highlighting the need for attention to and prevention of the long-term impacts of wildfires. Full contents are presented in Chapter 6 and Appendix 5.

# Chapter 7. Discussion and conclusions

This thesis provides a systematic review and original evidence on the long-term impacts of wildfires on mortality and morbidity, an area of research that remains largely underexplored. By focusing on the delayed, cumulative, and long-lasting effects of wildfires, it provides critical insights that inform public health strategies and long-term risk adaptation and mitigation efforts, filling an important gap in existing wildfire health research. Specifically, Chapter 1 provides an overview of wildfires, including the determinants and impacts, the relationship with climate change, the composition of WFS, as well as the associated health impacts, and the existing knowledge gaps. Chapter 2 presents a systematic review of long-term impacts of wildfires, summarizing previous findings and identifying potential gaps, while also recommending further research directions. In Chapters 3-6, original investigations were performed using data from the UK and Brazil to partially address these gaps by adding new scientific evidence.

## 7.1 Main findings of this thesis

Chapter 2 provides a systematic review on long-term impacts of wildfires with the inclusion of 36 articles published during 1987-2022. Through this systematic review, I found that existing evidence was predominantly of low quality, came from developed countries with high-fire exposure (e.g., Australia, Canada), and focused on the prevalence of mental issues. Although limited evidence exists reporting long-term impacts of wildfires on mortality from COVID-19 and CVD,

morbidity from RESP disease, height, lung function, and general health, high-quality quantitative evidence was limited. In addition, high-heterogeneity in study methods and confounders was observed. Finally, vulnerable populations were poorly explored. Further high-quality quantitative risk assessments are recommended to explore the associations and potential vulnerabilities of extensive wildfire measurements with extensive health outcomes across wider geographical areas (e.g., multiple regions, developed countries with low-fire exposure, developing countries).

Chapter 3 presents an original analysis to assess the association and potential vulnerability of WFS $PM_{2.5}$ with mortality using the UKB national cohort collection involving approximate 500,000 participants by the method of time-varying Cox regression. This study filled the abovementioned gaps by focusing on the UK, a developed country with low-fire exposure[2], while also providing high-quality prospective evidence through the comprehensive quantitative analyses on the associations and potential vulnerabilities of WFS $PM_{2.5}$ with mortality. After adjusting for a range of confounders (e.g., sociodemographic factors, socioeconomic status, behavioral risks), I found statistically significant associations between 3-year cumulative WFS $PM_{2.5}$ and all-cause, nonaccidental, and neoplasm mortality. However, non-statistically significant associations were observed between WFS $PM_{2.5}$ and CVD, RESP, or mental

mortality. Moreover, the potential vulnerable groups for all-cause mortality associated with WFS $PM_{2.5}$ were not observed through stratified analysis.

In Chapter 4, building on the increased risk of neoplasm mortality identified in Chapter 3, I performed a deeper analysis investigating the associations and potential vulnerabilities of WFS $PM_{2.5}$ with cancer-specific mortality, focusing on the most concerning subtypes of neoplasm. The comprehensive analysis provided prospective evidence, which identified the most sensitive cancer subtypes and vulnerable populations associated with WFS $PM_{2.5}$, offering rigorous findings to guide targeted prevention strategies. I found that, after controlling a series of confounders, statistical associations were found between WFS $PM_{2.5}$ and lung, LOCP cancer mortality. More pronounced effects were found among retired individuals.

Although no statistically significant association was observed between WFS $PM_{2.5}$ and CVD mortality using the UKB collection, the potential cannot be ruled out due to study limitations and heterogeneities (e.g., study design, population characteristics). Therefore, in Chapter 5, I performed another original analysis to investigate the associations and potential vulnerabilities of WFS $PM_{2.5}$ with CVD-specific mortality using the national Brazil data by the method of variant difference-in-differences analysis. This study filled the research gap by focusing on Brazil, a developing country with high-fire exposure. After controlling

spatiotemporally varying confounders, statistically significant concentration-response associations were found between WFS $PM_{2.5}$ and mortality from total-CVD, ischaemic heart disease and stroke. The modification effects of age and gender were not observed. During 2010-2018, WFS $PM_{2.5}$ was estimated to account for 35,847 CVD deaths, equivalent to 17.77 per 100,000 populations in Brazil.

In Chapter 6, my focus shifted to the impacts of wildfires on morbidity, which is also a research gap identified in the systematic review. I performed an original analysis to investigate the associations and potential vulnerabilities of WFS $PM_{2.5}$ with dementia incidence using the UKB collection by the method of time-varying Cox regression. After controlling potential confounders (e.g., age, sex, education, income), statistically significant associations were found between WFS $PM_{2.5}$ and all-cause, AD, and VAD. More pronounced effects were found among low-educated individuals. Longer-term effects were observed for AD (4-year), and VAD (5-year).

In summary, I found that different long-term WFS $PM_{2.5}$ exposure metrics showed significant associations with different health outcomes. 1-year exposure was associated with CVD mortality (especially total-, ischaemic heart disease, stroke), lung cancer mortality, and all-cause dementia incidence. 3-year exposure was associated with mortality from total causes and neoplasm

causes (especially total-cancer, lung cancer, LOCP cancer). 2-year and 5-year exposure was associated with mortality from total causes and neoplasm causes, and morbidity from VAD. While 4-year exposure was associated with mortality from total causes and neoplasm causes, and morbidity from AD and VAD. These results suggested that the long-term effects of WFS $PM_{2.5}$ might vary across different tissues, organs and systems, potentially due to factors such as the toxic effects, immune system responses, and tissue-organ-specific susceptibility[71].

### 7.2 Comparison with previous studies

The results of this thesis indicated that long-term risks of WFS $PM_{2.5}$ exposure for mortality from all-cause, non-accident, neoplasm (especially total-cancer, lung cancer, LOCP cancer), CVD (especially total-CVD, ischaemic heart disease, stroke), and morbidity from dementia incidence (especially all-cause, AD, and VAD), most of which were consistent with findings from previous studies[72-75], although the risk effect estimates might not be directly comparable due to differences in exposure metrics (e.g., mean vs. cumulative exposure). Specifically, a US study found that 12-month moving average WFS $PM_{2.5}$ exposure was associated with increased mortality from non-accidental causes, and CVD (especially ischaemic heart disease), contributing to an estimated 11,415 (95% CI: 6,754, 16,075) non-accidental deaths annually, with stronger effects observed in individuals aged $\geqslant$ 65 years and significant positive

interactions with extreme heat[72]. A Brazilian retrospective study reported that each 1-μg/$m^3$ increase in the 2-year moving average of WFS $PM_{2.5}$ exposure was associated with a 2% (1,3) increase in the total cancer mortality[73]. However, the statistical association between WFS $PM_{2.5}$ and mortality from lung cancer and LOCP cancer was not found[73]. Possible reasons for heterogeneity include study design, study population, exposure selection, and study methods. A cohort study from California reported that each 1-μg/$m^3$ increase in the 3-year mean of WFS $PM_{2.5}$ exposure was associated with an 18% (3, 34) increase in the dementia incidence with stronger effects observed among participants being < 75 years, racial minorities, and high-poverty[74]. Another US cohort study reported that each interquartile range increase in the 10-year mean of WFS $PM_{2.5}$ exposure was associated with a 5% (2, 8) increase in the dementia incidence[75].

### 7.3 Implications of this thesis

Before this thesis, little was known about the long-term wildfire risks and potential vulnerability[4]. At the beginning of this thesis (Chapter 2), I systematically summarized and critically evaluated previous research evidence on the long-term impacts of wildfires, which contributed greatly to understanding current research status and identifying potential research gaps and further directions. Then, this thesis (Chapters 3-6) observed long-term risks of WFS $PM_{2.5}$ on mortality from all-cause, non-accident, neoplasm (especially

all-cause cancer, lung cancer, LOCP cancer), CVD (especially all-cause, ischaemic heart disease, stroke), and incidence from all-cause dementia, AD, and VAD. Higher-vulnerability to WFS $PM_{2.5}$ was observed in retired individuals for lung cancer and low-educated individuals for all-cause dementia. The findings add new knowledge on the risks and potential vulnerabilities of wildfires on mortality and morbidity. This thesis not only partially fills knowledge gaps by expanding the geographical scope, broadening the examined health outcomes, and providing robust research findings, but also provides a theoretical basis for mitigation and adaptation strategies in the context of climate change, especially for high-vulnerability groups and regions. Tailored strategies and targeted measures are suggested as follows.

At the country and government level, both in UK and Brazil, several mitigation and adaptation measures can be considered. First, mitigation measures can be taken to prevent human-induced wildfire occurrences by targeting the determinants of wildfires, such as implementing effective ignition and fuel management (e.g., prescribed burns, fuelbreaks), establishing comprehensive wildfire prevention policies, developing effective wildfire risk monitoring and warning systems[4,76,77]. Second, adaptation measures can be taken to suppress incipient wildfires and prevent their spread, such as improving land-use planning and implementing effective emergency response[78]. Third, tailored wildfire intervention measures and health promotion strategies are encouraged

to be customized according to the vulnerabilities of regions and populations. For example, a higher vulnerability WFS $PM_{2.5}$ was identified among retired individuals for lung cancer and low-educated individuals for all-cause dementia in the UK. Additionally, larger wildfire-attributed CVD deaths were observed in older adults ($\geqslant$60 years) and in the Southeast region of Brazil. Enhanced interventions targeting these vulnerabilities could yield greater health benefits.

At the health sector level, enhanced regional protective measures are advised for UK and Brazil based on local long-term health risks and vulnerabilities of wildfires to achieve greater health benefits through lower investments. First, more academic explorations are encouraged in order to more comprehensively identify local long-term health threats and vulnerabilities, thereby facilitating the development of more targeted protective measures. Second, targeted measures can be tailored to mitigate known long-term health threats and vulnerabilities, such as establishing health risk monitoring and surveillance system, organizing regular sensitive disease screening, implementing targeted health education and intervention measures, strengthening fire-affected health support and services, and enhancing healthcare preparedness and responses.

At the community level, five components of a good disaster-resilience community are socialization and networking, knowledge and learning, leadership and governance, preparedness and responses, infrastructure and

resources[79]. Potential community-based mitigation and adaptation measures encompass resource and response coordination, social cooperation and communication (e.g., establishing community support forums), knowledge education and dissemination (e.g., organizing workshops, hosting community lectures, utilizing online platforms for resource sharing), emergency response training and exercises, high-resistance infrastructures and resources (e.g., constructing fire-resistant buildings, maintaining wildfire-emergency access roads), and accessible medical and health support services[4,79,80].

At the individual level, individual health promotion measures mainly include protection awareness education and protection strategy implementation, especially for high-risk populations, although there is little evidence to evaluate the effectiveness of interventions. Potential individual promotion measures encompass enhancing risk awareness, avoiding wildfire area, checking air quality, wearing air purifiers and masks, reducing outdoor activities, and seeking timely medical services and psychological support[3-5,81].

In conclusion, the essential protective measure, regardless of long-term or short-term health impacts, is to reduce wildfire incidence and exposure. Although wildfires are an unavoidable and essential component of ecosystems, effective mitigation and adaptation strategies can reduce their human-induced incidence, spread, and exposure. At the same time, it is crucial to acknowledge

that existing risk assessments of long-term health risks and vulnerabilities associated with wildfires are significantly lacking. This inadequacy potentially hinders comprehensive risk perception and effective protection implementation. Further exploration of associations, vulnerabilities and mechanisms is highly expected to support and expand existing knowledge.

### 7.4 Strengths of this thesis

This thesis has some strengths. Chapter 2 presents the first systematic summary and critical evaluation of previous evidence on long-term health impacts of wildfires, which contributed significantly to synthesizing previous findings, identifying research gaps, and guiding further directions. On the basis of this systematic review, I conducted four high-quality novel quantitative explorations on long-term impacts of WFS $PM_{2.5}$ on mortality and morbidity using national health data from UK and Brazil.

A key strength of this thesis was the refined exposure assessment, which enhanced the accuracy and reliability of the results. In addition, this thesis employed rigorous and robust statistical methods, including adjustments for both individual- and area-level confounders, stratified analyses to assess vulnerabilities, and rigorous model specifications to ensure the stability and reliability of the findings. The large national sample sizes further enhanced the statistical power and generalizability of the results. Furthermore, the health

outcomes were determined using medical and death records, which to some extent minimized recall bias compared to self-reported data, ensuring greater reliability and accuracy in the assessments.

This thesis also has made significant contributions to the field of long-term health risks associated with wildfires. Chapter 3 is the first study to explore the associations and vulnerabilities of WFS $PM_{2.5}$ with all-cause and cause-specific mortality. Chapters 5 and 6 investigate CVD-specific mortality and dementia-specific incidence, respectively, while Chapter 4 presents the first prospective study in the UK examining cancer-specific mortality associated with WFS $PM_{2.5}$. Importantly, the health outcomes were determined using medical and death records, which minimized recall bias compared to self-reported data and ensured the reliability of the findings.

### 7.5 Limitations of this thesis

Although this thesis provides robust evidence on the long-term impacts of wildfires, some limitations should be reported. First, the UK cohort sample is subject to volunteer-based selection bias[82]. The representativeness of the UKB sample has been criticized, as the 5.5% of voluntary respondents were likely healthier and of higher socioeconomic statue than the general population[83]. This limitation might result in an underestimation of the risk estimates rather than a change in the risk direction[84]. Second, potential exposure bias might be

introduced during exposure estimation and allocation; however, the findings are unlikely to be substantially affected due to the relatively low residential mobility of participants[31,85]. Specifically, uncertainties existed in the exposure estimation process, such as the fire emission inventory used, unconsidered plume rise, and limited station observations[2]. The spatial resolution of the exposure data in the UK (0.1°×0.1°) and in Brazil (0.25°×0.25°) might lead to spatial exposure misclassification. The individual-based exposure allocation in the UK was based on baseline residential addresses, while the municipality-based exposure allocation in Brazil introduced the potential for exposure misclassification. Third, although my analysis adjusted for extensive individual- and area-level confounders, potential residual confounding bias was inevitable due to unconsidered confounders. Fourth, considering the heterogeneity (e.g., regions, populations), the generalization and interpretation of the findings should be approached with caution. For example, the study area for this thesis was restricted to UK with low-fire exposure, and Brazil with high-fire exposure, which might limit the generalizability of the findings to other developed countries with high-fire exposure and developing countries with low-fire exposure.

### 7.6 Recommendations for future studies

Based on the findings of the systematic review (Chapter 2) and original research (Chapters 3-6) in this thesis, future studies are recommended to focus on two key areas: epidemiological assessment, and basic medical exploration.

The following research directions are recommended for future epidemiological studies. First, although this thesis explored the long-term impacts of WFS $PM_{2.5}$ on mortality and dementia incidence using data from the UK and Brazil, there is still limited high-quality quantitative evidence regarding the long-term health impacts of wildfires. High-quality explorations of extensive health outcomes (e.g., CVD morbidity, RESP mortality and morbidity) and vulnerabilities (e.g., hazardous time windows, populations, regions) associated with extensive wildfire components (e.g., WFS ozone, WFS $PM_{10}$) are recommended, such as using comprehensive methods, applying prospective designs, controlling thorough confounders, implementing multi-country studies, and pooling individual findings by meta-analysis. Second, while this thesis focused on the health impacts of WFS $PM_{2.5}$, the comparison with $PM_{2.5}$ from other sources (e.g., traffic emissions, industrial emissions, agricultural emissions) as well as with $PM_{2.5}$ from different types of wildfires (e.g., forest fires, grassland fires), is an important avenue for future research. A more explicit exploration of this topic could offer valuable insights into the unique pathways or mechanisms through which WFS may affect long-term health risks. Third, while the exposure assessments employed in this thesis demonstrated high accuracy, uncertainties and limitations remain[2]. Future studies should focus on enhancing exposure accuracy by developing and refining exposure assessment and calibration methods. Fourth, the interactive effects of WFS components and

weather variables (e.g., temperature, humidity) on health are recommended. Fifth, implementing interventions for long-term effects and evaluating their effectiveness and associated health benefits is recommended. Sixth, assessments and future projections of the health burden and economic burden attributable to wildfires are recommended.

The toxicity and mechanism of WFS $PM_{2.5}$ and ambient $PM_{2.5}$ might be different, possibly associated with fuel type and epigenetic factors[4,33]. Although the biological mechanisms of ambient $PM_{2.5}$ hazards have been extensively explored, the mechanisms of complex WFS are still less studied. Therefore, animal and human experiments are recommended to further investigate and elucidate the biological mechanisms by which WFS components impair health at the cellular, molecular, and epigenetic levels. Such explorations could help clarify the biological mechanisms underlying the long-term health effects associated with WFS and facilitate the development of biomarkers for predicting the health risks posed by long-term wildfire exposure[86].

### 7.7 Conclusions

Using national health data of UK and Brazil, this thesis observed long-term risks of WFS $PM_{2.5}$ on mortality from all-cause, non-accident, neoplasm (especially total-cancer, lung cancer, LOCP cancer), CVD (especially total-CVD, ischaemic heart disease, stroke), and morbidity from all-cause dementia, AD, and VAD.

Higher-vulnerability to WFS $PM_{2.5}$ was observed in retired individuals for lung cancer and low-educated individuals for all-cause dementia. These findings are important for expanding the existing knowledge base and guiding targeted mitigation and adaptation strategies. Tailored strategies and targeted measures are needed to protect the public health, especially for higher-vulnerability groups. However, further exploration of associations, vulnerabilities and mechanisms is highly needed to support and expand existing knowledge.

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## Appendix 1. Supplementary materials for Chapter 2

Long-term impacts of non-occupational wildfire exposure on human health: a systematic review

Table of Contents

Table S1. PRISMA 2020 Checklist

| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review. | In the Title |
| **ABSTRACT** | | | |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. | In the Abstract |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | In the para 1-2 of Introduction |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | In the para 3 of Introduction |
| **METHODS** | | | |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | In the para 3 of Methods |
| Information sources | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | In the para 2 of Methods |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | In the Table S2 |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | In the para 3-6 of Methods |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | In the para 3-6 of Methods |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | In the para 3-6 of Methods |
| | 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | In the para 3-6 of Methods |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | In the para 5 of Methods |
| Effect measures | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or | In the para 7 of Methods |

| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| | | presentation of results. | |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | In the para 3-7 of Methods |
| | 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | Not applicable |
| | 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | In the para 7 of Methods |
| | 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | In the para 7 of Methods |
| | 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | Not applicable |
| | 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | Not applicable |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | Not applicable |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | Not applicable |
| **RESULTS** | | | |
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | In the Figure 1 |
| | 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | In the Figure 1 |
| Study characteristics | 17 | Cite each included study and present its characteristics. | In the Results and Table 1 |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | In the Table S7 |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | In the Table 1 |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | In the Results |
| | 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the | In the Results |

| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| | | summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | |
| | 20c | Present results of all investigations of possible causes of heterogeneity among study results. | Not applicable |
| | 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | Not applicable |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | Not applicable |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | Not applicable |
| **DISCUSSION** | | | |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | In the Discussion |
| | 23b | Discuss any limitations of the evidence included in the review. | In the Current research evidence and potential research gaps of Discussion |
| | 23c | Discuss any limitations of the review processes used. | In the Strengths and limitations of the review of Discussion |
| | 23d | Discuss implications of the results for practice, policy, and future research. | In the Current research evidence and potential research gaps of Discussion |
| **OTHER INFORMATION** | | | |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | In the para 1 of Methods |
| | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | In the para 1 of Methods |
| | 24c | Describe and explain any amendments to information provided at registration or in the protocol. | In the para 1 of Methods |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | In the Funding |
| Competing interests | 26 | Declare any competing interests of review authors. | In the Declaration of conflicts of interest |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | In the Availability of data |

Table S2. Search strategies used for online databases

| Databases | Search Strategy |
|---|---|
| Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations | # Searches<br>1 Wildfires/<br>2 (bushfire* or bush fire* or wildfire* or wild* fire* or forest fire* or wildland fire* or wild land fire* or woodland fire* or wood land fire* or brushfire* or brush fire* or rural fire* or grassfire* or grass fire or vegetation fire* or landscape fire*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]<br>3 1 or 2<br>4 morbidity/ or mortality/ or "cause of death"/<br>5 patient care/ or hospitalization/ or patient admission/ or patient discharge/ or patient readmission/<br>6 patients/ or inpatients/<br>7 exp disease/ or exp disease attributes/<br>8 emergency service, hospital/ or trauma centers/<br>9 exp Emergency Medical Services/<br>10 Ambulances/ or Air Ambulances/<br>11 exp "Wounds and Injuries"/<br>12 exp "diseases (non mesh)"/ or exp respiratory tract diseases/ or bronchial diseases/ or exp asthma/ or exp lung diseases/ or exp respiration disorders/<br>13 exp Sleep Wake Disorders/<br>14 mental health/ or mental disorders/ or exp anxiety disorders/ or exp mood disorders/ or exp "trauma and stressor related disorders"/ or mental health services/<br>15 exp pregnancy/ or exp pregnancy outcome/<br>16 exp pregnancy complications/ or exp cardiovascular diseases/<br>17 (health* or disease* or mortalit* or morbidit* or incidence* or hospital* or admission* or injur* or traum* or emergency or emergencies or ambulanc*).mp.<br>18 (asthm* or cardio* or allerg* or respirator* or COPD or lung diseas* or lung function* or mental health* or sleep* or disorder* or insomni*).mp.<br>19 (pregnan* or gestation* or maternal or preterm* or pre term* or pre matur* or prematur* or post matur* or postmatur* or abortion* or stillbirth* or still birth*).mp.<br>20 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19<br>21 3 and 20<br>22 exp animals/ not humans.sh.<br>23 21 not 22 |
| Embase | 1 wildfire/<br>2 (bushfire* or bush fire* or wildfire* or wild* fire* or forest fire* or wildland fire* or wild land fire* or woodland fire* or wood land fire* or brushfire* or brush fire* or rural fire* or grassfire* or grass fire* or vegetation fire* or landscape fire*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]<br>3 1 or 2<br>4 morbidity/ |

| | |
|---|---|
| | 5 cancer mortality/ or maternal mortality/ or all cause mortality/ or in-hospital mortality/ or cardiovascular mortality/ or hospital mortality/ or mortality/<br>6 hospital discharge/ or hospital patient/ or hospital admission/ or hospital/ or hospital emergency service/<br>7 emergency patient/ or emergency health service/ or emergency medical dispatch/ or emergency/<br>8 ambulance/<br>9 exp diseases/<br>10 exp sleep disorder/<br>11 exp wound/<br>12 exp injury/<br>13 exp mental health/<br>14 exp pregnancy outcome/ or exp pregnancy/<br>15 (health* or disease* or mortalit* or morbidit* or incidence* or hospital* or admission* or injur* or traum* or emergency or emergencies or ambulanc*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]<br>16 (asthm* or cardio* or allerg* or respirator* or COPD or lung diseas* or lung function* or mental health* or sleep* or disorder* or insomni*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]<br>17 (pregnan* or gestation* or maternal or preterm* or pre term* or pre matur* or prematur* or post matur* or postmatur* or abortion* or stillbirth* or still birth*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]<br>18 hospitalization/ or patient/ or hospital/ or patient/<br>19 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18<br>20 3 and 19<br>21 exp animals/ not humans.sh.<br>22 20 not 21 |
| Scopus | (TITLE-ABS-KEY ( "bushfire*" OR "bush fire*" OR "wildfire*" OR "wild* fire*" OR "forest fire*" OR "wildland fire*" OR "wild land fire*" OR "woodland fire*" OR "wood land fire*" OR "brushfire*" OR "brush fire*" OR "rural fire*" OR "grassfire*" OR "grass fire*" OR "vegetation fire*" OR "landscape fire*" ) AND TITLE-ABS-KEY ("health*" OR "disease*" OR "mortalit*" OR "death*" OR "morbidit*" OR "incidence*" OR "hospital*" OR "admission*" OR "injur*" OR "traum*" OR "emergency*" OR "emergencies" OR "ambulanc*" OR "asthm*" OR "allerg*" OR "cadio*" OR "respirator*" OR "copd" OR "lung diseas*" OR "lung function*" OR "mental health*" OR "sleep*" OR "disorder*" OR "insomni*" OR "pregnan*" OR "gestation*" OR "maternal" OR "preterm*" OR "preterm" OR "prematur*" OR "postmatur*" OR "abortion*" OR "stillbirth*" OR "still birth*" ) AND NOT TITLE-ABS-KEY ( "animal*" OR "not human*" )) |

Table S3. Criteria for the risk of bias assessment for included studies, adapted from the OHAT tool

| Bias | Risk of Bias Domains and Ratings | Answer |
|---|---|---|
| **Selection bias** | Did selection of study participants result in appropriate comparison groups? | -LOW risk: The descriptions of the studied population were sufficiently detailed to support the assertion that risk of selection effects was minimal.<br>-PROBABLY LOW risk: There is insufficient information about population selection to permit a judgment of low risk of bias, but there is indirect evidence that suggests low risk of bias.<br>-PROBABLY HIGH risk: There is insufficient information about population selection to permit a judgment of high risk of bias, but there is indirect evidence that suggests high risk of bias.<br>- HIGH risk: There were indications from descriptions of the studied population of high risk of bias. |
| **Confounding bias** | Did the study design or analysis account for important confounding and modifying variables?<br>The selected potential confounders for cross-sectional, cohort and case-control studies: age, gender, race/ethnicity, education level, household income, health status, employment status; for ecological studies: social-economic status, region, variation in expected number of outcome; for time-series and case-crossover studies: time trend, seasonality, temperature, day of week, public holiday, variation in expected number of outcome. | - LOW risk: Study accounted for 4/5 of the selected potential confounders.<br>-PROBABLY LOW risk: Study accounted for 3/5 of the selected potential confounders.<br>-PROBABLY HIGH risk: Study accounted for 2/5 of the selected potential confounders.<br>-HIGH risk: Study accounted for ≤ 1/5 of the selected potential confounders. |
| **Detection bias, exposure assessment** | Can we be confident in the exposure characterization? | -LOW risk: There is high confidence that the exposure to wildfire is the true average population exposure.<br>-PROBABLY LOW: There is indirect evidence that suggests low risk of bias, or one of the three listed considerations is not applied.<br>-PROBABLY HIGH risk: There is insufficient information to permit a judgment of high risk of bias, but there is indirect evidence that suggests high risk of bias.<br>-HIGH risk: There is direct evidence of high risk of misclassification bias, or all three of the listed considerations are not applied. |
| **Detection bias, outcome assessment** | Can we be confident in the outcome assessment? | -LOW risk: Outcome was classified based on diagnosis standard criteria (e.g., International Classification System code) and provided by a national or regional database.<br>-PROBABLY LOW: Outcome was assessed based on diagnosis standard criteria and collected by researcher.<br>-PROBABLY HIGH risk: Outcome was not assessed based on standard diagnosis |

| | | |
|---|---|---|
| | | criteria AND is accompanied by validation sub-study or sensitivity analysis to suggest that the risk is minimum.<br>-HIGH risk: Outcome was assessed based on self-reports (parents, family) and data collected by the researcher. |
| **Attrition/exclusion bias** | Were outcome data complete without attrition or exclusion from analysis? | -LOW risk: There were no missing outcome data or missing data unrelated to true outcome<br>-PROBABLY LOW: There was insufficient information about incomplete data to judge for low risk, but indirect evidence that suggests low risk of bias<br>-PROBABLY HIGH risk: There was insufficient information about incomplete data to judge for high risk, but indirect evidence that suggests high risk<br>-HIGH risk: Missing outcome data is related to true outcome |
| **Selective reporting bias** | Were all measured outcomes reported? | -LOW risk: All of the studies pre-specified outcomes and findings are reported<br>-PROBABLY LOW: There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report<br>-PROBABLY HIGH risk: There was insufficient information about selective reporting to judge for high risk, but indirect evidence suggests that study was not free of selective reporting<br>-HIGH risk: Not all pre-specified outcomes and findings were reported, or one/more of the primary outcomes or analyses were assessed or executed with other methods than the pre-specified one, or one/more of the reported outcomes/findings was/were not pre-specified |

Table S4. Quality assessment of included studies using the Newcastle-Ottawa Scale (NOS) for cohort and case-control studies

| Authors, year | Study design | Representativeness of the exposed cohort (*) | Selection of the non-exposed cohort (*) | Ascertainment of exposure (*) | Demonstration that outcome of interest was not present at start of study (*) | Comparability based on design and analysis (**) | Assessment of outcome (*) | Follow-up long enough for outcomes to occur (*) | Adequacy of follow up of cohorts (*) | Score (9) |
|---|---|---|---|---|---|---|---|---|---|---|
| Mott et al. 2005 | cohort | - | * | - | * | * | * | - | - | 4 |
| Tse et al. 2015 | cohort | - | * | - | - | * | - | - | * | 3 |
| Orr et al. 2020 | cohort | - | * | * | * | * | * | - | * | 6 |
| Singh et al. 2021 | cohort | - | * | * | * | * | * | * | * | 7 |
| Bryant et al. 2021 | cohort | - | * | - | - | * | * | * | - | 4 |
| Galletly et al. 2011 | cohort | - | - | - | - | - | - | * | - | 1 |
| Marshall et al. 2010 | cohort | - | - | - | - | - | * | - | - | 1 |
| McFarlane et al. 2009 | cohort | - | * | - | - | * | * | * | - | 4 |
| Pfitzer et al. 2016 | cohort | - | - | - | - | * | * | - | * | 3 |
| McFarlane et al. 1987 | cohort | - | - | - | - | * | * | - | * | 3 |
| Blando et al. 2022 | cohort | - | * | * | - | ** | * | - | - | 5 |
| Korsiak et al. 2022 | cohort | * | * | * | * | ** | * | * | * | 9 |
| Parslow et al. 2006 | cohort | - | - | - | - | - | * | - | - | 1 |
| **Authors, year** | **Study design** | **case definition adequate (*)** | **Representativeness of the cases (*)** | **Selection of Controls (*)** | **Definition of Controls (*)** | **Comparability of cases and controls on the basis of the design or analysis (**)** | **Ascertainment of exposure (*)** | **Same method of ascertainment for cases and controls (*)** | **Non-Response rate (*)** | **Score (9)** |
| Xue et al. 2021 | case-control | * | - | * | * | ** | * | * | * | 8 |

Note: Maximum score in brackets.

Table S5. Quality assessment of included studies using the adapted form of Newcastle-Ottawa Scale (NOS) for cross-sectional studies

| **Authors, year** | **Representativeness of the sample (*)** | **Sample size (*)** | **Non-respondents (*)** | **Ascertainment of exposure** (**) | **Comparability based on design and analysis (**)** | **Assessment of outcome** (**) | **Statistical test (*)** | **Score (10)** |
|---|---|---|---|---|---|---|---|---|
| Ontawong et al. 2020 | - | * | * | - | * | * | * | 5 |
| Agyapong et al. 2020 | - | - | - | * | * | * | * | 4 |
| Belleville et al. 2021 | - | * | - | * | * | * | * | 5 |
| Ducy et al. 2021 | - | - | * | * | - | - | - | 2 |
| Moosavi et al. 2019 | - | * | - | * | * | * | * | 5 |
| Ritchie et al. 2020 | - | - | - | * | * | * | * | 4 |
| Verstraeten et al. 2021 | - | - | - | * | * | * | * | 4 |
| Dodd et al. 2018 | - | - | * | * | - | - | - | 2 |
| Humphreys et al. 2022 | - | - | - | - | - | - | - | 0 |
| Brown et al. 2021 | - | * | * | * | * | * | * | 6 |

Note: Maximum score in brackets.

Table S6. Quality assessment of included studies using the modified version of framework developed by Zaza et al. (2000) for other observational studies

| Authors, year | Study design | Study design (7) | Population Eligibility and Sampling Described (4) | Valid and Reliable Exposure Measures (2) | Valid and Reliable Outcome Measures (2) | Appropriate Statistical Methods (3) | Multilevel Analyses (2) | Interpretation (1) | Confounding and Bias Addressed (3) | Total (24) |
|---|---|---|---|---|---|---|---|---|---|---|
| Landguth et al. 2020 | time series | 3 | 3 | 2 | 2 | 2 | 1 | 1 | 1 | 15 |
| Brown et al. 2019 | ecological | 3 | 3 | 1 | 1 | 2 | - | 1 | - | 11 |
| Bryant et al. 2014 | ecological | 3 | 3 | 1 | 1 | 2 | - | 1 | - | 11 |
| Cowlishaw et al. 2021 | ecological | 2 | 3 | 1 | 1 | 2 | 1 | 1 | - | 11 |
| McFarlane et al. 1997 | ecological | 2 | 2 | 1 | 1 | 2 | 1 | 1 | - | 10 |
| Nunes et al. 2013 | ecological | 3 | 3 | 2 | 2 | 2 | 1 | 1 | 1 | 15 |
| Rosales-Rueda et al. 2020 | natural experiment | 5 | 3 | 2 | 2 | 2 | 1 | 1 | 1 | 17 |
| Kim et al. 2017 | natural experiment | 5 | 3 | 1 | 2 | 2 | 1 | 1 | 1 | 16 |
| Johnston et.al. 2021 | linear panel event-study design | 5 | 4 | 2 | 2 | 2 | 1 | 1 | 2 | 19 |
| Cohen et al. 2022 | retrospective crossover | 6 | 4 | 1 | 1 | 1 | - | 1 | - | 14 |
| Balasooriya et al. 2022 | natural experiment | 5 | 3 | 1 | 1 | 2 | 1 | 1 | 2 | 16 |
| Schroeder et al. 2022 | time series | 4 | 4 | 1 | 2 | 2 | - | 1 | 1 | 15 |

Note: Maximum score in brackets.

Table S7. Heat map for risk of bias rating and quality rating for the included studies

| Study | Risk of Bias | | | | | | Study quality | |
|---|---|---|---|---|---|---|---|---|
| | Selection bias | Confounding bias | Exposure assessment | Outcome assessment | Attrition/exclusion bias | Selective reporting bias | Quality score | Classification |
| Mott et al. 2005 | | | | | | | 4/9[a] | Low |
| Tse et al. 2015 | | | | | | | 3/9[a] | Low |
| Orr et al. 2020 | | | | | | | 6/9[a] | High |
| Singh et al. 2021 | | | | | | | 7/9[a] | High |
| Bryant et al. 2021 | | | | | | | 4/9[a] | Low |
| Galletly et al. 2011 | | | | | | | 1/9[a] | Low |
| Marshall et al. 2010 | | | | | | | 1/9[a] | Low |
| McFarlane et al. 2009 | | | | | | | 4/9[a] | Low |
| Pfitzer et al. 2016 | | | | | | | 3/9[a] | Medium |
| McFarlane et al. 1987 | | | | | | | 3/9[a] | Low |
| Blando et al. 2022 | | | | | | | 5/9[a] | High |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Korsiak et al. 2022 | | | | | | | 9/9[a] | High |
| Parslow et al. 2006 | | | | | | | 1/9[a] | Medium |
| Xue et al. 2021 | | | | | | | 8/9[a] | Medium |
| Ontawong et al. 2020 | | | | | | | 5/10[b] | Low |
| Agyapong et al. 2020 | | | | | | | 4/10[b] | Medium |
| Belleville et al. 2021 | | | | | | | 5/10[b] | Medium |
| Ducy et al. 2021 | | | | | | | 2/10[b] | Low |
| Moosavi et al. 2019 | | | | | | | 5/10[b] | Low |
| Ritchie et al. 2020 | | | | | | | 4/10[b] | Low |
| Verstraeten et al. 2021 | | | | | | | 4/10[b] | Low |
| Dodd et al. 2018 | | | | | | | 2/10[b] | Low |
| Humphreys et al. 2022 | | | | | | | 0/10[b] | Low |
| Landguth et al. 2020 | | | | | | | 15/24[c] | Medium |
| Brown et | | | | | | | 11/24[c] | Medium |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| al. 2019 | | | | | | | | |
| Brown et al. 2021 | | | | | | | 6/10[b] | Medium |
| Bryant et al. 2014 | | | | | | | 11/24[c] | Medium |
| Cowlishaw et al. 2021 | | | | | | | 11/24[c] | Medium |
| McFarlane et al. 1997 | | | | | | | 10/24[c] | Medium |
| Nunes et al. 2013 | | | | | | | 15/24[c] | High |
| Rosales-Rueda et al. 2020 | | | | | | | 17/24[c] | High |
| Kim et al. 2017 | | | | | | | 16/24[c] | Medium |
| Johnston et.al. 2021 | | | | | | | 19/24[c] | Medium |
| Cohen et al. 2022 | | | | | | | 14/24[c] | Low |
| Balasooriya et al. 2022 | | | | | | | 16/24[c] | Medium |
| Schroeder et al. 2022 | | | | | | | 15/24[c] | High |

[a] Study quality was assessed using Newcastle-Ottawa Scale (NOS).

[b] Study quality was assessed using an adapted form of the NOS scale.

[c] Study quality was assessed using an adapted version of a validated quality assessment framework developed by Zaza et al. (Zaza et al. 2000).

[d] Risk of bias assessment was adapted from the National Institutes of Environmental Health Sciences National Toxicology Program Office of Health Assessment and Translation (OHAT) tool. Each of domain was evaluated as “low,” “probably low,” “probably high,” or “high” risk according to specific criteria (Table S3).

## Appendix 2. Supplementary materials for Chapter 3

Association between long-term exposure to wildfire-related $PM_{2.5}$ and mortality: A longitudinal analysis of the UK Biobank

Table S1. Baseline statistics of included and excluded study participants.

| Variables | Number (%) or mean ± SD | | |
|---|---|---|---|
| | **Included participants (n=492394)** | **Excluded participants (n=10050)** | **P value *** |
| **Age at recruitment (years)** | 56.5 ± 8.1 | 56.7 ± 8.4 | < 0.0001 |
| **BMI (kg/m$^2$)** | 27.4 ± 4.8 | 27.9 ± 5.3 | < 0.0001 |
| **Sex** | | | < 0.0001 |
| Male | 224,119 (45.5) | 4,966 (49.4) | |
| Female | 268,275 (54.5) | 5,053 (50.3) | |
| **Ethnicity** | | | < 0.0001 |
| White | 435,170 (88.4) | 7,349 (73.1) | |
| Non-White | 57,224 (11.6) | 1,772 (17.6) | |
| **Education** | | | < 0.0001 |
| College or University degree | 159,795 (32.5) | 1,335 (13.3) | |
| A / AS / O / GCSEs / CSE / NVQ / HND / HNC levels or Equivalent and other Professional qualifications | 243,641 (49.5) | 2,254 (22.4) | |
| None of the above | 83,628 (17.0) | 1,631 (16.2) | |
| Prefer not to answer | 5,330 (1.0) | 160 (1.6) | |
| **Current employment status** | | | < 0.0001 |
| In paid employment or self-Employed | 282,834 (57.4) | 4,252 (42.3) | |
| Retired | 163,782 (33.3) | 3,186 (31.7) | |
| Other [#] | 43,791 (8.9) | 1,619 (16.1) | |
| Prefer not to answer | 1,987 (0.4) | 92 (0.0) | |
| **Smoking status** | | | < 0.0001 |
| Never | 268,952 (54.6) | 4,526 (45. 0) | |
| Previous | 170,024 (34.5) | 3,001 (29.9) | |
| Current | 51,444 (10.4) | 1,518 (15.1) | |

| | | | |
|---|---|---|---|
| Prefer not to answer | 1,974 (0.4) | 83 (0.8) | |
| **Alcohol drink status** | | | < 0.0001 |
| Never | 21,671 (4.4) | 710 (7.1) | |
| Previous | 17,494 (3.6) | 600 (6.0) | |
| Current | 452,533 (91.9) | 7,753 (77.1) | |
| Prefer not to answer | 696 (0.1) | 59 (0.6) | |
| **Average total household income before tax (GBP)** | | | < 0.0001 |
| <18000 | 96,000 (19.5) | 1,182 (11.8) | |
| 18000-30999 | 107,388 (21.8) | 770 (7.7) | |
| 31000-51999 | 110,105 (22.4) | 648 (6.4) | |
| ≥ 52000-100000 | 108,573 (22.0) | 605 (6.0) | |
| Do not know / Prefer not to answer | 70,328 (14.3) | 803 (8.0) | |
| **Townsend deprivation index** | | | < 0.0001 |
| Low (≤ -2.08) | 95,340 (19.4) | 3,531 (35.1) | |
| Middle (-2.08 - 1.40) | 145,928 (29.6) | 2,663 (26.5) | |
| High (≥ 1.40) | 251,126 (51.0) | 3,196 (31.8) | |

Note: A = Advanced; AS = Advanced Subsidiary; O = Ordinary; GCSEs = General Certificate of Secondary Educations; CSE = Certificate of Secondary Education; NVQ = National Vocational Qualification; HND = Higher National Diploma; HNC = Higher National Certificate.

* T-test for continuous variables and chi-square test for categorical variables.

# Other included: Looking after home and/or family; Unable to work because of sickness or disability; Unemployed; Doing unpaid or voluntary work; Full or part-time student; None of the above.

# Appendix 3. Supplementary materials for Chapter 4

Wildfire-related $PM_{2.5}$ and cause-specific cancer mortality

Table S1. Baseline summary of the study participants (n=492,394).

| Variables | Number (%) or mean ± SD | 3-year cumulative wildfire-related $PM_{2.5}$ |
|---|---|---|
| **Age at recruitment (years)** | 56.5 ± 8.1 | - |
| **BMI ($kg/m^2$)** | 27.4 ± 4.8 | - |
| **Sex** | | |
| Male | 224,119 (45.5) | 456.9 |
| Female | 268,275 (54.5) | 457.6 |
| **Ethnicity** | | |
| White | 435,170 (88.4) | 457.9 |
| Non-White | 57,224 (11.6) | 452.6 |
| **Education*** | | |
| High | 159,795 (32.5) | 455.2 |
| Middle | 243,641 (49.5) | 457.4 |
| Low | 83,628 (17.0) | 461.1 |
| Prefer not to answer | 5,330 (1.0) | 456.0 |
| **Current employment status** | | |
| In paid employment or self-employed | 282,834 (57.4) | 457.4 |
| Retired | 163,782 (33.3) | 457.2 |
| Other # | 43,791 (8.9) | 457.2 |
| Prefer not to answer | 1,987 (0.4) | 453.7 |
| **Smoking status** | | |
| Never | 268,952 (54.6) | 457.8 |
| Previous | 170,024 (34.5) | 456.4 |
| Current | 51,444 (10.4) | 457.1 |
| Prefer not to answer | 1,974 (0.4) | 456.1 |
| **Alcohol drink status** | | |
| Never | 21,671 (4.4) | 457.5 |
| Previous | 17,494 (3.6) | 457.0 |
| Current | 452,533 (91.9) | 457.3 |
| Prefer not to answer | 696 (0.1) | 452.0 |
| **Average total household income before tax (GBP)** | | |

| | | |
|---|---|---|
| <18000 | 96,000 (19.5) | 459.2 |
| 18000-30999 | 107,388 (21.8) | 457.8 |
| 31000-51999 | 110,105 (22.4) | 457.4 |
| ≥ 52000-100000 | 108,573 (22.0) | 455.3 |
| Do not know / Prefer not to answer | 70,328 (14.3) | 456.6 |
| **Townsend deprivation index^** | | |
| Low (≤ -2.08) | 95,340 (19.4) | 459.7 |
| Middle (-2.08 - 1.40) | 145,928 (29.6) | 457.1 |
| High (≥ 1.40) | 251,126 (51.0) | 456.5 |

Note: SD=standard deviation; BMI= body mass index.

*High: college or university degree; Middle: Level Advanced (A), Advanced Subsidiary (AS), Ordinary (O), General Certificate of Secondary Educations (GCSEs), Certificate of Secondary Education (CSE), National Vocational Qualification (NVQ), Higher National Diploma (HND), Higher National Certificate (HNC) or equivalent and other professional qualifications; Low: none of the above.

#Included: Looking after home and/or family, unable to work because of sickness or disability, unemployed, doing unpaid or voluntary work, full or part-time student, none of the above.

^A representative of area-level socioeconomic status (SES) based on unemployment, non-home ownership, non-car ownership and overcrowding. For each participant, this indicator was immediately drawn from the UK census according to the area of residence prior to recruitment and categorized into three groups based on the national thresholds in our study.

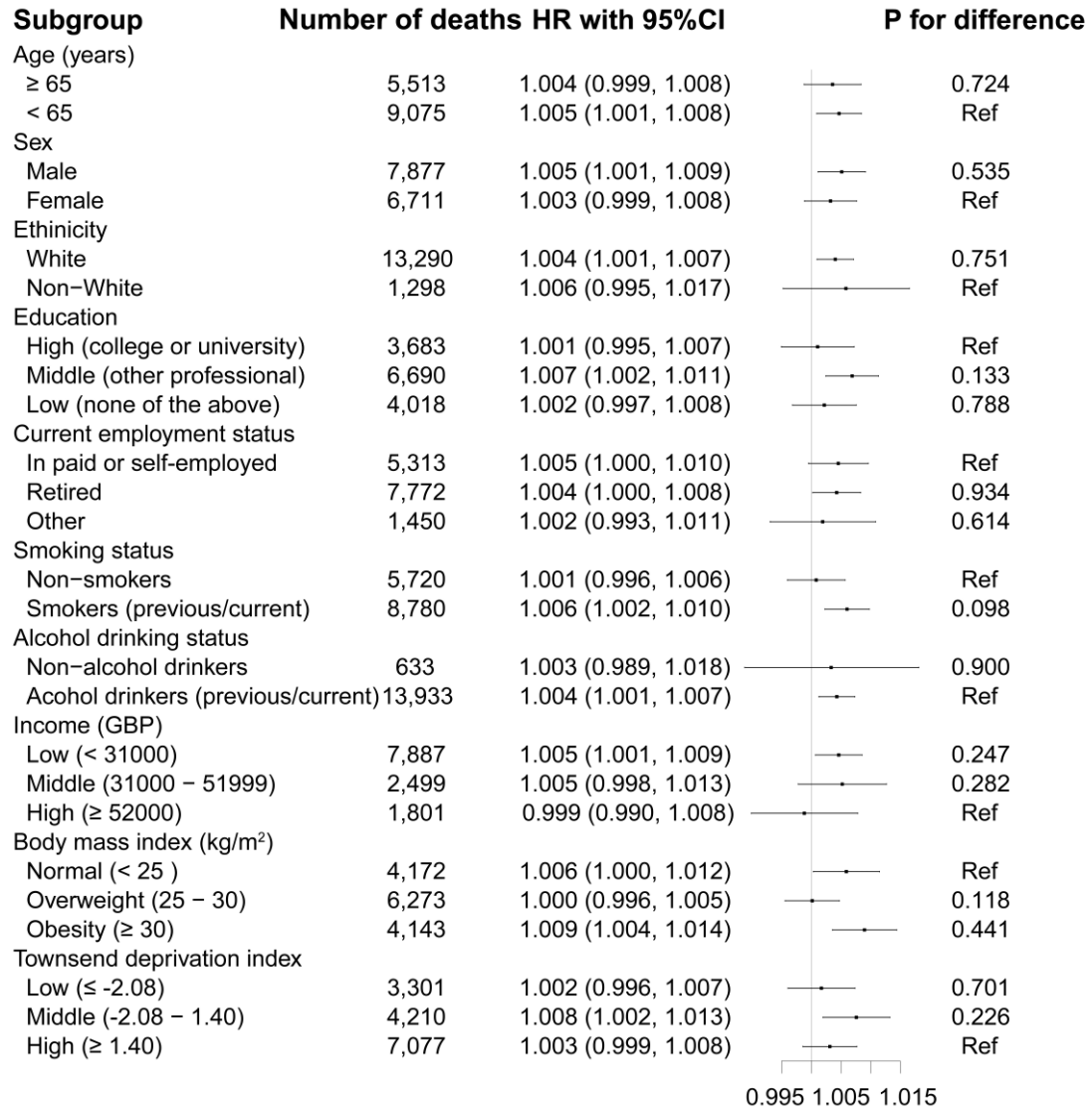


Figure S1. Stratified analyses of the association between wildfire-related $PM_{2.5}$ and total cancer mortality.

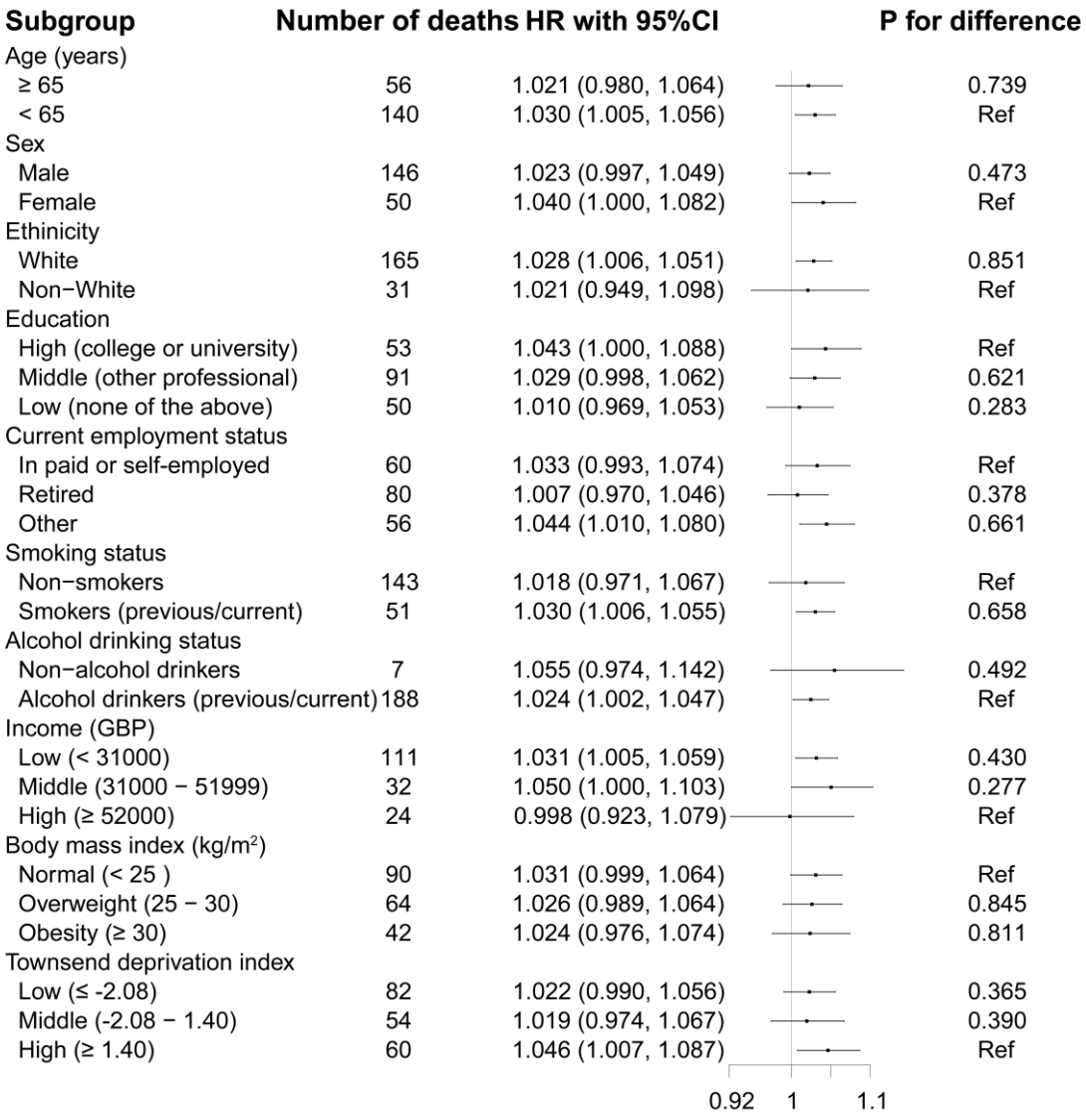


Figure S2. Stratified analyses of the association between wildfire-related $PM_{2.5}$ and lip, oral cavity and pharynx cancer mortality.

## Appendix 4. Supplementary materials for Chapter 5

Wildfire-related $PM_{2.5}$ and cardiovascular mortality: A difference-in-differences analysis in Brazil

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Table S1. Number of cause-specific cardiovascular death counts grouped by sex and age in Brazil during 2010-2018.

| | Male | | Female | | Aged < 60 years | | Aged ≥ 60 years | |
|---|---|---|---|---|---|---|---|---|
| Item | Number | % | Number | % | Number | % | Number | % |
| Total | 1,626,746 | 100 | 1,476,913 | 100 | 651,250 | 100 | 2,446,899 | 100 |
| Ischaemic heart disease | 572,138 | 35.17 | 408,601 | 27.67 | 236,693 | 36.34 | 742,026 | 30.33 |
| Heart failure | 118,067 | 7.26 | 128,183 | 8.68 | 33,485 | 5.14 | 212,415 | 8.68 |
| Hypertensive heart disease | 202,662 | 12.46 | 229,570 | 15.54 | 70,648 | 10.85 | 361,156 | 14.76 |
| Stroke | 382,636 | 23.52 | 371,858 | 25.18 | 143,908 | 22.10 | 609,541 | 24.91 |
| Peripheral vascular disease | 77,721 | 4.78 | 69,309 | 4.69 | 31,038 | 4.77 | 115,791 | 4.73 |

Table S2. Descriptive statistics of study participants by region in Brazil during 2010-2018.

| | Central-west | North | Northeast | South | Southeast |
|---|---|---|---|---|---|
| **Mortality data (%)** | | | | | |
| Total | 195,973 (6.31) | 151,852 (4.89) | 806,443 (25.98) | 486,283 (15.67) | 1,463,495 (47.15) |
| Ischaemic heart disease | 62,318 (6.35) | 44,133 (4.50) | 249,709 (25.46) | 153,971 (15.70) | 470,715 (47.99) |
| Heart failure | 15,007 (6.09) | 12,368 (5.02) | 60,396 (24.52) | 43,120 (17.51) | 115,386 (46.85) |
| Hypertensive heart disease | 27,432 (6.35) | 23,918 (5.53) | 135,133 (31.26) | 60,346 (13.96) | 185,446 (42.90) |
| Stroke | 43,809 (5.81) | 47,878 (6.34) | 213,314 (28.27) | 126,513 (16.77) | 323,085 (42.82) |
| Peripheral vascular disease | 9,445 (6.42) | 4,153 (2.82) | 28,757 (19.56) | 22,558 (15.34) | 82,131 (55.85) |
| **Demographic data** | | | | | |
| Population size (persons) | 136,940,721 | 154,822,575 | 499,505,551 | 259,353,928 | 764,565,872 |
| **Environmental data** | | | | | |
| Wildfire-related $PM_{2.5}$, mean (SD), $\mu g/m^3$ | 6.88 (2.45) | 4.92 (2.99) | 2.25 (1.38) | 3.27 (0.92) | 3.10 (1.33) |
| Mean winter temperature, mean (SD), ℃ | 24.27 (1.94) | 27.06 (1.08) | 25.22 (2.52) | 16.1 (2.18) | 20.32 (2.05) |
| Mean summer temperature, mean (SD), ℃ | 25.16 (1.00) | 26.06 (0.75) | 26.81 (1.31) | 23.19 (1.57) | 24.42 (1.54) |
| SD of winter temperature, mean (SD), ℃ | 2.56 (0.89) | 1.26 (0.50) | 1.02 (0.32) | 3.85 (0.63) | 2.43 (0.59) |
| SD of summer temperature, mean (SD), ℃ | 1.36 (0.28) | 1.07 (0.22) | 1.09 (0.41) | 2.06 (0.42) | 1.57 (0.26) |
| **Socioeconomic data** | | | | | |
| GDP per capita, USD | 6,150.90 | 3,073.57 | 2,139.81 | 6,312.00 | 5,211.16 |

Note: SD = standard deviation; $PM_{2.5}$ = fine particulate matter; GDP = gross domestic product.

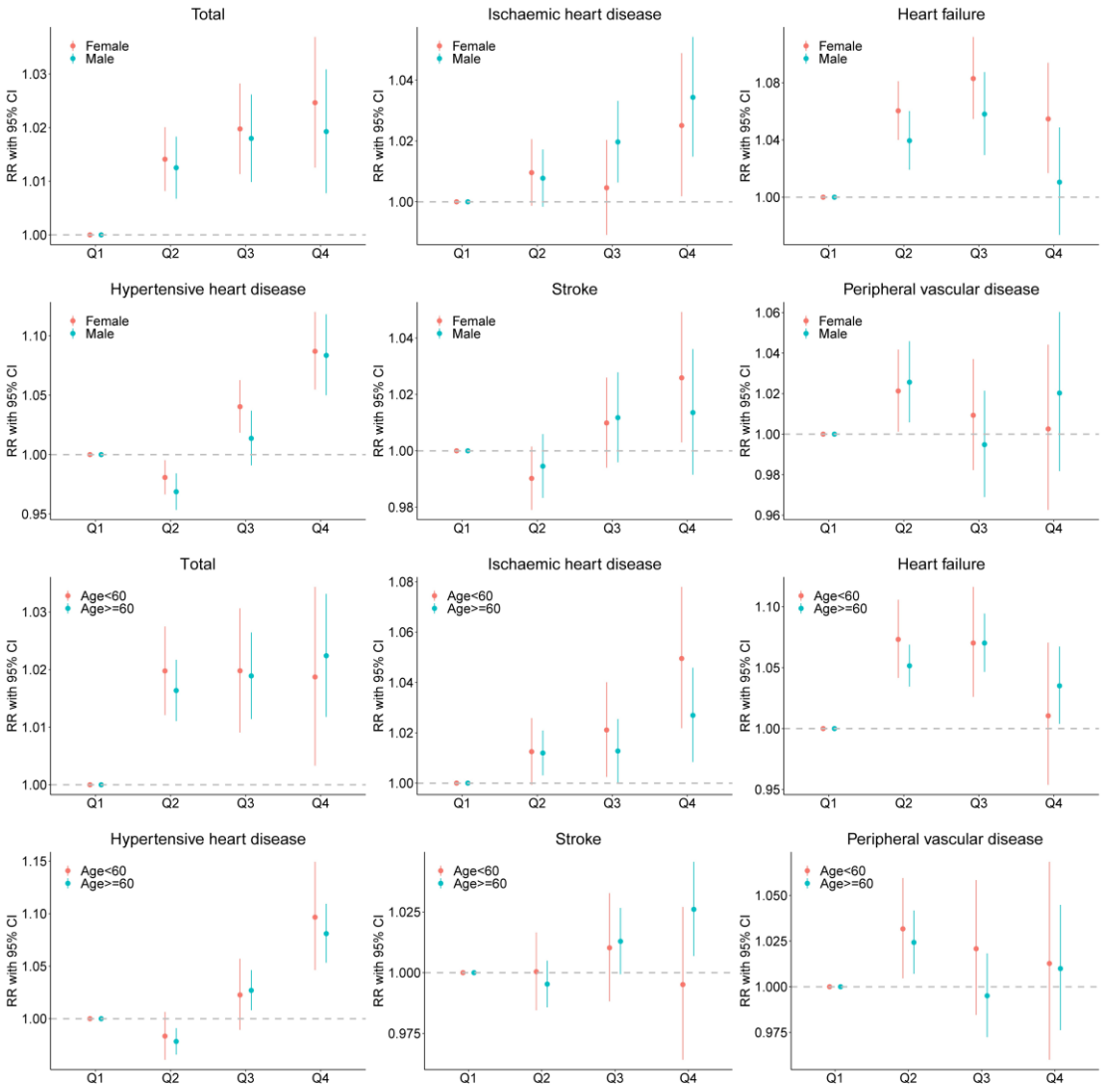


Figure S1. Subgroup analyses stratified by age and sex for associations between wildfire-related $PM_{2.5}$ and cause-specific cardiovascular mortality in Brazil during 2010-2018, compared with the lowest quartile (Q1) of wildfire-related $PM_{2.5}$ exposure.

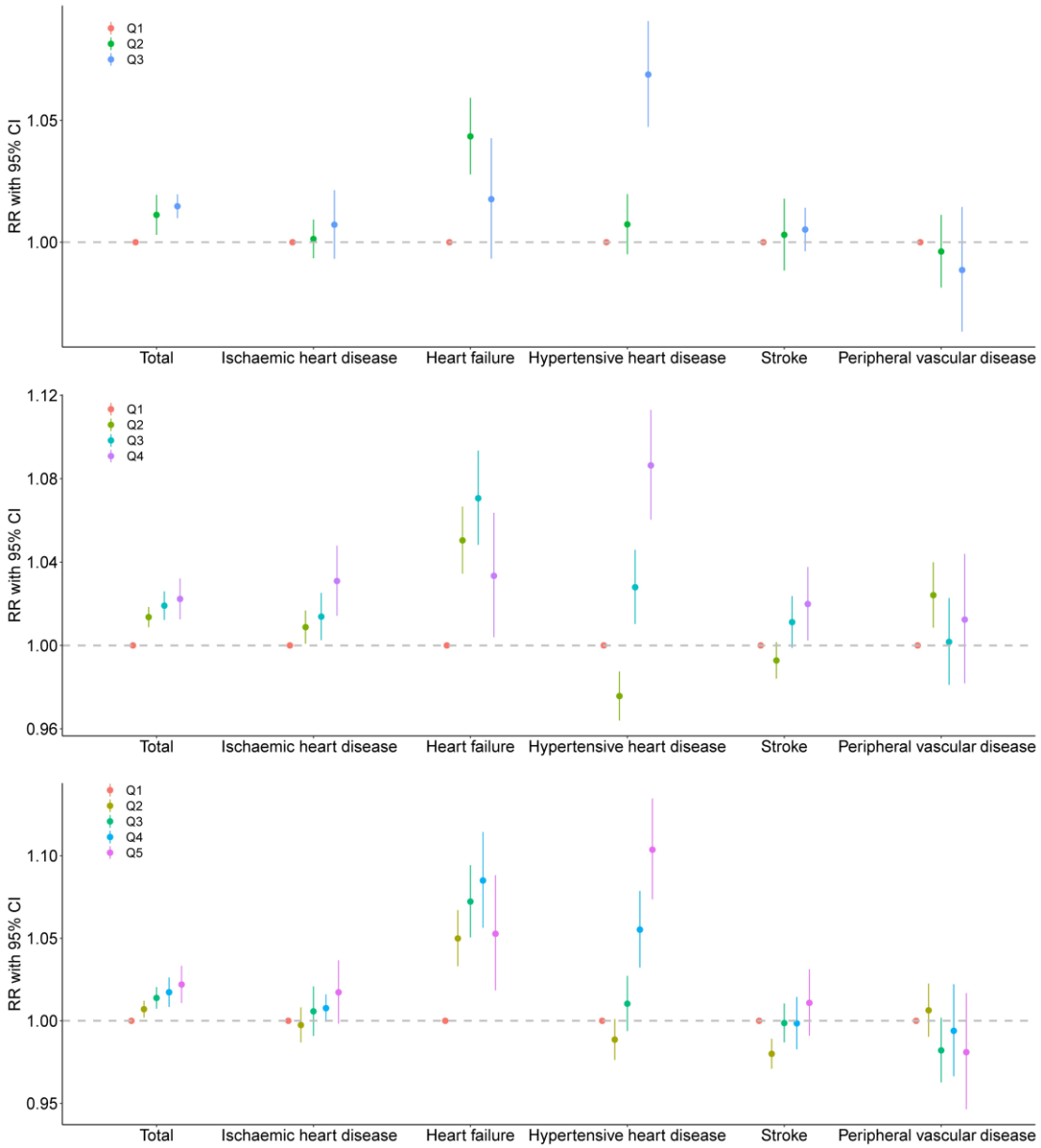


Figure S2. Sensitivity analyses by using different quantiles of wildfire-related $PM_{2.5}$.

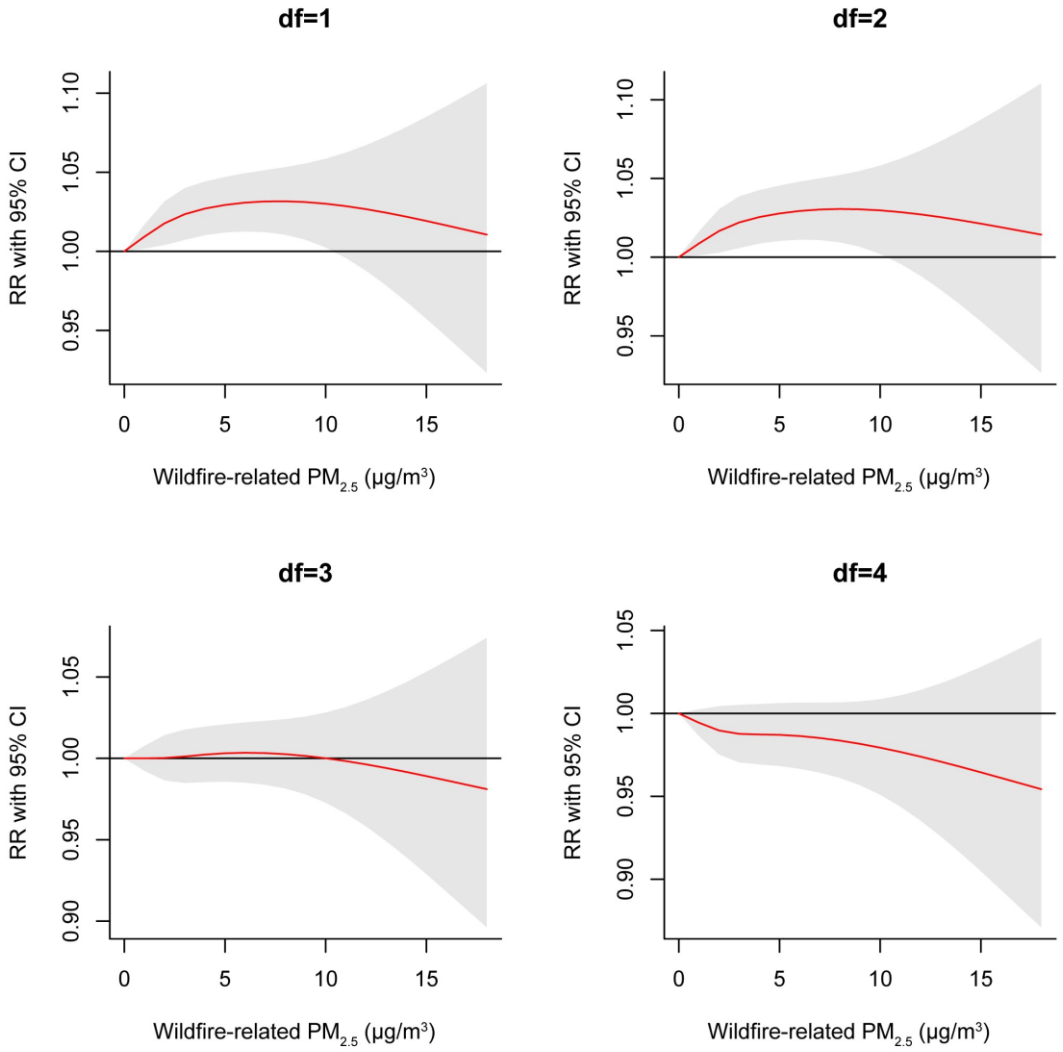


Figure S3. Sensitivity analyses by changing the degrees of freedom (df) of the year.

## Appendix 5. Supplementary materials for Chapter 6

Long-term exposure to low-level wildfire-sourced $PM_{2.5}$ and dementia incidence in the UK

Table S1. Sensitivity analyses by adding physical activity as an additional covariate.

| | All-cause dementia (n=5249) | Alzheimer's disease (n=2194) | vascular dementia (n=1217) |
|---|---|---|---|
| 1-year cumulative | 1.027 (1.004, 1.050) | 1.060 (1.024, 1.098) | 1.215 (1.162, 1.270) |
| 2-year annual cumulative | 0.992 (0.969, 1.016) | 1.028 (0.993, 1.065) | 1.117 (1.066, 1.171) |
| 3-year annual cumulative | 0.870 (0.846, 0.894) | 0.896 (0.860, 0.933) | 0.929 (0.880, 0.981) |
| 4-year annual cumulative | 1.012 (0.987, 1.037) | 1.043 (1.005, 1.082) | 1.072 (1.020, 1.127) |
| 5-year annual cumulative | 0.984 (0.959, 1.009) | 1.029 (0.992, 1.068) | 1.077 (1.025, 1.133) |

Table S2. Sensitivity analyses by adding healthy diet as an additional covariate.

| | All-cause dementia (n=5249) | Alzheimer's disease (n=2194) | Vascular dementia (n=1217) |
|---|---|---|---|
| 1-year cumulative | 1.028 (1.005, 1.051) | 1.062 (1.026, 1.099) | 1.216 (1.163, 1.272) |
| 2-year annual cumulative | 0.993 (0.970, 1.017) | 1.030 (0.994, 1.067) | 1.119 (1.068, 1.172) |
| 3-year annual cumulative | 0.871 (0.847, 0.895) | 0.898 (0.862, 0.935) | 0.931 (0.881, 0.983) |
| 4-year annual cumulative | 1.013 (0.989, 1.039) | 1.045 (1.007, 1.084) | 1.073 (1.021, 1.128) |
| 5-year annual cumulative | 0.985 (0.961, 1.011) | 1.031 (0.993, 1.070) | 1.079 (1.026, 1.134) |

Table S3. Sensitivity analyses by adding physical activity and healthy diet as additional covariates.

| | All-cause dementia (n=5249) | Alzheimer's disease (n=2194) | Vascular dementia (n=1217) |
|---|---|---|---|
| 1-year cumulative | 1.027 (1.005, 1.051) | 1.062 (1.026, 1.099) | 1.216 (1.162, 1.271) |
| 2-year annual cumulative | 0.993 (0.970, 1.017) | 1.030 (0.994, 1.067) | 1.118 (1.067, 1.171) |
| 3-year annual cumulative | 0.870 (0.847, 0.895) | 0.897 (0.862, 0.935) | 0.930 (0.881, 0.982) |
| 4-year annual cumulative | 1.013 (0.988, 1.038) | 1.045 (1.007, 1.084) | 1.073 (1.020, 1.128) |
| 5-year annual cumulative | 0.985 (0.960, 1.010) | 1.031 (0.993, 1.070) | 1.078 (1.026, 1.134) |

Table S4. Sensitivity analyses by excluding dementia cases before 2011.

| | All-cause dementia (n=5079) | Alzheimer's disease (n=2110) | Vascular dementia (n=1181) |
|---|---|---|---|
| 1-year cumulative | 1.037 (1.013, 1.061) | 1.057 (1.020, 1.095) | 1.237 (1.182, 1.295) |
| 2-year annual cumulative | 0.995 (0.971, 1.019) | 1.025 (0.988, 1.062) | 1.126 (1.074, 1.180) |
| 3-year annual cumulative | 0.866 (0.842, 0.890) | 0.887 (0.851, 0.925) | 0.929 (0.879, 0.982) |
| 4-year annual cumulative | 1.006 (0.981, 1.032) | 1.035 (0.997, 1.075) | 1.073 (1.020, 1.129) |
| 5-year annual cumulative | 0.981 (0.956, 1.006) | 1.023 (0.985, 1.062) | 1.082 (1.028, 1.138) |

Table S5. Sensitivity analyses by excluding dementia cases before 2012.

| | All-cause dementia (n=4920) | Alzheimer's disease (n=2034) | Vascular dementia (n=1140) |
|---|---|---|---|
| 1-year cumulative | 1.026 (1.002, 1.050) | 1.051 (1.013, 1.090) | 1.237 (1.180, 1.296) |
| 2-year annual cumulative | 1.003 (0.979, 1.028) | 1.024 (0.987, 1.063) | 1.143 (1.090, 1.200) |
| 3-year annual cumulative | 0.864 (0.840, 0.889) | 0.877 (0.840, 0.916) | 0.932 (0.881, 0.986) |
| 4-year annual cumulative | 1.013 (0.987, 1.039) | 1.038 (0.998, 1.078) | 1.084 (1.030, 1.141) |
| 5-year annual cumulative | 0.975 (0.949, 1.000) | 1.018 (0.979, 1.058) | 1.079 (1.025, 1.136) |

# Appendix 6. Ethical approval

MONASH University

**Monash University Human Research Ethics Committee**

**Approval Certificate**

This is to certify that the project below was considered by the Monash University Human Research Ethics Committee. The Committee was satisfied that the proposal meets the requirements of the *National Statement on Ethical Conduct in Human Research* and has granted approval.

**Project ID:** 27582
**Project Title:** Multi-Country Study on Health Effects of Bushfire Air Pollution
**Chief Investigator:** Professor Yuming Guo
**Approval Date:** 28/05/2021
**Expiry Date:** 28/05/2026

**Terms of approval - failure to comply with the terms below is in breach of your approval and the *Australian Code for the Responsible Conduct of Research*.**

1. The Chief Investigator is responsible for ensuring that permission letters are obtained, if relevant, before any data collection can occur at the specified organisation.
2. Approval is only valid whilst you hold a position at Monash University.
3. It is responsibility of the Chief Investigator to ensure that all investigators are aware of the terms of approval and to ensure the project is conducted as approved by MUHREC.
4. You should notify MUHREC immediately of any serious or unexpected adverse effects on participants or unforeseen events affecting the ethical acceptability of the project.
5. The Explanatory Statement must be on Monash letterhead and the Monash University complaints clause must include your project number.
6. Amendments to approved projects including changes to personnel must not commence without written approval from MUHREC.
7. Annual Report - continued approval of this project is dependent on the submission of an Annual Report.
8. Final Report - should be provided at the conclusion of the project. MUHREC should be notified if the project is discontinued before the expected completion date.
9. Monitoring - project may be subject to an audit or any other form of monitoring by MUHREC at any time.
10. Retention and storage of data - The Chief Investigator is responsible for the storage and retention of the original data pertaining to the project for a minimum period of five years.

Kind Regards,

Professor Nip Thomson

Chair, MUHREC

CC: Professor Michael Abramson, Professor Lidia Morawska, Associate Professor Fay Johnston, Professor Jane Heyworth, Associate Professor Geoffrey Morgan, Associate Professor Luke Knibbs, Professor Jonathan Samet, Professor Michelle Bell, Professor Alistair Woodward, Professor Bin Jalaludin, Professor Paulo Saldiva, Associate Professor Simon Hales, Associate Professor Sarah Henderson, Associate Professor Eric Lavigne, Professor Guy Marks

**List of approved documents:**

| Document Type | File Name | Date | Version |
|---|---|---|---|
| List of data variables | Section E2 | 10/05/2021 | 1.0 |