LA TROBE UNIVERSITY

LITERATURE REVIEW ON HEALTH IMPACTS OF EXPOSURE TO PARTICULATE MATTER EMITTED BY FIRE SMOKE

Final Report

January 2023

La Trobe University

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EXECUTIVE SUMMARY

Background

Fire Rescue Victoria (FRV) identified that incident controllers have limited guidance to assist them when responding to urban industrial fires in relation to exposure to smoke particulate matter (PM), especially fine PM ($PM_{2.5}$). La Trobe University was contracted to undertake a project to provide current research evidence to assist FRV develop guidance materials for Incident Controllers based on the best available evidence and expert opinion. The project comprised the following key components: rapid literature review of current research evidence; content analysis of available operational guidelines or standard operating procedures; and expert consultation regarding best-practice for smoke exposure mitigation for career firefighters. This report covers the literature reviews conducted for the project.

Six research questions were set by the Metropolitan Fire Brigade (now Fire Rescue Victoria) and addressed by this project through literature and document review. The first three (research questions 1 to 3) were addressed together, and were on the impacts of exposure to PM, while the remaining three (research questions 4 to 6) were about mitigation of health impacts:

1. What are the likely or documented adverse health effects (and clinical outcomes) from acute $PM_{2.5}$ exposure, in the short-term and longer-term?
2. What concentrations and exposure doses of smoke contaminants (primarily $PM_{2.5}$) from urban industrial fires are associated with adverse health effects following acute exposures (i.e., for up to 24 hours duration), taking the type of fire and/or fuel load into account)?
3. What is the potential impact of repeated exposures that may be experienced by emergency responders through the course of their careers?
4. What protocols have been shown to reduce health risks and/or improve outcomes for emergency responders?
5. How effective are various respiratory protective measures (e.g., $PM_{2.5}$ dust masks, but excluding self-contained breathing apparatus) at protecting emergency responders on or near the fire-ground?
6. What guidelines or procedures are other agencies or jurisdictions using for this type of exposure and what control actions are taken?

Articles on health impacts of exposure to PM were divided into those that provided direct evidence on health impacts (e.g., direct measures of lung function) and those that provided indirect evidence. Indirect evidence was of two kinds: type 1 used secondary databases such as data on health service use or mortality, and type 2 used indirect measures of health impacts (e.g., biomarkers of oxidative stress) or animal models.

Results

The combined literature search on Questions 1 – 3 resulted in identifying 137 sources: 134 peer-reviewed articles and three reports. The studies relied on a wide range of methods, including laboratory studies of human and animal exposure and statistical modelling linking fire events to hospital and medical records, as well as direct physiological measures taken from firefighters with field exposure to $PM_{2.5}$.

Question 4 resulted in identifying just seven peer-reviewed articles, and the search related to Question 5 resulted in 26 articles.

Health impacts of single acute exposure

Research indicated that acute PM exposure may be associated with the following:

- Changes in lung function.
- Decreased microvascular[1] function and altered heart rate variability
- Healthcare service utilisation for respiratory and/or cardiovascular conditions
- Medication use and prescription dispensing for respiratory conditions
- Eye injury
- An increase in diabetic complications
- Uptake of carcinogenic polycyclic aromatic hydrocarbons (PAH) metabolites and urinary mutagenicity due to dermal exposure
- Increases in morbidity and mortality
- Decreased immune response

In addition, among firefighters, on-shift emergency fire suppression significantly increases biomarkers of an inflammatory response and urinary concentrations of PAH metabolites and organic mutagens, and there is some evidence of DNA oxidative damage following exposure to PM. Adverse health effects are associated with smoking and duration of service.

Repeated exposure

Repeated exposure to PM has been associated with:

- Changes in lung and cardiovascular function, especially among vulnerable population such as children and older people
- Health service and medication use for breathing problems
- Skin problems
- Mortality

The community-level impacts of repeated exposure to $PM_{2.5}$ from wildfire may be more deleterious than the impacts from ambient sources.

Among firefighters, the impacts of exposure to $PM_{2.5}$ on biomarkers and genetic material may be cumulative. There may be incomplete recovery from repeated exposures to $PM_{2.5}$

[1] Relating to the smallest blood vessels.

Longer term impacts of single and repeated acute exposure

- Repeated exposure to PM in firefighters is related to the presence of inflammatory biomarkers but physiological impacts decrease post-exposure.
- Short term exposure to coal mine fire smoke may have long term impacts on nearby and surrounding communities.
- Repeated exposure to PM is related to relatively short-term, rather than longer term, impacts on respiratory health in the community.
- Exposures to $PM_{2.5}$ *in utero* (during pregnancy) and in children may have longer-term impacts.
- Impacts of exposure to PM in the community are related to the person's health status at birth.
- Repeated exposure to PM is not related to longer term impacts on cardiovascular health in the community.
- Limited evidence suggests possible longer-term impacts of exposures to fire smoke as evidence by the presence of biomarkers for oxidative stress
- Limited evidence suggests possible longer-term impacts of exposures to chemicals that may be present in fire smoke

Dose effects

Dose effects have not been found for direct measures of pulmonary function in firefighters and health volunteers. There is indirect evidence for dose effects of exposure to PM on:

- Pulmonary function and health service use for respiratory conditions in the community, especially for at-risk populations;
- Healthcare use associated with impaired cardiac function in the community;
- Ambulance call-outs;
- Antibiotic prescriptions in infants;
- Blood biomarkers.

Mitigation effects of protocols

Anticipatory smoke modelling has a positive impact on community outcomes during major fire events.

Mitigation effects of PPE

PPE is not used as consistently as it should be, especially during later firefighting phases. Use of PPE protects against some health impacts of exposure to PM, but the extent of protection depends on the kinds of PPE used. Emerging evidence suggests that PPE should be used even in "cold zones", previously considered safe from contaminants.

Existing guidelines and protocols

We were able to access broader guidance material from national and international firefighting peak bodies and regulatory organisations

International documents included a 2018 review report from the Dutch Institute for Safety (Instituut Fysieke Veiligheid - IFV), which outlined important measures to reduce on-field exposure to contaminants by firefighters in terms of appropriate use of protective clothing and breathing apparatus. The IFV reviewed safety guidelines for 16 European firefighting organisations, and found consensus on risks of exposure to smoke and soot. All reviewed guidelines recommended that turn-out garments be removed while still on site, but away from the fire zone, to minimise skin exposure to contaminants. Laundering of turn-out garments should ensure maximal removal of contaminants, with minimal numbers of garments to be laundered at once. Breathing apparatus was recommended to remain on for at least three minutes after deployment to allow for evaporation of toxic chemicals (or 'off gassing'), but it was noted that the usual length of time for off gassing was one hour. In terms of particulate protection, the IFV report recommended that firefighters continue to wear FFP3 masks after removing breathing apparatus to limit soot inhalation by on-field firefighters. This grouping of recommendations is referred to as 'clean(er) working' procedures, and have been adopted broadly and operationalised to varying degrees across European professional firefighting organisations.

The focus of national documents was on bushfires rather than urban firefighting; however, recommendations in terms of PPE were consistent with the above Dutch review report. Specifically, protective clothing was recommended to be removed away from the fire zone, before returning to the fire station, and laundered appropriately (AFAC, 2018). Types of respiratory protection were chosen in accordance with a risk assessment of the fire zone and associated smoke exposure risk.

CONCLUSIONS

Extent of the literature:

When expanded to cover not just urban fires but also landscape fires, we identified a substantial body of literature that addresses both individual-level health impacts and population-level health impacts of exposure to $PM_{2.5}$.

Impacts on health

Evidence is strengthening that exposure to particulate matter including $PM_{2.5}$ (and PM_{10} and ultrafine PM) has adverse impacts on human health, both in the short and longer term. The clear health impacts identified by this review include respiratory effects; cardiovascular and cerebrovascular impacts, which have both short-term and long-term consequences on individuals and communities; and impacts on health service use, including emergency department presentations, GP visits, and medication use.

The most obvious acute effects at the population level are asthma and COPD exacerbations, with some impacts on cardiovascular health. These impacts are observed particularly amongst communities where harm minimisation to smoke exposure has not been implemented. In addition, some studies have reported impacts on people's eyes.

Among firefighters, the PM exposure has impacts on heart rate and microvascular structures. The documented presence of inflammatory biomarkers circulating in the body may have long-term consequences that have not yet been identified, including impacts on the brain. In addition, PM exposure was associated with increased urinary secretions of potentially carcinogenic PAHs. Finally, impacts of PM exposure on immune responses have been documented; however, short and long-term health effects are not yet clear.

Concentrations and exposure doses

Importantly, there is no current evidence of a safe $PM_{2.5}$ threshold, and as little as 1 $\mu g/m^3$ may have noticeable effects on human health, with increasing concentrations having larger impacts on a range of acute and chronic cardiovascular and respiratory health outcomes. Based on the broader PM exposure literature, the relationship between $PM_{2.5}$ dose and physiological/health response is not linear but appears to plateau at high to very high concentrations (> 60 $\mu g/m^3$).

Impacts of protocols and PPE

It is important to note a general paucity of published, research-based evidence outlining impacts of protocols and/or PPE on smoke exposure mitigation for urban career firefighters. Furthermore, almost all available evidence was derived outside of the Australian context. However, there is apparent support from within the identified literature for the routine and consistent use of PPE by all firefighters during all phases of a fire event. Some internal documents, such as Standard Operating Procedures (SOPs), were able to be accessed, as well as key guiding documents, such as the International Agency for Research on Cancer (IARC) monograph (IARC, 2013)and the Instituut Fysieke Veiligheid review of safety guidelines (IFV, 2018), and these documents have helped inform the findings of this project.

More research is needed, particularly on the efficacy of protocols and guidelines in mitigating risk to firefighters from exposure to particulate matter.

RECOMMENDATIONS

- FRV should continue to monitor for emerging evidence on the efficacy of guidelines and protocols for mitigating health risks associated with exposure to all forms and size fractions of particulate matter.
- Based on current evidence, best practice risk mitigation protocols should be enacted, monitored, and evaluated for acceptability, effectiveness and adherence.
- FRV should continue to collaborate with environmental protection monitoring agencies and public health units to maintain consistent advice to their personnel and consistent public health messaging to exposed communities in events of urban fire smoke emergencies.
- If appropriate opportunities arise, FRV could consider participating in research to:
    - Directly monitor the impact of short-term and repeated exposures to particulate matter on FRV staff and other first responders during all stages of managing fire events.
    - Improve understanding of potential structural smoke particulate matter exposure levels for various suppression activities and fire conditions.
    - Improve knowledge of firefighters' understanding of smoke hazards and avoidance/risk mitigation options.
    - Improve understanding of potential health effects of residual particulate matter deposits on skin, clothing, or other personal effects.
    - Examine the cumulative effect of the factors that affect the probability and severity of health impacts, such as, intensity of combustion, duration of exposure, frequency of exposure, career length, and personal characteristics.

BACKGROUND

Smoke is generated by major fire emergencies in a range of urban settings such as urban structures (houses, warehouses, factories, buildings), vehicles (small, medium, large, and heavy), transport (trains, trams, light-rail, and buses), tyre stockpiles, landfill or transfer stations, and industrial sites where chemicals are stored. This smoke has the potential for significant and adverse impacts on both nearby and distant communities. In addition to the direct impact of flames, firefighters and other emergency responders working on or near the fire-ground may be exposed to a range of hazardous airborne chemicals, which may have both immediate and long-term impacts on health and safety.

Specific exposures to hazardous combustion by-products of burning materials of concern identified in the literature include: (1) asphyxiants[2], such as carbon monoxide, carbon dioxide, and hydrogen sulphide; (2) irritants, such as ammonia, hydrogen chloride, particulate matter (in particular fine particulate matter), volatile organic compounds (VOC), nitrogen oxides, phenol, and sulphur dioxide; (3) allergens; and (4) carcinogens, such as asbestos, benzene, styrene, polycyclic aromatic hydrocarbons [PAH][3], and certain heavy metals. Airborne toxic elements and compounds, such as metals and PAH, can bind to particulate matter, which becomes their vehicle to transport them throughout the body's systems (Fabian et al., 2010; Mouritz & Gibson, 2006).

The Metropolitan Fire Brigade, which became Fire Rescue Victoria on 1 July 2020, identified that Incident Controllers have limited guidance to assist them when responding to **urban industrial fires** and making evidence-based-decisions relating to minimising adverse health impacts from exposure to PM in smoke, both for emergency responders and surrounding communities.

Fine particulate matter

Particulate matter (PM) pollution is a complex and heterogeneous mixture of organic and inorganic solid particles and liquid droplets suspended in air that vary in size and chemical composition. Figure 1 illustrates the relative sizes of PM compared with a human hair and a grain of sand. PM with aerodynamic diameter of <10 µm is known as PM_{10} or coarse PM. The constituents of fine particulate matter (PM) are smaller than 2.5 micrometres (0.0025 mm) in aerodynamic diameter[4] and are commonly referred to as $PM_{2.5}$. They are up to 30 times smaller than the width of a human hair. $PM_{2.5}$ consists of two distinct components: PM <0.1 µm or ultra-fine particles (UFPs) and accumulation-mode particles. UFPs represent the largest portion in terms of concentration but little mass (Gong et al., 2014).

[2] An asphyxiant gas reduces or displaces the normal oxygen concentration in breathing air. Exposure for prolonged periods of oxygen depleted air will lead to death by asphyxiation (suffocation).
[3] Polycyclic aromatic hydrocarbons (PAHs) occur naturally in coal, crude oil, and gasoline and are also present in products made from fossil fuels, such as coal-tar pitch, creosote, and asphalt. Long-term health effects of exposure to PAHs may include cataracts, kidney and liver damage, and jaundice. Long-term exposure to low levels of some PAHs have caused cancer in laboratory animals.
[4] A micrometre (µm) is also known as a micron.

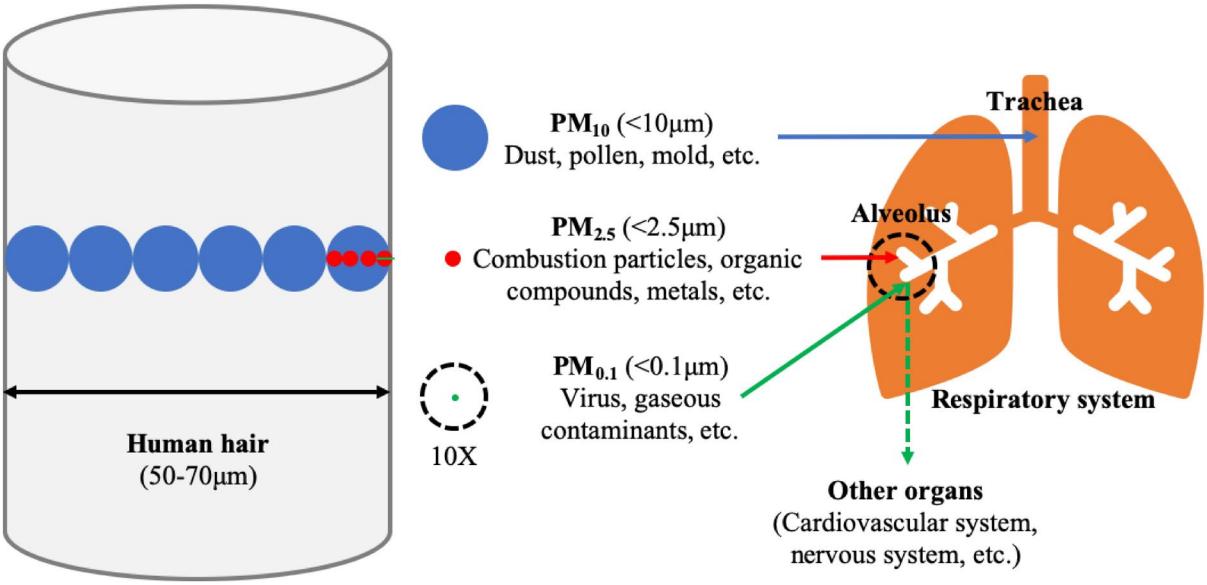

Figure 1: Size fractions of particulate matter in relation to a grain of sand and a strand of human hair; and how far each size fraction can enter the body via the respiratory system (Yang & Tang, 2020).

$PM_{2.5}$ is emitted from various sources, including motor vehicles, residential wood burning, urban fires, forest/vegetation fires, agricultural burning, power plants, airplanes, dust storms and volcanic eruptions. It may be emitted in a variety of forms including combustion by-products, metals, and organic compounds. $PM_{2.5}$ measures are frequently reported in mass per volume of air – micrograms per cubic metre ($\mu g/m^3$).

Horn et al. (2022) recently measured concentrations of airborne contamination at several stages post-fire in a suburban house, including directly after the fire had been suppressed and before overhaul[5]. Airborne particulate matter was elevated to potentially unhealthy levels (based on air quality index) shortly after fire suppression, with median $PM_{2.5}$ levels over 100 $\mu g/m^3$, which would be described by the Victorian Environment Protection Authority as "very poor"[6].

Health impacts of fine particulate matter

$PM_{2.5}$ is small enough to be inhaled deeply into the lungs, with consequent potential for negative impacts on respiratory health (Mouritz & Gibson, 2006; Xing et al., 2016). $PM_{2.5}$ is also fine enough to penetrate disrupted epithelial layers[7] and enter the blood stream (circulatory system) and may have adverse systemic effects related to systemic inflammation

[5] Overhaul is the practice of searching a fire scene to detect hidden fires or smouldering areas that may rekindle and to safeguard signs of arson.

[6] https://www.epa.vic.gov.au/for-community/monitoring-your-environment/about-epa-airwatch/calculate-air-quality-categories

[7] Epithelial tissue is a thin, continuous, protective layer of cells that lines to outer surfaces of organs and blood vessels throughout the body as well as the inner surfaces of cavities in many internal organs. A disrupted epithelium means alterations to normal epithelial layer integrity.

and oxidative stress[8] within the cardiovascular system (heart, circulatory system of arteries, veins, arterioles, and venules) and the organs (kidney, liver, etc.) (An et al., 2008). $PM_{2.5}$ may also directly enter the brain and central nervous system via the olfactory mucosa that separates the nose from the brain (Babadjouni et al., 2017). Over long-term exposure, it is one of the leading causes of global mortality and morbidity (Burnett et al., 2018; Stanaway et al., 2018). Pooled population studies examining acute exposure to $PM_{2.5}$ indicate that 10 $\mu g/m^3$ increases in $PM_{2.5}$ levels are associated with significantly increased risk for hospital admissions and mortality due to cardiac and respiratory conditions, and stroke (Requia et al., 2018; Gu et al., 2020).

Traditionally, literature related to combustion by-products is divided along arbitrary lines—urban versus wildland fires—to highlight differences in the nature of fuel source and associated by-products. The focus of the current literature review is evidence on the health impacts of urban fires. However, it is important to understand that airborne PM pollution is associated with all combustion by-products, regardless of fuel source. Significant extant literature outlines the toxic nature of biomass and wildland combustion by-products, with clear evidence of its deleterious effects on human health (Cascio, 2019; Johnston et al., 2014; Melody & Johnston, 2015).

Physiological responses to exposure to fine and ultrafine particles

The size of UFPs determines how far into the lung bed they penetrate. $PM_{2.5}$ size allows deep penetration into the lungs through to the alveolus and alveolar bed[9]. These compounds then dissociate within the moist environment of the alveolar bed, with UFPs diffusing across the alveolar membrane and into the bloodstream (Wu et al., 2018). There is evidence from studies of rats that some particles translocate to the pulmonary interstitium (area between cells) of the respiratory tract, the olfactory region of the brain, and the liver within four hours of exposure (Oberdörster et al., 2004). The most likely mechanism of transfer of UFPs into the brain/central nervous system (CNS) is from deposits on the olfactory mucosa of the nasopharyngeal region (upper throat area behind the nose) of the respiratory tract and subsequent translocation via the olfactory nerve (Oberdörster et al., 2004).

Physiological responses to exposure to UFPs fall into three main categories:

- Inflammatory response: translocation of particles into circulation resulting in oxidative stress and systemic inflammation.
- Cardiovascular response:

[8] Oxidative stress is an imbalance between free radicals and antioxidants in the body. Free radicals are oxygen-containing molecules with an uneven number of electrons. The uneven number allows them to react easily with other molecules. Free radicals can cause large chain chemical reactions in the body, called oxidation. They can be beneficial or harmful. Antioxidants are molecules that can donate an electron to a free radical without making themselves unstable. This causes the free radical to stabilize and become less reactive. https://www.healthline.com/health/oxidative-stress

[9] The alveolar bed is lung tissue densely packed with alveoli, which are tiny air sacks at the end of air tubes in the lungs. The alveoli are where the lung and the blood exchange oxygen and carbon dioxide during breathing. The alveolar membrane is the gas exchange surface. Across the membrane, oxygen is diffused into the capillaries and carbon dioxide is released from the capillaries into the alveoli to be breathed out.

    - Direct cause: autonomic nervous system disruption at the epithelial[10] and systemic[11] level, resulting in heart dysrhythmias[12] and heart rate variability, increased heart rate, and systemic vasoconstriction[13].
    - Indirect cause: secondary to systemic inflammation[14].
- Haemostatic response[15]: platelet[16] aggregation secondary to inflammatory mediators released in response to epithelial and systemic oxidative stress. Micro-clotting can lead to cardiovascular disorders and increase the risk of stroke and sudden death (Wu et al., 2018).

Individual biomarkers associated with PM exposure include:

- Autonomic biomarkers: heart rate; systolic blood pressure (SBP); and diastolic blood pressure (DBP).
- Lung inflammation biomarkers: Exhaled breathe condensate (EBC)[17] to assess airway pH (acidity), nitrogen oxides, molondialdehyde (MDA)[18]; and fractional exhaled nitric oxide (FeNO)[19].
- Haemostatic biomarkers: von Willebrand Factor (VWF); soluble CD40 Ligand (sCD40L); and P-selectin (sCD62P)[20].
- Systemic inflammation and oxidative stress markers: plasma fibrinogen[21]; white blood cells (WBCs); urinary MDA[22]; and urinary 8-hydroxy-2'-deoxyguanosine (8-OHDG)[23].

[10] Epithelial tissue is a thin, continuous, protective layer of cells that lines to outer surfaces of organs and blood vessels throughout the body as well as the inner surfaces of cavities in many internal organs.
[11] Pertaining to groups of organs, such as the gastrointestinal system or the nervous system.
[12] A dysrhythmia is an abnormality in a physiological rhythm, especially in the activity of the brain or heart.
[13] Vasoconstriction is the narrowing of blood vessels and can result in an increase in blood pressure.
[14] Inflammation is part of the complex, protective biological response of body tissues to harmful stimuli, such as pathogens, damaged cells, or irritants. The function of inflammation is to eliminate the initial cause of cell injury, clear out damaged cells and tissues, and initiate tissue repair. Chronic inflammation can eventually start damaging healthy cells, tissues, and organs, and can lead to DNA damage, tissue death, and internal scarring. Chronic inflammation has been linked to the development of diseases including cancer, heart disease, rheumatoid arthritis, obesity, asthma, and neuro generative diseases such as Alzheimer's disease.
[15] The haemostatic response is to retard or stop the flow of blood within blood vessels.
[16] Platelets are minute, disk-shaped bodies that assist in blood clotting by adhering to other platelets and to damaged epithelium.
[17] Exhalate from breath that has been condensed via a collection device.
[18] A marker for oxidative stress.
[19] Fractional exhaled nitric oxide is an gaseous molecule which can be measured in the human breath test and has been studied extensively as a marker of inflammation
[20] These biomarkers measure platelet activation. A raised blood platelet count is known as thrombocytosis.
[21] Fibrinogen is the major plasma protein coagulation factor. Low plasma fibrinogen concentrations are associated with increased risk of bleeding. High fibrinogen levels can indicate inflammation or tissue damage.
[22] Malondialdehyde (MDA) is an important indicator of oxidative degradation of polyunsaturated fatty acids. Urinary MDA is useful as a non-invasive test for monitoring oxidative stress.
[23] Urinary 8-OHdG is a good biomarker for oxidative lesions and is used in risk assessment of various cancers and degenerative diseases.

Health of firefighters

At the time of recruitment into firefighting roles, firefighters must meet strict fitness standards, so they tend to be much fitter and healthier than the general population and have lower rates of tobacco smoking. Despite this, studies have found that firefighters experience increased rates of certain types of cancer. For example, the 2014 Australian Firefighters' Health Study conducted by Monash University found that cancer incidence is significantly higher among male career firefighters than in the Australian population (Glass et al., 2014). There is also a statistically significant increase in prostate cancer incidence among career full-time firefighters overall, and particularly for those employed for more than 20 years. The risk of melanoma is also significantly elevated. However, there is no evidence of an increase in cardiovascular or respiratory mortality for firefighters compared to the general Australian population (Glass et al., 2014).

While the exact cause of the increased cancer incidence among firefighters is unknown, long-term exposure to low doses of chemicals from smoke may be one of the reasons.

Types of studies

Direct study of firefighters' health and wellbeing: The Monash University study of firefighters' health mentioned above was conducted by looking at the personnel records and incident records of individual firefighters. To obtain mortality and cancer outcomes, individuals in the cohort were linked to the National Death Index and the Australian Cancer Database held by the Australian Institute of Health and Welfare (AIHW). Australian population data were used to calculate the expected numbers of deaths and cancers, adjusted for age distribution, and these numbers were compared with those for groups of firefighters.

Analyses of large population databases: Large datasets can be used to estimate the impacts of exposure to smoke on community populations. Such datasets can be used to calculate, for example, rates of emergency department (ED) presentations and medication prescriptions in the wake of a fire event.

Chamber studies: A test chamber is a sealed enclosure whose content and temperature can be manipulated to mimic the effects of environmental conditions. Use of these chambers permits systematic variation in individual parameters under controlled conditions, unlike ambient air studies, where the continuous exposure to pollutants and the effects of weather and climate are often difficult to assess and incorporate quantitatively into data analyses (Finlayson-Pitts & Pitts, 1999). Environmental chamber studies are useful tools in examining the relationships between, for example, emissions, air quality and impacts on human or animal biomarkers.[24]

Fire simulations: Simulations are frequently used in training firefighters and in studies of the impacts of smoke and other exposures on firefighters, as they are a relatively safe, ethical, controlled, and cost-effective alternative to exposure to spontaneous or unplanned fires.

[24] A biomarker is a naturally occurring molecule, gene, or characteristic by which a particular pathological or physiological process, disease, etc. can be identified.

Animal toxicology studies: The use of mice as model organisms to study human biology is predicated on the genetic and physiological similarities between the species (Perlman, 2016). Mice are invaluable for studying biological processes that have been conserved during the evolution of the rodent and primate lineages. Mouse models can only approximate models of human functioning, however, because the networks linking genes to disease are likely to differ between the two species. The use of mice in biomedical research needs to take account of the evolved differences as well as the similarities between mice and humans (Perlman, 2016). Mouse models have proved a valuable tool for studying potential effects of pollutants such as tobacco smoke and diesel exhaust PM (Maes et al., 2010).

Literature reviews and desktop simulation studies: These studies rely on published literature and data to draw research conclusions.

Epidemiological health studies in humans related to exposure to urban fire smoke tend to be observational rather than experimental in design, for ethical and practical reasons. As such, it is not possible to identify causality (cause and effect relationships) between smoke exposure and health outcomes, however with the body of knowledge growing, the strength of evidence is increasing.

THE CURRENT PROJECT

The aims of the current project overall were to:

- Identify and analyse contemporary peer-reviewed literature on the potential health impacts of short-term exposure to PM, in particular $PM_{2.5}$.
- Develop background content for operational guidance materials for Incident Controllers to assist them to make informed decisions before, during, and after an urban fire/smoke event to minimise adverse health impacts from smoke on firefighters and other emergency responders.
- Develop background content for operational guidance materials for Incident Controllers to assist them to make informed decisions pertaining to advice and warnings to the community within a short-term period (less than 24 hours), particularly related to “shelter in place” and emergency evacuations, with the aim of minimising adverse health impacts from smoke exposure in the community.

Fire Rescue Victoria wished to focus on urban industrial fires to identify:

- Potential concentrations of $PM_{2.5}$ that may cause adverse health effects whilst considering the type of fire/fuel load.
- Evidence relating to the potential impact of repeated exposures that may be experienced by emergency responders throughout the course of their careers.
- Evidence of the efficacy of potential mitigation measures to minimise adverse exposure impacts for firefighters and other emergency responders on or near the fire-ground and for local communities affected by smoke.
- Additional data required to define guidelines more thoroughly for acute exposure to $PM_{2.5}$ from fires for emergency responders and communities, based on the available

health study data for acute exposure effects of $PM_{2.5}$, including possible toxicity; and development of a scope of work required to provide this data.

Project team at La Trobe University

La Trobe University was contracted to assist the Metropolitan Fire Brigade with the project early in 2020. The project lead, Professor Yvonne Wells PhD, is a senior staff member in the Australian Institute of Primary Care & Ageing at La Trobe University. When the project began, Dr Rachel Tham PhD was a Research Fellow in air pollution and noise research in the Behaviour, Environment and Cognition Research Program in the Mary MacKillop Institute for Health Research at the Australian Catholic University, and a Clinical Educator and Examiner in the Department of Dentistry at La Trobe University. In 2022, Rachel moved to the Allergy and Lung Health Unit in the Melbourne School of Population and Global Health at the University of Melbourne. The team included research assistants and research fellows—Kane Solly BPsychSci, Dr Nicholas Hunter PhD, Dr Samantha Clune, RN PhD, and Dr Anne-Marie Mahoney, RN PhD. The team also relied on assistance from La Trobe University library staff.

Aims of the literature review

Project methods included a series of systematic rapid evidence reviews accompanied by a broader "grey literature" review. The project focused on:

a) "**Acute exposure**," defined by the US Environment Protection Agency as "exposure by the oral, dermal, or inhalation route for 24 hours or less".[25]

b) **Urban**, industrial fires.

The research questions set by the Metropolitan Fire Brigade (now Fire Rescue Victoria) and addressed by this project through literature and document review include:

1. What are the likely or documented adverse health effects (and clinical outcomes) from acute $PM_{2.5}$ exposure, in the short-term and longer-term?
2. What concentrations and exposure doses of smoke contaminants (primarily $PM_{2.5}$) from urban industrial fires are associated with adverse health effects following acute exposures (i.e., for up to 24 hours duration), taking the type of fire and/or fuel load into account)?
3. What is the potential impact of repeated exposures that may be experienced by emergency responders through the course of their careers?
4. What protocols have been shown to reduce health risks and/or improve outcomes for emergency responders?
5. How effective are various respiratory protective measures (e.g., $PM_{2.5}$ dust masks, but excluding self-contained breathing apparatus) at protecting emergency responders on or near the fire-ground?

[25] https://iaspub.epa.gov/sor_internet/registry/termreg/searchandretrieve/glossariesandkeywordlists/search.do?details=&vocabName=IRIS%20Glossary

A further narrative literature and document review (including a search of internet-based resources) was employed to address the additional question:

6. What guidelines or procedures are other agencies or jurisdictions using for this type of exposure and what control actions are taken?

As noted above, population-level epidemiological health studies related to exposure to urban fire smoke tend to be observational rather than experimental in design, and it is not usually possible to identify causality (cause and effect relationships) between smoke exposure and health effects. Therefore, we aimed to report on levels of association between smoke exposure and the health outcomes and comment on the strength of the evidence within the relevant peer-reviewed scientific literature.

METHODS

To address the identified research questions for this project, a series of rapid literature reviews was completed. To meet the requirements of the project as efficiently as possible, within a rapid evidence review framework, we aimed to:

- Conduct a series of rapid reviews that were systematic and methodologically justifiable to deliver outputs within a short time frame.
- Use La Trobe University library expertise to assist with developing our search strategies.
- Use the Covidence software package to assist with managing identified literature.

A rapid review is not a full systematic review. Rather, strategic decision-making in the planning phase sets out parameters that limit the review to a project that is manageable within set timelines.

A commonly used strategy to limit the scope of literature reviews is to examine only peer-reviewed literature. However, this strategy would be likely to reduce the scope of the review too far, and we planned to scan the "grey literature" as well, including reports from other Australian jurisdictions, international government and non-government agencies, and key organisations with relevant expertise.

We intended to be as inclusive as possible in searching published information relevant to the key questions. We planned to include refereed literature such as Cochrane reviews and other systematic reviews; individual papers reporting randomised controlled trials (RCTs), quasi-experimental (e.g., pre- and post-intervention evaluations), observational, and cross-sectional studies; and Australian literature and literature from comparable countries written in English.[26]

However, being a rapid evidence review, the review process had to be constrained. Our plan was to constrain the review by:

- Limiting the databases searched to Medline and the Cumulative Index to Nursing and Allied Health Literature (CINAHL), given that the aim of the literature review was to identify health-related outcomes.
- Limiting the additional "grey" literature search to major reports readily available on-line.
- Employing a search strategy that maximises specificity rather than sensitivity. A sensitive search aims to receive all potentially relevant documents through a broad search strategy. A specific search, in contrast, aims to retrieve only highly relevant documents in a small, precise search. A specific search risks missing some evidence, but a sensitive search is often very time consuming.
- Relying on software designed to assist systematic literature review. Covidence (www.covidence.org) is a tool that assists with tracking the review process and

[26] Generally, other literature reviews were not included. The exception was Arriagada et al. (2019), which conducted a meta-analysis, thereby contributing new knowledge.

provides an auditable trail. The results of searches from electronic databases can be uploaded directly into Covidence and the data can be managed efficiently within the software.

Standard systematic literature review methods were planned for each research question, comprising:

- Identification of potential literature.
- Title and abstract screening (two people for each article).
- Full article screening (two people for each article).
- Data extraction of remaining articles (one person to extract, a second person to check).
- Risk of bias assessment (one person to assess, a second person to check).

Methods for this literature review had to evolve to address the research questions presented in this report. This involved several stages:

Stage 1: From sequential to integrated searches

Our initial approach to addressing each research question was sequential, addressing each question one at a time. This strategy was reviewed, considering the interrelated nature of the research questions. Relevant search terms were identified to address each question, and these were discussed with FRV staff.

Stage 2: Review of search terms

A widening of search terms used in the literature review was required to best capture relevant research that would address FRV's research questions, especially given the limited literature specifically on health impacts of urban fire smoke. This change in search strategy was discussed with FRV representatives, the Victorian Department of Health, and Human Services (DHHS), and the Environmental Protection Agency (EPA). Wider search terms were agreed upon by FRV, DHHS, and EPA representatives. The La Trobe University research team subsequently included chamber studies, as well as vegetation and landscape fires.

Once the revised search terms were agreed upon by all parties, the research team then examined how best to expedite an outcome for FRV. Three options were identified: (i) start again; (ii) re-frame the methods for efficiency; and (iii) re-frame the methods to consider the desired endpoint for FRV. It was decided that options (ii) and (iii) could run concurrently and was the recommendation of the research team. The revised literature searches were conducted in October 2020.

Stage 3: Update

Because of a long delay between the searches conducted in 2020 and final reporting to FRV, and because we were aware of new literature that had been published in the interim, we decided to update the literature search on health impacts of exposure to $PM_{2.5.}$ The results of this search have been integrated with those of the original search.

Many of the newly-identified studies provide evidence on the community impacts of exposure to wildfire smoke and have been included as indirect evidence under Topic 2 (short-term impacts of repeated acute exposure) or Topic 3 (longer term impacts of single and repeated acute exposure). For example, the research literature on the community impacts of the Hazelwood mine fires in Victoria has increased substantially over the past two years.

A further minor update was made in May 2022 in response to a question on whether PPE could be required in fire "cold zones"[27].

Direct and indirect evidence

Studies were included if they provided direct or indirect evidence on the research questions:

- Direct evidence was defined as studies that directly measured health outcomes from exposure to fire smoke.
- Indirect evidence (type 1) included secondary analyses of existing databases, and included:
    - Community studies where the outcome is an indirect measure of health outcomes, such as use of health services or medications.
    - Community studies of mortality rates.
    - Community studies where exposure could not readily be described as acute or repeated. (These studies are included because they are important additions to the literature, although they do not meet FRV's inclusion criterion of short-term exposure.)
- Indirect evidence (type 2) included:
    - Studies that directly measured compounds that are known to attach to PM derived from fire smoke (as defined) as an exposure.
    - Non-human studies (e.g., mouse models or statistical modelling).
    - Studies that implied links between exposure and outcomes rather than demonstrating them.
    - Studies that lacked generalisability.
    - Studies that focused largely on pathophysiological effects (e.g., fatigue).

Search parameters

The search terms used in the literature review for Phase 1a (Health effects of $PM_{2.5}$ exposure) and Phase 1b (Mitigation of health effects) are set out in the tables below:

[27] The US Environmental Protection Authority defines a cold zone as an area that is free from contamination and may be used safely as a planning and staging area. Emergency responders in the cold zone are not required to wear PPE or SCBA.

Table 1: Search terms for health effects of PM2.5 exposure (RQ 1 – 3)

Search	Search String
1	urban fire* OR industrial fire* OR structur* fire OR car fire* OR building fire* OR *chemical fire OR t*re fire OR house fire* OR home fire* OR office fire* OR city fire* OR suburban fire* OR residential fire* OR commercial fire* OR *fire OR biomass fire* OR vegetation fire OR coal mine fire* OR wildfire* OR bushfire* OR landscape fire* OR prescribed burn* OR planned burn* OR fuel reduction burn* OR forest fire* OR peat fire* OR overhaul* OR knockdown* OR suppression*
2	particulate matter OR fine particle* OR PM10 OR ultrafine particle* OR UFP OR "$PM_{2.5}$" OR smoke contaminant* OR smoke
3	1 AND 2
4	emergency department* OR ED OR emergency ward OR emergency room OR Emergency unit OR hospital* OR hospital admission* OR hospital presentation* OR Out-of-hospital OR ambulance* OR physician visit* OR medical visit* OR doctor visit* OR diagnosis OR general practitioner*
5	myocardial infarct* OR cardiac OR cardiovascular OR cardiorespiratory OR Respirat* OR pulmon* OR asthma* OR cerebrovascular OR stroke OR mortality OR morbidity OR ocular OR eye OR lung* OR cancer*
6	4 AND 5
7	biomarker* OR inflam* OR lung capacity OR urinary excretion* OR irritat* OR metabolite* OR spirometr* OR hypoxem* OR hypoxaem* OR heart rate variability OR HRV OR FVC OR FEV OR clara cell OR blood pressure OR prescription* OR pharmaceutic* OR medication use OR medication* OR in vivo OR in vitro OR chamber stud* OR human experiment* OR oxidative stress OR physiological
8	6 OR 7
9	3 AND 8

Table 2: Search terms for mitigating effects of protocols (RQ 4)

Search	Search String
1	urban fire* OR industrial fire* OR structur* fire OR car fire* OR building fire* OR *chemical fire OR t*re fire OR house fire* OR home fire* OR office fire* OR city fire* OR suburban fire* OR residential fire* OR commercial fire* OR *fire OR biomass fire* OR vegetation fire OR coal mine fire* OR wildfire* OR bushfire* OR landscape fire* OR prescribed burn* OR planned burn* OR fuel reduction burn* OR forest fire* OR peat fire* OR overhaul* OR knockdown* OR suppression*
2	particulate matter OR fine particle* OR PM10 OR ultrafine particle* OR UFP OR "$PM_{2.5}$" OR smoke contaminant* OR smoke
3	1 AND 2
4	protocol* OR guideline* OR SOP OR "Standard operating procedure" OR "Systematic operating procedure" OR checklist OR guidance OR standard* OR advisory statement* OR risk communication
5	3 AND 4

Table 3: Search terms for mitigating effects of PPE (RQ 5)

Search	Search String
1	urban fire* OR industrial fire* OR structur* fire OR car fire* OR building fire* OR *chemical fire OR t*re fire OR house fire* OR home fire* OR office fire* OR city fire* OR suburban fire* OR residential fire* OR commercial fire* OR *fire OR biomass fire* OR vegetation fire OR coal mine fire* OR wildfire* OR bushfire* OR landscape fire* OR prescribed burn* OR planned burn* OR fuel reduction burn* OR forest fire* OR peat fire* OR overhaul* OR knockdown* OR suppression*
2	particulate matter OR fine particle* OR PM10 OR ultrafine particle* OR UFP OR "$PM_{2.5}$" OR smoke contaminant* OR smoke
3	1 AND 2
4	PPE OR "personal protective equipment" OR SCBA or "self-contained breathing apparatus" OR mask* OR "respiratory protection"
5	3 AND 4

The databases included in the literature review were CINAHL, Embase, and Medline.

RESULTS

In light of the large body of work generated from the numerous research questions addressed by the literature review, results from each aspect of inquiry will be presented separately, according to research question.

RESULTS FOR RESEARCH QUESTIONS 1 – 3: HEALTH EFFECTS OF EXPOSURE TO PARTICULATE MATTER

Screening process and results

This section sets out the overall results for research questions 1 to 3.

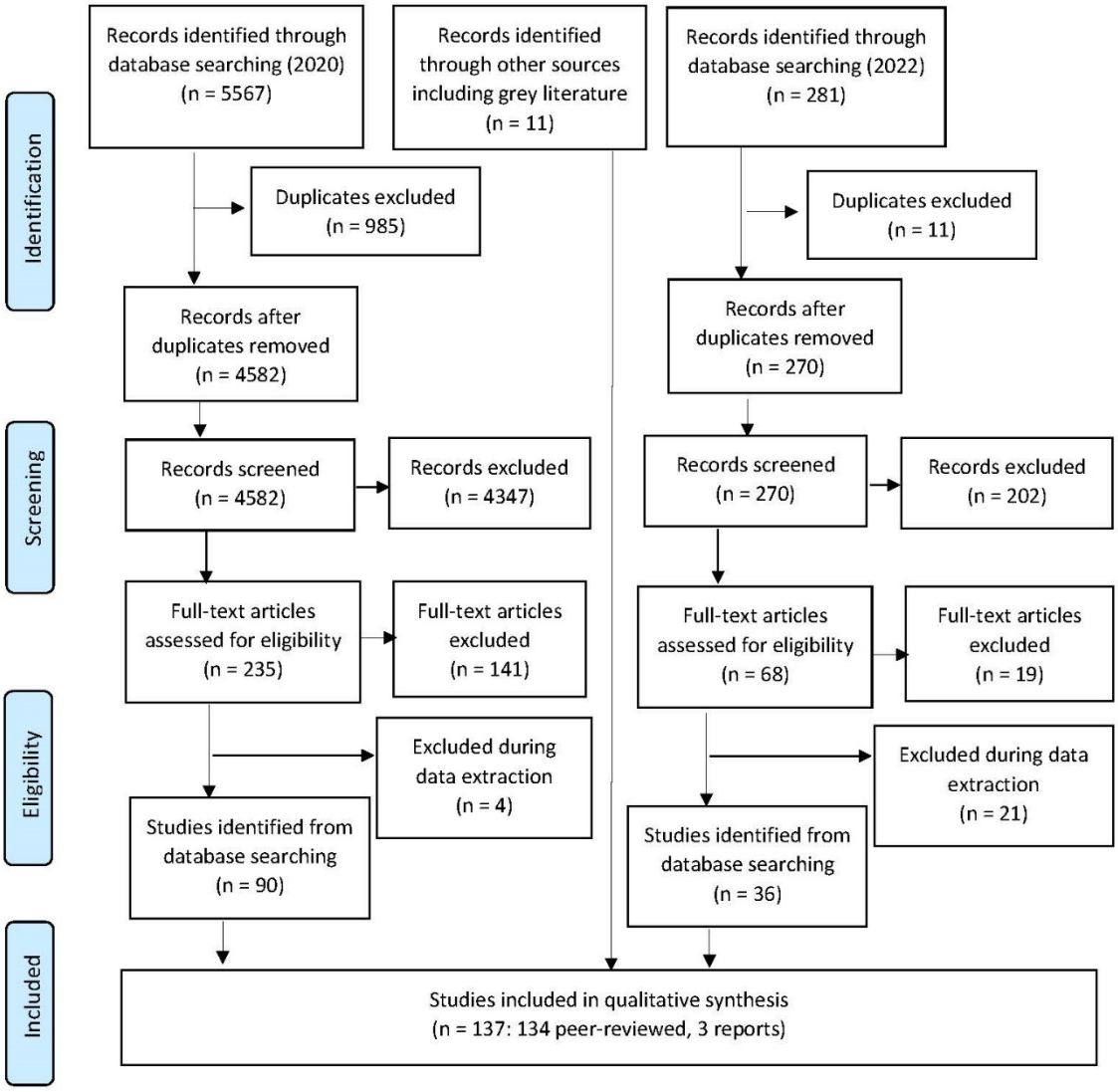

Figure 2: PRISMA diagram for literature search on research questions 1 -- 3

The combined literature search on Questions 1 – 3 resulted in identifying 137 sources: 134 peer-reviewed articles and three reports.

Description of identified studies

The following figures illustrate results by year of publication, nationality of the research team, and type of study.

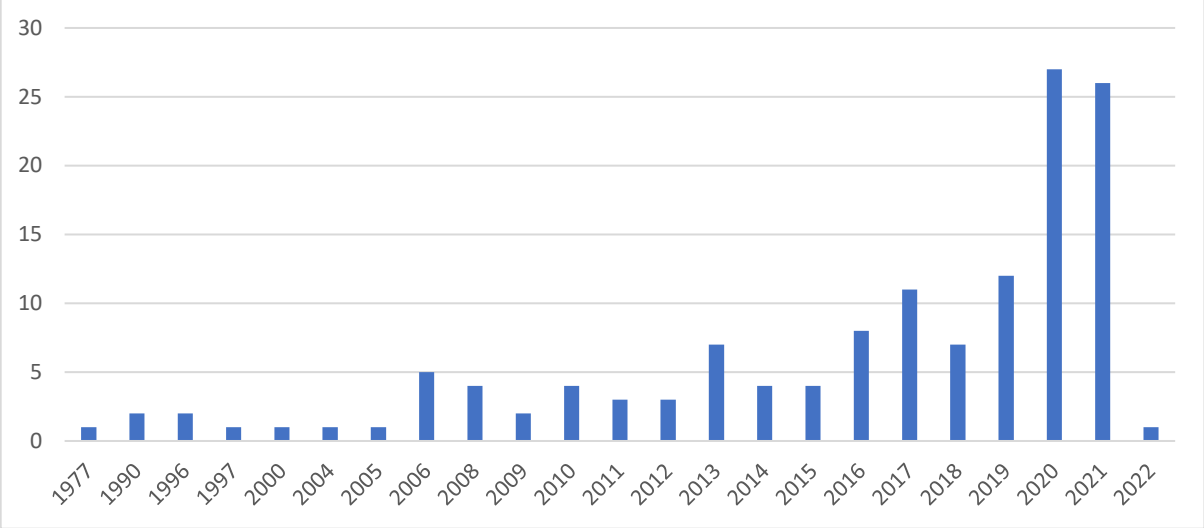

Figure 3: Year of publication of identified sources for research questions 1 -- 3

Figure 3 clearly shows the explosion in relevant literature, with over half (54%) of the articles in this review published in 2017 or later.

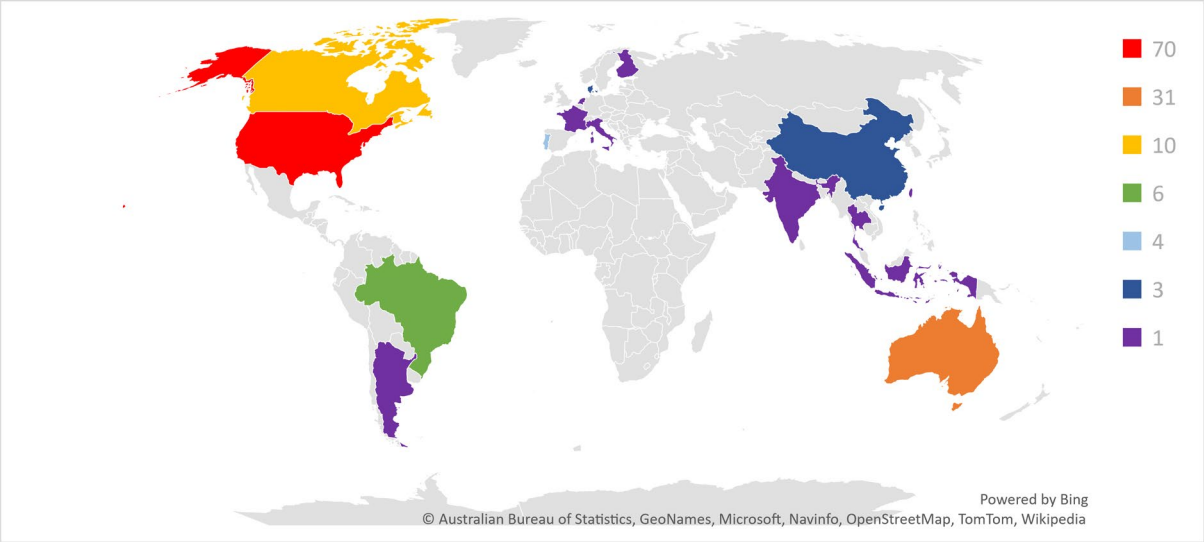

Figure 4: Country of origin of identified sources for research questions 1 -- 3

Figure 4 illustrates the major sources of data for the current review: The USA (n = 70), Australia (n = 31), and Canada (n = 10), with smaller numbers from a wide range of other countries (see table below).

Table 4: Country of study by study setting for research questions 1 – 3

	Study setting				
Country	**Community**	**Firefighters**	**Laboratory**	**Desktop[1]**	Total
Argentina	1				1
Australia	29	1		1	31
Brazil	4		2		6
Canada	6	3			9
China			3		3
Denmark		3			3
Finland	1				1
France		1			1
India			1		1
Indonesia	1				1
Italy			1		1
Korea			1		1
Portugal	1	3			4
Singapore		1			1
Taiwan		1			1
Thailand	1				1
The Netherlands		1			1
USA	37	16	16	1	71
Total	82	30	24	2	137

1. Includes meta-analysis (n = 1) and statistical modelling (n = 1)

Most studies (n = 83, 59%) were based in community populations, with a further 30 (22%) on firefighters and 24 (18%) based in the laboratory. Australia and the USA contributed the largest number of population-based studies, while the USA contributed most studies on firefighters and most laboratory-based studies.

The literature review results for research questions 1-3 were divided into four topics:

- Short-term impacts of acute exposure to PM
- Short-term impacts of repeated exposure to PM
- Longer term impacts of single and repeated acute exposure to PM
- Dose effects of PM exposure.

The following sections of the report deal with each of these topics before addressing other research questions (on mitigation effects and existing guidelines and protocols).

RESULTS FOR TOPIC 1: SHORT-TERM IMPACTS OF ACUTE EXPOSURE TO PM

Peer-reviewed literature

This rapid literature review identified 32 studies with direct evidence on impacts of exposure to PM on health, and a further 59 studies with indirect evidence (45 type 1 [secondary data], and 14 type 2). Three studies were identified in the grey literature.

Studies with direct evidence of PM exposure

General characteristics: Studies of the acute impact of fire-smoke related PM exposure on individual-level health effects comprised mostly pre-test/post-test studies of cohorts of healthy firefighters. Study settings were predominantly in the USA, Canada, and Australia.

Outcome measures: Individual-level health effects included lung function, vascular function, cardiac impacts, immune responses, inflammatory responses, and uptake of carcinogenic PAH metabolites.

What the studies tell us: At the individual-level, acute fire-smoke related PM exposure may be associated with altered heart rate, decreased microvascular function, changes in lung function, and increased presence of inflammatory biomarkers. Exposure to PM is also associated with airways inflammation and biomarkers of oxidative stress. Emergency fire suppression activities increase heart rate but may decrease systolic blood pressure.

- **PM exposure may lead to changes in lung function**

Ten studies collected lung function data using spirometry (forced expiratory volume in 1-second [FEV_1], forced vital capacity [FVC], and peak expiratory flow [PEF]).

An early study by Genovesi et al. (1977) described widespread symptoms of mildly-to-moderately severe hypoxemia[28] in firefighters exposed to smoke during suppression of a building fire. Three early studies (Chia et al., 1990; Gu et al., 1996; Large et al., 1990) found that firefighters exposed to smoke mixtures have poorer respiratory measures, such as reduced forced expiratory volume after one second (FEV_1), than control groups. These changes in airway responsiveness carry increased risks of impaired and irreversible respiratory function. Additional symptoms reported by firefighters exposed to smoke included hoarseness, cough, shortness of breath, wheezing, nasal/throat irritation, chest pain, and fatigue (Large et al., 1990).

Six later studies have confirmed that $PM_{2.5}$ exposure is associated with significant reductions in lung function, including reduced FEV_1, FVC, FEV_1/FVC ratio, and PEF in healthy firefighters (Gaughan et al., 2014; Lipner et al., 2019; Miranda et al., 2012; Nelson et al., 2020), healthy volunteers (Ferguson et al., 2017), and mixed community populations (Orr et al., 2020). In the Gaughan et al. study (2014), impacts were limited to those aged over 25 years. In contrast, three studies found no significant associations between $PM_{2.5}$ exposure and lung function changes. One of these studies involved a sample of 10 healthy adult male volunteer firefighters in a controlled exposure experiment (Ferguson et al., 2016); and two studies

[28] Low oxygen levels in the blood.

involving people with diagnosed asthma (Johnston et al., 2006; Vora et al., 2011). Johnston et al. suggested that this effect may be due to the effectiveness of asthma medication in minimising lung function effects.

Cherry et al. (2021a, 2021b) examined the effects on respiratory health of firefighters recruited from 12 fire services attending a catastrophic wildfire at Fort McMurray, Canada, in 2016. Blood samples were taken from a subsample (n = 68) of non-smoking firefighters in May and August/September 2016 and used to measure concentrations of inflammatory markers in plasma and the relation of these markers to exposures and reports of respiratory ill-health. Spirometry showed decreased FEV_1 and FVC with increasing exposure.

Finally, two studies found no overall association between $PM_{2.5}$ exposure and lung function in aggregated data but reported age-specific effects. A study of 17 firefighters (Gaughan et al., 2014) found that mean FEV_1 did not change pre-post shift, or cross-shift (across 4 days). However, mean FEV_1 did change when stratified by age, with a mean increase (0.02 Litres/second) for younger firefighters (those aged under 24) but significant greater mean decreases for those aged 25-29 years (-0.08 L/sec) and 30-36 years (-0.10 L/sec). Higher concentrations of respirable levoglucosan[29] were associated with FEV_1 decline (-0.25 L/sec), adjusted for age, job, and crew operations (Gaughan et al., 2014). It is not known whether effects on lung function reversed when firefighters were not exposed to smoke.

In a study of children and adolescents aged from 4 to 21 years and younger (n = 1404), Lipner et al. (2019) found no significant associations between $PM_{2.5}$ exposure and decreased FEV_1 in the full sample. However, they reported that one day after exposure, while children in the older group—those aged 12-to-21 years—had significantly decreased mean FEV_1 (-0.190 L/sec), and on the following day there was borderline increased mean FEV_1 (0.106 L/sec), this pattern was absent in younger children. In addition, they reported that White, but not African-American, children had significantly improved FEV_1 two days after exposure.

- **PM exposure may lead to decreased microvascular[30] function and altered heart rate variability**

In a human exposure study of 43 healthy firefighters, Andersen et al. (2017a) reported that exposure to fire smoke $PM_{2.5}$ during training exercises was associated with significantly decreased microvascular function, altered heart rate variability, and increased urinary excretion of 1-hydroxypyrene (1-OHP)[31]. Additional observations included: (i) Firefighters were primarily exposed to PM while in the 'bystander position', when not actively engaged in fire suppression activities; (ii) Exposure risks were increased where firefighters removed their self-contained breathing apparatuses (SCBA); (iii) Altered cardiovascular disease endpoints after firefighting were most likely due to complex effects from a combination of PM exposure, physical exhaustion, and increased core body temperature; and (iv) No differences in results

[29] Levoglucosan is an organic compound formed from burning carbohydrates such as starch and cellulose. It is often used as a chemical tracer for biomass burning in atmospheric chemistry studies, particularly with respect to airborne particulate matter.
[30] Relating to the smallest blood vessels.
[31] A human metabolite found in the urine of outdoor workers exposed to air pollution. It indicates exposure to polycyclic aromatic hydrocarbons (PAHs).

were apparent between fire environments (i.e., a constructed firehouse vs. a flashover container). A notable limitation of the study was that authors were unable to differentiate the effects of smoke exposure from those of increased body heat and physical activity associated with the fire suppression, as the firefighting exercises involved simultaneous exposure to all three. It is possible that the observed short-term vascular effects reflect increased blood flow to ameliorate build-up of waste products from the physical exercise and reduce core body temperature.

In a blinded randomised trial of 16 male firefighters, Hunter et al. (2014) found that controlled exposure to 1 μg/m^3 UFP in wood smoke during intermittent exercise significantly increases carboxyhaemoglobin[32] levels in the blood but has no significant effect on arterial blood flow when compared to dose-dependent forearm blood flow changes in response to vasodilators. These findings suggest that wood smoke exposure does not appear to impair vasomotor[33] or fibrinolytic function[34] or increase thrombus formation[35]. The authors suggested that acute cardiovascular events may be precipitated by other pollutants.

Wu et al. (2021) studied resting systolic/diastolic blood pressure (SBP/DBP) and heart rate (HR) of wildland firefighters before (pre-shift), after (post-shift), and the next morning immediately following prescribed burn shifts (burn days) and regular work shifts (non-burn days) in 38 firefighters. On burn days, HR significantly increased from pre-to-post-shift (13.25 beats per minute [bpm], 95% CI: 7.47 to 19.02 bpm), while SBP significantly decreased in the morning following the prescribed burns compared to pre-shift (6.25 mmHg,[36] 95% CI: 12.30 to 0.20 mmHg). However, this was due to the decrease of SBP in the firefighters who were hypertensive (8.46 mmHg, 95% CI: 16.08 to 0.84 mmHg). Significant cross-shift reductions (post-shift/next morning vs. pre-shift) were observed in SBP on burn days compared to non-burn days (7.01 mmHg, 95% CI: 10.94 to 3.09 mmHg and 8.64 mmHg, 95% CI: 13.81 to 3.47 mmHg, respectively). A significant reduction on burn days was also observed from pre-shift to the following morning for HR compared to non-burn days (7.28 bpm, 95% CI: 13.50 to 1.06 bpm) while HR significantly increased in pre-to-post-shift on burn days compared to non-burn days (10.61 beats per minute (bpm), 95% CI: 5.05 to 16.17 bpm). The authors suggested that the decreased BP observed in wildland firefighters might be due to a high level of carbon monoxide exposure and exercise-induced hypotension. On the other hand, the increase in HR immediately after prescribed burns might be attributable to wildfire smoke exposure and physical exertion in prescribed burn shifts. Altogether, the results suggest that wildland firefighting exposure might cause a distinct hemodynamic[37] response, including SBP

[32] Carboxyhemoglobin (COHb) is a stable complex of carbon monoxide that forms in red blood cells when carbon monoxide is inhaled.
[33] Vasomotor refers to actions that alter the diameter of a blood vessel (vasodilation or vasoconstriction).
[34] The fibrinolytic system functions to remove a blood clot after the vascular system is repaired and to degrade clots that form in the bloodstream.
[35] A thrombus is a blood clot that forms in a vessel and remains there.
[36] A unit of pressure equal to the pressure exerted by a column of mercury 1 millimetre high at 0°C and under the acceleration of gravity.
[37] The dynamics of blood flow

reduction and increased HR increment, especially for those who have pre-existing hypertension.

Studies with indirect evidence (Type 1) of PM exposure

General characteristics: Sixty-eight studies were identified in this category. Studies examining the impact of PM exposure on the community's health (i.e., population-level) were largely epidemiological and included time series, ecological, cross-sectional, and cohort designs. Study settings were predominantly in the USA, Canada, and Australia.

Outcome measures: Community-level health effects included respiratory, cardiovascular, cerebrovascular, and eye conditions. Individual-level health effects included lung function, vascular function, and inflammatory responses and were usually measured by use of health services. Mortality data have also been used as a proxy for community-level health effects.

What the studies tell us: The evidence indicates that acute fire-smoke related PM exposure may be associated with increased emergency department (ED) attendances and hospitalisations for a range of cardiovascular and respiratory conditions, stroke (cerebrovascular disease), and eye irritations. Increased demand for ambulance dispatches for respiratory and cardiac health problems has been noted within one hour of exposure to $PM_{2.5}$. Exposure is also associated with increased use of medications for asthma. Exposure to PM is also associated with increased mortality.

- **Exposure to PM can be associated with healthcare service utilization for respiratory and/or cardiovascular conditions**

Thirty-five studies examined rates of health care presentations, including ambulance attendances, visits to the general practitioner (GP)/physician, emergency departments (ED) visits or hospitalisation for cardiovascular, respiratory, and cerebrovascular conditions.

Respiratory conditions

Twenty-one studies (Chen et al., 2006; Crabbe, 2012; Deflorio-Barker et al., 2019; Delfino et al., 2009; Guo et al., 2020; Hanigan et al., 2008; Hutchinson et al., 2018; Johnson et al., 2020; Le et al., 2014; J. C. Li & Casher, 2020; Liu et al., 2017; Machin et al., 2019; K. L. Martin et al., 2013; Rappold et al., 2011; Reid et al., 2019; Reid et al., 2016; Resnick et al., 2015; Schranz et al., 2010; Stowell et al., 2019; Wettstein et al., 2018; Yao et al., 2020) examined the effect of $PM_{2.5}$ exposure on demand for health services for respiratory symptoms and diagnoses. The respiratory conditions most commonly examined were upper respiratory infections, 'all-cause' respiratory conditions, pneumonia, acute bronchitis, asthma, and other chest symptoms. All studies reported positive associations between increases in $PM_{2.5}$ levels and respiratory attendances to ED, GPs/physicians, and hospitalisations. For example, Chen et al.'s (2006) study, based in Brisbane, modelled the impacts of PM_{10} related to bushfire events on daily respiratory hospital admissions. A dose-response relationship between PM_{10} and hospital admissions was apparent, and stronger during bushfire periods than in non-bushfire periods.

Martin et al. (2013) studied the association between validated bushfire smoke pollution events and hospital admissions in Sydney, Wollongong, and Newcastle (NSW) from 1994 to 2007. In Sydney (and to a smaller extent in the other cities), associations with respiratory outcomes were generally observed on the day of a smoke event and the day after a smoke event. The same day increase was 5% for all respiratory admissions, 12% for all asthma admissions, and 13% for COPD[38] admissions.

A Canadian study (Yao et al., 2020) examined the immediate and lagged relationships (from 1 hour to 48 hours) between exposure to $PM_{2.5}$ and ambulance dispatches during wildfire seasons in British Columbia. Increased adverse respiratory health outcomes were observed within one hour of exposure to a 10 $\mu g/m^3$ increase in $PM_{2.5}$. There was a 3.8% increase (95%CI: 1.0 - 6.7%) for breathing problems; and a 9.8% increase (95%CI: 1.3 – 18.9%) for asthma/COPD.

In studies from the USA, adults aged 65 years and over have been found to be especially vulnerable to atmospheric PM (Li et al., 2016; Rappold et al., 2011; Resnick et al., 2015; Delfino et al., 2009; Hutchinson et al., 2018), as well as youth (Tinling et al., 2016; Hutchinson et al., 2018). Additionally, in the Northern Territory of Australia, Hanigan et al. (2008) found that the association between smoke PM and hospital admissions was especially strong among Indigenous Australians. The analysis found approximately three-fold higher associations between same-day estimated ambient PM_{10} and total respiratory admissions in Indigenous people than non-Indigenous people.

Schranz et al. (2010) found a lag in the presentations over the first two days; similarly, Ignotti et al. (2010) and Pope et al. (2017) both found a lag of 2-5 days before presentations increased, with Ignotti et al. (2010) finding children were more affected over time, but older adults were more likely to present immediately.

Asthma

Twenty-one studies, including one systematic review of 20 other studies, examined the effects of $PM_{2.5}$ exposure on people with, or presenting with, asthma. Eighteen studies (Alman et al., 2016; Arriagada et al., 2019; Borchers-Arriagada et al., 2020; Gan et al., 2020; Guo et al., 2020; Haikerwal et al., 2016; Huang et al., 2019; Jalaludin et al., 2000; F. Johnston et al., 2002; F. Johnston et al., 2006; Kiser et al., 2020; Kunzli et al., 2006; Lipner et al., 2019; Machin et al., 2019; Rappold et al., 2011; Reid et al., 2019; Reid et al., 2016; Tinling et al., 2016) reported positive associations between $PM_{2.5}$ exposure, from wildfire and other fire sources, and GP/physician visits, ED presentations and hospitalisations; and salbutamol (asthma reliever medication) use, dispensations, and refills. These associations were seen on the day of elevated $PM_{2.5}$ levels and up to 5 days later in some studies. For example, Cherry et al. (2021a, 2021b) examined the effects on respiratory health of firefighters attending a catastrophic wildfire at Fort McMurray, Canada, in 2016. Firefighters had two and a half times increased risk of needing an asthma consultation post-fire. In contrast, one relatively old

[38] Chronic obstructive pulmonary disease.

study (Smith et al., 1996) found no significant increase in the number of asthma-related emergency department presentations during a wildfire period.

Six studies (Rappold et al., 2011; Jalaludin et al., 2000; Lipner et al., 2019; Arriagada et al., 2019; Gan et al., 2020) explored the differential effects of age on response to $PM_{2.5}$ exposure and found that adults aged over 65 years were more at risk of asthma-related presentations, and/or that hospital presentations increasing with age. Children (younger than 21 years) were more likely to have increased bronchial hyper-reactivity and decreased FEV_1 values after $PM_{2.5}$ exposure.

Cardiovascular and cerebrovascular conditions

Increased $PM_{2.5}$ exposure was associated with health care utilisation for cardiovascular conditions in 17 studies (Alman et al., 2016; Crabbe, 2012; Deflorio-Barker et al., 2019; Delfino et al., 2009; Dennekamp et al., 2015; Guo et al., 2020; Haikerwal et al., 2015; Jones et al., 2020; Le et al., 2014; Moore et al., 2006; Rappold et al., 2011; Reid et al., 2019; Reid et al., 2016; Resnick et al., 2015; Sarnat et al., 2008; Wettstein et al., 2018; Yao et al., 2020), with a majority of studies examining this across a wildfire season using modelled daily or hourly $PM_{2.5}$ exposures. Results are grouped below by the heath care setting or utilisation to differentiate the severity of the conditions.

Ambulance attendances

In Melbourne, Dennekamp et al. (2015) analysed ambulance dispatches for cardiac arrests in people aged 35 years or over during a season when Melbourne was blanketed in bushfire smoke. They observed 8.05% and 11.1% increases in ambulance dispatches, for men only, with cardiac arrest within 48 hours of $PM_{2.5}$ levels increasing by 6.1 $\mu g/m^3$ and PM_{10} levels increasing by 13.7 $\mu g/m^3$, respectively. Although, the same associations were not observed with women, it should be noted that twice as many men as women were diagnosed with cardiac arrest. Another study in Melbourne found consistent significant associations between 9.0 $\mu g/m^3$ increases in wildfire smoke $PM_{2.5}$ and 6.98% increases in out-of-hospital cardiac arrests, which was stronger amongst men (9.05% increases) and people aged over 65 years (7.25%) (Haikerwal et al., 2015).

In Canada, Yao et al. (2020) used estimated hourly $PM_{2.5}$ levels and found that ambulance dispatches for acute myocardial infarction and ischaemic heart disease were highest in the hour immediately after exposure to 10 $\mu g/m^3$ increases in $PM_{2.5}$ from baseline levels. In the US, Jones et al. (2020) analysed emergency medical service-treated out-of-hospital cardiac arrests, and found risk increased in association with heavy smoke (defined as >22 $\mu g/m^3$ $PM_{2.5}$) across multiple lag days and was strongest on lag day 2. Risk was elevated in both sexes and groups aged 35 years and over.

ED attendance and hospitalisations

The majority of studies examined the impact of fire smoke related PM on ED and hospitalisations for cardiovascular conditions, as these are commonly acute events and represent the most severe health effects. Martin et al. (2013) studied the association between validated bushfire smoke pollution events and hospital admissions in Sydney, Wollongong,

and Newcastle (NSW) from 1994 to 2007. They found no associations between cardiovascular hospitalisations and acute increases in wildfire-smoke-related PM_{10} and $PM_{2.5}$. In contrast, in Portugal, 472 excess cardiovascular hospitalisations were attributed to wildfire smoke $PM_{2.5}$ in one year (2017: Oliveira et al., 2020).

Vulnerable populations have been identified, including people aged over 65 years (Haikerwal et al., 2015; Le et al., 2014; Rappold et al., 2011; Resnick et al., 2015; Wettstein et al., 2018). Specifically, Haikerwal et al. (2015) found a 2.07% increase in the risk of ED attendances and hospitalisations for ischaemic heart disease[39] associated with exposure to $PM_{2.5}$ during wildfires, with stronger associations among women (a 3.2% increase) and older adults (a 2.41% increase). Jones et al. (2020) studied data on out-of-hospital cardiac arrest and wildfire smoke density in California from 2015-2017 and reported increased risk for people in low socio-economic status groups on medium and heavy smoke days.

Le et al. (2014) reported short-term increases in $PM_{2.5}$ concentrations (haze period compared with non-haze period) due to forest fires in the Province of Quebec (Canada) were associated with a consistent significant increase in cardiovascular (64.9%) hospitalisations for older people (>65 years) across 11 north-eastern and mid-Atlantic states in the USA. Affected communities were thousands of kilometres from the original site of the forest fires. Similar relationships were observed by Resnick et al. (2015) in Albuquerque, USA. High levels of wildfire-smoke-associated $PM_{2.5}$ were associated with increased risk of ED presentations for cardiovascular conditions (RR=1.08), particularly in the group aged 20-64 years (RR=1.11). Rappold et al. (2011) reported short-to-medium term exposure to $PM_{2.5}$ generated from peat fire smoke was associated with increased risk of ED visits for heart failure[40] (RR=1.37) but not for myocardial infarction[41] or cardiac dysrhythmia[42] among older people.

Together, these studies suggest that exposure to $PM_{2.5}$ has potentially harmful effects on both frontline firefighters on the ground and the surrounding communities, both nearby and more distant, depending on the dispersion of the $PM_{2.5}$.

GP/Physician visits

Relatively few studies have explored the impact of smoke PM exposure on visits to the GP/physician, as these data are more difficult to obtain and subject to both higher reporting bias and inconsistent coding of the health outcome. Moore et al. (2006) reported that short term wildfire smoke exposure had no significant effect on physician visits for cardiovascular conditions in a region within Canada. In contrast, in a more recent Canadian study, McLean et al. (2015) were able to show that smoky days (those with $PM_{2.5}$ levels > 25 $\mu g/m^3$) were associated with excess physician visits and salbutamol (asthma reliever medication) dispensations.

[39] Heart problems caused by narrowed coronary arteries that supply blood to the heart muscle.
[40] Heart failure is a condition in which the heart is unable to pump enough blood to meet the body's needs.
[41] A myocardial infarction (MI), commonly known as a heart attack, occurs when blood flow decreases or stops to a part of the heart, causing damage to the heart muscle.
[42] Heart arrhythmias occur when the heart beats too quickly, too slowly, or irregularly.

Cerebrovascular diagnoses

Wettstein et al. (2018) studied ED visits associated with wildfire smoke exposure in California in 2014 and found that rates of ED visits for cerebrovascular disease were elevated across all lag days but were highest on dense smoke days when $PM_{2.5}$ concentrations were > 22 μg/m^3. Resnick et al. (2015) reported significant associations between wildfire smoke $PM_{2.5}$ and increased risk of ED presentations for cerebrovascular disease in the age group 20-64 years (RR=1.69).

- **Medication use and prescription dispensing can be associated with smoke exposure**

Five studies and one systematic review (including 20 studies) examined the effects of $PM_{2.5}$ exposure from wildfires on medication use of community-dwelling people. A consistent pattern was observed with medication (for respiratory and cardiovascular conditions) dosage and salbutamol (asthma reliever medication) dispensations being higher during wildfire episodes. Increased dosage was related to higher $PM_{2.5}$ concentrations (Arriagada et al., 2019; Elliot et al., 2013; Johnson et al., 2019; McLean et al., 2015; Vora et al., 2011).

One older study by Fay Johnston et al. (2006) on vegetation fires, particulate air pollution, and asthma conducted in Darwin found no association between $PM_{2.5}$ and asthma reliever medication use but reported positive associations with commencing asthma reliever medication and oral corticosteroids to prevent asthma attacks over a lag time (i.e., time between the smoke event and the outcomes) of 3-7 days. Approximately half of the study participants were under 18 years of age, and the oldest participants were over 70 years old. Over half (57%) of the participants identified vegetation fire smoke as a trigger of their asthma symptoms.

Amanda Johnson et al.'s (2019) study of coalmine-fire-related $PM_{2.5}$ exposure from the 2014 brown coal mine fire south-eastern Victoria, adjacent to the Hazelwood power station, found a consistent association between elevated $PM_{2.5}$ levels and increased dispensation of cardiovascular and respiratory medications in the local community over a lag range of 3-7 days. A 10 mg/m^3 increase in coal mine fire-related $PM_{2.5}$ was associated with a 25% increase in respiratory medications and a 10% increase in cardiovascular medications.

- **Eye injury may be associated with smoke exposure**

Berra et al. (2015) studied 35 ophthalmology patients and 51 healthy volunteers during a wildfire event in Argentina. They found that there was a significant increase in bulbar conjunctival hyperaemia[43], corneal fluorescein staining[44], and rose bengal vital staining[45] in ophthalmological patients after the acute wildfire episode. Healthy volunteers showed only

[43] Conjunctival hyperemia is a conjunctival reaction that appears as dilation and redness of the conjunctival vessels.

[44] This test uses orange dye (fluorescein) and a blue light to detect foreign bodies in the eye and damage to the cornea.

[45] Rose Bengal is a mildly toxic bright red stain that is adsorbed to and absorbed by compromised epithelial cells, mucous membranes, fibrous tissue.

an increase in bulbar conjunctival hyperemia. During the fire event, both patients and volunteers showed a decrease in tear break-up time values (a sign of dry eyes).

- **An increase in diabetic complications may be associated with smoke exposure**

A Canadian study (Yao et al., 2020) examined the immediate and lagged relationships (from 1 hour to 48 hours) between exposure to $PM_{2.5}$ and ambulance dispatches (acute health outcomes) during wildfire seasons in British Columbia. Increased adverse respiratory health outcomes were observed within one hour of exposure to a 10 $\mu g/m^3$ increase in $PM_{2.5}$. The risk for ambulance dispatch for diabetic complications increased significantly: by 7.5% (95%CI: 1.0 – 15.3). Overall, the association between increased exposure to $PM_{2.5}$ during wildfire seasons and diabetic outcomes increased over time (up to 48 hours).

- **PM exposure may lead to uptake of carcinogenic PAH metabolites and urinary mutagenicity due to dermal exposure**

Keir et al. (2017) combined urine and dermal analyses of firefighters exposed to fire smoke. The study demonstrated that dermal PAH concentrations accounted for 54% of the variation in urinary PAH metabolites following fire suppression. Skin contamination from fire smoke was also suggested by Allonneau et al. (2019). Findings suggest that dermal exposure is an entry point for PAHs, and that post-event skin decontamination may be an important intervention.

- **Increases in morbidity and mortality can be associated with increased outdoor smoke exposure**

Mortality attributable to smoke PM was examined in four ecological time-series studies. Two studies of communities affected by wildfire (Hanninen et al., 2009; Zu et al., 2016) reported no significant associations between $PM_{2.5}$ levels and mortality rates. In contrast, two health impact assessment studies of Australian communities affected by wildfire smoke estimated the numbers of deaths that could be attributed to wildfire smoke over their study period. In Tasmania, Borchers-Arriagada et al. (2020) calculated the daily population-level exposure to $PM_{2.5}$ from wood heater smoke (WHS) and landscape fire smoke (LFS). They estimated that 26% of 69 deaths, 86 hospital admissions, and 15 asthma ED visits each year over a decade could be attributed to the impacts of wildfire smoke. A Sydney study examining air pollution over the period 2001 to 2013 (Horsley et al., 2018) identified a total of 184 LFS days (3% of all days). The study estimated that 197 premature deaths, 436 cardiovascular hospitalisations, and 787 respiratory hospitalisations were attributable to fire smoke on these days.

Studies with indirect evidence (Type 2) of PM exposure

Indirect studies included non-human studies and those that focused on associated chemicals rather than $PM_{2.5}$ per se; with poor linkage of outcomes; that lacked generalisable outcomes; or looked at largely pathophysiological effects.

General characteristics: Twenty-four studies were identified in this category.

Outcome measures: Most studies focused on measures of biomarkers of exposure including macrophages and markers of oxidative stress markers. Statistical modelling studies have also been included in this section.

What the studies tell us: The indirect evidence largely supports more direct studies. Polycyclic aromatic hydrocarbons (PAH), known to bind with $PM_{2.5}$ and to carry long-term cancer risks, may enter the body during industrial and residential fire smoke exposures. Health impacts have been shown to correlate with urinary PAH metabolite (OH-PAH) concentrations following smoke exposure.

The studies included here examined biomarkers in firefighters and laboratory rats to characterise the impacts of acute exposure to $PM_{2.5}$.

- **Blood sampling and use of biomarkers are effective tools for assessing physiological responses to smoke exposure**

Five studies used blood sampling techniques to examine changes in biomarkers of exposure for humans exposed to $PM_{2.5}$ from a range of sources. Biomarkers, macrophages, leukocytes, DNA damage, and reactive oxygen species[46] were examined. $PM_{2.5}$ was associated with some biomarkers (oxidative stress markers, 8-Oxo-7,8-dihydro-2'-deoxyguanosine (8-Oxo-dG), malondialdehyde (MDA), 8-isoprostane, IL-1b, and lactic acid dehydrogenase, lipid hydroperoxide: (Adetona et al., 2017; Ghio et al., 2012; Hejl et al., 2013; Peters et al., 2018), and DNA damage and cytokine release[47] (Alves et al., 2017). These studies indicate a relationship between exposure to $PM_{2.5}$ and alterations in biomarkers and that these changes are increasingly noted as smoke exposure increases. Evidence of oxidative stress as well as inflammatory markers has been noted more in early-career and non-smoking firefighters than in career firefighters or those who smoke.

- **PM exposure may lead to decreased immune response**

Andersen et al. (2018b) found that $PM_{2.5}$ exposure was associated with significant damage to peripheral blood mononuclear cells (PBMC)[48], including lymphocytes, monocytes[49], and macrophages[50], which are critical cells involved in immune responses.

[46] Free radicals. A build-up of reactive oxygen species in cells may cause damage to DNA, RNA, and proteins and may cause cell death.
[47] Cytokines are small proteins released by many different cells in the body, including those of the immune system, where they coordinate the body's response against infection and trigger inflammation. Excessive or uncontrolled levels of cytokines may be released in a "cytokine storm", resulting in hyperinflammation. This can seriously harm or even kill the person.
[48] A peripheral blood mononuclear cell (PBMC) is any peripheral blood cell with a round nucleus.
[49] Lymphocytes and monocytes are types of white blood cell. They help fight bacteria, viruses, and other infections.
[50] Macrophages are specialised cells involved in the detection and destruction of bacteria and other harmful organisms.

- **On-shift emergency fire suppression significantly increases biomarkers of an inflammatory response**

Main et al. (2020) studied the blood samples of 38 Australian volunteer firefighters before and after 12-hour firefighting shifts. Levels of interleukin-6 (IL6) and interleukin-8 (IL8) increased significantly following shifts, and interleukin-10 (IL10) decreased. The authors observed that this acute inflammatory response may have resulted from multiple stressors including physical exertion and thermal strain, as well as smoke inhalation experienced during the shift, and may be a necessary response for the body to adapt to stressor exposure.

Wu, Adetona, et al. (2020) studied lung function by examining exhaled breath condensate (EBC**).** Measures included levels of biomarkers of oxidative stress (8-isoprostane) and pro-inflammatory response (interleukin-6 [IL-6], interleukin-8 [IL-8], C-reactive protein [CRP], and soluble intercellular adhesion molecule-1 [sICAM-1]), which were collected from firefighters before, after, and the morning following prescribed burn and regular work shifts. Results showed only a marginal cross-shift increase in 8-isoprostane on burn days, suggesting wildfire smoke exposure may lead to only mild pulmonary[51] inflammation in firefighters.

- **On-shift emergency fire suppression significantly increases urinary concentrations of PAH metabolites and organic mutagens**

Seven studies focussed on the uptake and health effects of PAH, which were included due to the breadth of literature describing their ability to bind to PM (e.g., Feunekes et al., 1997). These eight studies examined urinary excretion of PAH metabolites.

Five studies (Andersen et al., 2017; Fent et al., 2019; Z. Li et al., 2016; Oliveira et al., 2020; Oliveira et al., 2017) found increases in urinary excretions of various PAH metabolites (e.g., benzene, 1-hydroxypyrene, 3hydroxybenzo(a)pyrene, 1- and 2-naphthols, 1-hydroxynaphthalene, 1-hydroxyacenaphthene, and 2-hydroxyfluorene) in firefighters exposed to smoke, compared to control groups of firefighters who were not similarly exposed. Fent et al. (2019) suggested that the larger increases in 1-hydroxypyrene observed in instructors compared with trainees was likely to be because of their repeated exposures (i.e., three training sessions per day).

Oliveira et al. (2020a) studied OH-PAH DNA-adducts[52] (including total OH-PAH) in firefighters in Portugal. The firefighters reported long-term exposure to forest fire emissions, with a median of 13 years. Forty-eight hours before the sampling, exposed firefighters were directly involved in firefighting activities for a median period of 3 consecutive hours. Samples of urine and blood were taken at the end of firefighters' 8-hour shifts. Concentrations of total OH-PAHs were up to 340% higher ($p \leq 0.05$) in (non-smoking and smoking) exposed workers than in control participants (non-smoking and non-exposed to combat activities). Levels of biomarker for oxidative stress were higher in non-smoking exposed workers than in the control group (316%; $p \leq 0.001$); inconclusive results were found for DNA damage.

[51] Pulmonary is a term meaning 'in the lungs'.

[52] DNA-adducts are a measure of pro-carcinogenic genetic damage and are considered a biomarker of increased cancer risk.

In contrast, one study (Robinson et al., 2008) found no increases in urinary PAH from pre-to-post exposure to "prescribed pile burns" (i.e., intentional burning of logging debris), but reported that particulate and PAH exposures in the study did not exceed occupational standards. A study from France (Allonneau et al., 2019) found that the increases for most metabolites were lower than their associated biological and occupational exposure limits.

Together, these findings suggest that PAH, known to bind with $PM_{2.5}$ and to carry long term cancer risks, may enter the body during acute industrial and residential fire smoke exposures. An in-depth review of the PAH literature would be needed to specifically understand the impacts of repeated or longer-term exposures. However, there is little evidence on the impacts of repeated exposures or longer-term consequences of exposure.

- **Increased cardiac frequency and DNA oxidative damage correlate with urinary OH-PAH concentrations following smoke exposure**

A cross-sectional study by Oliveira et al. (2020a) found correlations between increased cardiac frequency (heart rate), biomarkers of oxidative DNA damage and the uptake of monohydroxyl-polycyclic aromatic hydrocarbons (OH-PAH) in a group of 108 non-smoking firefighters following firefighting activities (see study description above). Further, the study found that more than 21% and 14% of firefighters in this study had, respectively, diastolic, and systolic blood pressures[53] higher than 90 and 140 mmHg respectively, indicating Stage 2 (relatively severe) high blood pressure (hypertension).

- **Controlled laboratory mice studies have found increased levels of biomarkers and inflammatory markers and decreased cardiac function on exposure to $PM_{2.5}$**

Williams et al. (2013) found that the lungs of smoke-exposed mice had more macrophages (~50%) and Clara cell secretory protein (CCSP)[54], dead cells, 8-isoprostane[55] and tumour necrosis factor (TNF)-α[56] than in those without exposure. Similarly, Ryu et al. (2019) found upregulated pro-inflammatory markers in a skin-exposed mouse model. Myatt et al. (2011), examining air samples, found mean TNF release and cell mortality in alveolar macrophages in mice and human volunteers were greatest for fire-related $PM_{2.5}$ sources.

Kim et al. (2014) studied mice exposed to PM from smouldering peat fire. The coarse fraction of this PM was found to be associated with respiratory and systemic effects (increases in bronchoalveolar lavage fluid protein, cytokines (IL-6, TNF-α, and MIP-2), neutrophils[57] and intracellular reactive oxygen species (ROS) production). Exposure to UFP was not associated

[53] Blood pressure is measured using two numbers: The first number, *systolic* blood pressure, measures the pressure in a person's arteries when their heart beats. The second number, *diastolic* blood pressure, measures this pressure in your arteries when the heart rests between beats.
[54] Clara cell secretory protein (CCSP) is a protein that is synthesised, stored, and secreted by Clara cells. Clara cells are tall, dome-shaped epithelial cells that occur in large numbers in the bronchioles. Altered Clara cell function is likely to be a significant factor contributing to declining lung function in airway disease.
[55] A marker of antioxidant deficiency and oxidative stress.
[56] Tumour necrosis factor (TNF) is a multifunctional cytokine that plays important roles in diverse cellular events such as cell survival, proliferation, differentiation, and death.
[57] A type of white blood cell. Neotrophil blood levels increase in response to infections, injuries and other types of stress.

with lung or systemic effects but these mice developed significantly decreased cardiac function and greater post-ischemia-associated myocardial infarction, and mouse lung slices indicated comparable patterns of cytokine production. Thompson et al. (2018) found exposure to peat smoke reduced ventilatory expiratory time (breathing rate).

Hu et al. (2017) found $PM_{2.5}$ exposure induced signs of systemic inflammation in mice (increased lung collagen[58] and hydroxyproline[59] content and reduced serum levels of IL-6, TNF-α, and TGF-β). Similarly, out studies (Kumar et al., 2010; Mazzoli-Rocha et al., 2008) have reported that woodsmoke exposure causes increased sensory irritation and lung alveolar collapse. While Migliaccio et al. (2013) found no changes in leukocyte concentrations in PM-exposed mice, Wegesser et al. (2010) found elevated concentrations of neutrophils, chemokines, cytokines and tumour-necrosis factor (TNF)-α in the lung lavage fluid obtained 6 hours and 24 hours after PM exposure. B. L. Martin et al. (2020) found rats exposed to peat fire PM had increased blood pressure, low-density lipoprotein cholesterol, C3 and C4 components[60], angiotensin-converting enzymes, which control blood pressure, and white blood cells (defence blood cells).

Li et al. (2021) exposed 36 rats to diverse dosages of $PM_{2.5}$ for 24 hours and compared them with a control group. After exposure, the rats were euthanised and lung tissues were collected for the experiment. The lung tissues were examined microscopically. The exposure group experienced increased expression of inflammatory cytokines and the release of chemokines. High exposure was linked to inflammatory responses and mitochondrial damage and apoptosis. [61] The authors of the study suggested that antioxidants could mitigate the damage triggered by exposure to $PM_{2.5}$.

Overall, these studies suggest that exposure to $PM_{2.5}$ smoke stimulates a biological response within mice and rats, manifesting in inflammatory responses in cardiovascular, pulmonary, immunological, and haematological/blood systems.

- **Co-morbidity may increase the risk of mortality**

Mortality as a result of $PM_{2.5}$ was explored in two *in vivo* studies evaluating acute inhalation toxicity. Hu et al. (2017) found an increased mortality in mice with bleomycin-induced lung fibrosis, but not in healthy mice. Kumar et al. (2010) found that the acute inhalation toxicity ("sensory irritancy") of smoke from 15 minutes of static woodsmoke exposure in mice was only about one-third for fibreglass reinforced plastic (FRP) samples than the level for teak wood shavings. The authors attributed this difference to the greater number of submicron particles and greater percentages of gases in wood smoke than FRP smoke.

[58] Collagen is a protein that provides structure to much of the body, including bones, skin, tendons, and ligaments.
[59] A component of collagen.
[60] C3 and C4 are complement proteins which are important in immune system function – their levels increase after injury or infection.
[61] Apoptosis is cell death.

- **PM and PAH exposure, and associated health effects, are reduced where personal protective equipment (PPE) is used**

Andersen et al. (2018a) studied the genotoxicity risks in 22 firefighters exposed to PM and PAH during their 24-hour work shift. The researchers observed: (i) reduced levels of DNA damage in peripheral blood mononuclear cells (PBMC)[62] at the end of firefighters' shifts; and (ii) similar levels of PAH on skin and urinary 1-OHP concentration before and after the work shift. Overall, increased levels of genotoxicity were not identified during the study, and no adverse health effects were found. The authors attributed these findings to the firefighters' use of personal protective equipment (PPE) equipment. Similarly, Andersen et al. (2018b), in a study of 53 volunteers participating in a course to become firefighters, found that PPE prevented inhalation exposure to PM. However, PM exposure occurred when the environment was perceived as safe by individual trainees and self-contained breathing apparatuses were removed.

In general, the role of PPE in mitigating health risks has not been well quantified. Participants in two studies (Genovesi et al., 1977; Gu et al., 1996) admitted that their breathing apparatus was not used consistently through the fire event under study.

- **Adverse health effects are associated with smoking and duration of service**

Some underlying demographic factors have been identified by authors as accelerating or worsening health outcomes. Gu et al. (1996) found that respiratory symptoms were aggravated significantly in firefighters who smoked cigarettes. Chia et al. (1990) found a significant relationship between firefighters' duration of service and increases in airway reactivity (difficulty breathing). Interestingly, Large et al. (1990) observed two participants with serious declines in respiratory function following smoke exposure; however, no correlation was found between smoking habit, breathing apparatus usage, or age. This suggests that additional unidentified factors may contribute to accelerated health declines in some individuals.

[62] Peripheral blood mononuclear cells (PBMC) comprise lymphocytes, monocytes and macrophages. These blood cells are a critical part of the human immune system.

GREY LITERATURE

This search provided three relevant reports.

1) Australian bushfires 2019-2020: Exploring the short-term health impacts (AIHW, 2020)

The Australian Institute of Health and Welfare (AIHW, 2020) released a report in 2020 outlining the health impacts of significant bushfires for the 2019-2020 bushfire season on the whole community. Relevant outcomes reported were respiratory health, cardiovascular health, and stroke (cerebrovascular health). For respiratory health, ED presentation data specific to the most impacted state (NSW) were collected. Presentation diagnoses included: respiratory disease (all); asthma; abnormalities of breathing; and COPD with acute exacerbation. Data broadly demonstrated a clear increase in presentations for respiratory type conditions, peaking at 13% higher than the same week in the previous year. Associated increases in dispensing rates for inhalers to manage shortness of breath showed a significant increase during the peak of the fire at 149% increase when compared with the same week in the previous year.

For cardiovascular health and stroke, ED presentations showed a modest decrease for the fire period when compared with the same months in the previous year. While evidence is vague, this decrease may be related to strong, consistent public health messaging to stay indoors and avoid exposure to smoke. Moreover, AIHW data included only ED presentations and not hospital admissions, which may provide clearer indicators of acute smoke exposure impacts on cardiovascular health and stroke.

2) Health impact of smoke exposure in wildland-urban interface fires: A literature review (Hvenegaard, 2012).

This report focuses on wildfire operations in which structures are also burnt, and identified significant gaps in the literature, including:

- Health impacts from short-term exposure to structural smoke.
- Combined health effects from simultaneous exposure to both wildland and structural smoke.
- Potential structural smoke exposure levels for various suppression activities and fire conditions.
- Level of firefighters' understanding of wildland/urban interface smoke hazards and avoidance options.
- Potential health hazards of residual chemical deposits on skin, clothing, or other personal effects.
- Cumulative effect of the factors that affect the probability and severity of health impact: intensity of combustion, duration of exposure, frequency of exposure, career length, and fitness level [sic, health status, personal behaviours such as tobacco smoking and alcohol consumption].

This report also highlights the significant overlaps between the research relevant to wildland and structural firefighting.

3) Final report of the NSW Bushfire Inquiry (Owens & O'Kane, 2020)

This report provided analysis and recommendations for system change in response to significant bushfires across NSW during 2019-2020. Among other recommendations, two are directly relevant to this report.

Recommendation 34 outlines the need for Government to invest in operational air quality forecasting and alert systems, and public health research and policy development. Public health research is required to understand health impacts of bushfire smoke that includes research on the long-term health impacts of poor air quality resulting from sustained exposure to severe bushfire smoke, particularly for vulnerable groups within the community:

- children
- older people
- firefighters and other first responders to emergency situations
- people with chronic diseases such as cardiovascular disease, respiratory disease, diabetes, and immune suppression
- people living in lower socio-economic areas
- pregnant women
- outdoor workers

Recommendation 35 calls for improved provision of evidence-based public health messaging about air quality, and for governments to develop public education programs along with supporting systems prior to the upcoming fire season. This should include:

- a public education program, similar to sun exposure programs, that allows individuals to make their own decisions about their exposure to bushfire smoke
- tailored and appropriate health messaging to target vulnerable communities and general practitioners
- assistance from employers with the development of appropriate workplace health and safety directives for outdoor workers.

RESULTS FOR TOPIC 2: SHORT-TERM IMPACTS OF REPEATED ACUTE EXPOSURE

Twenty-five studies were identified on this topic. Only two of these provided direct evidence on the impacts of repeated acute exposure.

Studies with direct evidence

General characteristics: One study examined training exposure of firefighters to $PM_{2.5}$, while another studied impacts on of wildfire on health in the community.

Outcome measures: Lung function (FEV_1, FVC) and cardiovascular outcomes.

What the studies tell us: The studies on this topic are relatively few, but those examining firefighters provide evidence of the cumulative impacts of exposure to $PM_{2.5}$ on lung function.

- **Repeated PM exposure may lead to changes in lung and cardiovascular function**

Cherry et al. (2021) studied firefighters recruited from 12 fire services deployed repeatedly to the 2016 Fort McMurray fire. Spirometry showed decreased FEV_1 and FVC with increasing exposure. Lower diffusion capacity[63] related to higher exposure.

In a rare study of direct impacts of exposure to PM in the community, Zaini et al. (2020) use spirometry and pulse oximetry[64] to measure the lung function of healthy community members exposed to wildfire in Sumatra, Indonesia. Lung function was impaired in 72.6% of the participants, mostly with mild obstruction and mild restriction. Low levels of predicted carboxyhemoglobin (COHb) indicated probably carbon monoxide poisoning.

Studies with indirect evidence (Type 1)

General characteristics: Fifteen studies were identified with indirect evidence on the topic. Most of these were studies of the community that provided indirect evidence on the short-term impacts of repeated exposures. Several recent studies have examined the community health impacts of the Hazelwood coal mine fire, which burned for 45 days in February and March 2014, in Victoria. Some of these studies are reported here, but others are included (as well or instead) under Topic 4, Dose effects.

Outcome measures: Use of hospital and other medical services.

What the studies tell us: At the population level, repeated exposure is associated with negative impacts on pulmonary/respiratory health and cardiovascular health, and skin problems. Impacts are evident in vulnerable populations, including children.

[63] Lung diffusion tests are used to measure how well a person's lungs exchange oxygen and carbon dioxide.
[64] A clip-like device called a probe is placed on a body part, such as a finger or ear lobe. The probe uses light to measure how much oxygen is in the blood.

- **Repeated exposure to $PM_{2.5}$ from wildfires may affect health service and medication use for breathing problems**

In an early study, Stowell et al. (2019) studied emergency department visits and hospitalisations for acute cardiorespiratory outcomes over a four-year period (2011-2014), using 2-3 day "windows" following fire events in Colorado. They found many respiratory disease outcomes increased during periods of wildfire activity, the largest of which was for asthma. However, analyses did not take the potentially cumulative impacts of exposure to smoke $PM_{2.5}$ into account.

Guo et al. (2021) examined the change in rates of hospital ED presentations or hospital admissions during the Hazelwood coal mine fire. Daily data on hospital emergency presentations were collected for the period January 01, 2009 to June 30, 2015. Coal mine fire-related $PM_{2.5}$ concentrations were modelled and change in rates of hospital ED presentations and hospital admissions during the coal mine fire period were estimated. The study found that, compared with non-fire periods, during the fire period there were increased risks of all-causes, respiratory diseases, and asthma-related ED presentations and hospital admissions, as well as chronic obstructive pulmonary disease (COPD)-related ED presentations. Associations between daily concentrations of coal mine fire-related $PM_{2.5}$ and ED presentations for all-causes and respiratory diseases, including COPD and asthma, appeared after two days' exposure. In contrast, associations with hospital admissions for cerebrovascular and respiratory diseases appeared on the same day of exposure. Similarly, Nguyen et al. (2021) estimated that impacts of air pollution in the 2019-2020 bushfire period in NSW included 1535 (CI: 493, 2087) respiratory disease hospitalisations.

Several recent studies have focused on impacts of fires in California, USA on hospitalisations for respiratory diseases. Cleland et al. (2021), in a study of the 2017 California wildfires, estimated there were an excess 240 (95% CI: 114 to 404), 68 (95% CI: −10 to 159), and 45 (95% CI: 18 to 81) respiratory, cardiovascular, and asthma hospital admissions, respectively, attributable to fire-originated $PM_{2.5}$ exposure. Similarly, Aguilera et al. (2020) examined data from Santa Ana in Southern California, including spatiotemporal variation in respiratory hospitalisations in areas contained by and immediately downwind of wildfire perimeters. They found that excess hospitalisations tend to follow the distribution of smoke plumes across space and time.

Casey et al. (2021) found that impacts of exposure to wildfire smoke may depend on the usual air quality. Between 2013 and 2018, California's Shasta County experienced 19 weeks with average wildfire $PM_{2.5} \geq 5.5$ μg/m^3 ("high wildfire $PM_{2.5}$ concentration"). Across all areas, the researchers detected no association between high wildfire $PM_{2.5}$ concentrations and respiratory or circulatory disease-related ED visits or mortality. However, when analyses were confined to areas with lower elevation and worse air quality in general, high wildfire $PM_{2.5}$ was associated with a 14.6% (95% CI = 4.2 to 24.9) increase in same-week respiratory disease-related ED visits. This effect did not persist into the subsequent two weeks. Hahn et al. (2021) similarly noted increased odds of asthma-related ED visits among Alaskan First Nations people during the 2015-2019 wildfire seasons.

Howard et al. (2021) in Canada determined healthcare service use for cardiorespiratory ED presentations and outpatient salbutamol dispensation associated with 2.5 months of severe wildfire smoke in Yellowknife in Canada's high subarctic. Compared with 2012 and 2013, salbutamol dispensations in 2014 increased by 48%; clinic visits for asthma, pneumonia and cough increased; ED visits for asthma doubled, with the highest rate in females, in adults aged ≥40 years and in Dene (First Nations) people; and incidence of pneumonia increased by 57%, with higher rates in males, in individuals aged < 40 years, and in Inuit (First Nations) people.

In a Brazilian study attempting to quantify the impacts of wildfire related $PM_{2.5}$ on hospital admissions to due to respiratory conditions, Requia et al. (2021) estimated an increase of 23% (95% CI: 12% to 33%). In the north of Brazil, this percentage increased to 38% (95% CI: 30% to 47%).

Crop-burning is an activity that increases ambient $PM_{2.5}$ levels. Rutlen et al. (2021) evaluated the impact of crop burning on the prevalence of asthma and COPD emergency department treatments in a rural Arkansas county, using administrative datasets. In counties where $PM_{2.5}$ levels were higher, the odds of being treated were 20.9% higher for asthma and 16.9% higher for COPD.

- **Repeated exposure to $PM_{2.5}$ from wildfires may have an impact on cardiovascular health in the community**

Sherwen et al. (2020) examined hospital admissions in the Albury-Wodonga and East Gippsland regions in the December-January 2019-2020 period, when these regions were affected by bushfires, and compared numbers with those from the two years prior. They estimated a 24.6% increase in hospital admissions compared with previous years, whereas hospital admissions in non-bushfire affected regions of Victoria remained stable. In another Australian study, Nguyen et al. (2021) in NSW estimated that impacts of air pollution in the 2019-20 bushfire period was associated with 437 (95%CI: 81 to 984) excess cardiovascular disease hospitalisations. Similarly, Guo et al. (2021) reported that associations with hospital admissions for cerebrovascular and respiratory diseases appeared on the same day of exposure to PM.

Studies from other countries have reported similar findings. Hahn et al. (2021) noted increased odds of heart failure-related ED visits among Alaskan First Nations people during the 2015-2019 wildfire seasons, with a lag of 5 days. The authors interpreted this finding as indicating that rural populations may delay seeking care. Similarly, in Requia et al.'s (2021) Brazilian study, the estimated impacts of wildfire related $PM_{2.5}$ on hospital admissions due to circulatory conditions were an increase of 21% (95% CI: 8% to 35%). In the north of Brazil, this percentage increased to 27% (95% CI: 15% to 39%).

In contrast, Stowell et al. (2019) studied emergency department visits and hospitalisations for acute cardiorespiratory outcomes over a four-year period (2011-2014), using 2-3 day "windows" following fire events in Colorado, and were able to differentiate between smoke and non-smoke $PM_{2.5}$. No link was identified between smoke $PM_{2.5}$ events and cardiovascular

outcomes, but analyses did not take the potentially cumulative impacts of exposure to smoke $PM_{2.5}$ into account.

Similarly, using retrospective data on air quality and health service use, Howard et al. (2021) found no impact of increased $PM_{2.5}$ on ED visits for cardiorespiratory diagnoses following 2.5 months of severe unabated wildfire smoke in Canada's high subarctic region.

- **Repeated exposure to $PM_{2.5}$ from wildfires may have an impact on skin problems in the community**

Fadadu et al. (2021) assessed the associations of air pollution resulting from the California Camp Fire in November 2018 and dermatology clinic visits at an academic tertiary care hospital system in San Francisco, 175 miles from the wildfire source. Participants included patients with atopic dermatitis (AD) or itch from before, during, and after the time of the fire (October 2018 through February 2019), compared with those with visits in the same time frame of 2015 and 2016, when no large wildfires were near San Francisco. The rates of visits for AD during the Camp Fire for adult patients were 1.15 (95% CI, 1.02 to 1.30) times the rate for non-fire weeks on the same day of exposure, adjusted for temperature, relative humidity, patient age, and total patient volume.

- **Repeated exposure to fire smoke may have an impact on respiratory health of children**

As reported above, Fadadu et al. (2021) assessed the impacts of air pollution resulting from the California Camp Fire in November 2018 on dermatology clinic visits in San Francisco, 175 miles from the wildfire source. Participants included paediatric (child) patients with atopic dermatitis (AD) or itch from before, during, and after the time of the fire (October 2018 through February 2019), compared with those with visits in the same time frame of 2015 and 2016. The adjusted rates of visits for AD during the Camp Fire for paediatric patients were 1.49 (95% CI: 1.07 to 2.07). Hence the risk for children attending hospital were higher than for adult patients in this study.

Liebel et al. (2020) quantified the impacts of the Lilac Fire in the San Diego County on children's presentations at ED and urgent care clinics. The fire was associated with 16.0 (95%CI: 11.2 to 20.9) excess respiratory visits per day at the ED across all paediatric age groups. Children aged 0 to 5 years had the highest absolute excess respiratory visits per day with 7.3 (95% CI: 3.0 to 11.7), whereas those aged 6 to 12 years had the highest relative increase in visits, with 3.4 (95% CI: 2.3 to 4.6).

Aguilera et al. (2021b) examined the daily hospital admissions of children for respiratory diseases. The authors found that wild-fire-specific $PM_{2.5}$ was about 10 times more harmful to children's respiratory health than $PM_{2.5}$ from other sources, particularly for children aged 0 to 5 years.

- **The community-level impacts of repeated exposure to $PM_{2.5}$ from wildfire may be more deleterious than the impacts from ambient sources**

Aguilera et al. (2021a) studied the impacts of the presence of $PM_{2.5}$, including from ambient levels and wildfire smoke, on daily hospital admissions for respiratory diseases, including asthma, chronic obstructive pulmonary disease (COPD), pneumonia, and interstitial lung disease.[65] They found increases in respiratory hospitalisations ranging from 1.3% to up to 10% with a 10 $\mu g/m^3$ increase in wildfire-specific $PM_{2.5}$, compared to 0.67% to 1.3% associated with non-wildfire $PM_{2.5}$. Aguilera et al. (2021b) repeated their previous study, examining the daily hospital admissions of children for the same set of respiratory diseases. They found that wild-fire-specific $PM_{2.5}$ was about 10 times more harmful to children's respiratory health than $PM_{2.5}$ from other sources, particularly for children aged 0 to 5 years.

- **Community-level impacts of repeated exposure to $PM_{2.5}$ from wildfire may include excess mortality**

Nguyen et al. (2021) estimated that impacts of air pollution in the 2019-20 bushfire period was associated in NSW with 247 (CI: 89, 409) premature deaths.

Studies with indirect evidence (Type 2)

General characteristics: Eight studies were identified with indirect evidence on the topic.

Outcome measures: Individual-level health effects included presence of biomarkers for oxidative stress.

What the studies tell us: Some biomarkers increase over time and with increasing exposures to $PM_{2.5}$. At the individual-level, there are changes from pre-shift to post-shift in the presence of biomarkers for oxidative stress.

- **The impacts of exposure to $PM_{2.5}$ on biomarkers in firefighters may be cumulative**

Wu, Warren, et al. (2020) collected 120 spot urine samples from 19 firefighters before (pre-shift), immediately after (post-shift), and the following morning after work shifts on prescribed burn days and non-burn days. Measures included biomarkers of urinary mutagenicity: 8-isoprostane, malondialdehyde, and oxidised guanine species (Ox-GS). They found that post-shift levels of creatinine-corrected urinary mutagenicity and 8-isoprostane were non-significantly higher than pre-shift levels. However, creatinine-corrected Ox-GS levels increased significantly in next-morning samples following wildfire smoke exposure and a significant difference in cross- shift changes between burn and non- burn days was observed in 8-isoprostane. The authors suggested that wildland firefighters in this study had a higher urinary mutagenicity and oxidative stress than noted in other studies, presumably due to repeated exposure to elevated levels of fire smoke emissions during prescribed burns.

[65] Lung scarring: includes 200 lung disorders that affect the interstitium, the tissue and space around the alveoli (air sacs).

Other studies have also examined the impacts of repeated exposure to $PM_{2.5}$ smoke. These studies showed that health impacts of repeated exposure include:

- Increased polycyclic aromatic hydrocarbon metabolites (OH-PAH) and indicators of exposure to volatile organic compounds (VOCs), increasing with each exposure (Fent et al., 2019) and in higher concentrations for smokers (Oliveira et al., 2017);
- Increased urinary mutagenicity[66] (Adetona et al., 2019) and urinary 1-hydroxypyrene (Andersen et al., 2017);
- Increases in interleukin-8[67], C-reactive protein[68], and serum amyloid A[69] (A. M. Adetona et al., 2017);
- Increased body temperature and heart rate variability and decreased microvascular function (Andersen et al., 2017).

The Fent et al. (2019) study concluded that a dermal absorption route was likely to have been responsible for increased levels of PAH metabolites in urine samples.

- **Animal studies also demonstrate impacts of exposure to $PM_{2.5}$ from wildfire on pulmonary function**

Bai et al. (2021) examined outdoor-housed nonhuman primates born during years of low and high wildfire smoke exposure. Twenty-one females were born during extreme wildfire season events in summer 2008; 22 were born in summer 2009, during low wildfire smoke exposure. Pulmonary function and circulating cytokines were measured three years later, in the animals' adolescence. Higher exposure in infancy was, on average, associated with lower lung functional residual capacity (FRC), lung residual volume (RV), tissue compliance (Ct),[70] and IL-8 secretion in adolescence. Exposure to wildfire smoke in infancy generally conferred lower adolescent respiratory volumes and higher inflammatory cytokines.

- **Evidence on the impacts of repeated exposure to $PM_{2.5}$ from wildfires on genetic material is emerging**

Gea et al. (2021) studied the biological impacts of $PM_{2.5}$ and PM_{10} collected in North-West Italy in 2017. The in vitro impacts of these particles on human bronchial epithelial cells were assessed. The PM_{10} and $PM_{2.5}$ extracts induced a significant mutagenicity[71] in all sites. In addition, all extracts induced a slight increase in estrogenic activity. No cytotoxicity or DNA damage was detected. Results confirm that fires could be relevant for human health, since

[66] Urinary mutagenicity is a biomarker associated with genetic damage.
[67] Interleukin-8 is one of the major mediators of the inflammatory response.
[68] C-reactive protein is often the first evidence of inflammation or infection in the body.
[69] Serum amyloid is a family of proteins produced in the liver that are elevated in an acute-phase response to inflammatory stimuli.
[70] Compliance is the ability of a hollow organ (vessel) to distend and increase volume with increasing transmural pressure or the tendency of a hollow organ to resist recoil toward its original dimensions on application of a distending or compressing force.
[71] Mutagenicity refers to the induction of permanent transmissible changes in the amount or structure of the genetic material of cells or organisms.

they can worsen the air quality, increasing PM concentrations, with mutagenic and estrogenic effects.

- **The future impacts of wildfire-related $PM_{2.5}$ on premature mortality have been modelled**

Neumann et al. (2020) estimated the impacts of climate change on premature mortality from exposure to wildfire-related $PM_{2.5}$ using a range of scenarios. They found that excess mortality could be up to 3.5 times larger than in the baseline period by the end of the 21st century.

- **There may be incomplete recovery from repeated exposures to $PM_{2.5}$**

Adetona et al. (2013) found that firefighters' age and length of career were associated with increases in some individual biomarkers (8-Oxo-7,8-dihydro-2'-deoxyguanosine (8-Oxo-dG) and malondialdehyde), but not overall biomarkers.

Using a mouse model, Noel et al. (2016) found that 10 days after a 21-day exposure to 5 µg/m^3 of 1,3-butadiene soot had ended, incomplete lung recovery promoted a pro-biotransformation, pro-oxidant, and pro-inflammatory milieu/environment, which may be a starting point for potential long-term cardio-pulmonary effects.

RESULTS FOR TOPIC 3: LONGER-TERM IMPACTS OF SINGLE AND REPEATED ACUTE EXPOSURE TO PM

Seventeen studies (seven with direct evidence on the topic) were identified in this category.

Studies with direct evidence

General characteristics: Three studies on longer-term impacts were undertaken with firefighters, and the remaining five in the community.

Outcome measures: Measures of respiratory health.

What the studies tell us: The relationship between respiratory symptoms and estimated exposure to PM in firefighters appears to be strong immediately post fire but weakens over time. Evidence on exposure to PM at the community level is inconsistent, with some studies showing little impact over time but other demonstrating longer-term impacts on respiratory function.

- **Repeated exposure to PM in firefighters is related to the presence of inflammatory biomarkers but impacts decrease post-exposure**

Two studies providing direct evidence were conducted with firefighters in Canada. Cherry et al. (2021a, 2021b) examined the effects on respiratory health of firefighters recruited from 12 fire services attending a catastrophic wildfire at Fort McMurray, Canada, in 2016. Firefighters were followed up with clinical assessments in 2018-2019. In this cohort, 14.3% of non-smokers without prior chronic respiratory disease reported respiratory symptoms many months after their deployment that they attributed to the fire. The authors concluded that massive exposures during a wildfire are associated with non-resolving airways damage. On the other hand, concentrations of persisting inflammatory markers in the plasma of firefighters, which were related to estimates of exposure, decreased over time.

Moitra and colleagues (2021) conducted a study looking at long-term impacts of short-term exposure to the Fort McMurray fire among a group of Royal Canadian Mounted Police. Exposure was estimated by combining duration of exposure with air quality parameters obtained from nearby monitoring stations. Lung function was measured using spirometry and body plethysmography[72]. Results demonstrated a marginal association between air pollution and higher residual volume (RV: i.e., poorer lung function) [β: 1.55; 95% CI: −0.28 to 3.37 per interquartile change of air pollution index]. No notable change was detected for any other lung function indices. Associations between air pollution and RV were significantly higher in those participants screened in the first three months post exposure.

[72] The volume of air remaining in the lungs after the most forcible expiration possible and amounting usually to 60 to 100 cubic inches (980 to 1640 cubic centimetres)

- **Short term exposure to coal mine fire smoke may have long term impacts on host communities**

Evidence on longer-term impacts of exposure to PM is beginning to emerge from research conducted in relation to the Hazelwood coal mine fire in 2014. Prasad et al. (2021) explored any association between $PM_{2.5}$ and incidences of chronic obstructive pulmonary disease (COPD). Altogether, 346 exposed and 173 unexposed adults participated in a longitudinal study using spirometry and gas transfer measurements, as validated against a respiratory survey, 3.5 to 4 years after the mine fire. Individual $PM_{2.5}$ exposure was modelled. A 10 $\mu g/m^3$ increase in mean $PM_{2.5}$ exposure was associated with a 69% (95%CI: 11% to 158%) increase in risk of lung function consistent with COPD amongst non-smokers and increased risk of chest tightness (OR: 1.30, 95%CI: 1.03 to 1.64) and chronic cough (OR: 1.24, 95%CI: 1.02 to 1.51) in the previous 12 months in all participants. For current smokers, higher increments in average $PM_{2.5}$ exposure were associated with higher risk of chronic cough in the preceding 12 months (OR: 2.13, 95%CI 1.24 to 3.65).

Taylor et al. (2020) also examined impact of coal fire smoke 3.5 years after the Hazelwood fire, looking for evidence of impacts on asthma symptoms among exposed participants with asthma living in Morwell (exposed) and Sale (unexposed). In contrast to Prasad et al.'s (2021) study, Taylor et al. identified no evidence that exposed participants had more severe asthma symptoms, worse lung function, or more airway inflammation. However, there was evidence that participants who lived closest to the fire site had more uncontrolled asthma than those participants who lived further away from the fire zone (adjusted risk 2.71, 95% CI: 1.02, 7.21).

In Thailand, Ontawong et al. (2020) studied the lung function of 115 residents in an area chronically affected by forest fire smog and compared measures with broader population data. They reported that exposed participants had a lower FEV_1 (forced expiratory volume in 1 second)/ FVC (forced vital capacity) ratio (56.49 ± 23.88 in men and 56.29 ± 28.23 in women) than the general Thai population. The authors suggested that these results imply that long-term smoke exposure induces obstructive lung abnormality.

Orr et al.'s (2020) US study examined long-term health effects from exposure to wildfire smoke immediately after an extreme wildfire event that resulted in "hazardous" and "very unhealthy" levels of smoke over a six-week period. Measures were also taken one year and two years after the event. The study recruited 95 people with an average age of 63 years. Analysis of spirometry data found a significant decrease in lung function (FEV_1/FVC ratio) and a more than doubling of participants with ratios below the lower limit of normal (10.2% in 2017, 45.9% in 2018[73]) following the wildfire event, and this ratio remained low two years (33.9%) post exposure. In addition, observed FEV_1 was significantly lower than normal values. Similarly, Adetona et al. (2013) analysed spirometry data in two wildfire smoke-exposed communities in the USA. They found that a significant decrease in lung function (FEV_1/FVC ratio) remained low two years (33.9%) post exposure. Both studies concluded that exposure

[73] > 70% is considered normal.

to wildfire smoke can have long-lasting effects on respiratory health in the general community.

Studies with indirect evidence (Type 1)

General characteristics: Only five studies were identified in this category.

Outcome measures: Medication use and contact with medical professionals following exposure to wildfire.

What the studies tell us: Limited evidence suggests that repeated exposure to wildfire smoke in adults does not have longer-term impacts on health service use and mortality.

- **Repeated exposure to PM is related to relatively short-term, rather than longer term, impacts on respiratory health in the community**

Haikerwal et al. (2016) examined lag in ED attendances for asthma following the Hazelwood coal mine fire. While there was a relationship between ED attendances on the days of exposure, lag periods of up to 2 days did not show any association.

Reid et al. (2016) studied the impacts on the health of the community of a large wildfire complex in northern California in 2008. The association identified between $PM_{2.5}$ exposure and ED visits for respiratory issues was larger during than after the fires. The authors investigated lags of up to 28 days but did not find sustained effects, suggesting that the impacts of exposure were short-term.

A Tasmanian study (Borchers-Arriagada et al., 2020) found longer-term impacts on hospital admissions and mortality in the case of wood heater smoke, but short-term impacts only in the case of smoke from bushfires.

- **Exposures to $PM_{2.5}$ in utero and in children may have longer-term impacts**

Willis et al. (2020) in a study on children exposed to $PM_{2.5}$ in utero, or up to age the age of 2 years, found that each 100 µg/m^3 increase in peak 24-hour $PM_{2.5}$ exposure during a wildfire episode was associated with a 26% increased use of asthma medication inhalers 2-4 years later, as well as self-reported increases in respiratory infections and wheeze.

- **Impacts of exposure to PM in the community are related to the person's health status at birth**

Haikerwal et al. (2021) investigated impacts of bushfire smoke among young adults born extremely premature (EP) or with extremely low birth weight (ELBW). When compared with controls, EP/ELBW respondents reported more overall respiratory problems and respiratory specific symptoms post bushfire smoke exposure, along with higher medication uptake and health service utilisation. Adjusting for FEV_1 attenuated differences between the study and control groups. This study highlights that these population groups are likely to be at much higher risk of negative health outcomes when exposed to bushfire smoke or other forms of fire smoke.

Studies with indirect evidence (Type 2)

General characteristics: Six studies provided indirect evidence on the longer-term impacts of exposure to $PM_{2.5}$. Five examined biomarkers: three in firefighters; one in the community; and one in young rhesus macaques (primates). One study examined the long-term effects of exposure to smoke in utero on PAH in newborn cord blood following the World Trade Centre Collapse.

Outcome measures: Biomarkers of inflammation associated with respiratory capacity and cardiovascular disease.

What the studies tell us: There is limited evidence of longer-term impacts of exposure to PM on cardiovascular or respiratory health. Exposure to PM may be detected in umbilical cord blood.

- **Repeated exposure to PM is not related to longer term impacts on cardiovascular health in the community**

Betts et al. (2021) studied the impacts of the Hazelwood coal mine fire with long-term clinical or subclinical cardiovascular disease (CVD) in adult residents of Morwell (exposed) and Sale (unexposed) four years after the fire. Adults highly exposed to smoke-related $PM_{2.5}$ from a 6-week duration mine fire, did not exhibit consistent evidence of clinical or subclinical CVD (as measured by serum biomarkers, blood pressure, flow mediated dilatation – indication of endothelial function, or ECG) approximately four years after the event.

- **Exposures to $PM_{2.5}$ in utero and in children may have longer-term impacts**

Perera et al. (2005) found that pregnant women who resided or worked within a two-mile radius surrounding the World Trade Centre at the time of the building collapse had higher concentrations of PAH-adducts in the maternal and umbilical cord blood, while there was no association with distance beyond two miles. The cord adducts were not associated with birth weight, child length, or head circumference, except in women who were also exposed to environmental tobacco smoke.

- **Limited evidence suggests possible longer-term impacts of exposures to fire smoke on biomarkers for oxidative stress**

Black et al.'s (2017) study explored the long-term effects of wildfire smoke on rhesus macaques exposed to ambient wood smoke in early life. When these macaques were three years old, cultures of peripheral blood mononuclear cells (PBMCs)[74] were taken. The study found that cultures from exposed animals had less interleukin-6 and interleukin-8 proteins than similar cultures from controls. In addition, animals exposed to wildfire smoke as infants had significantly reduced lung inspiratory capacity, residual lung volume, lung vital capacity, and functional residual lung capacity per unit of body weight as adolescents. The research team concluded that their findings supported an association between wildfire smoke

[74] A peripheral blood mononuclear cell (PBMC) is any peripheral blood cell (i.e., the cellular components of blood) with a round nucleus. PBMCs can be extracted from whole blood and can be cultured for 5-7 days.

exposure during the postnatal period of development and immune dysregulation and compromised lung function in adolescence.

- **Limited evidence suggests possible longer-term impacts of exposures to chemicals that may be present in fire smoke**

Miranda et al. (2012) measured firefighter exposure levels of carbon monoxide (CO), nitrogen dioxide (NO_2), and volatile organic compounds (VOC) in wildfires during three fire seasons in Portugal. Personal monitoring devices were used to measure exposure. Firefighters were also tested for exhaled nitric oxide (eNO) and carbon monoxide (CO) before and after (within 1.5 hours) their firefighting activities. Data indicated that exposure levels during firefighting activities were beyond limits recommended by the Occupational Exposure Standard (OES) values. Medical tests conducted on the firefighters also indicated a considerable effect on various parameters, with a significant increase in CO and decrease in NO in exhaled air of the majority of the firefighters. Further, firefighters experienced a reduction in respiratory function between evaluation in April 2008 and at the end of the 2010 fire season, measured using spirometric parameters (FEV_1, F_{25}, F_{50}, and mid-expiratory flow MEF).

RESULTS FOR TOPIC 4: DOSE EFFECTS OF PM EXPOSURE

This section of the report includes studies that focused on **change** in exposure to $PM_{2.5}$, for example, a 5 µg/m^3 or 10 µg/m^3 increase over "usual" exposure levels. Fifteen of the studies in this section are studies of community exposure to smoke events. One study examined lung function of firefighters and five studies were laboratory-based (with human volunteers or using mouse models).

Twenty-one studies were identified in this category: three with direct evidence of dose effects of exposure to PM.

Studies with direct evidence

General characteristics: Three studies were categorised to this topic: one each in the general community, in firefighters, and in healthy volunteers (for a laboratory study).

Outcome measures: Spirometric measures and self-report.

What the studies tell us: There is unclear evidence of a dose effect on direct measures of lung function.

- **There is a dose effect of exposure to $PM_{2.5}$ on pulmonary function in the community, especially for at-risk populations**

Prasad et al. (2021) explored any association between $PM_{2.5}$ from the Hazelwood coalmine fire in 2014 and incidences of COPD. A longitudinal study sample of 346 exposed and 173 unexposed adults were examined using spirometry and gas transfer measurements, as validated against a respiratory survey, 3.5 – 4 years after the fire. Individual $PM_{2.5}$ exposure was modelled with a regression analysis. A 10 µg/m^3 increase in mean $PM_{2.5}$ exposure was associated with a 69% (95%CI: 11% to 158%) increase in odds of spirometry consistent with COPD amongst non-smokers and increased risk of chest tightness (OR 1.30, 95%CI: 1.03 to 1.64) and chronic cough (OR 1.24, 95%CI: 1.02 to 1.51) in the previous 12 months in all participants. For current smokers, incremental increases in mean $PM_{2.5}$ exposure were associated with higher risk of chronic cough in the preceding 12 months (OR 2.13, 95%CI: 1.24 to 3.65).

- **There may not be dose effect of exposure to $PM_{2.5}$ on direct measures of pulmonary function in firefighters**

Slaughter et al. (2004) found that although lung function of firefighters declined following wildfire $PM_{2.5}$ exposure, this was not related to the dose of the exposure and was not attributable to any single component of the smoke.

- **There may not be a dose effect of exposure to $PM_{2.5}$ on direct measures of pulmonary function in healthy volunteers**

Ferguson et al. (2017) studied 10 healthy, non-smoking volunteers in a laboratory and measured FEV_1 and FVC in response to clean filtered air and 250 µg/m^3 or 500 µg/m^3 wood

smoke $PM_{2.5}$. The study found a slight post-exposure reduction of FEV_1 in the 250 µg/m^3 and 500 µg/m^3 trials.

Studies with indirect evidence (Type 1)

General characteristics: Fourteen studies were classified here: six from the USA, four from Australia, three from Canada, and one from Brazil.

Outcome measures: hospital admissions, emergency department presentations, physician visits, and (for children) parent-reported symptoms, medications, and contact with medical services.

What the studies tell us: At the community level, dose effects have now been established for exacerbating lung conditions and associated healthcare use. The evidence for dose effects on health service use associated with cardiac conditions, diabetes, and mental health is suggested but not as well supported by the evidence as the evidence on healthcare for lung conditions. Estimates of the size of this effect vary widely, depending on the outcome measure used and the sample or population studied, with increases ranging from 2% to 55% per 10 µg/m^3 increase in mean $PM_{2.5}$ exposure. Overall, there is no current evidence of a $PM_{2.5}$ safe threshold.

- **There is a dose effect of exposure to $PM_{2.5}$ on health service use for respiratory functioning**

Exposure doses of as little as 10 µg/m^3 $PM_{2.5}$ have been associated with increased risks of elevated respiratory/other chest symptoms, upper respiratory infections, hypertension, and 'all-cause' cardiac outcomes and in youth for respiratory/other chest symptoms, upper respiratory infections, 'all-cause' respiratory conditions, wheeze, and seeking advice from a health professional (Gan et al., 2017; Reid et al., 2019; Tinling et al., 2016; Wettstein et al., 2018; Willis et al., 2020; Yao et al., 2020). Wettstein et al. (2020) found that these effects were more pronounced when exposed to increasing concentrations of $PM_{2.5}$, with the greatest for concentrations > 10.5 – 21.5 µg/m^3.

Reid et al. (2016) studied the impacts on the health of the community of a large wildfire complex in northern California in 2008. They reported that 1 µg/m^3 increase in $PM_{2.5}$ was associated with increases in the 3-day average for both asthma and combined respiratory diseases ED visits and hospitalisations. A 5 µg/m^3 increase in $PM_{2.5}$ was associated with a 7% increase in asthma hospitalisations, a 6% increase in asthma ED visits, and a 2% increase ("exacerbations") in COPD ED visits. It is unclear whether exacerbations refer to new diagnoses or worsening of problems experienced by people with an existing diagnosis.

In an analysis of the impacts of early childhood exposure by Willis et al. (2020), each 10 µg/m^3 increase in peak 24-hour $PM_{2.5}$ exposure was associated with increased use of asthma inhalers. In contrast, Slaughter et al. (2004) found that although lung function of firefighters declined as a result of wildfire $PM_{2.5}$ exposure, this was not related to the dose of the exposure and was not attributable to any single component of the smoke.

Gan et al. (2020) explored an association between expected daily $PM_{2.5}$ estimates and emergency department visits and asthma morbidity during the 2013 wildfire season in Oregon in north-western USA. The study reported that a 10 μg/m^3 increase in wildfire smoke $PM_{2.5}$ resulted in increased risk in asthma diagnosis at ED (odds ratio [OR]: 1.089, 95%CI: 1.043–1.136), office visits (OR: 1.050, 95% CI: 1.038–1.063), and outpatient visits (OR: 1.065, 95% CI: 1.029–1.103); a positive association was also observed with asthma reliever medication prescriptions/purchases (OR: 1.077, 95% CI: 1.065–1.088). In other words, increased exposure led to between 5% and 9% increases in measures of asthma morbidity.

Howard et al. (2021) in Canada determined healthcare service use for cardiorespiratory presentations and outpatient salbutamol dispensation associated with 2.5 months of severe wildfire smoke in Canada's high subarctic. The median 24-hour mean $PM_{2.5}$ was fivefold higher in the summer of 2014 than in 2012, 2013 and 2015 (median=30.8 μg/m^3), with the mean peaking at 320.3 μg/m^3. A 10 μg/m^3 increase in $PM_{2.5}$ was associated with an increase in asthma-related (incidence rate ratio (IRR) = 1.11, 95%CI: 1.07 to 1.14) and pneumonia-related ED visits (IRR 1.06, 95%CI: 1.02 to 1.10), as well as an increase in COPD hospitalisations (IRR = 1.11, 95%CI: 1.02 to 1.20).

In a Brazilian study, Ye et al. (2021) estimated the association between daily exposure to wildfire-related $PM_{2.5}$ and hospital admissions. At the national level, a 10 μg/m³ increase in wildfire-related $PM_{2·5}$ was associated with a 5.09% (95% CI: 4.73 to 5.44) increase in respiratory hospital admissions over at 1-day after the exposure. The effect estimates were particularly high in children aged 4 years or younger (4.88%, 95% CI: 4·47 to 5·28]), children aged 5–9 years (2.33%, 95%CI: 1·77 to 2·90), and people aged 80 years and older (3.70%, 95%CI: 3·20 to 4·20).

- **There is a possible dose effect of exposure to $PM_{2.5}$ on healthcare use associated with impaired cardiac function in the community**

In Ye et al.'s (2021) Brazilian study, at the national level, a 10 μg/m³ increase in wildfire-related $PM_{2·5}$ was associated with a 1.10% (95%CI: 0.78 to 1.42) increase in cardiovascular hospital admissions, up to one day after the exposure.

Xu et al. (2021) evaluated hospitalisation rates in the five years after the Hazelwood mine fire. Almost 3000 residents were surveyed and matched to hospitalisation records with recurrent event survival rates used to evaluate any relationship between $PM_{2.5}$ concentrations and hospitalisations. Results demonstrated that each 10 μg/m^3 increase in mine-fire-related $PM_{2.5}$ was associated with a 9% (95%CI: 1% to 17%) increased risk of respiratory hospitalisation over the following five years, with stronger associations observed for females (16% increase, 95%CI: 6% to 27%) than males (no difference). In particular, increased risks were observed for hospitalisations for asthma (43%, 95%CI: 19% to 73%) and COPD (14%, 95%CI: 2% to 28%). No association was found with hospitalisations for cardiovascular diseases, mental illness, injuries, type 2 diabetes, renal diseases, or neoplasms.

In Canada, Mahsin et al. (2021) studied daily outpatient respiratory and cardiovascular physician visits and observed that for every 10 μg/m^3 increase in $PM_{2.5}$ level during and after wildfire, there was an elevated risk of respiratory disease morbidity both during and after the

fire: during, RR = 33% (95%CI: 10% to 59%) and after, RR = 55% (95% CI: 42% to 69%) respectively, relative to the pre-wildfire time period. Increased risk was observed for children aged 0–9 years during (RR = 1.57, 95% CI: 1.21 to 2.02) and after the wildfire (RR = 2.11, 95% CI: 1.86 to 2.40) especially for asthma, acute bronchitis, and acute respiratory infection. The risk of physician visits among seniors increased by 11% (95% CI: 3% to 21%), and 19% (95% CI: 7% to 33%) post-wildfire for congestive heart failure and ischaemic heart disease, respectively. Individuals with pre-existing diabetes had an increased risk of both respiratory and cardiovascular morbidity in the post-wildfire period (RR = 1.35, 95% CI: 1.09 to 1.67; RR = 1.22, 95% CI: 1.01 to 1.46, respectively).

- **There is a dose effect of exposure to $PM_{2.5}$ on ambulance call out and health service use over time**

Broder et al. (2022) examined whether individual level exposure to coal mine fire-related $PM_{2.5}$ was associated with a long-term increase in ambulance attendances. $PM_{2.5}$ exposure was estimated using self-reported location diary data and modelled $PM_{2.5}$ concentrations. The study found that for each 10 µg/m^3 increase in mean coalmine fire-related $PM_{2.5}$ exposure, there was a 10% (adjusted hazard ratio [HR]= 1.10, 95%CI: 1.03 to 1.17) increase in the overall risk of ambulance attendances within 3.5 years.

- **There may be a dose effect of exposure to $PM_{2.5}$ as an infant on antibiotic prescriptions**

Shao et al. (2020) also investigated impacts of the Hazelwood mine fire, looking at associations between: (i) Intrauterine exposure to $PM_{2.5}$ and frequency of GP attendance and dispensing of prescribed asthma inhalers, steroid skin creams, and antibiotics during the first year of life; and (ii) Infant exposure and those same outcomes during the year following the fire. Results demonstrated that 10 and 100 µg/m^3 increases in average and peak $PM_{2.5}$ exposure during infancy were associated with higher dispensations of antibiotics during the year: the adjusted incidence rate ratios were 1.24 (95% CI: 1.02 to 1.50) and 1.14 (1.00 to 1.31) respectively.

Studies with indirect evidence (Type 2)

General characteristics: Five studies were classified under this topic. Two were human studies completed in laboratory settings with volunteers, one was carried out in the general community, and two were animal studies.

Outcome measures: Inflammatory biomarkers.

What the studies tell us: There may be a dose effect of exposure to PM on biomarkers, but the evidence is not strong.

- **There may be a dose effect of exposure to $PM_{2.5}$ on blood biomarkers**

Peters et al. (2018) in a laboratory study of volunteers found that uric acid[75] decreased following low exposure (250 µg/m^3) to woodsmoke, while plasma trolox equivalent antioxidant capacity (TEAC) levels[76] increased post exposure and for one hour afterwards. Lipid hydroperoxide levels[77] decreased for one-hour post-exposure for high exposures (500 µg/m^3) to woodsmoke, while 8-Iso[78] increased following both smoke trials. Together, these markers indicate blood oxidative stress[79] responses to exposure to woodsmoke. However, Peters et al. concluded that the blood oxidative stress occurred largely independent of $PM_{2.5}$ concentrations.

Ferguson et al. (2016) conducted a laboratory-based simulation study of healthy non-smoking volunteers that compared impacts of exposure to 250 µg/m^3 or 500 µg/m^3 woodsmoke $PM_{2.5}$ and clean air for 1.5 hours while exercising on a treadmill. Exhaled breath condensate (EBC) and blood plasma samples were obtained before, immediately after, and one-hour after exposure. 8-isoprostane, pH[80], and myeloperoxidase were measured in EBC while hydrogen peroxide (H_2O_2), surfactant protein D, and pentraxin-3 (PTX3) were measured in both EBC and plasma. Only pH, 8-isoprostane, and PTX3 increased significantly from pre- to post-exposures at the 500 µg/m^3 concentration compared to the 250 µg/m^3 concentration. 8-isoprostane concentrations did not increase immediately following wood smoke exposures but were elevated one-hour post exposure.

- **PM exposure may cause increased airway inflammation**

Over a two-year period, O'Dwyer et al. (2021) assessed the effects of outdoor smoke from planned burns, wildfires, and the Hazelwood coal mine fire on biomarkers of inflammation in an exposed, predominantly older population. The study found exposure to 10 µg/m^3 increases in $PM_{2.5}$ levels from outdoor smoke at a 4-hour lag was associated with increased levels of airway inflammation as indicated by increased FeNO (fractional exhaled nitric oxide)[81] (β = 0.500, 95%CI: 0.192 to 0.808). These effects were also shown for wildfire smoke exposure at 4, 12, 24 and 48-hour lag periods and coal mine fire smoke at a 4-hour lag. Total white cell (β = −0.088, 95%CI: −0.171 to −0.006) and neutrophil counts (β = −0.077, 95%CI: −0.144 to

[75] A uric acid blood test, also known as a serum uric acid measurement, determines how much uric acid is present in your blood. The test can help determine how well your body produces and removes uric acid. Low levels of uric acid are less common than high levels and are less of a health concern but may indicate liver or kidney disorder.

[76] The main function of antioxidants is to protect the body against the destructive effects of free radicals damage. Total antioxidant capacity (TAC) is frequently used to assess the antioxidant status of biological samples. Trolox equivalent antioxidant capacity (TEAC) can determine the TAC of a sample.

[77] Lipid peroxidation is the oxidative degradation of lipids. Lipid hydroperoxides are reported to be toxic to the human body. They contribute to inflammation and cell death.

[78] 8-isoprostane (8-iso-$PGF_{2\alpha}$) is a biomarker for oxidative stress found in urine. Increased 8-iso is a marker of antioxidant deficiency.

[79] Oxidative stress is an imbalance between free radicals and antioxidants in the body.

[80] Salivary pH (acid vs. alkaline) is a diagnosis biomarker and a robust measure of asthma. EBC pH is inversely correlated with disease severity: the more acidic the EBC, the higher the severity of asthma.

[81] A non-invasive, safe, and simple method of quantifying airway inflammation.

−0.010) declined in response to a 10 μg/m^3 increase in $PM_{2.5}$. However, other blood biomarkers were not affected.

- **Animal studies indicate inflammatory responses following PM exposure**

Martin et al. (2018) investigated the impact of a high fat oral/dietary intake on metabolic and inflammatory responses in the context of peat smoke exposure in mice. Among the mice ingesting a high fat diet orally, the findings demonstrated metabolic dysregulation and increased inflammatory responses were associated with high peat smoke exposure. Increased circulating low-density lipoproteins (LDLs)[82], white blood cells, and ACE inhibitors were also noted after exposure to peat smoke.

One study (Zhang et al., 2021) was an animal study examining likely cognitive impairment associated with inflammatory axis stimulation in mice offspring exposed to various doses of $PM_{2.5}$ in utero. Levels of inflammatory biomarkers in the brain were three times higher in the high-dose groups than in the control. Results suggest that $PM_{2.5}$ exposure promotes the inflammatory response in the hippocampus[83] mediated by inflammation in microglia[84], resulting in cognitive dysfunction in offspring, which could be alleviated by simultaneous HMGB1[85] suppression. These findings provide a theoretical basis for preventing cognitive impairment in offspring caused by environmental pollution during pregnancy.

[82] High levels of LDL lead to a build-up of cholesterol in the arteries and raise the risk of heart disease and stroke.
[83] Part of the brain with a major role in learning and memory.
[84] Microglia regulate brain development. They mount the primary active immune defence in the central nervous system (CNS). They are constantly scavenging the CNS for plaques (clumps of protein that can disrupt communication between nerve cells), damaged neurons and synapses and infectious agents.
[85] A common biomarker; a proinflammatory cytokine.

RESULTS FOR RESEARCH QUESTION 4: MITIGATION EFFECTS OF PROTOCOLS

The literature search used the search terms outlined in Table 2. The results of the literature search are set out in the PRISMA diagram below:

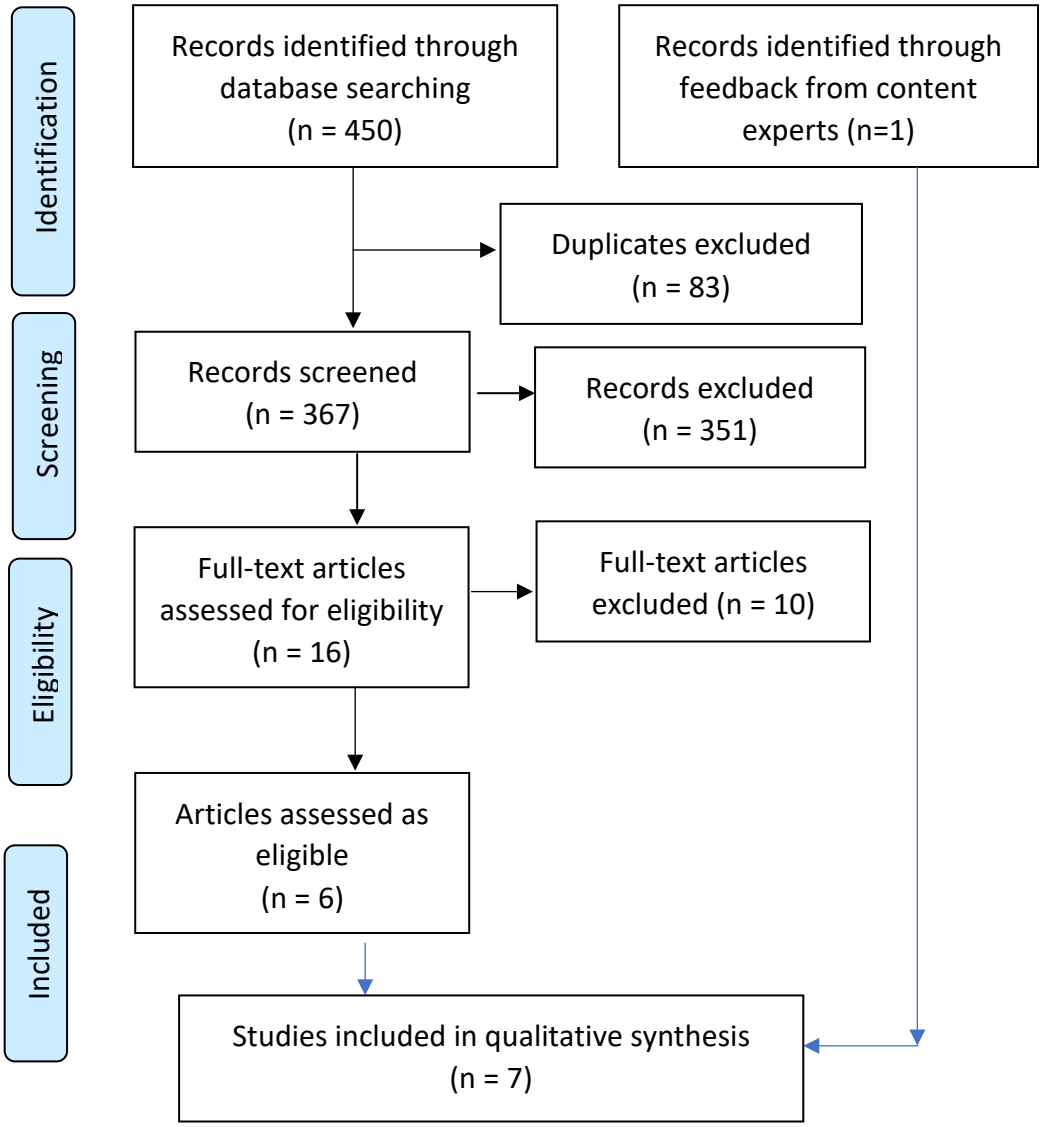

Figure 5: PRISMA diagram for literature search on mitigation impacts of protocols

General characteristics: Seven studies on impacts of use of protocols were identified.

Outcome measures: Injury data, feasibility ratings.

What the studies tell us: Anticipatory smoke modelling has a positive impact on community outcomes during major fire events.

In all, seven research articles were identified for inclusion in this report. Three articles discussed wildland fire protocols from the international context (Edwards et al., 2005; Koopmans et al., 2020; Vaidyanathan, Yip, & Barbe, 2018); one article (Luhar et al., 2020)

drew from a major industrial incident in the Australian context; one article discussed the development of an air quality monitoring service for use during major urban fire incidents in the UK (Griffiths et al., 2018); one article (van Deventer et al., 2020), discussed the impact of public messaging from government organisations during a major US wildland fire event; and one article reported on best-practice development of SOPs, with a focus on injury rates and SOPs (Duncan et al., 2014). While the Duncan et al. article did not focus on smoke exposure specifically, it is relevant to the current study in that it describes the best-practice methods for establishing SOPs to prevent fireground injuries.

It is important to note a general paucity of published, research-based evidence outlining impacts of protocols and/or PPE on smoke exposure mitigation for urban career firefighters. Furthermore, almost all available evidence was derived outside of the Australian context. Some internal documents, such as Standard Operating Procedures (SOPs), were able to be accessed, as well as key guiding documents, such as the International Agency for Research on Cancer (IARC) monograph, and these documents have helped inform this report.

Studies by Vaidyanathan et al. (2018), Luhar et al. (2020), and Griffiths et al. (2018) examined the impacts of smoke modelling on population health risk factors, with all research groups identifying the positive impact of anticipatory smoke modelling on community outcomes during major fire events. In contrast to the benefits of anticipatory modelling these researchers suggested delays in measuring air quality in relation to fire duration and intensity can have profound negative impacts on long term outcomes. Most relevant to this project is Griffiths et al.'s discussion of air quality monitoring, given its focus on short-term exposure (< 24 hrs) and urban context. Griffiths et al. (2018) reinforced the need to improve accuracy of the metrics used to measure levels of smoke exposure for fire responders and community. Griffiths et al. also identified the need for further evidence to support the development of effective metrics applied to protect responders and inform appropriate response for those communities at risk from smoke exposure.

Koopmans et al. (2020) outlined a study protocol for the evaluation of effective mitigation strategies or policies to reduce negative health impacts of occupational smoke exposure for wildland firefighters. This article was of interest in light of this project and the similar methodological applications to policy development. In addition to the work of Koopman et al., Duncan et al. (2014) outlined part of an international study that involved a panel of experts from Australia, Canada, Japan, United Kingdom, and the United States that focused on the development of best practice SOP development.

RESULTS FOR RESEARCH QUESTION 5: MITIGATION EFFECTS OF PPE

The literature search used the search terms outlined in Table 3. The results of the literature search are set out in the PRISMA diagram below:

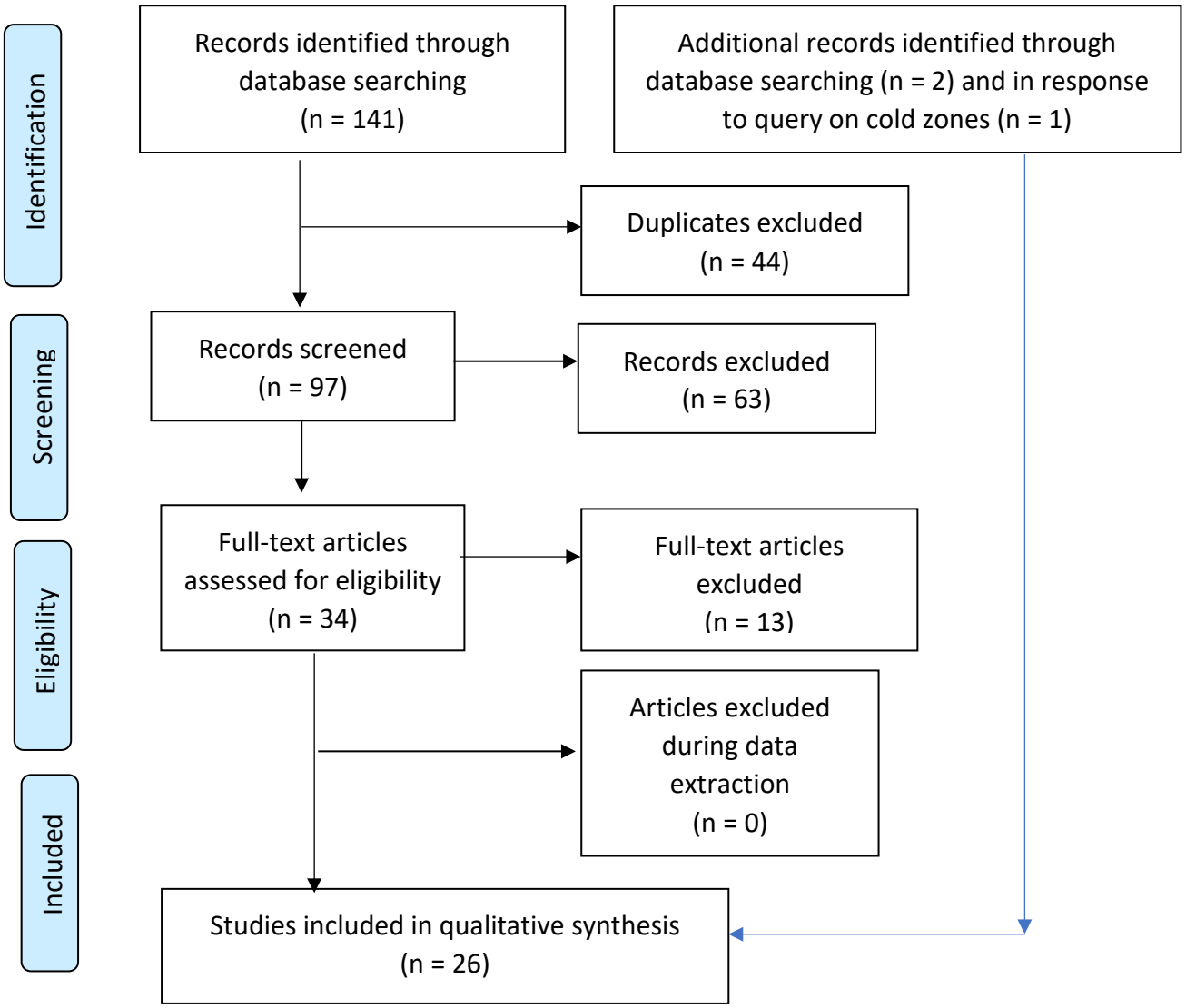

Figure 6: PRISMA diagram for literature search on mitigation impacts of PPE

General characteristics: Twenty-five studies on impacts of use of PPE were identified; 11 were laboratory-based or simulation studies.

Outcome measures: Extent of use of PPE; injury rates.

What the studies tell us: PPE is not used as consistently as it should be during all firefighting phases, especially when fire is not visible, such as during fire overhaul and outside fire "hot zones". Use of PPE protects against some health impacts of exposure to PPE, but the extent of protection depends on the kinds of PPE used.

Twenty-six articles were included as evidence in relation to impact of current PPE on smoke exposure mitigation (including one identified to address the question about whether

PPE might be required in fire "cold zones". While there was a general paucity of empirical evidence as to the efficacy of current PPE, some authors discussed the association between observed physiological changes during a fire event among firefighters and the use of any type of PPE (e.g., Andersen et al., 2017; Anthony et al., 2007).

Other included studies examined current firefighters and associated PPE use, with varying results under both controlled settings and on-field activity (Austin et al., 2001; Heineman et al., 1989; Large et al., 1990; Morgan et al., 2008). Austin et al. (2001) described use of PPE during various fire phases (knockdown and overhaul), noting that only 50% of firefighters who participated in the study used PPE (i.e., self-contained breathing apparatus [SCBA]) during the knockdown phase and only 6% of the time during all fire phases. There was a noted trend for lower PPE usage with more years worked. Heineman et al. (1989) compared 75 injured firefighters with 140 uninjured peers across three injury categories (smoke inhalation, burns, and falls). While no specific PPE was examined, a strong correlation between lower injury rates and the use of SCBA was noted.

There was also a positive correlation between a history of injury and previous firefighting experience. Large et al. (1990) noted a decrease in spirometric[86] or lung function measurements following exposure to house fires for all 60 participating firefighters, with two participants exhibiting significant decrease in measurements. Lung function was not associated with use of PPE or age, smoking history, or years of service.

Morgan et al. (2008) reviewed incidences of "health symptoms" in firefighters deployed to a fuel depot fire. No specific PPE was identified in the publication, and only "face mask" usage was assessed. Face masks could either be "fitted or paper." The study found a significantly greater likelihood of reporting respiratory symptoms among those firefighters who did not wear face masks (odds ratio = 2.33, 95%CI: 1.67 to 3.26).

Cherry et al. (2021) estimated firefighters' exposure to $PM_{2.5}$ during the Fort McMurray fire in Canada in May 2016. Firefighters were recruited from 13 fire services and included structural, woodland, and industrial firefighters. The research team estimated exposure to PM (including stage of fire and task type) and calculated an exposure mitigation index (EMI) from reports of use of respiratory protective equipment (RPE). If firefighters wore no RPE, the mitigation factor was set at 1. Sustained use of appropriate equipment reduced the EMI, with a calculated mitigation factor of 0.5 reducing the estimated exposure by 50%. Overall, 30% of structural and industrial firefighters wore no RPE, and none of the wildland firefighters did so. Among firefighters who did, only 12.5% of structural firefighters and 18.5% of industrial firefighters achieved an EMI of 0.5. The study found that shortly after the fire, self-reports of respiratory symptoms (i.e., cough, phlegm, breathlessness, wheezing and chest tightness) were strongly related to estimated PM exposures but these statistical associations declined over time (by the follow up in 2018-19). Chest tightness and cough were mitigated among firefighters who used PPE with an EMI of 10% or higher. Correlations between exposure and

[86] A common office test used to assess how well your lungs work by measuring how much air you inhale, how much you exhale, and how quickly you exhale.

reports of mental ill-health were also high, reflecting the impact of the ferocity of the fire on post-traumatic stress disorder (PTSD).

Eleven studies have examined exposure to particulates under laboratory, or simulation, conditions (e.g., Anthony et al., 2007; Cone et al., 2010; Currie et al., 2009; De Vos et al., 2009; Deitrich et al., 2015; Evans et al., 2015; Fent et al., 2018; Fent et al., 2019; Jones et al., 2015; Jones et al., 2016; Xu et al., 2019). Anthony et al. (2007) tested SCBA gas capture cartridges during simulated house fires and found clear evidence to support the efficacy of gas capture cartridges. The authors observed inconsistency among firefighters regarding use of SCBA during the overhaul phase and argued for more consistent use of SCBA during all phases of firefighting.

Several studies have compared the effectiveness or two or more devices. Cone et al. (2010) investigated differences in individual blood oxygen saturation levels using pulse oximetry[87] while deploying either regular SCBA or emergency escape device which is placed in a firefighter's mask and filters out PM and a number of hazardous smoke components but does not provide oxygen. The purpose of the emergency escape device is to provide additional time for a firefighter to escape after running out of oxygen in the SCBA. There were no differences in pulse oximetry between the groups, and protection from carbon monoxide (CO) was equal across the different mask types.

Currie et al. (2009) compared two gas purification canisters, one certified for chemical, biological, radiological, and nuclear (CBRN[88]) materials and one not certified under simulated overhaul conditions in a smoke chamber. The uncertified canister reduced irritant levels (carbon monoxide CO, nitrogen dioxide NO_2, and sulphur dioxide SO_2) below required levels, but levels of CO were higher in the non-certified canister. All respirator canisters demonstrated that they were able to filter respirable PM to their certified levels and penetration was <0.03%.

Particle penetration into PPE was examined by De Vos et al. (2009, 2006), Dietrich et al. (2015), and Mayer et al. (2020). Mayer et al. investigated the impact of laundering and/or on-site decontamination on PPE effectiveness and particulate penetration and found that garment design and fabric makeup were most strongly associated with greater protection from particulate penetration, rather than laundering or on-site decontamination. Evidence demonstrates that turnout jackets with zip closure (rather than 'hook and D closure') and particulate blocking hoods were more effective in reducing skin exposure to PAHs for firefighters.

De Vos et al. (2009, 2006) examined various mask filtration types under simulated urban and wildfire conditions and demonstrated statistically significant higher prevalence of cough, wheeze, and shortness of breath in those firefighters using 'particulate only' (P) filtration masks than when two other types of masks (particulate/organic vapor (POV), and particulate/organic/vapor/formaldehyde (POVF) masks) were used across both study groups. Deitrich et al. (2015) tested particle penetration of elastomeric (i.e., stretchy) face masks

[87] A non-invasive and painless test that measures your oxygen saturation level, or the oxygen levels in your blood.
[88] Chemical, Biological, Radiological and Nuclear materials

using Portable Aerosol Mobility Spectrometers (PAMS) inside and outside of the masks. Masked were deemed 'adequately fitted' by using a standardised 'Fit Factor' (FF) whereby mask application was demonstrated with careful adjustment of elastic straps and 'user seal' was established by removing positive pressure leak by further strap adjustment. Adequately fitted masks demonstrated lower penetration rates. The study concluded that PAMS could be used during overhaul operations to monitor real-time aerosols with potential reduction in risk of overexposure to fine and ultrafine PM.

A recent study (Kodros et al., 2021) attempted to quantify the potential of respirators of various designs to protect wearers from PM (i.e., the Protection factor [PF]). Measurements of mask filtration took place in an aerosol chamber. Face masks and respirators were attached to a cylinder and air flows approximated those of the flow rate during inhalation at rest. Mask efficiency was measured separately for each of four mask types—reusable natural-fibre (cotton) facemasks, disposable synthetic-fibre face masks, surgical masks, and N95 respirators—and three particle sizes corresponding to fossil fuel combustion (PM_1), wildfire smoke ($PM_{2.5}$), and dust (PM_{10}). Results showed that the efficiency of the masks depended on particle size. The N95 respirator offered the highest degree of protection against all three particle sizes, with a PF of more than 14 when worn with a leak rate of 5%. Conversely, the surgical mask had PFs of only 1.9. This is due to the poor fit typically reported for surgical masks, allowing a relatively high percentage (in this case 50%) of the air flow to bypass the filtering piece. The non-electrostatic filtering masks (the natural- and synthetic-fibre masks), worn with a bypass rate of 5%, had the lowest PFs for the aerosol size distribution corresponding to wildfire PM. When the impact of wearing a mask on risk of respiratory hospitalisation in the community was modelled, the natural-fibre masks reduced the risk from 66% in the no-mask case to 50%, and the poorly fitting surgical mask further reduced the increased risk down to 41%.

One study (Gainey et al., 2018) provided indirect evidence on the effectiveness of PPE, employing an animal-testing model to examine the impact of smoke exposure in the absence of PPE on lung gene expression in mice. Findings demonstrated genetic changes in mice exposed to fireground overhaul environment were greater than for those mice outside the overhaul environment. Implications for long-term exposure are a greater likelihood of inflammatory disease and emergence of lung disease; however, these findings are difficult to translate into the human context.

- **PPE use may be required in fire "cold zones"**

The urban fire response is divided into three areas – a hot zone, in which protective gear must be worn and immediate threat to life exists; a warm zone, in which potential but non-immediate threat to life and health exists; and a cold zone, which is considered safe from the fire and where the command post is established. By definition, use of PPE is considered unnecessary in cold zones. However, variability in toxic compound outputs makes it difficult to produce definite guidelines for where warm zone boundaries should lie (Bakali et al., 2021).

One study has identified health risks in areas previously identified as fire cold zones. Bakali et al. (2021) examined the distribution of toxic compounds within a localised fire incident

response arena. The study found that while PAHs with high molecular weight were deposited mainly in the hot zone, PAHs with low molecular weight were distributed throughout the area, including the cold zone. Bakali et al. concluded that fire responders may be exposed to carcinogens in all fire zones, especially where biomass is burnt, and maintained that the terms “warm zone” and “cold zone” do not indicate the level of chemical exposure that firefighters may sustain to carcinogenic compounds volatilized during fires.

RESULTS FOR RESEARCH QUESTION 6: EXISTING GUIDELINES AND PROTOCOLS

Systematic methods were not appropriate to address this research question. Instead, we sought existing guidelines and protocols using standard search engines (e.g., Google, ResearchGate) to identify online material.

We were unable to access current operational guidelines from urban firefighting organisations. However, we were able to access broader guidance material from national and international firefighting peak bodies and regulatory organisations (AFAC, 2018; Heus, 2018).

International documents included a 2018 review report from the Dutch Institute for Safety (Instituut Fysieke Veiligheid - IFV), which outlined important measures to reduce on-field exposure to contaminants by firefighters in terms of appropriate use of protective clothing and breathing apparatus (Heus, 2018). The IFV reviewed safety guidelines for 16 European firefighting organisations finding consensus on risks of exposure to smoke and soot. All reviewed guidelines recommended that turn-out garments be removed while still on site, but away from the fire zone, to minimise skin exposure to contaminants. Laundering of turn out garments was to ensure maximal removal of contaminants, with minimal numbers of garments to be laundered at once.

Breathing apparatus was recommended to remain on for at least three minutes after deployment to allow for evaporation of toxic chemicals (or 'off gassing'). However, a lack of clarity around removal of all respiratory PPE was raised in the IFV report, stating that the usual length of time for off gassing is one hour, not three minutes. In terms of particulate protection, the IFV report recommended that firefighters continue to wear FFP3 masks after removing breathing apparatus to limit soot inhalation by on-field firefighters. This grouping of recommendations is referred to as 'clean(er) working' procedures, which have been adopted broadly, and operationalised to varying degrees across European professional firefighting organisations.

National documents were significant in their focus on bushfire activity rather than urban firefighting; however, recommendations in terms of PPE were consistent with the above Dutch review report. The Australasian Fire and Emergency Service Authorities Council (AFAC), based on studies by the CSIRO (Reisen & Meyer, 2009a, 2009b; Reisen, Hansen, & Meyer, 2011), recommended protective clothing be removed away from the fire zone, before returning to the fire station, and laundered appropriately (AFAC, 2018). Types of respiratory protection were chosen in accordance with a risk assessment of the fire zone and associated smoke exposure risk (AFAC, 2021). In contrast to the IFV report, not attempt was made to form time-critical recommendations in terms of PPE removal.

CONCLUSION

Extent of the literature:

When expanded to cover not just urban fires but also landscape fires, there is a substantial body of literature that addresses both individual-level health impacts and population-level health impacts of exposure to $PM_{2.5}$. This review identified 103 studies, including seven grey literature reports and four studies on exposure to PAHs. The studies relied on a wide range of methods, including laboratory studies of human and animal exposure and statistical modelling linking fire events to hospital and medical records, as well as direct physiological measures taken from firefighters with field exposure to $PM_{2.5}$.

Impacts on health

Evidence is strengthening that exposure to particulate matter including $PM_{2.5}$ (and PM_{10} and ultrafine PM) has adverse impacts on human health, both in the short and longer term. The clear health impacts identified by this review include respiratory effects; cardiovascular and cerebrovascular impacts, which have both short-term and long-term consequences on individuals and communities; and impacts on health service use, including emergency department presentations.

The most obvious acute effects at the population level are asthma and COPD exacerbations, with some impacts on cardiovascular health. These impacts are observed particularly amongst communities where harm minimisation to smoke exposure has not been implemented. In addition, some studies have reported impacts on people's eyes.

Among firefighters, the PM exposure has impacts on heart rate and microvascular structures. The documented presence of inflammatory biomarkers circulating in the body may have long-term consequences that have not yet been identified, including impacts on the brain. In addition, PM exposure was associated with increased urinary secretions of potentially carcinogenic PAHs. Finally, impacts of PM exposure on immune responses have been documented, however short and long-term health effects are not yet clear.

Concentrations and exposure doses

Importantly, there is no current evidence of a safe $PM_{2.5}$ threshold, and as little as 1 $\mu g/m^3$ may have noticeable effects on human health, with increasing concentrations having larger impacts on a range of acute and chronic cardiovascular and respiratory health outcomes. Based on the broader PM exposure literature, the relationship between $PM_{2.5}$ dose and physiological/health response is not linear but appears to plateau at high to very high concentrations (> 60 $\mu g/m^3$).

Impacts of protocols and PPE

It is important to note a general paucity of published, research-based evidence outlining impacts of protocols and/or PPE on smoke exposure mitigation for urban career firefighters. Furthermore, almost all available evidence was derived outside of the Australian context. However, there is apparent support from within the identified literature for the routine and

consistent use of PPE by all firefighters during all phases of a fire event—even in "cold zones" previously considered to be uncontaminated by PM. *More research is needed, particularly on the efficacy of protocols and guidelines in mitigating risk to firefighters from exposure to particulate matter.*

Some FRV internal documents, such as Standard Operating Procedures (SOPs), were able to be accessed, as well as key guiding documents, such as the International Agency for Research on Cancer (IARC) monograph, and these documents have helped inform the findings of this project. In particular, recommendations to reduce on-field exposure to contaminants include appropriate use of protective clothing and breathing apparatus.

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