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REVIEW ARTICLE

Review of the health effects of wildland fire smoke on wildland firefighters and the public

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Abstract

Each year, the general public and wildland firefighters in the US are exposed to smoke from wildland fires. As part of an effort to characterize health risks of breathing this smoke, a review of the literature was conducted using five major databases, including PubMed and MEDLINE Web of Knowledge, to identify smoke components that present the highest hazard potential, the mechanisms of toxicity, review epidemiological studies for health effects and identify the current gap in knowledge on the health impacts of wildland fire smoke exposure. Respiratory events measured in time series studies as incidences of disease-caused mortality, hospital admissions, emergency room visits and symptoms in asthma and chronic obstructive pulmonary disease patients are the health effects that are most commonly associated with community level exposure to wildland fire smoke. A few recent studies have also determined associations between acute wildland fire smoke exposure and cardiovascular health end-points. These cardiopulmonary effects were mostly observed in association with ambient air concentrations of fine particulate matter ($PM_{2.5}$). However, research on the health effects of this mixture is currently limited. The health effects of acute exposures beyond susceptible populations and the effects of chronic exposures experienced by the wildland firefighter are largely unknown. Longitudinal studies of wildland firefighters during and/or after the firefighting career could help elucidate some of the unknown health impacts of cumulative exposure to wildland fire smoke, establish occupational exposure limits and help determine the types of exposure controls that may be applicable to the occupation.

Keywords

Cardiovascular effects, respiratory effects, toxicity mechanism, wildfire, wildland firefighter

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Background

Although smoke from burning wildland vegetation (wildland fire smoke) is known to be composed of many potentially harmful components, its impacts on human health are relatively understudied and inadequately understood. Vegetative biomass smoke under different exposure scenarios has been associated with various adverse health effects. However, fewer studies have investigated the adverse health effects of wildland (natural vegetation including forests, grasslands, chaparral, etc.) fire smoke compared with those experienced in association with residential combustion of wood or other vegetation based fuels; fewer still have examined the effects of occupational exposure among wildland/forest firefighters.

The current review of vegetative biomass smoke exposure specifically examines adverse health effects of exposure to smoke emissions from forest fires or prescribed burns. Wildland fire smoke exposure is typically experienced on two levels: the community/general public level and occupationally among wildland firefighters. Due to climate change (Bedia et al., 2014; Johnston et al., 2012; Keywood et al., 2013; Liu et al., 2013), past forest management practices that have contributed to increased fuel loads in forests (Stephens & Ruth, 2005), large scale deforestation fires in developing countries (Silvestrine et al., 2011; Tosca et al., 2011) and increase in the number of people working and/or living in areas adjacent to forested areas which has resulted in the growth of the wildland–urban interface (Radeloff et al., 2005), the risk of exposures to wildfire smoke in both scenarios and their resulting adverse health effects may be expected to rise.

A majority of the investigation into the community level health effects of wildfire smoke exposure has been conducted

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in association with ambient air particulate matter concentrations, while a few have also studied associations with other criteria air pollutants. However, wildland fire smoke contains many other potentially harmful substances such as mono- and polycyclic aromatic hydrocarbons, aldehydes and metals for which dose-response data are not always available (Naeher et al., 2007).

In addition, it is important to note that wildland fire smoke is a dynamic mixture, changing temporally and spatially in composition as it is dispersed from the source. Its composition at the source is dependent on combustion conditions, while its variation across space from the source is highly influenced by atmospheric and weather factors. Consequently, the exposures experienced by wildland firefighters deployed to the fire line would be expected to be rather different from those experienced within communities downwind from wildland fires. Due to their proximity to the source, wildland firefighters may be exposed to elevated concentrations of the more harmful constituents of wildland fire smoke such as particulate matter and aldehydes when compared to what is experienced by the public. They are also expected to be more frequently exposed.

Accordingly, we review the literature on and assess the evidence for the health effects of wildland fire smoke exposure on both wildland firefighters and the general public, and discuss the needs for research considering both exposure scenarios. Small but measurable acute pulmonary effects have been observed in studies of occupational and community exposures. However, results from various studies including those related to wood smoke exposures from occupational or residential sources indicate possible systemic and long-term effects. Systemic inflammation, acute cardiovascular responses and reduction in birth weight (a delayed effect) are some of the other effects that have been reported.

As part of an effort to characterize health risks of wildland fire smoke exposure to wildland firefighters and the public, we review the literature to identify the components that present the highest hazard potential to both populations. We also review the literature for evidence of the health effects of wildland fire smoke and for possible underlying mechanisms of toxicity. The specific objectives of the current review are to:

Discuss the composition of wildland fire smoke. Since a primary objective of this review is the evaluation of health hazards of wildland fire smoke exposure to wildland firefighters and the general public, focus is placed on wildland fire smoke components for which good exposure estimates can be obtained (either from the exposure assessment or emission factor literature), and for which relevant exposure standards are available. Although this is a pragmatic approach, it should be noted that the application of this set of criteria excludes many components of smoke that are known to be damaging to health, but are not currently regulated e.g. poly-aromatic hydrocarbons (PAHs). This discussion also highlights specific characteristics of wildland fire smoke derived particulate matter in terms of its chemical composition and size distribution.

Identify the components presenting the highest hazard ratios to wildland firefighters and the public based primarily on reported occupational exposure or ambient air concentrations.

Review the evidence for the adverse health impacts of wildfire smoke on wildland firefighters and the public.

Discussion of the possible mechanisms for wildland fire smoke toxicity.

Identification of research needs for determining the health effects of occupational and community level wildfire smoke exposure.

Methods

Wildland fire smoke components that are considered harmful based on available occupational or general population regulatory or recommended exposure limits were identified from the literature. Concentrations or emission factor data were then abstracted from the selected papers. Emission factors were used to calculate concentrations if the emission factor for carbon monoxide or carbon dioxide was available in the same study as these are indicators of incomplete and complete combustion respectively. Molar ratios of the components relative to carbon monoxide or carbon dioxide were then obtained from the emissions factor data and multiplied by the maximum mean concentration of fire line exposure to carbon monoxide or carbon dioxide reported in the most comprehensive published wildland firefighters exposure assessment study that is available (Reinhardt & Ottmar, 2004). The calculation of concentrations from emission factors is illustrated in Equation (1).

$$C_{component} = \left[N_{component}/N_{CO\ or\ CO_2}\right] \times C_{CO\ or\ CO_2} \quad (1)$$

$C_{component}$ is the concentration of a component of interest in wildland fire smoke; $N_{component}$ is the number of moles of the component based on its reported emission factor; $N_{CO\ or\ CO_2}$ is the reported emissions factor for carbon monoxide or carbon dioxide in the same study; $C_{CO\ or\ CO_2}$ is the maximum concentration of carbon monoxide or carbon dioxide as reported by Reinhardt & Ottmar (2004). The maximum estimate or reported average and/or individual concentrations were then used to determine hazard indices based on the most stringent occupational or general population regulatory or recommended exposure limits.

The review of the health effects of wildland fire smoke exposure is conducted using both epidemiological and experimental studies. The evidence analysis protocol of the Academy of Nutrition and Dietetics was adapted for conducting the review (Academy of Nutrition and Dietetics, 2012). Three databases: PubMed, SportsDiscus and Medline were used for a comprehensive literature search for the review of health effects of wildland fire smoke exposure. The terms used for the searches are presented in Table 1. Environmental Sciences and Pollution Management (ProQuest) and ACS Symposium Series, in addition to the first three databases were used for literature searches for emission factor or concentration data for components of wildland fire smoke.

Wildland fire smoke composition

Smoke from wildland fires is a complex mixture containing hundreds of constituents/compounds in both particulate and gaseous phases, and its composition often varies spatially and temporally depending on combustion conditions (especially the relative amounts of flaming and smoldering combustion).

Table 1. Literature search results.

Objective	Databases	Search terms	Years searched	Total number of papers	Number of papers selected for review	Number of papers excluded
Wildland fire smoke component and exposure	PubMed MEDLINE Web of Knowledge SportsDiscus Environmental Sciences and Pollution Management (ProQuest) ACS Symposium Series	Wildland fire smoke (or wildfire smoke, wood-smoke, peat fire smoke forest fire smoke, woodland fire smoke, vegetative fire smoke, vegetative fire smoke) and components (or emission, concentration)	1970–2014	219	107	112
Health effects (epidemiology)	PubMed MEDLINE Web of Knowledge SportsDiscus	Health effects (or cardiovascular, respiratory, reproductive, birth weight, preterm, perinatal, stillbirth, infant death) and wood smoke (or biomass smoke, biomass combustion, vegetation smoke, wildfire)	1970–2014	344	198[a]	146
Mechanism of toxicity	PubMed MEDLINE Web of Knowledge SportsDiscus	*In vitro* (or *in vivo*, human experiment, inflammation, oxidative stress, airway, cardiovascular) and wood smoke (or biomass smoke, biomass combustion, wildfire)	1970–2014	200	70[b]	130

[a]This total contains studies of the health effects related to vegetative smoke exposure situations other than wildland fire smoke exposure which were reviewed for supporting evidence. There were a total of 52 studies of health effects of occupational and general occupational exposure to wildland fire smoke.
[b]A total of 70 papers were reviewed with 67 included in the review for evidence directly relevant to the health effects observed in epidemiology studies.

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These in turn are a function of fuel characteristics such as its chemistry, bulk density, arrangement and moisture content (Alves et al., 2010b; Burling et al., 2010; Urbanski, 2014). Such emission can have significant impact on the earth's atmosphere by significantly altering the concentrations of some of its constituents, shifting radiative forcing and negatively impacting air quality on a regional and continental scale (Akagi et al., 2013; Anttila et al., 2008; Ferek et al., 1998; Heil & Goldammer, 2001; Urbanski, 2014; Yokelson et al., 2013).

Wildland fuels have relatively consistent carbon content with dry matter carbon content ranging between 35 and 55% (Urbanski, 2014). By far, most of the carbon is released as carbon dioxide (CO_2) which together with carbon monoxide (CO) and methane (CH_4) constitutes approximately 95% of carbon released during wildland fires (Urbanski, 2014). In addition, biomass burning is considered to be the second largest global atmospheric source of both total trace gases and gas-phase non-methane organic compounds (NMOC), and is the largest global atmospheric source of primary fine carbonaceous particles (Akagi et al., 2013; Yokelson et al., 2013). According to the National Emissions Inventory (NEI) estimate from the United States Environmental Protection Agency (USEPA), wildland fires (wildfires and prescribed burns) are the largest source of $PM_{2.5}$ emissions in the US, accounting for 29% of total emissions compared to 9.2% from transportation sources (Aurell & Gullett, 2013).

The classes of compounds/components that have been observed in biomass smoke include major inorganic gases, hydrocarbons, oxygenated hydrocarbons, trace metals and particulate matter (Naeher et al., 2007). Wildland fire smoke could also contain exotic persistent organic compounds such as dioxins and furans (Black et al., 2011; Ward & Lincoln, 2006). It may also, with possibly less potential impacts, contain radon-derived daughter radionuclides and absorbed accumulations of abiotic contaminants such as polychlorinated biphenyls (PCBs) and pesticides/herbicides (Commodore et al., 2012; McMahon & Bush, 1992; Molto et al., 2010; Yoschenko et al., 2006). Since this review is health risk-driven, components with reported or estimable exposure levels and which are of concern based on comparisons with established exposure limits are the main focus of this section of the review. The exposure standards for these components are presented in Table 2, while their maximum reported study mean or individual time-weighted average (TWA) concentrations and hazard ratios based on the most stringent regulatory or recommended occupational or ambient air (acute or chronic) exposure limits are presented in Table 3. Comparisons with chronic exposure limits applicable to the general population are made with the consideration that episodic wildland fire smoke exposure is experienced rarely in most communities. In preparing Table 3, preference is given to components with fixed area ground or personal exposure measurement data. Components without such measurements but which may be of concern based on exposures estimated from emissions factor data are mentioned at the end of this section.

Based on the maximum reported mean or individual TWA fixed area ground or personal exposure measurements and relevant regulatory or recommended occupational or general

Table 2. Occupational and public health exposure limits for components of concern.

Components	Lowest occupational exposure limit[a]	Lowest short term occupational exposure limit[a]	Lowest general public daily exposure limit[a]	Lowest short term general public exposure limit[a]	Unit	Agency/organization issuing exposure limit (period or form of limit)[b,c]
Respirable particles ($PM_{3.5/4}$)	3000				$\mu g/m^3$	LOcEL – ACGIH
Fine particles ($PM_{2.5}$)			35		$\mu g/m^3$	LGPDEL – USEPA
Carbon monoxide	25	200	9	20.08	ppm	LOcEL – CalOSHA, ACGIH LSTOEL – CalOSHA, NIOSH (ceiling) LGPDEL – USEPA (8 h) LSTGPEL - CalOSHA (1 h)
Nitrogen dioxide	0.20	1.00		0.1	ppm	LOcEL – ACGIH LSTOEL – CalOSHA, NIOSH (STEL) LSTGPEL – USEPA (1 h)
Sulfur dioxide	2	0.25		0.075	ppm	LOcEL – CalOSHA, NIOSH LSTOEL – ACGIH (STEL) LSTGPEL – USEPA (1 h)
Ozone	0.1[d]	0.1	0.075	0.092	ppm	LOcEL – OSHA, CalOSHA LSTOEL – NIOSH ceiling LGPDEL – USEPA (8 h) LSTGPEL – CalEPA (1 h)
Acrolein	0.1	0.1	0.00015	0.001	ppm	LOcEL – OSHA, NIOSH LSTOEL – CalOSHA, ACGIH (ceiling) LGPDEL – USEPA (RfC – chronic inhalation) LSTGPEL – CalEPA (1-h)
Formaldehyde	0.016	0.1		0.045	ppm	LOcEL – NIOSH (as potential carcinogen) LSTOEL – NIOSH (ceiling) LSTGPEL – CalEPA (1 h)
Benzene	0.1	1	0.0028	0.0085	ppm	LOcEL – NIOSH (as potential carcinogen) LSTOEL – NIOSH (STEL) LGPDEL – CalEPA (reference exposure level) LSTGPEL – CalEPA (1 h)
Toluene	10	150	0.08	9.82	ppm	LOcEL – CalOSHA LSTOEL – CalOSHA NIOSH (STEL) LGPDEL – CalEPA (reference exposure level) LSTGPEL – CalEPA (1 h)
Xylene	100	150	0.16	5.07	Ppm	LOcEL – CalOSHA, NIOSH, ACGIH LSTOEL – CalOSHA, NIOSH, ACGIH (STEL) LGPDEL – CalEPA (reference exposure level) LSTGPEL – CalEPA (1 h)

[a]Both regulatory and recommended exposure limits are considered.

[b]LOcEL – lowest occupational exposure limit; LSTOEL – lowest short term occupational exposure limit; LGPDEL – lowest general public daily exposure limit; LSTGPEL – lowest short term general public exposure limit; OSHA – Occupational Safety and Health Administration; CalOSHA – California Occupational Safety and Health Administration; NIOSH – National Institute for Occupational Safety and Health; ACGIH – American Council of Governmental Industrial Hygienists; USEPA – United States Environmental Protection Agency; CalEPA – California Environmental Protection Agency; STEL – short term exposure limit (15 min); RfC – reference concentration.

[c]Limits are for 8-h and 24-h exposure for lowest occupational exposure limit (LOEL) and lowest general public daily exposure (LGPDEL) when periods are not specified.

[d]ACGIH OEL is as low as 0.05 and as high as 0.20 depending on workload and time.

population exposure limits for acute and chronic exposures, the components of most concern are respirable or fine particulate matter, acrolein, carbon monoxide, nitrogen dioxide, benzene and formaldehyde.

Particulate matter

Particulate matter has been identified as the best single indicator of the health hazards of smoke from biomass combustion sources (Naeher et al., 2007). The size and composition of the particles are two of the characteristics that determine its toxicity (Bølling et al., 2009). Both unimodal and bimodal size distribution have been observed for particles emitted in vegetative biomass smoke (Barregard et al., 2008; Chakrabarty et al., 2006; Iinuma et al., 2007; Keywood et al., 2000; Tesfaigzi et al., 2002). However, results indicate that the particulate matter emission is dominated by smaller particles in the accumulation mode (aerodynamic diameter of 0.1–2 μm) (Barregard et al., 2008; Chakrabarty et al., 2006; Iinuma et al., 2007; Keywood et al., 2000). In addition, greater increases in concentrations of particles in the accumulation mode have been observed in studies of ambient air

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Table 3. Hazard indices for components of concern based on occupational and general public relevant exposure limits.

Components	Type of study + description[a]	Maximum occupational TWA value reported	Maximum occupational short-term or instantaneous exposure reported	Unit	Hazard ratio (daily occupational 8 h)	Hazard ratio (occupational short-term)[b]
Occupational hazard indices based on occupational exposures or fireline measurements						
Respirable particles ($PM_{3.5/4}$) (Reinhardt & Ottmar, 2004)	Personal exposure at fireline	10.500		$\mu g/m^3$	3.50	
Carbon monoxide (Reinhardt & Ottmar, 2004; Reisen et al., 2011)	Personal measurements	58	1085[c]	ppm	2.32	5.43[d]
Nitrogen dioxide (Miranda et al., 2012)	Personal exposure	2.5	7.00[c]	ppm	12.5	1.40[d]
Formaldehyde (Reinhardt & Ottmar, 2004)	Personal measurements	0.6	1.46	ppm	38	14.6
Acrolein (De Vos et al., 2006; Reinhardt & Ottmar, 2004)	Personal exposure; measurement inside experimental firefighter mask	0.153	0.129	ppm	1.53	1.29[e]
Benzene (Reinhardt & Ottmar, 2004; Barboni et al., 2010)	Personal measurements	0.384	16.9[f]	ppm	3.84	16.9
Hazard indices based on exposures measured in areas remote from the fireline						
Components	Type of study + description[a]	Maximum general public TWA value reported	Maximum general public short-term or instantaneous exposure reported	Unit	Hazard ratio (Public daily)	Hazard ratio (public short-term)[g]
Fine particles ($PM_{2.5}$) (Wu et al., 2006)	Area measurements	90		$\mu g/m^3$	2.57	
Carbon monoxide (Tan et al., 2000)	Area measurements	17.6		ppm	1.95[h]	
Ozone (Smith et al., 1996; Tham et al., 2009)	Area measurements	0.09	0.12[i]	ppm	1.20[h]	

[a]Personal measurements are reported where available. Area measurements are given only when personal measurements are not available.
[b]Comparison is with STEL or ceiling values.
[c]Instantaneous peak measurement.
[d]Comparison is between instantaneous measurements and ceiling value.
[e]Comparison of the short-term exposure with lowest ceiling value; note that TWA is also higher than the short-term exposure.
[f]15-min averages.
[g]Comparison with limits for exposure for 1-hour period or less.
[h]Comparison is with USEPA 8-h exposure standard.
[i]Hourly averages.

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during periods of wildland fire compared to periods without such events (Alonso-Blanco et al., 2012; Cashdollar et al., 1979; Portin et al., 2012; Sillanpää et al., 2005; Verma et al., 2009). Particle formation during combustion of vegetative biomass usually starts with the nucleation mode (aerodynamic diameter < 0.1 μm) with condensation nuclei consisting of compounds such as PAHs or low volatility organic compounds (LVOCs) depending on fuel characteristics and combustion conditions (Chakrabarty et al., 2006). Submicrometer airborne particles, which as noted are relatively abundant in vegetative biomass smoke, are transported by diffusion and penetrate deeper into the lungs compared to larger particles (Araujo & Nel, 2009; Invernizzi et al., 2006; Kristensson et al., 2013; Schwarze et al., 2006). They are also deposited more efficiently in the pulmonary region compared to the more proximal regions of the lungs (Alföldy et al., 2009).

The above observations are important as they indicate that wildland fire smoke derived particulate matter is comparable, in terms of its size, to particles in traffic exhaust or smoke particles from other combustion sources. It possesses more similarities to fumes or diesel particulate matter than to comminution-derived inert dust that is regulated for the workplace. The regulatory standard for inert or nuisance dust is based on its perceived low toxicity due to low solubility (and low quartz content), and its toxicity is thought to result from injury in the terminal airways and proximal alveoli due to accumulation from high level of exposure (Cherrie et al., 2013). However, wildland fire smoke-derived particles contain water soluble components, and redox reactive metals and polar organic compounds (Alves et al., 2011; Balachandran et al., 2013; Lee et al., 2005b, 2008a; Leonard et al., 2000, 2007; Wegesser et al., 2010). It may also induce measurable acute pulmonary and systemic responses at lower exposure levels (Naeher et al., 2007).

Particulate matter emitted from the combustion of vegetative biomass is mostly carbonaceous and is typically composed of at least 50% organic carbon by weight

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(Alves et al., 2010a,b; Chen et al., 2007a; Fine et al., 2001, 2002a,b, 2004a,b; Robinson et al., 2011; Schmidl et al., 2008). Elemental (the inorganic form of) carbon may constitute less than 10% of the particulate matter, but could sometimes be more substantial depending on the specie or type of vegetation (Alves et al., 2010a,b; Chen et al., 2007a; Fine et al., 2001, 2002a,b, 2004a,b; Robinson et al., 2011; Schmidl et al., 2008). Wildland fire smoke contains black carbon which is the strong light absorbing component of elemental carbon and is a climate forcing agent (Chen et al., 2007a; Ramanathan & Carmichael, 2008). Exposure to black carbon has also been associated with effects on cardiovascular and respiratory health (Jansen et al., 2005; Nichols et al., 2013).

Levoglucosan, which is a sugar anhydride and a pyrolytic product of cellulose, is the most abundant organic compound in wildland fire associated smoke particulate matter (Lee et al., 2005b). Other sugar anhydrides, aliphatic and oxygenated aliphatic hydrocarbons, sterols, methoxyphenols, which are pyrolytic products of lignin, PAHs and oxygenated PAHs, are also present (Fine et al., 2001, 2002ab, 2004a,b).

Although, the currently existing occupational standard for particulate matter may be inadequate for particles in wildland fire smoke as previously stated, ambient air concentration in the immediate vicinity of fires (12.5 mg/m^3) (Alves et al., 2010a,b) and personal wildland firefighter exposure (10.5 mg/m^3) (Reinhardt & Ottmar, 2004) that exceed the lowest occupational exposure limit (3 mg/m^3) recommended by the American Conference of Governmental Industrial Hygienists (ACGIH) have been reported. These levels also exceed the Occupational Safety and Health Administration's (OSHA) regulatory standard with a higher permissible exposure limit of 5 mg/m^3. These levels are of course well above the current 24-h National Ambient Air Quality Standard (NAAQS) for ambient air (35 μg/m^3). Although typically a lot lower than wildland firefighter exposure, ambient air concentrations at least two to three times higher than the NAAQS are not uncommon in urban areas downwind of wildland fire. These levels have been associated with various adverse health outcomes (Delfino et al., 2008).

Carbon monoxide

Carbon monoxide, along with particulate matter, has the most comprehensive exposure data from personal monitoring and area/ground measurements in the literature among the air pollutants emitted during wildland fires. Published study average TWA personal occupational exposures at wildfires or prescribed burns are lower than the lowest OEL occupational exposure limit (OEL) of 25 ppm (ACGIH) indicating that exposures of most wildland firefighting personnel are relatively low (Adetona et al., 2013a; Dunn et al., 2013; Miranda et al., 2012; Reinhardt & Ottmar, 2004; Reisen & Brown, 2009). Nonetheless, the maximum TWA personal occupational exposures in the literature exceeded 50 ppm (Reinhardt & Ottmar, 2004), the regulatory standard (permissible exposure limit – PEL) issued by OSHA. Similarly, the reported maximum instantaneous peak personal exposure of 1085 ppm was about 5.5 times the NIOSH and California OSHA recommended ceiling value of 200 ppm (Reinhardt & Ottmar, 2004). Exposure of the public during wild fire events is usually much lower than the published occupational exposures due to the dilution of carbon monoxide in air during transport from the fire to public receptor locations.

The toxicity of carbon monoxide is partly due to its ability to bind hemoglobin more strongly than oxygen (~240 times) causing the formation of carboxyhemoglobin (COHb) (Raub, 1999). This results in tissue hypoxia since the formation of COHb reduces the oxygen carrying capacity of the blood. COHb levels beginning at 5% saturation in the blood results in decreased work capacity in healthy young adults, while levels below 5% but greater than 2% have been associated with cardiovascular effects in persons with pre-existing cardiovascular diseases (Raub, 1999). Higher COHb concentrations could result in headache, dizziness, weakness, disorientation and impair decision making (Raub, 1999; Raub et al., 2000). The elimination half-life of COHb is 4–5 h without any intervention, and treatment of carbon monoxide poisoning involves speeding up the elimination rate (Annane et al., 2011; Guzman, 2012; Quinn et al., 2009; Wolf et al., 2008).

Although COHb levels measured in wildland firefighters are mostly below 5% (Dunn et al., 2009; Gaskill et al., 2010; Miranda et al., 2012), working in heavy smoke or for longer periods could contribute towards elevated COHb concentrations due to its potential to accumulate in the blood (Gaskill et al., 2010). Consequently, wildland firefighters and other persons potentially could experience elevated COHb levels when they are in close proximity to wildland fires. However, it should be noted that other sources of carbon monoxide such as pumps, generators and gasoline trucks could significantly contribute to the exposures of firefighters working at wildland fires (Gaskill et al., 2010).

Respiratory irritants: acrolein and formaldehyde

Both acrolein and formaldehyde are respiratory irritants at low concentrations. Exposure to these pollutants could result in respiratory symptoms, and nasal and respiratory tract irritation (Bein & Leikauf, 2011; Lang et al., 2008). Acrolein is a more potent irritant (Roemer et al., 1993), and exposure at higher concentrations could result in lung injury (Bein & Leikauf, 2011). Formaldehyde is also classified as a probable human carcinogen by the USEPA.

Olfactory detection of formaldehyde occurs between 0.04 and 0.40 ppm (Lang et al., 2008). Most of the published average occupational TWA exposures are below this range, and all maximum occupational TWA exposures reported in identified studies are below the OSHA PEL of 0.75 ppm (De Vos et al., 2009; Reinhardt & Ottmar, 2004; Reisen & Brown, 2009; Reisen et al., 2011). However, some of the average occupational TWA exposures reported for wildland firefighters in the US and Australia in these studies exceed the lowest OEL of 0.016 ppm (National Institute for Occupational Safety and Health [NIOSH] recommended exposure limit) which is based on the carcinogenic effect of formaldehyde. Exceedance of this OEL was by up to 3700% for the highest reported average TWA. The maximum short-term exposure in the literature (1.46 ppm) was reported among wildland firefighters at prescribed burns in the US (Reinhardt &

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Ottmar, 2004). This is an order of magnitude higher than the NIOSH recommended ceiling of 0.1 ppm.

Both average and maximum occupational TWAs reported for acrolein in the literature were all below the lowest OEL of 0.10 ppm (OSHA) and the recommended ceiling value of 0.1 ppm (California OSHA and ACGIH) except for a maximum TWA of 0.15 ppm measured in the respirator of a wildland firefighter working at a bushfire in Australia (De Vos et al., 2006). This TWA was also higher than the maximum reported short-term exposure of 0.129 ppm observed among wildland firefighters conducting prescribed burns in the US (Reinhardt & Ottmar, 2004). Additive effects from multiple irritants should be considered, and risk assessment of occupational wildland firefighters to wildland fire smoke indicates that their concurrent exposures to particulate matter, acrolein and formaldehyde at wildland fires may be of concern (Reinhardt & Ottmar, 2004). It is possible that cancer risk from formaldehyde exposure may be slightly increased above the acceptable 10^{-5} level for occupational exposure when the average duration of exposure at wildland fires, the frequency of exposure and career length of the wildland firefighter are considered (Booze et al., 2004).

Benzene

Five studies of the assessment of benzene exposure due to wildland fire from ground measurements or personal monitoring were identified (Barboni et al., 2010; Barboni & Chiaramonti, 2010; Evtyugina et al., 2013; Reinhardt & Ottmar, 2004; Reisen & Brown, 2009). Although repeated exposure to low levels of benzene may result in adverse non-cancer hematological, neurological and immunological effects (Galbraith et al., 2010; Gist & Burg, 1997), the average TWA concentrations reported are well below estimated or measured levels for which these adverse effects were observed in various studies. However, a maximum individual TWA personal exposure of 0.384 ppm observed in one study was 3.84 times the NIOSH recommended OEL which is based on carcinogenic effects (Reinhardt & Ottmar, 2004). In addition, a maximum 15-min fixed area measurement of 16.9 ppm reported in a study in France was 16.9 times the NIOSH recommended short-term exposure limit (Barboni et al., 2010). However, it is worth noting that the 15-min measurements in the France study may not be representative of typical occupational exposures since the measurements were conducted by firefighting personnel in very close proximity (1–10 m) to the fire line. It is possible that cancer risk from benzene exposure may contribute to a total risk above the acceptable 10^{-5} level for occupational exposure when the average duration of exposure at wildland fires, the frequency of exposure and career length of the wildland firefighter are considered (Booze et al., 2004).

Nitrogen dioxide

Nitrogen dioxide (NO_2) induces various pulmonary responses including decrement in lung function, airway hyper-responsiveness and bronchoconstriction (WHO, 2006). In addition, ambient air concentration of NO_2 has been associated with respiratory and cardiovascular events as indicated by increases in mortality and physician or emergency room visits due to morbidity (Poloniecki et al., 1997; Samoli et al., 2006). In general, susceptible individuals with pre-existing diseases such as asthma and chronic obstructive disease are more vulnerable to exposure to NO_2 (WHO, 2006). These adverse responses seem to be solely dependent on concentration more than the duration or total dose of exposure (WHO, 2006). Therefore, the short-term exposure may be the more relevant metric for NO_2 during wildland fires. The maximum personal TWA exposure and the maximum peak area measurement reported for nitrogen dioxide suggest that it may be of concern during wildland fires (Miranda et al., 2012). The maximum personal TWA exposure reported for nitrogen dioxide (2.5 ppm) also exceeded the ACGIH and California OSHA recommended ceiling of 1 ppm for the pollutant.

Ozone and others

Ozone is a secondary air pollutant formed through a series of reactions involving the interaction of light and other air pollutants including nitrogen dioxides and volatile organic compounds. In addition to being present in background ambient air, some of these primary air pollutants, as stated earlier in this section, are emitted in wildland fire smoke (Evtyugina et al., 2013; Simpson et al., 2011). Consequently, ozone could be a pollution problem in areas downwind from wildland fires. Eight studies reporting on the concentration of ozone in ambient air impacted by wildland fire smoke were identified (Evans et al., 1977; Hu et al., 2008; Phuleria et al., 2005; Portin et al., 2012; Smith et al., 1996; Tan et al., 2000; Tham et al., 2009; Wang et al., 2012). The maximum mean fixed area 24-h (90 ppb) and 1-h (120 ppb) ambient air concentrations of ozone under such conditions exceeded the USEPA 8-h NAAQS of 75 ppb by 20 and 60%, respectively (Smith et al., 1996; Tham et al., 2009). The recommended NIOSH ceiling of 0.1 ppm was also exceeded by the maximum mean 1-h concentration by 20% (Smith et al., 1996). Elevated concentration of ozone in ambient air is associated with acute effects including decline in lung function, enhancement of airway responsiveness, autonomic cardiovascular effects and morbidity and mortality related especially to respiratory illnesses (WHO, 2006). Some of these effects are observed in association with ambient air concentrations below the maximum concentrations referenced above (WHO, 2006).

Concentrations of 1,3-butadiene and hydrogen cyanide estimated from available emissions factor data and compared to USEPA reference concentrations for chronic inhalation exposure suggest that both could be pollutants of concern for the general public if exposure is experienced a few times a year (Burling et al., 2010; Urbanski, 2014; Yokelson et al., 2013).

The health impact of wildland fire smoke exposure

Virtually all of the health studies of wildland fire smoke have focused on the more immediate effects of acute exposures on the general public. Furthermore, a very limited number of health studies have been conducted among wildland firefighters, and most of the investigation has focused on

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acute physiological changes in response to exposures during the work shift at wildfires or prescribed burns. Therefore, little is known about the effects of more chronic cumulative exposures experienced by wildland firefighters. The primary information discussed in this section is from studies investigating the effects of exposures directly related to wildland/vegetation fire events. Health studies of related ambient or household air pollution are also discussed.

Health effects of exposure directly related to wildland fire smoke in the general public

The study of the effects of wildland fire smoke exposure is complicated by the sporadic unpredictable nature of wildfires. Consequently, most of the knowledge about the health impacts of exposures directly related to wildland fire smoke on the general public has come from retrospectively conducted ecological time series studies: 25 of the 36 (69%) of the articles that were identified were ecological studies with only population level measures for exposure and outcomes. It should be noted that the burning of agricultural residues or fields was the source of exposure in eight of the studies that were identified.

Acute cardiovascular and/or respiratory impacts with lagged effects mostly restricted to within 6 days of exposure were the focus of most (35/36) of the studies that were identified. Furthermore, outcomes in many of the studies were defined as the incidences of mortality, hospital admission, physician or emergency room visits due to events or symptoms resulting from diseases such as chronic obstructive pulmonary disease (COPD), asthma and cardiovascular episodes such as stroke, heart failure and cardiac dysrhythmia. Accordingly, health effects that have been examined have largely been those most relevant to people who are susceptible due to pre-existing diseases. Therefore, very little is known about the effects of wildland fire smoke exposure in individuals who are otherwise healthy. Knowledge is also lacking regarding the delayed effects of exposure over the longer term. The summary of all identified studies involving the general public are presented in Table 4.

Respiratory effects of wildland fire smoke in the general public

Naeher et al. (2007), in a major comprehensive review of the health effects of vegetative biomass smoke, concluded that exposure to smoke from wildland fires or burning of agricultural fields/residues resulted in respiratory symptoms and illnesses. They noted that the results were consistent across studies in different locations except for those that were conducted in Australia. Studies that have been published since the Naeher et al. comprehensive review in 2007, including six that were conducted in Australia, have reported results positive for the respiratory effects of wildland fire smoke exposure in the general public (Analitis et al., 2011; Crabbe, 2012; Delfino et al., 2008; Epton et al., 2008; Hanigan et al., 2008; Henderson et al., 2011; Johnston et al., 2007; Martin et al., 2013; Mirabelli et al., 2009; Morgan et al., 2010; Rappold et al., 2011; Tham et al., 2009).

Occurrence of wildfires (forest fires) in Athens, Greece, was associated with increases in mortality due to respiratory illnesses (Analitis et al., 2011). An apparent dose–response relationship was observed with more deaths occurring with increasing size of the forest area burned. While small fires (defined as fires burning 10 000–1 000 000 m^2) were not associated with increases in respiratory mortality, medium (defined as fires burning 1 000 000–30 000 000 m^2) and large fires (defined as fires burning >30 000 000 m^2) were associated with 16.2% (95% CLs: 1.3, 33.4%) and 92.0% (47.5, 150.0%) increases in respiratory mortality respectively. Sastry (2002) had similarly observed a significant doubling of respiratory mortality in Kuching, Malaysia, in association with reduced visibility (<0.91 km), which was used as a surrogate of ambient air pollution, during the 1997 Southeast Asia forest fire-related haze episode. An insignificant increase was observed in Kuala Lumpur, Malaysia during the same period (Sastry, 2002). Increase in respiratory mortality was not observed in association with ambient air PM_{10} concentrations on high pollution days that were heavily influenced by bushfires in Sydney, Australia (Morgan et al., 2010).

The adverse health effects of wildland fire smoke exposure in the general public have been most consistently observed as increases in hospital admissions, physician or emergency room visits due to respiratory illnesses. Effects of forest fires were observed among a cohort of registered individuals on the Medical Service Plan in the province of British Columbia, Canada (Henderson et al., 2011). While no relationship was observed between either physician visits or hospital admissions due to all respiratory diseases and the occurrence of fire on the same day, significant increases were observed for both effects (odds ratio [OR]: 1.02 and 1.05, respectively) in association with an increase of 10 $\mu g/m^3$ in the same-day 24-h average ambient concentration of PM_{10} recorded at fixed monitoring station during the forest fire season. Significant increases in hospital admissions due to all respiratory diseases (OR: 1.11) were also observed in association with an increase of 60 $\mu g/m^3$ in the same-day 24-h average ambient concentration of PM_{10} derived from the integration of satellite data with the CALPUFF smoke dispersion model in the same study (Henderson et al., 2011).

In a study of the effects of the 2003 southern California wildfires, the 10-day wildfire period seemed to be protective against hospital admissions for all respiratory diseases (relative risk [RR]: 0.903) when compared to the 3-week period before the wildfires in a model adjusting for the concentration of ambient air $PM_{2.5}$ (Delfino et al., 2008). Conversely, the risk for hospital admissions increased during the 2-week period immediately following the wildfires (RR: 1.173) indicating some delayed effects, although, the authors could not rule out a seasonal effect for the post-wildfire results (Delfino et al., 2008). It should be noted that results were in similar directions when the same comparisons were made in a model without adjustment for $PM_{2.5}$, but the difference in the risk of hospital admission for all respiratory diseases between the wildfire and pre-wildfire periods was not significant in this model. In addition to testing the effect of the period (relative to the wildfire) on hospital admissions, the authors tested the effect of the interaction term between the period and ambient air $PM_{2.5}$ concentration. Although, the positive exposure ($PM_{2.5}$)–response relationship was not statistically different between the periods, it was stronger

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Table 4. Summary of review of epidemiological studies of the general public.

Citation (Author.Year.Journal)	Location	Biomass type	Study design	Subject description	Sample size	Exposure measure	Health end-point(s)	Major confounders (apart from adjustment for trend and seasonal components in trend analyses)	Result summary
Holstius et al. (2012). Environ Health Perspect	Southern California, USA	Forest fire	Cohort	Singleton births	886 034 (747 590 births from pregnancy before or after wildfire events, 60 270 births from pregnancy with wildfire occurs during the first trimester, 39 435 – second trimester, 38 739 – third trimester)	Exposure versus non-exposure periods	Birth weight	Age, educational attainment, parity, race/ethnicity, infant's gender, gestational age	Mean birth weight was 7.0 g lower [95% CI: −11.8, −2.2] when the wildfire occurred during the third trimester, 9.7 g lower when it occurred during the second trimester (95% CI: −14.5, −4.8), and 3.3 g lower when it occurred during the first trimester (95% CI: −7.2, 0.6) compared with pregnancies before and after the wildfires
Torigoe et al. (2000). Pediatr Int	Niigata, Japan	Agricultural fire – rice straw	Cohort	Boys and girls with the average age of 7.3 years	438 boys and 262 girls	Burn season versus non-burn season (PM_{10} also measured but not used for associations with health end-points)	Asthma attack	The weather and pressure patterns, temperature, wind direction and velocity, daylight hours and precipitation	There was a significant increase in the number of children with asthma attack visiting emergency room among the exposed group ($p < 0.001$)
Jalaludin et al. (2000). Aust NZ J Public Health	Sydney, Australia	Bush fire	Cohort	Children with a history of wheeze	32	PM_{10} (O_3, NO_2 also measured but not used for associations with health end points)	Lung function (peak expiratory flow rate)	Asthma medications, time trend, mean temperature, mean humidity, number of hours spent outdoors, total pollen and alternaria counts	Overall, no significant association was observed between mean PM_{10} and peak expiratory flow rate ($\rho = -0.009$, $p = 0.86$). However, significant negative association between peak expiratory flow rate and PM_{10} $\rho = -0.1029$, $p = 0.03$) was observed among children without bronchial hyperreactivity. Bush fire period was not significantly associated with peak expiratory flow rate
Henderson et al. (2011). Environ Health Perspec	British Columbia, Canada	Forest fire	Cohort	Residents in the study area whose addresses were precisely geocoded	281,711	PM_{10}	Respiratory and cardiovascular (physician visit and hospital admission)	Effect modification by age, sex, and SES were examined	There were increases in odds for a 30 $\mu g/m^3$ increase in TEOM-based PM_{10} were for all respiratory physician visits – 1.05 (95% CI, 1.03–1.06); for asthma-specific visits – 1.16 (95% CI, 1.09–1.23); and for

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Table 4. Continued

Citation (Author.Year.Journal)	Location	Biomass type	Study design	Subject description	Sample size	Exposure measure	Health end-point(s)	Major confounders (apart from adjustment for trend and seasonal components in trend analyses)	Result summary
									respiratory hospital admissions – 1.15 (95% CI, 1.00–1.29). There were no associations with cardiovascular outcomes among the whole population in the study
Mott et al. (2002). West J Med	Hoopa, California, USA	Forest fire	Retrospective cohort	American Indians (92 had pre-existing cardiopulmonary conditions)	289	Exposure versus non-exposure periods	Respiratory illnesses (medical visits)	None listed or considered in analysis	Increase in medical visits for respiratory illnesses from 417 to 634 visits (52%) was observed during the weeks of the forest fire compared to the previous year, and those with preexisting cardiopulmonary conditions reported more symptoms before, during and after the smoke episode
Johnston et al. (2006). Int J Environ Health Res	Darwin, Australia	Bush fire	Cohort (panel study)	Adult and children	251	PM_{10} and $PM_{2.5}$	Acute respiratory symptoms on individuals with asthma	Minimum daily air temperature, relative humidity, pollen and spore counts, the weekly rate of consultations to general practitioners for influenza-like illness, temporal autocorrelation of outcomes, weekends and holiday periods	A rise of 10 $\mu g/m^3$ in PM10 ranged was significantly associated with onset of asthma symptoms (OR = 1.240, CI 1.106–1.39), commencing oral steroid medication (OR = 1.540, CI 1.01–2.34), the mean daily symptom count (OR = 1.020, CI 1.001–1.031) and the mean daily dose of reliever medication (OR = 1.020, CI 1.00–1.030) and similar results were observed for $PM_{2.5}$.More severe outcomes of asthma attacks, increased health care attendances or missed school/work days, were not associated with exposure measures.

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Sutherland et al. (2005). J Allerg Clin Immunol	Denver, Colorado, USA	Forest fire	Cohort (panel study)	Denver residents with COPD	21	Spike days indicated by elevated concentrations of $PM_{2.5}$ (PM_{10} and CO were also measured)	Respiratory symptoms in adult subjects with COPD	None listed or considered in analysis	Symptom scores were significantly elevated on spike days versus non-spike days (p = .0002). The symptom score on spike days was 21.5 (IQR = 3.0), and on non-spike days was 20.0 (IQR = 1.0)
Kunzli et al. (2006). Am J Respir Crit Care Med	Southern California, USA	Forest fire	Cross-sectional	High-school students	6424 (n = 873; 17–18 years old and n = 5551; age, 6–7 years old elementary-school children)	Number of days of fire smoke smell indoors	Respiratory symptoms	Sex, ethnicity, educational level of parents, asthma status before the fire (physician-diagnosed asthma) and cohort (high-school versus elementary-school cohort)	Various symptoms were 2–5.5 times more likely to occur among those with 6 or more days of fire smell indoors: general, sleep-disturbing and speech-limiting wheezing occurred 3.5, 4.9 and 5.5 times more often respectively among those with 6 or more days of fire smell indoors compared with those reporting no day of fire smoke smell indoors. Asthma attacks also significantly increased 63% among this group. The trend across the different levels of fire smell duration (0, 1–5 and >5 days) was highly significant for all outcomes except for asthma attacks (p = 0.12). There was significant difference between the communities with the highest and lowest PM_{10} levels (210 and 30 μg/m^3, respectively) for dry coughs at various times during the day, irritated eyes, watery/itchy eyes and sneezing/runny/blocked nose.
Long et al. (1998). Chest	Winnipeg, Canada	Agricultural residue	Cross-sectional	Adults (35 to 64 years old)	428	Exposure versus non-exposure periods (PM_{10}, CO, NO_2, and VOC were used but not measured for associations with health endpoints)	Respiratory symptoms	Age, gender, smoking status	Although 37% of subjects reported that they were not bothered by smoke at all, 42% of subjects reported that at least one symptom (cough, wheezing, chest tightness, shortness of breath) developed or became

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Table 4. Continued

Citation (Author.Year.Journal)	Location	Biomass type	Study design	Subject description	Sample size	Exposure measure	Health end-point(s)	Major confounders (apart from adjustment for trend and seasonal components in trend analyses)	Result summary
									worse due to the air pollution episode and 20% reported that they had breathing trouble: females compared to males and ex-smokers compared to smokers were more likely to be affected and subjects with asthma and chronic bronchitis were also more likely to be affected
Analitis et al. (2011). Occup Environ Med	Athens, Greece	Forest fire	Ecological time series	General population	Population size was not mentioned	Exposure versus non-exposure and size of burns	Non-accidental mortality including those due to respiratory and cardiovascular illnesses	Time trend and meteorological variables	No mortality effects were observed for small fires (10 000–1 000 000 m^2). Medium sized fires (1 000 000–30 000 000 m^2) were associated with an increase of 4.9% (95% CI 0.3–9.6%) in the daily mortality, 6.0% (95% CI 0.3–12.6%) in cardiovascular mortality and 16.2% (95% CI 1.3–33.4%) in respiratory mortality. Cardiovascular effects are larger in those aged <75 years, while respiratory effects are larger in older people. Large fires (>30 000 000 m^2) were associated with: 49.7% (95% CI 37.2–63.4%) increase in daily mortality, 60.6% (95% CI 43.1–80.3%) in cardiovascular mortality and 92.0% (95% CI 47.5–150.0%) in respiratory mortality. Respiratory and not cardiovascular mortality were more pronounced in persons >75 years old.

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Jacobs et al. (1997). Environ Health Perspec	Butte County. California. USA	Agricultural residue – rice straw	Ecological time series	General population	Population size was not mentioned	Burn acreage	Asthma hospitalization	Maximum daily temperature, seasonal factors, and yearly population	Burn acreage showed a small but statistically significant elevation of risk for hospitalization per acre of rice burned (RR = 1.0001; 95% CI, 1.00004-1.0002), after adjusting for confounders. An apparent dose-response was observed with days with the greatest acreage burned (>499 acre) having the largest risk of hospitalization (RR = 11.23; CI, 1.09-1.39), while days with moderate burning (between 100 and 499 acre) had a slightly lower risk of admission (RR = 1.2; CI, 1.05-1.37).
Johnston et al. (2002). Med J Aust	Darwin, Australia	Bush fire	Ecological time series	General population	Population size was not mentioned	PM_{10}	Asthma presentations (ER visits)	Weekly rates of influenza, day of week (weekend or weekday)	A 10 $\mu g/m^3$ increase in PM_{10} was associated with increase in asthma presentations even after adjusting for confounders (adjusted rate ratio, 1.20; 95% CI, 1.09–1.34; $p < 0.001$). The strongest effect was seen on days when the PM_{10} was above 40 $\mu g/m^3$ (adjusted rate ratio, 2.39; 95% CI, 1.46–3.90), compared with days when PM_{10} levels were less than 10 $\mu g/m^3$
Moore et al. (2006). Can J Public Health	Kelowna and Kamloops, British Columbia, Canada	Forest fire	Ecological time series	General population	Kelowna – average of 146 199 and Kamloops – average of 100 548 during study period	Exposure period versus non-exposure period ($PM_{2.5}$ and PM_{10} were also measured but not used for associations with health end-point)	Respiratory and cardiovascular (physician visit)	None listed and not evident that any were considered in analysis	In the Kelowna region PM level was more elevated, increases in physician visits due to respiratory illnesses of between 46 and 78% above 10-year mean rates were observed for three weeks during the forest fire period but similar effects were not observed in Kamloops. Effects on visits for cardiovascular diseases or mental disorders were not seen in either of the two communities.

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Table 4. Continued

Citation (Author.Year.Journal)	Location	Biomass type	Study design	Subject description	Sample size	Exposure measure	Health end-point(s)	Major confounders (apart from adjustment for trend and seasonal components in trend analyses)	Result summary
Rappold et al. (2011). Environ Health Perspect	Eastern North Carolina, USA	Peat forest fire	Ecological time series	General population	Population size was not mentioned	Exposed versus unexposed counties (aerial optical depth as a proxy for smoke pollution was used to determine exposed counties)	Respiratory and cardiovascular (ER visits)	None listed and not evident that any were considered in analysis	Significant increases in cumulative RR for ER visits for asthma [1.65 (95% confidence interval, 1.25–2.1)], chronic obstructive pulmonary disease [1.73 (1.06–2.83)] and pneumonia and acute bronchitis [1.59 (1.07–2.34)] were observed. ER visits associated with cardiopulmonary symptoms [1.23 (1.06–1.43)] and heart failure [1.37 (1.01–1.85)] were also significantly increased in exposed counties.
Vedal & Dutton (2006). Environ Res	Denver, Colorado, USA	Forest fire	Ecological time series	General population	>2 000 000	Exposure versus no exposure periods (PM_{10} and $PM_{2.5}$ were measured but not used for associations with health end-points)	Mortality from respiratory and cardiovascular illnesses	None listed or considered in analysis	Abrupt PM peaks associated with fires were not associated with differential increase in cardiorespiratory mortality between exposed and control counties.
Hanigan et al. (2008). Environ Health	Darwin, Australia	Bush fire	Ecological time series	General population	Population size was not mentioned	PM_{10}	Respiratory and cardiovascular illnesses (hospital admission)	Daily temperature and humidity	An increase of 10 $\mu g/m^3$ in same-day estimated ambient PM_{10} was associated with a non-significant 4.81% (95%CI: −1.04%, 11.01%) increase in total respiratory admissions, but a statistically different association was found between PM_{10} and admissions three days later for respiratory infections of indigenous people (15.02%; 95%CI: 3.73%, 27.54%) than for non-indigenous people (0.67%; 95%CI: −7.55%, 9.61%) (3). Null associations were observed for cardiovascular effects with ambient PM_{10} having positive (non-

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									significant) associations with cardiovascular admissions of indigenous people two and three days later.
Morgan et al. (2010). Epidemiology	Sydney, Australia	Bush fire	Ecological time series	General population	Population size was not mentioned	PM_{10}	Respiratory and cardiovascular illnesses (hospital admission and mortality)	Temperature, humidity, day of week, flu epidemic	A 10 $\mu g/m^3$ increase in bushfire PM_{10} was associated with same day increase of 1.24% (95% CI: 0.22–2.27%) in all respiratory disease admissions, a 3.80% (1.40–6.26%) increase in chronic obstructive pulmonary disease admissions 2 days later, and a same day 5.02% (1.77–8.37%) increase in adult asthma admissions. Bushfire PM_{10} was associated with a large increase in same day admissions for adult asthma (5.02, 1.77–8.37) and a moderate decrease in childhood asthma admissions 3 days later (3.10, 6.18–0.07) . Bushfire PM_{10} was not associated with all cardiovascular disease admissions, cardiac admissions or ischemic heart disease admissions.
Tham et al. (2009). Respirology	Victoria, Australia	Bush fire	Ecological time series	General population	Population size was not mentioned	PM_{10} and O_3	Respiratory illnesses (ER visits)	Day-of-the-week and trend effects (meteorological data)	After adjusting for confounders, the strongest associations were observed between PM_{10} and daily respiratory emergency department attendances in Melbourne (RR = 1.018, 95% CI: 1.004–1.033, p = 0.01) (3). Non-significant positive associations were observed for all respiratory outcomes with API and ozone after adjustment.

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Table 4. Continued

Citation (Author.Year.Journal)	Location	Biomass type	Study design	Subject description	Sample size	Exposure measure	Health end-point(s)	Major confounders (apart from adjustment for trend and seasonal components in trend analyses)	Result summary
Chen et al. (2006). Int J Environ Health Res	Brisbane, Australia	Bush fire	Ecological time series	General population	Population size was not mentioned	PM_{10}	Respiratory illnesses (hospital admissions)	Daily average maximum and minimum temperatures, relative humidity (at 9 am), rainfall and wind direction (at 3 pm), seasonality, day of the week, holidays, long-term trends and influenza	The relative risk for respiratory hospital admissions increased by 9 and 11% for the medium level of ambient PM_{10} concentration (15–20 $\mu g/m^3$) and by 19 and 13% for higher level of ambient PM_{10} concentration (>20 $\mu g/m^3$) during bushfire and non-bushfire periods, respectively compared with admissions when there was lower level of PM_{10} (<15 $\mu g/m^3$).
Mott et al. (2005). Int J Hyg Environ Health	Kuching, Malaysia	Forest fire	Ecological time series	General population	Population size was not mentioned	Exposure versus no exposure	Respiratory and cardiovascular illnesses (hospital admission)	None listed or considered in analysis	Statistically significant fire-related increases were observed for respiratory hospitalizations across all ages (more so for 40–64 year old adults), specifically related to COPD and asthma; no associations were observed for cardiorespiratory or circulatory diseases. The survival analyses indicated that persons over age 65 years with previous hospital admissions for any cause, any cardiorespiratory disease, any respiratory disease or COPD, were significantly more likely to be rehospitalized during the follow-up period in 1997 than during the follow-up periods in the pre-fire years of 1995 or 1996
Arbex et al. (2010). J Epidemiol Community Health	Araraquara, Brazil	Agricultural burn – sugar cane plantations	Ecological time series	General population	~200 000 inhabitants	TSP	Hypertension (hospital admission)	Temperature, day of the week, humidity	Increase in TSP concentration was associated with a low but statistically significant increase in the number of

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									hypertension-related hospital admissions (0.233, $p<0.001$) with association being significant only during burn period. Increase in hypertension hospital admission associated with a 10 $\mu g/m^3$ rise in 3-day average TSP lagged 1 day was 30% higher during burn periods compared to non-burn periods
Arbex et al. (2007). J Epidemiol Community Health	Araraquara, Brazil	Agricultural burn – sugar cane plantations	Ecological time series	General population	192 000 inhabitants	TSP	Asthma (hospital admission)	Temperature, day of the week, humidity	A 10 $\mu g/m^3$ increase in 5-day moving average TSP was associated with an increase of 11.6% (95% CI 5.4–17.7) in asthma hospital admission. No threshold effect seemed apparent.
Crabbe. (2012). Environ Geochem Health	Darwin, Australia	Bush fire	Ecological time series	General population	Population size was not mentioned	PM10, coarse particulate matter, fine particulate matter, carbon black	Respiratory and cardiovascular illnesses (hospital admission)	Meteorological data, holiday, day of week, periods of influenza epidemics	Ambient fine particulate matter, black carbon and PM_{10} concentrations lagged 1 day were associated with cardiovascular hospitalization, while ambient fine particulate matter, black carbon lagged 1 day were associated with respiratory hospitalization.
Johnston et al. (2007). BMC Public Health	Darwin, Australia	Bush fire	Case-crossover	General population	110 000 total residents: 11 500 indigenous persons	PM_{10}	Respiratory and cardiovascular illnesses (hospital admission)	Weekly influenza rate, days with rainfall >5 mm, same day mean temperature and humidity, the mean temperature and humidity of the previous 3 days and public holidays	There was a positive relationship between PM_{10} and admissions for all respiratory conditions (OR 1.08 95%CI 0.98–1.18) with a larger magnitude in the Indigenous subpopulation (OR1.17 95% CI 0.98–1.40). There was a positive association with ischemic heart disease in Indigenous people, greatest at a lag of 3 days (OR 1.71 95%CI 1.14–2.55), but no relationship between PM10 and

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Table 4. Continued

Citation (Author.Year.Journal)	Location	Biomass type	Study design	Subject description	Sample size	Exposure measure	Health end-point(s)	Major confounders (apart from adjustment for trend and seasonal components in trend analyses)	Result summary
Martin et al. (2013). Aust NZ J Public Health	Sydney, Newcastle and Wollongong, Australia	Bush fire	Ecological time series	General population	Sydney (3 862 000 residents), Newcastle (406 000 residents); Wollongong (278 000 residents)	Exposure versus no exposure periods (PM_{10}, $PM_{2.5}$ were measured but not used for associations with health end-points	Respiratory and cardiovascular illnesses (hospital admission)	None listed or considered in analysis	cardiovascular admissions overall. Bush fire events in Sydney were associated with a 6% (OR = 1.06, 95%CI = 1.02–1.09) same day increase in respiratory hospital admissions, same day increase of 13% (OR = 1.13, 95%CI = 1.05–1.22) in chronic obstructive pulmonary disease admissions and 12% (OR = 1.12, 95%CI = 1.05–1.19) in asthma admissions. Events were also associated with increased admissions for respiratory conditions in Newcastle and Wollongong. There were no associations with cardiovascular illnesses.
Sastry (2002). Demography	Malaysia	Forest fire	Ecological time series	General population	Population size was not mentioned	Exposure versus non exposure periods (determined by dichotomized variables - PM_{10} and visibility)	Mortality from respiratory and cardiovascular illnesses	weather factors and seasonal terms	In Kuala Lumpur, null associations were observed for all types of mortality; but significant relative risks of 1.218, 1.225 and 1.208 for total, nontraumatic and other mortality were observed with respect to visibility measure, while association was significant for total, nontraumatic and cardiovascular mortality among 65-74 year olds; In Kuching: significant relative risk for of 2.049 was observed only for respiratory mortality in overall population, but significant associations with total, nontraumatic and cardiovascular mortality was

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									observed among >75 year olds
Churches & Corbett. (1991). NSW Public Health Bull	Australia	Bush fire	Ecological time series	General population	Population size was not mentioned	Exposure versus non-exposure periods (PM, CO and other pollutants measured but not used in analyses)	Asthma (hospital admission)	None listed or considered in analysis	There were no differences between asthma hospital attendances between days when there were bushfires and on days when there were none
Duclos et al. (1990). Arch Environ Health	USA	Forest fire	Ecological time series	General population	Population size was not mentioned	Exposure versus non-exposure periods	Respiratory illnesses (ER visits)	None listed or considered in analysis	Wildfire event was associated with observed/expected ratio of 1.4 and 1.3 for emergency room visits for asthma and COPD, respectively. There was also an increase in emergency room visit for laryngitis and sinusitis while no association was observed for pneumonia, pharyngitis and coronary problems
Emmanuel (2000). Respirology	Singapore	Forest fire	Ecological time series	General population	Population size was not mentioned	PM_{10} (other measures recorded including CO, NO_2, O_3, SO_2 and pollutant standard index but not used)	Respiratory illnesses (Hospital admissions and ER visit)	Weather factors	An increase in PM concentration from 50 to 150 $\mu g/m^3$ was associated with a 12, 19 and 26% increase in upper respiratory tract illnesses, asthma and rhinitis. There was no increase in hospital admissions and mortality.
Smith et al. (1996). Int J Epidemiol	Australia	Bush fire	Ecological time series	General population	Population size was not mentioned	PM_{10}, NO_2, O_3	Asthma (ER visit)	Weather factors	There was no relationship between PM_{10}, NO_2 and O_3 concentrations and asthma emergency room visits.
Delfino et al. (2008). Occup Environ Med	USA	Forest fire	Ecological time series	General population	Population size was not mentioned	$PM_{2.5}$	Respiratory and cardiovascular illnesses (hospital admissions)	Weather factors, fungal spores	There were positive associations between 10 $\mu g/m^3$ rise in $PM_{2.5}$ and hospital admission for respiratory illnesses (all, asthma, pneumonia, COPD) during the wildfire event. The increase per 10 $\mu g/m^3$ rise in $PM_{2.5}$ was stronger during wildfire event compared to before except for pneumonia with the difference for asthma being marginally significant. There were

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Table 4. Continued

Citation (Author.Year.Journal)	Location	Biomass type	Study design	Subject description	Sample size	Exposure measure	Health end-point(s)	Major confounders (apart from adjustment for trend and seasonal components in trend analyses)	Result summary
									increases in admissions for various cardiovascular illnesses in association for the same rise in PM_{10} (all, ischemic heart disease, congestive heart failure, cerebrovascular disease + stroke) during the wildfire event but none of these was significant.
Golshan et al. (2002). Int J Environ Health Res	Iran	Agricultural burn – rice straw	Cohort study	1–80 years old male and female	994 in first phase (questionnaire) – dropped to 134 in clinical phase	Exposure versus no exposure period	Lung function (spirometry measures)	Previous respiratory illness history, confounding exposure (smoking)	Percent predicted FEV_1, FEV1/FVC, PEFR, FEF_{25-75} decreased after exposure to rice burning smoke while recent asthma attacks, using asthma medication, sleep disturbed by dyspnea, cough and exercise induced cough increased.
van Eeden et al. (2001). Am J Respir Crit Care Med	Singapore	Forest fire	Cohort (panel study)	Healthy young male	30	Exposure versus no exposure period	Acute systemic inflammation	None listed or considered in analysis	Concentrations of circulating cytokines (IL-1β, IL-6, GM-CSF) reduced from during the wildfire event to the period after the wildfire event.
Tan et al. (2000). Am J Respir Crit Care Med	Singapore	Forest fire	Cohort (panel study)	Healthy young male	30	Exposure versus no exposure period ($PM_{2.5}$, SO_2 measurements were collected but not used for association with health end-points)	Acute systemic inflammation	None listed or considered in analysis	Percentage of white blood cells that was polymorphonuclear leukocytes reduced from during the wildfire event to the period after the wildfire event and was associated with PM10 with no lag days and SO_2 with 3 lag days. There was no change in lung function as measured by FEV_1 and FVC or in the number of different white blood cell types.
Golshan et al. (2002). Int J Environ Health Res	Iran	Rice (agricultural burning) – whole vegetation	Cohort study	1–80 years old male and female	994 in first phase (questionnaire) – dropped to 134 in clinical phase	Rice straw burning smoke and PM_{10}	Lung function measured as spirometry; respiratory symptoms	Previous respiratory illness history, confounding exposure (smoking)	Percent predicted FEV_1, FEV_1/FVC, PEFR, FEF_{25-75} decreased after exposure to rice burning smoke while

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									recent asthma attacks, using asthma medication, sleep disturbed by dyspnea, cough and exercise induced cough increased.
Hanninen et al. (2009). J Exp Sci Environ Epidemiol	Finland	Wildfire – whole vegetation (long range transport)	Ecological time series	General population	3.4 million	$PM_{2.5}$	Daily all-cause mortality	Temperature, weekday	Non-significant 0.8–2.1% increase in daily all-cause mortality for exposure lagged 0–4 days and 5-day average exposure for every 10 $\mu g/m^3$ increase in $PM_{2.5}$
Cancado et al. (2006). Environ Health Perspect	Brazil	Sugar cane field burn	Ecological time series	General population	320 000	$PM_{2.5}/PM_{10}$	Respiratory hospital admissions	Relative humidity, temperature, weekday	Increases of 10.2 $\mu g/m^3$ in $PM_{2.5}$ and 42.9 $\mu g/m^3$ in PM_{10} were associated with 21.4% (4.3, 38.5%) and 31.03% (1.25, 60.21%) increases in child and elderly respiratory hospital admissions respectively. Associations were more positive on sugar cane burn days.

during the wildfire period. An increase of 2.8% in hospital admissions for all respiratory diseases was observed in association with an increase of 10 $\mu g/m^3$ in the 2-day average ambient air $PM_{2.5}$ concentrations during the wildfire period (Delfino et al., 2008). While the authors acknowledged the inconsistencies in the results obtained from the different models without providing an explanation of probable causes for them, the significant increase in hospital admission in the period immediately after the wildfire event, and the positive relationship between ambient air $PM_{2.5}$ concentration and hospital admissions during the wildfire period suggest a respiratory effect of wildfire smoke exposure.

Similarly, an increased risk for emergency room visits for all respiratory diseases (RR: 1.66) was observed in North Carolina counties that were determined to have been exposed to smoke from peat forest fires between 1 June 2008 and 14 July 2008 based on a satellite platform derived aerial optical density measure (Rappold et al., 2011). In addition, significant associations, which were stronger during the sugar cane field burning season, were observed between ambient air PM_{10} concentrations and hospital admissions for both children (>13 years) and the elderly (>64 years) in a city in Brazil (Cancado et al., 2006). The results referenced above for all respiratory diseases are supported by those reported in prior studies (those included in the Naeher et al. review) conducted in countries other than Australia (Chen et al., 2006; Moore et al., 2006; Mott et al., 2002, 2005). They are also supported by results reported in other more recent studies (published after the 2007 review by Naeher et al.) that were conducted in Australia with regards to bushfire smoke exposure (Crabbe, 2012; Hanigan et al., 2008; Johnston et al., 2007; Morgan et al., 2010; Tham et al., 2009). Although non-significant overall increases in risk were observed in two of the more recent Australian studies (a case-crossover study and an ecological time-series study) (Hanigan et al., 2008; Johnston et al., 2007), a significant increase was observed for indigenous people in one of these studies (Hanigan et al., 2008).

These two Australian studies also did not observe increases in hospital admissions for asthma in association with bushfire related air pollution (Hanigan et al., 2008; Johnston et al., 2007). However, significant increase in the odds (same day OR: 1.12) of having hospital admission for asthma was associated with the occurrence of bushfire related high pollution in Sydney, Australia (Martin et al., 2013). No association was found for asthma hospital admissions in two other Australian cities, Newcastle and Wollongong, in the same study. Associations of asthma hospital admissions or emergency room visits with various measures of particulate matter air pollution were observed with respect to peat forest fires in North Carolina (65% increase in emergency room visits in exposed counties) (Rappold et al., 2011), bushfire in Australia (5.02% increase in hospital admissions per same day 10 $\mu g/m^3$ rise in PM_{10} in 15–64 year old) (Morgan et al., 2010), forest fires in British Columbia (16% increase in odds of hospital admissions per 30 $\mu g/m^3$ rise in same-day PM_{10} during the forest fire season) (Henderson et al., 2011) and forest fires in California (4.8% increase in hospital admission per 10 $\mu g/m^3$ rise in 2-day average $PM_{2.5}$ during wildfire period) (Delfino et al., 2008). Results for asthma hospital

admissions from prior studies (those included in the Naeher et al. review) are more inconsistent. Significant positive associations were observed in three of the prior studies, including two which focused on burning of agricultural fields or residues (Arbex et al., 2007; Jacobs et al., 1997; Mott et al., 2005), while null results were reported in two studies (Churches & Corbett, 1991; Duclos et al., 1990). Weather factors, which are commonly controlled for in ecological time series studies were not adjusted for in these two prior studies that reported the null findings for asthma hospital admissions. One prior study reported null findings for asthma related physician visits (Johnston et al., 2006). Three prior studies reported significant positive associations for asthma emergency room visits (Duclos et al., 1990; Emmanuel, 2000; Johnston et al., 2002), while one prior study reported a null finding (Smith et al., 1996). Two prior studies (one, cohort and the other, a cross-sectional study) also observed associations with various asthma-related symptoms and wellness measures in relation to wildfire events (Johnston et al., 2006; Kunzli et al., 2006).

Wildland fire related air pollution exposure has also been associated with hospital admissions for COPD among the general public in two more recent ecological time-series studies (published after the 2007 review by Naeher et al.) (Delfino et al., 2008; Morgan et al., 2010). A bushfire related $10\,\mu g/m^3$ rise in ambient air PM_{10} was associated with an increase of 3.29% in hospital admissions for COPD among persons older than 65 years in Sydney, Australia. This was six times higher than the insignificant 0.57% increase in hospital admissions for COPD that was observed for a $10\,\mu g/m^3$ rise in PM_{10} in background ambient air in the same study (Morgan et al., 2010). Delfino et al. (2008) also reported a 3.8% increase in COPD hospital admissions among persons between 20 and 99 years old for every $10\,\mu g/m^3$ rise in $PM_{2.5}$ during the 2003 southern California wildfires. This association was stronger than those observed in the periods immediately preceding or following the wildfires. In a case-crossover study, the odds of subjects being admitted into the hospital for COPD during the bushfire season in Darwin, Australia increased by 21% for every $10\,\mu g/m^3$ rise in PM_{10} (Johnston et al., 2007). In another ecological time-series study conducted in Australia, significant increases in odds for COPD hospital admissions were observed in association for same day (12%) and previous day (10%) bushfire related severe pollution event in Sydney, Australia (Martin et al., 2013). However, null results were observed for Newcastle and Wollongong. No associations were also observed in Sydney in a different ecological time-series study (Hanigan et al., 2008). Significant positive associations were reported in studies included in the Naeher et al. (2007) review for various COPD outcomes: incidences of symptoms in Denver, CO (Sutherland et al., 2005), emergency room visits in California (Duclos et al., 1990) and hospital admissions in Malaysia (Mott et al., 2005).

Adverse effects of wildland fires for other respiratory outcomes among the general population have been reported. These include hospital admission for acute bronchitis and bronchiolitis (Delfino et al., 2008), and pneumonia (Delfino et al., 2008; Morgan et al., 2010). Significant effects were also observed for emergency room visits for pneumonia and acute bronchitis (Rappold et al., 2011), and upper respiratory tract illness including laryngitis, sinusitis and rhinitis (Duclos et al., 1990; Emmanuel, 2000). Although, null results were reported in one study for hospital admissions for pneumonia and acute bronchitis in Sydney and Wollongong in association with bushfire associated elevated pollution, significant positive associations were observed in Newcastle in the same study on the day immediately following or two days after the pollution event (Hanigan et al., 2008). Null results were also reported for emergency room visits for pneumonia and pharyngitis in association with forest fires in California (Duclos et al., 1990), and unspecified upper respiratory tract infection in association with forest fires in California and peat forest fires in North Carolina (Duclos et al., 1990; Rappold et al., 2011).

Cardiovascular effects of wildland fire smoke in the general public

In all, 13 peer-reviewed papers reporting on the possible cardiovascular effects of wildland fires were identified. The ecological time series design was employed in all the studies except for a cohort study that was conducted in British Columbia, Canada (Henderson et al., 2011), and a case-crossover study conducted in Australia (Johnston et al., 2007). Mostly, null findings were reported for the associations between wildland fire exposure and cardiovascular health end points among the general public. No positive association was reported for hospital admissions, physician or emergency room visits due to all cardiovascular diseases combined in ten studies conducted in North America, Asia or Australia (Crabbe, 2012; Delfino et al., 2008; Duclos et al., 1990; Hanigan et al., 2008; Henderson et al., 2011; Johnston et al., 2007; Moore et al., 2006; Morgan et al., 2010; Mott et al., 2005; Rappold et al., 2011).

However, positive association was reported for the association between cardiovascular mortality in Athens, Greece and the size of forest fires occurring in areas adjacent to the city (Analitis et al., 2011). An apparent dose-response effect was also observed with fires classified as medium being associated with a non-significant 6.0% (−0.3, 12.6%) rise in cardiovascular mortality, while fires classified as large were associated with a 60% (43.1, 80.3%) increase. In addition, the effect was observed to be more pronounced in the older population (>75 years). Conversely, no positive association was observed between mortality among all age groups and visibility which was used as a surrogate measure for particulate matter ambient air pollution in two Malaysian cities, Kuala Lumpur and Kuching, during the 1997 forest fire related haze in Southeast Asia (Sastry, 2002). Nevertheless, cardiovascular mortality was observed to increase among 65–74 year old (RR: 2.016) in Kuala Lumpur and persons who were 75 years and older (RR: 3.060) in Kuching on days with forest fire related reduced visibility in the same study.

Some of the identified papers report findings from studies investigating the associations between wildland fire smoke exposure and specific cardiovascular health end points among the general public. These end points include hospital admission and/or emergency room visits for hypertension, ischemic heart disease, cardiac dysrhythmia, myocardial infarction,

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Table 5. Summary of review of epidemiological studies of wildland firefighters.

Citation (Author.Year.Journal)	Location	Type of fire activity/burn	Study design	Subject description	Sample size	Exposure measures	Health end-point(s)	Major confounders accounted for	Result summary
Betchley et al. (1997). Am J Ind Med	Salem, Oregon, USA	Forest fire	Cohort (repeated measures)	Wildland firefighters	76 firefighters for cross-shift and 53 firefighters for cross-seasonal	Participation at work-shift and burn season with exposure to wildland fire smoke	FVC and FEV_1 by spirometry, and respiratory symptoms including cough, phlegm production, sore throat, chest tightness, chest pain and wheezing by questionnaire	Smoke exposure prior to preseason, smoking within 2 h, of pulmonary function tests, chest cold within the preceding 4 weeks, medications, allergies, wood use	The change of respiratory symptoms cross-shift and cross-seasonal were not statistically significant (2). There were significant mean individual cross-shift declines in FVC, FEV_1 and FEF_{25-75}, and significant cross-seasonal declines in FEV_1 and FEF_{25-75} decreases which continued after nearly 2.5 months. Recovery in all spirometry measures was observed across the winter months (171–380 days) when firefighting activities are minimal.
Jacquin et al. (2011). Am J Ind Med	Corsica, France	Forest fire	Cohort (repeated measures)	Wildland firefighters	108 (59 were smokers and 49 were non-smokers without any acute or chronic pulmonary disease)	Participation at work-shift and burn season with exposure to wildland fire smoke	FVC, FEV_1 and PEFR were measured by spirometer. Exhaled CO was also measured. Symptoms relating to related to smoke exposure or CO intoxication were recorded.	Smoking	FEV_1, FVC and PEF declined immediately after the end of exposure and greater declines was seen after 24 h (−0.531, −0.591 and −531 min^{-1}, respectively). Declines in spirometric parameters persisted through 3 months after the fire season in comparison with baseline values (FEV_1 −0.28 l; FVC −0.34 l; PEF −451 min^{-1}, $p < 0.05$ for each). No difference was observed in declines between smoking and non-smoking groups.
Gaughan et al. (2008). J Occup Environ Med	Rocky Mountain National Park, Yosemite National Park, Glacier National Park, USA	Forest fire	Cohort (repeated measures)	Wildland firefighters from two Interagency Hotshot Crews	58	Participation at work-shift and burn season with exposure to wildland fire smoke	Respiratory symptoms collected using a questionnaire, lung functions were assessed by spirometry, intracellular and airway inflammation (extracellular myeloperoxidase and eosinophilic cationic protein were measured through induced sputum and nasal lavage analyses)	Age, gender, height and race/ethnicity	Mean FEV_1, mean upper and lower respiratory symptom scores were higher immediately after exposure compared to preseason. FEV_1 recovered by post-season after subjects had spent time away from fighting fires. After adjusting for a significant association between an

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Table 5. Continued

Citation (Author.Year.Journal)	Location	Type of fire activity/burn	Study design	Subject description	Sample size	Exposure measures	Health end-point(s)	Major confounders accounted for	Result summary
									individual's preseason FEV_1 and subsequent FEV_1 values, lower FEV_1 values were associated with greater upper respiratory symptom scores, with higher sputum eosinophilic cationic protein concentration and with higher sputum myeloperoxidase concentrations. Individual increases in sputum and nasal eosinophilic cationic protein and myeloperoxidase from preseason to post-fire were all significantly associated with post-fire respiratory symptom scores.
Hejl et al. (2013). J Occup Environ Hyg	Savannah River Site, SC, USA	Prescribed burns	Cohort (repeated measures)	U.S. Forest Service wildland firefighters	12	Participation at work-shift and burn season with exposure to wildland fire smoke, $PM_{2.5}$ and CO	Inflammation (IL-1β, IL-6, IL-8, TNF-α and CRP, SAA, ICAM-1, VCAM-1 in dried blood spot samples)	Various confounders including task, residential use of wood, exposure to secondhand smoke collected but not controlled for in a multi-factor model	IL-8 concentration in dried blood spot samples significantly increased across the work shift as indicated by a post-/pre-work shift ratio of 1.70 (95% CL: 1.35, 2.13), while concentrations of IL-8, CRP, and ICAM-1 increased in 91.7, 75 and 67% of subject-days across work shift. Firefighters who lighted fires as opposed to other work tasks had the largest cross-work shift increase in IL-8 concentrations.
Adetona et al. (2011). Inhal Toxicol	Savannah River Site, SC, USA	Prescribed burns	Cohort (repeated measures)	Wildland firefighters	24	Participation at work-shift and burn season with exposure to wildland fire smoke, $PM_{2.5}$ and CO	Lung function measured by spirometry	Gender, race, work-time, cumulative burn days, smoking and allergies	Declines across work-shift on burn days were observed for mean individual FVC and FEV_1, but not for FEF_{25-75}, PEF and FEV_1/FVC, but changes on burn days were not significantly different from those on non-burn days. However, each additional day of working at a prescribed burn,

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									at any given point during the burn season, was associated with declines of 24 ml in pre-shift FVC and 24 ml in pre-shift FEV_1 in non-allergic firefighters, and 8 ml in FVC and 4 ml in FEV_1 in allergic firefighters.
Rothman et al. (1991). J Occup Environ Med	Northern California, USA	Forest fire	Cohort (repeated measures)	Wildland firefighters	52	Participation at work-shift and burn season with exposure to wildland fire smoke	Lung functions measured by spirometry	Age, race, gender, passive exposure to cigaret smoke, exposure to diesel exhaust, smoking status, history of asthma, history of hay fever, previous number of years as a firefighter, hours of fire-fighting occurring before baseline measurements and use of a bandanna for respiratory protection	The mean cross-seasonal change in FEV_1 and FVC were −1.2% (95% CI −0.5%, −2.0%) and −0.3% (95% CI 0.4%, −1.0%) respectively. Decreases in FEV_1 and FVC were most strongly associated with hours of recent fire-fighting activity. Firefighters in the high activity category (mean ± SE, 73 ± 7 h of fire-fighting in previous week) had a −2.9% (130 ml) change in FEV_1 and a −1.9% (102 ml) change in FVC. Most respiratory symptoms evaluated increased significantly across the fire season and several symptoms (eye irritation, nose irritation and wheezing) were associated with recent fire-fighting.
Slaughter et al. (2004). J Occup Environ Hyg	Western United States	Forest fire	Cohort (repeated measures)	Wildland firefighters	65	$PM_{3.5}$, acrolein, formaldehyde, and CO	Lung functions measured by spirometry	Gender, age, and current smoking status	FEV_1 declined significantly by −0.1251 from preshift to postshift. A 1000 μg/m^3 increase in PM3.5 was associated with a −0.0301 change in the cross-shift FEV_1 (95% CI [−0.087, 0.026]). Acrolein, formaldehyde, and carbon monoxide exposure were also not significantly associated with changes in FEV_1, FVC, or FEF_{25-75}

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Table 5. Continued

Citation (Author.Year.Journal)	Location	Type of fire activity/burn	Study design	Subject description	Sample size	Exposure measures	Health end-point(s)	Major confounders accounted for	Result summary
Swiston et al. (2008). Eur Respir J	British Columbia, Canada	Forest fire	Cohort (repeated measures)	Seasonal forest firefighters	52	Participation at work-shift and burn season with exposure to wildland fire smoke, CO	Pulmonary symptoms was assessed by question-naires; spirometry; local airway and systemic inflammation measured as cell counts and cyto-kine concentrations	Information collected and controlled for at the subject selection stage (smoking, co-mor-bidities). Study design eliminated the others.	The number of circulat-ing white blood cells, band cells and per-centage sputum gran-ulocytes increased significantly follow-ing fire-fighting shifts. Serum inter-leukin (IL)-6, IL-8 and monocyte chemotactic protein-1 levels also signifi-cantly increased fol-lowing fire-fighting, while there were no changes in band cells, IL-6 and IL-8 fol-lowing strenuous physical exertion without fire-fighting.
Gaughan et al. (2014). J Occup Environ Hyg	Rocky Mountain National Park, Colorado, USA	Forest fire	Cohort (repeated measures)	Wildland firefighters of the Alpine Interagency Hotshot Crew	17	Participation at work-shift and burn season with exposure to wildland fire smoke, CO, levoglucosan, respirable crystalline silica, respirable par-ticulate matter, exhaled breath CO	Lung functions measured by spirometry	Age, job and crew operation	Cross-shift declines in FEV_1 were associated with exposure to higher concentrations of respirable levoglu-cosan. FEV_1 declined across the work shift by −0.051 ($p = 0.08$), with participating wildland firefighters in the high levoglu-cosan exposure group having a mean FEV_1 decline of 0.231 compared to a mean decline of 0.021 in the low levoglucosan exposure group. Larger mean values of pre-shift exhaled breath CO were asso-ciated with larger declines in FEV_1.
Miranda et al. (2012). J Toxicol Environ Health	Leiria, Coimbra and Aveiro, Portugal	Forest fire	Cohort (repeated measures)	Wildland firefighters	40	CO, VOC and NO_2	Exhaled nitric oxide was measured; lung function measured by spirometry	None listed	FEV_1, F_{25}, F_{50} and MEF) significantly declined after exposure at work shifts. Exhaled nitric oxide concen-tration significantly decreased after exposure to smoke.
Adetona et al. (2013b). Sci Total Environ	USA	Prescribed burn – whole vegetation	Cohort (repeated measures)	Wildland firefighters	17	$PM_{2.5}$ and carbon monoxide	Urinary oxidative stress biomarkers	Age, length of fire-fighting career	There was no cross-shift increase in mean malondialdehyde concentrations. However, 8OHdG significantly increased across

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										workshift for only subjects who had been firefighters for 2 years or less, while decreases were observed for firefighters who had been firefighters for longer periods with a significant decrease observed for those working as firefighters for 10 years or more. This effect of career length was not evident when age which correlated with career length was added into the model.
Gaughan et al. (2014). Am J Ind Med	USA	Wildfire – whole vegetation	Cross-sectional	Wildland firefighters	38		Levoglucosan (particle)	Urinary oxidative stress biomarkers, inflammatory biomarkers, arterial stiffness and lung function was measured using spirometry	Smoking, historical occupational exposures, allergies, pre-existing asthma	Aortic augmentation index increased by 10.5% (2.5, 18.5%) with every unit increase in oxidative stress score (average of the z-scores of 8-OHdG and 8-isoprostane), while the oxidative stress score was positively associated with levoglucosan concentration.
Liu et al. (1992). Am Rev Respir Dis	USA	Wildfire – whole vegetation	Cohort (repeated measures)	Wildland firefighters	63		Wildland fire smoke	Lung function	Gender, smoking history, allergies/asthma, years as a firefighter, symptoms	FVC, FEV_1 and FEF_{25-75} declined by 0.091, 0.151 and 0.44 l/s across the wildfire season while airway responsiveness increased across the season.
Serra et al. (1996). Am J Ind Med	Italy	Wildfire – whole vegetation	Cross-sectional	Wildland firefighters as exposed group and policemen as control	92 wildland firefighters versus 51 policemen		Wildland fire smoke	Lung function	Age, height, smoking, previous work experience	Wildland firefighters had significantly ($p < 0.05$) lower spirometry measures compared to the policemen – FEV_1 (3.90 versus 4.04 l); FEF_{75} (8.37 versus 8.38 l/s); FEV_1/FVC (80.07 versus 83.89%); FEF_{25} (1.58 versus 1.99 l/s) and FEF_{50} (4.73 versus 5.54 l/s).

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stroke and heart failure. Of these, positive associations have only been reported for hospital admission due to hypertension in relation to exposure to smoke from the burning of sugar cane fields in Brazil (Arbex et al., 2010), emergency room visit due to heart failure in relation to exposure to peat forest fire smoke in North Carolina (Rappold et al., 2011), and hospital admission due to ischemic heart disease among indigenous people in Darwin, Australia (Johnston et al., 2007). However, these results should be interpreted with caution. No other study of the association between wildland fire smoke exposure and hypertension was identified. Two studies, one in Australia in relation to bushfires and another in the US with respect to forest fires, report null findings for hospital admissions due to heart failure (Delfino et al., 2008; Morgan et al., 2010). A null finding was reported for non-indigenous people in the Australian study which reported a positive finding for indigenous persons for hospital admissions for ischemic heart disease (Johnston et al., 2007). In addition, four other studies – one from Malaysia in relation to the 1997 forest fire haze episode in Southeast Asia, one from the US in relation to forest fires, and two from Australia in relation to bushfires – report null findings for hospital admission due to ischemic heart disease (Delfino et al., 2008; Hanigan et al., 2008; Morgan et al., 2010; Mott et al., 2005). Null findings were reported for cardiac dysrhythmia in two studies from the US (Delfino et al., 2008; Rappold et al., 2011), myocardial infarction in one study from the US (Rappold et al., 2011), and stroke from two studies, one from the US and the other from Australia (Delfino et al., 2008; Morgan et al., 2010).

Other health effects of wildland fire smoke in the general public

Several studies have investigated the association between wildland fire smoke exposure and all-cause, non-traumatic or ill-defined mortality among the general public (Analitis et al., 2011; Emmanuel, 2000; Hanninen et al., 2009; Morgan et al., 2010; Sastry, 2002; Vedal & Dutton, 2006). Hanninen et al. (2009) reported non-significant increases of 0.8–2.1% in daily mortality in provinces in Southern Finland per additional 10 $\mu g/m^3$ of $PM_{2.5}$ with varying lag periods (lag 0–3, 0–4 day average) during a 2-week period in September 2002 when air quality in the provinces was impacted by smoke from wildfires in Eastern Europe. Significant increases in non-traumatic and ill-defined mortality were observed among different age groups in association with dichotomous measures of air pollution (visibility <0.91 km and $PM_{10}>210\ \mu g/m^3$) in two cities in Malaysia during the 1997 Southeast Asia forest fire related haze episode (Sastry, 2002). However, results were inconsistent among the age groups across the two cities. Also, null findings for all-cause mortality among the general public in association with forest fires were reported in one study in Singapore and another in Denver, CO (Emmanuel, 2000; Vedal & Dutton, 2006). However, Analitis et al. (2011) reported increases in all natural deaths among the general public in Athens, Greece in association with forest fires in areas adjacent to the city. Medium fires were associated with a 4.9% (0.3, 9.6%) increase in all natural deaths while large fires were associated with a 49.7% (37.2, 63.4%) increase.

The effect of *in utero* acute exposure to wildland fire smoke on birth outcomes has been investigated in one study (Holstius et al., 2012). Compared to babies born from pregnancies occurring entirely during periods before or after the forest fires, birth weights of newborns were 7.0 g (2.2, 11.8 g), 9.7 g (4.8, 14.5 g) and 3.3 g (−0.6, 7.2 g) lower when the wildfires occurred in the first, second and third trimester of pregnancy respectively. Finally, increases in circulating immature polymorphonuclear (band cells) leukocytes and serum pro-inflammatory cytokine concentrations were increased in healthy male volunteers in Singapore during the 1997 Southeast Asia forest fire haze compared to the period immediately after the episode (Tan et al., 2000; Van Eeden et al., 2001). These results indicated that exposure to smoke from the forest fires caused systemic inflammation. However, the authors reported the lack of measurements prior to the forest fire related exposure as a limitation of their study.

Health effects of occupational exposure to wildland fires among wildland firefighters

Few studies of the health effects of occupational wildland fire smoke exposure have been conducted among wildland firefighters. The comprehensive review of the health effects of wood smoke by Naeher et al. (2007) included six studies of health effects among wildland firefighters, including one non-peer reviewed paper. Nine studies investigating the health effects of occupational wildland fire smoke among wildland firefighters have since been published. None of these studies has investigated direct linkages to diseases, and all have focused on various adverse physiological responses in the airways or blood.

Declines in lung function measures across the work shift have been observed in a few studies. Betchley et al. (1997) reported declines of 65 ml, 150 ml and 497 ml/s in forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1) and maximum mid-expiratory flow (FEF_{25-75}) across the work shift for wildland firefighters working at wildland fires in the states of Oregon and Washington. Similarly, corresponding declines of 59 ml, 53 ml and 53 L/min were also observed at the end of the first firefighting activity compared to baseline measurements collected before deployment of a group of firefighters in Corsica, France (Jacquin et al., 2011). A smaller non-significant cross-shift decline in FEV_1 of 30 ml was reported by Gaughan et al. (2008). No association was observed between cross-shift declines in lung function measures and work shift exposure to $PM_{3.5}$, carbon monoxide, acrolein or formaldehyde in the studies conducted in Oregon and Washington (Slaughter et al., 2004). However, Gaughan et al. (2014) reported an association between cross-shift declines in FEV_1 and work shift exposure to particulate levoglucosan.

Nonetheless, the results of the cross-shift studies referenced above are limited by the lack of comparisons to control days when the firefighters were not exposed to wildland fires. This is especially important due to the large variability that is associated with lung function measures

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(Borsboom et al., 1999; Troyanov et al., 1994), and the probable confounding effect of physical exertion that accompanies working at wildfires or prescribed burns. Moreover, Adetona et al. (2011) did not detect any differences in cross-shift changes in lung function measures between days when a crew of wildland firefighters in Southeastern US worked at prescribed burns and days when they did not.

However, there is evidence that continuous occupational wildland fire smoke exposure may have a cumulative effect on lung function. Adetona et al. (2011) observed decreases of 24 ml in FVC and 24 ml in FEV_1 for each additional day that the firefighters worked at a prescribed burn during the dormant winter burn season in Southeastern US (Adetona et al., 2011). Declines in lung function measures have also been observed across periods encompassing one or two burn seasons (Betchley et al., 1997; Gaughan et al., 2008; Liu et al., 1992; Miranda et al., 2012). Significant cross-season declines of 90 ml, 150 ml and 440 ml/s in FVC, FEV_1 and FEF_{25-75}, respectively, were in wildland firefighters in the state of California (Liu et al., 1992). Corresponding cross-season declines in these measures in another study of wildland firefighters in the states of Oregon and Washington were 33 ml, 104 ml and 275 ml/s (Betchley et al., 1997). Gaughan et al. (2008) also observed a cross-season decline of 224 ml in FEV_1 in hot-shot firefighters working at wildfires in the states of Alaska and California. In addition, Rothman et al. (1991) reported cross-season declines of 1.2% in FEV_1 and 0.3% in FVC that were mostly associated with hours of recent firefighting activities among wildland firefighters in California. However, it is unclear whether declines through the prescribed burn/wildfire season are sustained through non-exposure periods/months. No difference was observed in pre-season lung function measurements of a small number of wildland firefighters ($n = 9$) across two years in one study (Adetona et al., 2011), while Betchley et al. (1997) reported that cross-season declines in lung function measures tended to resolve over non-exposure periods ranging between 5.5 and 13 months among the subjects in their study. However, declines which had been observed across a work shift among wildland firefighters in Corsica, France persisted over a three month non-exposure period (Jacquin et al., 2011). FVC, FEV_1 and FEF_{25-75} remained 280 ml, 340 ml and 45 L/min below their baseline measurements, respectively. Wildland firefighters in Sardinia, Italy, also had lower measurements for various lung measurements including FVC, FEV_1 and the FEV_1/FVC ratio compared to policemen on the island after controlling for known confounding factors such as age, height and smoking (Serra et al., 1996). It should be noted that the authors considered that the two groups were similar with respect to their level of physical fitness and the non-sedentary nature of their jobs.

Acute airway and systemic inflammation among wildland firefighters have also been investigated in a few studies. No significant cross-shift changes in eosinophilic cationic protein and myeloperoxidase in induced sputum were observed among two hot-shot crews fighting wildfires in Alaska and California (Gaughan et al., 2008). However, concentrations of these inflammatory biomarkers were increased in their nasal lavage across the work shift. Furthermore, Swiston et al. (2008) reported cross-shift increases in percentage granulocytes, mostly neutrophils, in induced sputum among wildland firefighters in British Columbia. On the other hand, exhaled nitric oxide decreased across firefighting work-shifts in a group of firefighters in another study that was conducted in Portugal (Miranda et al., 2012). Although, the investigators were not expecting this result since reduction in exhaled nitric oxide indicates reduction in airway inflammation, they noted that their observation was similar to results observed in smokers. They noted that cigaret smoke may induce such effect due to the inhibition of nitric oxide synthetase; this in turn could contribute to increased risks of chronic and respiratory diseases in cigaret smokers since endogenous nitric oxide is important for protecting the respiratory tract and counteracting bronchoconstriction, vasoconstriction and platelet aggregation (Miranda et al., 2012).

Acute systemic inflammation consequent upon occupational wildland fire exposure among wildland firefighters has been investigated in two studies (Hejl et al., 2013; Swiston et al., 2008). Significant cross-shift changes in circulating band cells and serum concentrations of pro-inflammatory cytokines, interleukin-6 (IL-6) and IL-8, were observed after exposure to wildland fire in British Columbia (Swiston et al., 2008). Increases in the cytokine concentrations were not observed across a work shift when the firefighters were engaged in strenuous physical activities but had no wildland fire smoke exposure. A similar finding was observed among wildland firefighters in Southeastern US (Hejl et al., 2013). Post-shift concentrations of IL-8 in dried blood spot samples were 1.7 times higher than the pre-shift levels. Cross-shift differences were not observed for adhesion molecules (VCAM-1 and ICAM-1), IL-1β, serum amyloid A (SAA) and C-reactive protein (CRP). Comparisons to changes on days when there were no wildland fire smoke exposures were not made in this study.

Although wood smoke particles have been shown to generate reactive oxygen species (ROS) (Leonard et al., 2000, 2007) only two studies of oxidative stress among wildland firefighters were identified (Adetona et al., 2013b; Gaughan et al., 2014). Cross-shift changes were not observed for oxidative stress biomarkers, urinary 8-hydroxy-2′-deoxyguanosine (8-OHdG) and 8-isoprostane, in all wildland firefighters that were included in one study. However, cross-shift increases were observed for subjects who had worked as wildland firefighters for less than 2 years, while cross-shift decreases were observed for those with longer careers (Adetona et al., 2013b). The authors hypothesized that the acute oxidative stress response due to wildland fire smoke may be modified by the cumulative exposure of the wildland firefighter. The study was limited due to its very small sample size. Although many repeated measurements were collected, the total number of subjects was 17 and the number of subjects per career length group was five or less. Gaughan et al. (2014) also observed a positive association between urinary 8-OHdG and aortic augmentation among two hot shot crews in Colorado. Aortic augmentation is a measure of arterial stiffness which is involved in the pathogenesis of cardiovascular disease.

None of the study of wildland firefighters that were identified investigated the effect of occupational wildland fire

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smoke exposure over the longer term. Consequently, very little is known about the health effects of continuing occupational wildland fire smoke exposure across years among career wildland firefighters. However, such information is needed since the exposure of wildland firefighters, unlike that of the public, is more persistent and typically much higher. The summary of all identified studies involving wildland firefighters are presented in Table 5.

Evidence from the health effects of ambient air pollution indirectly linked to combustion of wood or vegetation

In all, 11 papers that reported on the adverse health effects of ambient air pollution indirectly linked to the combustion of wood or the vegetation were identified. Health outcomes were limited to cardiovascular and/or respiratory health end-points in most of the studies. Null results were reported for all-cause mortality in the whole population in a study involving a city-wide program to replace wood heaters as the primary source of residential heating in Launceston, Australia (Johnston et al., 2013). However, a significant reduction in all-cause mortality was reported for males in the population after the implementation of the stove replacement program. No association was observed between wood/vegetative smoke-associated particulate matter and all-cause mortality in Phoenix, Arizona or Washington, DC in two source apportionment studies (Ito et al., 2006; Mar et al., 2006). These two studies also reported no associations for cardiovascular or respiratory mortality (Ito et al., 2006; Mar et al., 2006). Although, no reduction in all-cause, cardiovascular and respiratory mortality among the whole population was observed in association with a stove intervention program in Launceston, Australia, significant reductions of 11.4, 17.9 and 22.8%, respectively, were observed for males in the city (Johnston et al., 2013). No reductions were observed during the period under study for Hobart, Australia, the control city where no specific air quality intervention had occurred. Sanhueza et al. (2009) reported an increase of 12.5 and 5.5% in respiratory and cardiovascular mortality respectively for every $100\,\mu g/m^3$ rise in PM_{10} in Temuco, Chile. The association between respiratory mortality and ambient particulate matter pollution was stronger during the winter with a rise of 15.7% in mortality for every $100\,\mu g/m^3$ rise in PM_{10}. Almost 70% of the population in Temuco is reported to use wood for cooking or heating during the winter, and 87% of the winter PM_{10} is estimated to originate from residential wood combustion (Díaz-Robles et al., 2014).

In a source apportionment method, Sarnat et al. (2008) did not find any association between admission for all respiratory diseases combined and wood smoke associated $PM_{2.5}$ determined using chemical balance, factor analysis or tracer technique in Atlanta, Georgia. However, a 2.3% rise was observed for every inter-quartile increase in total carbon, the tracer of vegetative burning in Spokane, Washington in another source apportionment study (Schreuder et al., 2006). Associations were also reported between ambient particulate matter concentrations and respiratory admission in Temuco, Chile and Christchurch, New Zealand (Mcgowan et al., 2002; Sanhueza et al., 2009) and outpatient visits for all respiratory illnesses combined in Temuco Chile (Díaz-Robles et al., 2014). Positive relationships were also observed between ambient particulate matter concentrations and respiratory infections including pneumonia and influenza in Christchurch, New Zealand where 90% of the particulate air pollution is estimated to originate from wood burners (Mcgowan et al., 2002). In addition, reduced ambient $PM_{2.5}$ was associated with decrease in the incidences of bronchitis, influenza and throat infection in a cohort study conducted among children in Libby, Montana after a wood stove replacement program (Noonan et al., 2012). Reductions in the incidences of wheeze and colds were also observed in the same study. On the other hand, the odds of experiencing respiratory symptoms within the previous twelve months were not different among study participants living in two cities with substantially different rates of wood stove use and levels of ambient wood smoke exposure in Australia (Bennett et al., 2010). Associations have been reported between residential wood combustion derived ambient air pollution and hospital admissions for asthma and COPD in Christchurch, New Zealand (Mcgowan et al., 2002), and clinical encounters (inpatient and outpatient) for infant bronchiolitis in British Columbia (Karr et al., 2009).

McGowan et al. (2002) did not find any association between residential wood combustion derived ambient particulate matter pollution and hospital admission for cardiac dysrhythmia, ischemic heart disease or heart failure in Christchurch, New Zealand. Conversely, a significant 1.26% increase in hospital admission for all cardiovascular diseases combined for every $14.8\,\mu g/m^3$ increase in PM_{10} was observed in the same study. In addition, Sarnat et al. (2008) reported a positive association between wood smoke derived ambient particulate matter pollution as determined by chemical balance, factor analysis or tracer technique and emergency room visits for all cardiovascular diseases combined in Atlanta, while a 5.8% increase in hospital admissions for all cardiovascular diseases combined in association with every $100\,\mu g/m^3$ increase in ambient air PM_{10} was observed in Temuco, Chile during the cold season (Sanhueza et al., 2009). Schreuder et al. (2006) did not observe an association between concentrations of total carbon, used as a tracer of vegetative burning and emergency room visits for all cardiovascular diseases combined.

Evidence from the health effects of household air pollution related to the combustion of wood or other vegetative materials

As with other exposure scenarios, most of the studies of the health effects of household air pollution associated with the combustion of wood and other vegetative materials investigate respiratory health end-points. There is strong evidence that continuous long-term exposures to smoke related to residential wood combustion is linked to the development of COPD and chronic bronchitis. A recent meta-analyses showed that the odds of having doctor diagnosed or lung function defined COPD increased more than four folds (OR: 4.29 [1.35, 13.70]) in populations using wood burners in their residences compared to those using cleaner fuels (Kurmi et al., 2010). The corresponding odds ratio for bronchitis in

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the same study is 2.64 (2.12, 3.29). Similar results are reported by two other recent meta-analyses of studies investigating residential combustion of all solid biomass fuel types including wood (Kurmi et al., 2012; Po et al., 2011). Similarities have been shown in the pathology of wood and tobacco smoke associated COPD (González-García et al., 2012; Guzmán-Grenfell et al., 2011; Montano et al., 2004; Moran-Mendoza et al., 2008; Sandoval et al., 1993). However, some of the indicators of the disease have been observed to be more severe in wood smoke associated COPD (González-García et al., 2012; Guzmán-Grenfell et al., 2011; Montano et al., 2004; Sandoval et al., 1993). Higher metalloproteinase activity was observed in patients with wood smoke associated COPD (Montano et al., 2004), while they also had more severe pulmonary arterial hypertension and bronchial hyper-responsiveness (González-García et al., 2012; Sandoval et al., 1993).

It is not clear that there is an association between exposure to smoke from residential combustion of wood and asthma. Ostro et al. (1994) reported an association (OR: 1.59 [1.28, 1.97]) between the use of wood stove or fireplace and nocturnal asthma and other asthma related symptoms among adult patients (18–70 years) diagnosed with asthma in Denver, CO (Ostro et al., 1994). Significant association (OR: 5.64 [1.1, 27.9]) was reported for asthma together with other "respiratory problems" among children less than 12 years in one study in Mexico (Graham et al., 2005). Lack of separation prevented firm conclusion specific to asthma to be drawn from the results of the study. No association was observed between wood stove use and acute asthma in young children (1 month to 5 years) in a hospital-based study that was conducted in Malaysia (Azizi et al., 1995). Eisner et al. (2002) reported no association between wood stove use and asthma health outcomes in Northern California. In a survey study, an insignificant increase in odds for the prevalence of doctor-diagnosed asthma was observed among children (4–6 years) living in homes in three rural communities in Guatemala where wood for cooking was combusted exclusively in open fires relative to those living in homes where improved stoves were used (Schei et al., 2004). On the other hand, significant positive associations were observed for asthma-related symptoms in the same study. Similar results have been reported for asthma-related symptoms including wheezing and shortness of breath among children and adults (Da Silva et al., 2012; Ingale et al., 2013; Mengersen et al., 2011; Romieu et al., 2009; Smith-Sivertsen et al., 2009). Residential wood combustion has also been linked with other respiratory symptoms and decreased lung function (Da Silva et al., 2012; Diaz et al., 2007; Fullerton et al., 2011; Guggisberg et al., 2003; Guneser et al., 1994; Ingale et al., 2013; Köksal et al., 2013; Mengersen et al., 2011; Rinne et al., 2006; Riojas-Rodríguez et al., 2001; Romieu et al., 2009; Saha et al., 2005; Smith-Sivertsen et al., 2009; Triche et al., 2002, 2005).

Results were inconsistent between two meta-analyses of studies of the relationship between asthma and household air pollution due to the combustion of solid biomass fuel without any specification of type (Kurmi et al., 2012; Po et al., 2011). While Kurmi et al. (2012) reported a doubling of the risk of developing asthma (OR: 1.96 [1.29, 2.99]) in children exposed to biomass smoke in the indoor environment, Po et al. (2011) reported non-significant reduction in risk among children (OR: 0.50 [0.12, 1.98]) and a non-significant increase in risk among women (OR: 1.34 [0.93, 1.93]). There was an overlap of only two studies out of a total of 12 that were considered by both meta-analyses. Kurmi et al. (2012) reported that the positive result from their meta-analysis be interpreted with caution because the methodology was imperfect in all the five papers they reviewed.

Acute lower respiratory disease and pneumonia, especially among children, is perhaps the most studied health end-point in association with household air pollution due to the combustion of solid biomass fuel including wood. Positive associations between exposure to smoke from residential combustion of wood and acute respiratory infections among children were reported in all seven papers that were identified (Collings et al., 1990; Etiler et al., 2002; Johnson & Aderele, 1991; Johnson et al., 2008; Mahalanabis et al., 2002; Smith et al., 2011; Taylor & Nakai, 2012). Association was positive but insignificant in the only study that reported results for adults (women) (Taylor & Nakai, 2012). In a randomized control trial involving replacement of open fires with chimney stoves, an intention-to-treat analysis showed that a 50% reduction in personal carbon monoxide exposure related to the intervention was associated with reduced odds of being diagnosed by the physician with pneumonia (OR: 0.82 [0.70, 0.98]) or hypoxemic pneumonia (OR: 0.72 [0.59, 0.92]) (Smith et al., 2011). Cooking with wood also increased the risk of mortality among children admitted into the hospital for acute lower respiratory infection in Nigeria (Johnson & Aderele, 1991; Johnson et al., 2008).

Residential wood combustion was linked to tuberculosis in two studies from Mexico. The odds of having active tuberculosis increased 1.5 (1.0, 2.4) times with past or present use of wood among subjects in Mexico City (Perez-Padilla et al., 2001), while cooking with wood for more than 20 years increased the odds of being diagnosed with tuberculosis among subjects living in rural areas in Southern Mexico (García-Sancho et al., 2009). These results are supported by the findings of two meta-analyses of studies that investigated the association between tuberculosis and household air pollution due to the combustion of solid biomass fuel without specification of type (Kurmi et al., 2014; Sumpter & Chandramohan, 2013). However, the authors of a third meta-analysis reported that the association is uncertain (Lin et al., 2007). Association in three of the five studies they included in the meta-analysis was significantly positive, while it was insignificantly negative in the other two. It should be noted that the findings that wood smoke exposure is a risk factor for tuberculosis are similar to those reported for tobacco smoke (Kurmi et al., 2012).

The authors of a pooled analysis of the International Lung Cancer Consortium of data from seven studies across Asia and North America reported an increased odds of 1.21 (1.06, 1.38) for having lung cancer among all subjects that combusted wood for cooking or heating in their homes (Hosgood et al., 2010). The odds (OR: 1.43 [0.97, 2.11]) were higher but not significant for lifetime wood users alone. Similar results were reported by Kurmi et al. (2012) in another meta-analysis of studies investigating the association between lung cancer and household air pollution due to

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residential combustion of solid biomass fuel (all types with and without coal). A higher effect estimate (odds ratio) was reported for females (1.81) compared to males (1.16) for residential combustion of all types of solid biomass fuel combined. This is probably because women experience higher exposure levels compared to men in many of the study areas since they are usually the primary cooks and spend more time in the home.

Household air pollution due to residential combustion of wood has also been linked to adverse birth outcome. Most of the studies have focused on birth weight. Newborns were 14–243 g lighter when they were born to mothers living in homes where wood was used for cooking and/or heating compared to mothers living in homes that used cleaner fuels (Abusalah et al., 2012; Amegah et al., 2012; Boy et al., 2002; Kadam et al., 2013; Siddiqui et al., 2008; Wylie et al., 2014). The results were marginally significant in the study recording the smallest difference (14 g) (Wylie et al., 2014), and another reporting a difference of 82 g (Siddiqui et al., 2008). The smallest difference reported in studies with significant results was 63 g (Boy et al., 2002). Children who were born to women who continued to use open fire to cook were 89 (range: 27–204) grams lighter than those who switched to chimney stoves in a randomized control trial in Guatemala (Thompson et al., 2011). Although the results were not always significant, the incidence of low birth weight (birth weight <2500 g) also tended to be higher among newborns of mothers cooking with wood compared to those cooking with cleaner fuels, and among newborns of mothers cooking with open fire compared to those cooking with chimney stoves. The risk of stillbirth was observed to be higher (PR: 1.24 [1.08, 1.41]) among births to mothers cooking with firewood compared to those cooking with liquefied petroleum gas or electricity in a national survey in India (Lakshmi et al., 2013). Stillbirth was also observed to be more common (4% versus 0%) among women cooking with wood in another Indian study (Wylie et al., 2014). The positive findings for reduced birth weight and stillbirth are supported by results of a meta-analysis of studies investigating the associations between adverse birth outcomes and exposure to household air pollution due to the combustion of solid biomass fuel without specification of type (Pope et al., 2010).

Very few studies have investigated the cardiovascular health effects of chronic exposure to household air pollution due to combustion of wood. Reduced blood pressure has been observed in association with the replacement of open fire with chimney stoves in Guatemala and Nicaragua (Clark et al., 2013; Mccracken et al., 2007). Probable cardiovascular effects of residential exposure to wood smoke have also been demonstrated by observed increase in reactive hyperemia index (a measure of endothelial function) and reduced incidence of non-specific ST-segment depression (a measure of ventricular repolarization) in association with exposure reduction interventions (Allen et al., 2011; Mccracken et al., 2011). The possibility that wood smoke could be a risk factor for adverse cardiovascular outcomes is also supported by results of studies of residential combustion of non-specified solid biomass fuel including wood. A recent study found a higher prevalence of atherosclerotic plaque and an increased mean carotid artery intima-media thickness, an indicator of the progression of atherosclerosis, in association with household solid biomass fuel use (Painschab et al., 2013). Higher blood pressure (Baumgartner et al., 2011), higher prevalence of arterial hypertension (Dutta et al., 2012) and worse measures of markers of pulmonary hypertension in association with residential biomass fuel use have also been reported in recent studies (Emiroglu et al., 2010). Schematics of the pathways involved in pulmonary and systemic effects of wildland fire smoke exposure are presented in Figures 1 and 2.

Mechanisms of toxicity

Most mechanistic studies of wood smoke toxicity relate to its adverse effects in the airways with one study involving both intratracheal instillation and oral gavage of wood smoke particles reporting that the strongest effects were exerted in the organ closest to the port of entry (Danielsen et al., 2010). However, systemic effects after inhalation exposures are reported in a few *in vivo* and human studies. The majority of the mechanistic studies investigated the effects of wood smoke particle exposure on oxidative stress, inflammation and cell toxicity. A few of the studies that attempt an elucidation of the toxicity pathways indicate that these effects are largely due to the endogenous generation of ROS. This indicates that toxicity by wood smoke particles may be induced in a way similar to the hierarchical cellular response model that has been proposed for the toxicity of diesel and ambient air particles (Li et al., 2002, 2008; Xiao et al., 2003). It should be noted again at this point that particulate matter has been identified as the chief indicator of the adverse effects of pollution from combustion sources (Naeher et al., 2007). A few studies have also reported that wood smoke inhalation may induce adverse effects through the action of its component pollutants on cells in the autonomic nervous system. It seems that these effects could be mediated without or together with particles in wood smoke, and that the generation of ROS is at least partially involved.

Oxidative stress and inflammation in the airways

Wood smoke particles contain and possess the potential to generate ROS including the hydroxyl radical, superoxide anions and hydrogen peroxide in cells (Danielsen et al., 2011; Lee et al., 2008b; Leonard et al., 2000, 2007; Liu et al., 2005). No increase in ROS generation was observed in one study (Forchhammer et al., 2012a). However, measurement of ROS in this study was done in human umbilical endothelial cells, unlike in the other studies in which measurements were conducted in airway cell lines. Due to its ability to cause cellular ROS generation, wood smoke exposure can clearly result in oxidative stress. This is measured as the induction of antioxidant enzymes, changes in antioxidant capacity or as changes in concentrations of products of oxidative degradation of macromolecules (lipid peroxidation or oxidative DNA damage). Results are consistent for oxidative stress in *in vitro* studies conducted with monocytes, macrophages, epithelial and endothelial cells. Upregulation of antioxidant enzymes such as heme oxygenase (HO-1) and superoxide dismutase (Cu/Zn SOD), depletion of endogenous antioxidant capacity such as reduction in glutathione (GSH) and increases

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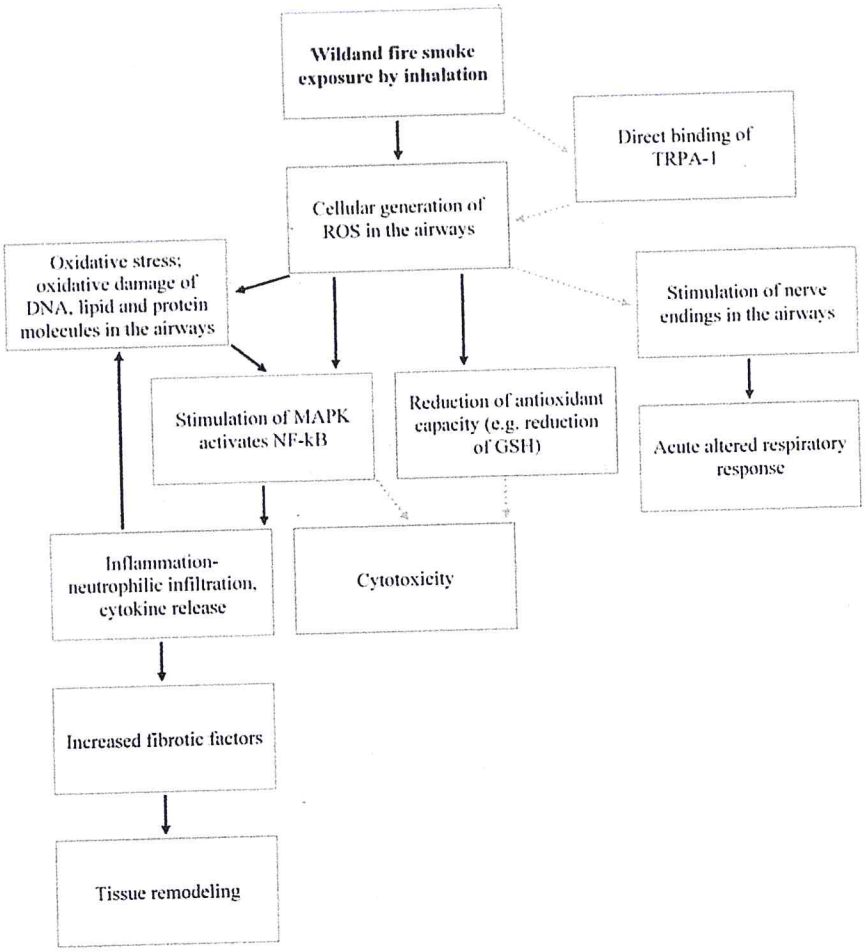


Figure 1. Schematic representation of the pathways for the effects of wildland fire smoke exposure by inhalation on the respiratory system. The solid black arrows represent pathways known with higher level of certainty, while the broken gray arrows represent pathways known with less certainty. *Abbreviations*: TRPA-1: transient receptor potential ankyrin-1; MAPK: mitogen-activated protein kinases; NF-kB: nuclear factor-κB; GSH: glutathione.

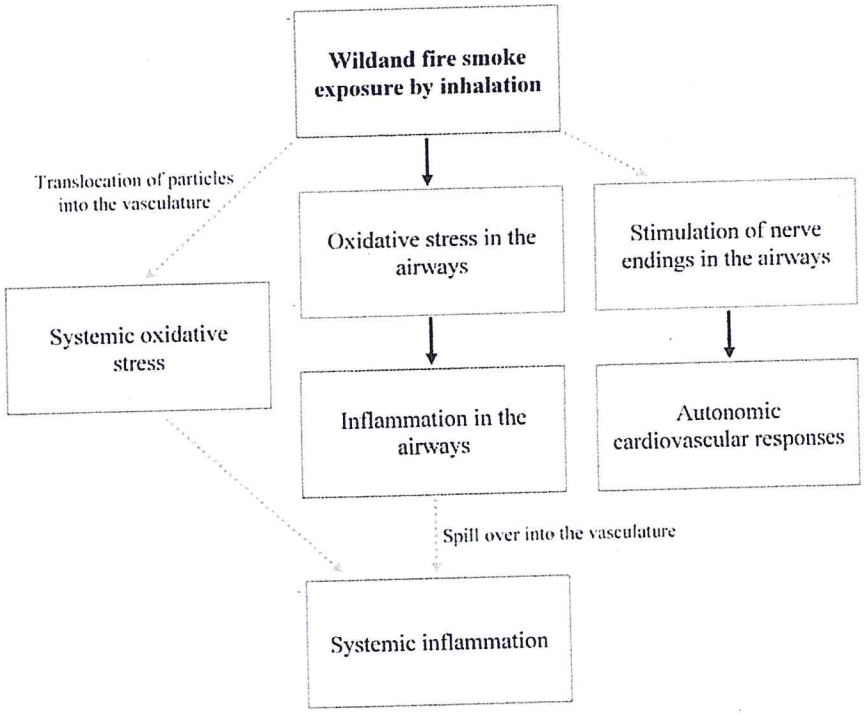


Figure 2. Schematic representation of the pathways for the systemic effect of wildland fire smoke exposure by inhalation. The solid black arrows represent pathways known with higher level of certainty, while the broken gray arrows represent pathways known with less certainty.

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in products of oxidative damage of macromolecules such as DNA strand breaks, oxidized guanines and lipid peroxides are observed across these airway cell lines (Corsini et al., 2013; Danielsen et al., 2009,2011; Forchhammer et al., 2012a; Karlsson et al., 2006; Kubátová et al., 2006; Lee et al., 2008b; Leonard et al., 2007; Liu et al., 2005). Dose-dependent increases in the formation of strand breaks and formamidopyrimidine DNA glycosylase (FPG) sites were observed in human A549 lung epithelial and THP-1 monocytic cell lines in a pair of studies (Danielsen et al., 2009, 2011). The induction of oxidative stress response by wood smoke is dependent on its composition. Non-polar and mid-polar fractions of wood smoke particle extracts caused more GSH depletion than the polar fraction in murine 264.7 macrophages (Kubátová et al., 2006). In addition, the organic extract of wood smoke particulate matter generated more strand breaks in human A549 epithelial cells (Danielsen et al., 2009). Oxidative responses including oxidative lipid damage and reduction in antioxidant capacity have also been observed in the airways in *in vivo* models (Park et al., 2004; Ramos et al., 2013; Wegesser et al., 2009; Williams et al., 2013). However, results about oxidative responses in the airways from human experimental studies are not as consistent as those reported for *in vitro* and *in vivo* studies (Barregard et al., 2008; Sehlstedt et al., 2010; Stockfelt et al., 2012). Although, Barregard et al. (2008) reported an increase in exhaled malondialdehyde, Stockfelt et al. (2012) observed no difference after experimental exposure of healthy adults to wood smoke. Possible reasons for this inconsistency include heterogeneity in the measured oxidative stress marker, timing of measurements, dose of exposure, the type of wood and exposure protocol as it relates to the combustion conditions.

Airway inflammation characterized by an increase in cytokine release by various airway cells (Bølling et al., 2012; Corsini et al., 2013; Danielsen et al., 2011; Forchhammer et al., 2012a; Karlsson et al., 2006; Kocbach et al., 2008a,b; Myatt et al., 2011), and infiltration of immune cells, especially neutrophils, in various *in vivo* models is also induced by exposure to wood smoke particles (Bhattacharyya et al., 2004, 1998; Danielsen et al., 2010; Karlsson et al., 2006; Park et al., 2004; Samuelsen et al., 2009; Wegesser et al., 2009, 2010; Williams et al., 2013; Zhu et al., 2012). There is evidence that ROS generated by wood smoke particles stimulate mitogen-activated protein kinases (MAPKs) such as Jun-N-terminal kinases (JNK). This in turn activates nuclear factor-κB (NF-κB) and other pro-inflammatory transcription factors, thus causing an up-regulation of cytokines. This pathway is similar to what has been described for pulmonary inflammation induced by ambient air particulate matter (Brook et al., 2010). Inhibition of endogenous generation of ROS by wood smoke particle extract and each of the following steps in the theorized pathway resulted in the reduction of the activities of subsequent steps and eventual expression of IL-8 in human bronchial epithelial cells (Perng et al., 2013). In addition, IL-8 release induced by extracts of beech wood smoke generated particles was completely blocked by a specific inhibitor of p38 MAPK in both A549 and THP-1 cells (Corsini et al., 2013). However, specific inhibition of NF-κB resulted in significant inhibition of smoke extract induced IL-8 in only the A549 cells in the same study. Activation of MAPKs by ROS may also result in the up-regulation of anti-oxidant genes. The induction of HO-1 in alveolar epithelial cell II by wood smoke particle extract was completely abolished by pre-treatment with a combination of MAPKs (JNK, p38 and ERK) inhibitors (Lee et al., 2008b).

While endotoxins could adhere to particles and cause inflammation, their inactivation results in only partial attenuation of the pro-inflammatory effects of wood smoke particles (Kocbach et al., 2008a,b). Rather there is evidence that organic components of the particles (which could be metabolized to produce ROS) are largely responsible (Bølling et al., 2012; Kocbach et al., 2008a,b; Wegesser et al., 2009, 2010; Wong et al., 2011). Inflammatory response to wood smoke exposure may also be dependent on combustion conditions which are a determining factor for the physico-chemical properties of the resulting particles (Bølling et al., 2012; Danielsen et al., 2010, 2011). This may account for the negative findings that have been observed with respect to inflammation in some human chamber experiment studies in contrast with actual exposure situations for wildland fire-fighters (Gaughan et al., 2008; Hejl et al., 2013; Riddervold et al., 2012; Sehlstedt et al., 2010; Stockfelt et al., 2012; Swiston et al., 2008). Furthermore, neutrophilic infiltration in the lungs, increased exhaled nitric oxide and serum/urine Clara cell protein (CC16) observed in some human experiment studies suggest a pulmonary pro-inflammatory effect of wood smoke in humans (Barregard et al., 2008; Ghio et al., 2012; Stockfelt et al., 2012).

Alternative mechanistic pathways may contribute to the oxidative stress and inflammatory potentials of wood smoke particles in the airways. The binding of the electrophile binding site of Transient Receptor Potential Ankyrin-1 (TRPA-1) has been postulated as a potential pathway (Shapiro et al., 2013). Although TRPA-1 is mainly expressed in C-fibers that innervate the airways, they are also expressed in non-neuronal airway cells including fibroblasts and small airway epithelial cells. It is hypothesized that the binding of TRPA-1 in these non-neuronal cells could result in their release of pro-inflammatory mediators. It is possible that other alternative pathways that have been described for ambient air particulate matter may also contribute to the pro-inflammatory effects of wood smoke particles (Brook et al., 2010).

Cytotoxicity in airway cells

Cytotoxicity measured as increase in the release of lactate dehydrogenase (LDH) due to membrane damage or reduction in the number of viable cells is induced *in vitro* by exposure to suspension of wood smoke particles (Bølling et al., 2012; Danielsen et al., 2009; Forchhammer et al., 2012a; Kocbach et al., 2008a; Kubátová et al., 2006). Increase in LDH (Samuelsen et al., 2009), increase in the number of dead macrophages and reduction in the number of viable macrophages in bronchoalveolar lavage have also been observed in *in vivo* models (Wegesser et al., 2009; Williams et al., 2013). It appears that macrophages are especially sensitive to toxicity from acute wood smoke particle (Franzi et al., 2011; Kubátová et al., 2006; Wegesser et al., 2009). Activation of

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NF-κB consequent upon phagocytosis of particles has been suggested as a possible pathway for wood smoke particles induced toxicity (Franzi et al., 2011; Williams et al., 2013), and diminution of antioxidant capacity (GSH depletion) may also contribute (Kubátová et al., 2006). Less efficient combustion conditions and higher organic content may also contribute towards more potent induction of cytotoxicity in airway cells (Bølling et al., 2012; Kocbach et al., 2008a; Kubátová et al., 2006).

Systemic oxidative stress and inflammation

It is unclear how wood smoke inhalation could cause systemic inflammation and uncertain how pulmonary oxidative stress and inflammation may spill over into the circulation. However, it has been demonstrated in a rat model that exposure to wood smoke by oral gavage causes increases in markers of oxidative stress and inflammation in the liver (Danielsen et al., 2010). Moreover, increases in MCP-1, a chemotactic cytokine, and HO-1 and 8-oxoguanine glycosylase (OGG1) increased in the liver 24 h after intratracheal instillation of wood smoke particles. These suggest that both inflammatory responses and the induction of antioxidant enzymes in the liver are caused by inhalation exposure to wood smoke.

Increases in the concentrations of markers of lipid peroxidation in circulation have been observed in other *in vivo* models consequent upon acute exposures to elevated levels of wood smoke (Park et al., 2004; Ramos et al., 2013). Inconsistent results have been observed in human experiments (Barregard et al., 2006, 2008; Danielsen et al., 2008; Forchhammer et al., 2012b; Sehlstedt et al., 2010; Stockfelt et al., 2012, 2013). Nonetheless, increases in mRNA levels of OGG1 in peripheral blood mononuclear cells (Danielsen et al., 2008), urinary concentration of 8-isoprostane (Barregard et al., 2006) and serum concentrations of inflammation markers have been observed in human subjects after experimental exposure to wood smoke compared to filtered air (Barregard et al., 2006, 2008; Stockfelt et al., 2012).

Exposure to elevated levels of wood smoke may cause neurological effects, and induce inflammatory responses and oxidative stress responses including lipid peroxidation and genotoxic DNA damage in brain tissues (Chen et al., 2007b; Gorgun et al., 2014; Lee et al., 2005a, 2010, 2011). These toxic effects have been linked to the ability of wood smoke to inhibit mitochondrial complexes and consequent augmentation of ROS generation, possibly from increased supply of nicotinamide adenine dinucleotide (NADH) from the glycolytic pathway (Gorgun et al., 2014; Lee et al., 2010). Glycolytic metabolism may serve as a compensatory mechanism for impaired mitochondrial respiration induced by wood smoke exposure (Gorgun et al., 2014; Lee et al., 2010). Overexpression of neuroglobin in mice has been shown to attenuate the inhibition of mitochondrial complexes, ameliorate the shift towards glycolytic metabolism and reduce oxidative DNA damage in brain tissue after exposure to wood smoke (Gorgun et al., 2014; Lee et al., 2011).

Inflammation and thrombosis are closely linked and it has been hypothesized that lower airway inflammation could induce production of coagulation in the liver (Barregard et al., 2006; Stockfelt et al., 2013). However, inconsistent results have been observed for the effects of acute wood smoke exposure on thrombosis in human exposure studies Both Barregard et al. (2006) and Stockfelt et al. (2013) observed a larger increase in plasma concentration of coagulation factor VIII after wood smoke exposure relative to filtered air exposure. However, Stockfelt et al. (2013) reported larger decreases in plasma concentration of fibrinogen and in platelet counts after exposure to wood smoke relative to exposure to filtered air. In addition, Hunter et al. (2014) reported no difference in platelet count, platelet activation and thrombus formation following experimental exposure to wood smoke relative to exposure to filtered air.

Immune suppression

Although initial activation of immune cells could result in a temporary bactericidal effect, immune suppression may be the long-term effect (Samuelsen et al., 2009). Whereas neutrophilic infiltration may result in some initial clearance of infection, the sensitivity of macrophages to cytotoxicity and the impairment by wood smoke exposure of their ability to phagocytize and kill bacteria may suppress immune response in the longer term (Samuelsen et al., 2009). Instillation of wood smoke particles reduced *in vivo* clearance of *Staphylococcus aureus* and Fc-receptor mediated phagocytosis (Zelikoff et al., 2002). In one study, macrophages from wood smoke exposed rabbits were less adherent, had reduced phagocytic ability, and a lower maximum number of associated bacteria (Fick et al., 1984). Although there was no change in macrophage phagocytic ability 24 h after exposure, there was an increase in bacterial load in lung tissue of wood smoke exposed mice inoculated with *Streptococcus pneumoniae* in another study (Migliaccio et al., 2013). Reduction in T-cell activation was also observed 2 h and up to 7 days after wood smoke exposure in macrophages co-cultured with $CD4^+$ cells accompanied by a reduction in the production of interferon-gamma (IFN-γ). Activation of the non-canonical NF-κB, RelB, with the possible involvement of the aryl-hydrocarbon receptor (AhR) activation by PAHs has been hypothesized as a possible pathway for suppression of macrophages (Migliaccio et al., 2013).

Tissue remodeling

Chronic wood smoke exposure has been identified as a cause of COPD in patients with the disease (González-García et al., 2012; Guzmán-Grenfell et al., 2011; Montano et al., 2004; Moran-Mendoza et al., 2008; Sandoval et al., 1993). *In vivo* experiments have recently been carried out to study the linkage (Ramos et al., 2009; Zou et al., 2014). Features that are characteristic of the pathogenesis of COPD were observed in the experiments. Increase in the expression and activities of metalloproteinases, which are involved in the degradation of the extracellular matrix, was observed in the chronic exposure (1–7 months) animal models (Ramos et al., 2009; Zou et al., 2014). Macrophage number in bronchoalveolar lavage increased after 1–4 months of exposure, while neutrophils

increased after 4–7 months of exposure (Ramos et al., 2009). Both cell types possess the secretor phenotype of metalloproteinases. Metalloproteinases can activate transforming growth factor beta (TGF-β) resulting in the proliferation of fibroblasts (Zou et al., 2014). In addition, the serum concentration of tissue inhibitor of metalloproteinase (TIMP-1) in rats increased after 4 or 7 months of exposure (Zou et al., 2014). This indicates a protease–antiprotease imbalance which is a hallmark of the disease.

The transition of epithelial cells to fibroblast phenotype or epithelial–mesenchymal transition in small airways has been proposed as a potential mechanism contributing to airway fibrosis in COPD. Evidence of this transition was observed *in vitro*. Increase in the expression of vimentin and type I collagen (mesenchymal markers) and a decrease in E-cadherin (epithelial markers) were observed in rat tracheal epithelial cells, while both types of markers were in the airway sub-epithelium *in vivo* indicating that bronchial fibroblasts may directly originate from epithelial cells in wood smoke exposed rats (Zou et al., 2014). The number of fibroblasts in the small airways also increased after wood smoke exposure.

Finally, emphysematous lesions also increased in the rats and guinea pig models after 7 months of exposure (Ramos et al., 2009; Zou et al., 2014). Collagen deposition was observed in the rat but not in the guinea pig model after 7 months of exposure. Twenty-eight days of exposure increased deposition of collagen protein, hydroxyproline, collagen I and III, in lung tissue in another rat model indicating that chronic wood exposure could cause pulmonary fibrosis (Zhu et al., 2012).

Interaction with the autonomic nervous system in the airways

Wood smoke interacts with vagal pulmonary afferent nerves. Rapidly adapting myelinated irritant receptors and nerve endings of the unmyelinated bronchopulmonary C-fibers can both be stimulated by wood smoke exposure (Lai & Kou, 1998a,b). Apparently, two distinct types of immediate ventilator responses are caused by the stimulation of these sensory receptors. The stimulation of the C-fibers causes inhibitory response observed as slow respiration after spontaneous wood smoke (~6 ml) inhalation by tracheostomy in Sprague–Dawley rats, while excitatory augmented inspiration resulted from the stimulation of irritant receptors (Kou et al., 1995). Pre-treatment with capsaicin which selectively blocks conduction by C-fibers abolished slow respiration in exposed animals, while cooling both cervical vagi at the higher temperature required for blocking conduction by only the myelinated fibers abolished augmented inspiration. Filtration of particles did not affect slow respiration while it prevented augmented inspiration in some of the exposed animals (Kou et al., 1995). Consequently, it can be concluded that the stimulation of C-fibers by the gas phase of wood smoke resulted in the inhibitory slow respiration response, and this effect is for example similar to that observed for acrolein (Faroon et al., 2008a,b). Gas and/or particulate phase components of wood smoke induced the excitatory augmented inspiration via the irritant receptors. Pre-treatment of animals with a hydroxyl radical scavenger or an iron chelator to prevent the formation of the radical abolished or attenuated both effects in most of the exposed animals (Ho & Kou, 2000; Kou et al., 1997).

Wood smoke induces bronchoconstriction as indicated by increased lung resistance and reduced dynamic lung compliance and hyper-responsiveness to itself or other bronchoconstrictors (Ho & Kou, 2002; Hsu & Kou, 2001; Hsu et al., 1998a,b, 2000). These effects are also mediated through the interaction of wood smoke with bronchopulmonary C-fibers. The involvement of both cholinergic mechanisms and tachykinins such as substance P and neurokinin A released due to the stimulation of C-fiber nerve endings has been determined (Ho & Kou, 2002; Hsu et al., 1998a,b). Pre-treatment of experimental animals with inhibitors of tachykinin and acetylcholine receptors attenuated bronchoconstriction effects. The endogenous production of free radicals subsequent to wood smoke exposure is also involved, as pre-treatment with a hydroxyl radical scavenger attenuated wood smoke induced airway hyper-responsiveness (Hsu et al., 2000). Tachykininergic and endogenous production of hydroxyl radicals have also been implicated in wood smoke-induced lung injury characterized by increased extravascular water, atelectasis and pulmonary parenchymal injury (Lin & Kou, 2000; Lin et al., 2001).

Cardiovascular effects

Various indicators of cardiovascular health in association with wood smoke exposure have been studied in a few human experimental studies. Non-smoking healthy human subjects had higher central arterial stiffness measures (augmentation index, augmentation pressure and pulse wave velocity) and decreased variability in the time domain of the electrocardiogram 1 h after exposure to wood smoke with an average PM_1 concentration of ~300 μg/m^3 for 3 h compared to filtered air exposure (Unosson et al., 2013). There were no changes immediately or 20 h after wood smoke exposure in both the time domain and repolarization variables of the electrocardiogram in another human experimental study (2 h exposure to particulate matter concentration of ~400 μg/m^3) (Ghio et al., 2012). Marginally significant minimal changes were observed in the frequency domain measures, while a significant 16.8% increase in maximal heart rate was observed in this second study. Compared to exposure to filtered air, there was no change in central arterial stiffness measures over a 24-h period following experimental 1-h exposure of firefighters to wood smoke with an average PM_1 concentration of 1115 μg/m^3 (Hunter et al., 2014). No change was observed in vascular function as measured by venous occlusion plethysmography with intra-arterial infusion of vasodilators 4–6 h after wood smoke exposure among the firefighters. Similarly, no change in vascular function as measured by peripheral arterial tonometry was observed among non-smoking healthy subjects immediately, 6 or 20 h following 3 h exposures to average $PM_{2.5}$ concentrations of 200 and 354 μg/m^3 (Forchhammer et al., 2012b). Timing of measurements and the healthy worker effect in the case of the firefighter study were given as possible reasons for the negative findings and the inconsistent results between the studies (Hunter et al., 2014).

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Table 6. Evidence summary.

Class of effects	Confidence level	Basis for rating
Public		
Acute respiratory	Strong evidence	Consistent results across epidemiological studies of different designs and across different study regions; dose-response with ambient air PM concentration; plausibility indicated by results of epidemiological studies of ambient PM and experimental studies of wood smoke.
Acute cardiovascular	Weak evidence	Inconsistent results with few positive findings from small number of ecological epidemiological studies; few relevant experimental studies with inconsistent results with some positive findings; plausibility indicated by results of ambient PM studies.
Birth outcome	Not enough evidence to conclude	Positive results from one ecological study; applicability of evidence from related exposure situation limited by various factors (lack of specificity in exposure, difference in exposure pattern, undefined temporality); no experimental evidence.
Wildland firefighter		
Acute respiratory	Weak evidence	Some effects observed in a few wildland firefighter studies; strong evidence from related exposure situation in humans; plausibility of effects supported by experimental studies; although lung function decline across the work-shift was observed in most studies, controls were not used to account for changes that may have otherwise occurred; no difference was observed in lung function decline between exposure and no exposure days in the only study that included controls.
Acute cardiovascular	Not enough evidence to conclude	Virtual lack of study among wildland firefighters; applicability of evidence from related exposure situation limited by various factors (lack of specificity in exposure, difference between public and healthy wildland firefighter; undefined temporality); few relevant experimental studies with inconsistent results.
Chronic respiratory	Not enough evidence to conclude	Virtual lack of study among wildland firefighters; applicability of evidence from related exposure situation limited by various factors (lack of specificity in exposure, difference in exposure pattern, undefined temporality); very few relevant experimental studies.
Chronic cardiovascular	Not enough evidence to conclude	Virtual lack of study among wildland firefighters; weak but limited evidence from related exposure situation; lack of relevant experimental studies.

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Three possible mechanisms that have been proposed for the cardiovascular effects of particulate matter inhalation exposure could apply to wood smoke. These include the spilling over of local airway inflammation from the lungs into the vasculature, translocation of ultrafine particles into circulation from the airways and the interaction with the autonomic nervous system through the stimulation of pulmonary vagal afferents by wood smoke constituents (Brook et al., 2002, 2010; Ghelfi et al., 2008; Kido et al., 2011; Mills et al., 2009). The first two pathways could also be involved in systemic oxidative stress and inflammation resulting from inhalation exposure to wood smoke.

Summary of evidence

The summary of evidence for the hazard associated with wildland fire smoke is presented in Table 6. The evidence that acute wildland fire smoke exposure adversely impacts respiratory health among the general public is strong. Although most of the evidence is from ecological studies without individual level measurements of exposure and outcomes, positive findings have been reported in cohort studies for COPD symptoms and various indicators of worsening of health in persons with asthma (Henderson et al., 2011; Johnston et al., 2006; Sutherland et al., 2005). Results from studies from different regions of the world (North and South America, Southeast Asia and Australia) are mostly consistent for positive findings for acute responses in persons with pre-existing diseases or for the development of respiratory infections resulting in hospital admissions, emergency room or physician visits. Dose–response relationships between exposure during wildland fire events to particulate matter, a major health hazard in wood smoke and respiratory end-points were also determined in many of the studies. Furthermore, persons who are more susceptible to adverse effects of wildland fire smoke due to pre-existing conditions would more likely take preventive measures to reduce their exposures during wildfire events. Such behavior would result in exposure misclassification which would bias estimates for effects sizes towards the null. This might have contributed to the null findings in some of the ecological studies.

No study of the effect of wood smoke on an experimental model with pre-existing airway disease was identified. However, as noted earlier, there is a preponderance of evidence from *in vivo* studies that wood smoke exposure could result in neutrophilic inflammation in the lungs and bronchoconstriction induced via tachykinin receptors in the airways. These responses could contribute to the exacerbation of COPD and asthma, respectively (Ling & Van Eeden, 2009; Papi et al., 2006; Ramalho et al., 2011). Mechanistic studies also reveal that wood smoke exposure could result in immune suppression subsequent to the initial pro-inflammatory response. This could plausibly explain the increases in medical visits for respiratory infections in association with wildland fire smoke exposure. Effects of wood smoke exposure on airway inflammation were not observed in most human experiment studies. The contrasting results with other types of studies could have been partly due to the use of healthy subjects in the human experiment studies, differences in exposure conditions and possibly differences in the physicochemistry of the emissions contributing towards the exposure. We thus conclude with high level of confidence that wildland fire smoke exposure is a respiratory hazard to the general public.

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Ambient PM concentration is associated with cardiovascular morbidity and mortality (Brook et al., 2010). However, results for the cardiovascular effects of PM exposure specific to wildland fire smoke among the general public is less unequivocal. Most of the studies focus on acute outcomes and reported null findings. Significant positive findings were reported for associations between measures of particulate matter exposure and hospital admissions for hypertension with respect to agricultural burns and emergency room visits for heart failure during a peat fire event (Arbex et al., 2010; Rappold et al., 2011). While two of the papers reported non-significant protective effects in association with wildland fire associated PM (Hanigan et al., 2008; Johnston et al., 2007), five others reported non-significant positive effects for various cardiovascular health end-points (Crabbe, 2012; Delfino et al., 2008; Duclos et al., 1990; Morgan et al., 2010; Rappold et al., 2011). However, all but (one cohort and one case-crossover) of the 13 studies identified for cardiovascular health end-points were based on the ecological time-series study design. These studies could therefore have been limited by probable misclassification of exposure (including avoidance by those with preexisting condition) and the lack of power to detect small differences on a population level. Consequently, we conclude that there is currently weak evidence that wildland fire smoke exposure is a cardiovascular hazard to the general public. No effect of wood smoke exposure on systemic inflammation, which contributes towards the precipitation of cardiovascular events, was observed in most of the human experiment studies that have been conducted. Yet, the use of healthy subjects limits the generalization of the results to the general population, and acute systemic inflammation in response to occupational wood smoke exposure has been observed among wildland firefighters.

Although there is evidence that cumulative exposure results in progressive lung function decline during the burn season among wildland firefighters, it is presently unclear whether this decline persists across off-seasons or whether this decline is larger than what would be expected for an average individual. Respiratory symptoms and biomarkers of airway and systemic inflammation have also been observed to increase in association with occupational wildland fire smoke exposure in a few studies. However, results in many of the studies are limited by small sample sizes and the determination of outcomes through self-reporting. Acute airway and systemic oxidative stress and inflammation, and effects on the autonomic nervous system were observed consequent upon wood smoke exposure in *in vivo* studies, but findings were mostly not positive in human experiments involving healthy subjects (firefighters in one study). The sample sizes in the human experiments were small by design and exposure was for limited periods. Emissions were also generated under combustion conditions very different from what is typical for the wildland firefighters. Given the significant differences in emissions of smoke constituents among combustion phases and different fuel/vegetation types, this is a critical deficiency in broadly applying results to the wildland firefighter population and the general public.

No study of long-term effects of continuing occupational smoke exposure among wildland firefighters was identified. Nevertheless, chronic exposure to household air pollution due to the residential combustion of wood is associated with COPD and chronic bronchitis. Such exposures have also been linked to acute lower respiratory infections, and possibly asthma, tuberculosis and lung cancer. However, the differences in combustion conditions and emissions, exposure patterns, susceptibility status and population characteristics make extrapolation of results of household air pollution studies to wildland firefighters difficult. Exposures are typically more frequent and occur over longer durations for household air pollution, while firefighters are more likely to be male and a healthier working population. Wildland firefighters are also more likely to be exposed to emissions generated under better oxygenated combustion conditions with a higher heat release rate. It is also unclear how immune suppression and fibrotic/emphysema-like effects observed in relation to wood smoke exposure *in vivo* studies may be interpreted with respect to wildland firefighter occupational exposure since exposure patterns in these studies are not reflective of what the wildland firefighter experiences. Taken together, we conclude that there is weak evidence for acute respiratory and systemic effects of occupational wildland fire smoke among wildland firefighters. However, it is unclear what these acute pulmonary and systemic physiological responses translate to in terms of the occurrence of acute and chronic diseases among wildland firefighters. Furthermore, the current lack of studies of health end-points of known clinical significance among this working population leads us to conclude that there is not enough information to determine the long-term cardiovascular and respiratory hazard of cumulative occupational wildland fire smoke exposure among wildland firefighters. A recent study demonstrated that organic constituents of combustion-generated ambient aerosols can aggravate and promote atherosclerosis and cardiovascular disease in a cumulative fashion (Keebaugh et al., 2015). The freshly emitted smoke from woodland fires may have greater percentage of toxic organic compounds than ambient particles, and thus might represent a greater potential health risk to firefighters over the course of their careers.

There is a need for studies of clinically significant health end-points including the incidences of diseases in relation to occupational wildland fire smoke among this population. Wildland firefighters would be expected to be healthier than the average population, and they have a very different wildland fire smoke exposure pattern compared to the exposure of the general public which is generally at a lower concentration and less frequent, or to exposure of individuals to smoke due to residential combustion of wood which typically is more continuous. In addition, the tasks in wildland firefighting can lead to greater exposures to particulates as the job is physically demanding and require elevated ventilation rates, which can result in substantially increased doses of smoke to the respiratory tract (Danielsen et al., 2008). Rothman et al. (1991) demonstrated that recent cumulative exposures were more strongly associated with greater changes in lung function, and it would be important to note if such was the case regarding cardiovascular function. The cumulative exposure effect previously mentioned would be particularly important for those who are at most risk occupationally as it is

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unknown whether cessation of exposure among wildland firefighters during the off-season may allow for recovery and reversibility of effects (Danielsen et al., 2008). Consequently, it is hard to extrapolate results from other populations to wildland firefighters.

Evidence for effects of wildland fire smoke exposure on birth outcomes is currently very limited. Only one study has so far been conducted with results of a small effect on birth weight. Extrapolation of the results from household air pollution studies is difficult for some of the same reasons that were discussed above for cardiovascular health end-points among the general public and health effects among wildland firefighter.

Conclusion

There is strong evidence that acute episodic wildland fire smoke exposure is associated with respiratory effects among the general population, while current evidence of an association with cardiovascular effects is weak. Most of the research of health effects among the general population that has been conducted is based on the ecological time series design, and relies on ambient air concentrations of PM as the measure of exposure and medical visits or mortality as the measure of health outcome. The inability to assess exposure on the individual level within this study design limits the power to detect small effect sizes that may be associated with an episodic event such as wildfires. The greater likelihood that protective action will be taken by susceptible persons would reduce their exposure, and result in misclassification of their exposure and the bias of effect sizes towards the null. Perhaps accounting for pre-existing disease in such analysis could help ameliorate this problem. The effect windows used in the studies are typically less than 6 days. However, effects may be delayed and patients may not make medical visits until symptoms become severe. As such effects of wildland fire smoke exposure may be underestimated especially for respiratory outcomes (Delfino et al., 2008). In addition, cardiovascular and respiratory effects of wildland fire smoke could be due to other components apart from PM (Delfino et al., 2008). Such association could be explored as has been done for typical ambient air pollution studies.

The available research on wildland firefighter occupational exposure is currently very limited, and there is not enough information to make conclusions with regards to cardiovascular and chronic respiratory effects. Only acute physiological responses have been investigated without any determination of the clinical significance of findings. Therefore, a conclusion could only be made with respect to acute respiratory effects. The evidence for wildland fire being an acute respiratory hazard for wildland firefighters is weak. The pattern of wildland firefighter occupational exposure is very different from those of the populations from which evidence of chronic effects are available. Their exposure is more frequent than that of the general public to wildland fire smoke but more intermittent than the exposure experienced by individuals in the case of household air pollution. In addition, the healthy worker effect makes the extrapolation of results difficult. Consequently, there is need to conduct studies of clinically significant health end-points among this population. Investigating such effects in association with the intermittent seasonal nature of wildland firefighters may help elucidate possible associations between exposure and disease initiation and/or progression. Experimental models with exposure patterns, fuel mix and combustion conditions similar to the populations of interest in this review could also help inform on the health effects of wildland fire smoke exposure.

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Declaration of interest

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