Chapter 2

Outdoor Air Pollution and Arterial Hypertension

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Additional information is available at the end of the chapter

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Abstract

Air pollution is a major environmental risk factor. There is accumulating evidence that air pollution could induce elevated blood pressure and potentiate hypertension. Acute elevations in the outdoor air pollution levels can trigger immediate or shortly delayed increases in arterial blood pressure. Moreover, few studies suggest that short-term increases in the levels of particulate and gaseous pollutants could lead to an acute onset of hypertension. Prolonged exposure to outdoor air pollution is associated with elevated blood pressure. Furthermore, some longitudinal studies have linked long-term exposure to air pollution with the incidence of hypertension. Various components of air pollution, such as inhalable particulate matter ($PM_{2.5}$, PM_{10}), nitrogen oxides, sulfur dioxide, and ozone, have shown associations with blood pressure in some studies. The hypothesized underlying mechanisms include inflammatory reactions and oxidative stress in lungs and in systemic circulation, imbalance of autonomous nervous system, and pathologic changes in vascular endothelium. In addition to "traditional" susceptible groups such as elderly individuals or patients with chronic diseases, children and pregnant women could be especially susceptible to the adverse effects of air pollution. The interplay of air pollution with the related environmental exposures, such as traffic noise and climate change, should be investigated further.

Keywords: ambient air pollution, particulate matter, nitrogen oxides, ozone, sulfur dioxide, cardiovascular effects of air pollution, high blood pressure, hypertension

1. Introduction

Atmospheric air pollution is a major environmental risk factor. It was estimated that outdoor air pollution caused 3 million premature deaths worldwide in 2012 [1]. Air pollution is a

heterogeneous mixture of substances, including particles and gaseous compounds, which are not normal air constituents and can harm living organisms.

Airborne particles, or particulate matter (PM), is a heterogeneous mixture of solid and liquid particles suspended in air [2]. PM is classified by its aerodynamic diameter, ranging from ≤0.1 micrometers (μm), which is comparable to the size of some molecules or smaller viruses, to very large particles of >100 μm at the limit of vision [3]. Particles ≤10 μm in diameter (PM_{10}), called thoracic, or inhalable particles, can be inhaled into lungs, while larger particles do not get past the nasopharynx [3]. Thoracic particles consist of fine, ultrafine, and coarse particles. Fine particles are small thoracic particles with aerodynamic diameter ≤ 2.5 μm ($PM_{2.5}$). The ultrafine particles (UFP) are a subfraction of fine PM with a diameter ≤ 0.1 $\mu g/m^3$. Coarse fraction particles include the thoracic particles, larger than $PM_{2.5}$. Smaller particles can be inhaled deeper into the respiratory tract and reach the alveoli. It is also hypothesized that very small particles could directly translocate into the circulation [4]. The chemical composition of the particles varies greatly. The most common constituents are nitrates, sulfates, carbon, organic compounds (such as polycyclic aromatic hydrocarbons), biological compounds (such as bacterial endotoxin and cell fragments), and metals [2]. Both the size and the chemical composition of PM change over time and space [2]. Fuel and biomass combustion produces large amounts of so-called carbonaceous PM, the most important combustion by-products besides carbon dioxide [5]. One of the fractions of the carbonaceous PM, called black carbon (BC), is a commonly used marker of traffic-related emissions.

Gaseous compounds comprise the second major group of air pollutants. Nitrogen oxides, cumulatively referred to as NO_x, consist of nitrogen dioxide (NO_2) and nitrogen monoxide (NO), and a lesser proportion of other nitrogen oxides and nitrogen-containing acids [2]. NO_x originates from fossil fuel combustion in motor vehicles and from industrial processes, such as power generation. It can also be formed naturally, e.g., through bacterial metabolism of nitrogen-containing compounds, from fires, volcano eruptions, etc., but to a lesser extent, than from anthropogenic sources. Tropospheric ozone (O_3) is a highly reactive gaseous secondary pollutant formed in photochemical smog reactions in the presence of sunlight, NO_x, and reactive hydrocarbons. O_3 can be formed from NO_2 by photolysis, producing NO [2]. O_3 can be scavenged by NO, regenerating NO_2 and O_2 [2]. Sulfur dioxide (SO_2) is a highly irritating gas with pungent odor and taste. It originates from power generation and industrial processes including combustion of sulfur-containing fuels in power generation, as well as from diesel car engines, household heating, etc. [2]. The formerly high levels of SO_2 in Western countries have reduced substantially over the past decades, through efficient technologies to remove sulfur from fuel prior to combustion. Similar trend of a rapid decline of the ambient SO_2 levels has been recently observed in China [6]. However, in other regions, such as India, the emission of SO_2 is still growing [6]. SO_2 and NO_x are major precursors for acid rains and secondary particle formation. Other gaseous components of air pollution include carbon dioxide (CO_2) or, in case of incomplete combustion, carbon monoxide (CO), volatile organic compounds (VOCs), and ammonia (NH_3).

Air pollution is an important risk factor for cardiovascular disease. More than a decade ago, the American Heart Association published a statement on the cardiovascular effects of air pollution, concluding that exposure to PM contributes to cardiovascular morbidity and

mortality [2]. Based on the reviewed evidence, the authors concluded that short-term exposure to elevated levels of PM leads to increases in cardiovascular mortality and morbidity, reflected in elevated hospital admissions for cardiopulmonary diseases [2]. Moreover, the longer duration of exposure can reduce overall life expectancy by few years [2]. In the updated review of the literature [7], published few years later, the authors concluded that there is a causal relationship between exposure to $PM_{2.5}$ and cardiovascular morbidity and mortality. The authors emphasized that acute exposure to $PM_{2.5}$ over a few hours to weeks can trigger cardiovascular disease–related mortality and nonfatal events, while long-term exposure (over months or years) contributes to a higher cardiovascular mortality and reduced life expectancy [7]. It is also hypothesized that long-term exposure to air pollution may have a greater effect on cardiovascular disease than the short-term exposure [7].

There is a growing interest to the effect of air pollution on traditional cardiovascular risk factors, such as hyperglycemia, dyslipidemia, and high blood pressure (BP). On one hand, the individuals with these risk factors might be particularly vulnerable to adverse cardiovascular effects of air pollution [7]. On the other hand, air pollution exposure could potentiate the development of these risk factors; thus, they could act as mediators of the adverse effect of air pollution on CVD [7].

High BP is, alongside air pollution, one of the top five risk factors for mortality and disability worldwide [8]. According to the recent Global Burden of Disease Study, 10.4 million deaths and 208.1 million disability adjusted life years were attributed to high systolic BP in 2013 globally [8]. It was estimated that in adults aged 40–69 years, an increase in systolic BP by 20 mmHg or in diastolic BP by 10 mmHg was associated with a twofold or an even higher difference in death rate from vascular events, such as ischemic heart disease or stroke [9]. Even a relatively small reduction in BP is associated with substantial health benefits. For example, a decrease in the systolic BP by 2 mmHg can reduce stroke mortality by 5%, coronary heart disease (CHD) mortality by 4%, and total mortality by 3% [10]. The same reduction in diastolic BP was associated with a 6% decrease in the risk of coronary heart disease and 15% reduction in the risk of stroke and transient ischemic attack [11]. A factor with a relatively small impact on BP, but affecting the large proportion of the population, is therefore of high importance for public health.

There is evidence that air pollution could induce elevated blood pressure and potentiate hypertension [3]. Short- and long-term elevations in outdoor $PM_{2.5}$ have been linked to higher BP, hypertension, and a raise in emergency visits for hypertension to hospitals [12]. Different components of air pollution, such as gases, larger or smaller particles, carrying various chemical substances on their surface, could be responsible for blood pressure elevation. Inflammatory and pro-oxidative reactions, triggered by pollutants in lungs and later in systemic circulation, imbalance of autonomous nervous system, and pathologic changes in vascular endothelium could be underlying pathways of this elevation. Despite extensive research in the past decades, the evidence is still quite heterogenic with regard to the study methods, population characteristics, pollutants' assessment and composition, research questions, etc. We aim to provide a comprehensive review of the available literature on the evidence of short- and long-term effects of air pollution on BP and hypertension in the general population and susceptible population groups, discuss pathophysiologic mechanisms, which could be responsible for the prohypertensive effect of air pollution, and consider related environmental factors.

2. Short-term effects of air pollution

A growing number of studies have investigated the short-term effects of ambient air pollutants on blood pressure and hypertension. We identified 30 studies on short-term associations of air pollution with BP or hypertension, performed in healthy volunteers or in general population [13–42]. Sixteen studies were conducted in North America [14, 16–19, 21, 22, 24, 25, 32, 34, 36–39, 43], four studies were conducted in South America [13, 23, 35, 41], four studies took place in Europe [28–31], and six studies were performed in Asia [15, 20, 26, 27, 40, 42]. While the vast majority of the publications have focused on acute changes in BP [14–25, 28, 31–35, 37–39, 42, 44], five studies have investigated hypertension as outcome [13, 26, 27, 36, 41], and one study has included both BP and hypertension [29]. Consistent with the previous reviews [7, 12], we found that in most of the investigated studies a transient increase in BP following short-term exposure to air pollution or some of its components was observed. Here, we briefly summarize the observed results by the type of the respective air pollutant.

2.1. Black carbon (soot)

Short-term associations of BC with BP were investigated in five studies [31, 32, 34, 38, 39]. Four of them reported positive associations with BP [31, 32, 34, 45], while one study found no associations [38]. The exposure duration ranged from very acute (2 hours) to a longer period (7 days). A controlled two-hour exposure to BC from traffic was positively associated with postexposure elevation in systolic BP (1.22 mmHg (95% confidence interval (CI): 0.28, 2.17) per interquartile range) [31]. In a panel study with 28 nonsmoking seniors, 24-hour mean BC was positively associated with systolic (estimated increase of 3.2 mmHg (standard error (SE) 1.46 mmHg) per 487 ng/m^3 BC) and diastolic (4.32 mmHg (1.33)) BP [32]. Weekly average BC concentration was associated with increased BP in a cohort of 461 elderly men: per increase in BC by 0.43 μg/m^3, the estimated increase in systolic BP was 1.46 mmHg (95% CI: 0.10, 2.82), and the estimated increase in diastolic BP was 0.87 mmHg (95% CI: 0.15, 1.59) [34]. Similar positive associations were reported in a reanalysis of this cohort with a larger sample of 789 elderly men [39]. No study has investigated the short-term associations of soot with hypertension.

2.2. Coarse particles: PM_{10}, total suspended particles (TSP)

In total, 12 studies investigated the association of short-term PM_{10} with BP and hypertension [15, 16, 18–20, 23, 27, 28, 31, 35, 36, 42]. Nine of them observed positive associations [15, 16, 18–20, 27, 31, 35, 36]. For example, in a study with 120 healthy volunteers, a 10 μg/m^3 increase in 8-day ambient PM_{10} was associated with an increase in systolic BP by 0.98 mmHg (95% CI: 0.34, 1.61) and an increase in diastolic BP by 0.71 mmHg (95% CI: 0.18, 1.24) [15]. Similarly, increased systolic and diastolic BP were observed in few controlled exposure studies with healthy volunteers, following short-term exposure to coarse concentrated ambient particles (CAPs) [16, 18, 19].

Few studies observed positive associations of short-term PM_{10} elevations with hypertension: for example, a 10 μg/m^3 increase in ambient PM_{10} was associated with an odds ratio (OR) of

1.060 (95% CI: 1.020, 1.101) for hospital admissions for hypertension in China [27]. A similar effect estimate was reported in a comparable study in Canada [36].

Two studies assessed coarse PM exposure as total suspended particles (TSP) [13, 29]. This measure stands for the fraction of particles with diameters <50–100 μm and could be seen as a crude surrogate for PM_{10}. In a study with 2607 adults from a population-based MONICA cohort in Germany, 24-hour and 5-day mean TSP was positively associated with systolic BP: for example, an increase by 70 $\mu g/m^3$ in the 5-day mean TSP was associated in an increase in systolic BP by 1.96 mmHg (95% CI: 0.75, 3.15) [29]. The authors also observed a weaker positive relationship with diastolic BP and a positive association with hypertension: OR 1.63 (95% CI: 1.21, 2.20). [29]. Similarly, in an ecological time-series study in Brazil, TSP generated from sugarcane burning was associated with an increase in hypertension-related hospital admissions [13].

Interestingly, two studies with the same professional group (traffic controllers) from Brazil reported divergent results: one study observed an acute increase in systolic and diastolic BP [35], while another study reported no associations with PM_{10} [23]. A study with 2612 elderly subjects in France reported an inverse association of ambient PM_{10} with systolic BP: an increase in PM_{10} during the fifth lag hour by 10 $\mu g/m^3$ was associated with a decrease in systolic BP by 1.12 mmHg (95% CI: −1.90; −0.30) [28]. Similarly, inverse associations of 1- to 3-day lag PM_{10} with systolic BP and pulse pressure were observed in a large population-based study in Taiwan (N = 9238) [42].

2.3. Fine and ultrafine PM

The short-term associations of ambient fine particles ($PM_{2.5}$) with BP and hypertension were investigated in 17 studies [14–17, 22, 24, 25, 27, 30, 32–34, 36–38, 40, 41] and overall showed more mixed results, than studies with coarse particles. Four studies with healthy volunteers observed positive associations with at least one BP metrics [16, 32, 37, 40]. Moreover, two studies with larger population-based samples observed similar results [14, 24]. An increase in 5-day mean $PM_{2.5}$ by 10 $\mu g/m^3$ was associated with an increased systolic BP (4.7 mmHg, $p = 0.05$) and pulse pressure (4.04 mmHg, $p = 0.03$), and no association was observed with diastolic BP in a random sample of 347 residents of Detroit, USA [24]. Similar results were reported in an analysis with a population-based cohort from six US communities (N = 5112): a 10 $\mu g/m^3$ increase in a 30-day mean $PM_{2.5}$ was associated with an increase in pulse pressure by 1.12 mmHg (95% CI: 0.28, 1.97) [14]. Likewise tendency, though not statistically significant, was found with systolic BP (0.99 mmHg; 95% CI: –0.15, 2.13), while no association was observed with diastolic BP [14].

The associations of short-term exposure to $PM_{2.5}$ with hospital admissions for hypertension were investigated in three studies, all reporting positive findings [27, 36, 41]. A study in Canada found that per increase in 3-day lag $PM_{2.5}$ concentration by 6.2 $\mu g/m^3$ the estimated OR for hospital admissions for hypertension was 1.07 (95% CI: 1.01, 1.11) [36]. Similarly, a study in Brazil reported a positive association of ambient $PM_{2.5}$ with hospital admissions for hypertension: per 10 $\mu g/m^3$ increase in $PM_{2.5}$ lags 0–4, the estimated relative risks (RR) were 1.018–1.021 ($p < 0.05$) [41]. A study in China also reported a very comparable estimate: p OR 1.084 (95% CI: 1.028, 1.139) per 10 $\mu g/m^3$ increase in short-term $PM_{2.5}$ [27]

Some studies report different results by subgroup or by exposure measurement. For example, a positive association of $PM_{2.5}$ CAP exposure with systolic BP was observed in a group of 12 healthy volunteers, while in the group of 12 participants with asthma, this association was inverse [25]. One study observed no association with ambient $PM_{2.5}$ from an urban monitoring station, but found a positive association of personal-level exposure, measured with personal environmental monitors [17]. In another study, the positive association of outdoor $PM_{2.5}$ with systolic BP was observed only in subjects taking antihypertensive medication (N = 57 (65% of the total sample) [30]. No associations with BP were reported in five studies [15, 22, 33, 34, 38].

Only three studies so far have investigated the associations of ultrafine particles (UFP) with acute changes in BP: two of them reported positive associations with systolic BP [31] and pulse pressure [33], while one study found no association [38]. We could not find studies on the association of UFP with hypertension.

2.4. Ozone

Very few studies have investigated the acute effects of gaseous pollutants on BP and hypertension. The effect of short-term O_3 exposure was investigated in four studies so far [20, 33, 38, 42]. In a large population-based cohort from Taiwan (N = 7578), an increase in 3-day O_3 by 12.15 particles per billion (ppb) was associated with an increase in diastolic BP by 0.37 mmHg (95% CI: 0.04, 0.69); no association with systolic BP was found for O_3 [20]. However, in a similarly large cohort from Taiwan (N = 9238), 1- to 3-day lag O_3 was associated with decreased systolic BP and pulse pressure, and not associated with diastolic BP [42]. In a small study with healthy female volunteers from Canada, 3-hour exposure to O_3 was positively associated with both systolic and diastolic BP: the estimated increase per 24 ppb O_3 was 2.49% (95% CI: 0.141, 4.84) and 3.26% (95% CI: 0.012, 6.51) systolic and diastolic, respectively [38]. No association with BP was observed in a controlled exposure study with air pollution from a steel plant [33].

2.5. Nitrogen oxides

The acute effects of nitrogen oxides on BP and hypertension have been investigated in eight studies so far [22, 23, 26, 31, 33, 36, 38, 42]. Positive associations with BP and hypertension were observed in four studies [22, 26, 31, 36]. For example, in a study with 39 healthy volunteers and exposure to air pollution at a bus stop in Canada, an increase in NO_2 by 1 ppb resulted in an increase of systolic BP by 0.44 mmHg ($p < 0.05$) [22]. Similarly, in a study with 28 healthy volunteers in Spain, elevated NO_x was associated with higher systolic BP [31]. Two studies reported short-term associations with quite comparable OR estimates: per increase in NO_2 by 10 $\mu g/m^3$, the estimated OR was 1.101 (95% CI: 1.038, 1.168) in a study from China [26], and per increase in NO_2 by 12.8 ppb, the estimated OR was 1.06 (95% CI: 1.00, 1.12) in a study from Canada [36]. Three studies reported no associations of NO_x with BP [23, 33, 38]. Interestingly, discordant associations with different BP metrics were observed in a large Taiwanese cohort (N = 9238): per 14.9 ppb of NO_2 at lag day 2, diastolic BP increased by 1.15 mmHg (95% CI: 0.56, 1.73), while systolic BP and pulse pressure decreased by 0.87 mmHg (95% CI: −1.74, −0.01) and −1.56 mmHg (95% CI: −2.25, −0.88), respectively [42].

2.6. Sulfur dioxide

The short-term associations of SO_2 with BP and hypertension were investigated in six studies [23, 26, 29, 33, 36, 42], and five of them reported positive associations [23, 26, 29, 36, 42]. In a large population-based cohort from Germany (N = 2607), an increase in 5-day SO_2 by 75 μg/m^3 was associated with an increase in systolic BP by 1.07 mmHg (95% CI: 0.41, 1.73) [29]. Similar findings were reported in a population-based study in Taiwan (N = 9238): per increase in a 2-day lag SO_2 by 2 ppb, systolic BP increased by 0.32 mmHg (95% CI: 0.06, 0.59), and diastolic BP increased by 0.79 mmHg (95% CI: 0.61, 0.97) [42]. However, an inverse association with pulse pressure was reported in the latter study [42]. Similar to NO_2, SO_2 elevations were positively associated with hospital admissions for hypertension in two studies: per 10 μg/m^3 increase in daily SO_2 concentration, the estimated OR was 1.037 (95% CI: 1.004, 1.071) [26], and per increase in lag 3 SO_2 by 2.3 ppb, the estimated OR was 1.04; (95% CI: 1.00, 1.08) [36].

2.7. Other exposures

For the short-term exposure to CO, mostly null effects were reported with BP and hypertension as outcomes [29, 33, 36]. Inverse associations of short-term exposure to CO with systolic BP and pulse pressure, and null effects with diastolic BP were reported in one study [42]. Controlled exposure to diesel exhaust was associated with increased systolic but not diastolic BP in a study with 49 nonsmoking adults [21].

3. Long-term effects of air pollution

The number of studies on long-term effects of air pollution on BP is smaller, than the number of studies focusing on short-term effects, but has also increased tremendously in the last years. We identified 17 publications presenting individual studies investigating the long-term associations of air pollutants with arterial BP and hypertension [46–62]. Some of these studies have been included to the previous reviews [7, 12]. In addition to one cohort study, there has also been one metastudy, performed as a part of the European Study of Cohorts for Air Pollution Effects (ESCAPE; [63–65]). The ESCAPE study aimed to investigate the long-term effects of ambient air pollution on human health in Europe. More than 40 cohorts from 17 countries in Europe participated in the ESCAPE study [65]. Ambient air pollution concentrations in the participating cohorts were assessed according to the standard ESCAPE procedure [63]. The statistical analyses in ESCAPE contained two stages: (1) cohort-specific analyses using uniform statistical protocols and centrally developed analysis codes and (2) centrally conducted meta-analyses, followed by the publication of results in the peer-review articles.

Of the individual studies, seven were performed in North America (Canada and USA; [46, 56, 57, 59, 61, 62, 66, 67], five were performed in Southeast Asia (China and Taiwan; [47–51], and five studies were performed in Europe (Denmark, Germany, and Spain; [52, 53, 55, 58, 68]. The study samples in most studies included men and women [47–52, 54, 55, 58, 61, 66, 69]. Two cohorts included only women [56, 57, 59, 62], and one cohort included only men [46].

Most studies on long-term associations of air pollution with BP investigated systolic and diastolic BP as outcomes, and one study [59] investigated mean arterial pressure and additionally pulse pressure. The investigated exposures included $PM_{2.5}$, PM_{10}, soot, O_3, NO_x, and SO_2. All of the individual studies reported a statistically significant association with at least one of the BP parameters. However, only six studies observed concordant results with both systolic and diastolic BP [46, 48–50, 54, 58, 69]. In five studies, results varied across the BP metrics [47, 51, 52, 55, 59].

Nine studies investigated associations of air pollution with prevalent hypertension [47, 49–52, 55, 59, 63, 66, 67], five studies assessed only incident hypertension [56, 57, 61, 62, 64], and two studies analyzed both incident and prevalent hypertension [54, 58]. The majority of these studies reported positive associations of at least one pollutant with hypertension [49, 51, 55, 57, 61, 64, 66], indicating that air pollution is likely to have a prohypertensive effect. However, some studies observed negative [54, 57] or null [47, 52, 53, 58, 59, 63] associations.

3.1. Black carbon (soot)

Two markers of soot were used in the studies on long-term associations with BP and hypertension: BC [46] and absorbance $PM_{2.5}$ [47, 55, 63, 64]. Absorbance $PM_{2.5}$ is measured as the blackness of the $PM_{2.5}$ exposed filter in the particle sampler, determined by measurement of light reflectance. BC was positively associated both with systolic and diastolic BP [46]. The estimated associations with BP, adjusting for relevant confounders, were as follows: increase by 2.64 mmHg systolic (95% CI: 1.47–3.80) and 2.41 mmHg diastolic (1.77–3.05) per 0.32 $\mu g/m^3$ increase in black carbon [46]. Absorbance $PM_{2.5}$ was associated only with diastolic BP in single cohort analysis: 1) per increase by 10^{-5}/m, estimated increase in systolic BP was 0.15% (−0.49, 0.78) and in diastolic BP, 0.62% (0.24, 0.99); 2) per increase by 0.2 10^{-5}/m, the estimated mean change in systolic BP was 0.5% (95% CI: −0.1; 1.0), and in diastolic BP, 0.6% (95% CI: 0.1; 1.1; [55]). In the ESCAPE meta-analysis, where the association was assessed in medicated and nonmedicated participants separately, no association of long-term concentrations of absorbance $PM_{2.5}$ with BP was observed [63].

At 0.05 level of significance, none of the studies found an association with prevalence of hypertension. However, a weak positive relationship was observed in a German cohort: per increase by 0.2 10^{-5}/m in absorbance $PM_{2.5}$, percent change in hypertension prevalence was 10.8% (−1.1; 24.0; [55]). Incident self-reported hypertension (but not measured hypertension) was positively associated with absorbance $PM_{2.5}$ in the ESCAPE meta-analysis: per 10^{-5}/m increase in absorbance $PM_{2.5}$, the estimated RR was 1.13 (1.02, 1.24; [64]).

3.2. Coarse particles (PM_{10})

Three individual studies found positive associations of PM_{10} with both systolic and diastolic BP. An increase in PM_{10} per 48 $\mu g/m^3$ was associated with an increase in systolic BP by 16.34 mmHg (95% CI: 12.27, 20.42) and diastolic BP by 14.87 mmHg (95% CI: 12.73, 17.02) [48]. An increase in PM_{10} by 19 $\mu g/m^3$ was associated with an increase in systolic BP by 0.87 mmHg (95% CI: 0.48–1.27) and diastolic BP by 0.32 (95% CI: 0.08–0.56; [49]), and an increase per 3.9 $\mu g/m^3$ with an increase in systolic BP by 1.1 mmHg (95% CI: 0.2, 2.0) and diastolic BP by 0.8 mmHg (95% CI: 0.3, 1.2). In one study, PM_{10} was positively associated with

diastolic, but not systolic, BP [47]; in another study, systolic BP, pulse pressure, and mean arterial pressure were increased in association with PM_{10}, but not diastolic BP [59]. In the ESCAPE meta-analysis, no association of PM_{10} with BP was observed [63].

Two individual studies found positive associations of PM_{10} with hypertension, and per 10-μg/m^3 increase in PM_{10}, a hazard ratio (HR, a measure similar to the RR) for hypertension of 1.02 (95% CI: 1.00, 1.04) [67] was reported. In another study, per 20 μg/m^3 increase in PM_{10}, an increase in OR of 1.12 (95% CI: 1.08, 1.16; [49]) was reported. Two individual studies, on the contrary, reported no significant associations of PM_{10} with hypertension [47, 53, 58]. In the ESCAPE meta-analyses, no association of PM_{10} with incident or prevalent hypertension was observed [63].

3.3. Fine particles ($PM_{2.5}$)

So far, $PM_{2.5}$ is the most frequently investigated pollutant: 9 studies in total included it in the analyses with BP [47, 48, 50, 51, 55, 58, 63, 64, 69], and 10 studies included it in the analyses with hypertension [47, 50, 55, 56, 58, 61–64, 66, 67, 69].

Three individual studies reported a positive association of $PM_{2.5}$ with both systolic and diastolic BP [48, 50, 55, 58, 69]. Per increase in $PM_{2.5}$ by 20.42 μg/m^3, systolic BP increased by 32.08 mmHg (95% CI: 21.57, 42.58), and diastolic BP increased by 31.29 mmHg (95% CI: 25.43, 37.14) [48]. Another study has per 10 μg/m^3 increase in ambient $PM_{2.5}$ a 1.30 mmHg (95% CI: 0.04–3.56) increase in systolic BP and 1.04 mmHg (95% CI: 0.31–1.78) increase in diastolic BP [50]. The third study reported, per increase of $PM_{2.5}$ by 2.4 μg/m^3, an increase in systolic BP by 1.4 mmHg (95% CI: 0.5, 2.3) and an increase in diastolic BP by 0.9 mmHg (95% CI: 0.4, 1.4; [69]). Two studies reported a positive association with one of the BP parameters: per increase in $PM_{2.5}$ by 41.7 μg/m^3, an increase in systolic BP by 0.60 mmHg (95% CI: 0.05, 1.15; [51]), and per increase in $PM_{2.5}$ by 1 μg/m^3, an increase in diastolic BP by 0.7% (95% CI: 0.2; 1.2) [55]. No consistent associations were found in one individual study [47] and in the ESCAPE meta-analysis [69].

Six individual studies reported positive associations of $PM_{2.5}$ with hypertension: per increase in $PM_{2.5}$ by 10 μg/m^3, OR for hypertension of 1.05 (95% CI: 1.00–1.10) [66], HR for hypertension of 1.11 (95% CI: 1.03–1.19) [61], and OR for hypertension of 1.14 (95% CI: 1.07, 1.22) [50]. Per increase in $PM_{2.5}$ by 41.7 μg/m^3, OR of 1.11 (1.05,1.17; [51]), and per increase by 1 μg/m^3, an estimated OR of 1.145 (1.025; 1.280; [55]) were reported. Two individual studies reported no association of $PM_{2.5}$ with hypertension ([53, 56]). In the ESCAPE meta-analyses, no associations were observed for $PM_{2.5}$ with prevalent or incident measured hypertension [63, 64]. However, 5 μg/m^3 increase in $PM_{2.5}$ was associated with incident self-reported hypertension: RR of 1.22 (95% CI: 1.08, 1.37; [64]).

3.4. Ozone

Only two studies, both from the Asian region, investigated the association of long-term O_3 exposure with BP and both reported positive associations [48, 49]. The associations with BP were as follows: per increase in O_3 by 8.95 ppb, the estimated increase in systolic BP was 21.51 mmHg (95% CI: 16.90, 26.13) and in diastolic BP, was 20.56 mmHg (18.14–22.97; [48]), and per increase

in O_3 by 22 μg/m^3, systolic BP increased by 0.73 mmHg (95% CI: 0.35, 1.11), and diastolic BP increased by 0.37 mmHg (95% CI: 0.14, 0.61; [49]). Positive associations were also reported with hypertension: per increase in O_3 by 6.7 ppb, the estimated HR was 1.09 (95% CI: 1.00, 1.18; [57]) and per increase in O_3 by 22 μg/m^3, OR for hypertension was 1.13 (95% CI: 1.06, 1.20; [49]).

3.5. Nitrogen oxides

A 12.83 ppb increase in long-term concentration of NO_2 was associated with an increase in systolic BP by 14.40 (10.98–17.82) and diastolic BP by 12.43 (10.63–14.23; [48]). In a large cohort from Taiwan (N = 27,752), a positive association of nitrogen oxides with diastolic, but not systolic, BP was observed: per increase in NO_x by 20 μg/m^3, diastolic BP increased by 0.34 mmHg (95% CI: 0.19, 0.50) [47]. Another analysis with a Spanish cohort, vice versa, found association only with systolic BP: per 10 μg/m^3, increase in NO_2 systolic BP increased by 1.35 mmHg (95% CI: 0.23, 2.47). One study observed a positive association of long-term exposure to NO_2 with pulse pressure, but neither with systolic nor with diastolic BP [59]. No association of NO_2 with BP was found in two individual studies [49, 55] and also in the ESCAPE meta-analysis [63]. [52]. Contrary to the other studies, a negative association of NO_x with BP was observed in a large Danish cohort: per doubling of long-term NO_x, the estimated change in systolic BP was −0.50 (95% CI: −0.84, −0.16) and in diastolic BP was −0.24 (95% CI: −0.42, −0.07) [54].

NO_x was associated with incident hypertension in a longitudinal female cohort from the USA: per increase by 12.4 ppb, the estimated HR was 1.14 (95% CI: 1.03–1.25) [62]. However, in a later reanalysis with a larger sample, an inverse association was observed: per increase in NO_2 by 9.7 ppb, the estimated HR was 0.92 (95% CI: 0.86, 0.98) [57]. The authors do not consider the latter finding indicative of a causal relationship, but attribute it to the confounding relationship between NO_2 and neighborhood socioeconomic status in their study sample [57]. An inverse association of NO_x with prevalent hypertension was observed in the Danish study, similar to the findings with BP, but no clear associations with incident hypertension were reported [54]. At 0.05 level, no statistically significant associations were reported in six individual studies [47, 49, 52, 55, 59] and in the ESCAPE meta-analyses [63, 64].

3.6. Sulfur dioxide

The effects of SO_2 on BP and hypertension were investigated in two studies so far [48, 49]. One of these studies reported positive associations: per increase in SO_2 by 20 μg/m^3, systolic BP increased by 0.80 mmHg (95% CI: 0.46, 1.14), diastolic BP increased by 0.31 mmHg (95% CI: 0.10, 0.51), and OR for hypertension was 1.11 (95% CI: 1.04, 1.18; [49]). No association with BP was reported in the other study [48].

4. Effects in vulnerable subgroups

4.1. Children

Compared with adults and elderly, children are in the period of body growth and development. Therefore, children may be more susceptible to the effect of environmental pollution

exposure compared to adults. So far, six studies investigated the relationship between air pollution and blood pressure in children [43, 70–74], reporting mixed results.

Two of these studies investigated short-term effects of air pollution, reporting few positive associations [72, 74]. In a sample of 130 children aged 6–12 years, a positive association of daily ambient UFP exposure with systolic, but not diastolic, BP was observed: per increase in nano-sized UFP fraction by 860 particles/cm^3, systolic BP increased by 6.35 mmHg (95% CI: 1.56, 11.14) [72]. No associations with BP were observed for $PM_{2.5}$ and PM_{10} [72]. In a large Seven Northeastern Cities (SNEC) study from China (N = 9354, aged 5–17 years), PM_{10} and O_3, but not NO_2 and SO_2, were positively associated with hypertension, defined as ≥95th percentile of BP distribution by gender, age, and height [74]. An increase in 5-day mean PM_{10} by 47.4 μg/m^3 was associated with OR 2.17 (95% CI: 1.61, 2.93), and an increase in 5-day mean O_3 by 51.4 μg/m^3 was associated with OR 2.77 (95% CI: 1.94, 3.95) [74].

Four studies investigated long-term associations of air pollution with BP in children [43, 70, 71, 73]. In a cohort of German children (N = 2368, aged 10 years), long-term exposure to soot, $PM_{2.5}$, and PM_{10} was not associated with BP, and NO_2 showed a negative association, which diminished to null after adjustment for traffic noise [43]. In a cohort of Dutch children (N = 1147, aged 12–13 years), no consistent associations with short- and long-term exposure to PM and gaseous exposures were observed [70]. However, in a subgroup of children who have never changed their residence, a positive association of long-term exposure to NO_2 with diastolic BP was found [70]. A cross-sectional study (n = 179, aged 8–12 years) from Pakistan found systolic and diastolic BP in children living in areas with heavy traffic air pollution (mean daily value of $PM_{2.5}$: 183.0 μg/m^3) than in children living in areas with less traffic air pollution (mean daily value of $PM_{2.5}$: 28.5 μg/m^3) [73]. The most consistent positive signal was found in the analysis with the long-term exposure estimates in the SNEC study in China: 4-year mean PM_{10}, O_3, NO_2, and SO_2 were positively associated with BP and hypertension [71].

It is possible that short-term effect of air pollution on BP in children is stronger than long-term effect. The estimated short-term associations of exposure with hypertension in the SNEC study were stronger than the long-term associations [71, 75]. For example, the estimated ORs of PM_{10} with hypertension in boys, given per interquartile range, were 1.79–2.22 for short-term and 1.55 for long-term exposure [71, 75]. The same tendency was also observed with exposure to O_3 [71, 75].

There might be factors modifying individual susceptibility to adverse physiologic effects of air pollution in children. Stronger associations of air pollution with BP were observed in nonbreastfed children, compared to breastfed ones [71], in overweight/obese children, compared to those with normal weight [75], and in children with mood disorders or unfavorable emotional symptoms, compared to those with no emotional symptoms [76].

4.2. Pregnant women

Pregnant women usually are at particular risk for hypertensive complications since changes in pregnancy can lead to increased stress on the cardiovascular system [77]. Studies evaluating the relationship of ambient air pollution with BP and/or hypertensive disorders among pregnant women have been summarized in a recent review [12] and a systematic review and meta-analysis [77]. The meta-analysis revealed positive associations of multiple pollutants with

hypertensive disorders of pregnancy [77]. In particular, the following ORs were reported for combined pregnancy-induced hypertensive disorders: per 5 μg/m^3 of $PM_{2.5}$ 1.57 (95% CI: 1.26, 1.96), per 10 μg/m^3 of NO_2 1.20 (95% CI: 1.00. 1.44), and per 10 μg/m^3 of PM_{10} 1.13 (95% CI: 1.02, 1.26) [77]. The authors also found weak positive relationships with NO_x and O_3 [77]. No association with CO was found [77]. There is evidence of positive associations of air pollution with continuous BP levels in pregnancy, although the individual study findings differ by trimester [77].

5. Hypothesized pathophysiology

There are three potential pathways of how air pollution could affect BP: (1) triggering systemic inflammation and oxidative stress, (2) autonomous nervous system (ANS) imbalance, and (3) translocation of PM or its constituents into blood [7, 12]. It is suggested that pathways may, to some point, overlap in their action, although the exact interplay is unknown [12]. It is possible that a "vicious cycle" occurs, when reactive oxygen species (ROS) and pro-inflammatory cytokines, originating from the reaction of particles in the lungs or from particles penetrating into the blood flow, contribute to even more oxidative stress and damage to the vascular system.

Inhalation of air pollutants could trigger an inflammatory response in the alveoli [12]. The inflammatory response is reflected in generation and release of the endogenous pro-inflammatory mediators, such as cytokines (interleukins 1 and 6 (IL-1, IL-6), tumor necrosis factor, acute phase response molecules (c-reactive protein and fibrinogen), activated white blood cells, platelets, and vascular-active molecules such as endothelin in the lung. Further, these mediators could reach the systemic circulation, potentiating the systemic inflammatory response and oxidative stress. This results in excessive generation of ROS and reactive nitrogen species (RNS). Under normal conditions, these substances help maintain vascular integrity [78]. However, the abundance of ROS and RNS can harm the vessels, triggering endothelial dysfunction, smooth muscle cell apoptosis, and inflammatory and other damage to vessels [79].

According to the second proposed mechanism, the sympathetic branch of ANS, which directs the "fight and flight" response, gets activated, while the parasympathetic ANS, leading the group of so-called rest and digest reactions, gets inhibited [12]. It is likely that inhaled particles trigger autonomic imbalance through activation of afferent pulmonary autonomic reflexes [12]. In a controlled human exposure study, acute imbalance of autonomic nervous system, which is characterized in the activation of sympathetic nervous system and withdrawal of parasympathetic nervous system, was the most likely underlying mechanism of the rapid increase in diastolic BP following particle inhalation [80]. The autonomic imbalance, resulting from the short-term exposure to elevated levels of air pollutants, is characterized by reduced heart rate variability and a rapid increase in BP [12]. Apart from the acute response, it is possible that autonomic imbalance is involved in chronic adverse cardiovascular effects of air

pollution, since there are some indications that sympathetic ANS is involved in long-term regulation of BP [81].

The third hypothesized mechanism suggests that nanoparticles and soluble compounds (e.g., metals) of the air pollution mixture can translocate to the systemic circulation [4]. In addition to translocation by diffusion, the particles could be ingested by alveolar macrophages [4]. The particles or their soluble components, having entered the circulation, can interact with the vascular endothelium or induce local inflammatory response and oxidative stress, similar to the response in the lung [4].

The core pathophysiologic process underlying cardiovascular effects of air pollution is oxidative stress, an imbalance between the production of ROS and RNS, and their neutralization through antioxidant defense [7]. Oxidative stress is a generic mechanism of injury involved in many pathologic processes and plays a very important role in the pathogenesis of cardiovascular disease [82]. Elevated levels of ROS, reduced bioavailability of NO, and inhibited antioxidants in blood have been observed in animal and human studies of hypertension [78, 82]. Though it has not been proved that oxidative stress may cause hypertension, it can augment the existing prehypertensive condition [78]. The elevated levels of ROS can lead to adverse processes such as endothelial dysfunction, increased contraction, vascular inflammation, and vascular remodeling [78]. Oxidative stress can lead to cell proliferation, hypertrophy, and collagen deposition in vascular wall; can stimulate the expression of pro-inflammatory molecules, such as adhesion molecules and chemotactic proteins; and can mediate the oxidation of lipids and cell migration [79]. In the outer vascular layer, ROS can lead to vascular remodeling [78]. Vascular remodeling, which is considered to have a causal relationship with hypertension, is a combination of pathological changes of small arteries characterized by a reduced lumen and increased media-to-lumen ratio [83]. Oxidative stress within the renal medulla can also promote renal dysfunction and contribute to elevated BP [78, 82]. Oxidative stress in the central nervous system could, through the activation of the sympathetic ANS, also contribute to hypertension development [82].

Vascular endothelium maintains vascular homeostasis through the interactions with the cells in the vessel wall [84]. Endothelial dysfunction is a combination of impaired vasomotion and vascular tone, the prothrombotic and pro-inflammatory changes, and proliferation in the arterial wall, characterized by the inability of the endothelium to dilate in response to vasodilator stimuli [82, 84]. Inflammation and oxidative stress can potentiate the development of endothelial dysfunction. For example, vascular oxidative stress can result in decreased bioavailability of NO [79]. Combined with an inflammatory response, this may promote endothelial dysfunction [79]. Oxidative stress and endothelial dysfunction are prevalent in subjects with hypertension and therefore have been suggested to play causal roles in hypertension development [85]. It is possible that the prohypertensive response to long-term exposure is potentiated through endothelial dysfunction, as a delayed (24 hours postexposure) endothelial dysfunction was observed in the controlled air pollution exposure study with healthy volunteers [80]. Authors hypothesized that this response was triggered by inflammatory reactions [80].

6. Related environmental exposures

6.1. Interaction of noise and air pollution on hypertension

Alongside air pollution, ambient noise is a major environmental risk factor in the urbanized societies. Noise is a stressor that can affect the endocrine and sympathetic ANS and trigger unspecific physiological responses, such as elevated BP, heart rate, vasoconstriction, release of stress hormones, and so on [86]. Such responses favor development and progression of cardiovascular disease, such as hypertension. Two systematic meta-analyses showed positive statistically significant associations of road traffic and aircraft noise with hypertension: per 5 dB of traffic noise, OR of 1.034 (95% CI: 1.011, 1.056) [87], and per 10 dB of aircraft noise, OR of 1.13 (95% CI: 1.00, 1.28) [88]. The evidence for railway noise is rather limited, but positive associations with residential exposure to railroad noise were reported in a population-based Swiss study [89]. Noise annoyance was also positively associated with hypertension in a systematic meta-analysis [90].

Long-term ambient noise exposure shares many sources with outdoor air pollution. Therefore, if not properly controlled for, it may confound air pollution estimates in the analyses. A systematic review was conducted to assess whether the associations of traffic noise or traffic-related air pollution with cardiovascular outcomes could be mutually confounded [91]. The authors concluded that traffic-related air pollution and noise do not mutually confound each other in most of the reviewed studies [91]. The effects of air pollution and noise are likely independent, and there is no interaction between them, or such interaction is probably very small [91]. Indeed, few studies appear to suggest that traffic noise and air pollution may independently contribute to the risk of hypertension [53, 55, 63, 64]. However, more research is recommended to estimate the extent of potential confounding factors [91, 92].

6.2. Ambient temperature, climate change, and BP

It is well known that ambient temperature can affect BP [93]. A recent random-effects meta-analysis, which included 14 studies, indicated that a decrease of 1°C in mean daily outdoor temperature was associated with an increase in SBP and DBP of 0.26 mmHg (95% CI: 0.18–0.33) and 0.13 mmHg (95% CI: 0.11–0.16), respectively [94]. A stronger response was observed in subgroups of subjects with CVD conditions [94].

Ambient air pollution and temperature show synergistic effects on BP. A recent panel study with healthy volunteers found that the association of air pollution with BP was stronger at lower temperatures and, vice versa, the effect of outdoor temperature on BP was only found at high air pollution levels [95]. Also, the effects of individual pollutants may vary by season: in a large cohort study, the associations of PM_{10} and NO_2 with BP were found in the warm season, while SO_2 and O_3 were associated with BP in the cold season [96].

Climate change might contribute to the association of air pollution with BP and hypertension beyond the temperature effects. For example, the concentration of tropospheric O_3 is expected to increase due to global climate change [97]. O_3 was linked to various CVD events, such as

ventricular arrhythmias, myocardial infarction, and ischemic heart disease in the recent studies [97]. Soil drying, deforestation, drought- and climate change-induced dust storms, and wildfires reduce air quality and can increase the concentration of PM dramatically, therefore escalating respiratory and CVD disease burden [97]. It is expected that concentrations of $PM_{2.5}$ from anthropogenic sources will increase with climate change, as, in addition to emissions, there will be changes in meteorology and in physical and chemical transformations of particles in the atmosphere [98].

7. Conclusions

The number of studies on short-term effects of air pollution in the general population has grown in the recent years. Based on the reviewed evidence, we can conclude that an acute increase in air pollution was associated with a transient increase in arterial BP within the following hours or days. Moreover, short-term elevations in air pollution were associated with hospital admissions for hypertension, even at relatively low exposure levels. Most studies focused on PM exposure. Despite some heterogeneity in results, the evidence is in favor of acute increase in BP and hypertension episodes following exposure to fine and coarse PM.

The evidence of short-term effects of gaseous pollutants is still rather scarce and more heterogeneous. Most consistent findings are observed in studies with NO_2 and SO_2, reporting short-term associations with BP and emergency visits for hypertension. There are fewer studies with less consistent results with O_3 and CO, as well as for other types of air pollutants, calling for more research in this field.

As for long-term effects of air pollution, the evidence is somewhat more limited, than for the short-term effects. However, the number of studies is increasing over years, allowing comprehensive comparisons of the effect estimates for different types of air pollutants. Similar to the studies on short-term effects, most cohort studies on long-term effect report positive associations of at least one pollutant with systolic and/or diastolic BP. The majority of studies also report some positive associations of hypertension, though there are more null findings, than with BP. The vast majority of publications on long-term air pollution with BP focused on PM as exposure, similar to the studies on short-term effects. The most consistent positive associations with BP and hypertension were reported for fine particles (PM_{10} and $PM_{2.5}$). Only few studies investigated the associations with gaseous pollutants. Results with NO_x were rather mixed. There are few studies investigating O_3 and SO_2, reporting some positive associations. More longitudinal studies, assessing a simultaneous effect of (1) short- and long-term exposures and (2) various pollutants separately and combined is needed for complete understanding of the effect size, relevant time window of exposure, and the responsible pollutants.

These findings are similar to the previous reviews [7, 12]. However, we expanded the previous reviews by focusing on studies in the general population and by a detailed investigation of the evidence by the type of pollutant, duration of exposure, and type of BP-related outcome studies.

There is accumulating evidence on positive association of air pollution with BP in children. Childhood growth and development of cardiovascular system might be the age of special vulnerability of the cardiovascular system toward the environmental influences. It is also possible that short-term effects of air pollution are stronger in children than in adults. Pregnant women may be another specifically vulnerable population group in regard to prohypertensive effect of air pollution.

Plausible biologic pathways, involving inflammation, oxidative stress, sympathetic ANS activation, endothelial dysfunction, vasoconstriction, and small artery remodeling, are proposed to explain how air pollution could affect blood pressure. Longitudinal epidemiologic studies with extensive clinical examinations, repeated over years, could provide more information for better understanding on the sequence of events in the air pollution–related cardiovascular disease development or progression.

It is important to consider air pollution together with other environmental risk factors. For example, ambient noise shares many common causes with air pollution. It is possible that the associations of air pollution and noise with BP are independent and not confounded by each other. However, some studies do not confirm this, and it is advisable to account for potential confounding factors by adjusting for ambient noise when investigating the cardiovascular effects of air pollution. Another important environmental factor is climate change. It can affect human health independently of air pollution, but it can also influence the composition and toxicity of air pollution mixture. It is possible that climate factors and air pollution act synergistically on BP and hypertension.

Conflict of interest

The authors declare no conflict of interests.

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References

[1] World Health Organization. Ambient (outdoor) Air Quality and Health. Available from: http://www.who.int/mediacentre/factsheets/fs313/en/ [Accessed: Dec 14, 2017]

[2] Brook RD, Franklin B, Cascio W, et al. Air pollution and cardiovascular disease: A statement for healthcare professionals from the expert panel on population and prevention science of the American Heart Association. Circulation. 2004;**109**:2655-2671

[3] Brook RD. Why physicians who treat hypertension should know more about air pollution. Journal of Clinical Hypertension. 2007. Available from: http://www3.interscience.wiley.com/journal/119918183/abstract

[4] Mills NL, Donaldson K, Hadoke PW, et al. Adverse cardiovascular effects of air pollution. Nature Clinical Practice. Cardiovascular Medicine. 2009;**6**:36-44

[5] Petzold A, Ogren JA, Fiebig M, et al. Recommendations for reporting 'black carbon' measurements. Atmospheric Chemistry and Physics. 2013;**13**:8365-8379

[6] Li C, McLinden C, Fioletov V, et al. India is overtaking China as the world's largest emitter of anthropogenic sulfur dioxide. Scientific Reports. 2017;**7**:14304

[7] Brook RD, Rajagopalan S, Pope CA, et al. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. Circulation. 2010;**121**:2331-2378

[8] Forouzanfar MH, Alexander L, Anderson HR, et al. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015;**386**:2287-2323

[9] Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002;**360**:1903-1913

[10] Whelton PK, He J, Appel LJ, et al. Primary prevention of hypertension: Clinical and public health advisory from The National High Blood Pressure Education Program. Journal of the American Medical Association. 2002;**288**:1882-1888

[11] Cook NR, Cohen J, Hebert PR, et al. Implications of small reductions in diastolic blood pressure for primary prevention. Archives of Internal Medicine. 1995;**155**:701-709

[12] Giorgini P, Di Giosia P, Grassi D, et al. Air pollution exposure and blood pressure: An updated review of the literature. Current Pharmaceutical Design. 2016;**22**:28-51

[13] Arbex MA, Saldiva PHN, Pereira LAA, et al. Impact of outdoor biomass air pollution on hypertension hospital admissions. Journal of Epidemiology and Community Health. 2010;**64**:573-579

[14] Auchincloss AH, Diez Roux AV, Dvonch JT, et al. Associations between recent exposure to ambient fine particulate matter and blood pressure in the multi-ethnic study of atherosclerosis (MESA). Environmental Health Perspectives. 2008;**116**:486-491

[15] Baccarelli A, Barretta F, Dou C, et al. Effects of particulate air pollution on blood pressure in a highly exposed population in Beijing, China: A repeated-measure study. Environmental Health. 2011;**10**:108

[16] Bellavia A, Urch B, Speck M, et al. DNA hypomethylation, ambient particulate matter, and increased blood pressure: Findings from controlled human exposure experiments. Journal of the American Heart Association. 2013;**2**:e000212

[17] Brook RD, Bard RL, Burnett RT, et al. Differences in blood pressure and vascular responses associated with ambient fine particulate matter exposures measured at the personal versus community level. Occupational and Environmental Medicine. 2011;**68**: 224-230

[18] Brook RD, Bard RL, Morishita M, et al. Hemodynamic, autonomic, and vascular effects of exposure to coarse particulate matter air pollution from a rural location. Environmental Health Perspectives. 2014;**122**:624-630

[19] Byrd JB, Morishita M, Bard RL, et al. Acute increase in blood pressure during inhalation of coarse particulate matter air pollution from an urban location. Journal of the American Society of Hypertension. 2016;**10**:133-139.e4

[20] Chuang K-J, Yan Y-H, Cheng T-J. Effect of air pollution on blood pressure, blood lipids, and blood sugar: A population-based approach. Journal of Occupational and Environmental Medicine. 2010;**52**:258-262

[21] Cosselman KE, Krishnan RM, Oron AP, et al. Blood pressure response to controlled diesel exhaust exposure in human subjects. Hypertension. 2012;**59**(5):943-948

[22] Dales R, Liu L, Szyszkowicz M, et al. Particulate air pollution and vascular reactivity: The bus stop study. International Archives of Occupational and Environmental Health. 2007; **81**:159-164

[23] de Paula Santos U, Braga ALF, Giorgi DMA, et al. Effects of air pollution on blood pressure and heart rate variability: A panel study of vehicular traffic controllers in the city of São Paulo, Brazil. European Heart Journal. 2005;**26**:193-200

[24] Dvonch JT, Kannan S, Schulz AJ, et al. Acute effects of ambient particulate matter on blood pressure differential effects across urban communities. Hypertension. [Epub ahead of print]. 2009. DOI: 10.1161/HYPERTENSIONAHA.108.123877

[25] Gong H, Sioutas C, Linn WS. Controlled exposures of healthy and asthmatic volunteers to concentrated ambient particles in metropolitan Los Angeles. Research Reports – Health Effects Institute. 2003;**1**:1-36-1-47

[26] Guo Y, Tong S, Li S, et al. Gaseous air pollution and emergency hospital visits for hypertension in Beijing, China: A time-stratified case-crossover study. Environmental Health. 2010;**9**:57

[27] Guo Y, Tong S, Zhang Y, et al. The relationship between particulate air pollution and emergency hospital visits for hypertension in Beijing, China. Science of the Total Environment. 2010;**408**:4446-4450

[28] Harrabi I, Rondeau V, Dartigues J-F, et al. Effects of particulate air pollution on systolic blood pressure: A population-based approach. Environmental Research. 2006;**101**:89-93

[29] Ibald-Mulli A, Stieber J, Wichmann HE, et al. Effects of air pollution on blood pressure: A population-based approach. American Journal of Public Health. 2001;**91**:571-577

[30] Jacobs L, Buczynska A, Walgraeve C, et al. Acute changes in pulse pressure in relation to constituents of particulate air pollution in elderly persons. Environmental Research. 2012; **117**:60-67

[31] Kubesch N, De Nazelle A, Guerra S, et al. Arterial blood pressure responses to short-term exposure to low and high traffic-related air pollution with and without moderate physical activity. European Journal of Preventive Cardiology. 2015;**22**:548-557

[32] Liu L, Ruddy T, Dalipaj M, et al. Effects of indoor, outdoor, and personal exposure to particulate air pollution on cardiovascular physiology and systemic mediators in seniors. Journal of Occupational and Environmental Medicine. 2009;**51**:1088-1098

[33] Liu L, Kauri LM, Mahmud M, et al. Exposure to air pollution near a steel plant and effects on cardiovascular physiology: A randomized crossover study. International Journal of Hygiene and Environmental Health. 2014;**217**:279-286

[34] Mordukhovich I, Wilker E, Suh H, et al. Black carbon exposure, oxidative stress genes, and blood pressure in a repeated-measures study. Environmental Health Perspectives. 2009;**117**:1767-1772

[35] Sérgio Chiarelli P, Amador Pereira LA, Nascimento Saldiva PH, et al. The association between air pollution and blood pressure in traffic controllers in Santo André, São Paulo, Brazil. Environmental Research 2011;**111**:650-655

[36] Szyszkowicz M, Rowe BH, Brook RD. Even low levels of ambient air pollutants are associated with increased emergency department visits for hypertension. The Canadian Journal of Cardiology. 2012;**28**:360-366

[37] Urch B, Silverman F, Corey P, et al. Acute blood pressure responses in healthy adults during controlled air pollution exposures. Environmental Health Perspectives. 2005;**113**: 1052-1055

[38] Weichenthal S, Hatzopoulou M, Goldberg MS. Exposure to traffic-related air pollution during physical activity and acute changes in blood pressure, autonomic and microvascular function in women: A cross-over study. Particle and Fibre Toxicology. 2014;**11**:70

[39] Wilker EH, Baccarelli A, Suh H, et al. Black carbon exposures, blood pressure, and interactions with single nucleotide polymorphisms in MicroRNA processing genes. Environmental Health Perspectives. 2010;**118**:943-948

[40] Wu S, Deng F, Huang J, et al. Blood pressure changes and chemical constituents of particulate air pollution: Results from the Healthy Volunteer Natural Relocation (HVNR) Study. Environmental Health Perspectives. 2013;**121**:66-72

[41] Costa Nascimento LF, Francisco JB. Particulate matter and hospital admission due to arterial hypertension in a medium-sized Brazilian city. Cadernos de Saúde Pública. 2013; **29**:1565-1571

[42] Chen S-Y, Su T-C, Lin Y-L, et al. Short-term effects of air pollution on pulse pressure among nonsmoking adults. Epidemiology. 2012;**23**:341-348

[43] Liu C, Fuertes E, Tiesler CMT, et al. The associations between traffic-related air pollution and noise with blood pressure in children: Results from the GINIplus and LISAplus studies. International Journal of Hygiene and Environmental Health. 2014;**217**:499-505

[44] O'Neill MS, Diez-Roux AV, Auchincloss AH, et al. Airborne particulate matter exposure and urinary albumin excretion: The Multi-Ethnic Study of Atherosclerosis. Occupational and Environmental Medicine. 2008;**65**:534-540

[45] Ren C, Park SK, Vokonas PS, et al. Air pollution and homocysteine: More evidence that oxidative stress-related genes modify effects of particulate air pollution. Epidemiology. 2010;**21**:198-206

[46] Schwartz J, Alexeeff SE, Mordukhovich I, et al. Association between long-term exposure to traffic particles and blood pressure in the Veterans Administration Normative Aging Study. Occupational and Environmental Medicine. 2012;**69**:422-427

[47] Chen S-Y, Wu C-F, Lee J-H, et al. Associations between long-term air pollutant exposures and blood pressure in elderly residents of Taipei City: A cross-sectional study. Environmental Health Perspectives. 2015;**123**:779-784

[48] Chuang K-J, Yan Y-H, Chiu S-Y, et al. Long-term air pollution exposure and risk factors for cardiovascular diseases among the elderly in Taiwan. Occupational and Environmental Medicine. 2011;**68**:64-68

[49] Dong G-H, Qian ZM, Xaverius PK, et al. Association between long-term air pollution and increased blood pressure and hypertension in China. Hypertension (Dallas, Tex 1979). 2013;**61**:578-584

[50] Lin H, Guo Y, Zheng Y, et al. Long-term effects of ambient PM2.5 on hypertension and blood pressure and attributable risk among older chinese adults. Hypertension (Dallas, Tex 1979). 2017;**69**:806-812

[51] Liu C, Chen R, Zhao Y, et al. Associations between ambient fine particulate air pollution and hypertension: A nationwide cross-sectional study in China. Science of the Total Environment. 2017;**584–585**:869-874

[52] Foraster M, Basagaña X, Aguilera I, et al. Association of long-term exposure to traffic-related air pollution with blood pressure and hypertension in an adult population–based cohort in Spain (the REGICOR study). Environmental Health Perspectives. 2014;**122**: 404-411

[53] Fuks K, Moebus S, Hertel S, et al. Long-term urban particulate air pollution, traffic noise, and arterial blood pressure. Environmental Health Perspectives. 2011;**119**:1706-1711

[54] Sørensen M, Hoffmann B, Hvidberg M, et al. Long-term exposure to traffic-related air pollution associated with blood pressure and self-reported hypertension in a Danish cohort. Environmental Health Perspectives. 2012;**120**:418-424

[55] Pitchika A, Hampel R, Wolf K, et al. Long-term associations of modeled and self-reported measures of exposure to air pollution and noise at residence on prevalent hypertension and blood pressure. Science of the Total Environment. 2017;**593–594**:337-346

[56] Coogan PF, White LF, Yu J, et al. PM2.5 and diabetes and hypertension incidence in the black Women's health study. Epidemiology. 2016;**27**:202-210

[57] Coogan PF, White LF, Yu J, et al. Long-term exposure to NO_2 and ozone and hypertension incidence in the Black Women's Health Study. American Journal of Hypertension. 2017;**30**:367-372

[58] Fuks KB, Weinmayr G, Hennig F, et al. Association of long-term exposure to local industry- and traffic-specific particulate matter with arterial blood pressure and incident hypertension. International Journal of Hygiene and Environmental Health. 2016;**219**:527-535

[59] Chan SH, Van Hee VC, Bergen S, et al. Long-term air pollution exposure and blood pressure in the sister study. Environmental Health Perspectives. 2015;**123**:951-958

[60] Lewington S, Lacey B, Clarke R, et al. The burden of hypertension and associated risk for cardiovascular mortality in China. JAMA Internal Medicine. 2016;**176**:524-532

[61] Chen H, Burnett RT, Kwong JC, et al. Spatial association between ambient fine particulate matter and incident hypertension. Circulation. 2013;**129**:1-25

[62] Coogan PF, White LF, Jerrett M, et al. Air pollution and incidence of hypertension and diabetes mellitus in black women living in Los Angeles. Circulation. 2012;**125**:767-772

[63] Fuks KB, Weinmayr G, Foraster M, et al. Arterial blood pressure and long-term exposure to traffic-related air pollution: An analysis in the European Study of Cohorts for Air Pollution Effects (ESCAPE). Environmental Health Perspectives. 2014;**122**:896-905

[64] Fuks KB, Weinmayr G, Basagaña X, et al. Long-term exposure to ambient air pollution and traffic noise and incident hypertension in seven cohorts of the European study of cohorts for air pollution effects (ESCAPE). European Heart Journal. 2017;**38**:ehw413

[65] ESCAPE – European Study of Cohorts for Air Pollution Effects. Available from: http://www.escapeproject.eu/ [Accessed: Dec 14, 2017]

[66] Johnson D, Parker JD. Air pollution exposure and self-reported cardiovascular disease. Environmental Research. 2009;**109**:582-589

[67] Zhang Z, Laden F, Forman JP, et al. Long-term exposure to particulate matter and self-reported hypertension: A prospective analysis in the Nurses' Health Study. Environmental Health Perspectives. 2016;**1414**:1414-1420

[68] Sørensen M, Hvidberg M, Hoffmann B, et al. Exposure to road traffic and railway noise and associations with blood pressure and self-reported hypertension: A cohort study. Environmental Health. 2011;**10**:92

[69] Long-Term Urban Particulate Air Pollution, Traffic Noise and Arterial Blood Pressure. Environ Health Perspect. 2011. Available from: http://www.ehponline.org/ambra-doi-resolver/10.1289/ehp.1103564 [Accessed: Aug 10, 2011]

[70] Bilenko N, van Rossem L, Brunekreef B, et al. Traffic-related air pollution and noise and children's blood pressure: Results from the PIAMA birth cohort study. European Journal of Preventive Cardiology. 2015;**22**:4-12

[71] Dong G-H, Qian ZM (Min), Trevathan E, et al. Air pollution associated hypertension and increased blood pressure may be reduced by breastfeeding in Chinese children: The Seven Northeastern Cities Chinese Children's Study. International Journal of Cardiology. 2014;**176**:956-961

[72] Pieters N, Koppen G, Van Poppel M, et al. Blood pressure and same-day exposure to air pollution at school: Associations with nano-sized to coarse PM in children. Environmental Health Perspectives. 2015;**123**:737-742

[73] Sughis M, Nawrot TS, Ihsan-ul-Haque S, et al. Blood pressure and particulate air pollution in schoolchildren of Lahore, Pakistan. BMC Public Health. 2012;**12**:378

[74] Zeng X-W, Qian ZM, Vaughn MG, et al. Positive association between short-term ambient air pollution exposure and children blood pressure in China-result from the Seven Northeast Cities (SNEC) Study. Environmental Pollution. 2017;**224**:698-705

[75] Dong G-H, Wang J, Zeng X-W, et al. Interactions between air pollution and obesity on blood pressure and hypertension in Chinese children. Epidemiology. 2015;**26**:740-747

[76] Dales RE, Cakmak S. Does mental health status influence susceptibility to the physiologic effects of air pollution? A population based study of Canadian children. PLoS One. 2016; **11**:e0168931

[77] Pedersen M, Stayner L, Slama R, et al. Ambient air pollution and pregnancy-induced hypertensive disorders: A systematic review and meta-analysis. Hypertension. 2014;**64**: 494-500

[78] Montezano AC, Touyz RM. Oxidative stress, Noxs, and hypertension: Experimental evidence and clinical controversies. Annals of Medicine. 2012;**44**:S2-S16

[79] Touyz RM, Schiffrin EL. Oxidative stress and hypertension. In: Holtzman L, editor. Atherosclerosis and Oxidant Stress: A New Perspective. Boston, MA: Springer; 2008. pp. 51-78

[80] Brook RD, Urch B, Dvonch JT, et al. Insights into the mechanisms and mediators of the effects of air pollution exposure on blood pressure and vascular function in healthy humans. Hypertension. 2009;**54**:659-667

[81] Charkoudian N, Rabbitts JA. Sympathetic neural mechanisms in human cardiovascular health and disease. Mayo Clinic Proceedings. 2009;**84**:822-830

[82] Rodrigo R, González J, Paoletto F. The role of oxidative stress in the pathophysiology of hypertension. Hypertension Research. 2011;**34**:431-440

[83] Mulvany MJ. Small artery remodeling and significance in the development of hypertension. News in Physiological Sciences. 2002;**17**:105-109

[84] Widlansky ME, Gokce N, Keaney JF, et al. The clinical implications of endothelial dysfunction. Journal of the American College of Cardiology. 2003;**42**:1149-1160

[85] Lin C-P, Lin F, Huang P-H, et al. Endothelial progenitor cell dysfunction in cardiovascular diseases: Role of reactive oxygen species and inflammation. BioMed Research International. 2013;**2013**:845037

[86] Münzel T, Gori T, Babisch W, et al. Cardiovascular effects of environmental noise exposure. European Heart Journal. 2014;**35**:829-836

[87] van Kempen E, Babisch W. The quantitative relationship between road traffic noise and hypertension: A meta-analysis. Journal of Hypertension. 2012;**30**:1075-1086

[88] Babisch W, Van Kamp I. Exposure-response relationship of the association between aircraft noise and the risk of hypertension. Noise & Health. 2010;**11**:161-168

[89] Dratva J, Phuleria HC, Foraster M, et al. Transportation noise and blood pressure in a population-based sample of adults. Environmental Health Perspectives. 2012;**120**:50-55

[90] Twardella D, Ndrepepa A. Relationship between noise annoyance from road traffic noise and cardiovascular diseases: A meta-analysis. Noise Health. 2011;**13**:251

[91] Tétreault L-F, Perron S, Smargiassi A. Cardiovascular health, traffic-related air pollution and noise: Are associations mutually confounded? A systematic review. International Journal of Public Health. 2013;**58**:649-666

[92] Foraster M. Is it traffic-related air pollution or road traffic noise, or both? Key questions not yet settled! International Journal of Public Health. 2013;**58**:647-648

[93] Rose G. Seasonal variation in blood pressure in man. Nature. 1961;**189**:235

[94] Wang Q, Li C, Guo Y, et al. Environmental ambient temperature and blood pressure in adults: A systematic review and meta-analysis. Science of the Total Environment. 2017;**575**:276-286

[95] Wu S, Deng F, Huang J, et al. Does ambient temperature interact with air pollution to alter blood pressure? A repeated-measure study in healthy adults. Journal of Hypertension. 2015;**33**:2414-2421

[96] Choi J-H, Xu Q-S, Park S-Y, et al. Seasonal variation of effect of air pollution on blood pressure. Journal of Epidemiology and Community Health. 2007;**61**:314-318

[97] Giorgini P, Di Giosia P, Petrarca M, et al. Climate changes and human health: A review of the effect of environmental stressors on cardiovascular diseases across epidemiology and biological mechanisms. Current Pharmaceutical Design. 2017;**23**:3247-3261

[98] Orru H, Ebi KL, Forsberg B. The interplay of climate change and air pollution on health. Current Environmental Health Reports. 2017;**4**:504-513

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