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Review Article

A Systematic Review of the Association between Air Pollution and Cardiovascular Parameters: Blood Pressure, Arterial Stiffness, and Endothelial Function. (Review)

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Abstract

Exposure to air pollution is hypothesized to influence blood pressure, arterial stiffness, and endothelial function, all independent predictors of cardiovascular disease. Systematic literature search for articles reporting exposure to particulate matter (PM) or gaseous pollutants (carbon monoxide, ozone, sulfur dioxide, nitrogen oxide, and nitrogen dioxide) on blood pressure, arterial stiffness, and endothelial function. Short-term exposures studies presented heterogeneous results: 17 of 31 papers supported a rise in blood pressure after exposure to PM, and five of 13 studies of gaseous pollutants; impaired endothelial function in response to PM (six of 11 papers) and gaseous pollutants (three of six studies); and arterial stiffness after PM exposure in three of six studies. Blood pressure data from long-term air pollution studies were more consistent: Seven of nine PM and five of six gaseous exposure studies reported blood pressure elevation. Three studies reported arterial stiffness, with heterogeneous results. A single study was identified reporting PM impaired dilatation. This supports an association between long-term exposure to certain gaseous pollutants, particularly sulfur dioxide (SO_2), and PM with increased blood pressure, arterial stiffness, and possibly endothelial dysfunction. Acute exposure can impair endothelial function and may affect blood pressure, but not measures of vascular stiffness. The implication for researchers is that acute versus long-term air pollution conveys different patterns of confounding on these cardiovascular measures. Regarding population-based prevention strategies, data support air quality as potentially a modifiable risk factor in the development of cardiovascular diseases.

Key words: Air pollution, blood pressure, particulate matter, vascular endothelium, vascular stiffness

Introduction

Cardiovascular disease represents a significant contribution to the global burden of chronic disease, with annual mortality reaching 18.6 million in 2019.[1] The causes of cardiovascular disease are a complex interaction between genetic and environmental risk factors over an extended period of time. These include obesity, hypertension, hyperlipidemia, and diabetes mellitus, but there is increasing evidence that air pollution may be an additional environmental risk factor, with epidemiological studies demonstrating increased cardiovascular morbidity and mortality.[2,3]

Due to continuing industrialization in many parts of the world, high use of private vehicles and failure to divest from fossil fuels, air quality continues to decline in many parts of the world. Indeed, the Global burden of disease study estimates that mortality from air pollution increased by 5.8% between 2007 and 2017, with 5 million deaths caused by air pollution in 2017.[4] Some models forecast that the contribution of outdoor air pollution to premature mortality will double by 2050.[5] Air pollution is a heterogeneous mixture of gaseous pollutants, volatile, semi-volatile, and particulate matter (PM). Although many gaseous pollutants can have serious health effects such as ozone (O_3), carbon monoxide (CO) and nitrogen oxides (NO),

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the largest body of epidemiological evidence supports PM as having the strongest association with health problems.[6]

PM is subdivided into coarse, fine and ultrafine, collectively termed PM_{10} meaning particulate diameter <10 μm. Fine particles ($PM_{2.5}$) have diameter <2.5 μm, and ultrafine particles ($PM_{0.1}$) with diameter <100 nm. Size is important as it influences how easily they form aggregates of material that can readily deposit in the lungs and affects their inflammatory properties.[7] Outdoor air quality depends on a range of covariant factors including meteorological conditions, industrial activity, time of day and traffic. Hence, estimates of air pollution exposure in epidemiological models are limited by spatial and temporal variation in pollutant concentrations and must adjust for many covariates.[8]

Methodologically, air pollution exposure has been studied short-term, measuring acute effects of changes in pollutant concentrations over hours or days, or long-term exposure over several years. Contrasting attitudes regarding exposure reflect uncertainty of the biological mechanisms linking air pollution and cardiovascular disease, with various direct or indirect inflammatory, and endocrine pathways being proposed.[9]

Assessing cardiovascular health and predicting risk of cardiovascular disease can be aided by measurement of known risk factors such as blood pressure, and surrogate markers of arterial function, in particular endothelial function and arterial stiffness.[10] Arterial stiffness can be quantified using validated techniques such as pulse wave velocity (PWV) - the speed at which arterial pressure waves transmit representing stiffness of the arterial tree, and Pulse wave analysis (PWA) or "Augmentation index (AIx)," based on the morphology of reflected pulse wave as an indicator of arterial stiffness. Flow-mediated dilatation (FMD) and Peripheral artery tonometry (PAT) both assess for endothelial function with methods involving arterial occlusion and measuring the vascular response.

Our aim was to systematically review the available evidence to provide a comprehensive assessment of the association between air pollution exposure and cardiovascular risk parameters. This data informs health-care professionals and academics when considering air quality as a contributory or confounding factor in cardiovascular research, and policy decision makers tasked with prevention of cardiovascular diseases.

Methods

Protocol

The systematic review was written following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[11] A review protocol was developed, including eligibility criteria, databases searched, and the search terms.

Eligibility criteria

Studies had to meet pre-determined criteria to be included: published in a peer-reviewed journal; cross-sectional studies, case-control studies, case-crossover studies, time series, cohort studies, or panel studies; measured effect of long-term exposure ≥30 days or short-term exposure <30 days; at least ten subjects and conducted in humans; measured exposure to PM PM_{10} or $PM_{2.5}$ or gaseous pollutants CO, O_3, SO_2, NO, and nitrogen dioxide (NO_2). Outcome measures had to be validated tools, including FMD and PAT as measures of endothelial function; PWV, PWA, and AIx adjusted to 75 bpm (AI at 75) as measures of arterial stiffness; and blood pressure based on office, 24 h ambulatory, or standardized technique home readings.

Publications that were excluded from this systemic review: Case reports, editorials, comments, news items and letters; studies conducted in animals; duplicate reports; only measured exposure to pollutant not stated in eligibility criteria; measured outcome on cardiovascular health by methods other than endothelial function, arterial stiffness, and blood pressure; and measured exposure to indoor sources of air pollution.

Information sources

A comprehensive literature review was conducted using the databases Scopus and PubMed for publications between 2000 and July 2021 in the English language. The literature search of the databases was carried out on July 13, 2021, with an additional citation search on July 23, 2021.

The search terms were combined with Boolean operators "AND" and "OR" and asterisk "*": "(air pollution OR PM_{10} OR $PM_{2.5}$ OR PM OR particul* OR particle* OR CO OR O_3 OR SO_2 OR NO OR NO_2) AND (FMD OR FMD OR PWV OR PWV OR blood pressure OR hypertension OR hypertensive OR hypertens* OR endotheli* OR arterial stiffness)".

Study selection

Duplicates were removed from the initial records using software, then one reviewer read through titles and abstract of each remaining study to determine if they met the eligibility criteria and exclude those that although mention search terms did not meet the parameters of the eligibility criteria. Perusal of the remaining studies determined eligibility for inclusion in the review, Figure 1.

Data collection and analysis

Data items collated from eligible studies included study design, population characteristics, duration of exposure and follow-up, pollutants measured, and cardiovascular health parameter(s). Wherever possible the standard deviation, 95% confidence interval and *P* value were extracted from the study to quantify effect size. Meta-analysis was intended; however, outcome data were found to be inadequate for undertaking a valid assessment.

Risk of bias (ROB) assessment

The ROB of cross-sectional, case-control, case-crossover, cohort, and panel studies were analyzed using the Newcastle-Ottawa quality assessment tool adapted for use with cross-sectional studies [Table S1].[12] For randomized blinded trials, the revised Cochrane ROB tool (RoB 2) was used [Table S2].[13]

Table S1: Scores based on modified Newcastle-Ottawa scale measuring the risk of bias for non-randomised clinical trials, cohort studies, cross-sectional studies

Study	Selection	Comparability	Outcome	Total
Shan *et al*. 2014	****	*	**	7/10
Liu *et al*. 2018	***	*	***	7/10
Wu *et al*. 2016	**	*	***	6/10
Liu *et al*. 2014	**	*	***	6/10
Zhao *et al*. 2020	***	*	*	5/10
Fang *et al*. 2008	***	**	*	6/10
Briet *et al*. 2007	***	**	**	7/10
Cole *et al*. 2018	***	**	*	6/10
Gong *et al*. 2003	***	*	*	5/10
Adamopoulos *et al*. 2010	****	**	***	9/10
Jiang *et al*. 2016	*****	**	***	10/10
Krishnan *et al*. 2012	*****	**	***	10/10
Kumarathasan *et al*. 2018	***	**	***	8/10
Mehta *et al*. 2014	***	**	***	8/10
Lenters *et al*. 2010	****	**	*	7/10
Weichenthal *et al*. 2014	****	*	*	6/10
Chen *et al*. 2015	***	**	*	6/10
Babisch *et al*. 2014	***	**	*	6/10
Coogan *et al*. 2012	****	**	**	8/10
Dong *et al*. 2013	****	*	**	7/10
Foraster *et al*. 2014	****	**	**	8/10
Lin *et al*. 2017	****	**	***	9/10

Results

Literature search and study selection

The initial search strategy identified 4500 published articles that contained potentially relevant information. An additional 14 articles were retrieved through searching of citations. Duplicates were removed before the screening process. The titles and abstracts of the remaining 4512 articles were screened. One of the remaining 67 papers could not be retrieved, leaving 66 articles assessed in detail for eligibility. Perusal of the full text excluded 20 articles for the reasons listed in Figure 1, resulting in 46 articles being included in this review.

Study characteristics

The characteristics, design, and principal findings of the included studies are summarized in supplemental Tables S3 and S4. Of the 46 studies, 36 focused on short-term and ten reported long-term exposure to air pollution. Study design was cross-sectional in nine studies, three were panel studies, two were cohort studies, and 32 were crossover studies. Crossover designs were most frequently adopted for short-term exposure studies, and cross-sectional designs for long-term exposure studies. The included studies were conducted in 12 countries across, Asia, Europe, and America, with the sample size ranging from 12 to 27,752.

Several approaches were adopted by the studies in this review to account for the uncertainty regarding spatial and temporal variation in pollutant concentrations. The most common approach of long-term exposure studies was land-use regression modeling.[14-19] Other methods included spatio-temporal modeling;[20] satellite-derived column aerosol optical depth to estimate $PM_{2.5}$ concentrations;[21,22] and closest monitoring sites.[23,24] Short-term exposure methodologies included purpose-designed exposure chambers;[25] indoor filtration units to measure acute response to filtered versus unfiltered air; ambient exposure with high versus low pollution environs, and particulate filtering respirators. Pollutant concentrations were mainly measured using purpose designed monitors at the relevant locations. A small number of studies (14%) utilized personal exposure monitors.

Descriptive results

Short-term exposure

PM

The relationship of PM with blood pressure, endothelial function, and arterial stiffness was investigated by 31 observational studies (details in Table S3). Twelve studies included in this review found a statistically significant association between PM and blood pressure.[26-37] Elevations of up to 12 mmHg in SBP were demonstrated in a double-blind randomized cross-over trial (145 ± 4 mmHg diesel fume exposure, vs. filtered air 133 ± 3 mmHg, p=0.012).[36] This trial was an outlier however, with the remainder demonstrating much smaller changes in blood pressure, Table S3. Methods of reporting were too heterogeneous to allow meta-analysis. Two of the 12 employed ambulatory blood pressure measurements,[27-29] the remainder were "in-office" blood pressure. Adjustment for confounders was common; design details and outcome data are listed in Table S3.[26-37] In half of these studies, only the association with systolic, but not diastolic blood pressure (DBP) achieved statistical significance.[28,29,32,34,36,37] Eleven studies in contrast found no association between PM exposure and blood pressure.[38-48] Most of these studies (8 of 11) did report an acute rise in blood pressure following exposure to PM; however, statistical significance was not sustained following adjustment for confounding variables.[38-43,45,46] Considering methodology as a source of data variability; 89% of exposure chamber studies reported an association,[28,30,32-37] conversely, 78% of air filtration studies concluded no association.[39,42-47] Aggregated, there does appear to be evidence of short-term effects of PM on blood pressure, though the effect size does not appear to be large. Strength of the evidence is limited by heterogeneous methodology and the large number of variables determining air pollution exposure.

Table S2: Scores based on revised Cochrane risk of bias tool (RoB 2) measuring the risk of bias for blinded randomised clinical trials, randomized single, and double-blinded crossover studies

Study	Domain 1. Randomization process	Domain 2. Deviations from intended interventions	Domain 3. Mising outcome data	Domain 4. Measurement of the outcome	Domain 5. Selection of the reported result	Domain 6. Overall Bias
Cui *et al*. 2018	L	SC	L	SC	L	SOME CONCERNS
Rich *et al*. 2018	L	SC	L	L	L	LOW RISK OF BIAS
Barath *et al*. 2010	L	L	L	L	L	LOW RISK OF BIAS
Bellavia *et al*. 2013	L	SC	L	L	L	LOW RISK OF BIAS
Brook *et al*. 2002	L	SC	L	SC	L	LOW RISK OF BIAS
Brook *et al*. 2009	L	L	L	L	L	LOW RISK OF BIAS
Brook *et al*. 2014	L	L	L	L	L	LOW RISK OF BIAS
Chen *et al*. 2015	L	L	L	L	L	LOW RISK OF BIAS
Cosselman *et al*. 2012	L	L	L	L	L	LOW RISK OF BIAS
Langrish *et al*. 2010	L	SC	L	L	L	LOW RISK OF BIAS
Fakhri *et al*. 2009	L	SC	L	SC	L	SOME CONCERNS
Frampton *et al*. 2015	L	L	L	SC	L	LOW RISK OF BIAS
Kajbafzadeh *et al*. 2015	L	SC	L	SC	L	SOME CONCERNS
Karottki *et al*. 2013	L	L	L	L	L	LOW RISK OF BIAS
Mills *et al*. 2011	L	L	L	SC	L	LOW RISK OF BIAS
Morishita *et al*. 2015	L	L	L	L	L	LOW RISK OF BIAS
Morishita *et al*. 2018	L	L	L	L	L	LOW RISK OF BIAS
Padró-Martínez *et al*. 2015	L	SC	L	L	L	LOW RISK OF BIAS
Törnqvist *et al*. 2007	L	L	L	L	L	LOW RISK OF BIAS
Allen *et al*. 2011	L	SC	L	SC	L	SOME CONCERNS
Shi *et al*. 2017	L	SC	L	SC	L	SOME CONCERNS
Tank *et al*. 2011	L	L	L	L	L	LOW RISK OF BIAS
Weichenthal *et al*. 2019	L	L	L	L	L	LOW RISK OF BIAS
Arjomandi *et al*. 2015	L	SC	L	L	L	LOW RISK OF BIAS

Endothelial dysfunction was linked to PM exposure in six studies. This included exposure studies,[35,36,49] an air filtration study,[50] a high- and low-pollution bicycle route crossover-trial,[51] and a cross-sectional study.[26] Five studies conversely concluded no association between PM exposure and endothelial function.[33,47,52-54] Such divergent results may indicate an exposure interaction; one such proposed interaction is between PM and gaseous pollutants, though even here authors disagree on directionality: Briet *et al*. 2007[53] reporting PM exaggerates dilatory response of small arteries to ischemia, contradicting evidence of particular matter-induced lower serum NO levels[26] and reduced vasodilation.[36,49] The method used to measure endothelial function (reactive hyperemic index [RHI] from PAT, and FMD) did not appear affect the outcome.

Three studies found an association between arterial stiffness and PM exposure, all adjusted for confounding variables. Two were panel studies and one was cross-sectional, sample size ranging from 26 to 371.[26,55,56] Three smaller sample size studies (n = 25–70), all adjusted for confounding variables, did not demonstrate a statistically significant association.[33,38,46] Contrasting outcomes may relate to methodology, the three studies reporting an association were all based on AIx,[26,55,56] with carotid-femoral PWV (cfPWV)[38,46] and PWA[33] not demonstrating significant change with exposure. AIx and PWV are not interchangeable as measures of arterial function; AIx is an index of pressure wave reflection and is affected by vasoactive substances that do not produce parallel changes in PWV.[57] Many of the studies included multiple outcome measures of BP, endothelial function and arterial stiffness, Table S3. For example, Jiang *et al*.[26] reported participants who lived within 50 m of a major road compared with those lived more than 200 m away had higher average personal $PM_{2.5}$ (111.1 vs. 68.2 μg/m^3), 4.3-fold higher AIx ($P < 0.05$), 1.6-fold higher SBP ($P < 0.05$), 1.9-fold higher DBP ($P < 0.01$), and 4.6-fold lower NO production ($P < 0.01$). Data would suggest that air pollution is a confounding factor that should be taken into consideration when measuring AIx, but not PWV.

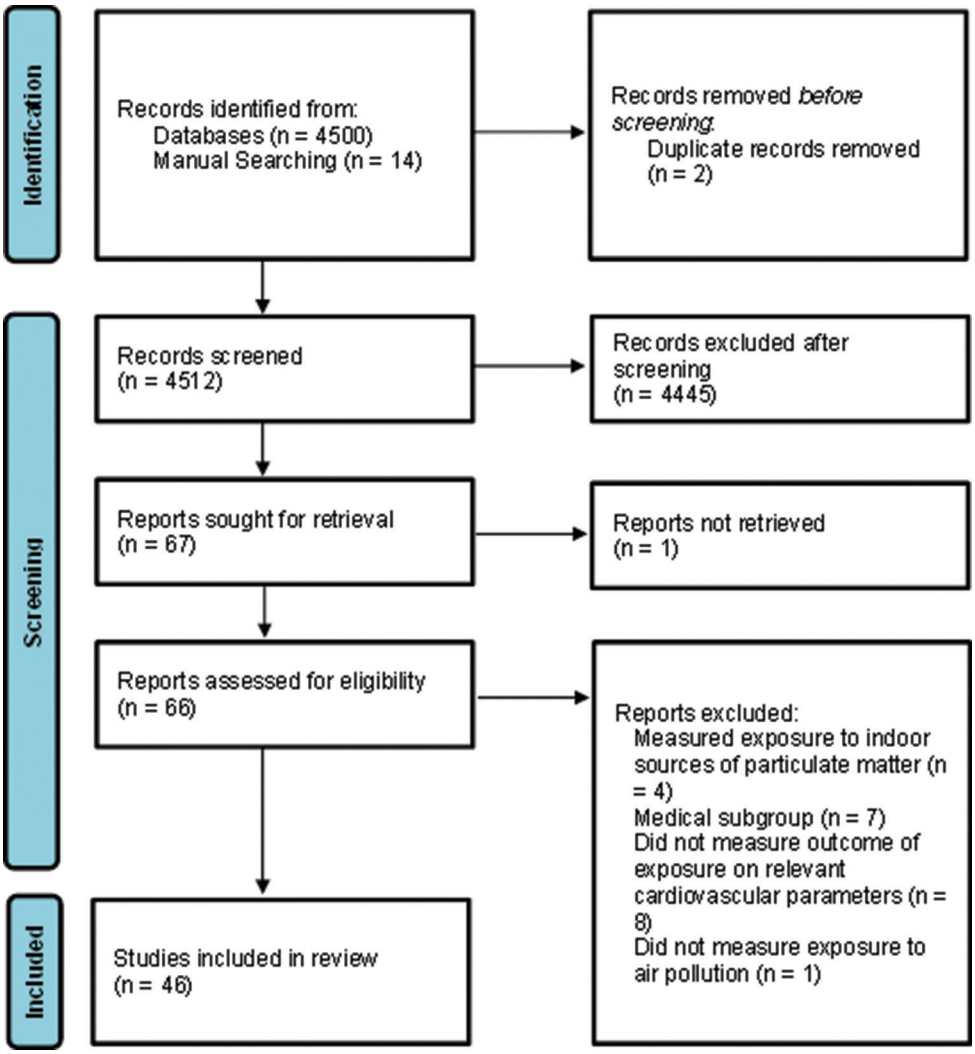

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart of study selection process

Gaseous pollutants

The relationship between gaseous pollutants with blood pressure and endothelial function was investigated by 13 crossover studies [Table S3]. There were no articles reporting the association between short-term exposure to gaseous pollutants with arterial stiffness.

A minority (three of eight) studies reported an association between O_3 and blood pressure,[30,35,51] five demonstrating no association.[46,47,58-60] Two of the studies only demonstrated an association when exposed to $PM_{2.5}$ 150 μg/m^3 in combination with O_3 120 ppb, but not O_3 in isolation.[30,35] Only two studies investigated exposure to NO_X, one air filtration study and one diesel exposure study; both reporting no statistically significant effect on blood pressure.[46,48] Of gaseous pollutant exposure studies concluding no association, three did not assess O_3 or NO_X exposure specifically, but rather filtered air versus unfiltered air[46,47] or diesel exhaust[48] that was measured to confirm higher O_3 or NO_X concentration.

Six studies in this review investigated the association between gaseous pollutants and endothelial function. Two found an association between endothelial dysfunction as measured by FMD and exposure to CO or NO_x, Breit *et al.* also reported a reduction in FMD with SO_2 exposure, but not supported by Liu *et al.*[41,53] Both studies had similar designs, both used fixed site air quality monitors to measure exposure at either two different locations or two different times. Although, both studies found an association between endothelial dysfunction and NO_X, only NO demonstrated a statistically significant association for Breit *et al.*, only NO_2 for Liu *et al.*, and neither NO or NO_2 reached statistical significance for Langrish *et al.*,[61] who did differ in their use of an exposure chamber rather than fixed site air quality monitors. Only one study found an association between O_3 with endothelial dysfunction[35] with three studies reporting no association after adjustment for confounding variables.[47,59,62] Most studies used FMD to measure endothelial function,[35,41,53,59] but one study measured response to vasodilators[61] and one used RHI.[62]

Table S3: Evidence table of studies investigating association between short-term exposure to air pollution and blood pressure, endothelial dysfunction, and arterial stiffness

Reference	Quality Rating	Population Characteristics	Air Pollution Measurement	Cardio-Vascular Measurement	Principal Findings
Cross-Sectional					
Shan *et al*. 2014	7/10	Sichuan Province; *n*=25 Age range: 38–85 Mean age: 59 Sex: male 0% female 100% Smoking status: Never smoked Inclusion criteria: Not pregnant, never smoked, used biomass fuel for cooking Adjusted for age, waist circumference, daily salt intake with statistical methods	Average 24 h exposure to $PM_{2.5}$ using personal exposure monitors with a d_{50} of $_{2.5}$ µm at 1.8 lpm (±10%) and a greased impaction surface.	Brachial artery and central SBP and DBP with 3 measurements using mean of final 2 measurements. cfPWV up to 3 readings in supine position	Difference between high $PM_{2.5}$ (>58 µg/m^3) and low $PM_{2.5}$ (<58 µg/m^3): Brachial SBP (95% CI) = 4.6 (−7.8, 16.9) *P*=0.4 Brachial DBP (95% CI) = −1.2 (−7.3, 4.9), *P*=0.54 Central SBP (95% CI) = 3.1 (−8.4, 14.5), *P*=0.53 Central DBP (95% CI) = −1.0 (−7.3, 5.3), *P*=0.61 cfPWV (95% CI) = −0.1 (−0.9, 0.7). *P*=0.97
Jiang *et al*. 2016	10/10	Urban Shanghai, China, *n*=371 Age range: 45–79 Mean age: 56.5±10.3 Sex: male 139 female 232 Smoking status: 14.8% smoker Adjusted for age, gender, BMI, educational status, smoking status, history diseases, and medication use	Categorsied by residential distance from major road. Personal $PM_{2.5}$ exposure measured with AM510, with plastic tube inlet port close to patients mouth to estimate $PM_{2.5}$ exposure	AIx, SBP, DBP, NO production in serum	Participants who lived within 50 m of a major road compared with those lived more than 200 m away had higher average personal $PM_{2.5}$ (111.1 vs. 68.2 µg/m^3) and 4.3×higher AIx (*P*<0.05), 1.6×higher SBP (*P*<0.05), 1.9×higher DBP (*P*<0.01), 4.6×lower NO production (*P*<0.01)
Panel Study					
Mehta *et al*. 2014	8/10	Participants of Normative Aging Study in Massachusetts, USA; *n*=370 Age range: 21–80 Mean age: 78.0±6.2 Sex: male 100% female 0% Smoking status: 1.9% smoker, 65.7% ex-smoker Adjusted for: Age, BMI, HDL, years of education, race, alcohol intake, smoking status, diabetes status, , seasonality, weekend of examination, average temperature, relative humidity	$PM_{2.5}$: Ambient $PM_{2.5}$ concentrations from local monitoring station. Short-term exposure windows of 4 h, 24 h, and 3, 7, 14 days preceding each examination.	AIx; mixed effects regression model as continuous functions of moving averages of air pollution exposure.	% change in AIx for 3.6-µg/m^3 increase in $PM_{2.5}$ (95% CI): 0.8% higher AIx (0.2–1.4) (*P*<0.05) Concluded that data support an association between exposure to air pollution and vascular function.
Fang *et al*. 2008	6/10	Construction workers regularly exposed to welding fumes; *n*=26 Age range: 24–64 Mean age: 41.2±11.7 Sex: male 100% female 0% Smoking status: 39% smoker Adjusted for age, smoking and smoking by time interaction	Exposure to $PM_{2.5}$ Gravimetric particle samplers in workers breathing zones.	AIx; measured radial artery pulse wave pressure forms with high fidelity micro manometer, before work, after work and following morning.	Increase in afternoon AIx (95% CI): 2.8% (−1.4, 7.0). Decrease in next morning AIx: −2.4% (−6.9, 2.2). Authors conclude welding fume exposure increases same day and decreases next morning augmentation index.
Randomized Crossover					
Liu *et al*. 2018	7/10	Elderly residents of Peking, China, *n*=35 Mean age: 66.26±7.71 Sex: male 20 female 15 Smoking status: smokers excluded Exclusion criteria: smoker Adjusted for age, gender, BMI, air filtration (yes vs. no) and time of day with statistical methods	$PM_{2.5}$: 4-week observational intervention - 2-weeks with filter and consecutive 2-weeks without. Air pollution monitoring devices measured 12 h real-time indoor and outdoor $PM_{2.5}$	12 h daytime ambulatory BP measurement, measured SBP and DBP every 30 min.	% increase in SBP per 10 µg/m^3 increase in indoor $PM_{2.5}$ (95% CI): 0.39 (0.03–0.75) (*P*<0.05) % increase in DBP per 10 µg/m^3 increase in indoor $PM_{2.5}$ (95% CI): 0.57 (0.05–1.10) (*P*<0.05). Concluded that short-term indoor air filtration intervention can be of cardiovascular benefits in elderly living with high pollution episodes.

(Contd...)

Table S3: Evidence table of studies investigating association between short-term exposure to air pollution and blood pressure, endothelial dysfunction, and arterial stiffness *(Continued)*

Reference	Quality Rating	Population Characteristics	Air Pollution Measurement	Cardio-Vascular Measurement	Principal Findings
Zhao *et al*. 2020	5/10	Peking University students, China, *n*=29 Age range: 18–25 Mean age: 21.8±2.1 Sex: male 16 female 13 Inclusion criteria: non-smoker, no history of CVD, BMI<30 Adjusted for sex, age, BMI, indoor temperature, indoor humidity	$PM_{2.5}$: Aerosol spectrometer was used to monitor real-time indoor $PM_{2.5}$ during active filtration and sham filtration	SBP and DBP measured from upper arm. 3 measurements, mean of last 2 used.	No statistically significant effect on $PM_{2.5}$ on SBP or DBP. Hypothesised that $PM_{2.5}$ could still affect health through systematic oxidative stress, platelet activation and respiratory inflammation.
Gong *et al*. 2003	5/10	Los Angeles, USA, *n*=12 Age range: 18–45 Mean age: 28±10 Sex: male 6 female 6 Inclusion criteria: healthy, non-smoker, non-asthmatic	$PM_{2.5}$: Exposure laboratory single person exposure chamber delivered air to chamber containing 8×outdoor $PM_{2.5}$ concentration	Measured BP, heart rate and heart rate variability	DBP showed no significant differences. SBP (baseline 120 mmHg) increased marginally at 4 h relative to filtered air, slope –0.30 mmHg/(μg/m^3), *P*=0.02. Concluded that $PM_{2.5}$ exposure elicits inflammation and heart rate variability consistent with systemic rather than respiratory effects.
Cole *et al*. 2018	6/10	Cyclists in downtown Vancouver, Canada, *n*=38 Age range: 20–39 Mean age: 29±5.6 Sex: male 28 female 10 Inclusion criteria: healthy, non-smoker, not taking medication for respiratory disease or CVD, no exposed to passive tobacco smoke Adjusted for route differences, pollutant exposure, BMI, age, sex	PM_1, $PM_{2.5}$ and PM_{10}: Exposure to low pollution residential route and high pollution downtown route. Ultrafine particle counter mounted onto wire panier measuring particle number concentration at 1 s intervals. GRIMM dust monitors measured PM10, $PM_{2.5}$ and PM1 at 6 s intervals	RHI measured 1 h before beginning cycle route and 15 min after completing route.	Mean difference downtown (pre-post change in RHI) vs residential (pre-post change) (95% CI): −0.39 (−0.77–0.017). Association between route and RHI were independent of pollutant exposure, suggesting other confounders.
Weichenthal *et al*. 2014	6/10	Montreal females (Canada); *n*=53 Age range 18–44 Mean age: 25±6.0 Sex: male 0 female 53 Smoking status: all non-smokers; 13.3% 2nd hand smoke exposure Adjusted for: caffeine/alcohol consumption, age, race, BMI, recent illness, or second hand smoke exposure in the past 24-h	$PM_{2.5}$ and $PM_{0.1}$, O_3: 3 separate days 2 h high traffic routes, low traffic routes, indoor cycling. 5 day washout period between 3 visits. Personal air pollution exposure measured with instruments mounted onto the bicycle. Harvard impacts measure $PM_{2.5}$ and $PM_{0.1}$ concentration. Ogawa sampling bags measured O_3 concentration.	Measured SBP, DBP and RHI Evaluated before and 3 h after each 2 h exercise period. 3 BP measurements average of 2 closest values.	$PM_{0.1}$ exposure was associated with a 4.91% (95% CI: −9.31, −0.512) decrease in RHI 24 ppb increase in O_3 exposure corresponded to a 2.49% (95% CI: 0.141, 4.84) increase in SBP and a 3.26% (95% CI: 0.0117, 6.51) increase in DBP 3-h after exposure. Exposure to traffic pollution may contribute to acute changes in blood pressure, autonomic and micro-vascular function in women
Kumarathasan *et al*. 2018	8/10	Residents with adjacent steel mill; Canada *n*=52 Age range: 18–34 Medium age: 23.0 Sex: male 24 female 28 Smoking status: smokers were excluded Adjusted for: date of exposure, carry-over effect, age, sex, body mass index (BMI), ambient air pressure, humidity and temperature.	$PM_{2.5}$, SO_2, NO_X, O_3: fixed site ambient air quality monitor measured pollutant concentration hourly. Participant spend 5×8 h days adjacent to Steel plant and 5×8 h days on college campus or in air filtered. 9-day washout period	Measured SBP, DBP, heart rate	College site vs Steel plant change SBP (mmHg) (95% CI): – 0.4733 (−3.1738–2.2272) (*P*=NS). College site versus Steel plant change DBP (mmHg) (95% CI): −0.1021 (−2.2438–2.0396) (*P*=NS). Conclude that air pollutants in the proximity of steel mill site can influence inflammatory and vascular mechanisms.

(Contd...)

Table S3: Evidence table of studies investigating association between short-term exposure to air pollution and blood pressure, endothelial dysfunction, and arterial stiffness *(Continued)*

Reference	Quality Rating	Population Characteristics	Air Pollution Measurement	Cardio-Vascular Measurement	Principal Findings
Liu *et al*. 2014	6/10	Ontario, Canada from University campuses; *n*=61 Age range: 18–34 Medium age: 22±1.6 Sex: male 28 female 33 Exclusion criteria: smoker, occupational exposure to Iron and Steel industry, history of CVD or Respiratory disease, diabetes, exercise limiting disorders, pregnancy or breastfeeding Adjusted for sex, temperature, humidity	Steel plant in proximity; randomized cross over study with fixed site air quality monitor at two sites Measured exposure to $PM_{2.5}$, NO_2, CO and SO_2	SBP and DBP were calculated from 6 consecutive readings, mean of last 5 used. FMD subject supine scanned basal brachial artery diameter following 5 min of cuff occlusion	Resting and post-exercise BP were not significantly different between two sites. % change in FMD for IQR increase in NO2 (95% CI) = −0.14% (−0.31, 0.02) (P<0.1), % change in FMD for IQR increase in CO (95% CI) = −0.02% (−0.03, −0.00) (P<0.05). Conclude NO2 and CO inversely associated with FMD.
Briet *et al*. 2007	7/10	France, *n*=40 Age range: 18–35 Sex: male 100% female 0% Inclusion criteria: non-smoker, no passive smoke exposure, normal creatinine and cholesterol levels, no proteinuria, normotensive. Adjusted for R53R/R53H genotype, diet, subject factor, visit, and air temperature	Measured exposure to NO, NO_2, SO_2, CO, PM_{10}, $PM_{2.5}$ Air pollution data extracted from AIRPARIF, Paris air pollution monitoring network, used monitoring station closest to HEGP hospital	Measured endothelium dependent FMD of brachial artery in response to 5 min hand ischemia.	Correlation between SO2 with FMD: P<0.001 Correlation between NO with FMD: P<0.01 Correlation between CO with FMD: P<0.05 Correlation NO_2, $PM_{2.5}$, PM_{10} with FMD: P=NS. SO_2 levels explained 19% of the variance of FMD. An increase in gaseous pollutants, 2 weeks apart, was significantly associated with a decreased FMD. Endothelial function was impaired by ordinary levels of urban pollution in healthy young males.
Randomized Single-blind Crossover					
Shi *et al*. 2017	Some Concerns	Healthy college students, Shanghai, China; *n*=24 Mean age: 23 Sex: male 13 female 11 Smoking status: smokers were excluded Adjusted for: age, sex, body mass index, $PM_{2.5}$ concentration, 48-h mean temperature, and 48-h mean humidity.	$PM_{2.5}$: Randomized; wore N95 disposable particulate filtering respirators for 48 h alternating with 3-week washout period. $PM_{2.5}$ was continuously monitored indoors and outdoors using personal aerosol monitors.	Heart rate variability and ABPM BP measured every 15 min during day and 30 min at night)	Mean % change in SBP: −2.7 (−5.2, −0.1) (P=0.049) Mean % change in DBP: −0.5 ($-_{2.5}$, 1.5) (P=0.622) Concluded that short-term wearing of particulate-filtering respirators may reduce BP.
Kajbafzadeh *et al*. 2015	Some Concerns	Residents of Vancouver, Canada, *n*=68 Age range: 19–72 Mean age: 43.8±12.8 Sex: male 32 female 36 Exclusion Criteria: pregnant women, recent surgery, diabetes, heart disease, hypertension, metabolic syndrome, asthma, COPD, or Raynaud's syndrome, use of anti-inflammatory medication Adjusted for average indoor temperature and relative humidity	$PM_{2.5}$: 7 days with filtration device followed by 7 days with placebo filtration device. Indoor and outdoor $PM_{2.5}$ concentration was measured.	RHI at the end of each 7-day period	Mean RHI non-filtration±SD: 2.1±0.6 Mean RHI with air filtration±SD: 2.1±0.6 P=0.71 Concluded no relationship between $PM_{2.5}$ exposure and endothelial function.

(Contd...)

Table S3: Evidence table of studies investigating association between short-term exposure to air pollution and blood pressure, endothelial dysfunction, and arterial stiffness *(Continued)*

Reference	Quality Rating	Population Characteristics	Air Pollution Measurement	Cardio-Vascular Measurement	Principal Findings
Allen *et al*. 2011	Some Concerns	Canada, *n*=45 Age range: 20–63 Mean age: 43.0±9.9 Sex: male 21 female 24 Smoking status: smokers were excluded Inclusion criteria: healthy, non-smoking, non-smoking households Adjusted for: age, sex, BMI, temperature	$PM_{2.5}$: Each home was monitored for 2 consecutive 7 day periods during filtration and placebo filtration. During exposure $PM_{2.5}$ filter samples were collected indoor and outdoors to calculate $PM_{2.5}$ mass concentration.	Measured microvascular endothelial function with RHI	RHI unfiltered air±SD: 2.06±0.63, RHI filtered air±SD: 2.28±0.72 (*P*=0.03) Increases in RHI during filtration HEPA filtration was associated with a 9.4% (95% CI, 0.9–18%) increase in RHI.
Fakhri *et al*. 2009	Some Concerns	Canada, *n*=50 Age range: 19–48 Mean age: 27.08±7.13 Sex: male 24 female 26 Inclusion criteria: healthy, non-smoker, no history of CVD or CVD risk factors Adjusted for age, sex, asthmatic status	$PM_{2.5}$, O_3: 4×2 h exposures to sham filtered air, $PM_{2.5}$ 150 μg/m^3, O_3 120 ppb, $PM_{2.5}$ and O_3 Exposures were separated by 2 weeks. $PM_{2.5}$ and O_3 concentrations were continuously monitored. Human exposure chamber used.	Measured heart rate variability and BP: SBP and DBP were measured every 30 mins throughout 2 h exposure.	Change in DBP after $PM_{2.5}$ and O_3 exposure (mmHg)±SE: 1.97±1.21 (*P*=0.02). Change in SBP after $PM_{2.5}$ and O_3 exposure (mmHg)±SE: 0.90±2.00 (*P*=0.48).
Randomised Double-blind Crossover					
Padró-Martínez *et al*. 2015	Low Risk of Bias	Residents living within 200 m of Massachusetts State highway, USA; *n*=20 Mean age: 53.6±9.2 Sex: male 4 female 16 Inclusion criteria: healthy, non-smoking, not allow smoking in home, lived 200 m form Massachusetts state highway Adjusted for: time activity, subjects served as own control	$PM_{2.5}$: 21-day period for each exposure to filtered air and unfiltered air. Particle counter and filtration units were installed in each living room.	Measured SBP and DBP	Difference in SBP unfiltered vs filtered air (mmHg) (95% CI): 8.19 (−0.991, 17.4) (*P*=NS) Difference in DBP unfiltered vs filtered air (mmHg) (95% CI): 4.23 (−3.89, 12.4) (*P*=NS) Concluded no evidence that the filtration improved BP
Morishita *et al*. 2018	Low Risk of Bias	Reducing air pollution in Detroit intervention study: participants living in a low income residential building for senior citizens; USA; *n*=40 Mean age: 67±8 Sex: male 25 female 15 Inclusion criteria: healthy, non-smoking, not receiving supplementary oxygen, Adjusted for: outdoor $PM_{2.5}$ exposure	$PM_{2.5}$: 3 day period for each intervention unfiltered air, low efficiency filtration, high efficiency filtration. Participant wore personal air monitors. Daily $PM_{2.5}$ samples were collected at each participant's residence both indoor and outdoor.	Measured SBP and DBP of Brachial artery,	Mean decrease SBP using high efficiency filtration mmHg (95% CI): 2.9 (−6.2–0.5) (*P*=0.75). Mean decrease DBP using high efficiency filtration mmHg (95% CI): 0.8 (−2.8–1.2) (*P*=0.14). Concluded: short-term use of portable air filtration systems reduced personal $PM_{2.5}$ exposures and may reduce SBP.
Karottki *et al*. 2013	Low Risk of Bias	Elderly residents of Copenhagen, Denmark, *n*=48 Age range: 51–81 Mean age: 67±6.5 Sex: male 22 female 26 Exclusion criteria: smokers Adjusted for: baseline level, BMI, age, and gender	$PM_{2.5}$: exposure to particle filtered and sham filtered indoor air over 14-day period each exposure. Particle number concentrations of $PM_{2.5}$ were continually monitored every 16 s	Measured BP	No effect of air filtration on BP (data not reported)

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Table S3: Evidence table of studies investigating association between short-term exposure to air pollution and blood pressure, endothelial dysfunction, and arterial stiffness *(Continued)*

Reference	Quality Rating	Population Characteristics	Air Pollution Measurement	Cardio-Vascular Measurement	Principal Findings
Weichenthal *et al*. 2013	Low Risk of Bias	First nations reserve, Canada. *n*=37; age range 11–64; mean age: 32. Sex: male 47% female 53%. Smoking status: 64% current smokers. Adjusted for: outdoor temperature, indoor CO2 concentration, air filtration, and mean number of cigarettes smoked.	PM_{10}, $PM_{2.5}$, PM_1: Air filter placed in each home. 1 week filtered air, 1 week unfiltered air with 1 week washout period. Weekly average PM_{10}, $PM_{2.5}$, PM_1 was determined with cascade impactors.	DBP, SBP, RHI: collected at start and end of each exposure period. BP measurements in duplicate. Participant was seated in quiet dimly lit room.	Change after exposure to $PM_{2.5}$ (95% CI): SBP −0.54 (−5.5, 4.5), *P*=NS; DBP 1.8 (−1.7, 5.3) *P*=NS; RHI −0.085 (−0.34, 0.17), *P*=NS. Concluded: air pollutants not strongly associated with cardiovascular parameters.
Chen *et al*. 2015	Low Risk of Bias	College students in Shanghai, China, *n*=35 Age range: 18–35 Mean age: 23±2 Sex: male 10 female 25 Inclusion criteria: healthy, non-smoker, no cardiopulmonary disease Adjusted for age, sex, BMI, indoor temperature, and indoor relative humidity.	$PM_{2.5}$: air purifier in room for 48 h, 2-week washout period, then sham purifier in room for 48 h. Measured indoor and outdoor $PM_{2.5}$ using personal aerosol monitor 1 m away from air purifier and outdoor monitor on rooftop.	BP measured 3 consecutive readings, mean of final 2 measurements to obtain SBP and DBP.	% change SBP (95% CI): −2.7% (−5.1, −0.4). % change DBP (95% CI): −4.8% (−8.5, −1.2). Concluded: cardiopulmonary benefits of indoor air purification among healthy adults living in urban areas with severe particulate air pollution.
Cui *et al*. 2018	Some Concerns	Medical and nursing students, China; *n*=70 Age range: 19–26 Mean age: 22±1.6 Sex: male 29 female 41 Smoking status: smokers were excluded Adjusted for filtration duration, temperature and relative humidity	$PM_{2.5}$, O_3, NO_2: Two indoor air filtration sessions. Measured exposure before, during and after air filtration.	SBP and DBP at start and end of filtration session. cfPWV average value of 3 consecutive measurements	% change between true and sham filtration: PWV 0.39% (−2.36, 3.15) (*P*=0.78). SBP −0.13% (−2.06, 1.79) (*P*=0.89). DBP 2.67% (−0.01, 5.34) (*P*=0.06) Concluded: changes in PWV and BP not significantly different from sham filtration.
Bellavia *et al*. 2013	Low Risk of Bias	Canada; *n*=15 Age range: 18–60 Mean age: 27.7±8.06 Sex: male 8 female 7 Exclusion criteria: fasting total cholesterol >6.2 mmol/L, fasting glucose >7 mmol/L hypertension, pregnancy or lactation, ECG abnormalities	PM_{10} and $PM_{2.5}$: 3 exposures in random order, volunteers and study personal were blinded. Human exposure facility.	BP measured when seated 10 min before and 5 min after exposure.	Post exposure to $PM_{2.5}$ difference in SBP relative to control: $_{2.5}$3 mmHg (*P*=0.001). Post exposure to PM_{10} difference in SBP relative to control: 1.56 mmHg (*P*=0.03). Post-exposure differences in DBP were not statistically significant. Concluded that PM elevates BP.
Brook *et al*. 2014	Low Risk of Bias	USA, *n*=32 Age range: 18–46 Mean age: 25.9±6.6 Sex: male 16 female 16 Inclusion criteria: healthy, non-smoker, without CVD or risk factors eg hypertension, hyperlipidemia, diabetes; not taking medication that may affect vascular function	PM_{10} and filtered air: PM_{10} generated by a system that concentrates ambient course particles. PM_{10} mass levels continuously monitored during exposure using personal DataRAM. Human exposure chamber used.	Measured endothelium dependant FMD from brachial artery, PWV, AIx, RHI and brachial artery BP	SBP (mean difference = 0.32 mmHg; 95% CI: 0.05, 0.58; *P*=0.021) and DBP (0.27 (0.003, 0.53); *P*=0.05) linearly increased per 10 min of exposure during the inhalation of $PM_{10.}$ FMD, AIx, PWV were not significantly altered by exposure to PM_{10}. Reported inhalation of coarse PM was associated with a rapid elevation in BP and heart rate during exposure.

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Table S3: Evidence table of studies investigating association between short-term exposure to air pollution and blood pressure, endothelial dysfunction, and arterial stiffness *(Continued)*

Reference	Quality Rating	Population Characteristics	Air Pollution Measurement	Cardio-Vascular Measurement	Principal Findings
Morishita *et al*. 2015	Low Risk of Bias	USA, *n*=32 Age range: 18–46 Mean age: 25.9±6.6 Sex: male 16 female 16 Inclusion criteria: healthy, non-smoking, without CVD, BP <140/90 mmHg, fasting glucose <126 mg/dl, not taking medications that may alter outcomes. Unadjusted data.	2 h long exposure to $PM_{2.5}$-10 vs filtered air, 1–3 week washout period. Virtual impact or system generated $PM_{2.5}$-10. Filtered air generated with high efficiency PM filter.	Left upper arm BP and heart rate measured every 10 min	Report concentration–response associations between $PM_{2.5}$-10 exposure and SBP, but not DBP. Particulate composition was not an important determinant of these responses. Values not reported.
Brook *et al*. 2002	Low Risk of Bias	Canada, *n*=25 Age range: 18–50 Mean age: 34.9±10 Sex: male 15 female 10 Inclusion criteria: healthy, non-smoker. Exclusion criteria: CVD; fasting glucose ≥126 mg/dL, total cholesterol ≥240 mg/dL, hypertension.	Measured exposure to concentrated ambient $PM_{2.5}$ O_3, vs filtered air 2 h inhalation to $PM_{2.5}$ and O_3 in human exposure facility to $PM_{2.5}$ = 150 μg/m^3 and O_3 = 120 ppb	Measured endothelium dependant FMD, SBP and SBP	% change FMD polluted air vs filtered air: +0.29±4.11% vs −0.03±6.63%, (*P*=0.88), % change SBP polluted air vs filtered air: +0.4±8.6% vs +0.8±10.3%, (*P*=0.61), % change DBP polluted air vs filtered air: +0.9±7.2% vs −0.4±7.3%, (*P*=0.77) FMD and BP responses did not significantly differ between the exposure types.
Brook *et al*. 2009	Low Risk of Bias	Canada, *n*=31 Age range: 18–50 Mean age: 27±8 Sex: male 16 female 15 Smoking status: smokers excluded Inclusion criteria: healthy, non-smoker, without CVD or CVD risk factors, not taking medications Exclusion criteria: fasting glucose ≥126 mg/dL, fasting total cholesterol ≥240 mg/dL	Measured exposure to concentrated ambient $PM_{2.5}$ O_3, filtered air 2 h inhalation to $PM_{2.5}$ and O_3 in human exposure facility or virtual impact system to $PM_{2.5}$ = 150 μg/m^3 and O_3 = 120 ppb. $PM_{2.5}$ level monitored using tapered element oscillating microbalance during exposure.	Measured endothelium dependent FMD SBP and SBP calculated from mean of 3 supine measurements.	% change FMD 24 h after exposure to $PM_{2.5}$ and O_3: 8.8±4.2 (*P*=0.016); $PM_{2.5}$ alone: 5.8±5.3 (*P*<0.05). Change in DBP after exposure to $PM_{2.5}$ and O_3: 0.89±0.22 (*P*=0.01); $PM_{2.5}$ alone: 0.71±0.21 (*P*=0.002), Concluded: immediately post-exposure, FMD not significantly impaired (data not shown), but decreased 24 h post-exposure. DBP increased linearly during $PM_{2.5}$ containing exposures.
Frampton *et al*. 2015	Low Risk of Bias	USA, *n*=12. Age range: 18–40 Mean age: 27.3±4.2 Sex: male 7 female 5 Inclusion criteria: healthy, non-smoker, no pulmonary disease or CVD, normal spirometry, normal ECG, not pregnant, not using anti-inflammatory drugs, no respiratory infections	Measured exposure (3 h) to 100 ppb O_3, 200 ppb O_3, and filtered air. Washout: 2 weeks between exposures.	Measured vascular endothelial function with RHI using peripheral artery tonometry.	No significant effect of O_3 on RHI. Figures not shown.
Tank *et al*. 2011	Low Risk of Bias	Germany, *n*=14. Age range 22–47 Mean age: 33.7±9.5 Sex: male 11 female 3 Inclusion criteria: healthy, forced expiratory volume in 1st s >80%. Exclusion criteria: respiratory tract infections, medication, hormone replacement therapy	Measured exposure (3 h) to 100 ppb O_3, 250 ppb O_3, and filtered air. Washout: 2 weeks between exposures. O_3 concentration was monitored	Measured brachial artery BP After overnight fast in the morning.	Resting SBP (clean air: 121±3 mmHg; ozone: 121±2 mmHg), DBP (clean air: 71±2 mmHg; ozone: 71±2 mmHg). *P* value not reported No significant effect for BP.

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Table S3: Evidence table of studies investigating association between short-term exposure to air pollution and blood pressure, endothelial dysfunction, and arterial stiffness *(Continued)*

Reference	Quality Rating	Population Characteristics	Air Pollution Measurement	Cardio-Vascular Measurement	Principal Findings
Rich *et al.* 2018	Low Risk of Bias	Multicentre Ozone Study in oldEr Subjects (MOSES); USA; *n*=87 Age range: 55–70 Mean age: 59.9±4.5 Sex: male 35 female 52 Inclusion criteria: healthy non-smoker, normal resting ECG, normal spirometry Adjusted for filtration duration, temperature and relative humidity	Exposure to O_3 in ventilated climate-controlled chambers.	SBP and DBP FMD	% change SBP pre-post exposure (95% CI): −1.3% (−3.7, 1.2) *P*=0.950, % change DBP: -0.1% (−1.2, 1.0) (*P*=0.816), % change FMD pre-post exposure (95% CI): −0.1% (−1.1, 0.9) (*P*=0.637) No statistically significant effect of Ozone on SBP and DBP, slight increase in FMD wasn't statistically significant.
Arjomandi *et al.* 2015	Low Risk of Bias	USA, *n*=26; Age range: 18–50 Mean age: 31.8±7.6 Sex: male 13 female 13 Smoking status: non-smokers Inclusion criteria: ability to perform exercise, healthy, no recreational drug use Adjusted for age and smoking	O_3 Exposure in ventilated chambers for 4 h with subjects exercising for 30 min. Exposed to 0, 100, 200 ppb O_3. 3-week washout period between exposures.	BP and heart rate measured at 0 h, 4 h, 24 h with subjects placed in supine position	Data not provided. Concluded: no significant trends between the changes in BP and heart rate with level of ozone exposure from 0 h to either 4 h or 24 h.
Langrish *et al.* 2010	Low Risk of Bias	Sweden, *n*=10; all male Age range: 22–28 Medium age: 24 Inclusion criteria: male, healthy, no respiratory infections, non-smoker, no current illness, no regular medications, normal lung function	NO_2, NO: NO_2 or filtered air in exposure chamber. Monitored for NOX using oxides of Nitrogen analyser. NOX concentration maintained at 4 ppm	Measured endothelial function with forearm blood flow following infusion with endothelium dependant and independent vasodilators	No difference in vascular response to any vasodilator following NOX exposure.
Barath *et al.* 2010	Low Risk of Bias	Sweden; *n*=18 Age range: 21–30 Mean age: 27 Sex: male 100% female 0% Smoking status: smokers were excluded inclusion criteria: healthy, non-smoking, free from respiratory tract infection	PM_{10}, NO and NO_2: exposure chamber with diesel exhaust generated by diesel engine. Standard glass fiber sampling and tapered element microbalance to measure PM_{10}. Chemiluminescence to measure NO and NO_2	Measured forearm blood flow using the fusion of vasodilators into brachial artery, BP and heart rate	SBP filtered air vs exhaust (mmHg)±SD: 142±3.2 versus 142±2.7 (*P*=NS), DBP filtered air vs exhaust±SD: 68±2.9 vs 68±1.8 (*P*=NS) Concluded: no differences on resting heart rate, BP, or forearm blood flow after diesel exposure.
Mills *et al.* 2011	Low Risk of Bias	UK, *n*=16; Age range: 18–32 Sex: male 100% female 0% Smoking status: smokers were excluded Exclusion criteria: taking regular medication, chronic health conditions, occupational exposure to air pollution	PM: Purpose built exposure chamber. Air was continuously monitored for NOx, CO, SO_2, O_3, PM concentrations. Diesel exhaust from diesel engine.	Measured SBP, DBP, and endothelial function: forearm blood flow following infusion with endothelium dependent and independent vasodilators	SBP following diesel exhaust inhalation±SD: 145± 4, versus filtered air 133± 3 (*P*=0.012) DBP± SD: 69±8 vs 69± 8 (*P*=NS) Infusion response diesel versus filtered: bradykinin (*P*=0.005), acetylcholine (*P*=0.008), and sodium nitroprusside (*P*<0.001) Concluded: Reduced vasodilation following exposure to diesel exhaust.

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Table S3: Evidence table of studies investigating association between short-term exposure to air pollution and blood pressure, endothelial dysfunction, and arterial stiffness *(Continued)*

Reference	Quality Rating	Population Characteristics	Air Pollution Measurement	Cardio-Vascular Measurement	Principal Findings
Cosselman *et al*. 2012	Low Risk of Bias	USA, *n*=31; Age range: 18–49 Mean age: 28±8.6 Sex: male 22 female 9 Exclusion criteria: smoker, hypertension, other chronic medical conditions, pregnancy. Adjusted for diesel exhaust exposure, metabolic syndrome, sex	$PM_{2.5}$: Diesel exhaust fumes generated to maintain $PM_{2.5}$ concentration at 200 μg/m^3. $PM_{2.5}$ measured with tapered element oscillating microbalance and adjusted.	Measured resting BP and heart rate during exposure at 5, 30, 60, 90, 110 min from exposure start and 3 h, 5 h, 7 h, 24 h after exposure	No significant effect on heart rate or DBP, but a rapid, increase in SBP in young non-smokers: Mean SBP increased, peaking 30 to 60 min after exposure 3.8 mmHg (95% CI 0.4–8.0) at 30 min, 5.1 mmHg (95% CI 0.7–9.5) at 60 min
Törnqvist *et al*. 2007	Low Risk of Bias	UK, *n*=15 Age range: 18–38 Mean age: 26 Sex: male 15 female 0 Smoking status: smokers were excluded Inclusion criteria: healthy, non-smoking, ,	PM: Exposed to filtered ambient air or diesel exhaust at 300 150 μg/m^3 for 1 h in exposure chamber. 2 week washout period	Measured response to various endothelium dependant and independent vasodilators Vascular measurements 2-4h and 24 h after exposure.	After exposure to diesel exhaust, endothelium-dependent vasodilatation was reduced with acetylcholine (*P*=0.01), bradykinin reduction did not reach significance (*P*=0.08). No effect on endothelium-independent vasodilatation: Sodium nitroprusside and Verapamil.

Long-term exposure

PM

The relationship between long-term exposure to PM with blood pressure was investigated by five observational studies [Table S4]. All studies defined hypertension as SBP ≥140 mm Hg and/or DBP ≥90 mm Hg, or physician diagnosis with use of antihypertensive medication,[63] and all found an association.[14,16,18,22,23] Endothelial function was not widely reported, with only one study identified. This concluded an inverse association, that is, elevated long-term (but not short-term) $PM_{2.5}$ concentrations impaired endothelial function as measured by FMD, independent of other cardiovascular risk factors.[20]

The association between arterial stiffness and long-term PM exposure was investigated by three studies. Wu *et al.*[17] reported an increase in arterial stiffness measured with brachial-ankle PWV (baPWV) when exposed to $PM_{2.5}$, but not when exposed to NO_2. In contrast, Lenters *et al.*[15] using cfPWV found an association with NO_2 and SO_2, but not $PM_{2.5}$. Adamopoulos *et al.*[24] also used cfPWV to measure arterial stiffness, and failed to find an association with long-term PM_{10} exposure.

Gaseous pollutants

The relationship between long-term exposure to gaseous pollutants with blood pressure and arterial stiffness was investigated by six observational studies; no articles reported the association with endothelial function; and four studies investigated the association with blood pressure [Table S4].

Dong *et al.*[23] using data from the nearest monitoring site found a positive association between O_3 and SO_2 exposure (but not NO_2) with odds of hypertension. Three other studies that used land-use regression models did conclude an association between NO_X exposure and increased blood pressure.[16,18,19] The association of arterial stiffness with gaseous pollutant exposure was investigated by two studies. Lenters *et al.*[15] found a positive association between SO_2 and NO_2 with arterial stiffness, in contrast Wu *et al.*[17] found no association. Considering the discrepancy, both studies used similar methods (PWV and land-use regression models), thus the long-term effect of gaseous pollutants on arterial stiffness remains unclear.

Risk of bias across the studies

Modified Newcastle-Ottawa scale applied to the cross-sectional studies gave scores between 5/10 and 10/10, and the revised Cochrane risk of bias tool (RoB 2) gave "some concerns" to "low risk of bias" for the randomized trials; detailed information regarding each study is reported in the supplemental data [Tables S1 and S2]. Potential sources of bias affecting the quality of the included studies included representativeness of the sample, lack of justification of sample size, and failure to control or adjust for exposure uncertainties or confounding variables, selection bias.

Discussion

Long-term exposure studies consistently report an association between air pollution and elevated blood pressure. These have largely been cross-sectional from which one cannot infer causation; however, one cohort study measuring exposure to $PM_{2.5}$ and NO_X over 10 years also supported a temporal association with air pollution.[18] Arterial stiffness and endothelial function were reported less frequently, but the majority of the studies supported an association. Data [Table S4] support the hypothesis that longer exposures to air pollution represent cumulative biological effects.

Table S4: Evidence Table of studies investigating association between long-term exposure to air pollution and blood pressure, endothelial dysfunction, and arterial stiffness

Author, Title, Country	Quality Rating	Population Characteristics	Air Pollution Measurement	Cardio-Vascular Measurement	Principal Findings
Cross-Sectional					
Krishnan *et al*. 2012	10/10	MESA Air (Multi-Ethnic Study of Atherosclerosis and Air Pollution); USA; *n*=3040 Age range: 45–84 Mean age: 61.2±9.9 Sex: male 1545 female 1495 Smoking status: smokers were excluded Inclusion: free from cardiovascular disease Adjusted for multiple factors	$PM_{2.5}$: Long term exposure hierarchical spatio-temporal model using EPA air quality monitoring stations used to predict exposure at home locations for year 2000. Short term exposure control site air quality monitoring station on day of examination and 2 days prior	Measured FMD	For every 3-μg/m^3 increase in the annual average $PM_{2.5}$ FMD % ↓ by 0.3% (0.6, 0.03) (*P*=0.03). Short-term $PM_{2.5}$ concentrations were associated with a small ↓ in FMD% 0.1% (0.2, 0.04) *P*=NS. Concluded: inverse association between long-term $PM_{2.5}$ concentrations and FMD, independent of cardiovascular risk factors.
Babisch *et al*. 2014	5/10	KORA-survey 2000; Germany; *n*=4166 Age range: 25–74 Mean age: 74.8±6.4 Sex: male 2046 female 2120 946 smoker, 132 occasional, 1305 ex-smoker Adjusted for: age, sex, smoking, alcohol intake, BMI, physical activity, socio-economic status.	$PM_{2.5}$: annual average $PM_{2.5}$ concentration at residential address from land use regression modeling using data from 20 monitoring sites 2008 to 2009.	Hypertension: 3 BP measurements. SBP ≥140 and/ or DBP ≥90 mm Hg or physician diagnosed with use of antihypertensive medication.	OR of hypertension: 1.15 (95% CI 1.02, 1.30) per 1 μg/m^3 ↑ increase in $PM_{2.5}$
Lin *et al*. 2017	9/10	Chinese respondents to WHO's SAGE study Hypertensive: *n*= 7777 Normotensive: *n*= 4888 Age range: ≥50 Mean age: 63 Sex: male 5895 female 6770 Smoking: 8417 none, 1655 0–8 cigs/day, 2588 >8 cigs/day.	$PM_{2.5}$: Van Donkelaar *et al*. method to estimate average $PM_{2.5}$ exposure in each participant communities. Used data from 3 years preceding the Survey.	Hypertension: SBP ≥140 and/or DBP ≥90 mmHg or physician diagnosed with use of antihypertensive medication. BP measured in triplicate.	OR of hypertension: 1.14 (95% CI 1.07, 1.22) per 10 μg/m3 ↑ in $PM_{2.5}$
Lenters *et al*. 2010	7/10	Young adults; Netherlands, *n*=745 Age range: 45–84 Mean age: 28.4±0.9 Sex: male 47% female 53% 31% smoker, 14% former smoker Adjusted for: age, sex, mean BP, PWV analysis, BMI, pack-years smoking, alcohol, socio-economic status, diabetes.	NO_2, $PM_{2.5}$, SO_2: Regression models were developed using land use data and population density. Long term exposure characterized as the sum of regional, urban and local traffic. NO_2, $PM_{2.5}$ and SO_2 from air monitoring sites were averaged for the year 2000.	Measured carotid artery intima media thickness, cfPWV, AIx.	cfPWV: 4.9% ↑ (95% CI 1.2, 8.7)/20-μg/m NO2. AIx: 37.6% ↑ (2.2, 72.9)/25-μg/m^3 ↑ NO_2 *P*<0.04. cfPWV: 5.26% ↑ (0.09, 10.43)/5-μg/m^3↑ SO2. Concluded: association between gaseous pollutant exposure and arterial stiffness; but not $PM_{2.5}$ which showed a weak association with PWV after adjustment for covariates.

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Table S4: Evidence Table of studies investigating association between long-term exposure to air pollution and blood pressure, endothelial dysfunction, and arterial stiffness *(Continued)*

Author, Title, Country	Quality Rating	Population Characteristics	Air Pollution Measurement	Cardio-Vascular Measurement	Principal Findings
Chen *et al*. 2015	6/10	Taiwan elderly health screening programme 2009 *n*=27752; Mean age: 74.8±6.4 Sex: male 14414 female 13338 Smoking status: 6.7% smoker, 93.3% ex-smoker Inclusion criteria: age >65, BP 120–60 to 190–90 mmHg Adjusted for: sex, age, BMI, smoking, alcohol, education, BP, diabetes, traffic proximity	NO_2, PM_{10}, $PM_{2.5}$, NOx: Land use regression to model annual average concentration for each participant using 40 monitoring sites. One-year exposures.	Hypertension: SBP ≥140 and/or DBP ≥90 mm Hg or physician diagnosed with antihypertensive medication use. BP performed seated, 1 measurement taken.	PM10, $PM_{2.5}$–10, and NOx were associated with higher DBP (but not $PM_{2.5}$) in generalised linear models: mmHg (95% CI) – PM10 (10 μg/m^3) 0.77 (0.46, 1.09); $PM_{2.5}$–10 (5 μg/m^3) 0.46 (0.29, 0.63); $PM_{2.5}$ (5 μg/m^3) –0.05 (–0.20, 0.11); NOx (20 μg/m^3) 0.41 (0.23, 0.59) None of the air pollutants was associated with SBP.
Dong *et al*. 2013	7/10	Communities <1 km from monitoring site, China *n*=24845; Age range: 18–74; Mean age: 46±13 Sex: male 12661 female 12184 Smoking status: approx. 1/3 smokers Adjusted for: age, race, education, income, smoke, drink, exercise, diet, sugar, family history of hypertension, and district.	PM10, SO_2, NO_2, O_3 concentrations were obtained from monitoring stations. Calculated 3-year average concentrations between 2006 and 2008	Hypertension: SBP ≥140 and/or DBP ≥90 mm Hg or physician diagnosed with antihypertensive medication use. BP was measured 3 times	OR of hypertension: A) 1.12 (95% CI 1.08, 1.16) per 19 μg/m^3 ↑ in PM_{10}. B) 1.11 (1.04, 1.18) per 20 μg/m^3 ↑ in SO_2. C) 1.13 (1.06, 1.20) per 22 μg/m^3 ↑ in O_3. D) 1.09 (1.00, 1.20) per 9 μg/m^3 ↑ in NO_2
Foraster *et al*. 2014	8/10	Population based Cohort of REGICOR study; Spain Hypertensive: *n*= 704, non-hypertensive: *n*= 1222 Age range: 36–82 Mean age: 56±18 Sex: male 876 female 1050 Smoking status: 406 smoker, 539 former smoker Adjusted for: age, sex, education, diet, exercise, alcohol, smoking, BMI, diabetes, deprivation, daily temperature, and indoor railway noise.	NO_2: outdoor levels at each subjects address with land use regression models using data from outdoor monitoring sites.	Hypertension: SBP ≥140 and/or DBP ≥90 mm Hg, or physiciandiagnosedwith use of antihypertensive medication. BP measured in duplicate.	OR of hypertension: 1.16 (95% CI 0.99, 1.36) per 10 μg/m^3 ↑ in NO_2. Concluded: association between long-term exposure to NO_2/traffic-related air pollution and hypertension.

(Contd...)

Table S4: Evidence Table of studies investigating association between long-term exposure to air pollution and blood pressure, endothelial dysfunction, and arterial stiffness *(Continued)*

Author, Title, Country	Quality Rating	Population Characteristics	Air Pollution Measurement	Cardio-Vascular Measurement	Principal Findings
Panel Study					
Wu *et al*. 2016	6/10	Residents of a Metropolitan area of Taiwan, *n*=89 Age range: 18–79 Mean age: 43.7; Sex: male 35 female 54 Exclusion criteria: incomplete health outcome data. Adjusted for sex, age, body mass index, waist, SBP.	$PM_{2.5}$ and NO_2: Outdoor air pollutants measured at air quality monitoring stations. Indoor air pollution sampled within a finance office in Taipei using personal dust and chemiluminescence methods. Land use regression modeling to estimate exposure levels.	baPWV 2 examinations, 8 months apart.	Increase in baPWV: 2.4% (95% CI 0.8, 4.0) per 10 μg/m^3 increase in $PM_{2.5}$ concentration (1 day lag), *P*<0.05. Increase in baPWV: 1.9% (95% CI–0.3, 4.1) per 10 ppb increase in NO_2 concentration (1-day lag) *P*=NS. Concluded: $PM_{2.5}$ increases baPWV as a measure of arterial stiffness, no significant association for NO_2.
Cohort Study					
Adamopoulos *et al*. 2010	9/10	Hypertension Outpatients in Athens, Greece; *n*=1222 Mean age: 51±13; Sex: male 649 female 573 42.1% smokers Inclusion criteria: hypertension outpatient clinics	PM10: Ambient PM10 obtained from 7 air quality monitoring station in Athens. Mean daily and mean 5-day values were calculated.	Cohort Study Length: 3 years Measure BP, cfPWV	Change in cfPWV: −1.99 m/s (95% CI −4.19, 0.19) per 43.4 μg/m^3, *P*=NS. Change in SBP: 0.26 mmHg (−2.02– $_{2.5}$4) per 43.4 mg/m^3, *P*=NS. Multiple-linear regression analysis revealed no significant associations between environmental variables and arterial stiffness.
Coogan *et al*. 2012	8/10	Black Women's Health Study; USA; *n*=4204 Age range: 21–69; all female Smoking tertiles: non-smoker, <25, ≥25 cigs/day Inclusion criteria: age 21–69, black, female Adjusted for: age, BMI, income, number of people in the household, smoking, alcohol, physical activity, socioeconomic status.	$PM_{2.5}$ and NOx: 23 state and local monitoring stations used to calculate long term mean $PM_{2.5}$ at ZIP code area. Land use regression models to estimate mean annual NOx based on 183 measurement sites in LA.	10 year follow up. SBP ≥140 mm Hg and/or DBP ≥90 mm Hg or physician diagnosed with use of antihypertensive medication.	Incidence Rate Ratio (IRR) for hypertension with a 10 μg/m^3 increase in $PM_{2.5}$ (95% CI): 1.48 (0.95–2.31). IRR for hypertension for a interquartile range increase in NOX (95% CI):1.14 (1.03–1.25) Concluded: exposure to traffic-related pollutants, may increase the risk of hypertension.

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, PWV: Pulse wave velocity, baPWV: Brachial-ankle pulse wave velocity, cfPWV: Carotid-femoral pulse wave velocity, FMD: Flow mediated dilatation, RHI: Reactive hyperemic index, AIx: Augmentation index, CVD: Cardiovascular disease, BMI: Body Mass Index, SD: Standard deviation, CI: Confidence interval, OR: Odds ratio, NS: Not significant, ABPM: Ambulatory blood pressure measurement, PM10: Coarse particulate matter diameter is <10 μm, $PM_{2.5}$: Fine particulate matter diameter $<_{2.5}$ μm, CO: Carbon monoxide , O_3: Ozone , SO_2: Sulfur dioxide, NO: Nitrogen oxide, NO_2: Nitrogen dioxide, NOX: Nitrogen oxide and/or nitrogen dioxide, USA: United States of America. All BP reported in mmHg, all PWV reported in m/s

Although a greater number of studies have reported short-term exposure, they proffer conflicting conclusions, likely in part reflecting heterogeneity in pollutant, design, and methodologies. In summary, data on blood pressure outcomes were mixed; there was no association with arterial stiffness techniques, but evidential support that endothelial function is impaired after exposure to both PM and gaseous air pollution. This fits with the hypothesis that endothelial dysfunction occurs earlier in the natural history of arterial disease and hypertension, with arterial stiffening indicating more established pathology. Endothelial effects were rapid, but also transient,[64] such that timing of outcome measures becomes a key methodological aspect.

For example, Cosselman *et al.*,[37] report SBP (although still elevated) had reduced towards baseline over 24 h following the exposure. However, most short-term exposure studies did not measure the aftereffects of exposures beyond 1–2 h, so duration of acute effects of air pollution exposure and relation to longer-term cardiovascular dysfunction remains unclear.

PM is a complex mixture ammonium, sulfate, nitrate, elemental carbon matter, organic carbon matter, sodium, and silicon.[65] The effects of these individual components were modeled by Krall *et al.* with time series data from 72 communities in USA; reporting that only silicon and sodium were associated with an increase in mortality.[66] This was reinforced by Dai *et al.*, using a city season specific Poisson regression model for 75 cities; they estimated $PM_{2.5}$ effects on approximately 4.5 million deaths for all causes. This epidemiological data suggested that silicon, calcium, and sulfate were associated with increased all-cause mortality,[67] but not carbon or nitrate exposure. Furthermore, despite reports that exposure to ultrafine carbon particles alters peripheral blood leukocyte distribution and expression of adhesion molecules,[68] they have no consistent effects on systemic vascular function.[69] This suggests the with regard to vascular function, the effects of carbon are smaller than other major components of PM, and highlights that the composition of pollutants is a determinant of the health consequences, as well as a factor contributing to the inconsistency in the results of short-term exposure studies.[36]

The adverse effects of diesel exhaust exposure persist even after the removal of PM,[70] indicating that gaseous pollutants also have a role in mediating the negative effects of air pollution. SO_2 was the only gaseous pollutant consistently associated with increase blood pressure and endothelial dysfunction from the studies included in this review. Increased oxidative stress caused by exposure to SO_2 may also lead to impaired bioavailability of NO contributing toward endothelial dysfunction.[71] Spirometry and venous sampling on military recruits with identical daily activities has also demonstrated that SO_2 and PM have a pro-inflammatory effect, elevating numbers of circulating polymorphonuclear leukocytes and release of white blood cells from the bone marrow. This may be stimulated by alveolar macrophages as they phagocytose fine particulates,[72] the final result of systemic inflammation being endothelial damage.

Other groups have previously performed systematic review investigating the association between air pollution and blood pressure,[73,74] or arterial stiffness[75] all concluding with varying degrees of certainty that there was an association. To the best of our knowledge, this is the first to look at endothelial function and the first to aggregate evidence on a range of cardiovascular risk parameters. However, this review is only as robust as the original data, for example, all the long-term studies included are observational, mainly cross-sectional studies and none of the studies investigated the effect of reducing exposure to air pollution to ascertain reversibility, nor measured the persistence of any acute changes beyond 24 h. Future studies should focus on investigating these aspects. There was high heterogeneity between trials in the concentration of pollutants, duration of exposure, measurement of outcome and the population sampled with highly variable inclusion and exclusion criteria. This is likely the most important factor in the inconsistent results reported by this review and makes comparability between trials difficult.

Conclusion

The results of this systematic review support the hypothesis of an association between long-term exposure to certain gaseous pollutants (particularly SO_2) and PM with increased blood pressure, arterial stiffness, and possibly endothelial dysfunction. Conversely, acute exposure demonstrates evidence of association with endothelial function and may effect blood pressure, but not measures of vascular stiffness. This carries implications for cardiovascular research, as a source of confounding or bias, but also inferences for public health policy and population-based prevention strategies, as air quality is potentially a modifiable risk factor in the development of cardiovascular disease.

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References

1. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, *et al*. Global burden of cardiovascular diseases and risk factors, 1990-2019: Update from the GBD 2019 study. J Am Coll Cardiol 2020;76:2982-3021.
2. Franklin BA, Brook R, Pope AC. Air pollution and cardiovascular disease. Curr Probl Cardiol 2015;40:207-38.
3. Samet JM, Dominici F, Curriero FC, Coursac I, Zeger SL. Fine particulate air pollution and mortality in 20 U.S. cities, 1987-1994. N Engl J Med 2000;343:1742-9.
4. GBD 2017 Risk Factor Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: A systematic analysis for the global burden of disease study 2017. Lancet 2018;392:1923-94.
5. Lelieveld J, Evans JS, Fnais M, Giannadaki D, Pozzer A. The contribution of outdoor air pollution sources to premature mortality on a global scale. Nature 2015;525:367-71.
6. Newby DE, Mannucci PM, Tell GS, Baccarelli AA, Brook RD, Donaldson K, *et al*. Expert position paper on air pollution and cardiovascular disease. Eur Heart J 2014;36:83-93.
7. Donaldson K, Stone V, Clouter A, Renwick L, MacNee W. Ultrafine particles. Occup Environ Med 2001;58:211.
8. Huang G, Lee D, Scott EM. Multivariate space-time modelling of multiple air pollutants and their health effects accounting for exposure uncertainty. Stat Med 2018;37:1134-48.
9. Hamanaka RB, Mutlu GM. Particulate matter air pollution: Effects on the cardiovascular system. Front Endocrinol (Lausanne) 2018;9:680.
10. Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: A systematic review and meta-analysis. J Am Coll

Cardiol 2010;55:1318-27.
11. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med 2009;6:e1000097.
12. Modesti PA, Reboldi G, Cappuccio FP, Agyemang C, Remuzzi G, Rapi S, *et al*. Panethnic differences in blood pressure in Europe: A systematic review and meta-analysis. PLoS One 2016;11:e0147601.
13. Sterne JA, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, *et al*. RoB 2: A revised tool for assessing risk of bias in randomised trials. BMJ 2019;366:l4898.
14. Babisch W, Wolf K, Petz M, Heinrich J, Cyrys J, Peters A. Associations between traffic noise, particulate air pollution, hypertension, and isolated systolic hypertension in adults: The KORA study. Environ Health Perspect 2014;122:492-8.
15. Lenters V, Uiterwaal CS, Beelen R, Bots ML, Fischer P, Brunekreef B, *et al*. Long-term exposure to air pollution and vascular damage in young adults. Epidemiology 2010;21:512-20.
16. Chen SY, Wu CF, Lee JH, Hoffmann B, Peters A, Brunekreef B, *et al*. Associations between long-term air pollutant exposures and blood pressure in elderly residents of Taipei city: A cross-sectional study. Environ Health Perspect 2015;123:779-84.
17. Wu CF, Shen FH, Li YR, Tsao TM, Tsai MJ, Chen CC, *et al*. Association of short-term exposure to fine particulate matter and nitrogen dioxide with acute cardiovascular effects. Sci Total Environ 2016;569-570:300-5.
18. Coogan PF, White LF, Jerrett M, Brook RD, Su JG, Seto E, *et al*. Air pollution and incidence of hypertension and diabetes mellitus in black women living in Los Angeles. Circulation 2012;125:767-72.
19. Foraster M, Künzli N, Aguilera I, Rivera M, Agis D, Vila J, *et al*. High blood pressure and long-term exposure to indoor noise and air pollution from road traffic. Environ Health Perspect 2014;122:1193-200.
20. Krishnan RM, Adar SD, Szpiro AA, Jorgensen NW, Van Hee VC, Barr RG, *et al*. Vascular responses to long- and short-term exposure to fine particulate matter: MESA air (multi-ethnic study of atherosclerosis and air pollution). J Am Coll Cardiol 2012;60:2158-66.
21. van Donkelaar A, Martin RV, Brauer M, Kahn R, Levy R, Verduzco C, *et al*. Global estimates of ambient fine particulate matter concentrations from satellite-based aerosol optical depth: Development and application. Environ Health Perspect 2010;118:847-55.
22. Lin H, Guo Y, Zheng Y, Di Q, Liu T, Xiao J, *et al*. Long-term effects of ambient PM(2.5) on hypertension and blood pressure and attributable risk among older chinese adults. Hypertension 2017;69:806-12.
23. Dong GH, Qian ZM, Xaverius PK, Trevathan E, Maalouf S, Parker J, *et al*. Association between long-term air pollution and increased blood pressure and hypertension in China. Hypertension 2013;61:578-84.
24. Adamopoulos D, Vyssoulis G, Karpanou E, Kyvelou SM, Argacha JF, Cokkinos D, *et al*. Environmental determinants of blood pressure, arterial stiffness, and central hemodynamics. J Hypertens 2010;28:903-9.
25. National Center for Environmental Assessment. Office of Research and Development U.S. Environmental Protection Agency. Washington, DC: National Center for Environmental Assessment, Washington Office; 2002.
26. Jiang S, Bo L, Gong C, Du X, Kan H, Xie Y, *et al*. Traffic-related air pollution is associated with cardio-metabolic biomarkers in general residents. Int Arch Occup Environ Health 2016;89:911-21.
27. Liu S, Chen J, Zhao Q, Song X, Shao D, Meliefste K, *et al*. Cardiovascular benefits of short-term indoor air filtration intervention in elderly living in Beijing: An extended analysis of BIAPSY study. Environ Res 2018;167:632-8.
28. Gong H Jr., Linn WS, Sioutas C, Terrell SL, Clark KW, Anderson KR, *et al*. Controlled exposures of healthy and asthmatic volunteers to concentrated ambient fine particles in Los Angeles. Inhal Toxicol 2003;15:305-25.
29. Shi J, Lin Z, Chen R, Wang C, Yang C, Cai J, *et al*. Cardiovascular benefits of wearing particulate-filtering respirators: A randomized crossover trial. Environ Health Perspect 2017;125:175-80.
30. Fakhri AA, Ilic LM, Wellenius GA, Urch B, Silverman F, Gold DR, *et al*. Autonomic effects of controlled fine particulate exposure in young healthy adults: Effect modification by ozone. Environ Health Perspect 2009;117:1287-92.
31. Chen R, Zhao A, Chen H, Zhao Z, Cai J, Wang C, *et al*. Cardiopulmonary benefits of reducing indoor particles of outdoor origin: A randomized, double-blind crossover trial of air purifiers. J Am Coll Cardiol 2015;65:2279-87.
32. Bellavia A, Urch B, Speck M, Brook RD, Scott JA, Albetti B, *et al*. DNA hypomethylation, ambient particulate matter, and increased blood pressure: Findings from controlled human exposure experiments. J Am Heart Assoc 2013;2:e000212.
33. Brook RD, Bard RL, Morishita M, Dvonch JT, Wang L, Yang HY, *et al*. Hemodynamic, autonomic, and vascular effects of exposure to coarse particulate matter air pollution from a rural location. Environ Health Perspect 2014;122:624-30.
34. Morishita M, Bard RL, Wang L, Das R, Dvonch JT, Spino C, *et al*. The characteristics of coarse particulate matter air pollution associated with alterations in blood pressure and heart rate during controlled exposures. J Expo Sci Environ Epidemiol 2015;25:153-9.
35. Brook RD, Urch B, Dvonch JT, Bard RL, Speck M, Keeler G, *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;54:659-67.
36. Mills NL, Miller MR, Lucking AJ, Beveridge J, Flint L, Boere AJ, *et al*. Combustion-derived nanoparticulate induces the adverse vascular effects of diesel exhaust inhalation. Eur Heart J 2011;32:2660-71.
37. Cosselman KE, Krishnan RM, Oron AP, Jansen K, Peretz A, Sullivan JH, *et al*. Blood pressure response to controlled diesel exhaust exposure in human subjects. Hypertension 2012;59:943-8.
38. Shan M, Yang X, Ezzati M, Chaturvedi N, Coady E, Hughes A, *et al*. A feasibility study of the association of exposure to biomass smoke with vascular function, inflammation, and cellular aging. Environ Res 2014;135:165-72.
39. Zhao Y, Xue L, Chen Q, Kou M, Wang Z, Wu S, *et al*. Cardiorespiratory responses to fine particles during ambient PM(2.5) pollution waves: Findings from a randomized crossover trial in young healthy adults. Environ Int 2020;139:105590.
40. Kumarathasan P, Vincent R, Blais E, Bielecki A, Guénette J, Filiatreault A, *et al*. Cardiovascular and inflammatory mechanisms in healthy humans exposed to air pollution in the vicinity of a steel mill. Part Fibre Toxicol 2018;15:34.

41. Liu L, Kauri LM, Mahmud M, Weichenthal S, Cakmak S, Shutt R, *et al*. Exposure to air pollution near a steel plant and effects on cardiovascular physiology: A randomized crossover study. Int J Hyg Environ Health 2014;217:279-86.
42. Padró-Martínez LT, Owusu E, Reisner E, Zamore W, Simon MC, Mwamburi M, *et al*. A randomized cross-over air filtration intervention trial for reducing cardiovascular health risks in residents of public housing near a highway. Int J Environ Res Public Health 2015;12:7814-38.
43. Morishita M, Adar SD, D'Souza J, Ziemba RA, Bard RL, Spino C, *et al*. Effect of portable air filtration systems on personal exposure to fine particulate matter and blood pressure among residents in a low-income senior facility: A randomized clinical trial. JAMA Intern Med 2018;178:1350-7.
44. Karottki DG, Spilak M, Frederiksen M, Gunnarsen L, Brauner EV, Kolarik B, *et al*. An indoor air filtration study in homes of elderly: Cardiovascular and respiratory effects of exposure to particulate matter. Environ Health 2013;12:116.
45. Weichenthal S, Mallach G, Kulka R, Black A, Wheeler A, You H, *et al*. A randomized double-blind crossover study of indoor air filtration and acute changes in cardiorespiratory health in a first nations community. Indoor Air 2013;23:175-84.
46. Cui X, Li F, Xiang J, Fang L, Chung MK, Day DB, *et al*. Cardiopulmonary effects of overnight indoor air filtration in healthy non-smoking adults: A double-blind randomized crossover study. Environ Int 2018;114:27-36.
47. Brook RD, Brook JR, Urch B, Vincent R, Rajagopalan S, Silverman F, *et al*. Inhalation of fine particulate air pollution and ozone causes acute arterial vasoconstriction in healthy adults. Circulation 2002;105:1534-6.
48. Barath S, Mills NL, Lundbäck M, Törnqvist H, Lucking AJ, Langrish JP, *et al*. Impaired vascular function after exposure to diesel exhaust generated at urban transient running conditions. Part Fibre Toxicol 2010;7:19.
49. Törnqvist H, Mills NL, Gonzalez M, Miller MR, Robinson SD, Megson IL, *et al*. Persistent endothelial dysfunction in humans after diesel exhaust inhalation. Am J Respir Crit Care Med 2007;176:395-400.
50. Allen RW, Carlsten C, Karlen B, Leckie S, van Eeden S, Vedal S, *et al*. An air filter intervention study of endothelial function among healthy adults in a woodsmoke-impacted community. Am J Respir Crit Care Med 2011;183:1222-30.
51. Weichenthal S, Hatzopoulou M, Goldberg MS. Exposure to traffic-related air pollution during physical activity and acute changes in blood pressure, autonomic and micro-vascular function in women: A cross-over study. Part Fibre Toxicol 2014;11:70.
52. Cole CA, Carlsten C, Koehle M, Brauer M. Particulate matter exposure and health impacts of urban cyclists: A randomized crossover study. Environ Health 2018;17:78.
53. Briet M, Collin C, Laurent S, Tan A, Azizi M, Agharazii M, *et al*. Endothelial function and chronic exposure to air pollution in normal male subjects. Hypertension 2007;50:970-6.
54. Kajbafzadeh M, Brauer M, Karlen B, Carlsten C, van Eeden S, Allen RW, *et al*. The impacts of traffic-related and woodsmoke particulate matter on measures of cardiovascular health: A HEPA filter intervention study. Occup Environ Med 2015;72:394-400.
55. Mehta AJ, Zanobetti A, Koutrakis P, Mittleman MA, Sparrow D, Vokonas P, *et al*. Associations between short-term changes in air pollution and correlates of arterial stiffness: The Veterans Affairs Normative Aging Study, 2007-2011. Am J Epidemiol 2014;l179:192-9.
56. Fang SC, Eisen EA, Cavallari JM, Mittleman MA, Christiani DC. Acute changes in vascular function among welders exposed to metal-rich particulate matter. Epidemiology 2008;19:217-25.
57. Sakurai M, Yamakado T, Kurachi H, Kato T, Kuroda K, Ishisu R, *et al*. The relationship between aortic augmentation index and pulse wave velocity: An invasive study. J Hypertens 2007;25:391-7.
58. Tank J, Biller H, Heusser K, Holz O, Diedrich A, Framke T, *et al*. Effect of acute ozone induced airway inflammation on human sympathetic nerve traffic: A randomized, placebo controlled, crossover study. PLoS One 2011;6:e18737.
59. Rich DQ, Frampton MW, Balmes JR, Bromberg PA, Arjomandi M, Hazucha MJ, *et al*. Cardiovascular function and ozone exposure: The multicenter ozone study in older subjects (MOSES). Environ Int 2018;119:193-202.
60. Arjomandi M, Wong H, Donde A, Frelinger J, Dalton S, Ching W, *et al*. Exposure to medium and high ambient levels of ozone causes adverse systemic inflammatory and cardiac autonomic effects. Am J Physiol Heart Circ Physiol 2015;308:H1499-509.
61. Langrish JP, Lundbäck M, Barath S, Söderberg S, Mills NL, Newby DE, *et al*. Exposure to nitrogen dioxide is not associated with vascular dysfunction in man. Inhal Toxicol 2010;22:192-8.
62. Frampton MW, Pietropaoli A, Dentler M, Chalupa D, Little EL, Stewart J, *et al*. Cardiovascular effects of ozone in healthy subjects with and without deletion of glutathione-S-transferase M1. Inhal Toxicol 2015;27:113-9.
63. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr., *et al*. Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. Hypertension 2003;42:1206-52.
64. Lundbäck M, Mills NL, Lucking A, Barath S, Donaldson K, Newby DE, *et al*. Experimental exposure to diesel exhaust increases arterial stiffness in man. Particle Fibre Toxicol 2009;6:7.
65. Dominici F, Wang Y, Correia AW, Ezzati M, Pope CA 3rd, Dockery DW. Chemical composition of fine particulate matter and life expectancy: In 95 US counties between 2002 and 2007. Epidemiology 2015;26:556-64.
66. Krall JR, Anderson GB, Dominici F, Bell ML, Peng RD. Short-term exposure to particulate matter constituents and mortality in a national study of U.S. urban communities. Environ Health Perspect 2013;121:1148-53.
67. Dai L, Zanobetti A, Koutrakis P, Schwartz JD. Associations of fine particulate matter species with mortality in the United States: A multicity time-series analysis. Environ Health Perspect 2014;122:837-42.
68. Frampton MW, Stewart JC, Oberdörster G, Morrow PE, Chalupa D, Pietropaoli AP, *et al*. Inhalation of ultrafine particles alters blood leukocyte expression of adhesion molecules in humans. Environ Health Perspect 2006;114:51-8.
69. Shah AP, Pietropaoli AP, Frasier LM, Speers DM, Chalupa DC, Delehanty JM, *et al*. Effect of inhaled carbon ultrafine particles on reactive hyperemia in healthy human subjects. Environ Health Perspect 2008;116:375-80.
70. Wooding DJ, Ryu MH, Hüls A, Lee AD, Lin DT, Rider CF, *et al*. Particle depletion does not remediate acute effects of traffic-related air pollution and allergen. A randomized, double-blind crossover study. Am J Respir Crit Care Med 2019;200;565-74.
71. Fichtlscherer S, Breuer S, Schächinger V, Dimmeler S,

Zeiher AM. C-reactive protein levels determine systemic nitric oxide bioavailability in patients with coronary artery disease. Eur Heart J 2004;25:1412-8.
72. Tan WC, Qiu D, Liam BL, Ng TP, Lee SH, van Eeden SF, *et al*. The human bone marrow response to acute air pollution caused by forest fires. Am J Respir Crit Care Med 2000;161:1213-7.
73. Yang BY, Qian Z, Howard SW, Vaughn MG, Fan SJ, Liu KK, *et al*. Global association between ambient air pollution and blood pressure: A systematic review and meta-analysis. Environ Pollut 2018;235:576-88.
74. Cai Y, Zhang B, Ke W, Feng B, Lin H, Xiao J, *et al*. Associations of short-term and long-term exposure to ambient air pollutants with hypertension: A systematic review and meta-analysis. Hypertension 2016;68:62-70.
75. Zanoli L, Lentini P, Granata A, Gaudio A, Fatuzzo P, Serafino L, *et al*. A systematic review of arterial stiffness, wave reflection and air pollution. Mol Med Rep 2017;15:3425-9.

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