Online Supplement:

Noise and air pollution as risk factors for hypertension: part II – pathophysiologic insight

Short title: Noise/air pollution and hypertension-pathophysiology

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Supplemental Table S1: Effect of Air Pollution filtration intervention on Blood Pressure

Author(s)	Experimental Design and Outcomes	Population	Intervention	Details on Intervention	Main outcomes	
Brauner et al. **(Copenhagen, Denmark)**	Randomized, crossover study. Outcomes: Microvascular flow measured by digital tonometry, SBP, DBP	21 nonsmoking couples	Home Air Filter	Two 48-hour exposures to particle-filtered or non-filtered air (2,533–4,058 and 7,718–12,988 particles/cm^3, respectively) at home	Air filtration led to improvement in microvascular flow. No significant difference in SBP or DBP was seen between intervention and non-intervention.	[1] Brauner EV, Forchhammer L, Moller P, Barregard L, Gunnarsen L, Afshari A, Wahlin P, Glasius M, Dragsted LO, Basu S, Raaschou-Nielsen O, Loft S. Indoor particles affect vascular function in the aged: An air filtration-based intervention study. American journal of respiratory and critical care medicine. 2008;177:419-425
Allen et al. **(British Columbia, Canada)**	Randomized crossover study Outcome: endothelial function (RHI), IL6, CRP, band cells, malondialdehyde, 8-iso-prostaglandin F2α, SBP, DBP	45 adults living in woodsmoke-impacted community	Home Air Filter	7-day periods of home air filters. Indoor air filters reduced indoor fine particle concentrations by 60% (from 11.2 mg/m^3 with HEPA off to 4.6 mg/m^3 with HEPA on)	Air filtration led to improved endothelial function (9.4% increase in RHI), and a trend towards decrease in CRP levels (-32.6%, P=0.06). No difference in other markers. No significant difference in SBP or DBP was seen between intervention and non-intervention.	[2] Allen RW, Carlsten C, Karlen B, Leckie S, van Eeden S, Vedal S, Wong I, Brauer M. An air filter intervention study of endothelial function among healthy adults in a woodsmoke-impacted community. American journal of respiratory and critical care medicine. 2011;183:1222-1230
Weichenthal et al. **(Manitoba, Canada)**	Randomized, double-blind, crossover Outcome: lung function, BP, and endothelial function	37 residents in 20 homes	Home Air Filter	Electrostatic air filter or a placebo filter for 7 days in random order. PM2.5 decreased by 37 ug/m3	Air filtration led to 7.9 mm Hg (95% CI: -17, 0.82) decrease in SBP and a 4.5 mm Hg (95% CI: -11, 2.4) decrease in DBP. Air filtration also led to improvement in FEV1	[3] Weichenthal S, Mallach G, Kulka R, Black A, Wheeler A, You H, St-Jean M, Kwiatkowski R, Sharp D. A randomized double-blind crossover study of indoor air filtration and acute changes in cardiorespiratory health in a first nations community. Indoor air. 2013;23:175-184
Chen et al· 2015 **(Shanghai, China)**	Randomized, double-blind crossover Outcomes: 14 circulating biomarkers of inflammation, coagulation, and vasoconstriction; lung function; BP; and	35 healthy young university students	Home Air Filter	Air filtration or sham filtration for 48 h with a 2-week washout interval. Air filtration reduced indoor $PM_{2.5}$ concentration by more than one-	After 48 h of air filtration exposure, SBP(7.9mmHg), DBP (4.5mmHg), MCP-1, IL-1β, MPO, sCD40L were significantly reduced	[4] Chen R, Zhao A, Chen H, Zhao Z, Cai J, Wang C, Yang C, Li H, Xu X, Ha S, Li T, Kan H. Cardiopulmonary benefits of reducing indoor particles of outdoor origin: A randomized, double-blind crossover trial of air purifiers. Journal of the American College of Cardiology. 2015;65:2279-2287

	fractional exhaled nitric oxide			half, from 96.2 to 41.3 μg/m^3.		
Shao et al. 2017 **(Beijing, China)**	Randomized, double-blind, crossover Outcomes: BP, cardio-respiratory biomarker levels	35 non-smoker senior participants with or without COPD	Home Air Filter	Portable air filtration units randomly allocated to active filtration (filter in) vs sham (filter out) for 2 weeks.	Air filtration reduced IL-8 by 59% but had no impact on BP, lung function tests, IL6, CRP, fibrinogen, Urinary 8-OHdG, or HRV measures	[5] Shao D, Du Y, Liu S, Brunekreef B, Meliefste K, Zhao Q, Chen J, Song X, Wang M, Wang J, Xu H, Wu R, Wang T, Feng B, Lung CS, Wang X, He B, Huang W. Cardiorespiratory responses of air filtration: A randomized crossover intervention trial in seniors living in beijing: Beijing indoor air purifier study, biapsy. Sci Total Environ. 2017;603-604:541-549
Karottki et al. (Copenhagen, Denmark)	Randomized, double-blind, crossover Outcome: microvascular function (PAT), BP	48 healthy non-smoking volunteers > 51 years	Home Air Filter	Periods with or without filter in living room/bedroom for 2 weeks	Air filtration did not lead to change in microvascular; however, microvascular function was associated with $PM_{2.5}$ decrease in the bedroom. No significant difference in SBP or DBP was seen between intervention and non-intervention.	[6] Karottki DG, Spilak M, Frederiksen M, Gunnarsen L, Brauner EV, Kolarik B, Andersen ZJ, Sigsgaard T, Barregard L, Strandberg B, Sallsten G, Moller P, Loft S. An indoor air filtration study in homes of elderly: Cardiovascular and respiratory effects of exposure to particulate matter. Environ Health. 2013;12:116
Langrish et al. **(Beijing, China)**	Open-label cross-over randomised controlled trial. Outcome: BP, HRV	15 healthy volunteers	Personal Mask	2-hour city walk with or without an air filter mask Mask efficiency of a range of masks tested prior to human intervention study Mask penetrance was highly dependent on mask type. PM2.5 levels lower with mask (86 vs.140 mg/m3). No change in particle numbers.	Air filter mask led to reduction in SBP (114 ± 10 vs 121 ± 11 mmHg, $P < 0.01$) compared with control, but no difference in heart rate. Over the 24-hour period heart rate variability increased (SDNN 65.6 ± 11.5 vs 61.2 ± 11.4 ms, $P < 0.05$; LF-power 919 ± 352 vs 816 ± 340 ms^2, $P < 0.05$) when subjects wore the facemask.	[7] Langrish JP, Mills NL, Chan JK, Leseman DL, Aitken RJ, Fokkens PH, Cassee FR, Li J, Donaldson K, Newby DE, Jiang L. Beneficial cardiovascular effects of reducing exposure to particulate air pollution with a simple facemask. Particle and fibre toxicology. 2009;6:8
Langrish et al.	Open randomized crossover trial	98 patients with	Personal Mask	Walking on a predefined route in	Mask reduced maximal ST segment	[8] Langrish JP, Li X, Wang S, Lee MM, Barnes GD, Miller MR, Cassee FR, Boon NA, Donaldson

(Beijing, China)	Outcomes: blood pressure, heart rate, and 12-lead electrocardiography over 24 hours	coronary heart disease		Beijing with or without a face mask (Dust Respirator) in. Estimated exposure with mask (assuming 97% efficiency) reduced from 89 μg/m^3 and 43,900 particles/cm^3 to 2 μg/m^3 and 1,200 particles/cm^3 respectively.	depression, mean BP (93±10 vs. 96±10 mmHg, p = 0.03) and increased heart rate variability.	K, Li J, Li L, Mills NL, Newby DE, Jiang L. Reducing personal exposure to particulate air pollution improves cardiovascular health in patients with coronary heart disease. Environ Health Perspect. 2012;120:367-372
Chuang 2017 (Taipei, Taiwan)	Randomized, cross over study Outcomes: BP and blood biomarkers	200 homemakers	Home Air Filter	Air conditioners were fashioned with a widely available filter or with a false air conditioner filter and run continuously for 1 year. After 1 year the type of filter was switched and air conditioners were run for another year.	False air conditioner filter use resulted in increased levels of PM2.5 and total VOCs; these elevated levels were associated with increased high-sensitivity-C reactive protein, 8-hydroxy-2'-deoxyguanosine, and blood pressure. False air conditioner filter use resulted in a greater percent change in blood pressure, than real air filtration (SBP: 3.01 vs 0.12; DBP: 2.14 vs -1.21)	[9] Chuang HC, Ho KF, Lin LY, Chang TY, Hong GB, Ma CM, Liu IJ, Chuang KJ. Long-term indoor air conditioner filtration and cardiovascular health: A randomized crossover intervention study. Environ Int. 2017;106:91-96
Shi 2017 (Shanghai, China)	Randomized, crossover trial Outcomes: Heart rate variability, ambulatory BP, and circulating biomarkers	24 healthy young adults	Personal Respirators	Participants were randomized to wear or not wear a particulate-filtering respirator for 48 hours, and alternate after a 3-week washout interval. Mean daily average PM2.5	Wearing respirators was associated with a 2.7mmHg decrease in SBP. With respect to heart rate variability, there was a 12.5% increase in high frequency power, 10.9% increase in the root mean square of	[10] Shi J, Lin Z, Chen R, Wang C, Yang C, Cai J, Lin J, Xu X, Ross JA, Zhao Z, Kan H. Cardiovascular benefits of wearing particulate-filtering respirators: A randomized crossover trial. Environ Health Perspect. 2017;125:175-180

				concentration during intervention was 74.2 μg/m^3	the successive differences, and 22.1% increase in the percentage of normal RR intervals with duration >50 msec different from the previous normal RR interval (pNN50). There was also a 7.8% decrease in the ratio of low frequency/high frequency power.	
Morishita 2018 (Michigan, USA)	Randomized, double-blind, 3-way crossover study Outcomes: Brachial BP, noninvasive aortic hemodynamics, pulse-wave velocity and heart rate variability	40 nonsmoking older adults	Portable Air Filtration	High-efficiency air purifiers, low-efficiency air purifiers and sham filters were placed in the bedroom and main living space for 3 days follow by a 1-week washout periods between switching filter types.	High-efficiency and low-efficiency filtration lead too decreased brachial systolic and diastolic BP by 3.2mmHg and 1.5mmHg respectively. Other outcomes were not significantly affected.	[11] Morishita M, Adar SD, D'Souza J, Ziemba RA, Bard RL, Spino C, Brook RD. 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;178:1350-1357
Morishita 2019 (Michigan, USA)	Randomized, single-blind, crossover study Outcomes: Brachial BP, aortic hemodynamics, heart rate variability, and reactive hyperemia index	50 healthy adults	Personal N95 Respirator	Multiple 2-hour near-roadway exposures with either not wearing, or wearing an N95 respirator for 1 week. Cross-over to alternate intervation occurred week 2.	Not wearing an N95 respirator resulted in acutely worsened aortic hemodynamics (aortic augmentation pressure and augmentation index) No significant difference was seen between the groups for brachial BP and aortic BP	[12] Morishita M, Wang L, Speth K, Zhou N, Bard RL, Li F, Brook JR, Rajagopalan S, Brook RD. Acute blood pressure and cardiovascular effects of near-roadway exposures with and without n95 respirators. Am J Hypertens. 2019;32:1054-1065
Zhao 2020 (Beijing, China)	Randomized, crossover trial Outcomes: BP, pulmonary function, fractional exhaled nitric	29 healthy young adults	Home Air Filter	Sham or High-efficiency particulate air filter was placed in the center of the subject's dormitory	Sham purification showed a significant increase in fractional exhaled nitric oxide and soluble P-selectin. Pollution waves lead to	[13] Zhao Y, Xue L, Chen Q, Kou M, Wang Z, Wu S, Huang J, Guo X. Cardiorespiratory responses to fine particles during ambient pm2.5 pollution waves: Findings from a randomized crossover trial in young healthy adults. Environ Int. 2020;139:105590

	oxide, circulating biomarkers for platelet activation, blood coagulation and systemic oxidative stress			during PM2.5 pollution waves for 2 weeks.	a decrease in pulmonary function. The above changes in biomarkers were attenuated and insignificant in the high-efficiency air filter group There was no significant association between personal PM2.5 exposure and BP and no significant difference in BP between the treatment groups.	
Guo 2021 (Chongqing, China)	Randomized, double-blind, crossover study Outcomes: 15 systemic biomarkers of inflammation, coagulation and oxidative stress; lung function; BP, HR, and fractional exhaled nitric oxide	24 healthy aged-care center adults	Home Air Filter	High-efficiency particulate air filter air purifiers or a placebo air purifier was used for 2 consecutive days, with a 12-day wash-out period before switching intervention groups	Air filtration resulted in a significant decrease concentration of inflammatory and coagulation biomarkers, but not oxidative stress and lung function biomarkers. HR decreased significantly with air filtration. There was no significant difference between the groups for BP.	[14] Guo M, Du C, Li B, Yao R, Tang Y, Jiang Y, Liu H, Su H, Zhou Y, Wang L, Yang X, Zhou M, Yu W. Reducing particulates in indoor air can improve the circulation and cardiorespiratory health of old people: A randomized, double-blind crossover trial of air filtration. Sci Total Environ. 2021;798:149248
Han 2021 (Nankai, China)	Randomized, double-blind, crossover study Outcomes: BP, HR, and heart rate variability	39 healthy university students	Personal Mask	2-hour exposure to air nearby a busy road. Participants wore either an N95 mask, a PM filter mask, a VOCs filter mask, or a sham filter mask. Participants had a washout period of at least 1 week between intervention change.	HRV measurements increased during and following exposure for all interventions. Systolic and diastolic BP increased slightly during exposure for all interventions. HR decreased during and after exposure, and was lower in all intervention vs sham.	[15] Han B, Zhao R, Zhang N, Xu J, Zhang L, Yang W, Geng C, Wang X, Bai ZD, Vedal S. Acute cardiovascular effects of traffic-related air pollution (trap) exposure in healthy adults: A randomized, blinded, crossover intervention study. Environ Pollut. 2021;288:117583

Hudda 2021 (Massachusetts, USA)	Randomized, crossover study Outcomes: Change in Systolic BP and Diastolic BP, and HR	77 participants, with an average age of 60 years	Home Air Filter	2-hour exposures to air near an interstate highway, a total of 3 times at high, medium and low traffic-related air pollution levels.	Systolic BP increased with increased exposure duration, with a correlation between the amount of increase and magnitude of exposure. Mean change in Systolic BP was 0.6mmHG, 1.3mm HG, and 2.8mm HG for low, medium and high exposure levels respectively. No significant changes were seen in diastolic BP and HR.	[16] Hudda N, Eliasziw M, Hersey SO, Reisner E, Brook RD, Zamore W, Durant JL, Brugge D. Effect of reducing ambient traffic-related air pollution on blood pressure: A randomized crossover trial. Hypertension. 2021;77:823-832
Wang 2021 (Beijing, China)	Randomized, crossover study Outcomes: Cardiorespiratory biomarkers	54 healthy students	Home Air Filter	Real or sham high-efficiency particulate air filter for 1 week, and change of group after a washout period	Diastolic BP, fractional exhaled nitric oxide, and 8-isoprostane levels all decreased significantly in real air filtration. FEV1, PEF and $FEF_{25\%-75\%}$ were significantly improved with real air filtration.	[17] Wang Y, Zhao Y, Xue L, Wu S, Wang B, Li G, Huang J, Guo X. Effects of air purification of indoor pm2.5 on the cardiorespiratory biomarkers in young healthy adults. Indoor Air. 2021;31:1125-1133
Eom 2022 (Cheongju, South Korea)	Randomized, double-blind, crossover study Outcomes: BP, heart rate variability, baroreflex sensitivity, autonomic function tests and endothelial function	38 patients with coronary artery disease	Home Air Filter	Real or sham air filtration for 2 weeks, with a 2-week washout period	Real filtration significantly associated with a decrease in 8-hydroxy-2'-deoxyguanosine (indicator of oxidative stress). Blood pressure was not significantly different between the groups.	[18] Eom SY, Kim A, Lee JH, Kim SM, Lee SY, Hwang KK, Lim HJ, Cho MC, Kim YD, Bae JW, Kim JH, Lee DI. Positive effect of air purifier intervention on baroreflex sensitivity and biomarkers of oxidative stress in patients with coronary artery disease: A randomized crossover intervention trial. Int J Environ Res Public Health. 2022;19
Faridi 2022 (Tehran, Iran)	Randomized, crossover study Outcomes: Brachial BP, heart rate variability, high-sensitivity cardiac troponin	28 healthy young adults	Personal Respirator	48-hour intervention with particulate-filtering respirator and 6-day washout period between change in intervention. Study took place in a	No significant difference between interventions was seen for brachial BP. High frequency power and heart rate increased significantly with respirator intervention	[19] Faridi S, Brook RD, Hassanvand MS, Nodehi RN, Shamsipour M, Tajdini M, Naddafi K, Sadeghian S. Cardiovascular health effects of wearing a particulate-filtering respirator to reduce particulate matter exposure: A randomized crossover trial. J Hum Hypertens. 2022;36:659-669

				dormitory 200m from a major 4-lane street and 2m away from a major 2-lane street with 2000 and 550 vehicle flow per hour respectively.		

Abbreviations: RHI: reactive hyperemia index; SBP: systolic blood pressure; DBP: diastolic blood pressure; FEV1: forced expiratory volume in 1 minute; MCP1: monocyte chemoattractant protein 1; MPO: myeloperoxidase; IL1beta: interleukin-1beta; COPD: chronic obstructive pulmonary disease. IL6: interleukin 6; CRP: c-reactive protein; HRV: heart rate variability; HEPA: High efficiency particulate air; PAT: peripheral artery tonometry; IA: inside air; OA: outside air; PAPR: powered air purifying respirator; CRH: Corticotropin-releasing hormone; ACTH: Adrenocorticotropic hormone; VOCs: Volatile organic compounds; peak expiratory flow; $FEF_{25\%-75\%}$: forced expiratory flow between the 25^{th} and 75^{th} percentile of forced vital capacity.