

Effect of environmental air pollution on cardiovascular diseases

S.A. MEO¹, F. SURAYA²

¹Department of Physiology, ²Department of Surgery (Plastic Surgery); College of Medicine, King Saud University, Riyadh, Saudi Arabia

Abstract. – OBJECTIVE: Environmental air pollution has become a leading health concern especially in the developing countries with more urbanization, industrialization and rapidly growing population. Prolonged exposure to air pollution is a risk factor for cardiovascular diseases. The present study aimed to investigate the effects of environmental air pollution on progression of cardiovascular problems.

METHODS: In this study, we identified 6880 published articles through a systematic database including ISI-Web of Science, PubMed and EMBASE. The allied literature was searched by using the key words such as environmental pollution, air pollution, particulate matter pollutants PM 2.5 μm -PM 10 μm . Literature in which environmental air pollution and cardiac diseases were discussed was included. Descriptive information was retrieved from the selected literature. Finally, we included 67 publications and remaining studies were excluded.

RESULTS: Environmental pollution can cause high blood pressure, arrhythmias, enhanced coagulation, thrombosis, acute arterial vasoconstriction, atherosclerosis, ischemic heart diseases, myocardial infarction and even heart failure.

CONCLUSIONS: Environmental air pollution is associated with increased risk of cardiovascular diseases. Environmental pollution exerts its detrimental effects on the heart by developing pulmonary inflammation, systemic inflammation, oxidative stress, endothelial dysfunction and prothrombotic changes. Environmental protection officials must take high priority steps to minimize the air pollution to decrease the prevalence of cardiovascular diseases.

Key Words:

Air pollution, Environmental pollutants, Cardiac problems.

Introduction

Over the last two decades, there has been an increasing concerns globally about the environmental air pollution and its impact on human health. Large number of health problems are related with longterm exposure to environmental

pollution. The environmental related diseases acquired during childhood, manifested during adulthood and are not easily diagnosed¹. Air pollution is a heterogeneous and a complex mixture of dust, fumes, gases, carbon monoxide (CO), nitrogen dioxide (NO₂), sulfur dioxide (SO₂) and ozone (O₃)²⁻⁴. The particle pollution also called Particulate Matter [PM] is a composite mixture of very small particles and liquid droplets made up of chemicals, acids, metals and soil or dust. The adverse health effects of air pollutants are highly dependent on the pollutant's nature, type, content, chemical composition and an individual's genetic makeup⁵⁻⁷. Particulate matter [PM] are broadly categorized by aerodynamic diameter. The particles with an aerodynamic diameter [PM-2.5-10 μm] are called coarse thoracic particles [PM-2.5 μm] fine particles and [PM-0.1 μm] are ultrafine particles⁸. Air pollutants have their own health risk profile and have been linked with pulmonary, systemic inflammation, oxidative stress, endothelial dysfunction, prothrombotic and coagulant changes and the progression of atherosclerosis⁹⁻¹⁰. There is a growing evidence that exposure to air pollution is not only associated to respiratory problems but the current perception is that air pollution is the main source of cardiovascular diseases⁵, although the evidence is limited and diverse. Therefore, the aim of this study was to assess the association between exposure to environmental air pollution and progression of cardiac problems.

Research Methodology

Selection of studies: For this study, we identified 7038 published articles from systematic database searches including ISI-Web of Science, PubMed and EMBASE. We examined the allied literature by using the key terms including air pollution, environmental pollution, dust, fumes, PM 2.5 μm , PM 10 μm , and gases, carbon monoxide (CO), ozone (O₃), nitrogen dioxide [NO₂] and sulfur dioxide (SO₂). In

addition, we also entered the keywords in the Google Scholar search engine and after getting any related article, we re-entered the title of that article in the ISI-Web of Science and PubMed to verify for any missing article. The title and abstract of the articles were evaluated to determine the eligibility for the documents. All studies in which cardiac problems and environmental air pollution were discussed were considered eligible for inclusion. Studies such as brief communication, editorials, case reports, small sample size studies, non-English language of publications were excluded while cohort, cross sectional studies, systematic review, studies which estimated the effect of long-term exposure to air pollution, including PM 2.5 μm , PM 10 μm , and NO₂, on risk of cardiac problems were included. The studies published in non-ISI and non-

pubmed indexed journals were also excluded. We reviewed 6880 papers, finally we included 67 studies and remaining articles were excluded.

Data extraction and quality assessment: Findings were extracted by both investigators; the results were determined by using a standardized form including a full description of the study characteristics.

Ethics statement: For this study we reviewed the database literature on environmental air pollution and cardiac problems, hence we did not require the ethical approval.

Results

Table I demonstrates the effect of various types of environmental air pollutions and their

Table I. Effect of various types of air pollutants and their association with cardiovascular diseases.

Author and year	Pollutants	Cardiovascular diseases
Stanković et al 2015 ¹¹	Black smoke, sulphur di oxide	Increased blood pressure
Giorgini et al 2015 ¹²	PM 2.5 μm	Increased blood pressure
Dong et al 2015 ¹³	PM 2.5 μm	Increased blood pressure
Pieters et al 2015 ¹⁴	Ultrafine particles	Increased blood pressure
Chan et al 2015 ¹⁵	PM _{2.5} and NO ₂	Increased blood pressure
Xu and Guo 2013 ¹⁶	PM ₁₀	IHD
Bennett et al 2014 ¹⁷	NO _x , Ben	Hear failure
Yang et al 2014 ¹⁸	PM, NO ₂ , SO ₂	Heart failure
Siponen et al 2015 ¹⁹	PM 2.5 μm	Systemic inflammation
Dutta et al 2015 ²⁰	PM 2.5-PM10 μm	Hypertension, CVD
Li and Chen 2015 ²¹	PM; 10 μm , SO ₂ , NO ₂	CHD
Ghosh et al 2015 ²²	PM, Carbon, gases	CHD
Chen and Weng 2015 ²³	PM _{2.5} -10 μm	IHD, CHF, arrythmia
Bartel et al 2013 ²⁴	PM	Ventricular tachycardia
Hsieh and Tsai 2013 ²⁵	PM _{2.5}	CHF
Shah et al 2013 ²⁶	CO, SO ₂ , NO ₂	HF
Wang et al 2013 ²⁷	PM10, SO ₂ , NO ₂	CHD
Xie et al 2014 ²⁸	PM 10, SO ₂ ,NO ₂	Acute MI, ischemic cardiomyopathy, angina, sudden death
Goldberg et al 2015 ²⁹	PM _{2.5} , CO	Tachycardia and increased systolic BP
Morishita et al 2015 ³⁰	Coarse PM, Cu, Mo	Tachycardia and increased systolic BP
Bloomfield and Lagat 2012 ³¹	House-hold air pollution	Pulmonary hypertension, right heart failure
Padula et al 2013 ³²	PM 10 μm , heavy traffic Density	Pulmonary valve stenosis and ventricular septal defects,
Agay et al 2013 ³³	PM10	Multiple congenital heart defects
Dominguez et al 2013 ³⁴	NO ₂	Heart failure
Huang and Deng 2013 ³⁵	PM _{2.5} , Black Carbon, CO	Autonomic cardiac dysfunction
Beckerman et al 2012 ³⁶	NO ₂	IHD
Gan and Davies 2012 ³⁷	Noise, Black Carbon, NO ₂ , NO	CHD
Scarborough et al 2012 ³⁸	Air pollution	CHD

PM: Particulate matter with aerodynamic diameter; SO₂; Sulfure dioxide, NO₂; Nitrogen dioxide, CO; Carbon monoxide, IHD: Ischemic heart diseases, MI: Myocardial infarction, CHD: Coronary heart diseases, HF: Heart failure. CVD: Cardiovascular diseases, CAD: Coronary artery disease.

association with cardiovascular diseases (CVD). There is a strong association between CVD and dust, fumes, gases, particulate material PM 2.5 μm -PM 10 μm , nitrogen dioxide (NO_2), carbon monoxide (CO) and sulfur dioxide (SO_2). The air pollutants can cause systemic inflammation, increased blood pressure, pulmonary hypertension, arrhythmias, ventricular septal defect, congenital heart diseases, ischemic heart diseases, cardiomyopathy, angina, myocardial infarction and heart failure.

In addition, vehicular related environmental air pollution can cause high systolic blood pressure, atherosclerosis, arrhythmias, ST-depression and myocardial infarction (Table II).

Discussion

Air pollution is the mixture of dust, fumes, gases, chemicals, particulate matter and biological materials that may cause damage to natural environment and harm to living organisms. The group of molecules and pollutants identified as highly heterogeneous, including dust, fumes, synthetic chemicals, industrial solvents, lubricants, plastics, pesticides and fungicides. Pollutants are different on multiple time scales, emission rates, weather patterns and diurnal/seasonal

cycles. The behavior of pollutants is governed by its formation rate and the length of time it remains in the atmosphere. In the present study, we found that environmental pollution can cause pulmonary inflammation, systemic inflammation, increased blood pressure, atherosclerosis, arrhythmias, ischemic heart diseases, cardiomyopathy, heart failure and myocardial infarction.

Literature indicates that particulate matter amount is associated to increase in arterial blood pressure. 1-4 mmHg blood pressure increase per 10 g/m^3 elevation in PM⁵⁷. Long term exposure to increase PM 2.5 μm has been linked with higher concentration of circulating endothelin (ET-1) with an increase pulmonary arterial pressure⁵⁸. Wu et al⁵⁹ found a significant interaction between temperature and traffic-related air pollutants PM \leq 2.5 μm , organic carbon, elemental carbon and nitrogen dioxide on blood pressure. They conclude that, air pollution affects blood pressure more at low temperature levels than at high temperature levels. Jung et al⁶⁰ found that, high systolic and diastolic blood pressure was associated with overweight or obese subjects when they were exposed to longterm pollution. Similarly, Stanković et al¹¹ reported that exposure to low levels of air pollution increases the blood pres-

Table II. Effect of motor vehicle pollutants and their association with cardiovascular diseases.

Author names and study year	Traffic pollutant	Cardiovascular diseases
Kluizenaar et al 2013 ³⁹	Air pollution, noise	Ischemic heart disease
Dzhambov et al 2015 ⁴⁰	Air pollution, noise	Myocardial infarction
Kälsch et al 2014 ⁴¹	Air pollution, noise	Atherosclerosis
Halonen et al 2013 ⁴²	Noise exposure	Ischemic heart disease
Hart et al 2013 ⁴³	Traffic, NO_2	Myocardial infarction
Hansell et al 2013 ⁴⁴	Aircraft noise	CAD
Selander et al 2013 ⁴⁵	Noise, job strain	MI
Sørensen et al 2012 ⁴⁶	Traffic exposure	Myocardial Infarction
Floud et al 2013 ⁴⁷	Aircraft noise	Myocardial Infarction
Gan et al 2012 ⁴⁸	Air pollution	CHD
Woodcock et al 2009 ⁴⁹	Motor vehicles	Ischemic heart disease
Hoffmann et al 2007 ⁵⁰	Traffic pollution	Atherosclerosis
Selander et al 2009 ⁵¹	Traffic pollution	Myocardial infarction
Gan et al 2010 ⁵²	Traffic pollution	Hypertension heart disease,
Grahame et al 2010 ⁵³	Vehicular emissions	Atherosclerosis, arrhythmias, ST-depression, blood pressure
Su et al 2015 ⁵⁴	PM 2.5 μm , PM 10 μm , NO_2 , NO_x	Atherosclerosis
Bard et al 2014 ⁵⁵	Benzene, gasoline-fueled	Myocardial infarction
Katsoulis et al 2014 ⁵⁶	Traffic-related air pollution	CVD and IHD

PM: Particulate matter with aerodynamic diameter; SO_2 : sulfure dioxide, NO_2 : Nitrogen dioxide, CO: Carbon monoxide, IHD: Ischemic heart diseases, MI: Myocardial infarction, CHD: Coronary heart diseases, HF: Heart failure. CVD: Cardiovascular diseases, CAD: Coronary artery disease.

sure. Physical activity has proved to be statistically significant protective factor for the development of hypertension. Bilenko et al⁶¹ investigated the association between particulate matter composition and blood pressure. They found that, exposure to particulate matter constituents increases blood pressure in children. Similarly, Giorgini et al¹² and Chan et al¹⁵ reported that, short-term exposures to ambient PM 2.5 μm and residential air pollution associated with substantial increases in BP. Pieters et al¹⁴ also found that children attending school on days with higher UFP concentrations (diameter < 100 nm) had higher systolic blood pressure. Prolonged PM 2.5 μm and NO₂ exposures were associated with high blood pressure.

Lee et al⁶² reported that, the association of PM 2.5 μm and PM 10 μm , nitrogen dioxide (NO₂), and elemental carbon were associated with cardiovascular diseases, stroke, and altered blood pressure. Similarly, Kälisch et al⁴¹ investigated associations of long-term exposure to fine PM and road traffic noise with thoracic aortic calcification (TAC). They found that, exposure to fine PM and night-time traffic noise are associated with sub-clinical atherosclerosis.

The epidemiological and experimental studies demonstrated that short and long-term exposure to particulate matter PM2.5 μm is associated with cardiovascular diseases including myocardial infarction, stroke, heart failure, arrhythmias, and venous thromboembolism⁶³. To et al⁶⁴ found that, congestive heart failure, ischemic heart disease and cerebrovascular accident were 20% upsurge with increase in PM 2.5 μm after adjusting for risk factors. Moreover, risks were elevated in smokers and those with obesity. Colais et al⁶⁵ found that an increased risk of cardiac admissions was associated to 10 $\mu\text{g}/\text{m}^3$ PM 10 μm pollutants. The effect was higher for cardiac failure and acute coronary syndrome than for arrhythmias. Females were at higher risk of heart failure, whereas males were at higher risk of arrhythmias.

Furthermore, Li and Chen²¹, Ghosh et al²², Wang et al²⁷, Gan and Davies³⁸, Scarborough et al³⁸; de-Kluzenaar et al³⁹ determined the association between air pollutants and coarse particles levels (PM 2.5-10 μm) with frequency of hospital admissions and mortality due to cardiovascular diseases (CHD). They reported that environmental pollution increases the CHD with an increase in particulate matter and sulfur dioxide and nitrogen dioxide. Mustafic et al⁶⁶ also ob-

served that short-term exposure to air pollutants including carbon monoxide, nitrogen dioxide, sulfur dioxide and particulate matter PM 2.5-10 μm are linked with acute coronary syndrome and myocardial infarction. Pope et al⁶⁷ demonstrated that, fine particulate matter (PM 2.5 μm) air pollution contributes to risk of cardio-metabolic disorders and increasing risk of coronary artery disease. Padula et al³² found that PM 10 μm are associated with pulmonary valve stenosis and ventricular septal defects.

The literature confirmed that air pollution is a leading risk factor in the development of cardiovascular diseases. The possible mechanism for the adverse effect of air pollution on cardiovascular diseases is the pulmonary, systemic inflammation, endothelial damage, oxidative stress and prothrombotic changes (Figure 1).

Larger cohort studies, especially from developing countries, are needed to provide a more precise assessment of the adverse effects of long-term exposure to air pollution on cardiovascular diseases.

Conclusions

Exposure to air pollutants is associated with increased risk of cardiovascular diseases. Air pollutants exert their detrimental effects on heart by developing pulmonary inflammation, systemic inflammation, oxidative stress, endothelial dysfunction and platelets and prothrombotic changes, atherosclerosis, coronary artery disease and congestive heart failure. The findings suggest an important health impact on human populations, occupational and environmental health officials must develop policies to minimize air pollution to decrease the cardiovascular diseases. Moreover, the researchers and physicians must consider the environmental pollution as a serious and an emerging factor in the development of cardiovascular diseases.

Acknowledgements

The authors are thankful to the Deanship of Scientific Research, King Saud University, Riyadh, Saudi Arabia for supporting the work through Research Group Project (RGPVPP 181).

Conflict of Interest

The Authors declare that there are no conflicts of interest.

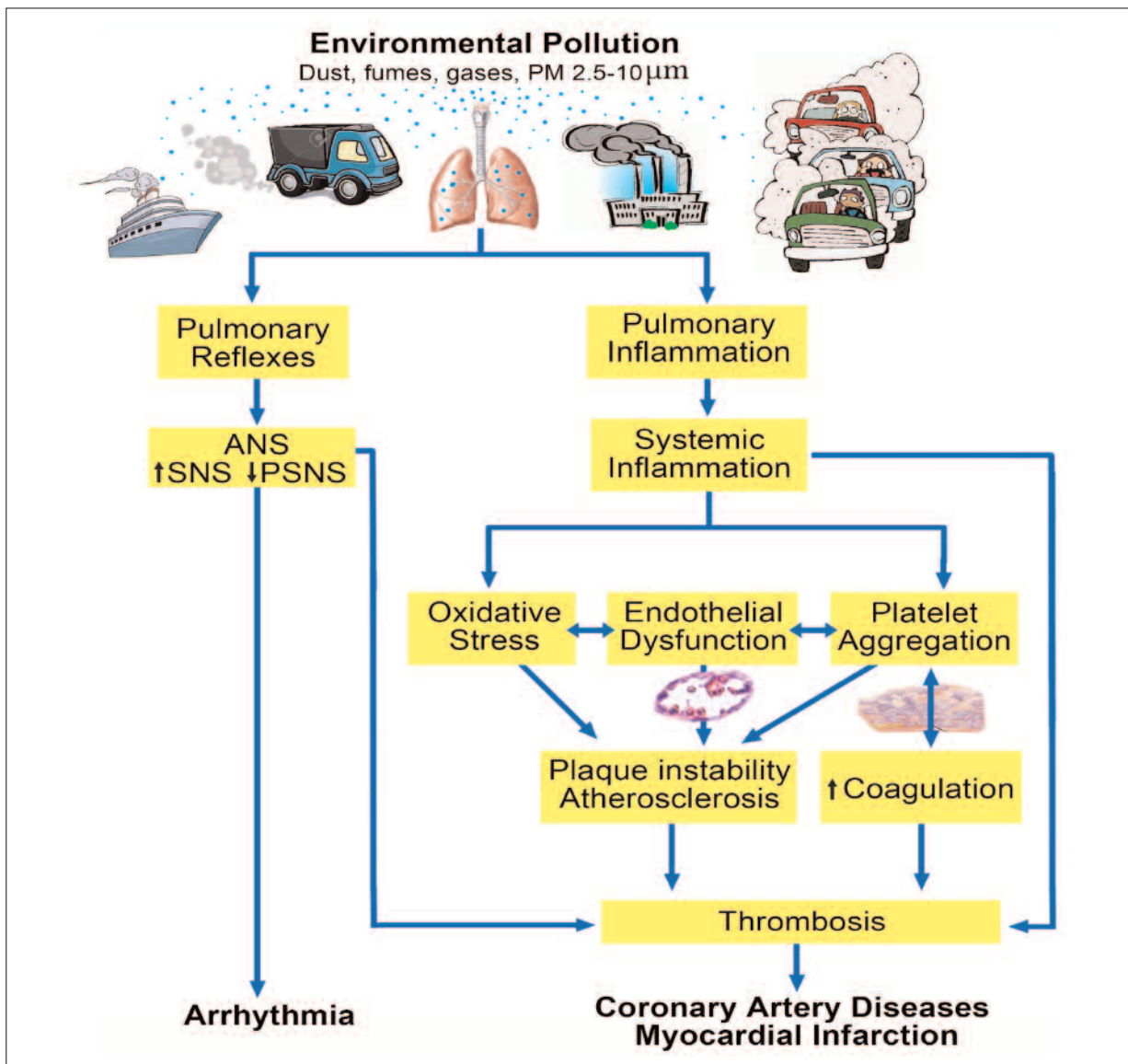


Figure 1. Mechanism involved in environmental pollution and cardiovascular diseases.

References

- 1) PERERA FP. Children are likely to suffer most from our fossil fuel addiction. *Environ Health Persp* 2008; 116: 987-990.
- 2) POPE CA, BURNETT RT, THUN MJ, CALLE EE, KREWSKI D, ITO K. Lung cancer, cardiopulmonary mortality and long-term exposure to fine particulate air pollution. *JAMA* 2002; 287: 1132-1141.
- 3) POPE CA, BURNETT RT, THURSTON GD, THUN MJ, CALLE EE, KREWSKI D. Cardiovascular mortality and long-term exposure to particulate air pollution: Epidemiological evidence of general pathophysiological pathways of disease. *Circulation* 2004; 109: 71-77.
- 4) GARELNABI M. Emerging Evidences from the contribution of the traditional and new risk factors to the atherosclerosis pathogenesis. *J Med Sci* 2010; 10: 136-44.
- 5) UZOIGWE JC, PRUM T, BRESNAHAN E, GARELNABI M. The emerging role of outdoor and indoor air pollution in cardiovascular disease. *N Am J Med Sci* 2013; 5: 445-453.
- 6) BROOK RD, RAJAGOPALAN S, POPE CA, BROOK JR, BHATTAGAR A, DIEZ-ROUX AV, HOLGUIN F, HONG Y, LUEPKER RV, MITTLEMAN MA, PETERS A, SISCOVICK D, SMITH SC JR, WHITSEL L, KAUFMAN JD. American Heart Association Council on Epidemiology and Prevention, Council on the Kidney in Cardiovascular Disease, And Council on Nutrition, Physical Activity and

- Metabolism, Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. *Circulation* 2010; 121: 2331-2378.
- 7) BROOK RD, FRANKLIN B, CASCIO W, HONG Y, HOWARD G, LIPSETT M, LUEPKER R, MITTLEMAN M, SAMET J, SMITH SC JR, TAGER I; EXPERT PANEL ON POPULATION AND PREVENTION SCIENCE OF THE AMERICAN HEART ASSOCIATION. Air pollution and cardiovascular disease: a statement for healthcare professionals from the Expert Panel on Population and Prevention Science of the American Heart Association. *Circulation* 2004; 109: 2655-2671.
 - 8) MIROWSKY J, HICKEY C, HORTON L, BLAUSTEIN M, GALDANES K, PELTIER RE, CHILLRUD S, CHEN LC, ROSS J, NADAS A, LIPPMANN M, GORDON T. The effect of particle size, location and season on the toxicity of urban and rural particulate matter. *Inhal Toxicol* 2013; 25: 747-757.
 - 9) KAMPFRATH T, MAISEYEU A, YING Z, SHAH Z, DEJULIS JA, XU X, KHERADA N, BROOK RD, REDDY KM, PADTURE NP, PARTHASARATHY S, CHEN LC, MOFFATT-BRUCES S, SUN Q, MORAWIETZ H, RAJAGOPALAN S. Chronic fine particulate matter exposure induces systemic vascular dysfunction via NADPH oxidase and TLR4 pathways. *Circ Res* 2011; 108: 716-726.
 - 10) POURSAFA P, KELISHADI R, LAHJANZADEH A, MODARESI M, JAVANMARD SH, ASSARI R, AMIN MM, MOATTAR F, AMINI A, SADEGHIAN B. The relationship of air pollution and surrogate markers of endothelial dysfunction in a population-based sample of children. *BMC Public Health* 2011; 11: 115.
 - 11) STANKOVI A, NIKOLI M. Long-term ambient air pollution exposure and risk of high blood pressure among citizens in Nis, Serbia. *Clin Exp Hypertens* 2015; 11: 1-6.
 - 12) GIORGINI P, RUBENFIRE M, DAS R, GRACIK T, WANG L, MORISHITA M, BARD RL, JACKSON EA, FITZNER CA, FERRI C, BROOK RD. Particulate matter air pollution and ambient temperature: opposing effects on blood pressure in high-risk cardiac patients. *J Hypertens* 2015; 33: 2032-2038.
 - 13) DONG GH, WANG J, ZENG XW, CHEN L, QIN XD, ZHOU Y, LI M, YANG M, ZHAO Y, REN WH, HU QS. Interactions between air pollution and obesity on blood pressure and hypertension in Chinese children. *Epidemiology* 2015; 26: 740-747.
 - 14) PIETERS N, KOPPEN G, VAN POPPEL M, DE PRINS S, COX B, DONS E, NELEN V, PANIS LI, PLUSQUIN M, SCHOETERS G, NAWROT TS. Blood pressure and same-day exposure to air pollution at school: associations with nano-sized to coarse PM in children. *Environ Health Perspect* 2015; 123: 737-742.
 - 15) CHAN SH, VAN HEE VC, BERGEN S, SZPIRO AA, DEROO LA, LONDON SJ, MARSHALL JD, KAUFMAN JD, SANDLER DP. Long-term air pollution exposure and blood pressure in the Sister Study. *Environ Health Perspect* 2015; 123: 951-958.
 - 16) XU M, GUO Y, ZHANG Y, WESTERDAHL D, MO Y, LIANG F, PAN X. Spatiotemporal analysis of particulate air pollution and ischemic heart disease mortality in Beijing, China. *Environ Health* 2014; 13: 109.
 - 17) BENNETT O, KANDALA NB, JI C, LINNANE J, CLARKE A. Spatial variation of heart failure and air pollution in Warwickshire, UK: an investigation of small scale variation at the ward-level. *Br Med J Open* 2014; 4: e006028.
 - 18) YANG C, CHEN A, CHEN R, QI Y, YE J, LI S, LI W, LIANG Z, LIANG Q, GUO D, KAN H, CHEN X. Acute effect of ambient air pollution on heart failure in Guangzhou, China. *Int J Cardiol* 2014; 177: 436-441.
 - 19) SIPONEN T, YLI-TUOMI T, AURELA M, DUFVA H, HILLAMO R, HIRVONEN MR, HUTTUNEN K, PEKKANEN J, PENNANEN A, SALONEN I, TIITTANEN P, SALONEN RO, LANKI T. Source-specific fine particulate air pollution and systemic inflammation in ischaemic heart disease patients. *Occup Environ Med* 2015; 72: 277-283.
 - 20) DUTTA A, RAY MR, BANERJEE A. Systemic inflammatory changes and increased oxidative stress in rural Indian women cooking with biomass fuels. *Toxicol Appl Pharmacol* 2012; 261: 255-262.
 - 21) LI H, CHEN R, MENG X, ZHAO Z, CAI J, WANG C, YANG C, KAN H. Short-term exposure to ambient air pollution and coronary heart disease mortality in 8 Chinese cities. *Int J Cardiol* 2015; 197: 265-270.
 - 22) GHOSH R, LURMANN F, PEREZ L, PENFOLD B, BRANDT S, WILSON J, MILET M, KUNZLI N, MCCONNELL R. Near-roadway air pollution and coronary heart disease: burden of disease and potential impact of a greenhouse gas reduction strategy in southern California. *Environ Health Perspect* 2015; [Epub ahead of print].
 - 23) CHEN YC, WENG YH, CHIU YW, YANG CY. Short-term effects of coarse particulate matter on hospital admissions for cardiovascular diseases: a case-crossover study in a tropical city. *J Toxicol Environ Health A* 2015; 78: 1241-1253.
 - 24) BARTELL SM, LONGHURST J, TJOA T, SIOUTAS C, DELFINO RJ. Particulate air pollution, ambulatory heart rate variability, and cardiac arrhythmia in retirement community residents with coronary artery disease. *Environ Health Perspect* 2013; 121: 1135-1141.
 - 25) HSIEH YL, TSAI SS, YANG CY. Fine particulate air pollution and hospital admissions for congestive heart failure: a case-crossover study in Taipei. *Inhal Toxicol* 2013; 25: 455-460.
 - 26) SHAH AS, LANGRISH JP, NAIR H, McALLISTER DA, HUNTER AL, DONALDSON K, NEWBY DE, MILLS NL. Global association of air pollution and heart failure: a systematic review and meta-analysis. *Lancet* 2013; 382: 1039-1048.
 - 27) WANG DZ, JIANG GH, ZHANG H, SONG GD, ZHANG Y. [Effect of air pollution on coronary heart disease mortality in Tianjin, 2001-2009: a time-series study. *Zhonghua Liu Xing Bing Xue Za Zhi* 2013; 34: 478-483.
 - 28) XIE J, HE M, ZHU W. Acute effects of outdoor air pollution on emergency department visits due to five clinical subtypes of coronary heart diseases in Shanghai, China. *J Epidemiol* 2014; 24: 452-459.
 - 29) GOLDBERG MS, WHEELER AJ, BURNETT RT, MAYO NE, VALOIS MF, BROPHY JM, GIANNETTI N. Physiological

- and perceived health effects from daily changes in air pollution and weather among persons with heart failure: a panel study. *J Expo Sci Environ Epidemiol* 2015; 25: 187-199.
- 30) MORISHITA M, BARD RL, WANG L, DAS R, DVONCH JT, SPINO C, MUKHERJEE B, SUN Q, HARKEMA JR, RAJAGOPALAN S, BROOK RD. 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: 153-159.
 - 31) BLOOMFIELD GS, LAGAT DK, AKWANALO OC, CARTER EJ, LUGOGO N, VEDANTHAN R, VELAZQUEZ EJ, KIMAYO S, SHERMAN CB. Waiting to inhale: An exploratory review of conditions that may predispose to pulmonary hypertension and right heart failure in persons exposed to household air pollution in low- and middle-income countries. *Glob Heart* 2012; 7: 249-259.
 - 32) PADULA AM, TAGER IB, CARMICHAEL SL, HAMMOND SK, YANG W, LURMANN F, SHAW GM. Ambient air pollution and traffic exposures and congenital heart defects in the San Joaquin Valley of California. *Paediatr Perinat Epidemiol* 2013; 27: 329-339.
 - 33) AGAY-SHAY K, FRIGER M, LINN S, PELED A, AMITAI Y, PERETZ C. Air pollution and congenital heart defects. *Environ Res* 2013; 124: 28-34.
 - 34) DOMINGUEZ-RODRIGUEZ A, ABREU-AFONSO J, RODRIGUEZ S, JUAREZ-PRERA RA, ARROYO-UCAR E, GONZALEZ Y, ABREU-GONZALEZ P, AVANZAS P. Air pollution and heart failure: Relationship with the ejection fraction. *World J Cardiol* 2013; 5: 49-53.
 - 35) HUANG J, DENG F, WU S, LU H, HAO Y, GUO X. The impacts of short-term exposure to noise and traffic-related air pollution on heart rate variability in young healthy adults. *J Expo Sci Environ Epidemiol* 2013; 23: 559-564.
 - 36) BECKERMAN BS, JERRETT M, FINKELSTEIN M, KANAROGLOU P, BROOK JR, ARAIN MA, SEARS MR, STIEB D, BALMES J, CHAPMAN K. The association between chronic exposure to traffic-related air pollution and ischemic heart disease. *J Toxicol Environ Health A* 2012; 75: 402-411.
 - 37) GAN WQ, DAVIES HW, KOEHOORN M, BRAUER M. Association of long-term exposure to community noise and traffic-related air pollution with coronary heart disease mortality. *Am J Epidemiol* 2012; 175: 898-906.
 - 38) SCARBOROUGH P, ALLENDER S, RAYNER M, GOLDACRE M. Contribution of climate and air pollution to variation in coronary heart disease mortality rates in England. *PLoS One* 2012; 7: e32787.
 - 39) DE-KLUIZENAAAR Y, VAN LENTHE FJ, VISSCHEDIJK AJ, ZANDVELD PY, MIEDEMA HM, MACKENBACH JP. Road traffic noise, air pollution components and cardiovascular events. *Noise Health* 2013; 15: 388-397.
 - 40) DZHAMBOV AM, DIMITROVA DD. Evaluation of the social and economic burden of road traffic noise-attributed myocardial infarction in Bulgarian urban population. *Arh Hig Rada Toksikol* 2015; 66: 15-21.
 - 41) KÄLSCH H, HENNIG F, MOEBUS S, MÖHLENKAMP S, DRAGANO N, JAKOBS H, MEMMESHEIMER M, ERBEL R, JÖCKEL KH, HOFFMANN B; HEINZ NIXDORF RECALL STUDY INVESTIGATIVE GROUP. Are air pollution and traffic noise independently associated with atherosclerosis: the Heinz Nixdorf Recall Study. *Eur Heart J* 2014; 35: 853-860.
 - 42) HALONEN JI, HANSELL AL, GULLIVER J, MORLEY D, BLANGIARDO M, FECHT D, TOLEDANO MB, BEEVERS SD, ANDERSON HR, KELLY FJ, TONNE C. Road traffic noise is associated with increased cardiovascular morbidity and mortality and all-cause mortality in London. *Eur Heart J* 2015; 36: 2653-2661.
 - 43) HART JE, RIMM EB, REXRODE KM, LADEN F. Changes in traffic exposure and the risk of incident myocardial infarction and all-cause mortality. Epub 2015 Jun 23. *Epidemiology* 2013; 24: 734-742.
 - 44) HANSELL AL, BLANGIARDO M, FORTUNATO L, FLOUD S, DE HOOGH K, FECHT D, GHOSH RE, LASZLO HE, PEARSON C, BEALE L, BEEVERS S, GULLIVER J, BEST N, RICHARDSON S, ELLIOTT P. Aircraft noise and cardiovascular disease near Heathrow airport in London: small area study. *Br Med J* 2013; 347: f5432.
 - 45) SELANDER J, BLUHM G, NILSSON M, HALLOVIST J, THEORELL T, WILLIX P, PERSHAGEN G. Joint effects of job strain and road-traffic and occupational noise on myocardial infarction. *Scand J Work Environ Health* 2013; 39: 195-203.
 - 46) SØRENSEN M, ANDERSEN ZJ, NORDSBORG RB, JENSEN SS, LILLELUND KG, BEELEN R, SCHMIDT EB, TJØNNELAND A, OVERVAD K, RAASCHOU-NIELSEN O. Road traffic noise and incident myocardial infarction: a prospective cohort study. *PLoS One* 2012; 7: e39283.
 - 47) FLOUD S, BLANGIARDO M, CLARK C, DE HOOGH K, BABISCH W, HOUTHUIJS D, SWART W, PERSHAGEN G, KATSOUYANNI K, VELONAKIS M, VIGNA-TAGLIANTI F, CADUM E, HANSELL AL. Exposure to aircraft and road traffic noise and associations with heart disease and stroke in six European countries: a cross-sectional study. *Environ Health* 2013; 12:89.
 - 48) GAN WQ, DAVIES HW, KOEHOORN M, BRAUER M. Association of long-term exposure to community noise and traffic-related air pollution with coronary heart disease mortality. *Am J Epidemiol* 2012; 175: 898-906.
 - 49) WOODCOCK J, EDWARDS P, TONNE C, ARMSTRONG BG, ASHIRU O, BANISTER D, BEEVERS S, CHALABI Z, CHOWDHURY Z, COHEN A, FRANCO OH, HAINES A, HICKMAN R, LINDSAY G, MITTAL I, MOHAN D, TIWARI G, WOODWARD A, ROBERTS I. Public health benefits of strategies to reduce greenhouse-gas emissions: urban land transport. *Lancet* 2009; 374: 1930-1943.
 - 50) HOFFMANN B, MOEBUS S, MÖHLENKAMP S, STANG A, LEHMANN N, DRAGANO N, SCHMERMUND A, MEMMESHEIMER M, MANN K, ERBEL R, JÖCKEL KH; HEINZ NIXDORF RECALL STUDY INVESTIGATIVE GROUP. Residential exposure to traffic is associated with coronary atherosclerosis. *Circulation* 2007; 116: 489-496.

- 51) SELANDER J, NILSSON ME, BLUHM G, ROSENLUND M, LINDOVIST M, NISE G, PERSHAGEN G. Long-term exposure to road traffic noise and myocardial infarction. *Epidemiology* 2009; 20: 272-279.
- 52) GAN WQ, TAMBURIC L, DAVIES HW, DEMERS PA, KOEHOORN M, BRAUER M. Changes in residential proximity to road traffic and the risk of death from coronary heart disease. *Epidemiology* 2010; 21: 642-649.
- 53) GRAHAME TJ, SCHLESINGER RB. Cardiovascular health and particulate vehicular emissions: a critical evaluation of the evidence. *Air Qual Atmos Health* 2010; 3: 3-27.
- 54) SU TC, HWANG JJ, SHEN YC, CHAN CC. Carotid intima-media thickness and long-term exposure to traffic-related air pollution in middle-aged residents of Taiwan: a cross-sectional study. *Environ Health Perspect* 2015; 123: 773-778.
- 55) BARD D, KIHAL W, SCHILLINGER C, FERMANIAN C, SÉGALA C, GLORION S, ARVEILER D, WEBER C. Traffic-related air pollution and the onset of myocardial infarction: disclosing benzene as a trigger? A small-area case-crossover study. *PLoS One* 2014; 9: e100307.
- 56) KATSOLIS M, DIMAKOPOULOU K, PEDELI X, TRICHOPOULOS D, GRYPARIS A, TRICHOPOULOU A, KATSOUYANNI K. Long-term exposure to traffic-related air pollution and cardiovascular health in a Greek cohort study. *Sci Total Environ* 2014; 490: 934-940.
- 57) CHOI JH, XU QS, PARK SY, KIM JH, HWANG SS, LEE KH, LEE HJ, HONG YC. Seasonal variation of effect of air pollution on blood pressure. *J Epidemiol Community Health* 2007; 61: 314-318.
- 58) CALDERÓN-GARCIDUEÑAS L, VINCENT R, MORA-TISCAREÑO A, FRANCO-LIRA M, HENRÍQUEZ-ROLDÁN C, BARRAGÁN-MEJÍA G, GARRIDO-GARCÍA L, CAMACHO-REYES L, VALENCIA-SALAZAR G, PAREDES R, ROMERO L, OSNAYA H, VILLARREAL-CALDERÓN R, TORRES-JARDÓN R, HAZUCHA MJ, REED W. Elevated plasma endothelin-1 and pulmonary arterial pressure in children exposed to air pollution. *Environ Health Perspect* 2007; 115: 1248-1253.
- 59) WU J, REN C, DELFINO RJ, CHUNG J, WILHELM M, RITZ B. Association between local traffic-generated air pollution and preeclampsia and preterm delivery in the south coast air basin of California. *Environ Health Perspect* 2009; 117: 1773-1779.
- 60) JUNG CC, SU HJ, LIANG HH. Association between indoor air pollutant exposure and blood pressure and heart rate in subjects according to body mass index. *Sci Total Environ* 2016; 539: 271-276.
- 61) BILENKO N, BRUNEKREEF B, BEELEN R, EEFSENS M, DE HOOGH K, HOEK G, KOPPELMAN GH, WANG M, VAN ROSSEM L, GEHRING U. Associations between particulate matter composition and childhood blood pressure--The PIAMA study. *Environ Int* 2015; 84: 1-6.
- 62) LEE BJ, KIM B, LEE K. Air pollution exposure and cardiovascular disease. *Toxicol Res* 2014; 30: 71-75.
- 63) MARTINELLI N, OLIVIERI O, GIRELLI D. Air particulate matter and cardiovascular disease: a narrative review. *Eur J Intern Med* 2013; 24: 295-302.
- 64) TO T, ZHU J, VILLENEUVE PJ, SIMATOVIC J, FELDMAN L, GAO C, WILLIAMS D, CHEN H, WEICHENTHAL S, WALL C, MILLER AB. Chronic disease prevalence in women and air pollution--A 30-year longitudinal cohort study. *Environ Int* 2015; 80: 26-32.
- 65) COLAIS P, FAUSTINI A, STAFOGGIA M, BERTI G, BISANTI L, CADUM E, CERNIGLIARO A, MALLONE S, PACELLI B, SERINELLI M, SIMONATO L, VIGOTTI MA, FORASTIERE F; EPI-AIR COLLABORATIVE GROUP. Particulate air pollution and hospital admissions for cardiac diseases in potentially sensitive subgroups. *Epidemiology* 2012; 23: 473-81.
- 66) MUSTAFIC H, JABRE P, CAUSSIN C, MURAD MH, ESCOLANO S, TAFFLET M, PÉRIER MC, MARIJON E, VERNEREY D, EMPANA JP, JOUVEN X. Main air pollutants and myocardial infarction: a systematic review and meta-analysis. *JAMA* 2012; 307: 713-721.
- 67) POPE CA 3RD, TURNER MC, BURNETT RT, JERRETT M, GAPSTUR SM, DIVER WR, KREWSKI D, BROOK RD. Relationships between fine particulate air pollution, cardiometabolic disorders, and cardiovascular mortality. *Circ Res* 2015; 116: 108-115.