View metadata, citation and similar papers at core.ac.uk
brought to you by CORE
provided by OAR@UM

Review Article

Pollution and Cardiovascular Health in Malta – A Review

Jeremy Fleri-Soler, Andrew J Cassar-Maempel

Introduction

The leading cause of global mortality is cardiovascular disease (CVD) and in 2016 alone over 17 million premature deaths were attributed to CVD.[1] Whilst previously there was only weak evidence to suggest an association of air pollution as a risk factor for CVD,[2] in recent years, the impact of air pollution has emerged as an independent, strong and modifiable risk factor for CVD. The importance of air pollution on CVD is now being considered above other more traditional factors such as high cholesterol and reduced physical activity.[3]

Exposure to fine particulate matter has been shown to increase the risk of acute coronary syndromes, yet more concerning are the studies which have shown the greater extent of its effects over a longer period of time, reducing life-expectancy by a number of years and being responsible for 19% of cardiovascular mortality (>3 million deaths)[1]

The purpose of this review is to identify significant studies investigating air pollution and its effects on cardiovascular health while also considering our situation in Malta, as a small, highly populated country.

Jeremy Fleri-Soler MD, MRCP (UK)
Higher Specialist Trainee in Cardiology,
Mater Dei Hospital
Msida, Malta

Andrew J Cassar-Maempel* MD, MRCP (UK), FACC, FSCAI, FESC
Consultant Cardiologist
Mater Dei Hospital
Msida, Malta
andrew-j.cassar-maempel@gov.mt

**Corresponding Author*

Epidemiology – prevalence / impact

Air pollution is a worldwide problem with almost all people exposed to some degree.[1] When discussing health care, the term air pollution encompasses gaseous pollutants present at ground level (ozone, carbon monoxide (CO), nitrous dioxide (NO_2) and sulfur dioxide (SO_2)) as well as airborne particulate matter (PM), all of which are able to enter the body through the airways. The latter is subdivided into three categories according to size of particles: coarse matter (<10μm - ≥2.5 μm), fine matter (<2.5 μm - ≥0.1μm) and ultrafine particles (<0.1 μm).[3]

Primary pollutants, such as soot particles, nitrous dioxide and sulphur dioxide, are emitted directly into the air by combustion of fossil fuels. Secondary pollutants are formed in the atmosphere from other components, such as ozone which is formed through complex photochemical reactions of nitrogen oxides and volatile organic components. Sources of coarse matter (PM_{10}) include dust, soil and dirt physically thrown into the air by wind or movement of vehicles. Once airborne, PM_{10} may be inhaled and deposited into the throat and upper airways. On the other hand fine matter ($PM_{2.5}$) is mostly found in smoke and haze and is attributable to combustion processes taking place in human industry, power plants, motorized vehicles and residential heating using oil, coal, or wood. $PM_{2.5}$ is of particular health concern as it is able to travel deeply into the respiratory tract and into the small airways.[4] It is also important to highlight that $PM_{2.5}$ can travel over long distances (>100km) imposing its effect over a wider area.[3]

There is major variability in the levels of air pollution globally. As expected, lower-income countries have higher household pollution due to consumption of solid fuels for domestic heating and cooking. However this is also a problem in the west where despite spending most of their lives indoors, people are still exposed to $PM_{2.5}$ which has been shown to infiltrate buildings. More concerning is a shift to using 'environmentally-friendly' biomass fuels for heating over traditional electrical means, particularly prevalent in Northern Europe, creating major indoor air quality problems.[3] Large urban-rural differences are found for soot (average 38% higher), NO_2 (63% higher), and ultrafine particle numbers. Temporal variation of daily air pollution concentrations is also present. For example, ozone concentrations are highest during the warmest, high-intensity sunlight hours of the day; traffic-related pollutants, such as ultrafine particles and soot, often peak during the morning and evening rush hours resulting in high exposures for people commuting. Wind direction, wind speed and atmospheric stability also effect daily pollution levels.

Air Pollution and Mortality

Cardiovascular Mortality

In 2004 the American Heart Association (AHA) first released a statement on their position of the effect on air pollution on health, concluding that exposure to particulate matter is indeed an adverse factor in cardiovascular morbidity and mortality.[5] In a further review in 2010 the AHA consolidated their position by claiming exposure to $PM_{2.5}$ in the short term may trigger cardiovascular events but that there is an even greater effect in long-term exposure, reducing life expectancy by a few years.[5] One meta-analysis found a pooled effect of a 6% increased risk per 10 μg/m^3 increase in $PM_{2.5}$ in all-cause mortality and as much as an 11% per 10 μg/m^3 $PM_{2.5}$ increased risk in cardiovascular mortality, which was higher when compared to death from non-malignant respiratory disease.[6]

In recent years, the European Study of Cohorts for Air Pollution Effects (ESCAPE study) was launched with an aim to investigate the effect of pollution on the health of >300,000 individuals across Europe. They used standardized models for measurements of exposure and subsequent health effects whilst trying to eliminate confounding factors such as race and social status that may exist between regions.[7] ESCAPE revealed a statistically significant effect of $PM_{2.5}$ on all-cause mortality, with a non-significant association with cardiovascular mortality specifically. The effect was exerted with mean $PM_{2.5}$ levels lower than those currently recommended, a trend that will be found across many studies.[8]

Cardiovascular Disease

Cardiovascular effects of air pollution are now well-recognized and studies have increasingly shown pollution to both exacerbate existing heart conditions as well as predispose the individual to the development of cardiovascular disease including coronary artery disease, cerebrovascular disease and peripheral artery disease.[3]

Coronary artery disease

Long-term exposure to $PM_{2.5}$ was associated with an increased risk of coronary artery disease in previously healthy, post-menopausal women. In the Women's Health Initiative Study, exposure to >65,000 women over 4 years in 36 different cities showed that risk of cardiovascular events was increased with increase in air pollution exposure. There was a hazard ratio of 1.21 for developing a first coronary event and a hazard ratio of 2.21 to die of the coronary event for every 10μg/m^3 increase in $PM_{2.5}$.[9]

The ESCAPE study involved more than 100 000 participants without a previous history of cardiovascular disease from 11 cohorts across Europe over the period 1997-2007. It found a 12% increased risk of coronary events per 10 μg/m^3 in PM_{10} and a 13% increased risk of coronary events per 5 μg/m^3 increase in $PM_{2.5}$. Most importantly, positive associations were also observed below the current recommended annual European limit for $PM_{2.5}$ and PM_{10}.[10-11] Both of these studies found a higher risk in people over 60 years of age and non-smokers, with $PM_{2.5}$ exerting its effect at less than 25μg/m^3, the current legal limit recommended. These findings suggest pushing for the lowering of European limits of air pollution so as to better protect the public from cardiovascular disease.

Another study investigated the increased risk of myocardial ischemia with exposure to $PM_{2.5}$ in patients known to suffer from ischemic heart disease, through repeated exercise stress testing. There was an increased risk of myocardial ischemia (as defined by ST-segment depression on exercise stress testing) in those people who had been exposed to higher levels of $PM_{2.5}$ or the gaseous pollutants NO_2 and CO.[12]

More recently, a study involving six metropolitan areas in the United States, showed an association between air pollution and the development / progression of coronary artery calcium over 10 years, with a particular stronger association in people aged over 65, the hypertensive and non-obese. Also of interest was that the mean $PM_{2.5}$ level in these areas was lower and acceptable by international standards.[2]

Cerebrovascular disease

The Women's Health Initiative study reported a 35% increased risk of stroke and death from cerebrovascular disease and 83% increased risk of death from cerebrovascular disease per 10μg/m^3 increase in long-termPM2.5 exposure.[9]

The ESCAPE study found a 19% increased risk of stroke per 5 mg/m3 increase in PM2.5 in nearly 100 000 participants from 11 cohorts across Europe.[10]

Peripheral artery disease

Furthermore, air pollution and living closer to a main road was also been associated with peripheral artery disease as defined by worse ankle brachial indexes.[13]

Heart failure

While much research has suggested a link between coronary artery disease and air pollution, studies into its possible association with heart failure in the long-term are still unsubstantial. One meta-analysis included 35 studies from across North and South America, Europe and Asia looking into more than 4 million events. It linked an increased risk of hospitalization or mortality due to heart failure with increased levels of both CO (per 1ppm), SO_2 (per 10ppb), NO_2 (per 10ppb), $PM_{2.5}$ (per 10μg/m3) and PM_{10} (per 10μg/m3), as much as 3.5%, 2.4%, 1.7%, 2.1% and 1.6% respectively.[14]

Arrhythmias and arrest

The effect on ventricular arrhythmias is unclear, with studies providing inconsistent evidence. While studies investigating a clear relationship between arrhythmias and pollution by measuring the rate of activation of implantable cardio-defibrillators have so far come up short, (15)other studies have reported an association between sudden cardiac death and out-of-hospital arrest with pollution.[16]

Pathophysiology

Although recent data has shown a strong influence of air pollution on cardiovascular disease, the exact mechanism by which air pollution increases the risk of cardiovascular problems remains unclear. Several hypothesis of pathophysiology have been suggested.[3]

Vascular Dysfunction

One proposed mechanism is that exposure to air pollution predisposes to vascular dysfunction with an increase in vascular tone and thus blood pressure, contributing to long-term sequelae. A study discovered that short-term inhalation of $PM_{2.5}$ and ozone contributed to an acute rise in mean arterial blood pressure, secondary to acute arterial vasoconstriction. Subjects had been exposed to concentration levels comparable to the urban environment.[17] Meanwhile larger observational studies have shown that exposure to $PM_{2.5}$ has led to persistent vascular dysfunction, and the lowering of $PM_{2.5}$ concentration exposure was associated with a drop in the mean blood pressure and a reduction in cardiovascular events.[18]

Atherosclerosis

Several studies have showed the association of formation of atherosclerosis with exposure to air pollution, in particular $PM_{2.5}$.[7] Using CIMT as marker for subclinical atherosclerosis, the Multi-Ethnic Study of Atherosclerosis (MESA) examined the progression of CIMT in comparison with $PM_{2.5}$ levels. Despite a mean follow-up of only 2.5 years, it showed a positive but not significant association between pollution and CIMT and a greater reduction on $PM_{2.5}$ levels was associated with a slower rate of CIMT progression.[19]

A cross-sectional meta-analysis of data from studies, including the previously mentioned ESCAPE, showed a 0.78% increase in CIMT per 5μg/m^3 increase in $PM_{2.5}$ as well as showing a positive association between CIMT and living proximity to high vehicular traffic.[7]

Increased Thrombogenicity

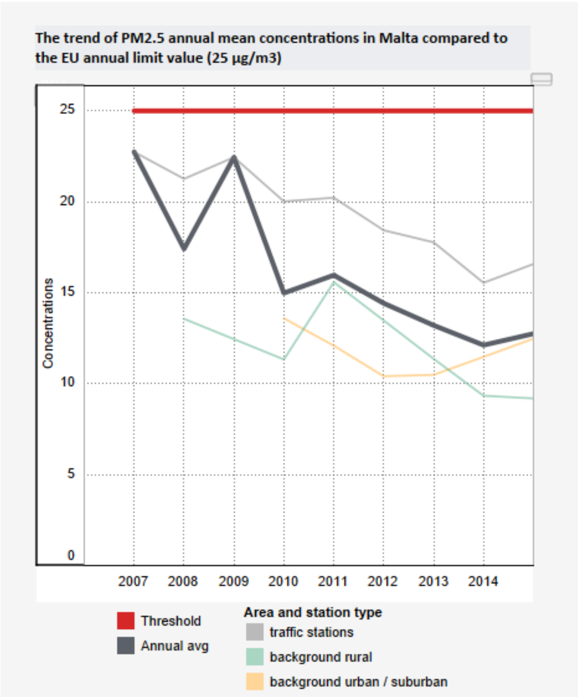
One hypothesis for the association of short-term exposure to $PM_{2.5}$ with acute cardiovascular events is the suggestion that prolonged exposure to air pollution results in endothelial damage and an increased likelihood of thrombosis through chronic inflammation and transient increases in plasma viscosity.[20]

This effect seems to be particularly increased in patients who suffer from diabetes. A study confirmed this by investigating platelet function in adults with diabetes. The study concluded that a relative increase in $PM_{2.5}$ was associated with a greater prothrombotic tendency of platelets as well as an increase in blood leukocyte number that was used as a marker for inflammation.[21]

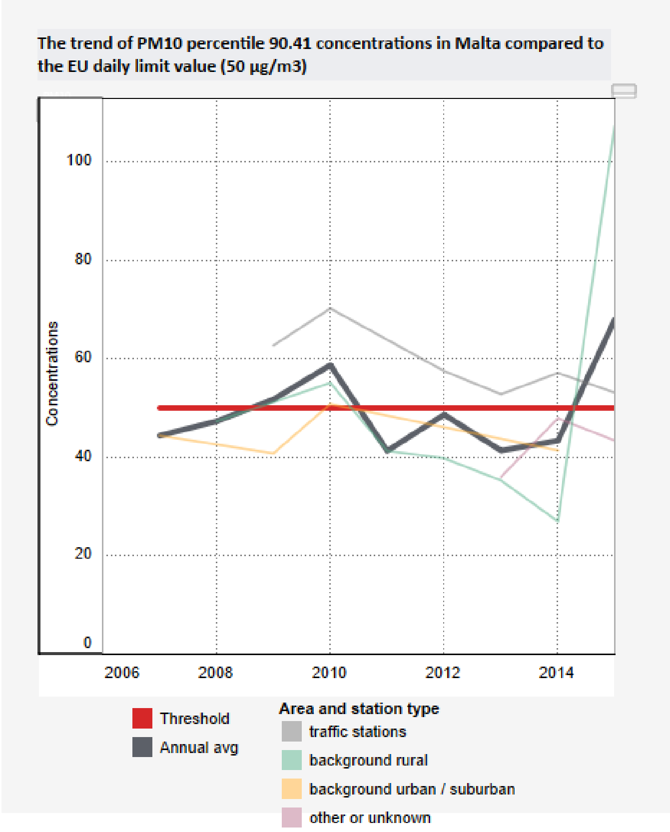
Air Quality in Malta

In recent years the European Union (EU) has recognized the negative impact that air pollution has on European health and economy and has set air quality limits which are regularly exceeded, especially in urban areas, the most troublesome pollutants being PM and ground-level NO_2.[22] Since joining the EU, Malta has committed itself to monitoring pollution levels and striving to reach targets agreed upon. The European Environmental Agency (EEA) monitors air pollution levels in all EU-28 member states through air quality data, which are submitted by each country to the EEA. The most recently published data encompasses the years of 2011-2015.[22]

As depicted below in Figure 1, taken from of the EEA report published in 2017, Malta has managed to remain below the EU's $PM_{2.5}$ limit of 25µg/m^3 with a mean of 10-20µg/m^3. The main contribution of $PM_{2.5}$ in Malta is identified as road traffic and energy production, with road traffic accounting for approximately 6 times of emissions when compared to energy production in 2013. More worryingly, emissions from traffic are on the upward trend.[22]



Data regarding PM_{10} in Malta can be found in Figure 2. The daily limit of 50µg/m^3 is regularly exceeded, peaking at a mean of 70µg/m^3 in 2015.[22] However no data was available in tracking sources of emissions.



Using this data, the EEA has been able to quantify the effect of air pollution and express it as premature deaths. Malta, with a population of 425,000 people at the time of the study, was found to have an annual mean $PM_{2.5}$ of 12µg/m^3. By extrapolation this was calculated to contribute to 220 premature deaths annually.[22]

The EU recommends annual mean levels of $PM_{2.5}$ and PM_{10} of 25µg/m^3 and 40µg/m^3 respectively, however no standards have been set for the chemical composition of PM and no standards set for $PM_{0.1}$ levels, the so-called "ultrafine particles".[3]

Although Malta reached $PM_{2.5}$ levels as recommended by the EU, it is important to also mention that in 2005 the World Health Organization (WHO) published global guidelines for air quality standards, in which the $PM_{2.5}$ limit was recommended at 10µg/m^3 as an annual mean and the PM_{10} limit was recommended at 20µg/m^3. Therefore at $PM_{2.5}$ of 12µg/m^3 Malta exceeds this.[23] In fact it is estimated that one third of Europeans live in substandard air quality according to EU guidelines however as much as 90% are exposed harmful levels according to WHO criteria.[3]

A Timely Intervention

Since the harmful effects of air pollution have been clearly defined, the issue turns to the value of intervention on air quality control. A study from the United States investigated changes in life expectancy associated with changes in $PM_{2.5}$ levels during the 1980s and 1990s. A significant increase in mean life expectancy by 0.61 years was associated with a reduction of $10\mu g/m^3$ in $PM_{2.5}$ concentration, accounting for almost 15% of overall increase in life expectancy in areas studied.[24]

Another study used the ban on coal sales in Dublin in 1990 as a pivotal point in examining air quality, investigating mortality rates over the 6 years prior and comparing to the following 6 years. Average black smoke concentrations fell by $35\mu g/m^3$ and, in conjunction, non-trauma mortality decreased by 5.7% and cardiovascular deaths fell significantly by 10.3%.[25]

Strategy Propositions

In 2017 the *Lancet* Commission on Pollution and Health was published, which not only highlighted the effect of pollution on health but also proposed that global pollution can be controlled and pollution-related health problems prevented, advocating for several interventions. As Table 1 summarizes, such interventions are needed at population and individual level and as healthcare professionals we have a role to play too.

***Table 1**: Summary of Proposed Interventions at Different Levels of Society*[1,26]

	Government	Individual	Healthcare Professionals
Determine Exposure & Health Risks	• Scientific monitoring of population exposure • Funding research in adverse effects on health	• Increase awareness of susceptibility to exposure	• Promote research in public health, environmental science
Reduce Emissions at Source	• Regulations and enforcement towards reduction of emissions • Develop renewable energy	• Use of clean burning fuels • Use of active / public transport	• Using health economics to demonstrate to policy makers the long-term financial benefit of pollution reduction
Reduce Exposures Downstream	• Incentivize cleaner industry through use of air filters • Identify and intervene at exposed sub-populations	• Identify and avoid potential sources of exposure to self • Installation of home ventilation systems	• Public education in risks of exposure, encouraging behavioural change

Pollution control strategies are dependent on a determined government and an engaged, informed and empowered civil society, with necessary collaboration between different government agencies and non-governmental organizations (NGO's) both nationally and internationally. Successful intervention relies on primary prevention by eliminating pollution at the source, and an efficient system able to control pollution once present in the environment. Such proposals do not come into fruition overnight and therefore it is important that ambitious but attainable targets are devised, guided by both national and supranational standards such as WHO or the EU. For interventions to be effective they must have public support and be prioritized according to health effects, environmental damage and cost-effectiveness. Once implemented it is important to establish systems for monitoring the effects of such interventions and seek improvement in their significance.[26]

Examples of high impact interventions to reduce air pollution are the energy and transport sectors. Highly relevant to Malta, the recent shift of energy production from coal power plants to cleaner gas plants while also incentivizing industry to move towards cleaner, more efficient production technologies is a step in the right direction being taken along with many developed countries. An even better strategy would be funding research and converting to low-polluting energy production such as wind and solar plants which would not only improve cardiovascular health of the population but also reduce greenhouse gases and increase the economic efficiency of energy generation.

Transportation also carries a heavy impact on air pollution, significantly so with the Maltese population who are so reliant on personal transportation. Upgrading public transportation to be more efficient and affordable for the populous as well as restricting motorized vehicles from city centres and encouraging active transport with the creation of appropriate walkways and cycle-lanes will significantly improve air-quality.[26] Moving toward electric cars rather than diesel / petrol will be an inevitable step in the future which should rather be done sooner than later. Paris have already targeted a ban on non-electric cars by 2030 and Copenhagen recently announced a plan for a total ban on diesel cars by 2019.

On an individual level, one can limit the effect of air pollution on health by personally reducing contribution to pollution through reduction of energy or transport use as well as the use of clean fuels in energy consumption. In preventing personal exposure to pollution an increased awareness of susceptibility to pollution is needed with subsequent behavioral change to reduce exposure.[1]

Finally, as health professionals, we can contribute by emphasizing the relationship between pollution and adverse health effects, contributing research in environmental science, public health and health economics and supporting education in environmental health science in the younger generations.[26]

Conclusion

In recent years, the problem of air pollution and its harmful effects have been highlighted with ample evidence published supporting the significant association of air pollution with risk of adverse cardiovascular effects. As a nation, Malta has elevated levels of air pollution and trends towards further worsening in recent years as industry and economy are booming. This is most likely resulting in significant morbidity and mortality due to cardiovascular disease to the Maltese people. We must now turn to solution through determination of the population including taking care of our own roles as individuals in society, by pressuring policy makers and supporting interventions carried out on a national scale so as to reverse the trend.

References

1. Hadley MB, Vedanthan R, Fuster V. Air pollution and cardiovascular disease: a window of opportunity. Nat Rev Cardiol. 2018;15(4):193-4.
2. Kaufman JD, Adar SD, Barr RG, Budoff M, Burke GL, Curl CL, et al. Association between air pollution and coronary artery calcification within six metropolitan areas in the USA (the Multi-Ethnic Study of Atherosclerosis and Air Pollution): a longitudinal cohort study. Lancet (London, England). 2016;388(10045):696-704.
3. Newby DE, Mannucci PM, Tell GS, Baccarelli AA, Brook RD, Donaldson K, et al. Expert position paper on air pollution and cardiovascular disease. European heart journal. 2015;36(2):83-93b.
4. 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(8):445-53.
5. Brook RD, Rajagopalan S, Pope CA, 3rd, Brook JR, Bhatnagar A, Diez-Roux AV, et al. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. Circulation. 2010;121(21):2331-78.
6. Hoek G, Krishnan RM, Beelen R, Peters A, Ostro B, Brunekreef B, et al. Long-term air pollution exposure and cardio- respiratory mortality: a review. Environmental Health. 2013;12(1):43.
7. Perez L, Wolf K, Hennig F, Penell J, Basagaña X, Foraster M, et al. Air Pollution and Atherosclerosis: A Cross-Sectional Analysis of Four European Cohort Studies in the ESCAPE Study. Environmental Health Perspectives. 2015;123(6):597-605.
8. Beelen R, Raaschou-Nielsen O, Stafoggia M, Andersen ZJ, Weinmayr G, Hoffmann B, et al. Effects of long-term exposure to air pollution on natural-cause mortality: an analysis of 22 European cohorts within the multicentre ESCAPE project. The Lancet.383(9919):785-95.
9. Miller KA, Siscovick DS, Sheppard L, Shepherd K, Sullivan JH, Anderson GL, et al. Long-Term Exposure to Air Pollution and Incidence of Cardiovascular Events in Women. New England Journal of Medicine. 2007;356(5):447-58.

10. Stafoggia M, Cesaroni G, Peters A, Andersen ZJ, Badaloni C, Beelen R, et al. Long-term exposure to ambient air pollution and incidence of cerebrovascular events: results from 11 European cohorts within the ESCAPE project. Environ Health Perspect. 2014;122(9):919-25.
11. Cesaroni G, Forastiere F, Stafoggia M, Andersen ZJ, Badaloni C, Beelen R, et al. Long term exposure to ambient air pollution and incidence of acute coronary events: prospective cohort study and meta-analysis in 11 European cohorts from the ESCAPE Project. The BMJ. 2014;348.
12. Pekkanen J, Peters A, Hoek G, Tiittanen P, Brunekreef B, de Hartog J, et al. Particulate Air Pollution and Risk of ST-Segment Depression During Repeated Submaximal Exercise Tests Among Subjects With Coronary Heart Disease: The Exposure and Risk Assessment for Fine and Ultrafine Particles in Ambient Air (ULTRA) Study. Circulation. 2002;106(8):933-8.
13. Hoffmann B, Moebus S, Kroger K, Stang A, Mohlenkamp S, Dragano N, et al. Residential exposure to urban air pollution, ankle-brachial index, and peripheral arterial disease. Epidemiology. 2009;20(2):280-8.
14. Shah ASV, Langrish JP, Nair H, McAllister DA, Hunter AL, Donaldson K, et al. Global association of air pollution and heart failure: a systematic review and meta-analysis. The Lancet. 2013;382(9897):1039-48.
15. Anderson HR, Armstrong B, Hajat S, Harrison R, Monk V, Poloniecki J, et al. Air pollution and activation of implantable cardioverter defibrillators in London. Epidemiology. 2010;21(3):405-13.
16. Raza A, Bellander T, Bero-Bedada G, Dahlquist M, Hollenberg J, Jonsson M, et al. Short-term effects of air pollution on out-of-hospital cardiac arrest in Stockholm. European heart journal. 2014;35(13):861-8.
17. Brook RD. Inhalation of Fine Particulate Air Pollution and Ozone Causes Acute Arterial Vasoconstriction in Healthy Adults. Circulation. 2002;105(13):1534-6.
18. Langrish JP, Li X, Wang S, Lee MM, Barnes GD, Miller MR, et al. Reducing personal exposure to particulate air pollution improves cardiovascular health in patients with coronary heart disease. Environ Health Perspect. 2012;120(3):367-72.
19. Adar SD, Sheppard L, Vedal S, Polak JF, Sampson PD, Diez Roux AV, et al. Fine particulate air pollution and the progression of carotid intima-medial thickness: a prospective cohort study from the multi-ethnic study of atherosclerosis and air pollution. PLoS Med. 2013;10(4):e1001430.
20. Smeeth L, Thomas SL, Hall AJ, Hubbard R, Farrington P, Vallance P. Risk of Myocardial Infarction and Stroke after Acute Infection or Vaccination. New England Journal of Medicine. 2004;351(25):2611-8.
21. Jacobs L, Emmerechts J, Mathieu C, Hoylaerts MF, Fierens F, Hoet PH, et al. Air pollution related prothrombotic changes in persons with diabetes. Environ Health Perspect. 2010;118(2):191-6.
22. Malta Air Pollution - Country Fact Sheet: European Environment Agency; 2017 [updated 15/11/2017. Available from: https://www.eea.europa.eu/themes/air/country-fact-sheets/malta.
23. WHO Air Quality Guidelines for particulate matter, ozone, nitrogen dioxide and sulfur dioxide - a global update. World Health Organization. 2005.
24. Pope CAI, Ezzati M, Dockery DW. Fine-Particulate Air Pollution and Life Expectancy in the United States. New England Journal of Medicine. 2009;360(4):376-86.
25. Clancy L, Goodman P, Sinclair H, Dockery DW. Effect of air-pollution control on death rates in Dublin, Ireland: an intervention study. The Lancet.360(9341):1210-4.
26. Landrigan PJ, Fuller R, Acosta NJR, Adeyi O, Arnold R, Basu N, et al. The Lancet Commission on pollution and health. The Lancet. 2018;391(10119):462-512.