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Exposure to air pollution and cancer risk

Zorana J. Andersen

Epidemiology at the Centre for Epidemiology and Screening, Department of Public Health, University of Copenhagen, Copenhagen, Denmark

Outdoor air pollution and particulate matter (PM) were recently classified as carcinogenic to humans by International Agency for Research on Cancer (IARC) monograph 'Air Pollution and Cancer' from 2013 (Loomis et al. 2014). Air pollution has been studied most frequently with respect to lung cancer. A number of studies, mainly from Europe and USA, over last two decades have clearly established that air pollution is a risk factor for lung cancer. Long-term exposure to PM with diameter $< 2.5 \mu\text{g}/\text{m}^3$ (PM_{2.5}) and PM with diameter $< 10 \mu\text{g}/\text{m}^3$ (PM₁₀) have been linked to increase in lung cancer morbidity (incidence) and mortality (Cui et al. 2014), though with majority of studies on lung cancer mortality. Cui et al. reported in meta-analyses from 2014 that $10 \mu\text{g}/\text{m}^3$ increase in PM_{2.5} and PM₁₀ led to 9% and 5% increase in mortality due to lung cancer, respectively (Cui et al. 2014). Similarly, long-term exposure to nitrogen oxide (NO_x) and nitrogen dioxide (NO₂) have also been linked to lung cancer. Meta-analyses by Hamra et al. showed that $10 \mu\text{g}/\text{m}^3$ increase in NO_x and NO₂ leads to 4% and 3% increase in lung cancer risk, respectively (Hamra et al. 2014). IARC concluded in the 2013 report that "there is sufficient evidence that exposure to air pollution causes lung cancer" (<https://www.iarc.fr/wp-content/uploads/2018/07/AirPollutionandCancer161.pdf>) Current research is focused on what components of PM and which air pollution sources are most relevant for lung cancer risk, and whether association with lung cancer is subtype specific.

More recently, and especially since 2013 IARC Monograph there has been an increasing interest in association between air pollution and other cancer sites than lung. Breast cancer has been of particular interest, as this is the most common cancer type in non-smoking women, with known risk factors explain only a portion of cases. A number of studies in last ten years have suggested an association between breast cancer and NO_x (Andersen et al. 2017) and possibly ultrafine particles (PM with diameter $< 0.1 \mu\text{g}/\text{m}^3$), while results on PM have been inconsistent, calling for more evidence. Recently established association between tobacco smoking in early age (active smoking between first childbirth) and breast cancer risk suggests possible relevance of similar, early exposures to air pollution for breast cancer, but so far, no studies had data on exposure to air pollution during teenage years and adolescence. Future research on air pollution and breast cancer calls for studies with long-term exposure to air pollution, dating back to early life, before woman's childbirth, and better data on breast cancer subtypes, by menopausal and estrogen and progesterone receptor status.

Associations of air pollution with brain cancer and benign brain tumor incidence and mortality have been examined in several studies (Andersen et al. 2018), though all with conflicting results. Although suggestive evidence of an association has been provided by current literature, small number of cases for this rare disease and poor statistical power to detect association between air pollution and brain tumor, call for more research on this area. Other cancer types studied with respect to air pollution include bladder, kidney, liver, stomach, colorectal, and cervical cancer.

European Study of Cohorts for Air Pollution Effects (ESCAPE, <http://www.escapeproject.eu/>) project utilized data on over 300,000 people from 17 European cohorts, to examine associations between long-term exposure to PM_{2.5}, PM₁₀, NO₂, and NO_x and a number of cancer sites, including: lung cancer (Raaschou-Nielsen et al. 2013), breast cancer (Andersen et al. 2017), brain tumor

(Andersen et al. 2018), cancer of gastric and upper aerodigestive tract (Nagel et al. 2018), kidney parenchyma cancer (Raaschou-Nielsen et al. 2017), bladder cancer (Pedersen et al. 2018), and liver cancer (Pedersen et al. 2017). Some of the major findings from ESCAPE project include association of PM_{2.5} with lung cancer, NO_x with breast cancer, and PM_{2.5} with gastric cancer. Project also provided suggestive evidence (positive but statistically non-significant associations) of an association between PM_{2.5} and kidney, liver, and brain cancers, and no association of air pollution with bladder cancer, benign brain tumor, or upper aerodigestive tract cancers.

Another recent large study based on the US Cancer Prevention Study II (CPS-II) studied association between long-term exposure to air pollution and all non-lung cancer deaths among 632,048 subjects. Turner et al. found association of PM_{2.5} with kidney and bladder cancer, NO₂ with colorectal cancer, and strong positive but statistically non-significant association of PM_{2.5} with cervical cancer (Turner et al. 2017). This presentation will provide the overview over the epidemiologic evidence regarding the association between air pollution measures and cancer risk in adult populations, including lung cancer, breast cancer, brain tumor, kidney cancer, bladder cancer, liver cancer, gastric cancer, cervical cancer, and colorectal cancer.

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Updates on cardiovascular effects of air pollution

Francesco Forastiere

King's College, London, UK and CNR-Ibim, Palermo, Italy

The recent statement of the European respiratory Society (ERS) and the American Thoracic Society (ATS) (1) recognizes the cardiovascular system as the first target organ of air pollution, in particular of particulate matter (PM_{2.5}). The aim of this short review is to provide updates on recent advances of the scientific knowledge regarding the effects of air pollution on the cardiovascular system. A comprehensive assessment of the issue has been recently prepared by the Journal of the American College of Cardiologists (2).

Several cardiovascular clinical outcomes related to air pollution should be considered including coronary and cerebrovascular events, heart failure, atrial fibrillation, hypertension, venous thromboembolism, and cardiovascular mortality. Increases in the frequency of coronary (myocardial infarction and unstable angina) and cerebrovascular (stroke) events have been observed in several time-series (or case-crossover) studies on short-term effects but the effects of long-term exposure have been less studied. The ESCAPE study provided some evidence that long-term exposure to PM_{2.5} and PM₁₀ are related to an increase in myocardial infarction and stroke. More recently, a cohort in the Netherlands (3) provided compelling evidence that exposure to ultrafine particles (defined as particles less than or equal to 0.1 μm in diameter), rather than larger particles, are related to cardiovascular health. Long-term UFP exposure was associated with an increased risk for all incident cardiovascular diseases (HR=1.18 per 10,000 particles/cm³; 95% confidence interval (CI): 1.03, 1.34], myocardial infarction (MI) (HR=1.34; 95% CI: 1.00, 1.79), and heart failure (HR=1.76; 95% CI: 1.17, 2.66). HRs for UFP and cerebrovascular events were positive, but with large confidence intervals. Indications of an effect of particles on incidence of heart failure comes from a recent Canadian study (4). Incidence of major CVD events were evaluated in a population-based cohort study in Toronto including more than a million individuals. Each interquartile-range increase in UFP exposure was associated with increased incidence of heart failure (HR = 1.03, 95% CI: 1.02, 1.05) and acute myocardial infarction (HR = 1.05, 95% CI: 1.02, 1.07). Adjustment for fine particles and nitrogen dioxide did not materially change these estimated associations. Finally, long-term exposures of PM_{2.5} on air pollution-related incident atrial fibrillation (AF) in general population have not yet been investigated well. A large cohort study conducted in Korea indicated that long-term exposure of PM_{2.5} is associated with the increased incidence of new-onset AF. The effects were larger in obese male subjects > 60-year old and individuals who have a history of hypertension or previous myocardial infarction (5).

Some longitudinal studies have provided strong evidence of the PM_{2.5} effects on atherosclerosis. The Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air), for example, is a prospective longitudinal study of relationships between air pollution and cardiovascular health that combines fine-scale air pollution exposure models with a wide range of outcomes (6). MESA measured coronary artery calcium (CAC) and carotid artery wall thickness (Intima-Media Thickness or IMT) to determine the extent and rate of development of atherosclerosis. For each additional 5 μg PM_{2.5}/m³, CAC progression was accelerated by 4.1 units/yr [95% confidence interval: 1.4, 6.8] and for each 40 ppb NO_x, CAC progression was accelerated by 4.8 units/yr [CI: 0.9, 8.7]. Therefore, fine particulate matter is associated with progression in coronary artery calcification, consistent with acceleration of atherosclerosis.

In summary, new evidence has been accumulating on the long-term effects of particles on the cardiovascular system and a recent investigation, using data from cohort studies on air pollution, clearly indicate that the burden of mortality due to PM_{2.5} worldwide may have been underestimated (7).

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Updates on the respiratory effects of air pollution

Sergio Harari

*Division of Pulmonary Disease and Reference centre for pulmonary rare diseases
Ospedale San Giuseppe Milan, Italy*

Exposure to air pollutants is associated with chronic obstructive pulmonary disease (COPD), acute respiratory infections, lung cancer and respiratory allergies. The evaluation of the effects of exposure to air pollution in children has documented a deleterious effect on lung function, respiratory tract infections and asthma episodes. A close relationship exists between indoor air pollution, particularly that due to cigarette smoke and the risk of developing a wide array of respiratory diseases.

Idiopathic pulmonary fibrosis (IPF) is a chronic and progressive fibrotic lung disease with a severe prognosis and a median survival of 3–5 years from diagnosis.

Although the mechanisms that cause the development of IPF are still under debate, there is evidence that both genetic and environmental factors, such as cigarette smoking, occupational exposure to metal and wood dusts and exposure to viruses, such as Epstein–Barr virus, may play a role.

Lombardy is characterised by high air pollution levels, heterogeneous among subregional areas. The stagnation of air pollutants over its lowland areas is facilitated by weather, climate and orographic characteristics which cause frequent thermal inversion. In a prior study, among the Minion Pro ~10 million inhabitants of the region, we identified >2000 IPF incident cases from 2005 to 2010. The number of IPF cases, together with the variability of environmental exposures makes Lombardy an interesting context for this analysis. The aim of this study was to investigate the long-term relationship between exposure to three criteria pollutants, namely particulate matter with an aerodynamic diameter <10 μm (PM₁₀), NO₂ and O₃, and the incidence of IPF in Lombardy, Northern Italy, from 2005 to 2010.

Acute exacerbations and worsening of idiopathic pulmonary fibrosis (IPF) have been associated with exposure to ozone (O₃), nitrogen dioxide (NO₂) and particulate matter, but chronic exposure to air pollution might also affect the incidence of IPF. We investigated the association between chronic exposure to NO₂, O₃ and particulate matter with an aerodynamic diameter <10 μm (PM₁₀) and IPF incidence in Northern Italy between 2005 and 2010.

Daily predictions of PM₁₀ concentrations were obtained from spatiotemporal models, and NO₂ and O₃ hourly concentrations from fixed monitoring stations. We identified areas with homogeneous exposure to each pollutant. We built negative binomial models to assess the association between area-specific IPF incidence rate, estimated through administrative databases, and average overall and seasonal PM₁₀, NO₂, and 8-hour maximum O₃ concentrations.

Using unadjusted models, an increment of 10 $\mu\text{g}\cdot\text{m}^{-3}$ in NO₂ concentration was associated with an increase between 7.93% (95% CI 0.36–16.08%) and 8.41% (95% CI –0.23–17.80%) in IPF incidence rate, depending on the season. After adjustment for potential confounders, estimated effects were similar in magnitude, but with larger confidence intervals.

Although confirmatory studies are needed, our results trace a potential association between exposure to traffic pollution and the development of IPF.

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The World Health Organization (WHO) global estimates of the impact of air pollution

Monica Guxens

IS Global Barcelona Institute for Global Health

Campus MAR, Barcelona Biomedical Research Park (PRBB)

Air pollution is the biggest environmental health crises we face, being the main environmental contributor to the global burden of disease and one of the top preventable causes of disease over time. Respiratory and cardiovascular morbidity and mortality related to exposure to air pollution has been extensively investigated. Conversely, evidence indicating that air pollution has a deleterious impact on the central nervous system through chronic neuroinflammation, oxidative stress, microglia activation, and alterations in myelin sheaths that can lead to neuronal damage and myelin abnormalities is accumulating. The human brain starts forming very early in fetal life, just three weeks after conception, and continues to mature well across the entire childhood and adolescence. Therefore, exposure to air pollution during this period might be determinant for brain development.

In the last decade, evidence from epidemiological studies demonstrating a negative impact of fetal and childhood air pollution exposure on child's brain development is growing. Most compelling evidence suggests that air pollution exposure during pregnancy and childhood affects executive functions including attentional function, working memory, and inhibitory control, and increases the risk of autism spectrum disorders. These studies used neuropsychological or clinical instruments to assess brain development and failed in understanding which brain structural and functional alterations underlie these associations. Just few studies have started using magnetic resonance imaging (MRI), a non-invasive technique that provides detailed information about brain structure and function and less biased results, finding promising results. Air pollution exposure during fetal life and childhood has been associated with alterations of the grey matter structure and of the myelination, and with a lower functional integration and segregation in key brain networks in children.

Moreover, although human brain development is a continuous phenomenon, brain structures and functions are being formed at different developmental periods. Hence, air pollution might affect different processes of the brain development at specific periods. Although very few studies have been performed, air pollution exposure at specific weeks during fetal life and childhood was associated to impaired attentional function, alterations of the myelination, and increased risk of autism spectrum disorders in children. However, there is still limited evidence on which are the critical developmental periods in relation to air pollution exposure to draw solid conclusions.

In conclusion, air pollution exposure during early life has been related to an impaired brain development. However, there is still a need for understanding whether this impairment is permanent until adolescence and adulthood, which are the long-term clinical implications of the observed alterations, and which are the most susceptible time-windows of exposure. ted indicators for monitoring progress against the Sustainable

Mechanisms of particulate matter (PM) toxicity

Frank J. Kelly; Julia Fussell

*MRC-PHE Centre for Environment and Health, Franklin-Wilkin Building,
King's College London, UK*

The WHO is of the opinion that the air we breathe is dangerously polluted, with nine out of ten people now breathing polluted air, leading to 7 million premature deaths every year. The health effects of air pollution are serious with one third of deaths from stroke, lung cancer and heart disease are due to air pollution (1). Of the major air pollutants particulate matter (PM) is thought to be the most dangerous. PM is a complex, heterogeneous mixture that changes in time and space. It encompasses many different chemical components and physical characteristics, many of which have been cited as potential contributors to toxicity. Each component has multiple sources, and each source generates multiple components. Identifying and quantifying the influences of specific components or source-related mixtures on measures of health-related impacts, especially when particles interact with other co-pollutants, therefore represents one of the most challenging areas of environmental health research (2).

Current knowledge does not allow precise quantification or definitive ranking of the health effects of PM emissions from different sources or of individual PM components and indeed, associations may be the result of multiple components acting on different physiological mechanisms. Some results do suggest a degree of differential toxicity, namely more consistent associations with traffic-related PM emissions, fine and ultrafine particles, specific metals and elemental carbon and a range of serious health effects, including increased morbidity and mortality from cardiovascular and respiratory conditions. Exposure to combustion-related PM, at concentrations experienced by populations throughout the world, contributes to pulmonary and cardiac disease through multiple mechanistic pathways that are complex and interdependent (3). Current evidence supports an interactive chain of events linking PM-induced pulmonary and systemic oxidative stress, inflammatory events, and translocation of particle constituents with an associated risk of vascular dysfunction, atherosclerosis, altered cardiac autonomic function, and ischemic cardiovascular and obstructive pulmonary diseases. Because oxidative stress is believed to play such an instrumental role in these pathways, the capacity of particulate pollution to cause damaging oxidative reactions (the oxidative potential) has been used as an effective exposure metric, identifying toxic components and sources within diverse ambient PM mixes that vast populations are subjected to from traffic emissions on busy roads in urban areas to biomass smoke that fills homes in rural areas of the developing world (4).

The ambitious 10 year US NPACT initiative has made a valuable contribution to the policy arena by demonstrating that no particle components can as yet be conclusively ruled out as not having an effect on public health. Upon focusing on studies conducted in different regions of world, within air sheds that vary with respect to a PM composition, size and source the very complex issue of differential toxicity is reaffirmed. Not only are individual PM characteristics and sources associated with certain effects in some locations and not in others but also, strengths of associations between effects and individual chemical components of the ambient mix vary from one effect to another. To further our understanding so that we can definitively conclude, or otherwise, that additional indicators have a role in protecting public health more effectively than the targeting total PM mass, comparison and synthesis of existing data through systematic reviews and quantitative meta-analysis must continue.

To further understanding of this complex area a carefully targeted programme of contemporary toxicological and epidemiological research, incorporating more refined approaches (e.g. greater speciation data, more refined modelling techniques, accurate exposure assessment and better definition of individual susceptibility) and optimal collaboration amongst multidisciplinary teams, is needed to advance our understanding of the relative toxicity of particles from various sources, especially the components and reactions products of traffic. This will facilitate targeted abatement policies, more effective pollution control measures and ultimately, a reduction in the burden of disease attributable to ambient PM pollution.

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Combining evidence from studies on the effects of air pollution at low level

Gerard Hoek

Institute for Risk Assessment sciences, Utrecht University, The Netherlands

In Europe and North-America concentrations of most major air pollutants have decreased in the past decades due to environmental policies. In large areas air quality is in compliance with current air quality limit values. Intervention studies have documented significant public health benefits related to improved air quality. Health effects may however still occur at current day relatively low air pollution concentrations. In this presentation we will examine the evidence for health effects at low air pollution levels.

We will interpret low level air pollution as pollution concentrations below the current air quality limit values of the EU and US-EPA. We will also assess evidence for health effects below the guideline values of the World Health Organization (WHO), particularly the guideline value for annual average PM_{2.5} concentrations of 10 µg/m³. The focus will be on long-term exposure to regulated air pollutants, particularly fine particulate matter (PM_{2.5} and PM₁₀), nitrogen dioxide (NO₂) and ozone (O₃). We will include studies with the full concentration distribution below current limit values and studies that have assessed the shape of the concentration response function typically using non-parametric smoothing methods. We will build on recent systematic reviews of WHO and other organizations.

A recent large multi-center study in Europe (ESCAPE), reported clear associations between PM_{2.5} and NO₂ and mortality, lung cancer and circulatory disease incidence, lung function and birth outcomes below current limit values. Recently results of large administrative cohort studies in Europe and North-America have been published. In these studies, several million subjects are followed over time, providing adequate power to assess health effects at low pollution levels. Cause-specific mortality was associated with PM_{2.5} also below the EU, US-EPA and even the WHO guideline value of 10 µg/m³ in Canadian and US studies. With funding of the US-based Health Effects Institute, further analyses are ongoing in large cohorts in Europe, Canada and the USA to evaluate mortality and morbidity effects at low air pollution levels. Preliminary results of the European cohorts will be presented. Other studies in especially Europe and North-America have documented that especially PM_{2.5} and NO₂ are associated with a range of morbidity endpoints at low pollution levels.

In conclusion, there is clear evidence that below current limit values air pollution is related to a significant morbidity and mortality burden. Several studies have also documented mortality associations below the WHO guideline value for annual average PM_{2.5}. Further reductions in outdoor air pollution will likely result in substantial health benefits at current day low air pollution levels.

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Evidence on the health risks from highly polluted regions

Haidong Kan

School of Public Health, Fudan University, Shanghai, China

Most of the air pollution-related deaths occur in low and middle-income highly polluted regions such as China and India. The economic expansion in these regions is largely driven by the use of fossil fuels, which leads to a dramatic increase in emissions of air pollutants. Compared to relatively complete air monitoring data, data on the association between air pollution and human health are limited in these regions. So far, a number of epidemiological studies on air pollution and population health have been conducted in highly polluted regions, using time-series, case-crossover, panel, cross-sectional, cohort, or intervention designs. The health outcomes usually include changes in mortality of all causes and of cardiopulmonary disease, and morbidity, as well as number of out-patients and emergency-room visits. The relationships between air pollution and respiratory and other clinical symptoms, lung functions and immune functions have also been assessed. Generally, time-series or case cross-over studies captured the acute effects of air pollution by examining the association between daily mortality (or morbidity) and daily or multi-day changes in air pollution, while the cohort and cross-sectional studies revealed that long-term exposure to air pollution might lead to an increased risk of health hazards in the population. Recently, a number of panel studies in China and India examine the short-term association between air pollution and sub-clinical parameters. Compared with association studies of short-term effect, there are even fewer studies in highly polluted regions examining the association between long-term exposure to air pollution and human health. So far, there have been several published air pollution cohort studies in these regions. Air pollution intervention study provides evidence regarding the potential health benefits from specific intervention-induced reduction in air pollution. For example, a unique opportunity emerged during the 2008 Beijing Olympic Games when the air quality in Beijing was significantly improved due to unprecedented efforts taken at that time in Beijing and surrounding regions. Health benefits gained from the improvement of air quality were observed not only in high-risk vulnerable groups but also in young, healthy adults. Generally, the observed health risks in highly polluted regions are somewhat lower in magnitude, per amount of pollution, than the risks found in relatively clean areas. However, the importance of these increased health risks is greater than that in clean areas, because the levels of air pollution in these regions are very high in general and huge population live in these regions. Finally, pollution needs to be substantially reduced and air quality and health indicators need to be monitored in these regions; this will enable the people and relevant authorities to be aware of the trends and consequences of air pollution, so they can determine how to ameliorate the situation.

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Casual approaches to study the effects of air pollution

Michela Baccini, Laura Forastiere, Michele Carugno

*Department of Statistics, Computer Science, Applications “G. Parenti” (DiSIA),
Florence, Italy*

The opportunity to assess the short term impact of air pollution relies on the causal interpretation of the exposure-outcome association. Up to now, this causal interpretation has been mainly supported by the fact that studies carried out in different countries and contexts provided consistent findings, as well as by evidences substantiating the possible existence of biological mechanisms tying exposure and health damage.

The potential outcome approach to causal inference, commonly referred to as the Rubin’s Causal Model, encourages thinking in terms of causes and action’s consequences, within a formal mathematical framework (Holland 1986, Imbens and Rubin 2015). Despite its increasing popularity in many fields, including epidemiology and medical sciences, only recently it was adopted in the analysis of short-term and long-term effects of air pollution on population health (e.g. Zigler et al. 2016, Schwartz et al. 2015, Baccini et al. 2017).

In a previous work (Baccini et al. 2017), we reformulated the problem of assessing the short term impact of air pollution on health within the potential outcome approach to causal inference. Relying on the fact that the number of attributable deaths (AD) can be expressed as a difference between potential outcomes under different exposure levels, we estimated the impact of high daily levels of particulate matter $\leq 10 \mu\text{m}$ in diameter (PM₁₀) on mortality in the metropolitan area of Milan (Italy), during the period 2003–2006, according to a procedure based on propensity score matching. After having defined a binary version of the exposure (“exposed” day: PM₁₀ > 40 $\mu\text{g}/\text{m}^3$; control day: PM₁₀ < 40 $\mu\text{g}/\text{m}^3$), we reconstructed a pseudo-randomized experiment by selecting for each “exposed” day a matched control, i.e. a day with similar covariate distribution (as summarized by the propensity score), but PM₁₀ level lower than 40 $\mu\text{g}/\text{m}^3$. Then, we estimated AD by comparing the mortality observed in the “exposed” days with the mortality occurring in the matched controls.

The main drawback of this procedure is that a binary version of the exposure is used. Moreover, it does not allow to investigate the shape of the exposure-response curve, which, as it is known, has important regulatory implications, being related to the existence of a safe threshold for the air pollution concentration. With the present study, we thus explored the possibility to estimate AD on the basis of the exposure-response function, treating the airborne particles level as a continuous exposure. At this purpose, we developed a method based on the generalized propensity score (GPS). The GPS extends the propensity score to the case of discrete treatments, continuous treatments and arbitrary treatment regimens, and, like propensity score, can be used for covariate adjustment (Hirano and Imbens 2004, Imai and Van Dyk 2004).

We employed it to estimate the average exposure-response function that described the relationship between PM₁₀ and mortality. In particular, we adapted the semiparametric approach proposed by Bia (2014), which assumes a Normal distribution on the outcome variable, to the case of counts having a quasi-Poisson distribution. Moreover, we proposed and implemented a novel procedure for the estimation of the attributable number of events according to the estimated exposure-response curve, through comparison of the number of deaths in days having level of air pollutant concen-

tration larger than a counterfactual threshold with the expected level of mortality at the threshold itself.

According to this procedure, we estimated that during the study period, daily exposures exceeding $20 \mu\text{g}/\text{m}^3$ were responsible of 657 deaths per year (95% Confidence Interval: 334,1006). This result confirmed the existence, already highlighted by previous studies based on “standard” regression approaches, of a not negligible impact of PM₁₀ exposure on mortality in the city of Milan.

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Particulate Matter Integrated Science Assessment (External Review Draft): Evaluation of Health Effects Attributed to Exposures to PM Components and Sources

Jason D. Sacks

Office of Research and Development, U.S. Environmental Protection Agency, RTP NC, USA

Disclaimer: This abstract is based on information provided in the external review draft of the Integrated Science Assessment for Particulate Matter. This information is distributed solely for the purpose of pre-dissemination peer review under applicable information quality guidelines.

The Clean Air Act requires the U.S. Environmental Protection Agency (U.S. EPA) to periodically review the National Ambient Air Quality Standards (NAAQS) for the six criteria pollutants, of which particulate matter (PM) is one, to determine the adequacy of current standards to protect public health and welfare. As part of this process, the U.S. EPA evaluates the current state of the science for each individual criteria pollutant in an Integrated Science Assessment (ISA). The ISAs represent rigorous evaluations of the scientific evidence spanning scientific disciplines, including atmospheric chemistry, exposure science, and health sciences (i.e., epidemiology, animal toxicology, and controlled human exposures) using a structured and transparent framework, which is described in the Preamble to the ISAs (U.S. EPA, 2015). The Preamble in combination with the Integrated Review Plan for the PM NAAQS review (U.S. EPA, 2016) forms the basis of the approach used to evaluate the current PM literature in the ongoing PM NAAQS review, including the evaluation of the health effects of PM components and sources. The evaluation of the health effects of PM components and sources in the 2018 PM ISA External Review Draft (PM ISA ERD) (U.S. EPA, 2018) is intended to support decisions as to whether the current mass-based indicators of the PM NAAQS (i.e., PM_{2.5} and PM₁₀) should be retained or revised.

Based on the systematic evaluation of the sources and components literature in the 2009 PM ISA, the U.S. EPA concluded “the results [of studies] indicate[s] that many [components] of PM can be linked with differing health effects and the evidence is not yet sufficient to allow differentiation of those [components] or sources that are more closely related to specific health outcomes.” To further facilitate an evaluation of the PM components and sources evidence in the 2018 PM ISA ERD, a defined scope was outlined to aid in addressing whether specific PM components or sources are more strongly associated with health effects than PM mass. To inform this evaluation, the 2018 PM ISA ERD focuses on studies that: (1) include a composite measure of PM (e.g., mass of PM_{2.5}); (2) applied some approach to assess the particle effect (e.g., particle trap) of a mixture; or (3) conducted formal statistical analyses using source-based exposures that were not defined a priori.

Since the completion of the 2009 PM ISA, a large body of literature has been published examining the health effects of specific PM components and sources. This includes single and multi-city epidemiologic studies, a limited number of experimental studies, and the largest coordinated research effort spanning multiple scientific disciplines of PM sources and components in the Health Effects Institute funded National Particle Component Toxicity (NPACT) Initiative (Lippman et al. 2013; Vedal et al. 2013). In the evaluation of the sources and components evidence, the 2018 PM ISA ERD focuses on those health effects categories where there is the greatest confidence in the relationship between PM_{2.5} exposure and health effects (i.e., a causal or likely to be causal relationship). Specifically, when evaluating PM_{2.5} sources and components, the 2018 PM ISA ERD focuses on studies

of short- and long-term exposure and cardiovascular or respiratory effects, or mortality.

Among epidemiologic studies of cardiovascular and respiratory effects, elemental carbon (EC) and organic carbon (OC) are the most commonly examined components and the pattern of positive associations reported are generally the same as those observed for PM_{2.5}. Studies of short- and long-term exposures and mortality did not focus more prominently on any one component and reported evidence of some positive associations for each of the components evaluated, though the pattern of associations was less consistent than reported for PM_{2.5}. Compared to the 2009 PM ISA, fewer studies, both epidemiologic and experimental, examined health effects attributed to PM_{2.5} sources. When evaluating studies that examined associations between short- and long-term exposures to PM_{2.5} sources and respiratory or cardiovascular effects, or mortality, positive associations were more often observed for sources representative of combustion-related activities.

The concentration and composition of PM_{2.5} within the U.S. has changed over time. Even with this change, the assessment of the collective body of evidence as detailed in the 2018 PM ISA ERD is consistent with the 2009 PM assessment that many PM_{2.5} components and sources are associated with many health effects and the evidence does not indicate that any one source or component is consistently more strongly related with health effects than PM_{2.5} mass.

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Ultrafine particles and health effects

Barbara Hoffmann

Institute for Occupational, Social and Environmental Medicine, Centre for Health and Society, Medical Faculty, University of Düsseldorf, Germany

Background/Aim: Due to their small size, ultrafine particles (UFP) with an aerodynamic diameter of <100 nm are believed to exert higher toxicity than larger particles. This higher toxicity is related to their large mass-specific surface area, their capacity to escape alveolar defense mechanisms, and their capacity to penetrate through biologic membranes, gaining access to the systemic circulation and thereby reaching all organs including the nervous system. The last systematic review conducted by the Health Effects Institute, Boston, USA, in 2013 came to the conclusion that scientific evidence pointed towards adverse short-term health effects of UFPs in human populations, but current evidence from toxicological, experimental and epidemiological studies, when considered together, was not sufficiently strong to conclude that short-term exposures to UFPs have effects that are dramatically different from those of larger particles. Moreover, evidence did not allow differentiating the effect of UFPs from other pollutants to assess the independent effect of UFPs. Finally, no studies on long-term UFP exposure had been conducted (HEI 2013).

Since then, numerous epidemiological studies have been published. Therefore, the aims of this study were to review the epidemiological literature on the health effects of UFPs, to evaluate the independence of effects of UFPs and to identify future areas of research in this field.

Methods: We systematically searched MEDLINE (Medical Literature Analysis and Retrieval System Online) for eligible studies published between 01.01.2011 until 11.5.2017 investigating health effects of ambient air pollution related UFPs. In addition, we searched the LUDOK-database, a specialized literature search, database and retrieval system, provided by the Swiss Tropical and Public Health Institute (Zitat). We included epidemiologic studies with either measured or modeled air pollution exposure, containing at least one UFP measure, quantifiable measures of associations and at least one health outcome, and extracted and evaluated the relevant data on the basis of previously defined criteria.

Results: We identified 85 original studies, with most studies being conducted in North America (n=37) or Western Europe (n=27). The vast majority of studies investigated short-term associations (n=75) with a panel study design (n=32), scripted exposure design with predefined exposure situations (n=16), or time-series studies (n=11). We identified 10 studies investigating long-term effects using exposure estimates averaged over a period of months to years. Long-term studies most frequently applied cohort (n=4) and cross-sectional (n=4) study designs. Thirtyfour studies adjusted for at least one other pollutant. Most consistent associations were identified for short-term effects on pulmonary/systemic inflammation, heart rate variability and blood pressure.

Conclusion: The evidence suggests adverse associations of short-term UFP exposure with pulmonary and systemic inflammation, autonomic tone and blood pressure, which may be at least partly independent of other pollutants. For the other studied health outcomes the evidence on independent health effects of UFP remains inconclusive or insufficient. Specifically, while a number of stu-

dies have investigated mortality and emergency department/hospital admission outcomes, the relatively few studies with co-pollutant adjustment reveal mixed and, up to now, inconclusive evidence. A future challenge is the development of enhanced spatiotemporal models which can contribute to a more precise exposure assessment across larger areas as well as incorporating multi-pollutant models to elucidate the independence of effects.

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AIRUSE-LIFE PM_x source apportionment and measures to abate urban air pollution in Southern Europe

Xavier Querol

Institute of Environmental Assessment & Water Research, IDAEA-CSIC, Barcelona, Spain

AIRUSE LIFE+ was active in 2013-2017 (<http://airuse.eu/project/>). We focused on assessing causes of urban air pollution (with a major focus on particulate matter, PM₁₀ and PM_{2.5}) in Southern Europe, but with special focus on Athens, Barcelona, Florence, Milan and Porto.

The focus on Southern Europe was due to various factors that favor high concentrations of atmospheric pollutants, such as an elevated level of emissions; the high density architecture of many cities, which impedes the dispersion of locally emitted pollutants; low rainfall, weak winds and high solar radiation, which all favor the formation and accumulation of pollutants; and the proximity to the deserts of North Africa. These peculiar features might require specific air quality measures.

Atmospheric PM is complex and comes from many different sources, deriving from both human activities (anthropogenic sources) and natural processes. According to EEA (2018) around 80% of the urban population in EU breathes air that exceeds the WHO AQ guidelines in PM_{2.5}, causing around 390,000 premature deaths in 2015. Typical anthropogenic PM contributions in Southern Europe are in most cases dominated by vehicle exhaust, domestic and industrial emissions. Additionally, there is an important contribution of urban dust (from deposited dust arising from brake, tyre and road abrasion, construction/demolition, and to a minor extent from regional dust emissions due to the wind). In addition to road traffic, important sources are biomass burning from residential heating (notably wood-burning stoves); forest fires and the burning of agricultural wastes; and harbor and shipping emissions. Industrial PM emissions arise from both channeled and fugitive sources; the latter can be of great relevance, especially in dry areas. Finally, the African dust contribution may increase the PM load either directly or indirectly, in the latter case by deposition on the ground and subsequent resuspension by vehicles or wind.

The current policy efforts at different levels have not fully delivered the expected results, especially regarding attainment of WHO (guidelines). In spite of the numerous efforts and significant improvements, serious air pollution impacts still persist in specific areas. Several urban and industrial areas in Europe are not capable of meeting the current EU standards for PM.

Most of the cost effective strategies and measures devised and implemented in the central regions are directly applicable to the southern ones; however, taking into account the above peculiarities, specific measures should also be implemented in action plans to abate ambient air concentrations of PM in Southern European regions. The first goal of the AIRUSE-LIFE+ project is to harmonize source apportionment methods and to prioritize the sources for evolving cost-effective air pollution mitigation strategies. The second goal is to assess the impact of sources on ambient air quality for different mitigation measures, mostly for PM and NO₂. The overall objective is to develop, demonstrate and adapt measures that considered appropriate and cost effective to ensure better air quality in urban areas.

We will present a summary of the following results:

1. The quantifications the source contributions to ambient PM levels and identifying those that are responsible for the PM pollution episodes and increased annual averages.
2. Proposing and quantitatively evaluating the effect of air quality mitigation measures for road dusts and fugitive industrial dust.
3. Developing and propose effective air mitigation measures to abate emissions from biomass burning domestic emissions with bi-fuels and stoves from Southern Europe.
4. Scientific evaluating the effect of measures implemented in Northern and Central Europe to Southern Europe (congestion taxes, low emission zones, shipping policy, domestic heating, eco-labeling of vehicles, climate/air quality measures, among others) and proposing pathways to, directly or after modifications, adapt them to Southern Europe.
5. Critical review of best available techniques used by industrial processes in and around the 5 cities and measures to abate pollution.

Results allowed us to propose an air quality strategy based on 7 major pillars that we will describe during RESPIRAMI, these are:

1. Developing air quality plans at metropolitan scale instead of municipal scale.
2. Improving metropolitan public transport as far as pricing, comfortability, speed and eco-efficiency.
3. Reducing number of circulating private cars by applying congestion charges (first) and restricting parking areas to residents.
4. Converting the reduced fleet of private and public vehicles to more eco-efficient one. Specially, by i) implementing German-style Low Emission Zones (applying to all vehicles, including passenger cars and with a strict enforcement) modified to include motor cycles, and ii) progressive hybridization and electrification of the fleets.
5. Applying measure to the urban freight distribution (UFD) and taxis, with measures to accelerate the e-mobility for these vehicles, ban UFD during traffic rush hours, intelligent logistic platforms to supply goods to markets, supermarkets, restaurants,....., and promoting nocturnal and unattended e-UFD.
6. Urban re-design: bikes, green areas, superblocks, schools, pedestrian streets.
7. Complementary measures, street washing, speed reductions, among others

We support the selection of these major fields of the strategy by systematic reviews of scientific papers on the topics or by evaluating effect of specific measures on air quality or reduction of circulating vehicles in specific cities.

We elaborated a 179 pp Guidebook on Measures to Improve Urban Air Quality that describe the above measures and support their selection, and that can be free downloaded from <http://www.cleanaircities.net/>, in English, Greek, Italian, Portuguese, or Spanish. The AIRUSE strategy is also described in a free downloadable book on air quality measures from <http://www.fundacionnaturgy.org/publicacion/libro-la-calidad-del-aire-las-ciudades-reto-mundial/>. And finally detailed reports on the specific measures and efficiency tests are available from: <http://airuse.eu/outcomes/reports/>.

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Non-exhaust emissions: sources and health effects

Fulvio Amato

Institute of Environmental Assessment and Water Research (IDÆA)

Spanish National Research Council (CSIC), Barcelona, Spain

Abstract

Air pollution, especially from particulate matter (PM), is widely recognized as one of the main risk factors for premature deaths and disability-adjusted life-years (DALYs) [1–3]. PM is a heterogeneous mix of chemical elements and origins, with road traffic being the major source of PM and related toxicity in cities. The increasing urbanization in developing countries and aging of population in developed countries enhance considerably the risk for the future. Over the last two decades most of the attention regarding this risk has been focused on vehicle exhaust emissions and their successful remediation and regulation. Consequently, nowadays about half of traffic emissions derive from non-exhaust processes such as direct emissions from the wear of brakes, tires, and road surfaces, and the suspension of particles previously deposited on road surfaces (road dust suspension) due to vehicle-induced turbulence and wind. Non-exhaust emissions are projected to dominate traffic emissions within a few years. As the relative contribution from non-exhaust emissions to total urban PM increases, so should our understanding of their health impact and abatement. Nevertheless, the current knowledge on this topic is quite limited, mostly concerning effective mitigation.

The first part of the talk will describe the main physico-chemical features of the non-exhaust sources and the processes involved in the generation of emissions. The talk will then review the state-of-the-art of current knowledge on the following points: Impact on air quality, Impact on health, Current regulations, Emission inventorying, and Mitigation measures.

Impact on air quality

A recent literature review[4] on the impact of non-exhaust emissions on air quality resulted in 256 source contribution estimates worldwide. Most of the studies were carried out by means of receptor models and performed in the last 15 years, with a significant increasing trend.

Among non-exhaust sources, the road dust category was the most commonly identified source with slightly higher contributions range (22% as mean) than vehicle exhaust (21%) in PM₁₀, and sensibly higher than brake wear (7%) and tire wear (4%). In PM_{2.5} the road dust contribution is still the highest (mean of 11% of PM_{2.5}) among non-exhaust ones (9% from brake wear and 2% from tire wear), but sensibly lower than vehicle exhaust (24%). This comparison allows concluding that globally, regardless of the environment studied, non-exhaust emissions are already at least as important as exhaust ones for PM₁₀. For PM_{2.5} they represent at least a third of total traffic contribution while they dominate the PM coarse (>1.5 mm) mode (>80%).

However, there is still limited information on brake (17 estimates) and tire wear (15 estimates) contributions. Based on these few studies, there is evidence that brake wear particles include an important portion (about half of the mass) of disc wear. Backward trend analysis of source contributions and PM concentrations indicate a relative increment of the share of non-exhaust particles versus the exhaust ones.

Impact on health

The preliminary results of the “WHO systematic review of health effects from non-exhaust sources and metals”[5] will be presented. Seventy-two epidemiological studies were found investigating the health effects of one (or more) indicator of road traffic non-exhaust emissions (brake wear, tire wear, road wear and road dust resuspension). Most of the studies were based on elemental characterization rather than on source contributions. In spite of the typically coarse size distribution of non-exhaust particles, PM_{2.5} was studied more often (49 studies) than PM₁₀ (35 studies), due to the fact that non-exhaust emissions were not the primary target source of the studies.

European Emission Inventories and Projections

Stringent EU policies succeed in reducing the road transport exhaust PM emissions, but do not address “non-exhaust” emissions from brake wear, tire wear, road abrasion, and road dust suspension. The engine exhaust emissions dominated the road transport emissions pre-2000, but since about 2012, wear emissions contribute more to road transport PM₁₀ emissions than exhaust emissions in the EU15, Norway, and Switzerland[6].

Comparing the official EU reported emissions, a substantial number of countries still report incomplete, despite the improvements over the years. Some countries do not report any wear emissions, or do not separate between exhaust and wear emissions. Moreover, the quality of reported wear emissions data seems questionable since the observed ranges of implied emission factors are much larger than can be understood due to different climatic conditions or vehicle fleets. An important conclusion is that resuspension of road dust may well be the dominant source of road transport PM₁₀ in many cities but is currently excluded from official emission reporting. It would be highly recommendable to include road resuspension as a separate category. Finally, the overall conclusion is that in the European urban environment, where most Europeans live and spend their time, the contribution of wear emissions to urban road transport PM₁₀ emissions already reaches more than 50% in many countries and is predicted to grow to about 80%-90% after 2020, even when resuspension is not or only incompletely taken into account.

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The BEEP project

G. Viegi^{1,2}, S. Fasola¹, S. Maio², M. Stafoggia³, P. Michelozzi³, F. Forastiere¹, C. Silibello⁴, C. Gariazzo⁵, on behalf of the BEEP group.

¹ *Institute of Biomedicine and Molecular Immunology (CNR-IBIM), Palermo, Italy;*

² *Institute of Clinical Physiology (CNR-IFC), Pisa, Italy;*

³ *Department of Epidemiology, Lazio Regional Health Service / ASL Roma 1, Rome, Italy;*

⁴ *ARIANET Srl, Milan, Italy;*

⁵ *INAIL-Research Center, Monteporzio Catone, Rome, Italy.*

Summary

The analysis of big data is an emerging topic in environmental health that may help scientists to assess large amounts of structured and unstructured information. The BEEP (Big data in Environmental and occupational Epidemiology) project is ongoing. It aims to collect, link and analyze data from different sources to support exposure assessment and epidemiological evaluations. The health effects of environmental factors in the general population and in workers are being investigated at different levels ranging from the national to the urban scale.

Introduction

One of the biggest challenges of the modern environmental epidemiology is to collect and link a huge amount of heterogeneous geographic, environmental and health data to get information otherwise not available.

The project started on June 2017 and will last two years. It is structured in specific objectives focused on different spatial domains, from the whole national territory to the urban micro-scale. A special focus is being devoted to the risk of hospitalizations and mortality at the national level and within the major metropolitan areas, the risk of occupational injuries and road accidents related to environmental factors, population mobility and extreme meteorological conditions.

General and specific objectives

General Objective:

1. To estimate the health effects of several environmental risk factors (air pollution, noise, temperature and other meteorological conditions) on the Italian population.
2. To evaluate the risk of injuries in sub-populations of workers in relation to environmental exposures.

Specific Objectives

1. To estimate the exposure of the Italian population to different environmental risk factors and their health effects, in terms of hospitalizations or occupational accidents on a national scale, using the municipality as the spatial unit.
2. To evaluate the risk of non-accidental and cardio-respiratory mortality induced by different environmental exposures among the residents of five Italian regions, at the municipality level.
3. To evaluate the adverse effects of air pollution and extreme temperatures on mortality and oc-

cupational accidents within six urban metropolitan areas, at the census block spatial resolution.

4. To evaluate the health effects of environmental exposures at the individual level in the longitudinal studies of Rome and Pisa-Cascina.

Materials and methods:

The applied methodologies entail the inter-correlation among huge spatial-temporal databases as well as the implementation of advanced statistical models for assessing short-term health effects at population level and long-term effects at individual level.

In particular, the following items are being explored:

1. Satellite data at high spatiotemporal resolution
2. Environmental monitoring data
3. Land use data
4. Dynamic population distribution data
5. Modeling of environmental parameters at national, regional, urban and address levels
6. Mortality and hospitalizations data
7. Follow-up of cohorts of resident population at urban and individual level
8. Data on occupational injuries and road accidents while commuting.

Results

In the first year of the BEEP project, estimates of air pollution concentration and meteorological parameters were performed at national and regional level:

1. particulate matter (PM₁₀, PM_{2.5}) concentration with a 1x1 Km spatial resolution and daily temporal resolution, for the period 2006-2015 at national level;
2. NO₂ and O₃ concentration with a 1x1 Km spatial resolution and daily temporal resolution, for the period 2013-2015 at national level;
3. air temperature, with the same spatial-temporal resolution, for the period 2001-2010 at national level.

Associations among air pollution, extreme temperatures and health effects have been assessed:

1. PM and hospitalizations and mortality: the preliminary results have shown an increased risk of natural mortality and of cardiovascular and respiratory hospitalizations in subjects exposed to PM₁₀ and PM_{2.5}; higher effects of PM on mortality in the older age group (> 75 years) and on respiratory admissions in males have been observed. Furthermore, significant associations have been found also in the municipalities of medium and low urbanization.
2. Extreme temperatures and hospitalizations and mortality: the analysis on mortality has shown a non-linear relationship, with increased risk for both high and low temperatures. The largest effects have been observed on respiratory causes, among the very elderly (75+ years), for heat in women and for cold in men. Similar mortality effects have been found by urbanization. Significant associations of high temperatures with respiratory admissions and of low temperatures with both cardiovascular and respiratory admissions have been found. Larger effects of heat and cold have been estimated in the elderly and in municipalities at a higher urbanization.
3. Extreme temperatures and occupational accidents: the results have shown a larger risk of occu-

pational accidents in the construction industry for hot temperatures and in the transport sector for cold temperatures.

Conclusions

Results of the BEEP project, beside addressing new directions in the scientific research, may provide decision makers with important information in the fields of air quality, urban planning and public health.

Acknowledgement

This BEEP project is supported by INAIL “Bando Ricerche in Collaborazione (BRiC) 2017”. More info on the BEEP project can be found in the project website: www.progettobeep.it.

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Fine resolved daily PM₁₀ and PM_{2.5} predictions in Italy using satellite data

Massimo Stafoggia^{a,b}, Tom Bellander^b, Simone Bucci^a, Marina Davoli^a, Kees de Hoogh^{c,d}, Francesca de' Donato^a, Claudio Gariazzo^e, Alexei Lyapustin^f, Paola Michelozzi^a, Matteo Renzi^a, Matteo Scortichini^a, Alexandra Shtein^g, Giovanni Viegi^h, Itai Kloog^g, Joel Schwartzⁱ, on behalf of the BEEP group

^a Department of Epidemiology, Lazio Regional Health Service / ASL Roma 1, Rome, Italy

^b Karolinska Institutet, Institute of Environmental Medicine, Stockholm, Sweden

^c Swiss Tropical and Public Health Institute, Basel, Switzerland

^d University of Basel, Basel, Switzerland

^e INAIL, Department of Occupational & Environmental Medicine, Monteporzio Catone, Italy

^f National Aeronautics and Space Administration (NASA) Goddard Space Flight Center (GSFC), Greenbelt, MD, USA

^g Department of Geography and Environmental Development, Ben-Gurion University of the Negev, Beer Sheva, Israel

^h Institute of Biomedicine and Molecular Immunology "Alberto Monroy", National Research Council, Palermo, Italy

ⁱ Department of Environmental Health, Harvard T. H. Chan School of Public Health, Cambridge, MA, USA

Introduction

Air pollution, especially particulate matter (PM), is one of the major causes of death. Recently, the last report of the World Health Organization estimated around 3 million of deaths attributable to PM exposure worldwide for 2012. Similarly, the latest update of the Global Burden of Diseases (GBD) study ranked PM as the sixth leading cause of death out of a list of 79 risk factors, being responsible for over 4 million casualties on 2015.

During the last decades, the epidemiological literature has reported consistent effects of PM from both short-term (i.e. daily variability) and long-term (i.e. annual averages) exposures. Most studies have however historically been conducted in major cities, where monitoring networks are more dense, and allow estimation of spatiotemporal PM variability with more accuracy.

We have previously developed a multivariate linear mixed model aimed at predicting daily PM₁₀ for each 1-km² of Italy for the years 2006-2012 using satellite measurements of Aerosol Optical Depth (AOD) interpreted with the MAIC algorithm, land use variables, and meteorology.

Objective

In this study we developed a novel five-stage modelling strategy to predict PM₁₀, PM_{2.5} and PM_{2.5-10} daily concentrations at 1-km² spatial resolution across Italy for the period 2013-2015.

Methods

We developed a five-stage machine-learning approach, the random forest, aimed at: Stage 1: Expanding the data base of PM_{2.5} and PM_{2.5-10} monitoring data by borrowing data from the co-located PM₁₀ monitors, Stage 2: Imputing missing MAIAC-AOD data using co-located multi-band AOD estimates available from atmospheric models, Stage 3: Calibrating the spatiotemporal PM concentrations with AOD data, meteorological parameters and land-use terms, Stage 4: Predicting the

output of the stage 3 model over all 1-km² grid cells of Italy and all days in 2013-2015, and Stage 5: Improving the stage 4 predictions by using additional information at a finer spatial resolution (monitor coordinates or 150-m buffer), with the aim of capturing local sources of PM not accounted for by the wider 1-km² resolution.

Predictive properties of the models have been checked by applying 10-fold cross-validation (CV) on individual monitors, for each year and PM metric.

Results

Our models were able to capture most of the PM variability, with mean CV R² 0.75 and 0.80 (stage 3), and 0.84 and 0.86 (stage 5), for PM₁₀ and PM_{2.5}, respectively. Model fitting was less optimal for PM_{2.5-10}, in summer months and in southern Italy. Finally, predictions were equally good in capturing annual and daily PM variability, lending themselves as reliable exposure estimates for investigating long-term and short-term health effects.

Conclusions

Machine learning methods in general, and random forests in particular, can be valid tools to be used in combination with satellite data, meteorological variables and land use parameters for predicting ground level air pollutants concentrations at fine spatial and temporal resolution. While the theory behind machine learning methods is still under development, and more research is required to better characterize all the possible sources of uncertainties inherent to such large estimation processes, we think that our PM predictions will provide novel evidence on the short-term and long-term health effects of fine and coarse particles in Italy.

Acknowledgement

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New evidence from the Rome Longitudinal Study

Giulia Cesaroni, Chiara Badaloni, Francesco Cerza,
Riccardo Orioli, Paola Michelozzi, Francesco Forastiere
Epidemiology Department, Regional Health Service Lazio, Rome, Italy

The Rome Longitudinal Study is a continuing project aimed at evaluating the health effects of long-term exposure to air pollution and its interplay with socioeconomic factors in Rome, Italy. The database is a large cohort of about 1.2 million residents in Rome at the 2001 census, with exposure assessment at the residential address, followed through record linkage procedures using administrative databases. All the linkage procedures are implemented under the National Statistical Program that protect individual confidentiality. The cohort contains all individual information from 2001 census, i.e. level of education, occupational status, and type of job, marital status, family composition, and demographic data. From Municipal Register, all the residential history and vital status are available. From the Health Information System, which includes the Mortality Registry, the Hospital Discharge Registry, the Drug Prescription Registry, the Emergency Visits Registry, and the Birth Certificates, it is possible to describe the health status of the study population, providing data on the prevalence and incidence of major disease and data on health service utilization. Each subject included in the study has a characterization of the place of residence in terms of outdoor air pollution exposure (particulate matter and its metal components, nitrogen oxides, ozone), traffic noise, greenness, proximity to high traffic roads and to parks.

We conducted several studies on the association between long-term exposure to air pollution and sociodemographic characteristics (Cesaroni et al. 2010), mortality (Cesaroni et al. 2013; Badaloni et al. 2017), acute coronary events and stroke, diabetes (Renzi et al. 2018), Parkinson's Disease (Cerza et al. 2018). Of particular interest is the association between metal (copper, iron, zinc, sulfur, silicon, potassium, nickel, and vanadium) components of particulate matter and health outcomes. The different components represent diverse sources of emission (traffic, industry, non-tailpipe vehicle emissions, road dust resuspension, etc.), and although in general are highly correlated with the particulate mass, their spatial distribution differ. Two examples follow using different health outcomes: natural mortality and pregnancy outcomes.

We investigated natural and cause-specific mortality in the 1,249,108 adults of the Rome Longitudinal Study in relation to the long-term exposure to metal components of PM₁₀ and PM_{2.5} (Badaloni et al. 2017). We followed all 30+ year olds from October 2001 to December 2010. We used land use regression models to estimate annual average concentrations at residences and Cox models to estimate the associations between pollutants and cause-specific mortality, adjusting for individual and contextual characteristics. We expressed Hazard ratios (HRs) per increments equal to the 5th–95th percentile range of each pollutant distribution. We observed higher mortality risk with increasing exposure to both exhaust and non-tailpipe traffic pollutants. In addition, we found an increased mortality risk associated to components related to oil burning and industry such as vanadium and nickel. With increasing levels of nickel in PM₁₀, we found HR= 1.07 (95% CI: 1.05–1.09) for non-accidental mortality, HR=1.08 (95% CI: 1.05–1.11) for CVD, and HR =1.13 (95% CI: 1.08–1.18) for IHD mortality.

We then investigated the association between elemental constituents of PM and pregnancy outcomes: term low birth weight (LBW: weight < 2,500 g among births after 37 weeks of gestation), pre-

term births, and small for gestational age (SGA, according to the Italian curves). We considered all singleton livebirths from mother who lived in Rome for the entire pregnancy in the period 2006-2014.

We used logistic regression to evaluate the association between exposure and outcomes, taking account of maternal age, parity, maternal education, season of conception, sex of the newborn, census block index of socioeconomic position.

Among the 172,325 singleton livebirths, 2.31% were term low birth weight, 6.07% were preterm births, and 8.59% were SGA. All the elemental constituents considered were associated to LBW and SGA. A 200-ng/m³ increase in sulfur in PM10 was associated with an increased risk of LBW (OR = 1.38; 95%: 1.22-1.57), an increased risk in SGA (OR=1.13; 95%CI: 1.06-1.21), and an increased risk in preterm births (OR=1.09; 95%CI: 1.01-1.17). The association was independent of PM10. We found that the association between PM and pregnancy outcomes can be attributed to several components, in particular sulfur and nickel in PM10 resulted associated with low birth weight and other pregnancy outcomes.

In conclusion, in addition to vehicular exhaust pollutants, PM related to non-tailpipe emissions and mixed oil burning/industry plays an important role in health outcomes.

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Air pollution and health effects in children: the Piccolipiù project

Franca Rusconi, Federica Asta, Luigi Gagliardi, Elisa Gori, Daniela Porta, Massimo Stafoggia and the Piccolipiù research group

Franca Rusconi, Unit of Epidemiology, Meyer Children's University Hospital, Florence, Italy

While the negative effects of early smoke exposure on child health have been widely studied, the association of air pollution exposure in pregnancy and early in life with adverse outcomes in childhood still needs to be fully ascertained. Prenatal and birth cohort studies allow for the prospective investigations of early environmental threats, including air pollution.

Within the Piccolipiù birth cohort we aim at studying : a) the effects of prenatal and early postnatal exposure to PM10 and PM2.5 and residential green spaces on several respiratory outcomes (infections, wheezing and asthma) and lung function up to school age; b) to evaluate the effects of the same exposures on neurodevelopment in preschoolers; c) to evaluate to what extent the effects of exposure to air pollution and green spaces on respiratory and neurodevelopmental outcomes are mediated through growth and in particular i) in utero infant growth patterns; ii) birth weight and growth in the first year of infants life.

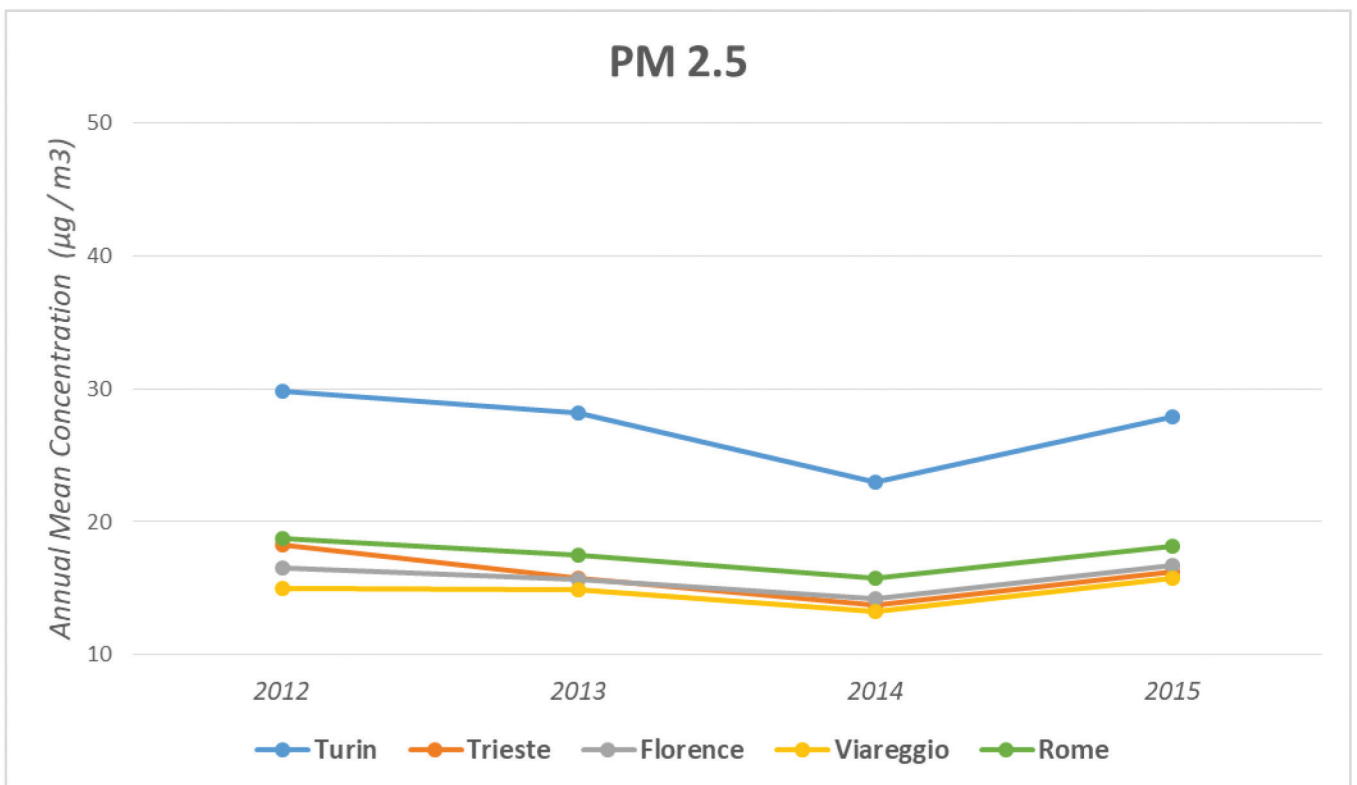
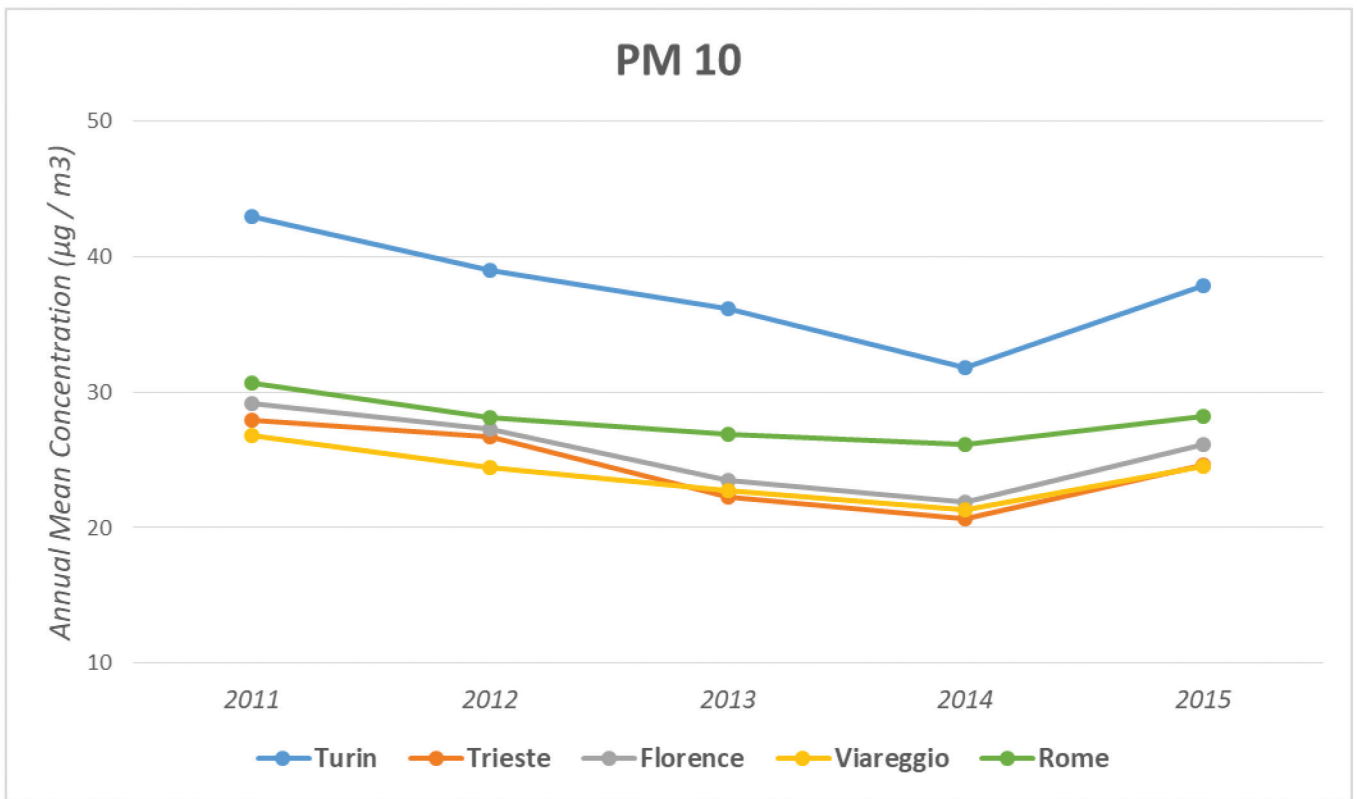
Between 2011 and 2015, the Piccolipiù birth cohort enrolled 3338 mother-infant pairs in Turin, Trieste, Viareggio, Florence and Rome. (Farchi et al, BMC Pediatrics 2014) Women completed a baseline questionnaire at the end of pregnancy and were then contacted when the child was 12, 24, 48 months and 6 years old (still ongoing); information on child health, development, and environmental exposures was collected through questionnaires. At 48 months of age children underwent neurodevelopmental tests and at 6 years lung function and atopic evaluation (still ongoing).

As for air pollution exposure, we developed a procedure to estimate daily concentrations of PM10 and PM2.5 over Italy (Stafoggia et al, Environ Int 2017). We combined finely resolved data on Aerosol Optical Depth- a satellite parameter of suspended aerosol- ground-level PM measurements, land-use variables and meteorological parameters into a four-stage mixed model to derive estimates of daily PM concentrations at 1-km² grid, for the years 2011-2015.

The residential address at birth and up to two years of age has been geocoded so far, and the annual mean concentrations for PM10 and PM2.5 in the period 2011-2015 are reported in figures 1 and 2. This will allow to look at the associations between exposures in pregnancy and in the first two years of infants' life, and outcomes of interest.

Neurodevelopmental tests at 4 years of age have been not completed and analyzed yet, and we are now therefore focusing on the relationship between air pollution and respiratory outcomes for which we have detailed information: recurrent upper respiratory infections (frequency: 9.5 and 10.3% at 12-24 and at 36-48 months); lower respiratory tract infections (21.7 and 20.2%); recurrent wheezing (10.2 and 5.8%); admission to hospital for lower respiratory tract infections or wheezing at 12-24 months of life (6.2%).

In preliminary analyses based on a more traditional indicator of traffic related air pollution (Land Use Regressions models) we found a clear association between density of busy roads near home and proximity to major roads with recurrent respiratory infections (Rusconi et al, ISEE 2016).



Noise and air pollution: mapping and incidence of diseases

Carla Ancona

Department of Epidemiology Lazio Regional Health Service, Rome, Italy

Background: Road traffic is highly prevalent and increasing across Europe and it is a source of both noise and air pollution. Until recently, both environmental exposures have been considered separately in the evaluation of their effects on health. Both noise and air pollution exposure have been related to increased risk of cardiovascular disease but the results have been controversial as to which pollutant is more important. These environmental stressors do not exist in isolation: there is a need for assessing and understanding both the individual role of these factors as well as the potential synergistic effects of combined exposure. Some of the inconsistencies that have been found in the associations between environmental noise and air pollution and health outcomes may be attributable to differential susceptibility to health effects based on genetic as well as other endogenous and exogenous factors related to predisposition. Recent studies are increasingly finding associations between aircraft and road traffic noise and hypertension and myocardial infarction but robust exposure-effect relationships are missing, the characterization of noise exposure could be improved, the role of confounding and moderating factors needs to be considered in more detail and more longitudinal studies are needed with validated health outcomes and less reliance on self-reported outcomes that are susceptible to response bias. Most studies of noise and health are cross-sectional and there is an urgent need for longitudinal studies to examine causal pathways, progression of effects and duration of noise exposure. Newly developed noise maps, such as those within the European Environmental Directive (END), are potentially a tool that can be used to link noise exposure data to individual respondent information in existing cohort studies. In Italy, there is not a standard national method and a defined common approach to treat and set input data and parameters for noise modeling, so even if cities followed indications from EU Commission, different noise mapping methods are adopted and exposure results are often not comparable. Air pollution has been traditionally measured with fixed monitors that are able to evaluate the variability of concentrations in time. However, data from fixed monitors are not suitable to assess the intra-urban spatial variability of pollutants and land use regression models are widely employed to estimate annual concentration of traffic related pollutants at the residential addresses of the individuals in epidemiological studies.

Objective: Our aim was to study whether long-term exposures to road traffic noise are associated with mortality, incidence of coronary events and stroke in a cohort of residents in three Italian metropolitan areas (Rome, Turin, and Pisa).

Methods: Population-based cohorts for a total of 1,902,521 people (aged ≥ 30 years) were enrolled on October, 31 2001 and followed for mortality and hospitalization until December, 31 2010. For all residential addresses we estimated average traffic noise levels (Lden) using the acoustic model Sound Plan 7.4 (reference to 2009 traffic flow data). We used a city and gender stratified Cox regression models with age as the time-scale to estimate associations while adjusting for individual characteristics (marital status, occupation, education place of birth) and contextual variables [annual NO₂ concentrations (from a land use regression model, ESCAPE protocol), residential addresses with a green area within 300m and area-based socioeconomic status (Hazard Ratios, HR, 95% CI)].

Results: During the 9 years of follow-up we identified 225,673 deaths, 58,989 incident coronary events, and 35,807 stroke cases. Noise and NO₂ were only moderately correlated ($r=0.36$). The ave-

rage level of Lden in the three cities was estimated at 60.1 (SD 7.1) dB (A), with very similar values in the three cities: 59.9 (SD 8.1) dB (A) in Rome, 60.4 (SD 4.9) dB (A) in Turin and 60.2 (SD 5.0) dB (A) in Pisa. The estimated mean NO₂ concentration in the three cities was 45.8 (SD 10.1) µg / m³, with 43.6 (SD 8.5) µg/m³ in Rome, 52.2 (SD 9.4) µg/m³ in Turin and 30.6 (SD 10.1) µg/m³ in Pisa. An association between Lden and natural mortality (HR = 1.013, CI95% = 1.007-1.019), acute fatal coronary events (HR = 1.032, CI95% = 1.011- 1.052) and fatal strokes (HR = 1.040, CI95% = 1.010-1.070) was found. NO₂ was also associated with natural mortality (HR = 1.016, IC95% = 1.011-1.021) and acute fatal coronary events (HR = 1.041, IC95% = 1.023-1.059). After mutual adjustment, the associations of Lden with natural mortality and acute fatal coronary events disappeared, while the effect of NO₂ exposure was confirmed (HR = 1.015, CI95%1.009-1.020, for natural mortality; HR = 1.035, IC95% = 1.015-1.055 for acute fatal coronary events). The positive associations of Lden with stroke and fatal stroke strengthened (for strokes: HR = 1.017, CI95% = 1,000-1.034, for fatal strokes: HR = 1.043, CI95 % = 1011-1077). However, NO₂ exposure was not associated with strke (fatal and not fatal)

Conclusions: This study supports an independent effect of long-term exposure to noise on mortality and on incidence of stroke in a large cohort of residents in metropolitan areas in Italy, while long term exposure to air pollution was associated with natural mortality and fatal AMI. The results are relevant for policy decisions to reduce population exposure and prevent large health effects.

Particulate matter components, sources and health effects

Andrea Ranzi

Centre for Environment Prevention and Health, ARPAE Emilia-Romagna, Italy

Multi-city time-series and long-term cohort studies showed associations between PM_{2.5} and health outcomes. Particulate matter is a complex mixture of chemical constituents, each of which may contribute to health adverse outcomes. However, the role of each PM component and the effects deriving from the interplay of chemicals with different toxicity is still poorly understood.

The Supersito project provided more than three years of atmospheric aerosol measurements, in five different sites in the Emilia-Romagna region, located within the Po Valley, in Northern Italy, in the aim of better understanding the PM chemical composition, mass closure, size distribution and source apportionment.

The toxicological profiles of atmospheric aerosol were investigated through an integrated approach, including in vitro tests and toxicogenomics, to highlight the effects of air particulate matter on toxicological relevant endpoints and to identify the key events at molecular and cellular level. 8 intensive campaigns with 2.500 experiments and 66.000 genes transcribed for each analyzed sample were performed.

More than 2 million subjects in four study areas with corresponding measurements sites were considered for detailed data collection and epidemiological analyses (66% in the 2 urban areas, 13% and 21% in the rural and coastal area). Epidemiological investigation of association between PM_{2.5} components and mortality and reproductive outcomes were performed. Survival analyses were used to analyze a retrospective cohort of residents in the period 2010-2014. Residential exposure to PM components was estimated monthly using a combined approach of LUR and dispersion models, and back extrapolation techniques.

Environmental investigations prove that the major sources of aerosols are road traffic, biomass burning, agriculture, long-range transport and industries. The primary and secondary organic matter from biomass burning and traffic vehicles is the principal component of PM_{2.5} and PM₁.

Cancer risk were detected only at high doses: the activation of inflammatory status, if persists over time at high concentrations, may lead to mutations, therefore to carcinogenic risk. There was the confirmation (already detected in previous studies) of activations of genes involved in inflammatory processes and identification of the possibility of autoimmune diseases and Pre-Term Births.

PM_{2.5} were associated with an increase of 7% in natural mortality. Biomass burning and oil combustion are the sources associated natural-cause mortality, regardless of the PM_{2.5} total concentration. Pre-term births was the only reproductive outcome associated with PM_{2.5} mass, with a specific role of traffic, oil combustion and secondary sulphates.

Results gave evidence for the modulation of genes playing a key role mainly in immune diseases and reproduction toxicity. The effect related to reproductive outcomes are reinforced by epidemiological investigation, with interesting indications of a possible role of secondary sulphates.

Important suggestions, such as the increasing role of biomass burning, the confirmed importance of traffic, the interesting role of long-range transport can be helpful to drive decisions. These results emphasize the importance of taking into account actions on all these sources to improve air quality in the Po valley.

Industrial pollution and health: experience from the Apulia Region

Lucia Bisceglia,
on behalf of the CSA Group - Apulia Region, Bari, Italy

The industrial areas of Brindisi and Taranto, two cities in the Apulia Region, have been recognized since 1998 as “areas at high environmental risk” and “sites of national relevance for cleanup” because of various industrial sources of environmental contamination, potentially affecting the residential communities: three thermoelectric power plants established in different time periods (1961, 1969, and 1991), two still operating in Brindisi, the second largest integrated iron and steel plant in Europe, built over a 15-year period (1960–1975) in Taranto. The productivity of the steel plant in Taranto changed during the period of its activity with an increase up to the eighties, a decline following the economic crisis (2009), a subsequent increase in the years 2010-2012, and a decline in 2013-2014. The production trend, and therefore the variation in emissions, influenced pollution levels in the neighboring districts. Several environmental monitoring studies and measurement campaigns of industrial emissions showed a relevant contribution of the industrial plants on the levels of measured pollutants in the area.

Descriptive epidemiological studies, since late '80, reported excess of mortality and morbidity from various diseases in the areas, strongly suggesting a role for industrial emissions. However, the causal relationship between industrial air pollutants and adverse health outcomes has been controversial. In 2012, a cohort study showed that residents living in Taranto in districts nearby the industrial area had higher mortality/morbidity levels compared to the reference area, even when their socioeconomic position has been taken into account.

Between 2014 and 2017 the Apulian Government supported large population-based cohort studies in the two areas with the aim to assess whether long-term exposure to industrial emissions is related to increased cause-specific mortality, cardiovascular and respiratory diseases hospital admissions, and cancer incidence, taking into account the independent effect of socioeconomic position (SEP), occupation and other contextual variables.

Individual exposure to industrial emissions was estimated at the residential address of all subjects using a Lagrangian dispersion model (SPRAY). Particulate Matter (PM₁₀) and Sulfur dioxide (SO₂) were considered as tracers of air contaminants emitted by the steel plant in Taranto and the power plants in Brindisi. Census data from 2001 at census block level were used to assess an area-based SEP index.

In both industrial areas, estimated exposures to industrial PM₁₀ and SO₂ were associated with several health outcomes, adjusting for SEP and occupational exposures, confirming that the industrial plant is an important risk factor for the health status of residents.

Focusing on Taranto, when we considered time-lags, increased mortality risks have been found associated with estimated concentration of PM₁₀ and SO₂ both for the most recent five years of exposure and for the far past (more than 25 years before the current exposure). Associations were even stronger when considering hospital admissions.

The “Difference-in Difference” approach was used to study the relationship between changes in exposure to industrial PM₁₀ and changes in cause-specific mortality rates at district level, included only deaths occurring on the last six years of follow up (2008-2014). We found evidence for a causal link between industrial PM₁₀ and mortality in Taranto. In particular, exposure to industrial PM₁₀ has been associated with an increased mortality risk for natural and respiratory causes.

More recently, in the context of a national project founded by Italian Health Ministry, a health impact assessment of industrial emissions in the two areas has been performed to evaluate the effectiveness of environmental measures to protect the health of people living near the industrial sites.

Concentrations of industrial pollutants, estimated with dispersion models, were used to obtain Population Weighted Exposures for three different emissions scenarios. Available concentration-response functions were used to estimate, for each scenario, the number of attributable premature deaths and the incremental lifetime cumulative mortality risk for lung cancer. Results showed that in Taranto current measures are not sufficiently protective and warrant remedial action to minimize the health impact of industrial pollution.

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CSA Group Apulia Region:

Lucia Bisceglia (1), Carla Ancona (2), Ester Alessandrini (2), Lisa Bauleo (2), Angela Morabito (3), Stefano Spagnolo (3), Alessandra Nocioni (3), Tiziano Pastore (3), Annalisa Tanzarella (3), Francesca Intini (3), Maria Serinelli (3), Ida Galise (3), Vito Laghezza (3), Susi Epifani (4), Antonino Arduzzone (4), Giuseppe Spagnolo (4), Simona Leogrande (5), Antonella Mincuzzi (5), Sante Minerba (5), Roberto Giua (3), Francesco Forastiere (2)

(1) Regional Health Agency, Bari, Puglia, Italy. (2) Department of Epidemiology Lazio Regional Health Service, Rome, Lazio, Italy; (3) Environmental protection Agency Apulia Region, Bari, Puglia, Italy; (4) Local Health Authority Brindisi, Brindisi, Puglia, Italy; (5) Local Health Authority Taranto, Taranto, Puglia, Italy

Studying the health effects of air pollution in Lombardy

Sara Conti

*Research Centre on Public Health, Department of Medicine and Surgery,
University of Milano-Bicocca, Monza, Italy.*

Lombardy region, that is located in Northern Italy, is a very heterogeneous context as for geographic conditions, land use, population densities, presence of industrial activities and climate. Currently, it has a population of roughly 10 million inhabitants (1/6th of the whole Italian population), that are exposed to heterogeneous concentrations of air pollutants, emitted by different sources, that reach high peaks especially in the Po Valley [1-2].

Since it has been shown that the composition of particulate matter (PM) affects its effect on health [3-4], Lombardy is a suitable context to investigate the potential heterogeneity of PM effects and what are the reasons behind such differences.

In order to address such issue, it is essential to involve the whole region in the analysis, without limiting the observation to well-known urban areas, such as that of Milan. In one previous study [5], we analysed 7 small and medium-sized cities of Lombardy, and we showed that exposure to PM₁₀ is associated with a short-term increase in the risk of drug prescription, a rarely investigated outcome, that is more frequent than hospitalization and is therefore suitable for investigating small areas.

We are now extending the analysis to the whole region, and we started by addressing the short-term relationship between exposure to PM₁₀ and the prescription of cardiovascular drugs, from 2007 to 2008.

In detail, we retrieved data on daily average PM₁₀ concentrations over the whole Lombardy from the regional environmental protection agency, that implemented a chemical transport model. Based on these estimates, we computed the daily mean PM₁₀ concentrations for each municipality of the region for the biennium 2007-2008.

Thereafter, we extracted all prescriptions of cardiovascular treatments that were effectively purchased by the inhabitants during the study period. Our data source were the administrative databases of the Lombardy Healthcare System.

Since our aim was to detect heterogeneity in the effect of the pollutant, we divided the region in the zones established by an administrative order of 2011 (Deliberazione della Giunta Regionale del 30 novembre 2011 - n. IX/2605), that identified areas that are homogeneous for pollutants emissions and meteorological conditions.

For each of them, we carried out a case-crossover study, using a time-stratified approach. Distributed lag models considering lags from 0 to 6 days allowed us to take the delayed effect of the pollutant into account. All models considered confounders such as influenza epidemics, holidays and other exceptional circumstances affecting the prescription frequency, and temperature.

We carried out stratified analyses in order to detect effect modifications due to season, gender and age. In detail, we separated warm and cold season, and we divided the population into three age classes (0-14, 15-64, 65+).

We also computed pooled estimates through a fixed effect metanalysis of the effects estimated for each zone.

Overall, our results showed an association between PM₁₀ concentrations and the prescription of drugs that are used in the management of mild episodes of hypertensive peaks and of congestive heart failure, namely diuretics, beta-blockers and calcium channel blockers. The estimates of the association were heterogeneous among zones, and in some of them they did not reach statistical significance. We observed an effect modification due to season and gender, with stronger effects during the cold season and among women.

Our results encourage further small area investigations, that could link the spatial differences that we detected among zones to the heterogeneity in PM composition and sources that characterizes Lombardy. Pharmaceutical prescriptions proved to be an outcome that deserves attention on a small area basis, because it allows drawing an inference even on small municipalities. Therefore, we are planning to continue our analysis in order to explain what drives the detected differences.

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Climate and air pollution: an integrated system to prevent acute health effect of temperature and air pollution in Italian cities

Paola Michelozzi,

Department of Epidemiology Lazio regional Health Service - ASL Roma 1, Rome, Italy

Italy and the Mediterranean have been identified as one of the areas most affected by climate change¹. Future climate change poses a significant health threat, especially considering the increase in the frequency and intensity of heat waves and worsening air quality.

Pollutant emission, transport, dispersion, and chemical transformation of pollutants is influenced by meteorological conditions (temperature, humidity, and wind characteristics). More than half of the world's population will be exposed to increasingly stagnant atmospheric conditions, which favor the build-up of air pollutants².

In order to contrast the acute health effects of extreme high temperatures, the national heat adaptation plan³ has been running since 2004 thanks to the collaboration between the Ministry of Health, the Department for Civil Protection and the Department of Epidemiology Lazio regional Health Service – ASL Roma 1. The plan has a national coverage, including 34 major cities thus 93% of urban residents aged 65 years and over. The main components of the heat plan include:

- City-specific Heat Health Watch Warning Systems (HHWWS) based on the association between temperature and mortality to identify weather conditions and temperature thresholds at risk. Three-day warnings are issued via the Ministry of Health website (www.salute.gov.it/caldo), via the APP “Caldo e Salute” and via email throughout the local dissemination networks to all emergency, health and social services involved. Heat prevention measures are modulated on the level of risk issued by the heat warnings.
- National prevention guidance and recommendations for at-risk subgroups have been developed and include the elderly, subjects with chronic conditions, children, pregnant women, outdoor workers.
- In Italy prevention programs are specifically addressed to high risk subgroups. Each summer lists of high risk subgroups to whom prevention measures are addressed are defined in each city using population registries, health information systems and direct notifications from GPs and social services. The proportion of susceptible subjects among the elderly ranges between 0.8% to 5.6% across cities.
- Near-real time mortality and ER visits surveillance allows the rapid monitoring of the impact of extreme weather events such as heat waves, cold spells. Thanks to over 15 years of data, a recent study has shown the number of heat attributable deaths has decreased, with 1200 deaths spared in the most recent years in 23 large cities⁴.
- Survey of local prevention plans, information campaigns and measures put in place such as help lines, education campaigns, social support services, opening of air conditioned spaces, active health surveillance of susceptible individuals and emergency protocols.

Thanks to this integrated system, public awareness on the issue and a better response from health

and social services have played a key role in improving adaptation to heat in Italy. Since 2018, the plan has been extended to air pollution since this is another environmental exposure that may benefit from such an inclusive and nationwide prevention effort. Air pollution is not only influenced by temperature and other meteorological parameters, but these are also competitive risks on survival of the same vulnerable subgroups, such as small children the elderly, and subgroups with pre-existing cardio-respiratory conditions. Specific actions towards air pollution are:

- Near real-time monitoring of air quality in urban areas. An evaluation of short-term effects and impacts during periods when air quality standards are exceeded is carried out in collaboration with the Italian Institute for Environmental Protection and Research (ISPRA). A website has been set up to allow general population, health workers and policy makers to follow current concentrations of ozone, particulate matter and nitrogen dioxide and forecasts for following days in the different cities from the regional environmental protection agencies (ARPA). The website allows a national “ at a glance” insight on air quality.
- Air pollution health warning systems based on the definition of air masses which have been associated with a higher mortality risk. These models are being defined in a selection of cities for which similar methodology is already in place for heat warnings. Typically in summer Dry tropical (DT) and moist tropical (MT) air masses are associated with anticyclonic conditions which favour the build-up of pollutants and are associated with higher pollutant concentrations, heat waves and a higher mortality risk. Similarly in winter, anticyclonic conditions with stable atmospheric stratification can lead to strong nocturnal temperature inversions due to rapid surface cooling. The resulting restriction in vertical air mixing near the surface consequently leads to the trapping of surface emissions and poor air quality in cities. Cold polar conditions together with poor air quality have been shown to be risk factors for cardio-respiratory conditions. These results are used to define a three day warnings to raise awareness and implement prevention measures.
- Prevention guidance, informative material and training on the health risks of air pollution. Based on air quality warnings, separate health advices are developed for at-risk groups and the general population⁵. Health workers (primary care and lung and heart specialties) guidance and training is focused to educate patients to reduce air pollution risks, and to influence policy makers to make changes toward air pollution mitigation.

Both consolidated and developing adaptation measures, within the integrated framework of the Italian plan, are strategic public health responses to built future capacity to cope with climate change and to succeed in reducing air pollution by protecting health of high risk subgroups.

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Approaches and challenges in estimating the health impact of air pollution

Michal Krzyzanowski

Environmental Research Group King's College London, UK

Combined evidence from epidemiological, clinical and toxicological research has provided solid evidence on the hazardousness of various air pollution components and types. Epidemiological studies have quantified relationships between various indicators of health status and the exposure level in many populations. Recently conducted studies are based predominantly on large data sets, covering sometimes 100s thousands of subjects or more, established a decade or more earlier for other purposes than research on health impacts of air pollution (1,2). Such large population and clinical data sets, combined with exposure estimates based on combination of air quality monitoring and modelling, assure good power of the studies and generate precise risk estimates. However, feasibility to conduct such studies is limited to a few countries and areas where such data bases have been established and are accessible to research. Consequently, availability of research results is still very poor in low and middle income countries, where population and health information collection, data base maintenance and access remain very limited. At the same time, these are the countries suffering from high exposures to air pollution and its health effects the most (3). Quantification of these effects is the key to triggering actions addressing major pollution sources and prevention of the impacts of air pollution on health. Recent global projects estimating national burden of disease due to air pollution resulted in significant increase of the awareness of the public as well as local and national governments about their air pollution problems and its importance to health (4,5). They generate questions about local estimates of burden of disease and health effectiveness of pollution reduction plans. Several risk assessment tools, ranging from rather simple AirQ+ of WHO to more complicated BenMAP, are available profiting from the global knowledge on exposure-health relationships (6, 7, 8). Their application provides practical alternative to epidemiological studies in support of local assessments of health impact of air pollution and pollution reduction planning.

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The World Health Organization (WHO) global estimates of the impact of air pollution

Sophie Gumy¹, Heather Adair-Rohani¹, Pierpaolo Mudu¹, Giulia Ruggeri¹, Francesco Forastiere^{1,2}

¹ *World Health Organization, Department of Public Health, Social and Environmental Determinants of Health, Geneva, Switzerland.*

² *Kings College, London, United Kingdom.*

Air pollution has been identified as a global health priority in the sustainable development agenda. The World Health Organization (WHO) has responsibility for stewarding three air pollution-related indicators for monitoring progress against the Sustainable Development Goals (SDGs): in health (Goal 3) – mortality from air pollution, in energy (Goal 7) – access to clean fuels and technologies, and in cities and communities (Goal 11) – air quality in cities (1).

This session will present WHO updated global estimates of exposure and burden of disease from ambient and household air pollution from particulate matter, which are used for SDG reporting at the global, regional and national level (2). These estimates are based on improved exposure estimates and integrated exposure risk models, two important inputs of the methodology for estimating the health impacts of PM_{2.5} for which there has been considerable improvement over the last two decades (3-8).

For ambient air pollution, the assessment of global exposure to PM_{2.5} using satellite data and its integration with ground measurements has greatly improved both because of new modelling techniques (3-6) and the increasing data availability (9). Air quality levels in cities, namely, is an SDG indicator and is now under global scrutiny.

Household air pollution from indoor smoke due to incomplete combustion of polluting fuels such as wood, coal, agricultural residues and kerosene for daily household needs such as cooking is still a major issue in low and middle income countries, putting women and children most at risks. The percentage of the population primarily relying on clean fuels and technologies for cooking, heating and lighting serves as one of the two main indicators (with electricity access) for monitoring progress towards the SDG 7 target on universal access to modern energy services. These estimates are also used in the calculation of the mortality attributed to the household air pollution. Recent development in modelling time-series of single fuel use by country is a useful tool to support countries to transition to cleaner household energy options and adopt efficient interventions (7).

Finally, the development of integrated exposure risk models (IERs) that relate the entire range of exposures to PM_{2.5} from various particle sources – namely ambient, household, second-hand smoke and active smoking - to cause-specific mortality risks has been a major breakthrough to fill to assess global estimates of burden of diseases particulate matter air pollution in the absence of direct evidence at higher PM_{2.5} concentration (8). Yet, recent studies shows that these IERs may be underestimating the real burden (10).

To date, air pollution – both ambient and household – is the biggest environmental risk to health, carrying responsibility for about one in every 8 deaths annually. Ambient (outdoor) air pollution alone kills around 4.2 million people each year, while household air pollution is responsible for about 3.8 deaths, both mainly from noncommunicable diseases.

To support countries in choosing policies aiming at reducing air pollution and promoting health, WHO is further developing and refining tools to support planning for clean household energy policies (the Clean Household Energy Solutions Toolkit); to quantify the health impacts of air pollution (AirQ+ software, (11)); and to estimate the expected health impacts from policies taken by other sectors (for example, transport, waste management, and land-use planning).

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Greenness mitigates the noxious effects of air pollution on health and wellbeing

Pier Mannuccio Mannucci

Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano

According to the United Nations, approximately half of the world population currently lives in urban or suburban areas, a proportion projected to increase to two-thirds by 2050. Urbanization is often associated with a decline in the quantity and quality of green space. Thus, health policies are increasingly advocating the promotion of more outdoor greenness (but also of plants growing indoor) in order to improve health and wellbeing.

Greenness and health benefits. The relationship between the degree of green space exposure and human wellbeing has been surmised for a long time but only recently it was substantiated with a scientific approach. A pioneer work from the Netherlands demonstrated a positive association between the amount of green space in the living environment and the perceived and declared general health of the residents (J Epidemiol Community Health 2006; 60: 587). More recently a systematic review and meta-analysis of 103 observational and 40 interventional studies that had explored the association between green space exposure and health status described an array of clinical benefits. However, the strength of this evidence was limited by the generally poor quality of the studies included in the analysis, as well as by their high level of heterogeneity (Environmental Res 2018;166:628).

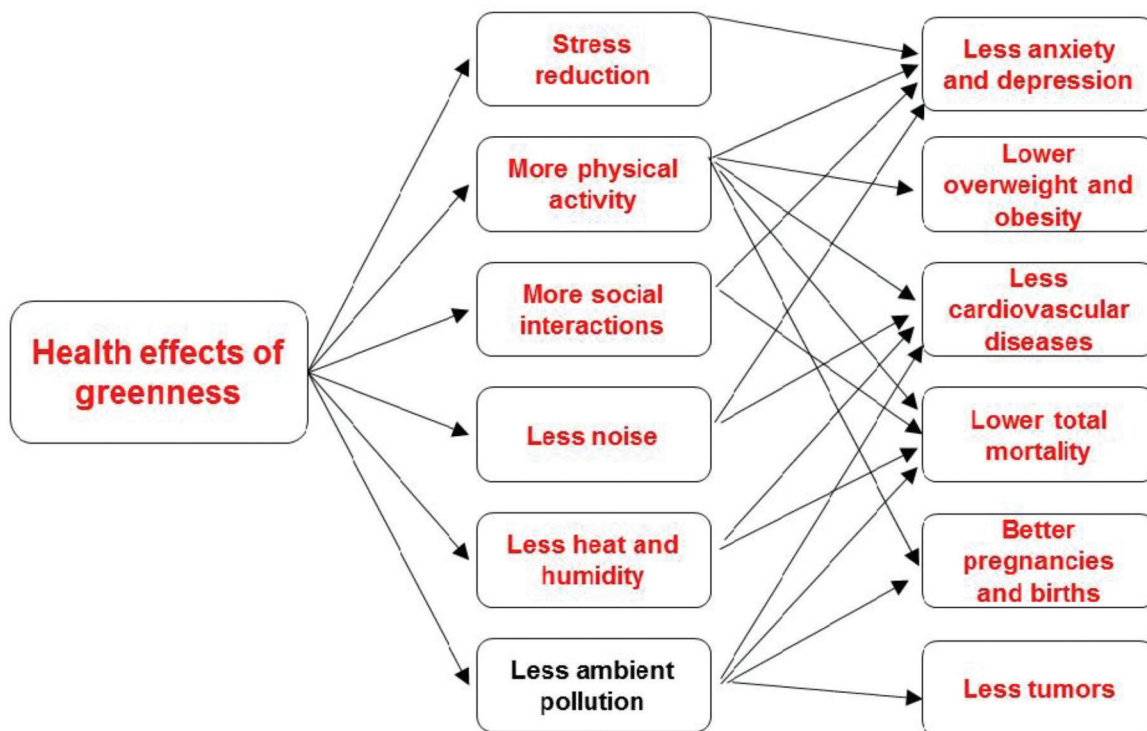
Seminal data were obtained in the frame of the US-based Nurses Health prospective cohort study carried out in 108.630 women. Epidemiologists from the Harvard School of Public Health showed that in nurses living in sites within the highest quartile of cumulative greenness exposure the rate of all-cause non accidental deaths was 12% lower than among nurses living in the lowest quartile of degree of exposure (Envir Health Perspect 2016;124:1344). These findings on a hard end-point such as all-cause mortality are consistent with previous smaller observational studies conducted in Europa and Canada, and with the results of a systematic review and meta-analysis from Barcelona by Gascon et al (Envir Int 2016;86:60).

Mechanisms of greenness benefits. The putative mechanisms underlying the beneficial effects of green space on health are multiple. Among of the main ones there is the promotion of physical exercise, with the ensuing reduction of obesity and improved cardiovascular and respiratory health. Other mechanisms pertain to mental health, because green space reduces cognitive fatigue, promotes emotional recovery and buffers the impact of stress on urban residents, with the related impact on anxiety and depression. Strikingly, a study carried out in a critical USA city as Philadelphia suggested that the implementation of greening in vacant city lots was associated with favorable effects on the rate of criminal behaviour, with a reduction of gun assaults and vandalism.

Greenness and air pollution. The forementioned cohort prospective study from Harvard suggests that one of the mechanisms of the favorable effect of greenness on mortality is its capacity to mitigate the noxious effects of air pollutants and particularly of particulate matter. A number of studies have indeed analyzed the relationship between the capacity of the natural environment to buffer exposure to air pollution. Greenness protects from air pollution by removing PM, O₃, CO, SO₂ and NO₂. The capacity of removal by a tree during its life cycle of excessive atmospheric CO₂ produced from fossil fuels is remarkable, ranging from 0.5 to 6 tons, and varies depending on the

vegetal species. Because the potency of air pollution mitigation varies from one species to another, trees suitable for a peculiar urban area should be chosen according to the main air pollutants to be removed in that area. Data stemming from an ecological study carried out by L. Chaparro and J. Terradas in Barcelona are very impressive. In 2009, trees and shrubs removed 305.6 tons of gaseous and particulate pollutants (166 tons of PM₁₀, 73 tons of O₃, 55 tons of NO₂, 7 tons of SO₂ and 6 tons of CO), with a monetary service value to the society estimated at 1.1 million Euros. A large degree of air pollution removal by greenness was also demonstrated by D.J. Novak et al in 2006 in 55 urban areas of the USA, and in 2012 by P.J. Villeneuve et al in Ontario, Canada.

Conclusions. Research exploring the relationship between environmental factors and health is increasing, and the emerging evidence supports a beneficial effect of more the outdoor green space. A number of studies and systematic reviews indicate that exposure to greenness reduces of all-cause, non accidental mortality, particularly from cardiopulmonary and cancer causes. There is also some evidence that green space residence may be associated with improved pregnancy and birth outcomes, and with better school performances in children. Furthermore, because at least one third of the premature deaths globally attributable to exposure to air pollution is due household agents, particularly in fragile populations living in low-income countries (i.e., children, older and deprived people, pregnant women), it must be realized that houseplants are an effective and economic mean for cleaning indoor air and thus reducing volatile organic compounds such as formaldehyde, benzene, toluene and others. On the whole more prospective studies are needed to further elucidate the mechanisms linking air pollution, greenness and health outcomes, although the multiple and interacting mechanisms depicted in this figure are all biologically plausible.



Policy issues: progress made and remaining challenges in neighbouring countries

Richard Ballaman

*Air Pollution Control and Chemicals Division, Swiss Federal Office for the Environment
Berne, Switzerland*

Air quality has continued to improve in Switzerland since 2000 and holds up well in comparison to other European countries. Nevertheless, the Swiss ambient limit values (in line with the WHO air quality guidelines) for ozone, particulate matter and nitrogen dioxide are still exceeded to some extent and a health risk remains. Additionally, atmospheric nitrogen deposition is still too high and has negative effects on ecosystems, biodiversity, soil, water and climate. To further improve air quality, additional national and international measures are necessary in the areas of transport, industry, combustion installation and agriculture.

Mandate of the Swiss legislation

Humans, animals, plants and ecosystems should not be exposed to any harmful effects or nuisances caused by air pollutants. For this protective goal, which is set out in the Environmental Protection Act (EPA),^[1] the Ordinance on Air Pollution Control (OAPC)^[2] sets ambient limit values for twelve air pollutants. To comply with the ambient limit values of the OAPC and the commitments under the UNECE Convention on Long-range Transboundary Air Pollution (CLRTAP) and its protocols^[3] the federal government set reduction targets for emissions of problematic pollutants (Federal Council 2009^[4]).

Current state of air pollution in Switzerland

Over the last decades, air quality has continuously improved^[5]. Yet, especially in winter during periods with temperature inversions and absence of precipitations, **particulate matter** concentrations continue to rise above healthy levels. During this season, the ambient limit value of **PM10** is frequently exceeded in urban agglomerations. The canton of Ticino is most affected, as it is exposed to higher emissions from transport as well as local wood-fired heating systems and also impacted by pollutants carried from the Lombardy region.

Peak levels of **tropospheric ozone**, the main compound of summer smog, have declined. Nevertheless, in summer the ambient limit values are still frequently exceeded in Switzerland. Ticino is the most heavily impacted due to the prevailing climate conditions and transboundary air pollution. The ambient limit value for the annual mean of **nitrogen dioxide** (NO₂) is still exceeded at locations with intensive traffic.

The effects of air pollution are wide-ranging and current levels still cause harmful effects on human health and ecosystems.

Emission sources

The emissions of primary **PM10** are divided in almost equal parts between industry, transport and agriculture, and households to a somewhat lesser extent. They decreased by 12% between 2005 and 2016. The goal is a reduction of 45% compared to 2005. Secondary particulate matter, which forms in the air from precursor substances such as nitrogen dioxide, ammonia, sulphur dioxide or volatile organic compounds, is not included in this target.

Nitrogen oxides (NO_x) are not only responsible for nitrogen dioxide pollution. They are a precursor substance in the formation of both tropospheric ozone and secondary particulate matter and are an important source of nitrogen deposition. Total emissions of NO_x decreased by 27% between 2005 and 2016. The target is a 50% reduction.

Ammonia (NH₃) originates almost exclusively from agriculture, where it escapes into the air from stables as well as manure storage and application. With a reduction of only 4% since 2005 major efforts are needed to achieve the targeted reduction of 40%.

Over 50% of **volatile organic compounds** (VOC), which can be toxic and carcinogenic and are important precursors in the formation of tropospheric ozone, are emitted by industry and commerce. The target is a reduction of around 30% compared to 2005. To date, a reduction of 24% has been achieved.

In the future, we expect a continued decrease of air pollutant emissions due to the consistent implementation of state-of-the-art technology even if the transport prospects until 2040 developed by federal offices show that the number of kilometres travelled is growing substantially. The reference scenario estimates an increase of 25% in the area of passenger transport and 37% in the area of freight transport.

Abatement measures

National regulations exist for pollutant emissions from combustion installations, industrial plants, construction machines, ships and rail vehicles. In addition, the OAPC defines the quality of fuels and combustibles. These requirements will become stricter as new commercially applicable technologies become available, which ensures that the best available technologies are always applied. The European-wide harmonised EURO standards are applied to all types of motor vehicles in Switzerland. Market-based instruments are also applied e.g. the performance-related heavy vehicle charge (HVC) or the incentive tax on volatile organic compounds.

The **cantons** play an important role in implementing air pollution control policy. They enforce the national regulations and issue their own action plans to improve the air quality in their territories. As a party to the UNECE Convention on Long-Range Transboundary Air Pollution (CLRTAP) and its protocols, Switzerland is actively involved in further reducing air pollutant emissions at the **international level**. Currently the ratification of the revised Gothenburg protocol is under treatment by the second chamber of the Parliament.

Synergies with other policy areas occur particularly in the area of energy and climate policy. Measures to increase efficiency and replace fossil energies with renewable ones are usually consistent with air pollution control policies. However, a conflict exists in the area of small-scale wood-fired heating systems which are desirable from the climate perspective, but still produce substantial amounts of particulate matter.

Further action required

To meet the Swiss ambient air quality standards as well as the internationally established critical loads, emissions of ammonia, nitrogen oxides, particulate matter and volatile organic compounds have to be further reduced at the national and international level. The best available technologies must be consistently promoted and used in vehicles, heat generators as well as industrial and agricultural installations.

- (1) Federal Act of 7 October 1983 on the Protection of the Environment (Environmental Protection Act, EPA), SR 814.01.
- (2) Ordinance on Air Pollution Controls of 16 December 1985 (OAPC), SR 814.318.142.1.
- (3) Convention on Long-Range Transboundary Air Pollution of 13 November 1979 (Geneva Convention), SR 0.814.32.
- (4) Strategia concernente i provvedimenti di igiene dell'aria adottati dalla Confederazione dell'11 settembre 2009. FF 2009 5723-5756.
- (5) OFEV (éd.) 2018 : La qualité de l'air en 2017. Résultats du Réseau national d'observation des polluants atmosphériques (NABEL). Office fédéral de l'environnement, Berne. État de l'environnement no 1825 : 28 p.

Europe's air quality legislation in review: the fitness check of the Ambient Air Quality Directives

Vicente Franco

*European Commission, Directorate-General for the Environment Clean Air unit,
Brussels, Belgium*

Europe's ambient air quality is slowly improving, but fine particulate matter and nitrogen dioxide in particular continue to cause serious impacts on health. Recent estimates point to about 400.000 premature deaths in EU 28 each year due to particulate matter and 75.000 due to nitrogen dioxide. Air pollution is estimated to cause at least € 24 billion per year in direct costs, while indirect costs (e.g., related to reduced life expectancy or broader societal impacts) are estimated in the range of €330 billion to € 940 billion annually. To determine whether and to what extent these improvements in ambient air quality are attributable to EU legislation on the matter, an evaluation exercise or 'fitness check' is being performed by the European Commission. Fitness checks are interim evaluations of EU policies and laws performed in the context of the European Commission's "Better Regulation" initiative. Fitness checks are used to assess if EU laws, policies and funding programmes are delivering the expected results at minimum cost. They also provide all stakeholders with increasing opportunities to contribute throughout the policy and law-making cycle.

In mid-2017, the European Commission initiated the fitness check of the two EU Ambient Air Quality (AAQ) Directives (Directives 2008/50/EC and 2004/107/EC) and the associated supporting regulatory acts (Implementing Decision 2011/850/EC and Commission Directive EU/2015/1480). These Directives set air quality standards and requirements to ensure that Member States monitor and/or assess air quality in their territory, in a harmonised and comparable manner.

Whereas the AAQ Directives themselves do not include a formal requirement for a comprehensive evaluation at a specific moment, an evaluation completed by 2020 appears to be timely for several reasons. First, the air quality standards set in the Directives have been in place for almost two decades (because they were 'inherited' from predecessor legislation). Also, since the conception of the Directives, the evidence base regarding health and environmental impacts has evolved significantly: WHO air quality guidelines are, in most instances, more stringent than EU air quality standards. Over the same period, the technical feasibility and implementation experience in Member States has also improved. Furthermore, the changing technological and legislative context should help deliver a sustained downward trend in emissions in the 2020-2030 timeframe. Relevant milestones in that sense include the major policy packages on Energy Union, Low Emission Mobility and climate objectives, the recently agreed national emission reduction commitments and the implementation of new source-oriented tools and instruments (e.g., new emission standards for light duty vehicles and non-road mobile machinery, on sulphur emissions of certain marine fuels, industrial emissions and eco-design of solid fuel boilers).

The fitness check of the AAQ Directives draws on experience from all Member States, focusing on the period from 2008 to 2018 (i.e., the period in which both Directives were in force). It covers all articles and provisions of the two Directives, looking at the role they have played in meeting the objectives. The fitness check evaluates the **relevance, effectiveness, efficiency, coherence and EU added value of the AAQ Directives**. The fitness check allows the public to participate effectively through a comprehensive stakeholder consultation. In order to receive feedback on this consulta-

tion, the European Commission has organised a number of events:

- Online Public Consultation: this consultation was used to collect views and opinions including via a survey, was carried out in the period 8 May to 31 July 2018.
- Side event during EU Green Week: this event (24 May 2018) provided the city-level perspective on what works well, and what does not, as regards EU Clean Air policies
- First Stakeholder Workshop (18 June 2018) collected stakeholders' views on the main objectives of the Directives within the framework of the evaluation criteria.
- Second Stakeholder Workshop: this event was organised on 15 January, with the objective to receive final feedback assisting in the completion of the evaluation.

The findings of the fitness check will inform further reflections on whether the AAQ Directives are fit for purpose and continue to provide the appropriate legislative framework to ensure protection from adverse impacts on, and risks to, human health and the environment.

Addressing emissions from domestic heating in Poland

Andrzej Guła

Polish Smog Alert/Institute of Environmental Economics Krakow, Poland

Solid fuel combustion in domestic heating is the major source of air pollution in Poland. Low-stack emissions account for 45% of total country PM10 and 88% of PAHs emissions¹. Benzo(a)pyrene annual mean concentrations in densely populated southern regions of Poland exceed even 10 ng/m³. Coal and wood are the prominent sources of heat in Polish households. Out of 5.4 million single family buildings 83% use coal and/or wood boilers for heating.

Significant regulatory reforms assisted by support measures are needed to successfully address low stack pollution. Since 2013 Polish regions have been introducing antismog laws forcing compulsory replacement of solid fuel appliances in the residential sector. So far the most stringent solution has been adopted in the Malopolska region. In Krakow (the capital city of the region) a total ban on using coal and wood enters into force on 1 September 2019, whereas in the whole region using solid fuel appliances that do not meet Ecodesign emission standard will be forbidden since 1 January 2023. Currently, nine out of sixteen regions have adopted antismog laws (setting different standards and time horizons).

Key regulations on the national level include standards for solid fuel appliances placed on the market and solid fuel quality standards. It is estimated that over 150 thousand solid fuel boilers and 100 thousand wood heaters are sold each year in Poland. The first step was made when the ban on marketing solid fuel boilers that do not meet emission standard of class 5 in line with EN 303:5-2012 norm entered into force on 1 July 2018. Introduction of market surveillance and control mechanism, however, is needed to stop illegal marketing of non-complying equipment. Similar regulations for space heaters have not been introduced yet.

In October 2018 the government of Poland launched 25 billion Euro Clean Air program for replacing heat sources and thermal refurbishment of single family buildings. Additionally to this measure, since 1 January 2018 an income tax relief is available for households that undertake thermal refurbishment investments.

The World Bank indicates the necessity to adopt two different financial approaches to non-poor (90%) and poor (10%) households. Whilst incentives for the former group would be based on commercial financing supported with fiscal incentives and small subsidy component, the incentives for the latter group require a much higher subsidy component (even up to 100%)³.

The natural pace of replacing solid fuel boilers amounts to 5 to 7% and relates to technical wear of such equipment. It means that approximately 200 thousand boilers are being replaced each year in the whole country⁴. Initial observations of the Clean Air subsidy program indicate the risk that without introduction of further regulatory and enforcement mechanisms the program will support to the large extend free-riders i.e. those who would replace the boilers even in the absence of the subsidy schemes.

¹The National Centre for Emissions Management. January 2018

²Energy Efficiency Review. Single family buildings. Institute of Environmental Economics. 2018

³Fighting Smog: Energy Efficiency and Anti-Smog in Single Family Buildings in Poland. The World Bank. May 2018

⁴Institute of Environmental Economics. Own estimations

Setting up proper combination of the regulatory, enforcement as well as financial/fiscal measures will be the key challenge in order to successfully address the low-stack emission problem Poland.

Andrzej Guła is an environmental economist. He has advised international financial institutions, governments, regional and local authorities in environmental programs and investments. He is co-founder and a leader of Polish Smog Alert - the social movement that has brought air quality into the mainstream policy discussion. Polish Smog Alert advocates for legal reforms, support schemes and undertakes public campaigns to raise public awareness around air pollution problem. He is also the chairman of the Institute of Environmental Economics, that is non-for profit think-tank developing solutions for environmental and energy efficiency policies.

WHO Urban Health Initiative: creating demand for action against air pollution through health knowledge and leadership

Thiago Herick de Sa, Pierpaolo Mudu, Michael Hinsch, Nathalie Roebbel,
World Health Organization (WHO), Geneva, Switzerland

The World Health Organization's Urban Health Initiative (UHI) aims to reduce deaths and diseases associated with air and climate pollutants, and to enhance health co-benefits from policies and measures to tackle air and climate pollution, particularly at the city level (WHO, 2019). The UHI aims to achieve this by mobilizing and empowering the health sector and using the sector's influential position to promote the implementation of air and climate pollutant reduction strategies, and by demonstrating to the public and decision-makers the full range of health and climate benefits to the local population, that can be achieved from implementing local emission reduction policies and strategies. These aims are based on the understanding that health arguments, incentives and linkages could be more effectively used to unleash action for clean air and better climate (WHO, 2016). Policy change at the municipal level can also inspire other cities and help trigger national decision making for healthier sector policies.

Proposed intervention

Interventions of the UHI rest on three pillars:

- (i) Building access to relevant **health evidence** (highlighting the societal, health care and environmental costs of mitigation inaction, modelling the benefits from mitigation actions, emphasizing the urgency for taking action, while providing clarity on a possible way forward);
- (ii) Building **health competencies** (providing key constituencies in health, environment and other sectors with the knowledge and arguments to support the mitigation of air and climate pollutants, engaging stakeholders in government, academia, civil society and communicating key messages to their patients and the public);
- (iii) Conducting **health communications** activities to raise public awareness on the connection between climate and air pollution and health and catalyzing increased local interest and engagement for action on emission reduction.

Model city process

UHI activities in pilot cities support the implementation of a model process that builds on existing capacities and resources to support the development of a road map, action plan and engaged support for scaling-up policies to tackle sources of air pollutant emissions. The model process includes the following steps:

• **Step I. Baseline and stakeholder analyses** conducted in pilot cities (i) to assess the current state of air quality, climate & air pollutant emissions and their sources (including their expected health impacts) and to identify gaps that need to be filled to allow for the comprehensive collection of data that can support policy action; (ii) to map the relevant parties that need to be engaged, including urban policy makers responsible for key sectors such as health, transport, household energy and waste management; academic institutions; civil society organizations; the media; the private sector, for engagement at various points in the project.**Step II.**

• **Step II. A visioning exercise** conducted as part of a wide stakeholder consultation and engagement process to take stock of results of the baseline analysis and to identify and agree on priority

areas of focus for action on air pollutants, also carefully considering socio-economic determinants and inequalities to orient policies.

- **Step III. In-depth analysis of policy scenarios/interventions on local level** to identify associated air pollution, climate and health risks and benefits, including in economic terms (e.g. impacts on health care costs). Relevant databases will be identified, and cross cutting analyses will be developed with project support. Capacity building activities, including training on the use of tools developed to support these analyses and to support health sector engagement with the public and relevant sectors will be conducted. A tailored communications strategy will be jointly developed and implemented.

- **Step IV. Support for the development of a city-level action plan/strategy or road-map** to support the implementation of the preferred policy scenario/intervention (that was identified by stakeholders and decision makers at the city level).

- **Step V. Development of a monitoring framework** to establish a tracking mechanism to follow up policy change and results from city initiatives to address air pollutants and its sources as well as their link to health.

Activities and preliminary results from pilot projects in Accra (Ghana) and Kathmandu (Nepal)

UHI activities in pilot cities support the implementation of a model process that builds on existing capacities and resources, in close collaboration with local and international partners and through relevant networks, such as the Climate and Clean Air Coalition (CCAC, 2019). This model process supports the development of a road map, action plan and engaged support for scaling-up policies to tackle sources of air pollutant emissions.

In both Accra and Kathmandu, there has been continued effort to develop and adapt analytical tools to identify and address the links between air pollution, its sources, climate and health that can be used across cities from low and middle-income countries (e.g. AirQ+ (WHO EURO, 2019); many of these tools are already available at the WHO website). Local and international experts have been working together to apply these tools and enrich the scientific evidence base about city-level policies and interventions to address air pollutants that have the greatest overall climate and health benefits, including in economic terms. Accra and Kathmandu projects have also facilitated activities to strengthen the capacity of health actors at the policy, programme and service delivery level to engage in cross-sector policy making processes, undertake relevant health analyses and effectively communicate with the general public on linkages between climate and air pollutants, and health.

Accra, the first UHI pilot project, is now at the stage of developing a city-level action plan, using a consultative process with local stakeholders, and building on results from cross cutting analyses of local data and competencies strengthened through UHI activities as well as stocktaking from global experiences. A communication strategy and local campaign has also been developed for the city, building on existing global efforts, and with active engagement from community leaders, experts and local authorities (BreatheLife, 2019). The campaign was tailored to local requirements to support and promote implementation on the ground and to communicate results and lessons learned. Initial trajectory is in line with the UHI expected outcomes, with decision makers already demonstrating an increased interest to adopt policies that address air pollution because of the benefits to health, related cost savings, and the demand from constituents and global interest groups. All these changes will be tracked with a mechanism to follow up policy change and results from city initiati-

ves to address air pollutants and its sources as well as their link to health.

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