The urban health effects and impact of anthropogenic and natural air pollution

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Preface

This doctoral thesis is based on the following publications, which will be referred by their Roman number in the text.

I. Perez L, Medina-Ramón M, Künzli N, Alastuey A, Pey J, Perez N, Garcia R, Tobias A, Querol X, Sunyer J. Size fractionate particulate matter, vehicle traffic, and case-specific daily mortality in Barcelona (Spain). Environ. Sci. Technol. 2009, 43, 4707–4714.

II. Perez L, Tobias A, Querol X, Künzli N, Pey J, Alastuey A, Viana M, Valero N, González-Cabré M, Sunyer J. Coarse particles from Saharan dust and daily mortality. Epidemiology. 2008 Nov;19(6):800-7.

III. Perez L, Sunyer J, Künzli N. Estimating the health and economic benefits associated with reducing air pollution in the Barcelona metropolitan area (Spain). Gac Sanit. DOI:10.1016/j.gaceta.2008.07.002

IV. Künzli N, Perez L, Lurmann F, Hricko A, Penfold B, McConnell R. An attributable risk model for exposures assumed to cause both chronic disease and its exacerbations. Epidemiology. 2008 Mar;19(2):179-85.

V. Perez L, Künzli N, Avol E, Hricko A, Lurmann F, Nicholas E, Gilliland F, Peters J, McConnell R. Global Goods Movement and the Local Burden of Childhood Asthma in Southern California. Am J Public Health. *In press.*

The main text of this doctoral thesis contains the following sections: introduction, background, aims, material and methods, results, discussion, conclusions, and an epilogue. The text is a synthesis of the aforementioned five published scientific papers. Detailed methods, results and discussions for each paper can be found directly in the published papers included in the results section of this text. In addition, an appendix includes a commentary to paper II by the journal that published our paper.

The data used in this thesis is derived in part from three different funded projects: (1) a project from the Department of the Environment from the autonomous government of Catalunya, the Plan Nacional de I&D from the Spanish Ministry of Education and Science and the Ministry of the Environment of Spain to measure mass and composition of particulate matter in Barcelona and to assess and investigate Saharan dust episodes; (2) a project commissioned by the Departament de Medi Ambient i Habitage and the Departament de Salut de la Generalitat de Catalunya (Spain), to evaluate the health impact of PM_{10} in the Barcelona Metropolitan Area; and (3) The studies that evaluate the health impact of air pollution in two communities of Southern California were supported by the USC Children's Environmental Health Center grant, the Hastings Foundation, the Center for Research in Environmental Epidemiology (CREAL), Fundacion IMIM, and ICREA (Barcelona, Spain). The Center for Research in Environmental Epidemiology (CREAL) has provided all the necessary additional support and funding to complete these research and associated thesis.

Based on original research guided by thesis directors, the doctoral candidate's contribution included data compilation, data management, data analyses, and the writing of the five scientific articles that constitute this doctoral thesis. Statistical analyses were conducted with the support of statisticians.

Abstract

The differential role that airborne particulate matter (PM) size fractions, components and sources play in producing adverse health effects is not fully understood. Specific gaps include the role of PM generated by traffic and the effects of PMs generated by natural sources. Source specific air pollution epidemiological research still lacks integration in the risk assessment process, a fundamental tool to inform policy makers and the public about the current situation or the impact of future or past air pollution policies. This thesis addresses both these gaps.

First, to explore the effects of traffic-related PMs, we investigated the association between three independent size fractions: coarse ($PM_{10-2.5}$), intermodal ($PM_{2.5-1}$), and very fine PMs (PM_1), and three health outcomes: short-term respiratory, cardiovascular, and cerebrovascular mortality during the period of March 2003 and December 2005 in Barcelona, Spain. Our results show that all PM size fractions have health effects, although effects vary for the different fractions. We found strong independent associations between daily PM_1 and $PM_{10-2.5}$ and cardiovascular and cerebrovascular mortality. In contrast, daily $PM_{2.5-1}$ was only associated with respiratory mortality. Chemical composition data showed that in Barcelona, PMs are generated in large proportion by vehicle traffic indicating that PMs generated by both traffic-related combustion and non-combustion processes should be considered in air pollution mitigation strategies in urban areas.

Second, to investigate the effects of natural PMs, we studied the interaction effects of Saharan dust days on the association between exposure to $PM_{10-2.5}$ and $PM_{2.5}$ (fine PMs) between March 2003 and December 2004 in Barcelona (Spain) and daily mortality. Winds from the Sahara-Sahel desert region regularly transport large amounts of dust to the Americas, North Africa and Europe. We found increase daily mortality risk from coarse PM exposure during Saharan dust days compared to non-Saharan dust days (*P* value for interaction: 0.05). Although further research is needed, our results support the conclusions that PMs generated by natural sources may have significant health effects.

Finally, to illustrate that local air pollution risk assessments are useful tools in evidence-based public health, we estimated the health and economic benefits that would result from two scenarios of improved air quality in the Barcelona metropolitan area. We developed methods to integrate the newly recognized chronic health effects due to traffic exposure into the risk assessment process. The consequence of this novel approach was illustrated by estimating the preventable burden of childhood asthma associated with air pollution in the southern California communities of Long Beach and Riverside, two communities highly impacted by port and traffic related activities. Our results show that local quantitative risk analyses can promote public health by identifying growing sources of health impact for communities and that the traditional risk assessment approach may underestimate the health impact of long-term environmental exposures that produce both chronic and acute diseases.

This thesis contributes to a better understanding of the link between particulate matter size fraction, sources, and components and health effects, and to improve air pollution health impact assessment methods. Both contributions have important implications for public health and air pollution public policy.

Resumen

El papel diferencial en que las diferentes fracciones de partículas en suspensión en el aire (PMs), sus fuentes y componentes producen efectos adversos para la salud no está completamente entendido. Las lagunas actuales incluyen el papel de las PMs generadas por el tráfico y los efectos de las PMs generadas por fuentes naturales. La investigación epidemiológica relacionada con fuentes todavía falta ser integrada en el proceso de evaluación de impacto, una herramienta fundamental para informar a los tomadores de decisiones y el público sobre la situación actual o el impacto de futuras o pasadas políticas de contaminación atmosférica. Esta tesis trata estas lagunas.

Primero, para explorar el papel de las PMs generadas por tráfico, se ha investigado la asociación entre tres fracciones independientes de PMs: gruesas ($PM_{10-2.5}$), intermodales ($PM_{2.5-1}$), y muy finas (PM_1), y tres indicadores de salud a corto plazo: mortalidad respiratoria, mortalidad cardiovascular y mortalidad cerebrovascular, durante el periodo de marzo 2003 y diciembre 2005 en Barcelona, España. Los resultados muestran que todas las fracciones de PM tienen efectos adversos, pero que los efectos varían según las fracciones. Se ha encontrado efectos independientes entre niveles diarios de PM_1 y $PM_{10-2.5}$ y la mortalidad cardiovascular y cerebrovascular. En contraste, los niveles diarios de $PM_{2.5-1}$ se han visto asociados únicamente con la mortalidad respiratoria. Los análisis químicos han mostrado que en Barcelona, las PMs son generadas en gran proporción por el tráfico de vehículos indicando que las PMs generadas tanto por los procesos de combustión vinculados al tráfico como por otros procesos tienen que ser consideradas en las estrategias de mitigación de la contaminación atmosférica en áreas urbanas.

En segundo lugar, para investigar los efectos de las PMs generadas por procesos naturales, se ha investigado los efectos interactivos entre los días con polvo de Sahara y la asociación con la exposición a $PM_{10-2.5}$ (PMs gruesas) y $PM_{2.5}$ (PMs finas) entre marzo 2003 y diciembre 2004 en Barcelona (España) y mortalidad diaria. Los vientos provenientes de la región desértica del Sahara-Sahel regularmente transportan grandes cantidades de polvo a las Américas, África del norte y Europa. Se ha encontrado un aumento del riesgo de mortalidad para exposición a PM gruesas durante los días de polvo del Sahara en comparación con días sin polvo (P de interacción: 0.05). Aunque se necesita investigación adicional, nuestros resultados respaldan que las PMs generadas por fuentes naturales pueden tener efectos adversos importantes en salud.

Finalmente, para ilustrar que las evaluaciones de impacto a nivel local son herramientas útiles en salud pública, se ha estimado el beneficio en salud y económico que resultaría de dos escenarios de mejora de la calidad del aire in el área metropolitana de Barcelona. Se ha desarrollado métodos que integran en estas evaluaciones los efectos crónicos nuevamente identificados asociados la exposición al tráfico. La consecuencia de este nuevo enfoque se ha ilustrado en estimando el número de casos de asma infantil prevenibles asociados con mejoras de la contaminación atmosférica en dos comunidades impactadas por las actividades del puerto y del trafico asociado en California del Sur, Long Beach y Riverside. Los resultados muestran que las evaluaciones de impacto a nivel local pueden promover la identificación de fuentes crecientes de contaminación y

que las evaluaciones de impacto tradicionales subestiman el impacto total de las exposiciones ambientales u otras que producen efectos tanto a corto como a largo plazo.

Esta tesis contribuye a un mayor entendimiento del vínculo entre las fracciones de PM, sus fuentes y componentes y los efectos en salud así como a la mejora de los métodos de las evaluaciones de impacto. Estas contribuciones tienen importantes implicaciones para la salud pública y las políticas públicas de contaminación atmosférica.

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1. Introduction

Numerous experimental studies conducted in cellular systems, animals, and humans, and as well as large number of epidemiological studies have shown that current levels of ambient anthropogenic air pollution lead to morbidity and mortality in humans. The associations between ambient air pollution and health outcomes established in these studies show small effects at the population level compared to other exposures such as smoking. However, the public health impact of air pollution is substantial in many regions because the whole population is exposed to air pollution, at least to some degree. In addition, exposure to air pollution is entirely involuntary. As a result, mitigation of air pollution health effects depends to a great extent on the decision-making process and public policy. Therefore, air pollution research is critical to guide policy-makers and protect public health.

Although air pollution research conducted in the last decade has dramatically improved the understanding of the link between air pollution and health effects, driving improvements of air quality in many countries, many challenges remain. Important gaps include the processes and mechanisms involved in affecting health of the many components of the air pollution mixture, especially the role of airborne particulate matter in relation to its source, and linking new air pollution source-specific research findings into policy relevant information. This thesis contributes to these areas.

2. Background

2.1 Particulate matter and health effects

The current epidemiological and toxicological air pollution literature indicates that there is no single air pollutant or source responsible for the full range of documented health effects. Various studies suggest that particulate matter (PM), the complex mixture of solid and liquid particles suspended in air, play an important role in these affects. [1, 2]

Consistent associations have been identified between exposure to PM and morbidity, mortality and other patophysiological events. [1, 3-5] Numerous epidemiological studies have shown that short-term PM exposure is associated with increased mortality, hospital admissions, and other respiratory and cardiovascular symptoms. Short-term studies have also shown that exposure to PM may advance death at least a few months for some cardiovascular and respiratory diseases.

Epidemiological long-term studies of PM effects, although less common, have shown associations between PM and a number of chronic diseases. Long-term exposure to current ambient PM concentrations may lead to a marked reduction in life expectancy. The reduction in life expectancy is primarily due to increase in cardio-pulmonary and lung cancer mortality. In addition, exposure to PM is likely to elicit increased lower respiratory symptoms and reduced lung function in children, and chronic obstructive pulmonary disease and reduced lung function in adults.

The epidemiological literature shows that there does not seem to be a threshold concentration below which ambient PM has no effect on health. It is thus likely that within any large human population, there is such a wide range of susceptibility, that some subjects are at risk even at the lowest end of the concentration exposure.

Although further studies are needed to identify susceptible groups, the recent reviews [3, 6, 7] show that in short-term studies, elderly subjects, and subjects with pre-existing health and lung disease are more susceptible to effects of ambient mortality and morbidity. In panel studies, asthmatics have also been shown to respond to ambient PM with more symptoms, larger lung function changes and with increased medication use than non-asthmatics. In long-term studies, it has been suggested that socially disadvantaged and poorly educated population respond more strongly in terms of mortality. PM is also related to reduced lung growth in children. No consistent differences have been found between men and women, nor between smokers and non-smokers in PM responses in long-term studies.

Toxicological and controlled human exposure studies have shown additive health effects for combinations of PM and ozone (O_3), and PM and allergens. [3, 8] Results confirmed by atmospheric chemistry tests demonstrated that PM interacts with gases to and alters its composition and toxicity. However, few epidemiological studies have successfully addressed the interaction of PM with other pollutants. APHEA2, a multi-city study of the short-term health effects of particulate air pollution associated with hospital admissions for respiratory diseases in Europe, found that PM effects on mortality were stronger in areas with high NO_2. This result has been interpreted as

showing that in areas with high NO_2, PM likely contains more toxic substances than in areas with low NO_2. [3]

2.2 Particulate matter composition, sources, and mechanisms of toxicity

PM represents a complex mixture of organic and inorganic substances. PM vary in number, size, shape, surface area, chemical composition, solubility, redox activity, and origin. PMs are generally categorized according to their diameter, with the most common categories including Total Suspended Particles (TSP) which include all particles up to some 30 µm in diameter; PM_{10} which includes particles with a diameter of less than or equal to 10 µm; $PM_{10-2.5,}$ which includes particles with a diameter between 2.5 µm and 10 µm, referred to as "coarse particles"; $PM_{2.5}$ which includes particles with a diameter of less than or equal to 2.5 µm referred to as "fine particles"; PM_1 which include particles with a diameter of less than or equal to 1 µm referred to as "very fine particles"; and $PM_{0.1}$ which include particles with a diameter of less than 0.1 µm (typically in the size range of 1 to 100 nanometers) referred to as "ultrafine particles" (UF). The level of PM pollution is commonly described in terms of mass ($\mu m/m^3$) or number (n per cm^3).

Effects of PM have principally been studied using $PM_{2.5}$ or PM_{10}. More recently, health effects of UF have been investigated. These studies suggest that health effects may be preferentially driven by the finer particles. [2] Fine particles are derived primarily from direct emissions from combustion processes, such as burning of gasoline and diesel in motor vehicles, wood burning, coal burning for power generation, and industrial processes, such as smelters, cement plants, paper mills, and steel mills. Fine particles also consist of transformation products, including sulfate and nitrate particles, which are generated by conversion from primary sulfur and nitrogen oxide emissions and secondary organic aerosol from volatile organic compound emissions. UFs are typically fresh emissions from combustion-related sources, such as vehicle exhaust and atmospheric photochemical reactions. Primary ultrafine particles have a very short life (minutes to hours) and grow rapidly through coagulation and/or condensation to form larger secondary complex aggregates, contributing to the $PM_{2.5}$ range. [2]

The association between fine and ultrafine PM generated by combustion processes, that include traffic-related emissions, and cardiopulmonary outcomes is well documented. [2] Source apportionment studies provide further evidence of this link. For example, a study in six United States (US) cities showed that fine PM generated by combustion processes was associated with daily mortality, while fine PM from crustal sources showed no association. [9] Another study in Phoenix Arizona (US), found that combustion-related pollutants and secondary aerosols were associated with cardiovascular mortality. [10]

Several epidemiological studies have detected short-term effects of coarse particle ($PM_{10-2.5}$) in urban areas for respiratory and cardiovascular mortality. [4, 5, 11-13] The results have been, however, less consistent than for finer PM fractions, suggesting that coarse particles may be harmful, but that their toxicity depends on their source and composition. Source and composition of coarse PM vary considerably between and within geographic areas. [11] Coarse particles can be derived from suspension or re-suspension of dust, soil, or other crustal materials from roads, farming, mining, brakes,

windstorms, or volcanos. Depending on their origin, coarse particles also include sea salts, pollen, mold, spores, and other biologic material.

Amongst the characteristics found to contribute to PM toxicity in epidemiological and controlled exposure studies are metal content, presence of poliaromatic hydrocarbons and other organic components, and presence of endotoxins. [2] A recent review indicated that organic carbon, and transition metals, such as V, Fe, Ni, Cr, Cu, Zn and Mn, are likely related to PM toxicity. [14] In addition, a study of PM in six California counties found consistent associations between elemental carbon, organic carbon, nitrates, Cu, K, Ti and Zn in PM and cardiovascular mortality, and Cu, Ti, V and Zn in PM and respiratory mortality, [15] and a study of PM in Atlanta found an association between elemental carbon, organic carbon, K and Zn and cardiovascular mortality, and sulfates and respiratory visits. [16]

Fine PM (below the $PM_{2.5}$ range) penetrate further into small airways and alveoli than larger PMs. For this reason fine PMs may elicit stronger health effects than coarse particles. [4] New studies also suggest that UFs may be more likely than larger particles to translocate from the lung to the blood, and may thus be responsible for cardiovascular outcomes. [2] A proposed mechanism of action for fine PM involves redox components which reach target sites in the respiratory and cardiovascular system and induce oxidative stress, inflammation, and acute thrombotic complications of atherosclerosis [1, 2] leading to other cerebrovascular outcomes. [17] Although not fully understood, the proposed current mechanism of action for coarse PM holds that pollutants have a direct involvement with neural reflexes [18, 19] or with changes in cardiac autonomic function. [1] There is some evidence that coarse particles may lead to oxidative stress and inflammation as well as neural and cardiac changes. [1] Several toxicologic studies also indicate that coarse particles can elicit inflammatory effects as potent as fine particles. [20-23] The differential role of PM sources, composition and mechanisms of toxicity needs to be explored more fully.

2.3 Air pollution health impact assessments and the decision-making process

Current epidemiological research has shown that individual effects of air pollution are in general rather small. However, the public health impact of air pollution can be substantial. The reason for this paradox is that the whole population is exposed to air pollution, at least to some degree. Air pollution is particularly high in the most densely populated areas, thus, the overall health burden is further increased.

The assessment of the public health impact of ambient air pollution, also referred to as air pollution Health Impact Assessment (HIA), takes into consideration the difference between individual and population risk. HIA translates research findings from the epidemiological or toxicological literature, for example the Relative Risk (RR) or Odds Ratio (OR), into rough quantifications of the total health problems in a given region, country, or city which may be attributable to air pollution.

The methods of the air pollution impact assessment have been developed during the last 15 years. These methods have been discussed in World Health Organization (WHO) committees which have generated recommendations by experts. Governmental agencies in the United Kingdom, Europe, the United States (US), particularly the Californian Environmental Protection Agency (EPA), employ these methods regularly to generate air pollution policy. The method consists of combining (1) the underlying frequency in the population of the disease to which air pollution may contribute; (2) the distribution of the exposure, or how many people are exposed to specific levels of pollution; and (3) the functions derived by epidemiological or toxicological studies which indicate the additional risk of disease due to air pollution.

Air pollution HIA have been applied to various geographic scales ranging from rough global assessments to more sophisticated international, national or local studies. [24-28] So far most evaluations have provided crude estimates for different health problems, such as death, hospital admissions, and respiratory problems attributable to air pollution and for selected changes in air pollution levels which represent future or past policy scenarios. In most evaluations, changes in regional air pollutant levels such as PM_{10}, $PM_{2.5}$, NO_2 or O_3 have been used as exposure scenario metrics. Some studies have attributed part of the regional pollutants to specific sources, such as traffic, to estimate source-specific impact. [29]

Every society has limited resources to allocate to projects. Policy makers need information that will help them make decisions on the suitability or prioritization of public policy development and plans. Cost-benefit analysis based on monetary valuation of health benefits are sometimes an integral part of HIAs.

2.4 Missing links

2.4.1 Linking particulate matter health effects, sources and components

PM levels in many countries are regulated according to their sizes with two fractions represented: $PM_{2.5}$ and PM_{10}. Although these size fractions may indirectly reflect different sources, the underlying assumption of this approach is of a uniform toxicity of all PM independently of their composition. However, it is unclear what PM components are causally related to the observed health effects. Therefore current legislation may not regulate the most relevant metric to protect health. Further research is needed to explore the link between different PM size fractions, components, sources and health effects to improve the air pollution regulation.

Of special interest is PM generated by traffic. Particle emissions from transport-related activities are recognized as the most important sources contributing to the PM mass concentrations in urban environments. [30] However, the role of traffic-related PMs in producing health effects is not clear. Traffic-related PMs are thus not directly regulated. The US removed annual threshold levels for PM_{10} from its regulation, arguing that most long-term health effects are due to exposure to fine combustion-related PMs only. Coarse PM has typically been associated with terragenous sources, [11] however, recent

studies have shown that a large fraction of coarse PM in urban areas is formed by re-suspended tire, brake and pavement residue, and that some of these components are similar to components found in combustion PM [31-35]. There is some toxicological evidence to suggest that this specific type of coarse particles may have similar effects to other combustion-generated fine PMs, although contrasting results exist [13, 36, 37]. If some components are common to fine and coarse PM fractions, the various chemicals adsorbed onto the surfaces of PM may be relevant in the toxicity of all size fractions and generate common mechanisms of toxicity. A further understanding of this link is thus necessary, before adverse health effects of all coarse particles can be disregarded.

In addition, recent studies using improved traffic exposure models have shown that residential exposure to traffic emissions is associated with a range of outcomes [38-40]. Reducing the traffic-related health burden requires mitigation strategies that take into account all the components of traffic exposure. The contribution of traffic-related PMs in generating these health effects remains to be resolved in order to identify the type of metric to be regulated to mitigate the effects of traffic exposure.

It is also necessary to consider the different health effects of PM generated by natural and urban sources. Most cities around the world affected by episodes of high wind blow dust from natural sources such as deserts, have implemented warning systems to advise vulnerable populations about days with high PM load. In contrast, new legislation in Europe has removed limits from so-called "natural" contributions to PM_{10} under the assumptions that these contributions are harmless.

Every year, winds from the Sahara-Sahel desert regions transport large amounts of dust across the Atlantic to the Americas, and across North Africa and the Mediterranean to Europe. [41, 42] Affected regions show increased ambient air dust concentrations that may last several days. In areas such as southern Europe, Saharan dust events are a recurrent air-quality problem. [43] While contrasting results have been found in other urban areas of the world also affected by desert dust, [44-48] there is a small but growing body of evidence showing that Saharan dust may contribute to exacerbate health effects. For example, Saharan dust cover, increased pediatric asthma accident and emergency admissions on the Caribbean island of Trinidad. [49] PM_{10} on Saharan dust events has also been associated with increase hospital admissions in the west Mediterranean. [50] Saharan dust has been shown to carry large amounts of biogenic factors, such as microbes and fungus, providing a biological plausibility for triggering health effects. [41, 42, 51-53] In light of the new regulation and to design sound public health warning plans, the health impact of dust outbreaks from Saharan dust need to be further explored for European and other populations.

2.4.2 Integrating sources and chronic diseases in air pollution health impact assessment

Regional air pollution HIAs rarely take into account local sources of pollution. Most assessments use large scale or global pollutant levels to evaluate the burden of air pollution in a region. These large-scale analyses obscure the local impact, and may provide only limited information to local policy making. For example, many coastal cities are planning large port development and related transportation infrastructure projects to facilitate the expected increase in goods moving throughout the world. [54,

55] Global and regional scale analysis has shown that shipping-related PM emissions are responsible for approximately 60,000 cardiopulmonary and lung cancer deaths annually, with most deaths occurring near coastlines in Europe, East Asia, and South Asia. [56] But there has been only limited formal evaluation of the health impact of these developments for these affected communities. Further studies to identify special local effects are necessary.

Another major limitation of regional air pollution HIAs is that they currently do not properly assess the impact specifically associated with traffic-related pollutant exposure. Of special interest is the emerging evidence indicating that living at proximity of traffic, as proxy for traffic-related exposure, is associated with chronic respiratory and cardiovascular morbidity. These studies have shown an association with severity and persistence of asthma and increased risk of asthma incidence. [38, 57] Another study on the effects of exposure to traffic on lung development showed that children who lived within 500m of a freeway had substantial deficits in 8-year growth of forced expiratory volume in one second (FEV_1) and maximum midexpiratory flow rate (MMEF) compared with children who lived at least 1500m from a freeway. [58] Living close to busy roads has also been associated with risk of term low birth weight and preterm birth. [59] In addition, results of recent studies in Germany also suggest a possible link between long-term residential exposure to high traffic, represented in that study by residential exposure within 150m of major highways and 100m of major road, and the prevalence of coronary heart disease and the degree of coronary atherosclerosis, respectively. [39, 60, 61] Cardiovascular disease is the main cause of death in many countries with development of atherosclerosis being a common underlying factor. Scientists have shown that exhaust pollutants, such as UFs, CO, or other primary gases, such as PMs, reach very high concentrations along streets. [62] Exposure to these pollutants can thus be very high during the commuting time and while walking, playing, or living close to such streets, further indicating an important role of traffic pollutants as a source of adverse health effects. However, HIAs using regional pollutants overlook the role of highly reactive local traffic-related pollutants. In addition, these recent studies point to an additional limitation. Standard HIAs quantify acute effects such as cardiorespiratory hospitalizations, bronchitis or asthma episodes, and myocardial infarction. However, as listed above, recent studies also show that local traffic exposure may be associated with chronic effects, such as asthma onset and atherosclerosis. Given this evidence, it is necessary to develop a more comprehensive approach to assessing the total disease burden in HIAs.

3. Aims

The objectives of this thesis are:

3.1 Objective 1

To investigate the health effects of different PM size fractions, components, and sources, with a focus on PM generated by traffic and PM from natural sources.

- We investigated the association between three independent size fractions; coarse ($PM_{10-2.5}$), intermodal ($PM_{2.5-1}$), and very fine PMs (PM_1), and three health outcomes: respiratory, cardiovascular, and cerebrovascular mortality in Barcelona (Spain). Using existing data, we examined the chemical composition of each fraction, to explore the effects of PM from different sources, and mechanisms of action (paper I).

- We investigated the effects of exposure to $PM_{10-2.5}$ and $PM_{2.5}$ in Barcelona (Spain) on daily mortality, and changes of effects between Saharan and non-Saharan dust days. We studied the chemical composition of particulate matter to explain changes of effects, and mechanisms of action (paper II).

3.2 Objective 2

To integrate impact of local sources and novel air pollution epidemiological research into the risk assessment process and illustrate implications for local public health and public policy.

- We estimated the health and economic benefits that would result from two scenarios of improved air quality in 57 municipalities of the metropolitan area of Barcelona (Spain) (paper III).

- We expanded traditional risk assessment methods to estimate the attributable risk for exacerbation under a “chronic disease model” (paper IV).

- We estimated the preventable burden of childhood asthma associated with air pollution in the southern California communities of Long Beach and Riverside, taking into account port and traffic-related sources (paper V).

4. Materials and Methods

This section provides a brief summary of the methods used in this thesis. Further methodological details for each paper can be found in the results section.

4.1 Objective 1

4.1.1 Study area

Studies from paper I and II were conducted in the city of Barcelona, located on the North-east Mediterranean coast. The city of Barcelona has a population of approximately 1.8 million inhabitants and is one of the densely populated cities in Europe. [63] The high population density results in the majority of people living and working in square-blocks type areas adjacent to streets and main arteries with high road traffic.

4.1.2 Air pollution data

Daily levels of particulate matter (PM) concentrations were obtained between March 27, 2003 and December 31, 2005 from real time measurements performed at a single monitor site. Paper I analyzed data from the whole period while paper II analyzed data until end of 2004. The PM monitoring site is an urban background station and is exposed to road traffic emissions from the Diagonal Avenue (approximately 150m distance), one of the largest arteries in the city.

An optical counter was used for real time PM_{10}, $PM_{2.5}$ and PM_1 measurements. The data was continuously validated and corrected by gravimetric methods. This was done by simultaneously collecting (three 24h samples/week for each size fraction for the whole study period) PM_{10}, $PM_{2.5}$ and PM_1 samples by high-volume samplers (30 m^3/h) equipped with DIGITEL cat off inlets and quartz microfiber filters (Schleicher & Schuell QF20). Daily mass concentrations for coarse particles ($PM_{10-2.5}$) and intermodal particles ($PM_{2.5-1}$) were obtained by subtracting $PM_{2.5}$ from PM_{10}, and PM_1 from $PM_{2.5}$, respectively. All days for which PM_{10}, $PM_{2.5}$ and PM_1 data was available were retained. Days on which at least one fraction measurement was missing or presented improbable results (i.e. $PM_{10-2.5}$ greater than $PM_{2.5}$) were discarded. In addition to PM mass, the chemical composition of PM was also determined on samples collected in filters approximately once a week from October 1, 2005 to October 1, 2006. The speciation scheme was based on the analysis of major and trace elements by inductively coupled plasma atomic emission spectroscopy (ICP-AES) and inductively coupled plasma-mass spectrometry (ICP-MS), soluble anions by ion chromatography, ammonium by selective electrode (the two last techniques on water extractions of a 1 4 of each filter) and total carbon by elemental LECO analyzer. Sampling, analytical, validation and quality control methods for masss and chemical analysis have been previously described in detailed. [31, 64] For reporting, major elements were grouped according to their major origin in non-mineral carbon (nmC), total carbon, crustal (silicates, carbonates and oxides) and marine (sodium and chloride) aerosol elements, inorganic secondary components (sulfate, nitrate and ammonium).

4.1.3 Identification of Saharan dust days

For paper II, we identified Saharan dust outbreaks using a two-step process. First, back-trajectory analysis (Hysplit model) was performed using information obtained from NRL [65], SKIRON [66], and BSC-DREAM dust maps, [67] as well as satellite images provided by the NASA SeaWiFS project. [68] These tools made it possible to identify days on which air masses from the Sahara-Sahel region were transported to Northeastern Spain. Second, days on which air mass transport occurred were classified as Saharan dust days in Barcelona, if levels of PM_{10} concentrations measured at a reference remote rural monitoring site reached at least 50% of the PM_{10} levels measured at the urban sampling site in Barcelona. The rural monitoring site (Montseny) is located approximately 60 km north of the city of Barcelona, (700 m above sea level). As for the urban site in Barcelona, we used laser spectrometers to determine real time $PM_{2.5}$ and PM_{10} measurements at the background monitor.

4.1.4 Daily mortality

Daily mortality in Barcelona was obtained from the Catalan mortality registry for years 2003 to 2005. For paper I, the outcomes of interest were respiratory mortality (ICD code, 10^{th} revision: J00-J99), cardiovascular mortality (ICD-10: I00-I99), and cerebrovascular mortality (ICD-10: I60-I69). For paper II the outcome of interest was all-cause natural daily mortality (ICD-10: A00-R99). Deaths from external causes (including injury, poisoning and accidents) were not included in the analysis.

4.1.5 Study design and statistical analysis

The association between daily concentrations of $PM_{10-2.5,}$ $PM_{2.5-1,}$ PM_1 and total and cause-specific mortality was investigated using a case-crossover design. The case-crossover design uses the day when the event of interest (i.e. death) occurred as a case day. Exposure at case days is compared with exposure at days in which the event did not happen (control days). [69] Thus, under the null hypothesis, exposure should not differ between control and case days. A time-stratified approach was followed for the selection of control days. Namely, we selected control days from the same day of the week, month and year as case days. The association between mortality and PM was estimated using conditional logistic regression models with adjustment for several variables. In paper I, to take into account the non-linear relationship between temperature and mortality, multivariable fractional polynomials were used to estimate the transformation on two temperature variables to determine their appropriate non-linear functional form with mortality. [70] We used one temperature average to control for the immediate effects dominated by heat (average of day of exposure and one day before exposure) and a second temperature average to control for effects of lower temperatures at longer lags (average third, fourth and fifth day before exposure). [71] In paper II, models were adjusted for four-day average temperature only. Models were also adjusted for the five-day average humidity (day of exposure and four days before exposure), for bank holidays and flu epidemic weeks using dummy indicators. Flu epidemic weeks were defined as weeks with relative deviation of incidence of flu cases compared to a baseline incidence defined by Spanish information. [72] [73] During the study period, the baseline incidence for a flu epidemic was 60 cases per 100,000 people. Between June and August 2003, record-breaking high temperatures were reported

across Europe including Spain. [74] Models were adjusted by heatwave days defined as days between the periods of June 10th-July 1st and July 8th-August 30st with daily average temperatures above 30ºC.

The effects of exposure to $PM_{10-2.5,}$ $PM_{2.5-1,}$ and PM_1 were examined for the same day (lag 0) and up to four days after exposure (lag 4) as well as for the multi-day average of exposure between lag0 and lag1. Results of models adjusted by the variables mentioned previously (one-pollutant model) were compared with models that were further adjusted by the other two size fraction mass concentrations (two or three-pollutant model, in paper II and I, respectively). In paper II, effect modification by Saharan dust outbreaks was examined by creating a dummy variable for the presence or absence of Saharan dust at exposure days. In paper I, we adjusted all models for the presence or absence of Saharan dust days without looking at interaction effects. In paper II, comparison of changes in adjusted mass and chemical concentration during Saharan and non-Saharan dust days was also carried out by multivariate linear regression.

Different sensitivity analyses were conducted to test the robustness of our models. Sensitivity analysis included changing the definition of heatwave days, restricting the analysis to individuals above 75 years old, and analysis of data using autoregressive Poisson regression models instead of case-crossover in case of paper I. Additional models also tested the effect of co-pollutants in our results by adjusting for both 24-hour mean NO_2 and 8-hour mean O_3 levels. NO_2 levels were derived from measurements at two urban background monitoring stations in the city, while 8-hour O_3 levels were derived from measurements at four different urban background monitoring stations.

4.2 Objective 2

4.2.1 Derivation of population attributable fractions

For paper III, IV, and V, we quantified the number of outcomes attributable to air pollution by deriving population attributable risk fractions (PAFs). The derivation of PAFs combines several elements. These include the concentration-response functions (CRF-the quantitative association between markers of air pollution and selected outcomes derived from epidemiological studies), the frequency of health conditions in the population of interest, the current population exposure to the markers of air pollution selected, and the population exposure hypothesized after scenarios of air pollution reduction. The detail of the methodological approach for each paper can be found in the original papers in the Appendix.

In all papers, we expressed results as the number of attributable cases for the change of exposure under consideration. Attributable cases are interpreted as the number of health events that could be prevented per year if air pollution was reduced. Attributable cases were derived from the attributable population fractions applied to number of outcome cases in the population. All calculations were conducted at the aggregated level of the different study areas. Attributable fractions were derived with the standard formula $AF_{pop}=[p_p (RR-1)] / [pp (RR-1)+1]$, where p_p represents the fraction of the population exposed to air pollution and assumed as one, and RR represents the relative risk (RR) of the CRF for the change in PM_{10} exposure considered. RR is derived as $RR=\exp(\beta x \Delta C)$

with β the slope of the CRF expressed for 1 μg/m^3 and ΔC the change in exposure considered in μg/m^3 in the case of regional pollutants The statistical models used to derive CRFs most often provide odds ratios (OR) from logistic regression models rather than RR. For rare events or small effects, RR and OR are similar, however, for frequent events and when the OR is large, OR may overestimate the true RR. To take this into account, we corrected OR with a standard formula. [75]

4.2.2 Modified attributable risk model

Paper V present results based on a modified risk model in comparison to the traditional "population attributable fraction" approach presented in 4.2.1. The modified risk analysis model operates under the assumption that the burden of air pollution is a combination of effects on both onset of disease and acute exacerbations among those with the underlying disease. The details of the methods, revised equations, and an illustrative example are provided in paper IV that can be found in the Appendix. The main steps of the modified methodology are summarized below.

The total attributable risk under the model of both chronic and acute effects is done in three steps. First, the fraction of chronic diseases attributable to the exposure of interest, in our case traffic-related pollution, is estimated. To date the studies that have found an association of traffic with chronic diseases used residential distance to busy road as exposure, thus for this quantification, the number of residents living at distance of busy roads was estimated using georeference tools. Second, the fraction of exacerbations triggered by exposure, in our case regional air pollution, among all those with the chronic disease is estimated. This represents the fraction of acute diseases attributable to the exposure. Third, among those with the chronic disease due to the exposure, the number of exacerbations due to causes, for example resulting from a range of other non-specified exogenous and endogenous triggers, is quantified.

4.2.3 Derivation of life years lost

The concept of attributable or preventable death is conceptually flawed as death is ultimately not preventable but can only be postponed. Those exposed to lower pollution would in fact in average have a longer life expectancy due to reduction in death rates. In paper III, we estimated average increase in life expectancy in addition to attributable death for our study population using standard life table methods. [76]

4.2.4 Monetary valuation of health benefits

In paper III, we attached a monetary valuation to our health estimates. Economists in different settings have attempted to develop alternative measures of values for benefits arising from clean air. [77] Ideally these measures should represent all the losses to individuals and to society that result from adverse health effects, and reflect preferences and decision-making processes similar to those of daily life. [77] In this evaluation, the value to attach to a reduction of the risk of death and other end points were based on the Willingness-To-Pay (WTP) approach. Unit monetary values based on WTP are derived from market choices that reduce risk to health or life indirectly. [77] We used same

monetary values as those proposed in the air pollution European cost-benefit analysis and derived from empiric studies. [25] In this latter evaluation, a mean and median value are proposed for some outcomes. Since no consensus has been reached as to which value reflects better the value of health, [25] we used a single mid monetary unit in the core estimates and discussed the impact of the variability of values in the sensitivity analysis. Values were transformed to 2006-price year using the real gross domestic product average annual increase for Spain. [78]. Economic benefits were calculated multiplying the unit monetary value by the number of attributable cases obtained for each scenario.

4.2.5 Expression of uncertainty

The various steps of the risk analysis come with a range of assumptions and uncertainties, which differ for the different outcomes. To reflect these uncertainties results in papers III, IV and V were presented with a point estimate as well as an upper and lower bound given by the 95% confidence interval (95%CI) of the CRF. In paper V, Monte Carlo simulations were also used to generate uncertainty distributions for outcomes that required combining two sets of CRF when taking into account asthma onset due to living close to busy roads. Several steps of the risk analysis have assumptions and uncertainties that limit our results. Some of the main limitations are addressed in the discussion section of this thesis. A series of additional sensitivity analyses were also conducted to illustrate the impact on our estimates of alternative approaches. Details of the sensitivity analysis results and a complete discussion of the limitations can be found in the original papers.

5. Results

This section provides the published papers constituting this thesis that include the detailed research results.

5.1 Objective 1

5.1.1 Paper I

Perez L, Medina-Ramón M, Künzli N, Alastuey A, Pey J, Pérez N, Garcia R, Tobias A, Querol X, Sunyer J.
Size Fractionate Particulate Matter, Vehicle Traffic, and Case-Specific Daily Mortality in Barcelona, Spain.
Environ Sci Technol. 2009 Jul 1;43(13):4707-14.

5.1.2 Paper II

Perez L, Tobias A, Querol X, Künzli N, Pey J, Alastuey A, Viana M, Valero N, González-Cabré M, Sunyer J.
Coarse particles from Saharan dust and daily mortality.
Epidemiology. 2008 Nov;19(6):800-7.

5.2 Objective 2
5.2.1 Paper III

Pérez L, Sunyer J, Künzli N.
Estimating the health and economic benefits associated with reducing air pollution in the Barcelona metropolitan area (Spain). Gac Sanit. 2009 Jul-Aug;23(4):287-94.

5.2.2 Paper IV

Künzli N, Perez L, Lurmann F, Hricko A, Penfold B, McConnell R. *An attributable risk model for exposures assumed to cause both chronic disease and its exacerbations.* Epidemiology. 2008 Mar;19(2):179-85.

5.2.3 Paper V

Perez L, Künzli N, Avol E, Hricko AM, Lurmann F, Nicholas E, Gilliland F, Peters J, McConnell R.
Global goods movement and the local burden of childhood asthma in southern California.
Am J Public Health. 2009 Nov;99 Suppl 3:S622-8.

Global Goods Movement and the Local Burden of Childhood Asthma in Southern California

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RUNNING HEAD

Ship emissions, traffic and childhood asthma

KEY WORDS

Ships, vehicle emissions, asthma, child, risk assessment, air pollution

ETHIC COMPLIANCES

This study complies with the Public Health Code of Ethics of the American Public Health Association.

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ABSTRACT

As part of a community-based participatory research effort, we estimated the preventable burden of childhood asthma associated with air pollution in the southern California communities of Long Beach and Riverside. Both have heavy automobile traffic corridors as well as truck traffic and regional pollution originating in the Los Angeles-Long Beach port complex, the largest in the United States. Novel features of the analysis include the assessment of newly recognized health effects due to residential proximity to major roads and an assessment of the impact of ship emissions. Approximately 1600 (9%) of all childhood asthma cases in Long Beach and 690 (6%) in Riverside were attributed to traffic proximity. Ship emissions accounted for 1400 (21%) bronchitis episodes and in more modest proportions of health care visits for asthma. Considerably greater reductions in asthma morbidity could be obtained by reducing NO_2 and O_3 concentrations to levels found in clean coastal communities. Community-based quantitative risk analyses can improve our understanding of health problems and help promote public health in transportation planning.

Word count 168 (max 180)

INTRODUCTION

Community groups in southern California have been increasingly concerned about the health effects of exposure to some of the highest urban air pollution in the United States. Statewide risk assessments have concluded that substantial cardiovascular and respiratory disease mortality and large numbers of cardio-respiratory emergency visits and hospitalizations, asthma exacerbations and chronic bronchitis are attributable to high levels of particulate matter and ozone (O_3) (1, 2). However, only rarely has this methodology been applied to smaller geographical scales taking into account local air pollution conditions and sources.

Information about the local health burden of air pollution would be useful for evaluating proposals to expand port facilities and transportation infrastructure in the Los Angeles air basin. Expansion at the adjacent ports of Long Beach and Los Angeles, the largest port complex in the country, has resulted in an increasing contribution to the region's air pollution. Air emissions from ships, yard equipment, railroads, and trucks account for about 10% of the daily particulate matter, 24% of nitrogen oxides, and 73% of the daily sulfur oxides, in the entire Los Angeles air basin (3). Ship emissions alone contribute substantially to coastal and inland air pollution (4). A doubling or tripling of cargo through the region by 2025 is predicted (5, 6), threatening decades of progress in reducing levels of air pollution.

As part of a community-based participatory research effort to provide information that could help communities evaluate plans for port expansion, we estimated the burden of childhood asthma due to air pollution in the Southern California cities of Long Beach (population 136 000) and Riverside (population 76 500). Residents from these communities have challenged

port expansion based on concerns about the health effects of ship emissions and of traffic proximity, which have not been well-characterized in prior health risk assessments (7, 8).

Novel features of our effort include an assessment of the impact of residential proximity to major roads on the burden of childhood asthma. Recent research suggests that traffic proximity is not only associated with severity and persistence of asthma in children but also with increased risk of asthma onset (9-11). In addition, we have evaluated the burden of childhood asthma attributable to ship emissions as an example of one specific source of port related pollution effects.

METHODS

We quantified the number of childhood asthma-related illnesses that could be prevented if air quality were improved in the Long Beach and Riverside community by deriving population attributable risk fractions (PAFs). The derivation of PAFs combines several elements. These include the concentration-response functions (the quantitative association between markers of air pollution and selected outcomes derived from epidemiological studies), the frequency of health conditions in the population of interest, the current population exposure to the markers of air pollution selected, and the population exposure hypothesized after scenarios of air pollution reduction.

The concentration-response functions (CRFs) for the outcomes selected for this study are shown in Table 1. Choice of outcomes was limited by the availability of the frequency of health conditions for the population under study. CRFs for bronchitis episodes among asthmatics, and lifetime asthma, were based on the Southern California Children's Health Study (CHS), a large population based study of air pollution and respiratory health, which included the Long Beach and Riverside areas (12). For other outcomes, appropriate studies had not been conducted in Southern California populations, so CRFs were selected if they had been used in previous peer-reviewed health impact assessments or were conducted in populations similar to the populations under study. If these criteria could not be met, recent studies were preferred over older studies. The comparability of results using alternative CRFs for these outcomes was tested in uncertainty analyses. The statistical models used to derive CRFs most often provide odds ratios (ORs) from logistic regression models rather than RR. To control for overestimation of the OR for frequent events, we corrected OR with a standard formula (13, 14). Table 1 presents published and corrected CRFs.

Burden of disease was estimated for NO_2 and O_3, which were available for both risk assessment scenarios considered below. NO_2 has been found to have a regional distribution and effects across southern California communities similar to that for particulate pollution (15). There are high levels of NO_2 in Long Beach and of both NO_2 and O_3 in Riverside. NO_2 in Long Beach is generated largely by combustion emissions from automobiles and other mobile sources related to goods movement (i.e. ships. harbor craft and other vehicles at the port, rail and truck traffic). O_3 is a product of atmospheric photochemistry, heavily influenced by upwind emissions of primary air pollutants (such as those from the port and vehicular traffic). Dominant regional wind trajectories transport emissions from the port communities (including Long Beach) to the Riverside area, approximately 50 miles inland (4). (Figure 1). The Riverside area is also one of several communities that has undergone rapid development to accommodate increased population and to facilitate cargo processing from the ports in large mega-warehouses before redistribution to the rest of the country, resulting in heavy truck and automobile traffic. Current community population exposures were estimated from the 8-year mean concentration (1996-2004) of NO_2 and O_3 measured at continuously-operating CHS monitoring stations in each community (4, 12) The frequency of health conditions in the population of interest and exposure levels in the two communities are shown in Table 2.

We provided estimates for two scenarios of exposure reduction. Scenario 1 quantified the burden of disease related to the contribution from ships alone while ignoring all other port-related activities. This scenario was based on a recent study that modeled the impact of emissions from ocean-going ships on NO_2 concentrations during episodic conditions in Southern California (4). Ship emissions were estimated to contribute 5.9 ppb and 2 ppb of NO_2 in Long Beach and Riverside, respectively (4) (although the contribution of ship emissions to O_3 was also estimated from this study, the episodic conditions were appropriate

only for estimating the contribution to long-term NO_2 exposure),. Scenario 2 estimated the reduction in disease that would result if NO_2 levels were reduced to concentrations present in the cleaner coastal southern Californian communities (about 15 ppb) (12). Under this scenario, current population exposure to NO_2 would have to be lowered by 18 ppb and 11 ppb in Long Beach and Riverside, respectively. For O_3, we assumed that the annual 8-hour mean concentration would be decreased to 30 ppb, corresponding to a 27 ppb exposure reduction in Riverside. Due to chemical reactions with high concentrations of NO, O_3 levels in Long Beach are, on average, below levels found in many coastal communities. Thus, O_3 burden was not evaluated for Long Beach. Population exposure under the two exposure reduction scenarios considered are presented in Table 2.

The CHS and other recent studies have demonstrated associations between living close to busy roads and asthma prevalence (10, 11, 16). For the asthma prevalence attribution, we used the CRF determined in a previous CHS study demonstrating an association with a busy road within 75m of children's homes (10). The detailed methods used to derive the number of children living within 75m of a busy road are described elsewhere (9). The census block population was uniformly assigned to grids representing households, and the distance from the nearest major road to these grids was assigned using geo-referenced software tools. As an exposure reduction scenario, we assumed that the current number of children living in the first 75 meters of busy roads would be reduced to zero, or that the high concentrations of toxicants along traffic arteries would fall to levels existing in areas more than 75 meters from busy roads.

The attribution of prevalent cases of asthma to residential traffic proximity has substantial implications for the burden of asthma-related exacerbation due to air pollution. If air pollution

increases risk of developing asthma, then all acute future consequences of having asthma should be attributed to air pollution in those individuals, regardless of subsequent causes of exacerbations. (17) Therefore, we extended our analysis to account for the burden of asthma associated with these effects using recently published methods (9). First, the number of asthma cases associated with living close to busy roads was estimated. Then, for each regional pollutant scenario described above, we estimated the yearly number of each asthma-related exacerbation outcome due to all causes (not just air pollution) among these cases using the attributable fraction formula.

For each regional pollutant scenario, we also estimated the yearly number of each respiratory outcome attributable to pollution among children with asthma not attributable to traffic proximity, a standard approach in health risk assessment of regional pollutant effects. These estimates were then added to the number of asthma exacerbations among children with asthma attributable to traffic proximity to obtain the total number of each exacerbation attributable to air pollution.

To reflect statistical uncertainty, results are presented with both a point estimate and an upper and lower bounds corresponding to the 95% confidence interval of the CRF. Monte Carlo simulations were used to generate uncertainty distributions for outcomes that required combining two sets of CRF when taking into account asthma onset due to living close to busy roads. Several steps of the risk analysis have assumptions and uncertainties that limit our results. These limitations are addressed in the discussion section. A series of additional sensitivity analyses were also conducted to illustrate the impact on our estimates of alternative approaches.

RESULTS

Approximately 1,600 cases of childhood asthma in Long Beach (9% of all cases) and 690 in Riverside (6% of all cases) were attributable to traffic proximity (Table 3), based on evidence that living close to busy roads causes new onset asthma. These local traffic proximity effects are independent of the effects of regional pollutants and so were the same for each regional pollutant scenario.

Without taking into account the impact of traffic-induced asthma, we estimated that eliminating ship emissions would result in reduction of the number of asthma related bronchitis episodes among asthmatics by 1,400 (21% of all cases) in Long Beach and 3,400 (8% of all cases) in Riverside, and that total number of health care facility visits, including emergency room visits, clinic visits and hospital admission, would decrease by 224 (1% of all visits) in Long Beach and 50 (0.4%) in Riverside. (See the first column under scenario 1 in Table 3). Further reduction of NO_2 concentrations to levels found in clean communities in Southern California would result in corresponding reductions in asthma exacerbation that are three- to five-fold those observed in scenario 1 (see first column under scenario 2). For example, if NO_2 were reduced to levels found in clean communities, 3,400 bronchitis episodes in Long Beach (50% of all episodes) and 1,600 in Riverside (36% of all episodes) could be prevented. O_3 reduction in Riverside to background levels would reduce the number of bronchitis episodes among asthmatics by 3,100 (70% of all episodes), and the number of health care facility visits for asthma by 482 (4% of all visits).

There was substantial impact of residential traffic proximity on asthma exacerbation, because exacerbation of asthma from any cause was attributable to traffic proximity among children who would not have developed asthma if they did not live near busy roadways. For example,

the preventable proportion of bronchitis episodes increased from 1,400 (21% of all episodes) to 1,900 (28% of all episodes) in Long Beach (third column under scenario 1) and from 3,400 (50% of all episodes) to 3,700 (55% of all episodes) (third column under scenario 2), after accounting for effects of NO_2 among children with asthma attributed to traffic proximity. The biggest relative impact of traffic proximity-attributable asthma on exacerbation was for asthma-related clinic visits, emergency department visits and hospital admissions.

Figure 2 shows selected sensitivity analyses for Riverside, which were conducted to evaluate the impact of assumptions made in the primary analyses and the associated uncertainty. The uncertainty is expressed as a percent change from estimates in Table 3 for cases attributable to O_3 and for asthma cases due to traffic proximity. The 95% confidence interval of the CRF is the source of large uncertainty, however, the available CRFs for the outcomes considered in this study were limited. The upper and lower bounds range around +/-30% for hospital admissions and +/-90% for clinic visits. Large bounds were also found for cases attributable to NO_2 (results not shown). Figure 2 also shows the impact of using alternative CRFs, which were generally less influential than statistical uncertainty but had important effects for some outcomes. For O_3, bounds varied between -10% for emergency room visits and -80% for bronchitis episodes. Error in asthma prevalence (+/- 20%) assumed for the risk assessment and in outcome incidence (+/-20%) had relatively modest impact on estimates of the burden of bronchitis, emergency room visits and other outcomes, compared to other uncertainties. The +/-20% error in outcome frequencies were selected to include a plausible range of diagnostic misclassification. For example, asthma frequencies in the CHS varied depending on alternative definitions of asthma definition, which was 14% if defined as physician-diagnosed asthma; 13% if defined as current severe symptoms and use of controller medications, or lifetime asthma with current wheeze, and 15% if defined as current wheeze

during the previous year (10). Finally, Figure 2 shows the impact on asthma prevalence of a reduction scenario in which 5% of the Riverside population were assumed to live within 75m of a busy road instead of 0% as in the primary analysis. In this case, the proportion of all Riverside asthma cases attributable to air pollution would be only 4 % lower than the primary estimate. However, this modest difference would have important impacts on the number of superimposed acute exacerbations attributable to reduction of regional air pollutants.

DISCUSSION

This health risk assessment was undertaken to provide credible estimates of the burden of air pollution-attributable childhood asthma for community groups concerned about the impact of the continued expansion of goods movement in southern California. We focused on childhood asthma, because its importance has been under-appreciated in traditional risk assessment, and this study is one of the first, to our knowledge, to estimate the population burden of asthma and asthma exacerbation caused by traffic proximity. Our results indicate that heavy traffic corridors in Long Beach and Riverside are responsible for a large preventable burden of childhood asthma prevalence, accounting for 6-9% of all cases of this most common chronic disease of childhood. O_3 from upwind sources and NO_2 from ships and from both regional and local sources were responsible for a significant burden of asthma exacerbation. Asthma cases attributable to traffic proximity had a large impact on the total burden of exacerbations, especially for common outcomes with weak (or no) association with regional air pollution in previous studies, because no exacerbation would have occurred in these children had asthma not developed due to residential traffic proximity.

The contribution of goods movement through the port to the burden of childhood asthma is difficult to quantify. However, the morbidity associated with ship emissions alone indicates that the port is an important contributor to the public health impact of air pollution in the Los Angeles basin. Port expansion has been promoted as an "economic engine" for the region (6), and there are currently several large transportation infrastructure development projects underway to facilitate the expected increase in goods moving through the region to the rest of the country. However, there has been only limited formal evaluation of the health impact of this development, and a comprehensive assessment of health costs has not been weighed against the potential benefit. Such an assessment would currently not be possible for specific downwind communities such as Riverside, because no model is available to estimate the contribution of all port activities to exposure to secondary pollutants in specific areas. Nevertheless, in a community already identified as having poor air quality, port-related growth is likely to contribute disproportionately to the pollution-related burden of disease, compared to projected changes in automobile pollution, which currently accounts for most regulated regional pollutants. Regulation of ship, locomotive and truck emissions has lagged behind that for automobiles. Moreover, increased expansion of cargo distribution centers in the Riverside area and associated influx of heavy duty diesel trucks carrying containers to warehouses will likely result in increased truck traffic on major roads in proximity to homes.

Transportation planning in local communities requires local information to develop effective policies, because state and national estimates of air pollution burden of disease that average effects over a large population are not adequate for evaluating local health impact in areas with high pollution. Although this study provides an example of how local health risk assessment might fill this need, our results underestimate the impact of air pollution. In addition, asthma morbidity results in impaired quality of life for the affected child and other

family members. School and corresponding work absenteeism and the added use of health care facilities due to air pollution also have an important impact on local economies (18, 19). World Health Organization guidelines list a range of other health outcomes that could be considered in children, including infant mortality, effects on birth weight, and bronchitis among non-asthmatics (20). Air pollution also may cause other adverse birth outcomes, cardio-respiratory ailments in adults, and lung cancer. In a recent health risk assessment in the port area, the largest carcinogenic risk from exposure to diesel and other air toxics in the Los Angeles air basin occurred in Long Beach area (21, 22).

Large statistical uncertainty of the CRFs and their limited availability for asthma-related outcomes affects the certainty of our results, as shown in Figure 2. Additional epidemiological studies for the outcomes and populations considered would be useful to generate more accurate CRF´s. Several other limitations and uncertainties may affect our estimates. Scenario 2 provided a more complete assessment of the burden of childhood asthma exacerbation attributable to air pollution because the reference levels were from clean coastal communities. Models of the regional consequences of primary emissions from the port and from port related goods movement are still incomplete, but it is clear that even if there were no port emissions, the levels of pollution in the study communities would not be reduced to “clean” levels.

We used regional air pollution exposure estimates that did not incorporate the children’s location and activity patterns in the assessment of the impact of pollution on asthma exacerbations. In communities located close to ports and next to busy roadways, children may experience higher personal levels of exposure than those measured at a single community monitoring site (which are intentionally located away from major roadways). Other

uncertainties include the attribution of uniform risk to children at all residential distances within 75m of a major roadway, a simplification of the continuous decline to approximately 200m we have observed (10). We also extrapolated the effects of traffic proximity on asthma prevalence developed from young school children in the CHS to the entire population of children up to age 17. These uncertainties can only be partially quantified, thus we did not perform sophisticated quantitative models of uncertainty. Finally, we did not estimate the additive benefits of disease prevented by reduction of NO_2 and O_3. Although the epidemiological evidence for the outcomes selected suggest that O_3 has independent effects from NO_2, there is some evidence that there may be some synergistic effects (23). The four exacerbation outcomes examined in this study may overlap in some children, as a child visiting an emergency room may also have been hospitalized. Therefore, summation of estimates of disease burden across outcomes may result in some duplicate counting. Also, it is likely that the same asthmatic children who experience chronic exacerbations of asthma symptoms are also more likely to require medical care. There are no data available to evaluate the extent of such duplicate counting on the individual level. However, air pollution represents both a burden on the quality of life of children, and on the health care system, and thus parallel presentation of all effects is appropriate.

We interpreted the attributable number of each outcome as those that would be prevented if air pollution were reduced. This assumption is supported by the few studies, including the CHS, that have observed a reduction of respiratory outcomes with periods of improvements in air quality due to annual fluctuations in air quality, or moving to another location (24-27). However, one generic limitation risk assessments of this type is that cases attributable to air pollution and to other exposures may together appear to cause more than 100% of all cases (or as interventions to prevent more than 100%), because disease attributable to air pollution in a

susceptible individual might well develop due to competing risk factors if there were no air pollution. For example, it is not known what fraction of children would develop asthma due to other causes if traffic proximity were eliminated. Competition between risk (or protective) factors is relevant to the correct interpretation of attributable cases, but these relationships are not well understood.

Another important uncertainty involves the causal relationship between asthma and pollutants associated with traffic proximity. Although the causal link between air pollution and asthma exacerbation is now recognized (28), some controversy remains as to whether air pollution causes asthma. However, emerging evidence from toxicological and epidemiological studies, including several from the CHS in these study communities, support a causal relationship (11) (29).

In conclusion, community-based quantitative risk analyses can improve our understanding of health problems and help promote public health in local transportation planning. Our results demonstrate that the burden of asthma prevalence and exacerbation due to traffic proximity can be substantial in communities with large numbers of homes in close proximity to major roadways. There is an urgent need for more detailed evaluation of the health consequences both of large-scale transportation infrastructure development and of port related air pollution in areas that already have high burden of disease associated with air pollution.

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Figure 1. Location of Long Beach and Riverside communities in Southern California in relation to the Los Angeles-Long Beach port complex and major roads and highways.

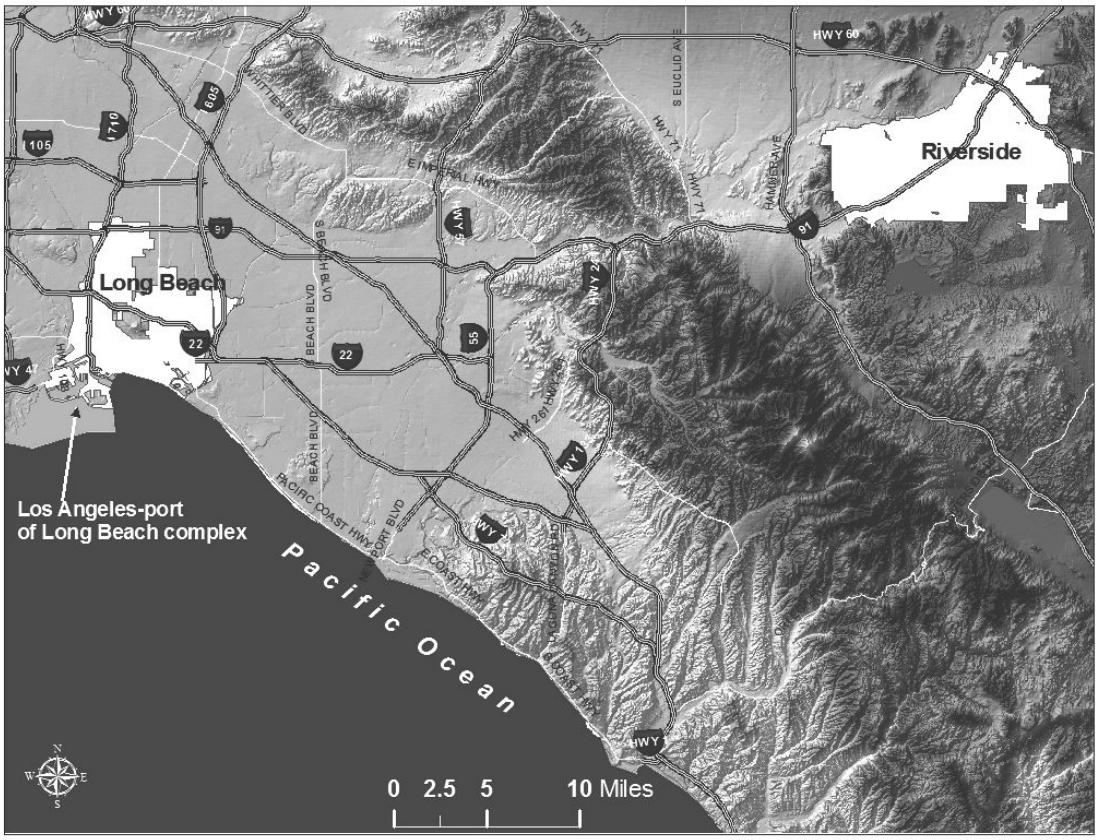


Table 1. Health outcomes and concentration response functions included in the study

Outcome	Pollutant	Unit of CRF/age	CRF (95%Confidence Interval)	Corrected CRF (95%Confidence Interval) *	Reference
Bronchitis episodes among asthmatics	NO_2	1 ppb (24-hr annual average) age 9-13	1.070 (1.020, 1.130)	1.042 (1.012-1.076)	(30)
	O_3	1 ppb (10am-6pm average) age 9-13	1.060 (1.000, 1.120)	1.057 (1.000-1.113)	(30)
Clinic visits for asthma	NO_2	24 ppb (24 hour average) age 0-14	1.061 (1.012, 1.113)	1.055 (1.011-1.102)	(31)
	O_3	50 ppb (daily average) age 2-14	1.054 (1.013, 1.096)	1.049 (1.012-1.086)	(32)
Emergency Department visits for asthma	NO_2	50 ug/m^3 (27 ppb†) (24-hr average) age ≤15	1.026 (1.006, 1.049)	1.024 (1.006-1.045)	(33)
	O_3	10 ppb (daily 1-hr max) age 1-16	1.024 (1.015, 1.033)	1.022 (1.014-1.030)	(2)
Hospital admissions for asthma	NO_2	27.1 ug/m^3 (14.4 ppb†) (average 24 hour) age≤15	1.079 (1.054, 1.090)	1.079 (1.054, 1.090)	(34)
	O_3	23 ug/m^3 (11.5 ppb§) (8-hour mean) age≤15	1.060 (1.041, 1.079)	1.060 (1.041, 1.079)	(34)
Prevalent asthma	Traffic exposure	living < 75m to busy road for long-term residents) age 5-7	1.64 (1.10-2.44)	1.515 (1.086-2.059)	(10)

*CRF: Concentration-Response Function; published CRF corrected with formula CRF/[1+I_tx(CRF-1)], where I_t is the frequency of the outcome in the population.

†Conversion factor for NO_2 1 ppb=1.88 μg/m^3

§Conversion factor for O_3 1 ppb= 2 μg/m^3

Table 2. Population baseline frequencies and exposure data

Description		Long Beach	Riverside	Reference
Population/baseline frequencies				
Total population of children, age 0-17		136,181	76,491	2000 USCB
Fraction of children with asthma (prevalence)*		0.1284	0.1488	CHS
Fraction of children with asthma reporting bronchitis symptoms‡		0.387	0.387	(30)
Fraction of children reporting clinic visits for asthma †		0.710	0.7521	CHS
Fraction of children with asthma reporting Emergency Department visits for asthma §		0.581	0.3793	CHS
Number of hospital admissions for asthma (ICD-9: 493)		264	120	California Breathing, 2003
Fraction children living <75m of busy roads		0.199	0.1291	Methods based on (17)
Population exposure-current conditions				
	NO_2	33 ppb	26 ppb	(12)
	O_3	29 ppb	57 ppb	(12)
Exposure reduction from current levels				
Scenario 1- no ship emissions				
	NO_2	-5.9 ppb	-2.0 ppb	(4)
	O_3	Not considered	Not considered	
Scenario 2-clean communities				
	NO_2	-18 ppb	-11 ppb	Clean CHS communities (12)
	O_3	Not considered	-27 ppb	Clean CHS communities (12)

2000 USCB: United States Census Bureau; CHS: Children Health Study, unpublished data.

*Defined as use of controller medications for asthma in previous year or physician diagnosed asthma with any wheeze in previous year.

‡Defined as daily coughs for 3 months in a row, congestion or phlegm for at least 3 months in a row, or bronchitis. Average 12 CHS communities

† Based on answer to the question " Has your child ever been to a doctor for wheezing?" among those that have ever had wheezing or whistling.

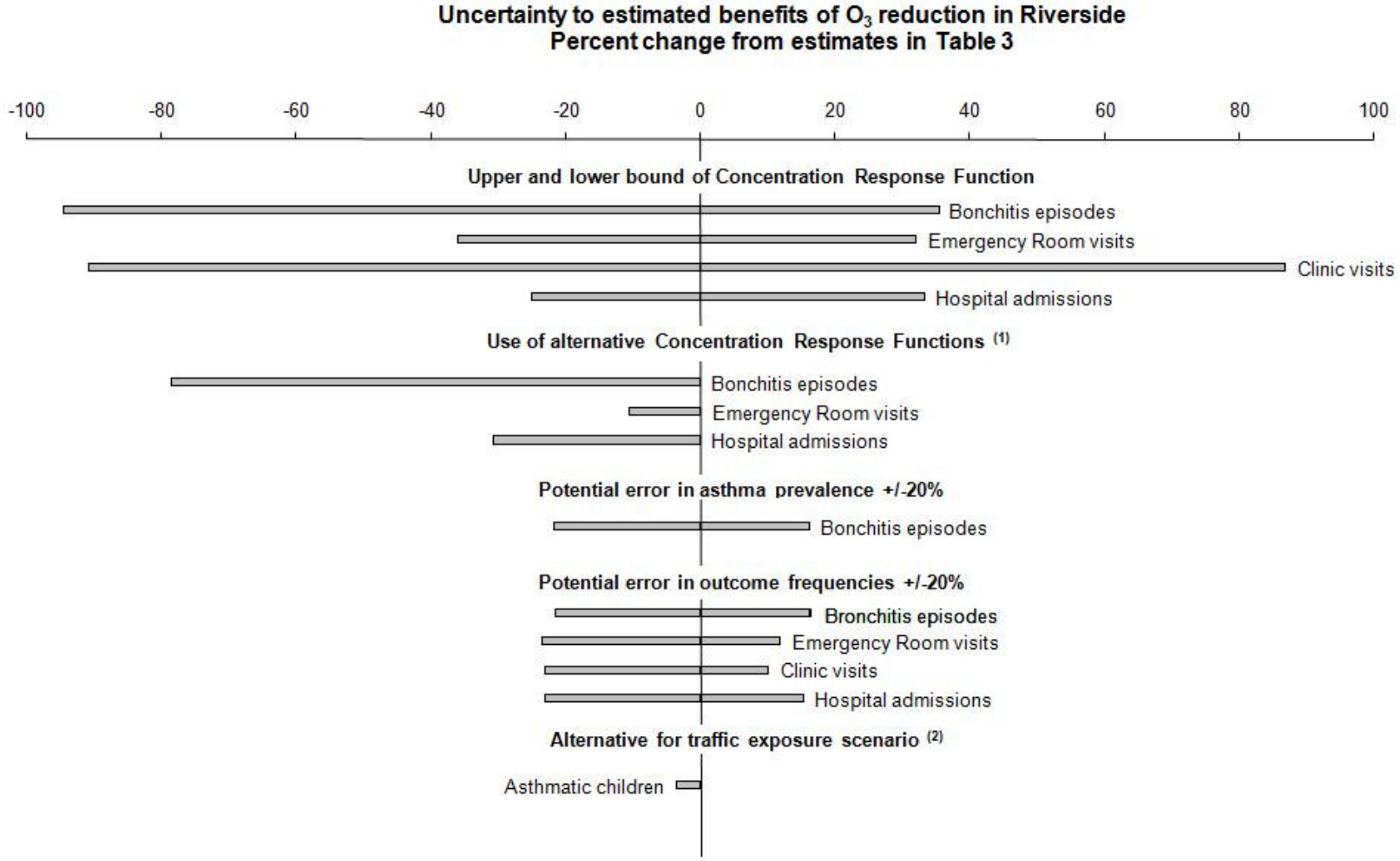
§ Based on answer to the question “Has your child ever been to an emergency room or a hospital for wheezing?” among those that have asthma.

Table 3. Number of outcomes (95%CI) attributable to air pollution per year for children living in Long Beach and Riverside

Pollutant/community	Outcome	Baseline estimates	Scenario 1-no ship emissions				Scenario 2-clean communities			
			Attributable to air pollution	Attributable to other causes among those with asthma due to air pollution	Total*		Attributable to air pollution	Attributable to other causes among those with asthma due to air pollution	Total*	
					Number cases	%			Number cases	%
Traffic exposure										
Long Beach	Asthma cases	17,486	1,600 (1,500-1,800)	na	1,600 (1,500-1,800)	9.2 (8.6-10.3)	1,600 (1,500-1,800)	na	1,600 (1,500-1,800)	9.2 (8.6-10.3)
Riverside	Asthma cases	11,382	690 (630-750)	na	690 (630-750)	6.1 (5.5-6-6)	690 (630-750)	na	690 (630-750)	6.1 (5.5-6-6)
NO_2 Long Beach	Bronchitis episodes among asthmatics	6,767	1,400 (400-2,300)	500 (400-600)	1,900 (980-2,700)	28.1 (14.5-39.9)	3,400 (1,200-4,900)	310 (170-530)	3,700 (1,700-5,100)	54.7 (25.1-75.4)
	Emergency Room visits for asthma	10,166	54 (7-100)	940 (860-1,020)	1,000 (910-1,100)	9.8 (9.0-10.8)	160 (20-300)	930 (860-1000)	1,100 (950-1,200)	10.8 (9.3-11.8)
	Clinic visits for asthma	12,410	160 (30-290)	1,100 (1,000-1,200)	1,300 (1,200-1,400)	10.5 (9.7-11.3)	500 (90-860)	1,100 (1,000-1,200)	1,600 (1,200-2,000)	12.9 (9.7-16.1)
	Hospital admissions for asthma	264	10 (8-12)	24 (22-26)	34 (31-36)	12.9 (11.7-13.6)	30 (24-35)	22 (20-24)	51 (46-57)	19.3 (17.4-21.6)
Riverside	Bronchitis episodes among asthmatics	4,405	340 (90-590)	250 (220-270)	590 (350-820)	13.4 (7.9-18.6)	1,600 (470-2,400)	170 (120-240)	1,700 (710-2,500)	38.6 (16.1-56.8)
	Emergency Room visits for asthma	4,317	8 (1-15)	260 (240-280)	270 (240-290)	6.3 (5.6-6.7)	42 (5-73)	260 (240-280)	300 (260-340)	6.9 (6.0-7.9)
	Clinic visits for asthma	8,560	40 (7-70)	510 (470-560)	550 (500-600)	6.4 (5.8-7.0)	200 (40-370)	500 (460-550)	710 (550-870)	8.3 (6.4-10.2)
	Hospital admissions for asthma	120	2 (1-2)	4 (4-4)	6 (5-6)	5.0 (4.2-5.0)	8 (7-10)	4 (3-4)	12 (11-14)	10.0 (9.2-11.7)
O_3 Riverside	Bronchitis episodes among asthmatics	4,405	--	--	--	--	3,100 (170-4200)	80 (14-250)	3,200 (420-4,200)	72.6 (9.5-93.3)
	Emergency Room visits for asthma	4,317	--	--	--	--	250 (160-330)	245 (223-267)	508 (417-595)	11.8 (9.7-13.8)
	Clinic visits for asthma	8,560	--	--	--	--	220 (20-410)	250 (220-270)	490 (410-580)	5.7 (4.8-6.8)
	Hospital admissions for asthma	120	--	--	--	--	12 (9-16)	4 (3-4)	16 (13-19)	13.3 (10.8-15.8)

* Not to be summed from other columns. Uncertainty distributions obtained by Monte Carlo simulations; --: not considered; na: not applicable

Figure 2. Sensitivity analysis examining uncertainty of results (expressed as percent change from the estimates in Table 3) for number of cases of asthma exacerbation attributable to O_3 and for number of cases of asthma due to traffic proximity in Riverside; Reference for alternative concentration response function are (35) for bronchitis episodes; (36) for Emergency department visits and (37) for Hospital admissions. [(2)] Difference in air pollution attributable asthma cases with a reduction scenario assuming that 5% of the population will remain living within 75m of busy road instead of 0% as in the core estimates.



6. Discussion

This section provides an integrative summary discussion of the results obtained and the limitations associated with the methods used in each study. More detailed discussions are provided in the original papers.

6.1 Particulate matter sizes, sources, components, and health effects

The link between the different size fractions of PMs, sources, components and health effects needs to be understood to improve air pollution regulation and public health.

Our results show that all PM size fractions associated with traffic have health effects; however effects vary for different health outcomes. In Barcelona, we found strong independent associations between daily PM_1 and $PM_{10-2.5}$ and cardiovascular and cerebrovascular mortality. In contrast, daily $PM_{2.5-1}$ was only associated with respiratory mortality.

The observed association between PM_1 and mortality is expected. Barcelona is one of the few cities in Europe for which chemical composition data for different PM size fractions exist. Results suggest that PM_1 in Barcelona arise mainly from combustion processes and specifically from traffic-related emissions. [31] The adverse health effects of fine PM generated by combustion processes and traffic emissions are well-documented, [2, 17] and several source apportionment studies confirm this link. For example, a study in six United States (US) cities showed that fine PM generated by combustion processes was associated with daily mortality, while fine PM from crustal sources showed no association. [9] Another study in Phoenix Arizona (US), found that combustion-related pollutants and secondary aerosols were associated with cardiovascular mortality, while terragenous elements showed no association. [10]

The observed association between $PM_{10-2.5}$ and mortality is more intriguing and suggests that non-combustion traffic-related PMs produce health effects. A previous study investigated the association between $PM_{10-2.5}$ and acute cerebrovascular mortality but results were not statistically significant. [17] Several other studies investigated the association between $PM_{10-2.5}$ and cardiovascular and respiratory mortality and found some positive associations. [4, 5, 11-13] However, lack of chemical composition data made it difficult or impossible to attribute $PM_{10-2.5}$ to specific sources.

Chemical composition data in Barcelona shows that $PM_{10-2.5}$ does contain the highest concentrations of crustal elements (Ti, Li, Rb, Sr, La, Ce, P, and Th), associated with soil and construction and demolition dust [31] However, $PM_{10-2.5}$ also contains the highest concentration of Sb, Cu, Mn, Cr, Co, Sn, Tl, Ba and Si, elements associated with road traffic abrasion products, such as the mechanical wear and degradation of tires, brakes and pavement. [31] This chemical signature indicates that a large part of $PM_{10-2.5}$ in Barcelona may be generated by non-combustion, traffic-related sources. Past studies in Barcelona provide some additional evidence to support this finding: at least 70-75% of the elements in PM_{10} and $PM_{2.5}$ was attributed, directly or indirectly, to non-combustion, traffic-related sources, [31, 34] and the concentrations of elements in

coarse PM attributed to non-combustion, traffic-related sources were generally higher than concentrations registered at an urban background site in Spain with relatively less traffic. [79]

The possibility that non-combustion traffic-related PMs produce health effects is supported by several studies. One study in 108 counties in the United States [13] found no significant association between $PM_{10-2.5}$ and hospital admissions for respiratory and cardiovascular disease, however, when the authors took into account the "urbanicity" of sites, an index considered to be a proxy for traffic exposure, the health risk of $PM_{10-2.5}$ increased. Two recent toxicological studies investigated the cytotoxic and inflammatory activities of size-segregated PM samples ($PM_{10-2.5}$, $PM_{2.5-0.2}$, and $PM_{0.2}$) from six European cities, including Barcelona. [22, 23] Results showed that $PM_{10-2.5}$ had a higher inflammatory effect than the other size fractions, and samples from Barcelona and Athens consistently induced the highest inflammatory activity in all parameters. The authors hypothesized that these effects could be due to a lack of rain and the subsequent accumulation of $PM_{10-2.5}$ on the road. Another study in Sweden found that PM_{10} generated by studded tires on pavement provoked an inflammatory response in cells as potent as that observed when cells were exposed to diesel exhaust. [37] This indicates that coarse PM from pavement degradation may induce health effects. In contrast, a study on cardiac re-polarization in mice, compared the effects of exposure to road dust and gasoline emissions, and only found effects for gasoline emissions. [80] The relatively small particles examined in this study (1.6 μm in diameter) may have a different chemical composition than larger particles, and this may explain the contrasting results. Although further studies linked to source apportionment are necessary, our results provide additional indirect evidence that non-combustion, traffic-related $PM_{10-2.5}$ may have significant adverse health effects in urban areas.

These results together with the large existing PM literature confirm that traffic sources of PM are a major contributor to the health effect and PM burden in urban areas. However, other PM sources may be of concern in specific geographic areas.

We found that in Barcelona Sahara dust outbreaks increase daily mortality. Specifically, results show that, the effects of short-term exposure to $PM_{10-2.5}$ on daily mortality are stronger during Saharan dust days than non-Saharan dust days. The effects of short-term exposure to $PM_{2.5}$ did not change during Saharan dust days.

It is important to disentangle the health effects of PMs from urban sources and natural sources. Past studies of the health effects of dust in arid regions have produced varied results. A study in Spokane, Washington (US) that examined windblown dust found no association between days with high PM_{10} and mortality. [46] A study in British Columbia that examined the impact of the 1998 Gobi dust event on hospital admissions also found no evidence of an association between PM_{10} and mortality [47]. Two studies in Taiwan and Korea investigated the health effects of Asian dust storms and found an increase of approximately 1% in total mortality per each 10 $\mu g/m^3$increase of PM_{10}, [44, 45] although those studies lacked power. A study on the impact of air pollution on hospital admissions in Tapei found that the risk of ischaemic heart disease admissions was associated with several sandstorm metrics, including indicators of high PM_{10} levels. [48]

The first observational studies investigating the health effects of Saharan dust at the population level were carried in the Caribbean islands, often impacted by winds from the Sahara. A study found that Saharan dust cover increased pediatric asthma accident and emergency admissions on the island of Trinidad. [49] The authors concluded that irritants or allergens in Saharan dust may have caused the increased asthma, although the measure of exposure was based on dust cover and not PM level. A more recent study which attempted to repeat these results, investigated the relationship between the daily concentrations of dust measured in Barbados and pediatric asthma attendance rates over two years. [81] No apparent relationship was found. However, the methods employed by these studies, particularly the statistical analysis, did not follow the standard methodology, which may have lead to inconclusive results. [82] Concurrently to our study, a study in Europe also examined the short-term effects of PM_{10} during Saharan dust storms with findings compatible with our results. [50] The study, conducted in Nicosia, Cyprus found an increased risk of hospitalizations on dust storm days, particularly for cardiovascular causes. All-cause and cardiovascular admissions were 4.8% (95%CI: 0.7%, 9.0%) and 10.4% (95%CI: -4.7%, 27.9%) higher on dust storm days respectively.

Additional studies have examined the health effects of various size fractions in arid regions. An initial study in the Coachella Valley in California (US) found an increase of approximately 1% in total mortality per each increase of 10 $\mu g/m^3$ PM_{10}. [83] Follow-up studies showed an association of PM_{10} and $PM_{10-2.5}$ with cardiovascular mortality, and also between $PM_{2.5}$ and total mortality. [84] Another study in the city of Phoenix in Arizona (US), showed a strong association of PM_{10} and $PM_{10-2.5}$ with cardiovascular mortality, and a weak association of PM_{10} and $PM_{10-2.5}$ with total mortality. [10] A strong association was also found between $PM_{2.5}$ and cardiovascular mortality. Factor analysis of $PM_{2.5}$ showed that elements with terrestrial origin (Al, Si, P, Ca, Mn, Fe, Sr, Rb) had no association with cardiovascular mortality, while combustion-related pollutants and secondary aerosols did. No factor analysis was performed for constituents of $PM_{10-2.5}$. These results, together with ours, are intriguing because all the studies were conducted in urban cities located in arid or relatively arid regions, where there are both natural and man-made dust, indicating that sources of dust play a role in influencing health effects.

Our investigations provide some insight into the mechanisms by which PM produce health effects. In Barcelona, we found that PM_1 and $PM_{10-2.5}$ do not share a similar chemical profile, however, they induce similar cardiovascular and cerebrovascular effects. This suggests that health effects may be produced by a range of elements, or from varying mixtures of reactive elements, and that these size fractions may share a common mechanism of action.

A proposed mechanism of action for fine PM involves redox components which reach target sites in the respiratory and cardiovascular system and induce oxidative stress, inflammation, and acute thrombotic complications of atherosclerosis. [1, 2] A recent study investigated the associations of particulate matter (PM) air pollution with systemic inflammation in a susceptible population of elderly individuals with coronary heart disease living in retirement communities in the Los Angeles, California, air basin. [85] This study used models based on size-fractionated PM mass, specifically UFs, $PM_{0.25}$, $PM_{2.5-0.25}$ and $PM_{10-2.5}$ and markers of primary and secondary aerosols. This study found that UFs and outdoor $PM_{0.25}$ concentrations were more strongly and

positively associated with biomarkers of inflammation (CRP, IL-6, sTNF-RII) than was $PM_{2.5-0.25}$ supporting hypotheses regarding the proinflammatory potential of UFs. In support to our findings, however, the study also found significant associations of sTNF-RII (marker of inflammation), sP-selectin (marker of platelet activation), and Cu,Zn-SOD (marker of enzymatic antioxidant activity) with coarse particles ($PM_{10-2.5}$). The authors mention that in the Los Angeles region, as in Barcelona, traffic contributes more to UFs and coarse PM (due to brake abrasion and road dust resuspension) than it does to accumulation-mode particles and that the size fractions < 0.25 and > 2.5 μm are more short-lived in ambient air. The authors hypothesize that the freshly generated reactive chemicals and transition metals on the particle surfaces of these two size fractions may explain the common biologic responses they observed. These processes may also explain our results.

Inflammatory exacerbation may also be linked with Saharan dust exposure. An hypothesis for the increase risk associated with Saharan dust exposure relates to a potential increase in the content of biological materials of these particles. The possibility that Saharan dust may contain irritants or allergens is supported by several studies. A study in the Virgin Islands showed that samples collected during Saharan dust outbreaks carried three times more microbes and fungi than normal samples. [41] The authors suggested that active biological agents may be transported in Saharan dust, shielded from inactivation by ultra violet light by attaching to crevasses within coarse particles. Numerous other species of fungi, bacteria and viruses have also been found in other desert dust samples. [42] A recent study examined the microbial quality of the PM aerosols for samples collected in the coastal city of Heraklion on the eastern Mediterranean during a north African dust storm. [53] Bacterial communities associated with aerosol particles of six different size ranges were characterized following molecular culture–independent methods. The study found that a large portion of the clones detected at respiratory particle sizes (< 3.3 μm) were phylogenetic neighbors of human pathogens that have been linked to several diseases such as pneumonia, meningitis, and bacteremia, or suspected to induce pathologic reactions such as endocarditis.

Toxicology studies have shown that endotoxin and other biologic compounds found in $PM_{10-2.5}$ activates inflammatory responses. [23, 86] A study in North Carolina found that ambient $PM_{10-2.5}$ exacerbated the response of allergic individuals to airborne bacteria; 13% of their mass was composed of pollens, spores and bacteria. [86] In study of six European cities, the highest inflammatory effect in Barcelona was for the $PM_{10-2.5}$ fraction. [23] Samples were collected during two episodes of Saharan dust events, although biologic composition of the samples was not available. [23] Taken together, these studies suggest that increased mortality detected during Saharan dust outbreaks may be related to biogenic factors associated with coarse particles.

Chemical analysis in Barcelona provides further indirect evidence about the components related to the health effects of Saharan dust. Analysis showed that chemical composition varied equally in $PM_{2.5}$ and $PM_{10-2.5}$ during Saharan dust days. In addition, metals involved in oxidative stress pathways, such as iron, copper, lead, and zinc [14] were similarly abundant during Saharan dust days and non-Saharan dust days in $PM_{10-2.5}$. This comparison indicates that some factor associated with $PM_{10-2.5}$, though not detected by chemical analysis, may be responsible for increased mortality. Biogenic factors carried by coarse particles in Saharan dust are a possible explanation of our observed effects. However, there may be other chemicals not measured in this study, such as

pesticides or industrial byproducts, transported within Saharan dust. Past studies have shown that soluble and insoluble chemical constituents may affect health in different ways, [87, 88] and these constituents may vary with different size fractions. [89] In our study only total metal mass amounts were available for analysis.

Our results should be interpreted in the context of several limitations. Detailed considerations of limitations are provided in the published papers. The following discussion considers those main limitations which identify gaps in understanding and suggest future research.

Our studies were based on the case-crossover method. One advantage of using case-crossover design is the ability to take into consideration individual characteristics such as age, sex, health status, or lifestyle factors to assess effects of air pollution among potentially susceptible subgroups or to explore modification of air pollution effects by individual characteristics. [90] Our studies only considered age and sex, however, it would be useful to consider a range of additional individual factors in the future.

A main disadvantage of case-crossover analysis relates to the fact that the exposure term relevant in case-crossover studies (i.e. exposure of case days and control days) can have rather narrow distributions compared to daily distributions, therefore statistical power may be jeopardized in some studies. [90] Although a time-period of study relatively short, our studies showed large distribution of the absolute difference between PM concentrations on case days and control days, which allowed for sufficient statistical power to detect marginally significant effects. In the future studies with longer lags may be considered, to capture events with low frequency like Saharan dust.

By design the case-crossover approach controls for potential individual confounders, and several time-dependent covariates were included in the models, thus most confounding effects may have been controlled for at this stage. We tested our models for several potential confounders that may have been important. These included the effect of temperature, the effect of the summer 2003 heatwave and effect by other co-pollutants. Sensitivity analysis showed that changing the definition of the heatwave did not change results and that the associations were independent of O_3 and NO_2 levels as shown in other areas. [17] Although we controlled for exposure to temperature differently in Paper II than paper I, sensitivity analysis showed that effects remained unchanged. Better availability of covariate data, such as co-pollutants, would improve future studies.

The most important limitation of short-term air pollution analysis is related to exposure misclassification, because no information on personal exposure is in general available. In our studies we used a single urban monitor to estimate individual exposure for PM fractions. This assumption is probably valid, because past observations have shown that fine and coarse PM levels at our monitoring station are strongly correlated with PM levels in other parts of the city (X. Querol, unpublished data, personal communication). However, in Barcelona most residences are located along busy roads. In light of the recent studies showing that traffic-related pollutants reach very high concentrations along streets [62] and the growing evidence of specific health effects related to these pollutants, [38-40] local validation studies would be needed to determine in more detail the spatial distribution of particles in Barcelona.

Our results and conclusions are based on a maximum study period of three years. We thus had to limit our analysis to investigate the effects of PMs on the same day to few days after exposure. Some studies on particulate exposure and O_3 have reported different time response for cardiovascular mortality compared with respiratory mortality, where cardiovascular mortality occurred within the first few days of exposure, whereas respiratory mortality showed a lag of up to two weeks. [91, 92] Air pollution has been associated with the triggering of cardiovascular events. [93] Exacerbation of respiratory infections would be expected to take more time. [92] Delayed effects may explain in part the lack of respiratory responses observed for very fine (PM_1) and coarse particles ($PM_{10-2.5}$) included in paper I. This hypothesis implies the existence of different mechanism of action between these particle sizes and the intermodal fraction ($PM_{2.5-1}$). Investigating cumulative effects is thus necessary to further understand biological processes. Finally, the chemical analysis for the different particle fractions available in the study helped us suggest potential connections with mechanism of actions of PMs. Further studies are necessary to understand the role of the different PM components in these processes including obtaining daily source apportionment data and improving population exposure models for the different size fractions and sources.

In summary, our study suggests that different PM size fractions generated by traffic-related combustion and non-combustion processes produce short-term health effects in urban areas. Studies which examine only aggregated fractions of PM, such as PM_{10} or $PM_{2.5}$, may obscure these health effects. Furthermore, a common mechanism of action may exist between different size fractions. Last, our studies suggest that some PM generated by natural sources, such as Saharan dust, may have adverse health effects, and that these effects may be related to allergens or biogenic factors.

These results are important to improve the regulatory process and public health. Our results may be used to develop new size- and source specific concentration-response functions (CRFs). It may be necessary to revise current PM legislation, particularly regarding traffic exposure, as the total impact of PMs may be underestimated in areas with high traffic density. Currently, CRFs based on one size fraction (i.e $PM_{2.5}$), may not take into account the differential effects of size fractions, and the whole range of effects associated with traffic related exposure. Finally natural PM sources such as Saharan dust must be taken into account in local air pollution policy.

6.2 Air pollution health impact assessment and local sources

Public health researchers and regulatory agencies use air pollution risk assessments – or health impact assessments – to either estimate the current public health burden attributable to air pollution, or the potential future impact of policies that will affect air quality.[26, 94, 95] Health impact assessment (HIA) is thus an important tool to translate research findings into quantitative information relevant to public health professionals, policy makers and the public.

We performed an air pollution health impact assessment in Barcelona (Spain) that used PM_{10} levels as exposure indicator for two scenarios of air pollution reduction. This study indicated that health and economic benefits would be substantial if air pollution

was reduced in the Barcelona metropolitan area, and showed that HIA provides a framework to evaluate the relevance of community-based policy decisions to public health.

Like many other HIAs, we employed exposure assessment methods and CRFs that did not capture local source-related differences within Barcelona, such as PM levels and effects related to traffic and harbor activities, two main sources of PM emissions in the area. Source-specific assessment in Barcelona was not possible because of lack of detailed population distributions relative to traffic and harbor activity, and source specific traffic CRFs. Greater understanding of such relationships, such as those outlined in paper I and II, may improve future HIAs. One can expect traffic to be a major contributor of the total air pollution health impact. The urban layout of Barcelona creates areas of high population density close to traffic. This population may thus be exposed to the contaminants with the greatest potential health effects. The contribution of the harbor activities to the total air pollution impact is unknown but is highly relevant because such activity is increasing while regulation lags in comparison to equivalent traffic regulation.

To illustrate the impact of local sources, we provided estimates of the burden of childhood asthma attributable to air pollution in communities affected by expanding goods movement in southern California. We developed case studies for southern California because of the availability of local data needed for this type of approach, including availability of population and source specific CRFs for asthma outcomes, detailed residential population distributions, and source-specific emission models. We estimated that eliminating ship emissions would result in reduction of the number of asthma related outcomes ranging from 5% to 28% depending on community and outcome considered. Further reduction of NO_2 concentrations to levels found in clean communities in Southern California would result in corresponding reductions in asthma related outcomes that are three- to five-fold the above figures. Our analysis showed the port is an important contributor to the public health impact of air pollution in the Los Angeles basin. Port expansion has been promoted as an “economic engine” for the region [96], and there are currently several large transportation infrastructure development projects underway to facilitate the expected increase in goods moving through the region to the rest of the country. However, there has been only limited formal evaluation of the health impact of this development, and a comprehensive assessment of health costs has not been weighed against the potential benefit. Such an assessment would currently not be possible for other downwind communities in Southern California and elsewhere, because no emission model is available to estimate the contribution of all port activities to exposure to secondary pollutants in specific areas. Nevertheless, in communities already identified as having poor air quality, such as Barcelona, port-related growth is likely to contribute disproportionately to the pollution-related burden of disease, compared to projected changes in automobile pollution, which currently accounts for most regulated regional pollutants.

A major local source of pollution is related to traffic. The full health effects of these sources of pollution may not be taken into account by HIAs which employ regional pollutants exposure; regional pollution represents a combination of many different sources and dilutes the full effects of traffic-related pollutants. Therefore, recent epidemiological studies use alternative traffic exposure proxies, such as traffic

proximity. Our results show that "traffic proximity" is responsible for a large burden of both asthma cases and asthma exacerbation. For example, in Long Beach and Riverside, heavy traffic corridors are responsible for 6-9% of all childhood asthma cases. Asthma cases attributable to traffic proximity contribute a large portion to the total asthma burden. This is especially true for some exacerbation outcomes, such as clinic visits, with small association with regional air pollution. Much fewer cases would be attributable to air pollution in these children had asthma not initially developed due to traffic exposure. This is a very important result because in many urban areas people live in close proximity to busy roads with high traffic density. For example, we estimated that in Long Beach, approximately 20% of children lived along traffic corridors, and are thus at risk for developing asthma due to traffic exposure. This proportion may even be higher in other densely populated urban areas, such as those found in Europe.

Our model partitions attributable cases of asthma exacerbation. Asthma exacerbation among those who have asthma because of traffic pollution, are distinguished from asthma exacerbation among those who have asthma because of other causes. Such partitioning is advantageous for risk assessors. Policies which prevent asthma onset may in some cases differ from those which prevent asthma exacerbation. For example, concentrated pollutants near busy roads may require different mitigation than large-scale regional air pollution. The partitioning of attributable cases may thus be useful in source-specific risk assessments.

This approach demonstrates that conventional HIA, which do not partition attributable cases, may underestimate the total burden of diseases such as asthma. We examined asthma because it is the most common chronic disease during childhood, and a major source of reduced quality of life for children and their families, [97] however, our approach can also be applied to other chronic diseases. Given the increasing evidence that air pollution may play a role in the onset and exacerbation of diseases such as asthma, Chronic Obstructive Pulmonary Disease (COPD) and atherosclerosis, [1] the integration of chronic and acute outcomes is necessary in the risk assessment process to inform policy makers about the real impact of air pollution.

The results of all HIAs must be discussed in the context of assumptions and uncertainties integrated in the evaluations. A main assumption when developing our evaluations involved the causal relationship between health effects and air pollution. This assumption is better supported for some outcomes than for others, especially for mortality as compared to morbidity. For example, many studies have shown an association between air pollution and mortality and reduced life expectancy [98-101] while the link between air pollution and chronic disease is less well documented. [102, 103] The relationship between air pollution and long-term effects remains unresolved.

In the case of asthma, the causal link between air pollution and asthma exacerbation is now recognized as highly suggestive or sufficient evidence [104]. But, we also assumed a causal relationship between traffic exposure and asthma based on CRFs that used proximity models as proxy for this exposure. These models are approximations, and may reflect exposure to factors associated with traffic, rather than traffic itself, such as socio-economic status (SES) or noise. While SES is usually controlled for, the latter co-exposure needs to be better integrated in future studies. More precise traffic exposure

models which take into account susceptibility factors are necessary to improve traffic-related CRFs.

Furthermore, many HIAs use regional estimates of air pollution to evaluate the burden of disease. However, these estimates may not be adequate in local areas with high pollution. For example, to estimate the number of exacerbation of asthma, we used CRFs derived from studying the effects of pollutants measured at central monitoring sites. This approach indirectly assumes that pollutants generated by different sources have the same health effects. Our results from Objective 1 confirm that this assumption is not true, because the toxicity of pollutants appears to be linked to specific sources. To date, no source-specific CRF exists for ship or port-related emissions. Developing such CRFs will be important in the future.

One generic limitation of HIAs is that cases attributable to air pollution and to other exposures may together appear to cause more than 100% of all cases , because diseases attributable to air pollution in susceptible individuals might well develop due to competing risk factors if there was no air pollution. For example, it is not known what fraction of children would develop asthma due to other causes if traffic proximity was eliminated. Competition between risk factors must always be taken into account in the interpretation of attributable cases, and this limitation is not specific to air pollution. These competitive relationships, are not well understood and were not addressed in our investigations, however this represents an important area for future research.

In summary, our HIAs indicate that local sources of air pollution must be taken into account to determine the health burden in urban areas. In addition, traffic exposure contributes considerably to the health burden, in part because large portions of the population live in close proximity to traffic, for example, along traffic corridors. Port-related emissions also contribute to the health burden, especially in urban areas where port and associated traffic activity are expanding. Finally, our HIAs indicate that it may be necessary to partition attributable cases, and integrate chronic and acute outcomes into risk assessments, given the increasing evidence that air pollution plays a role in the onset and exacerbation of asthma and other chronic diseases.

7. Policy implications and open research questions

Our studies propose several important public policy implications, and suggest important lines of future inquiry. More detailed discussions of policy implications and future research are provided in the original papers.

7.1 Traffic exposure and health

The growing awareness of the role of traffic related exposure in producing adverse health effects has raised concern among researchers, public health officials and policy makers that the efforts in place, including current air quality regulations, may not be sufficient to minimize these effects.

First, our findings suggest that further epidemiological studies are needed to understand the effects of $PM_{10-2.5}$ produced by vehicle traffic because results indicate that coarse road dust could represent an hazardous carrier of toxic compounds, similar to finer particles emitted from tail-pipe emissions.

Road dust can easily be re-suspended by passing vehicles and wind, resulting in an important source of atmospheric particulate matter. If the health effects of PMs are related to compounds generated both by traffic-related combustion and non-combustion related processes, mitigation strategies that go beyond the control of combustion related PMs must be implemented to reduce the health effects of PMs in urban areas. Thus, in urban areas, exposure to vehicle traffic emissions should be assessed by monitoring both coarse and fine PM.

Second, our results show that PM_1 provides a better measurement of exposure and effects to combustion-related sources than $PM_{2.5.}$ [31, 32] This indicates that it would be preferable to base PM air quality standards on PM_1 and PM_{10} or PM_1 and PM_{10-1} rather than the current $PM_{2.5}$ and PM_{10} standard. This alternative strategy takes into account the two types of relevant emissions, re-suspension and combustion, while $PM_{2.5}$ is a size fraction highly mixed with coarser material.

Third, the long-term effects of non-combustion traffic related coarse PMs may have to be reevaluated. Past studies show contrasting effects of coarse fraction on long-term health, however most of these studies have not considered sources of PMs. [5, 11, 105, 106] The long-term impact of PMs may have been underestimated in areas with high traffic density, because recent HIAs have used CRFs based preferably on $PM_{2.5}$.

Fourth, our studies illustrate how planning in local communities requires local health impact information to develop effective policies, especially regarding transportation, because state and national estimates of air pollution burden of disease that average effects over a large population are not adequate for evaluating local health impact in areas with high traffic exposure.

Finally, our results highlight the importance of developing more accurate CRFs to improve HIAs. There are major challenges in evaluating the burden of traffic exposure, because investigators have used a myriad of metrics to characterize exposure to

potential traffic pollutants. This makes it impossible to use common exposure metric, or to derive meta-analytics CRFs. Also, exposure data needs to be collected from a range of different areas, particularly along densely populated traffic corridors. Clarifying exposure metrics, targeting specific traffic-related pollutants, and incorporating population demographics, will greatly improve urban HIAs.

7.2 Natural sources of particulate matter and health

The new directive 2008/50/EC on air quality of the European Parliament states that "member States shall transmit to the Commission, for a given year, lists of zones and agglomerations where exceedances of limit values for a given pollutant are attributable to natural sources. Member States shall provide information on concentrations and sources and the evidence demonstrating that the exceedances are attributable to natural sources. Where the Commission has been informed of an exceedance attributable to natural sources in accordance with the above, that exceedance shall not be considered as an exceedance for the purposes of this Directive".

The removal of the limits from so-called "natural" contributions to PM_{10} is based on the assumptions that these contributions are harmless. Our results do not support this claim. Although further research is needed to investigate the biologic and chemical composition and associated allergenic and inflammatory properties of Saharan dust, our results suggest that coarse PM from Saharan dust affects public health.

The concentration-response relationships on which the European limit values are currently based include a 'natural' background. This approach takes into account impact due to natural sources. We do not expect that the direct impact of Saharan dust is large in many European areas, because its contribution represents only a small proportion of all PMs. For example, in Barcelona Saharan dust represents between 8% and 16% of all PM_{10} contributions. [31] However, if target levels do not account for natural background, even if this background is small, then the component of anthropogenic pollution, including PM from traffic, will be proportionally larger, producing greater health effects.

Many policy makers have argued that subtracting levels from natural sources is legitimate because impacted regions cannot do anything about these occurrences. However, to comply with international public health guidelines, areas affected by natural PM sources such as Saharan dust may have to control man-made sources of PMs more rigorously than other areas to compensate for the excess risk.

Finally, the health impact of natural sources, such as dust outbreaks, in relation to climate change must be explored. Climate change is likely to increase the frequency, intensity and distribution of Saharan and other desert dust outbreaks, [107, 108] with corresponding effects on public health. These changes must be incorporated into current and future air pollution mitigation strategies.

7.3 Acute versus chronic diseases

In most air pollution HIAs, the overall burden attributed to air pollution is heavily driven by mortality due to long-term exposure. [25, 29, 109] Most of these studies express results in terms of attributable deaths, a common approach used for other risk factors. [110] Long-term air pollution benefits are more appropriately expressed in terms of changes in life expectancy, because reducing pollution postpones rather than prevents death. [76, 111]

While expressing results in terms of changes in life expectancy may be more accurate, communicating these results to policy makers and lay people is more complex than communicating attributable deaths. In addition, postponement of death due to reduction in air pollution is the consequence of reductions in a range of acute and chronic pathologies. Expanding methods to incorporate morbidity burden in HIAs would avoid dealing with results dominated by mortality only and allow for integrating the sequence of development of acute and chronic pathologies related to the exposure.

Many chronic diseases are a combination of underlying disease pathology and acute triggers or events. Often the underlying disease determines an individual's susceptibility to acute events triggered by other factors. This model applies to conditions such as asthma, COPD, and cardiovascular diseases.

New epidemiological evidence shows that air pollution has a role in both onset and exacerbation of these diseases. Therefore, it is necessary to revise HIAs for situations where an environmental exposure of interest affects the incidence or prevalence of chronic conditions as well as the exacerbation of acute events. This partitioning is relevant to public health and public policy professionals because it can help prioritize actions.

To improve HIAs related to chronic disease, several lines of inquiry may be pursued. First, it is necessary to conduct more studies which relate exposure to pollutants, such as PM, to chronic conditions, such as cardiovascular disease. These studies are still scarce. [12, 39, 60, 61] Second, it is important to clearly distinguish between underlying pathologies and acute events. For example, asthma prevalence and asthma exacerbation are often defined using a combination of different responses from questionnaires, and may overlap. Last, the potential exists to employ preclinical markers of disease, such as lung function decrement, to indicate chronic pathology. Additional epidemiological studies which explore such markers are thus needed. The integration of such objective measures of health in HIA has not been accomplished yet but the proper development of methods may result in more comprehensive and complete assessments of the overall burden of air pollution.

8. Conclusions

8.1 Objective 1

- In urban areas, all PM size fractions have health effects, however effects may vary for different health outcomes.

- PMs generated by both traffic-related combustion and non-combustion processes may increase short-term mortality in urban areas.

- Studies which examine only aggregated fractions of PM may obscure the health effects of specific PM size fractions.

- PMs generated by both traffic-related combustion and non-combustion processes may share a common mechanism of action.

- In some areas exposure to coarse PMs from natural sources such as Saharan dust may increase daily mortality.

- The health effects of PMs from Saharan dust may be related to biogenic factors transported with dust particles.

8.2 Objective 2

- Reducing air pollution in highly impacted communities would greatly reduce mortality and morbidity among the population.

- Source-specific analysis is important for local decision-making to recognize growing local sources of health impact, such as port-related emissions.

- Traffic exposure is an important contributor to the local health burden in urban areas. This exposure may not be accounted for when using regional pollutant exposure in the traditional risk assessment models.

- HIAs for air pollution should be modified to account for the additional burden of long-term exposures which produce both chronic and acute diseases.

9. Epilogue

The differential role that airborne particulate matter (PM) size fractions, components and sources play in producing adverse health effects is not fully understood. Our investigations show that PMs generated by both traffic-related combustion and non-combustion processes, and coarse PMs from natural sources, specifically Saharan dust, contribute to health effects in urban areas.

Our results indicate that air pollution regulation in urban areas should take into account both PMs generated by traffic-related combustion and non-combustion processes. In addition, air quality regulations in areas affected by natural dust should take into account the health effects of these PM fractions, or they may not adequately protect public health. Further research is needed to determine the components and the biological processes by which traffic-related PMs, and PMs from natural sources, generate health effects.

Air pollution health impact assessment is an important tool to translate research findings into quantitative information relevant to public health professionals, policy makers and the public. Our studies show that local, source specific HIAs are necessary to improve public health. Air pollution mitigation strategies must take into account local exposures, such as high population density along traffic corridors, and port related emissions. Further research is needed to improve population exposure models, and clarify the relationship between air pollution and chronic and acute health effects.

In conclusion, our studies contribute to a better understanding of the link between PM size fraction, sources, components and health effects. Our results have important implications for public health and public policy. We hope that ongoing research will help improve knowledge about air pollution health impacts and help mitigation in urban areas.

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Glossary

$\mu g/m^{3:}$ micrograms per cubic meter

95%CI: 95% Confidence Interval

Al: Aluminum

Al_2O_3: Aluminium Oxide

Ba: Barium

BS: Black Smoke

Ca: Calcium

Ce: Cerium

Co: Cobalt

COPD: Chronic Obstructive Pulmonary Disease

Cr: Chromium

CRF: Concentration-Response Function

Cu: Copper

EPA: Environmental Protection Agency

EU: European Union

Fe: Iron

HIA: Health Impact Assessments

ICD: International Code of Diseases

La: Lanthanum

LE: Life Expectancy

Li: Lithium

Mn: Manganesese

Ni: Nickel

nmC: non mineral carbon=organic matter and elemental carbon

NO_2: Nitrogen Dioxide

O_3: Ozone

OR: odds ratio

P: Potassium

PM: Particulate Matter

PM_1: Particulate Matter with aerodiameter between inferior to 1 micrometer

$PM_{10:}$ Particulate Matter with aerodiameter inferior to 10 micrometers

$PM_{10-2.5}$: Particulate Matter with aerodiameter between 10 and 2.5 micrometers

$PM_{2.5}$: Particulate Matter with aerodiameter inferior to 2.5 micrometers

Rb: Rubidium

RR: Relative Risk

Sb: Antimony

Si: Silicon

Sn: Tin

Sr: Strontium

Th: Thorium

Ti: Titanium

Tl: Thallium

TSP: Total Suspended Particles

UF: Ultrafine particles

US: United States

V: Vanadium

VSL: Value of Statistical Life

WHO: World Health Organization

WTP: Willingness-to-pay

Zn: Zinc

Zr: Zirconium

Appendix

Commentary for paper II

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Desert dust: an unrecognized source of dangerous air pollution?
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