Air quality modeling and mortality impact of fine particles reduction policies in Spain

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A B S T R A C T

Background: In recent years, Spain has implemented a number of air quality control measures that are expected to lead to a future reduction in fine particle concentrations and an ensuing positive impact on public health.
Objectives: We aimed to assess the impact on mortality attributable to a reduction in fine particle levels in Spain in 2014 in relation to the estimated level for 2007.
Methods: To estimate exposure, we constructed fine particle distribution models for Spain for 2007 (reference scenario) and 2014 (projected scenario) with a spatial resolution of 16×16 km^2. In a second step, we used the concentration–response functions proposed by cohort studies carried out in Europe (European Study of Cohorts for Air Pollution Effects and Rome longitudinal cohort) and North America (American Cancer Society cohort, Harvard Six Cities study and Canadian national cohort) to calculate the number of attributable annual deaths corresponding to all causes, all non-accidental causes, ischemic heart disease and lung cancer among persons aged over 25 years (2005–2007 mortality rate data). We examined the effect of the Spanish demographic shift in our analysis using 2007 and 2012 population figures.
Results: Our model suggested that there would be a mean overall reduction in fine particle levels of 1 μg/m^3 by 2014. Taking into account 2007 population data, between 8 and 15 all-cause deaths per 100,000 population could be postponed annually by the expected reduction in fine particle levels. For specific subgroups, estimates varied from 10 to 30 deaths for all non-accidental causes, from 1 to 5 for lung cancer, and from 2 to 6 for ischemic heart disease. The expected burden of preventable mortality would be even higher in the future due to the Spanish population growth. Taking into account the population older than 30 years in 2012, the absolute mortality impact estimate would increase approximately by 18%.
Conclusions: Effective implementation of air quality measures in Spain, in a scenario with a short-term projection, would amount to an appreciable decline in fine particle concentrations, and this, in turn, would lead to notable health-related benefits. Recent European cohort studies strengthen the evidence of an association between long-term exposure to fine particles and health effects, and could enhance the health impact quantification in Europe. Air quality models can contribute to improved assessment of air pollution health impact estimates, particularly in study areas without air pollution monitoring data.

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1. Introduction

The epidemiological literature has signaled that exposure to air pollution, especially fine particles of less than 2.5 μm in aerodynamic diameter (hereinafter referred to as "fine particles"), can lead to cases of immediate (acute) or delayed (chronic) premature death, from cardiopulmonary diseases in particular (Pope and Dockery, 2006; Valavanidis et al., 2008). Epidemiological cohort studies, both in Europe (Beelen et al., 2008; Cesaroni et al., 2013) and in North America (Pope et al., 2002; Turner et al., 2011), have estimated the long-term health risk posed by exposure to air pollution. The Harvard Six Cities study reported a 14% increase in long-term all-cause mortality for every increase of 10 $\mu g/m^3$ in fine particle concentration (Lepeule et al., 2012). This last study and other recent European cohort studies (Cesaroni et al., 2013; Raaschou-Nielsen et al., 2013a) have reported increases in long-term mortality even at fine particle levels below the ambient air quality standards.

Evidence from a growing body of epidemiological studies has historically supported critical environmental policy decisions (Fann et al., 2011). Assessments of interventions which improve air quality show that a decrease in fine particle levels is accompanied by substantial health benefits (van Erp et al., 2008). By way of example, the 1990 ban on the use of coal in Dublin (Ireland) led to a 70% reduction in monthly mean particle concentrations, and a 6%, 15% and 10% decrease in all-cause, respiratory and heart disease mortality rates, respectively (Clancy et al., 2002).

Health impact assessment makes it possible to quantify the effect that public policies may have on the health of the population (WHO, 2000). Quantitative risk assessment methods are useful in providing point estimates, or a range of estimates, for the health risks associated with a variety of hazards, including air pollution, and are often used in health-based policy making (O'Connell and Hurley, 2009). For health impact assessment purposes, air quality information must be linked to the population subject to the exposure. The application of air quality models helps to examine potential air quality impacts and related health effects associated with emissions, and develop country-wide health impact assessment, especially in study areas without air pollution monitoring data (Dhondt et al., 2012).

In Spain, the Air Pollution Risk Assessment System (*Sistema de Evaluación de Riesgos por Contaminación Atmosférica – SERCA*) research project pioneered a nation-wide health impact assessment of air pollution, based on a reduction in fine particle levels in 2011 vis-à-vis 2004, as a result of a series of air quality control measures. Although such policy measures are not necessarily focused on health, they could nonetheless have an indirect effect on health. This study estimated that 1718 annual deaths were attributable to an average annual reduction of 0.7 $\mu g/m^3$ in fine particle levels in Spain (Boldo et al., 2011). The experience and knowledge acquired in this first stage of the project was used to undertake a new nation-wide health impact assessment, with more accurate estimates and a time horizon extended to 2014. This study now shows the impact of various air quality control measures on mortality, taking fine particle concentrations as an overall indicator of air pollution (WHO, 2006). In addition to total mortality, the study analyzes the impact of changes in fine particle levels on two of the leading principal causes of death in Spain (INE, 2013), namely, ischemic heart disease and lung cancer.

2. Materials and methods

Quantitative health impact assessment estimates were derived by linking together: (i) estimates of how proposed policies would affect population exposures; (ii) background mortality rates; and, (iii) concentration–response functions, typically expressed as percentage change in health effect per unit of exposure. This is an established approach when quantifying health impacts mediated by air pollution (O'Connell and Hurley, 2009).

2.1. Air pollution scenarios: 2007–2014

We defined a reference scenario corresponding to 2007, based on data drawn from the official National Emission Inventory for Spain (MARM., 2010), and designed a projected scenario to simulate air pollution distribution in 2014 in a case where air quality control measures planned in 2007 proved successful. This projected scenario was based on the reference scenario defined for Spain using emission projection methodology (Lumbreras et al., 2008), and assumed significantly decreased emissions of fine particle precursors (e.g., 51% reduction in primary fine particle emissions) resulting from technological measures targeting the road transport sector, industry and power generation (Table 1). The projected scenario reflected the most likely future situation, since it included expected outcomes from official plans and specific legislation (see Supplementary material, Table 1). Accordingly, the emissions and, by extension, the changes in air quality reported in this paper may be regarded as the most feasible evolution over the period considered. These measures affect a wide number of pollutants, with reduction in fine particle concentrations being chosen as an overall indicator of the health benefits to be obtained as a result of an improvement in air quality.

For both scenarios, emissions were initially processed using the Sparse Matrix Operator Kernel Emissions (SMOKE) modeling system (Borge et al., 2008). The US Environmental Protection Agency's (US EPA) Community Multiscale Air Quality model (CMAQ v4.6) was then applied (Byun and Schere, 2006) to simulate fine particle concentration levels ($\mu g/m^3$) for the entire Iberian Peninsula, Balearic Islands, Ceuta and Melilla, using a grid with a spatial resolution of 16×16 km^2 (4500 cells). Since the SERCA modeling domain was centered on the Iberian Peninsula, the Canary Islands were not included for estimation purposes. The Community Multiscale Air Quality (CMAQ) model is a next-generation 3D Eulerian Chemical-transport model which provides a comprehensive picture of air pollutants in the atmosphere under an holistic approach. Interactions among pollutants and processes are taken into account (emissions, physical transport and deposition phenomena, photochemical reactions, gas-particle interactions, secondary aerosols, etc.). Detailed information regarding the working principles and model formulation can be found elsewhere (Byun and Schere, 2006; Byun et al., 1999). The CMAQ modeling results provided the basis for the health impact estimates. Using the Environmental Benefits Mapping and Analysis Program (BenMAP: http://www.epa.gov/air/benmap/), a health impact assessment tool designed by the US EPA, air pollution changes in each cell were calculated by subtracting air pollution levels resulting from CMAQ models (projected minus reference).

2.2. Study population and mortality rates for the reference scenario

For each town in Spain (8109 municipalities), the Spanish National Statistics Institute furnished population data and the number of deaths corresponding to all-cause mortality, including external causes (International Classification of Diseases, 10th revision (ICD-10), codes A00-Y98), all non-accidental causes (ICD-10 codes A00-R99), ischemic heart disease (ICD-10 codes I20-I25) and lung cancer (ICD-10 code C33-C34), broken down by 5-year age groups, for the period 2005–2007, to make for more stable estimates. Lung cancer deaths included deaths due to malignant neoplasm of the trachea, bronchus, and lung. Mortality and municipal population data were used to calculate the mortality rates for each town. In addition, we also used municipal population data for year 2012 to consider the effect of the Spanish demographic shift on this health impact assessment.

In Spain, municipal centroids are computed by taking only the inhabited area of the designated town into account, and are situated in the center of the most populous zone. Each municipality was therefore assigned the geographical coordinates corresponding to its centroid, which were then deemed to be representative points of the location of the town's population. An overlapping grid identical to that used for the air quality models (spatial resolution of 16×16 km^2) was then applied, using geographic information system software to identify which centroids were located in each cell. In those cells that included more than one municipal centroid, mortality and population data were aggregated to obtain a unique cell value. Air pollution changes in each cell calculated as described above, were applied to all the centroids included. Fig. 1 shows the spatial distribution of the population, and includes a close-up of two specific Autonomous Regions, Madrid and Murcia. Towns in the Madrid Region tend to be smaller in terms of geographical area than those in Murcia, thereby making it possible for at least one centroid representative of the corresponding population to be included in all the grid squares. In Murcia, however, municipalities cover a greater surface area, so that there are blank squares that do not include population centroids.

2.3. Selection of concentration–response functions

We estimated attributable deaths using health impact functions based on studies of long-term exposure to fine particles conducted on large cohorts in Europe (Cesaroni et al., 2013; Raaschou-Nielsen et al., 2013a) and North America

Table 1
Primary fine particle emissions (*t*) and emission variation (%) in Spain (2007–2014).

Selected Nomenclature for Sources of Air Pollution group[a]	Activity	Emissions in 2007 (t)	Emissions in 2014 (t)	Emission variation (%)
01	Combustion in energy and transformation industries	13,808	5388	−61
02	Non-industrial combustion plants	23,048	22,516	−2
03	Combustion in manufacturing industry	10,770	4661	−57
04	Production processes	5086	4498	−12
05	Extraction and distribution of fossil fuels and geothermal energy	133	113	−15
07	Road transport	33,303	14,019	−58
08	Other mobile sources and machinery	43,369	10,092	−77
09	Waste treatment and disposal	72	76	6
10	Agriculture	2848	3951	39
	Total	132,437	65,314	−51

[a] Selected Nomenclature for Sources of Air Pollution 11 (Nature) was not included since no variation on natural sources was considered for this period.

(Crouse et al., 2012; Krewski et al., 2009; Lepeule et al., 2012; Pope et al., 2004, 2002). We calculated the mortality impact of a reduction in fine particles for all-causes (Krewski et al., 2009; Lepeule et al., 2012; Pope et al., 2002), all non-accidental causes (Cesaroni et al., 2013; Crouse et al., 2012), ischemic heart disease (Cesaroni et al., 2013; Crouse et al., 2012; Krewski et al., 2009; Pope et al., 2004) and lung cancer (Cesaroni et al., 2013; Krewski et al., 2009; Lepeule et al., 2012; Pope et al., 2002; Raaschou-Nielsen et al., 2013a). The concentration–response function relates a change in fine particle concentration to a change in mortality. In order to be consistent with the selected concentration–response functions, all mortality analysis targeted the age group examined in each cohort study. Table 2 summarizes the main characteristics of these cohort studies and their concentration–response functions, expressed as hazard ratios per 10 $\mu g/m^3$ increase in fine particles.

Several concentration–response functions used for this health impact assessment analysis were not included in the BenMAP. In these cases, the values of the regression coefficients (β), which is the natural logarithm of the hazard ratio for an increase in concentrations of fine particles of 1 $\mu g/m^3$, and their standard errors were calculated on the basis of the published confidence interval of concentration–response functions for specific causes (Abt Associates Inc, 2010a) and were then introduced into the BenMAP software.

2.4. *Estimation of attributable fine particle health impact*

The BenMAP tool is compatible with the US EPA's Community Multiscale Air Quality model. Following the application of Community Multiscale Air Quality software, the model's outputs were processed and introduced into the BenMAP, in order to estimate crude figures of all-cause, all non-accidental cause, ischemic heart disease and lung cancer mortality attributable to the changes in air quality. For each grid cell within Spain's territorial boundaries, we therefore supplied average population figures for the period 2005–2007, mortality rates broken down by 5-year age group, and estimated fine particle levels for 2007 and 2014. We repeated the analyses using the Spanish population in 2012.

Assuming that the entire population was exposed to fine particle air pollution, attributable deaths were calculated in absolute and relative numbers on a grid cell-by-cell basis in Spain. The following equation was used to calculate the change in the mortality rate based on differences in CMAQ-derived fine particle concentrations between the two simulations:

$$\Delta Y = Y_0(1 - 1/HR^{\Delta Q})P$$

where Y_0 is the mortality rate at the reference scenario; HR, the hazard ratio for an increase in concentrations of fine particles of 1 $\mu g/m^3$, as derived from the selected cohort studies (Table 2); ΔQ, the change in estimated air pollutant concentration between the reference and projected scenario; and *P*, the potentially affected population at the reference scenario.

The BenMAP software calculates a distribution of point estimates in each grid cell of the number of attributable deaths associated with changes in fine particles between the two scenarios considered. For each grid cell, we selected the median, and the 5th and 95th percentiles of this distribution to provide a range of uncertainty for health impact assessment results. National figures of deaths attributable to fine particle reduction were obtained by adding up all the cell estimates. When the lower estimate of the concentration–response function was below 1, as was the case for the effect of fine particles on lung cancer mortality in the framework of the European Study of Cohorts for Air Pollution Effects (Raaschou-Nielsen et al., 2013a), we considered that the minimum health benefits of reducing air pollution would be null, and set the lower limit of the range to 0. The methodology used in this study is described in detail elsewhere (Abt Associates Inc, 2010a, 2010b; Fann et al., 2009).

3. Results

In Spain, the main sectors responsible for emissions of primary fine particles in 2007 and 2014 were road transport and other mobile sources, machinery, non-industrial combustion plants, and combustion in the energy, transformation, and manufacturing industries. The combination of all these accounted for 94% of emissions of this pollutant in 2007. Among these sectors, note should be taken of transport (both road and off-road) with 58% of total fine particle emissions in 2007. By implementing air quality control measures, it is precisely these sectors, along with the combustion sector (in the energy, transformation, and manufacturing industries), that could most reduce their emissions, i.e., by 61% and 59% (Table 1).

With regard to the air quality simulation, the national average fine particle concentration in the reference scenario (2007) was 6.3 $\mu g/m^3$; the result of modeling for 2014 showed a generalized improvement throughout the territory, with the average fine particle concentration being reduced to 5.4 $\mu g/m^3$. The difference between the two scenarios amounts to an overall reduction of approximately 15% or 1 $\mu g/m^3$ (range 0.3–4.3 $\mu g/m^3$) in Spain. If air quality control measures were successfully implemented, reductions would be achieved in especially important fine particle levels, particularly in large Spanish cities such as Madrid (4.3 $\mu g/m^3$), Barcelona and the Greater Barcelona area (3.5 $\mu g/m^3$), and Valencia (3 $\mu g/m^3$). Fig. 2 displays the difference in simulated average fine particle concentration ($\mu g/m^3$) between the projected (2014) and reference scenario (2007) for each grid cell.

Spanish population was heterogeneously distributed across 8019 towns, though most of these subjects tend to congregate in large cities (Fig. 1). Spain had an annual population over the age of 30 years of 27,953,825 in 2007, and 30,889,710 in 2012. Table 3 shows the average annual number of deaths (period 2005–2007) for each selected mortality indicator, as well as population figures in 2007 and in 2012 according to the specific age range used in each cohort study.

Table 3 also summarizes the long-term mortality findings in terms of the total annual number of attributable deaths (50th, 5th–95th percentiles) and crude annual rates per 100,000 population, which could be potentially prevented by the fine particle reduction scenario in Spain. Using 2007 population figures and depending on the selected concentration–response functions, our analysis indicated a number of attributable deaths from all causes ranging from 2365 to 4163, corresponding to crude rates from 8 to 15 deaths delayed per 100,000 population, and it would account for approximately 0.7–1.1% of the total number of annual deaths in this population. Of the estimated mortality attributable to all causes, between 186 and 777 annual deaths (1–5 deaths per

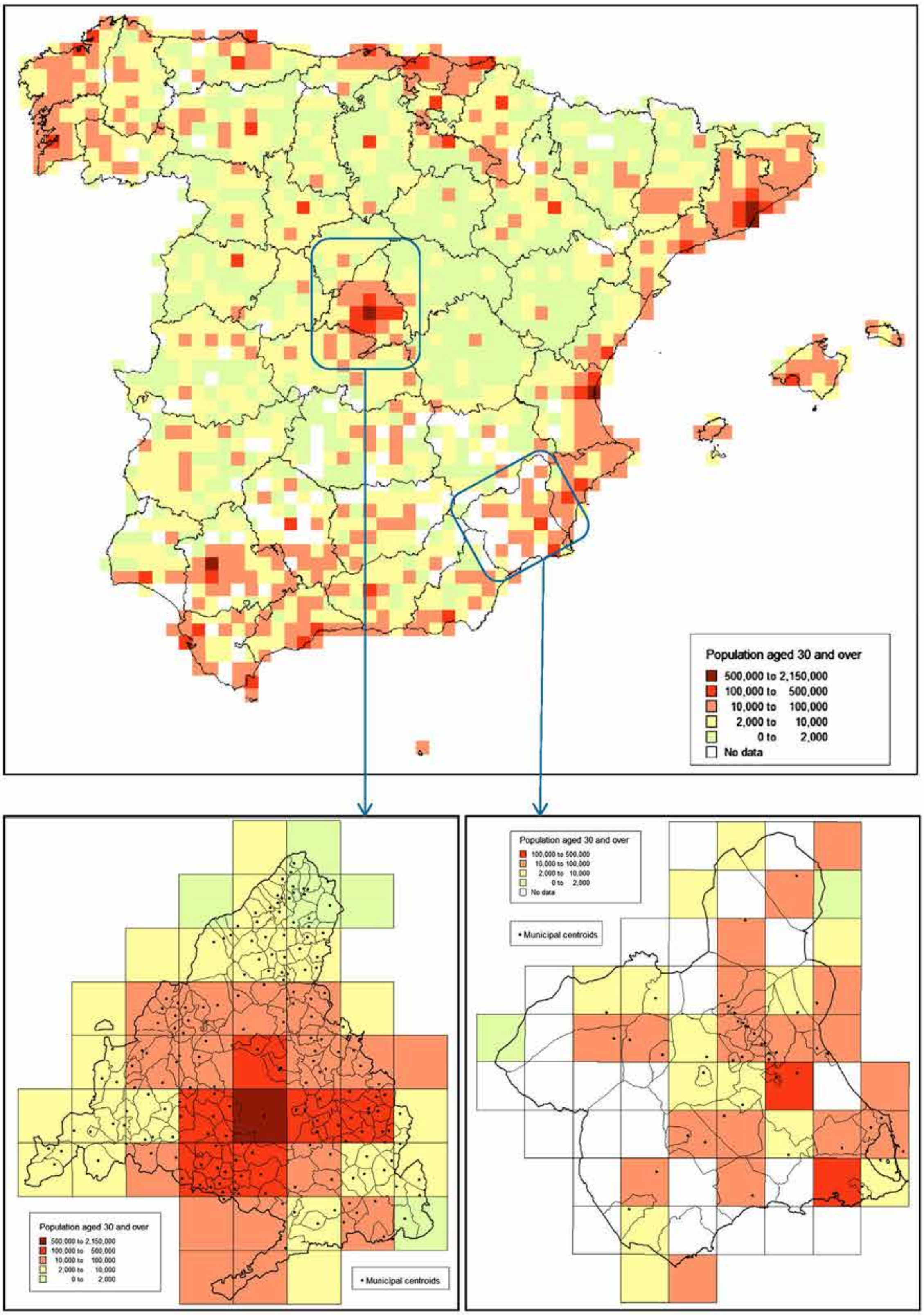

Fig. 1. Spatial distribution of Spanish population (annual average 2005–2007): detailed breakdown showing Madrid (bottom left) and Murcian Regions (bottom right) with municipal centroids.

100,000 population) were due to lung cancer and between 654 and 1817 annual deaths (2–6 deaths per 100,000 population) were due to ischemic heart disease. In relative terms, the impact of air pollution was greater when cause-specific mortality coefficients were used, i.e., 1.0–6.5% of annual deaths due to lung cancer and 1.8–5.1% of annual deaths due to ischemic heart disease.

On the other hand, we explored the effect of using different estimates from the same cohort study, i.e. American Cancer Society

Table 2
Main characteristics of the epidemiological studies and concentration–response functions used for long-term mortality impact assessment of fine particles.

Cohort study	Reference	Study area	Population		Follow-Up		Fine particles exposure assessment	Health outcome (mortality)	Hazard ratio (95%CI) (for 10 μg/m³ increase in fine particles)
			Number of Participants	Age range	Number of years	Last year			
American Cancer Society	Pope et al., 2002	USA	319,000	30–99	16	1998	Inhalable Particle Monitoring Network and Aerometric Information Retrieval System	All causes (ICD-10: A00-Y98)	1.06 (1.02–1.11)
	Krewski et al., 2009	USA	499,968	30–99	18	2000			1.03 (1.02–1.05)
Harvard Six Cities	Lepeule et al., 2012	USA	8096	25–74	35	2009	Central monitoring stations	All non-accidental causes (ICD 10: A00-R99)	1.14 (1.07–1.22)
Canadian national cohort	Crouse et al., 2012	Canada	2,145,400	> 25	10	2001	Satellite-derived estimates		1.15 (1.13–1.16)
Rome longitudinal study	Cesaroni et al., 2013	Italy	1,265,058	> 30	9	2001	Eulerian dispersion model		1.04 (1.03–1.05)
American Cancer Society	Pope et al., 2002	USA	319,000	30–99	16	1998	Inhalable Particle Monitoring Network and Aerometric Information Retrieval System	Lung cancer (ICD-10: C33-C34)	1.14 (1.04–1.23)
	Krewski et al., 2009	USA	499,968	30–99	18	2000			1.11 (1.04–1.18)
Harvard Six Cities	Lepeule et al., 2012	USA	8096	25–74	35	2009	Central monitoring stations		1.37 (1.07–1.75)
ESCAPE Project*	Raaschou-Nielsen et al., 2013a	European countries	273,838	43–73	13	2003	Land-use regression models		1.40 (0.92–2.13)
Rome longitudinal study	Cesaroni et al., 2013	Italy	1,265,058	> 30	9	2001	Eulerian dispersion model		1.05 (1.01–1.10)
American Cancer Society	Pope et al., 2004	USA	319,000	30–99	16	1998	Inhalable Particle Monitoring Network and Aerometric Information Retrieval System	Ischemic heart disease (ICD-10: I20-I25)	1.18 (1.14–1.23)
	Krewski et al., 2009	USA	499,968	30–99	18	2000			1.15 (1.11–1.20)
Canadian national cohort	Crouse et al., 2012	Canada	2,145,400	> 25	10	2001	Satellite-derived estimates		1.31 (1.27–1.35)
Rome longitudinal study	Cesaroni et al., 2013	Italy	1,265,058	> 30	9	2001	Eulerian dispersion model		1.10 (1.06–1.13)

* ESCAPE project: European Study of Cohorts for Air Pollution Effects. Data from 14 European cohort studies. Participants were recruited in the 1990s and the average follow-up was 13 years.

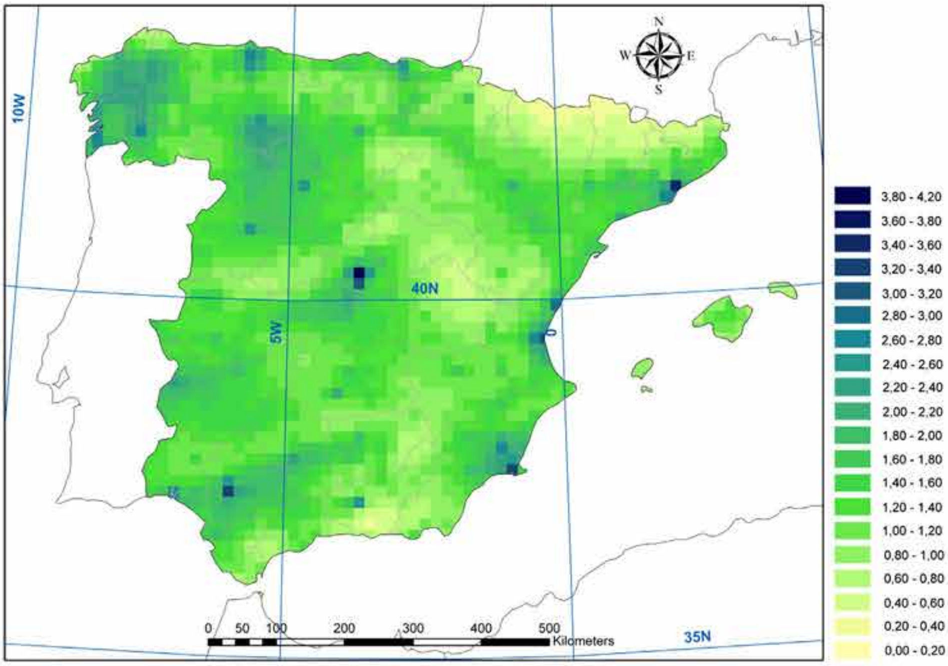

Fig. 2. Modeled fine particle reduction ($\mu g/m^3$) between reference and projected scenarios (2007–2014).

cohort (Krewski et al., 2009; Pope et al., 2004; Pope et al., 2002). We found a decrease by 43% for all causes (2365 deaths, range: 1306–3420), by 22% for lung cancer (389 deaths, range: 180–518), and by 15% for ischemic heart disease (972 deaths, range: 761–1181), when using the Krewski's concentration–response functions compared to those of Pope.

Finally, in relation to the 2012 population figures, our findings in terms of postponed deaths would increase by 18% for all causes, by 10% for lung cancer, and by 17% for ischemic heart disease, compared to the values using 2007 population data and Pope's estimates. In contrast, when we used the Harvard Six Cities concentration–response functions and its younger population range (Lepeule et al., 2012), the increase was limited to 5% for all-causes and to 7% for lung cancer.

Fig. 3 depicts the geographical distribution of the absolute number of annual attributable deaths and the annual crude rate of attributable deaths per 100,000 population expected in 2014 using population in 2007, and estimated using Pope's concentration–response functions (Pope et al., 2004; Pope et al., 2002). In terms of absolute numbers, the greatest health benefits resulting from a reduction in air pollution would be observed in large cities and provincial capitals, where the highest fine particle reduction concentrations are usually found. This is because of the wide difference in concentrations between the two scenarios and the great number of inhabitants that congregate in these population centers. In the country's capital, Madrid (2,146,146 inhabitants aged over 30 years), a total of 650, 168 and 80 annual deaths due to all causes, ischemic heart disease and lung cancer respectively (50th percentile) was estimated to be attributable to a 4.3 $\mu g/m^3$ reduction in fine particles. Something similar would occur in Barcelona and its outlying towns (Hospitalet de Llobregat, Prat de Llobregat, Sant Adrià de Besòs and Venturada) (with 1,346,419 inhabitants aged over 30 years), where there were an estimated 292, 69 and 37 annual deaths due to all causes, ischemic heart disease and lung cancer respectively. Other towns situated in the Greater Barcelona area and in Valencia and the Greater Valencia area also registered a reduction in fine particles of over 3 $\mu g/m^3$, so that they made a substantial contribution to the number of deaths attributable to air pollution. Nevertheless, the geographical distribution of the crude mortality rates indicates that the greatest health benefits in relative terms would be felt in certain areas of the Autonomous Regions of Galicia, Castile-Leon, Extremadura and Andalusia, and along the Mediterranean.

4. Discussion

This study reports the mortality impact in Spain expected in 2014, resulting from a mean reduction of 1 $\mu g/m^3$ in fine particle concentrations. Taking into account 2007 population data, between 8 and 15 all-cause deaths per 100,000 population could be postponed annually by the expected reduction in fine particle levels. For specific subgroups, estimates varied from 10 to 30 deaths for all non-accidental causes, from 1 to 5 for lung cancer, and from 2 to 6 for ischemic heart disease. For each mortality indicator, our results varied depending on the selected cohort studies, which included different age range and provided different hazard ratios.

If we consider the Spanish population growth occurring from 2007 to 2012 and Pope's estimates, the mortality impact would increase by 18%, 10% and 17% for all causes, lung cancer and ischemic heart disease, respectively (Pope et al., 2004, 2002). We should keep in mind that the American Cancer Society cohort included people over 30, while the Harvard Six Cities cohort recruited participants between 25 and 74 years old. This age variation could explain the lower increases – close to 5% – obtained applying the Harvard cohort risk functions to our data. Differences between both estimates could highlight the relevance of Spanish population ageing in our health impact assessment.

The results of this health impact assessment are in line with other previously conducted studies, both national (Perez et al., 2009) and international in scope (Anenberg et al., 2010; Ballester et al., 2008; Pascal et al., 2013). Our findings afford new reasons for reviewing the fine-particle-related provisions envisaged under Directive 2008/50/EC on ambient air quality and cleaner air for Europe.

With respect to the methodology, it should be noted that accurate assessment of population exposure to air pollution is crucial to estimating the health impact. This study used air quality

Table 3
Long-term mortality impacts of reducing fine particle concentrations in Spain by 2014 (absolute numbers and numbers per 100,000 population).

Mortality indicator	Reference	Age range	Average annual mortality (Period 2005–2007)	Long-term health impact assessment							
				Based on the Spanish population in 2007				Based on the Spanish population in 2012			
				Population	Annual number of attributable deaths		Annual number of attributable deaths per 100,000 population	Population	Annual number of attributable deaths		Annual number of attributable deaths per 100,000 population
					Median	5–95th percentile	Median		Median	5–95th percentile	Median
All causes											
	Pope et al., 2002	30–99	360,407	27,953,825	4163	1635–6669	15	30,889,710	4901	1925–7852	16
	Krewski et al., 2009				2365	1306–3420	8		2821	1557–4080	9
	Lepeule et al., 2012	25–74	114,796	28,081,812	2961	1729–4178	10	29,724,117	3108	1814–4384	10
All non-accidental causes											
	Crouse et al., 2012	> 25	348,330	31,572,075	9447	8712–10,173	30	33,857,417	11,273	10,400–12,140	33
	Cesaroni et al., 2013	> 30	347,661	27,953,825	2677	2128–3224	10	30,889,710	3197	2542–3851	10
Lung cancer											
	Pope et al., 2002	30–99	18,848	27,953,825	500	228–767	2	30,889,710	550	257–839	2
	Krewski et al., 2009				389	180–518	1		432	201–661	1
	Lepeule et al., 2012	25–74	11,915	28,081,812	777	274–1256	3	29,724,117	833	294–1345	3
	Raaschou-Nielsen et al., 2013a	43–73	8870	12,279,889	589	0–1157	5	14,054,059	662	0–1300	5
	Cesaroni et al., 2013	> 30	18,848	27,953,825	186	50–321	1	30,889,710	207	55–357	1
Ischemic heart disease											
	Pope et al., 2004	30–99	35,672	27,953,825	1143	922–1362	4	30,889,710	1343	1089–1596	4
	Krewski et al., 2009				972	761–1181	3		1159	907–1408	4
	Crouse et al., 2012	> 25	35,693	31,572,075	1817	1650–1984	6	33,857,417	2165	1966–2364	6
	Cesaroni et al., 2013	> 30	35,672	27,953,825	654	472–836	2	30,889,710	780	562–996	3

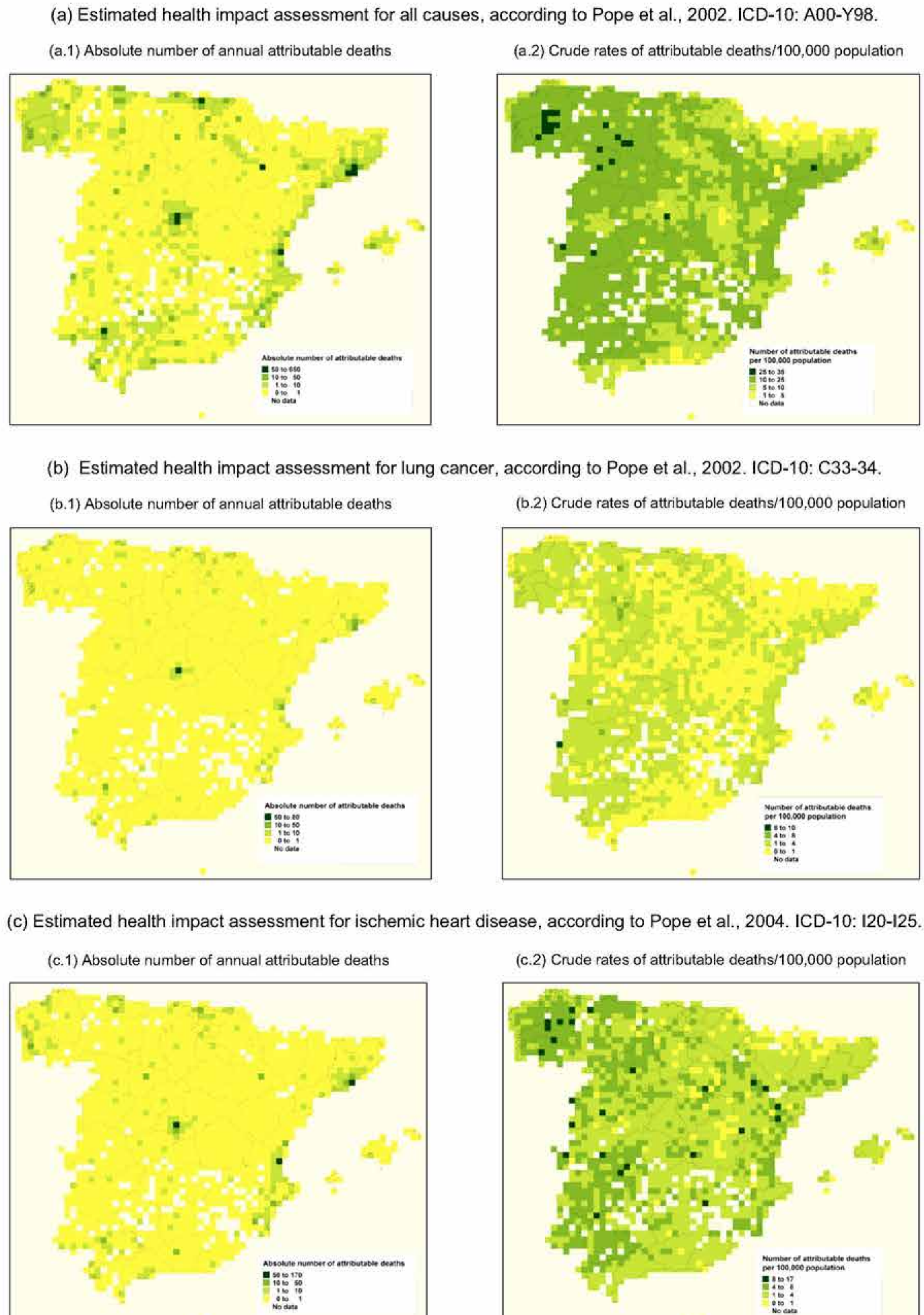

Fig. 3. Assessment of the annual long-term mortality impact of a reduction in fine particle levels (μg/m^3) in Spain. Air quality scenarios: reference year, 2007; projected year, 2014. Population and mortality rate: period 2005–2007.

models with a spatial resolution of 16×16 km^2 and incorporated air pollution control measures recently implemented in Spain (see Supplementary material, Table 1). Spatial comparisons of air pollution patterns are facilitated by the use of maps and are useful in health-based policy-making. In terms of a reduction in emissions, this would primarily take place in industries, essentially power plants in the north-western quarter of the country and the ceramics industry in areas lying along the Mediterranean seaboard. Nonetheless, the most important reductions are expected in urban settings, and are associated with technological improvements to vehicles (mainly the fitting of particle filters) and the application of sustainable urban transport and/or air quality control plans. These measures have already been partially implemented and have achieved a substantial reduction in fine particle emissions (e.g., at a national level the reduction in fine particle emissions in the period 2007–2009 was 20% (MARM., 2011)).

Our projections should be valid, since fine particle reduction levels have been described in European countries in recent years and have been attributed to various causes. On the one hand, the implementation of pollution-abatement strategies in Europe is having a direct effect on the levels of fine particles and their various components. A recently published study has stated that reductions in fine particles were observed across all stations in Spain and Europe to varying degrees (7–49%) over the period 2002–2010 (Cusack et al., 2012). This reduction has been gradual and consistent over time, implying the success of cleaner anthropogenic activities. On the other hand, the influence of the North Atlantic Oscillation has been noted, a large-scale meteorological phenomenon which is most prevalent during winter and modifies the frequency of Saharan dust intrusions across the Iberian Peninsula (Vicente-Serrano et al., 2011). As a result of the negative North Atlantic Oscillation, particulate matter levels have been considerably lower than in other winters (Pérez et al., 2008). Lastly, the ongoing economic crisis could also have caused a general fall in fine particle emissions (Cusack et al., 2012) and thus changed ambient trace element concentrations (Arruti et al., 2011; Santacatalina et al., 2012). Since 2008, many European countries have been in recession, which affects air pollutants through a reduction in activities associated with a healthy economy (e.g., increased road traffic, industrial processes and construction) (Cusack et al., 2012).

Since reductions in air pollution occur gradually after the implementation of environmental policies, the appearance of any concomitant health benefits could be expected to occur in a similar manner. Whereas any short-term health impacts might be expected to be seen almost immediately, in the case of the consequences of air pollution caused by a combination of short- and long-term causes, it might well take some years before the ensuing health benefits would be observable. Moreover, risk factors can be competitive, something that could also interfere in the appearance of any long-term benefits. Hence, greater uncertainty surrounds the nature of any possible long-term impacts and benefits than those in the short term (Kunzli et al., 2001). Intervention studies have been conducted to estimate the reduction in risk following a decrease in air-pollution levels (Clancy et al., 2002; Pope et al., 1992). Taking these studies into account, Roosli et al. proposed an exposure–response model to quantify dynamic changes in mortality following increases or decreases in air-pollution levels (Roosli et al., 2005). According to these authors, a substantial proportion of the benefit flowing from reducing contamination levels is seen to occur a few years after the reduction has taken place: in percentage terms, the effect was estimated as being 40% in the same year and 80% within 5 years (e.g., in our study a range of 1892–3330 attributable deaths). At all events, it should be noted that, while major benefits are to be expected in terms of public health, the real temporal pattern of such incremental health benefits is unknown and difficult to assess.

The choice of a concentration–response function between fine particle exposure and mortality can generate a considerable difference in the predicted health impact estimate at lower concentrations. To explore these variations, we used different hazard ratios provided by large cohort studies conducted in Europe (Cesaroni et al., 2013; Raaschou-Nielsen et al., 2013a) and North America (Crouse et al., 2012; Krewski et al., 2009; Lepeule et al., 2012; Pope et al., 2004, 2002), that could be considered the most updated evidence of the effects of long-term exposure to fine particles on mortality. Table 2 summarizes the main characteristics of the selected cohort studies for this health impact assessment. These studies reported different concentration–response functions for fine particles-related health effects. The disparities among them can be due to (a) the variability among different populations, i.e. disparities in susceptibility, baseline health conditions or lifestyles; (b) the environmental conditions, such as study area characteristics, geographic location or pollutant mixtures; and (c) the exposure assessment methodology.

In relation to the North American cohort studies, the American Cancer Society cohort (Krewski et al., 2009; Pope et al., 2004, 2002) is usually regarded as the largest cohort study available to date on the long-term effects of fine particles on mortality. The estimates furnished by this cohort are more conservative than those reported by similar studies (Crouse et al., 2012; Lepeule et al., 2012), and have already been used in other health impact assessment studies carried out in Europe (Ballester et al., 2008; Pascal et al., 2013). The Extended follow-up of the American Cancer Society cohort through 2000 (18 years) (Krewski et al., 2009) supported earlier findings (16 years follow-up) (Pope et al., 2004, 2002) of a positive association between long-term exposure to fine particles in ambient air and increased mortality rates in urban centers in the United States. The analysis conducted by Krewski and colleagues observed a decrease in the concentration–response function estimates for deaths attributable to fine particles compared with that of the initial follow-up period (Pope et al., 2004, 2002). According to Krewski and colleagues, the lower risk found could be due to exposure misclassification increasing over time. They assigned exposure based on residence location at the beginning of follow-up and cohort members who moved increased over time. In addition, fine particles concentrations declined over the follow-up period, so assigning a single exposure measure would not have fully captured this temporal pattern. Finally, as the cohort ages, air pollution effects may decline due to the healthy survivor effect (Krewski et al., 2009). The American Cancer Society cohort results showed how the health effect estimates of fine particles changed over time. When using hazard ratios from the Updated Analysis of the American Cancer Society cohort (Pope et al., 2004, 2002), we found that 4163 annual deaths could be delayed in 2014, including 500 due to lung cancer and 1143 deaths due to ischemic heart disease, in a population of nearly 28 million. These last findings decreased by 43%, 22% and 15%, when using the estimates from the Extended Analysis of the American Cancer Society study (Krewski et al., 2009). It is complicated to extrapolate these deviations when applying their estimates to target populations, and transferability issues can arise (Boldo et al., 2011).

Several studies undertaken in Europe have also estimated concentration–response functions for health outcomes attributable to long-term exposure to fine particles. In this report, we have used the most recent results of European cohort studies (Cesaroni et al., 2013; Raaschou-Nielsen et al., 2013a). For lung cancer, we used the latest results of European Study of Cohorts for Air Pollution Effects (Raaschou-Nielsen et al., 2013a), which combined 14 long-term cohort studies from nine European countries. They identified a hazard ratio of 1.40 (95% CI=0.92–2.13) for all lung cancers per 10 $\mu g/m^3$ in fine particles (Raaschou-Nielsen et al., 2013a), which is similar to the Harvard Six Cities estimate (Lepeule et al., 2012) and that from the Canadian study (Crouse et al., 2012), but higher than the estimate from the American Cancer Society study (Pope et al., 2002), and from the cohort study in Italy (Cesaroni et al., 2013).

The use of Rome longitudinal study risk estimates (Cesaroni et al., 2013) could be considered a cautious approach, as they were lower than those reported in other European (Brunekreef et al., 2009; Naess et al., 2007; Raaschou-Nielsen et al., 2013a) and North American settings (Crouse et al., 2012; Lepeule et al., 2012; Pope et al., 2002). These Italian risk functions could be more suitable for our health impact assessment due to the common characteristics between both countries. Italy and Spain share notable similarities on culture and environmental conditions, i.e. both are Mediterranean countries located in southern Europe. Additional similarities exist with respect to crucial socioeconomic indicators, such as labor markets or population educational attainment (Eurostat, 2013).

The health impact analysis estimated that an overall reduction of 1 $\mu g/m^3$ in fine particles by 2014 would succeed in preventing mortality attributable to this environmental risk factor. Taking into account the basic demographic components (mortality, fertility and migration), Spain is undergoing an ageing process which is accelerated by the decreasing birth rate and negative migratory balances. The Spanish National Statistics Institute has estimated that the greatest population growth would be concentrated among the higher age groups (INE, 2013). To incorporate population changes into the analysis, we repeated the calculations using 2012 population figures. Taking into account the population over the age of 30 years in 2012, the expected number of deaths attributable to fine particles exposure would be 4901, a figure substantially higher than the one estimated using the population data in 2007 (4163 deaths) (Table 3).

Our study also incorporated impact analysis for mortality due to specific causes, such as ischemic heart disease and lung cancer, since European studies on short- and long-term particulate matter exposure indicate a direct association with mortality in general, and mortality due to cardiopulmonary disease in particular (Fajersztajn et al., 2013; Hoek et al., 2013; Pope and Dockery, 2006). Our study focused on mortality because background country-wide rates of other health outcomes, such as hospital admissions or restricted activity days, were not available. In any event, further evidence has emerged of the effects of long-term exposure to fine particulate air pollution on diseases other than cardiovascular and respiratory diseases, such as adverse birth outcomes (Proietti et al., 2013), diabetes (Andersen et al., 2012; Raaschou-Nielsen et al., 2013b), neurological development in children and neurological disorders in adults (Ruckerl et al., 2011). There is a need to consider new health outcomes to be examined in health impact assessment studies.

The risk of ischemic heart disease has particularly strong and consistent associations with exposure to fine particles. Ischemic heart disease ranks as the leading cause of death in Spain, despite the fact that most of the risk factors (sedentarism, hypertension and dyslipidaemia) are known and modifiable. The trend in the mortality rate shows that from 1990 to 2007, risk in Spain fell by almost 30%, owing to improvements in treatment and lower exposure to risk factors (Bertomeu and Castillo-Castillo, 2008). Exposure to environmental particulate matter is another risk factor which potentiates cardiovascular morbidity and mortality due to acute (Peters et al., 2001) and chronic effects (Pope et al., 2004, 2002), and the mechanisms whereby this could cause systemic cardiovascular effects are being investigated (Bhaskaran et al., 2011; Brook et al., 2010). Evidence accumulated during the preceding decade indicates that the most important part of mortality caused by air pollution is due to cardiovascular disease, such that for every 10 $\mu g/m^3$ increase in fine particles, mortality due to ischemic heart disease increases from 10% (Cesaroni et al., 2013) to 31% (Crouse et al., 2012) in this mortality impact analysis. These findings have led to the proposal that exposure to these particles should be considered a new modifiable cardiovascular risk factor. According to our results, Spain could prevent a range of 2–5% of mortality due to this cause if the implementation of air quality control measures were effective.

In the case of lung cancer, smoking is considered the principal risk factor and gives rise to differences in mortality rate trends between men and women. Although it continues to be the tumor with the highest mortality rates, among men in Spain this rate decreased by 1% per annum from the 1990s, while among women it increased by 3% per annum over the same period (Cabanes et al., 2010). Epidemiological evidence that links air pollution to mortality from lung cancer is robust, particularly if only adenocarcinomas of the lung are considered (Raaschou-Nielsen et al., 2013a). Exposure to fine particulate matter is currently recognized as another of the principal modifiable risk factors for lung cancer (Fajersztajn et al., 2013; Thacker et al., 2005). New scientific evidence supports the relationship between exposure to fine particles and this disease (Fajersztajn et al., 2013), and it is estimated that a 10 $\mu g/m^3$ increase in fine particle concentrations is associated with a 15%–27% increase in lung cancer mortality (Turner et al., 2011). According to our results, Spain could prevent up to 6% of mortality due to this cause by reducing airborne fine particulate matter.

Recently, Pope et al. (2011) assessed the exposure–response relationship between fine particle exposure and cardiovascular and lung cancer mortality, reporting that the relationship for lung cancer (almost linear) was qualitatively different to that for cardiovascular mortality (nonlinear). These results are relevant, in view of the fact that health impact assessment studies conducted to date have tended to apply concentration–response functions, on the assumption of linear relationships between fine particle concentrations and the health effects assessed, something that might lead to the impact of exposure to low fine particle levels on cardiovascular mortality being underestimated.

5. Conclusions

In conclusion, air pollution constitutes one of the most significant environmental health risks and gives rise to both acute and chronic effects. In view of the fact that exposure to air pollution is a modifiable risk and that, to a great extent, this remains outside the control of the individual, public authorities must assume responsibility for adopting air quality control measures based on available scientific evidence. Compliance with European Directive guideline values should not only be a public health priority, so as to minimize any risks stemming from exposure to fine particles, but should also be a feasible goal, achievable through the interventions implemented in Spain. Nevertheless, since there is no known particulate matter threshold below which harmful health effects disappear, to improve the population's general state of health it is essential to continue setting increasingly ambitious targets, aimed at seeking a maximum reduction in air pollutant concentrations.

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Appendix A. Supplementary material

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References

Abt Associates Inc. 2010a. BenMAP. User's Manual. Appendices. Prepared for Office of Air Quality Planning and Standards, US EPA. Online at: ⟨http://www.epa.gov/air/benmap/models/BenMAPManualAppendicesAugust2010.pdf⟩. (accessed 12.05.12).

Abt Associates Inc. 2010b. BenMAP. User's manual. Prepared for Office of Air Quality Planning and Standards, US EPA. Online at: ⟨http://www.epa.gov/air/benmap/models/BenMAPManualAugust2010.pdf⟩. (accessed 12.05.12).

Andersen, Z.J., Raaschou-Nielsen, O., Ketzel, M., Jensen, S.S., Hvidberg, M., Loft, S., Tjonneland, A., Overvad, K., Sorensen, M., 2012. Diabetes incidence and long-term exposure to air pollution: a cohort study. Diabetes Care 35, 92–98.

Anenberg, S.C., Horowitz, L.W., Tong, D.Q., West, J.J., 2010. An estimate of the global burden of anthropogenic ozone and fine particulate matter on premature human mortality using atmospheric modeling. Environ. Health Perspect. 118, 1189–1195.

Arruti, A., Fernandez-Olmo, I., Irabien, A., 2011. Impact of the global economic crisis on metal levels in particulate matter (PM) at an urban area in the Cantabria Region (Northern Spain). Environ. Pollut. 159, 1129–1135.

Ballester, F., Medina, S., Boldo, E., Goodman, P., Neuberger, M., Iniguez, C., Kunzli, N., 2008. Reducing ambient levels of fine particulates could substantially improve health: a mortality impact assessment for 26 European cities. J. Epidemiol. Community Health 62, 98–105.

Beelen, R., Hoek, G., van den Brandt, P.A., Goldbohm, R.A., Fischer, P., Schouten, L.J., Jerrett, M., Hughes, E., Armstrong, B., Brunekreef, B., 2008. Long-term effects of traffic-related air pollution on mortality in a Dutch cohort (NLCS-AIR study). Environ. Health Perspect. 116, 196–202.

Bertomeu, V., Castillo-Castillo, J., 2008. Situación de la enfermedad cardiovascular en España. Del riesgo a la enfermedad. Rev. Esp. Cardiol. 08 (Supl.E), 2–9.

Bhaskaran, K., Wilkinson, P., Smeeth, L., 2011. Cardiovascular consequences of air pollution: what are the mechanisms? Heart 97, 519–520.

Boldo, E., Linares, C., Lumbreras, J., Borge, R., Narros, A., Garcia-Perez, J., Fernandez-Navarro, P., Perez-Gomez, B., Aragones, N., Ramis, R., Pollan, M., Moreno, T., Karanasiou, A., Lopez-Abente, G., 2011. Health impact assessment of a reduction in ambient PM(2.5) levels in Spain. Environ. Int. 37, 342–348.

Borge, R., Lumbreras, J., Rodriguez, E., 2008. Development of a high-resolution emission inventory for Spain using the SMOKE modeling system: a case study for the years 2000 and 2010. Environ. Modeling Software 23, 1026–1044.

Brook, R.D., Rajagopalan, S., Pope III, C.A., Brook, J.R., Bhatnagar, A., ez-Roux, A.V., Holguin, F., Hong, Y., Luepker, R.V., Mittleman, M.A., Peters, A., Siscovick, D., Smith Jr., S.C., Whitsel, L., Kaufman, J.D., 2010. Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. Circulation 121, 2331–2378.

Brunekreef, B., Beelen, R., Hoek, G., Schouten, L., Bausch-Goldbohm, S., Fischer, P., Armstrong, B., Hughes, E., Jerrett, M., Van Den, B.P., 2009. Effects of long-term exposure to traffic-related air pollution on respiratory and cardiovascular mortality in the Netherlands: the NLCS-AIR study. Res. Rep. Health Eff. Inst. 139, 5–71.

Byun, D., Schere, K.L., 2006. Review of the governing equations, computational algorithms, and other components of the models-3 community multiscale air quality (CMAQ) modeling system. Appl. Mech. Rev. 59, 51–77.

Byun, D., Ching, J., 1999. Science algorithms of the EPA models-3 community multiscale air quality (CMAQ) modeling system [microform]. In: Byun, D.W., Ching, J.K.S. (Eds.), U.S. Environmental Protection Agency. Office of Research and Development, Washington, DC.

Cabanes, A., Vidal, E., Aragones, N., Perez-Gomez, B., Pollan, M., Lope, V., Lopez-Abente, G., 2010. Cancer mortality trends in Spain: 1980–2007. Ann. Oncol. 21 (Suppl. 3), iii14–iii20.

Cesaroni, G., Badaloni, C., Gariazzo, C., Stafoggia, M., Sozzi, R., Davoli, M., Forastiere, F., 2013. Long-term exposure to urban air pollution and mortality in a cohort of more than a million adults in Rome. Environ. Health Perspect. 121, 324–331.

Clancy, L., Goodman, P., Sinclair, H., Dockery, D.W., 2002. Effect of air-pollution control on death rates in Dublin, Ireland: an intervention study. Lancet 360, 1210–1214.

Crouse, D.L., Peters, P.A., van, D.A., Goldberg, M.S., Villeneuve, P.J., Brion, O., Khan, S., Atari, D.O., Jerrett, M., Pope, C.A., Brauer, M., Brook, J.R., Martin, R.V., Stieb, D., Burnett, R.T., 2012. Risk of non-accidental and cardiovascular mortality in relation to long-term exposure to low concentrations of fine particulate matter: a Canadian National-level cohort study. Environ. Health Perspect. 120, 708–714.

Cusack, M., Alastuey, A., Perez, N., Pey, J., Querol, X., 2012. Trends of particulate matter (PM2.5) and chemical composition at a regional background site in the Western Mediterranean over the last nine years (2002–2010). Atmos. Chem. Phys. Discuss. 12, 10995–11033.

Dhondt, S., Beckx, C., Degraeuwe, B., Lefebvre, W., Kochan, B., Bellemans, T., Int Panis, L., Macharis, C., Putman, K., 2012. Health impact assessment of air pollution using a dynamic exposure profile: Implications for exposure and health impact estimates. Environ. Impact. Assess. Rev. 36, 42–51.

Eurostat, 2013. Europe indicators. Online at: ⟨http://epp.eurostat.ec.europa.eu/⟩. (accessed 04.10.13).

Fajersztajn, L., Veras, M., Barrozo, L.V., Saldiva, P., 2013. Air pollution: a potentially modifiable risk factor for lung cancer. Nat. Rev. Cancer 13, 674–678.

Fann, N., Bell, M.L., Walker, K., Hubbell, B., 2011. Improving the linkages between air pollution epidemiology and quantitative risk assessment. Environ. Health Perspect. 119, 1671–1675.

Fann, N., Fulcher, C.M., Hubbell, B.J., 2009. The influence of location, source, and emission type in estimates of the human health benefits of reducing a ton of air pollution. Air Qual. Atmos. Health 2, 169–176.

Hoek, G., Krishnan, R.M., Beelen, R., Peters, A., Ostro, B., Brunekreef, B., Kaufman, J. D., 2013. Long-term air pollution exposure and cardio-respiratory mortality: a review. Environ. Health 12, 43.

INE. Spanish National Statistics Institute. Online at: ⟨http://www.ine.es⟩. (accessed 04.09.13).

Krewski, D., Jerrett, M., Burnett, R.T., Ma, R., Hughes, E., Shi, Y., Turner, M.C., Pope III, C.A., Thurston, G., Calle, E.E., Thun, M.J., Beckerman, B., DeLuca, P., Finkelstein, N., Ito, K., Moore, D.K., Newbold, K.B., Ramsay, T., Ross, Z., Shin, H., Tempalski, B., 2009. Extended follow-up and spatial analysis of the American Cancer Society study linking particulate air pollution and mortality. Res. Rep. Health Eff. Inst. 140, 5–114.

Kunzli, N., Medina, S., Kaiser, R., Quenel, P., Horak Jr., F., Studnicka, M., 2001. Assessment of deaths attributable to air pollution: should we use risk estimates based on time series or on cohort studies? Am. J. Epidemiol. 153, 1050–1055.

Lepeule, J., Laden, F., Dockery, D., Schwartz, J., 2012. Chronic exposure to fine particles and mortality: an extended follow-up of the Harvard Six Cities study from 1974 to 2009. Environ. Health Perspect. 120, 965–970.

Lumbreras, J., Borge, R., de Andres, J.M., Rodriguez, E., 2008. A model to calculate consistent atmospheric emission projections and its application to Spain. Atmos. Environ. 42, 5251–5266.

MARM, 2010. Inventario Nacional de Emisiones a la Atmósfera 1990-2008. Dirección General de Calidad y Evaluación Ambiental, Ministerio de Medio Ambiente y Medio Rural y Marino.

MARM, 2011. Inventario Nacional de Emisiones a la Atmósfera 1990-2009. Dirección General de Calidad y Evaluación Ambiental, Ministerio de Medio Ambiente y Medio Rural y Marino.

Naess, O., Nafstad, P., Aamodt, G., Claussen, B., Rosland, P., 2007. Relation between concentration of air pollution and cause-specific mortality: four-year exposures to nitrogen dioxide and particulate matter pollutants in 470 neighborhoods in Oslo, Norway. Am. J. Epidemiol. 165, 435–443.

O'Connell, E., Hurley, F., 2009. A review of the strengths and weaknesses of quantitative methods used in health impact assessment. Public Health 123, 306–310.

Pascal, M., Corso, M., Chanel, O., Declercq, C., Badaloni, C., Cesaroni, G., Henschel, S., Meister, K., Haluza, D., Martin-Olmedo, P., Medina, S., 2013. Assessing the public health impacts of urban air pollution in 25 European cities: results of the Aphekom project. Sci. Total Environ. 449, 390–400.

Perez, L., Sunyer, J., Kunzli, N., 2009. Estimating the health and economic benefits associated with reducing air pollution in the Barcelona metropolitan area (Spain). Gac. Sanit. 23, 287–294.

Pérez, N., Pey, J., Querol, X., Alastuey, A., López, J.M., Viana, M., 2008. Partitioning of major and trace components in PM10-PM2.5_PM1 at an urban site in Southern Europe. Atmos. Environ. 42, 1677–1691.

Peters, A., Dockery, D.W., Muller, J.E., Mittleman, M.A., 2001. Increased particulate air pollution and the triggering of myocardial infarction. Circulation 103, 2810–2815.

Pope III, C.A., Burnett, R.T., Thurston, G.D., Thun, M.J., Calle, E.E., Krewski, D., Godleski, J.J., 2004. Cardiovascular mortality and long-term exposure to particulate air pollution: epidemiological evidence of general pathophysiological pathways of disease. Circulation 109, 71–77.

Pope III, C.A., Schwartz, J., Ransom, M.R., 1992. Daily mortality and PM10 pollution in Utah Valley. Arch. Environ. Health 47, 211–217.

Pope, C.A., Burnett, R.T., Turner, M.C., Cohen, A., Krewski, D., Jerrett, M., Gapstur, S. M., Thun, M.J., 2011. Lung cancer and cardiovascular disease mortality associated with ambient air pollution and cigarette smoke: shape of the exposure–response relationships. Environ. Health Perspect. 119, 1616–1621.

Pope, C.A.I., Burnett, R.T., Thun, M.J., Calle, E.E., Krewski, D., Ito, K., Thurston, G.D., 2002. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. JAMA 287, 1132–1141.

Pope, C.A.I., Dockery, D.W., 2006. Health effects of fine particulate air pollution: lines that connect. J. Air Waste Manag. Assoc. 56, 709–742.

Proietti, E., Roosli, M., Frey, U., Latzin, P., 2013. Air pollution during pregnancy and neonatal outcome: a review. J. Aerosol. Med. Pulm. Drug Deliv. 26, 9–23.

Raaschou-Nielsen, O., Andersen, Z.J., Beelen, R., Samoli, E., Stafoggia, M., Weinmayr, G., Hoffmann, B., Fischer, P., Nieuwenhuijsen, M.J., Brunekreef, B., Xun, W.W., Katsouyanni, K., Dimakopoulou, K., Sommar, J., Forsberg, B., Modig, L., Oudin, A., Oftedal, B., Schwarze, P.E., Nafstad, P., De, F.U., Pedersen, N.L., Ostenson, C.G., Fratiglioni, L., Penell, J., Korek, M., Pershagen, G., Eriksen, K.T., Sorensen, M., Tjonneland, A., Ellermann, T., Eeftens, M., Peeters, P.H., Meliefste, K., Wang, M., Bueno-de-Mesquita, B., Key, T.J., de, H.K., Concin, H., Nagel, G., Vilier, A., Grioni, S., Krogh, V., Tsai, M.Y., Ricceri, F., Sacerdote, C., Galassi, C., Migliore, E., Ranzi, A., Cesaroni, G., Badaloni, C., Forastiere, F., Tamayo, I., Amiano, P., Dorronsoro, M., Trichopoulou, A., Bamia, C., Vineis, P., Hoek, G., 2013a. Air pollution and lung cancer incidence in 17 European cohorts: prospective analyses from the European Study of Cohorts for Air Pollution Effects (ESCAPE). Lancet Oncol. 14, 813–822.

Raaschou-Nielsen, O., Sorensen, M., Ketzel, M., Hertel, O., Loft, S., Tjonneland, A., Overvad, K., Andersen, Z.J., 2013b. Long-term exposure to traffic-related air pollution and diabetes-associated mortality: a cohort study. Diabetologia 56, 36–46.

Roosli, M., Kunzli, N., Braun-Fahrlander, C., Egger, M., 2005. Years of life lost attributable to air pollution in Switzerland: dynamic exposure-response model. Int. J. Epidemiol. 34, 1029–1035.
Ruckerl, R., Schneider, A., Breitner, S., Cyrys, J., Peters, A., 2011. Health effects of particulate air pollution: a review of epidemiological evidence. Inhal. Toxicol. 23, 555–592.
Santacatalina, M., Yubero, E., Mantilla, E., Carratala, A., 2012. Relevance of the economic crisis in chemical PM10 changes in a semi-arid industrial environment. Environ. Monit. Assess. 184, 6827–6844.
Thacker, S.B., Ikeda, R.M., Gieseker, K.E., Mendelsohn, A.B., Saydah, S.H., Curry, C.W., Yuan, J.W., 2005. The evidence base for public health informing policy at the Centers for Disease Control and Prevention. Am. J. Prev. Med. 29, 227–233.
Turner, M.C., Krewski, D., Pope III, C.A., Chen, Y., Gapstur, S.M., Thun, M.J., 2011. Long-term ambient fine particulate matter air pollution and lung cancer in a large cohort of never-smokers. Am. J. Respir. Crit. Care Med. 184, 1374–1381.
Valavanidis, A., Fiotakis, K., Vlachogianni, T., 2008. Airborne particulate matter and human health: toxicological assessment and importance of size and composition of particles for oxidative damage and carcinogenic mechanisms. J. Environ. Sci. Health C Environ. Carcinog. Ecotoxicol. Rev. 26, 339–362.
van Erp, A.M., O'Keefe, R., Cohen, A.J., Warren, J., 2008. Evaluating the effectiveness of air quality interventions. J. Toxicol. Environ. Health A 71, 583–587.
Vicente-Serrano, S.M., Trigo, R.M., pez-Moreno, J.I., Liberato, M.L.R., Lorenzo-Lacruz, J., Beguerxed, S., Tejeda, E., El, K.A., 2011. Extreme winter precipitation in the Iberian Peninsula in 2010: anomalies, driving mechanisms and future projections. Clim. Res. 46, 51–65.
WHO, 2000. Evaluation and use of epidemiological evidence for environmental health risk assessment: WHO guideline document. Environ. Health Perspect. 108, 997–1002.
WHO, 2006. WHO Air quality guidelines for particulate matter, ozone, nitrogen dioxide and ulfur dioxide. Global update 2005. Summary of risk assessment. World Health Organization Regional Office for Europe. Online at: ⟨http://whqlibdoc.who.int/hq/2006/WHO_SDE_PHE_OEH_06.02_eng.pdf⟩.