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Air quality modeling and mortality impact of fine particles reduction policies in Spain.  
Boldo E, Linares C, Aragonés N, Lumbreras J, Borge R, de la Paz D, Pérez-Gómez B,  
Fernández-Navarro P, García-Pérez J, Pollán M, Ramis R, Moreno T, Karanasiou A, López-  
Abente G.  
Environ Res. 2014 Jan;128:15-26

which has been published in final form at

<https://doi.org/10.1016/j.envres.2013.10.009>

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

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## Abstract

### 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 16x16 km<sup>2</sup>. 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 30 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<sup>3</sup> 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.

**Key words:** Air quality policies, fine particles, ischemic cardiac events, lung cancer, air quality models.

**Funding sources:**

This study was funded by a grant from the Spanish Ministry of Agriculture, Food & Environment (058/PC08/3-18.1).

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## 1. Introduction

The epidemiological literature has signalled 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 et al., 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 µg/m<sup>3</sup> 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 et al., 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 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 1,718 annual deaths were attributable to an average annual reduction of 0.7 µg/m<sup>3</sup> 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

1 assessment, with more accurate estimates and a time horizon extended to 2014. This study  
2 now shows the impact of various air quality control measures on mortality, taking fine particle  
3 concentrations as an overall indicator of air pollution (WHO, 2006). In addition to total mortality,  
4 the study analyses the impact of changes in fine particle levels on two of the leading principal  
5 causes of death in Spain (INE, 2011), namely, ischemic heart disease and lung cancer.  
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## 8 **2. Materials and methods**

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11 Quantitative health impact assessment estimates were derived by linking together: (i) estimates  
12 of how proposed policies would affect population exposures; (ii) background mortality rates;  
13 and, (iii) concentration-response functions, typically expressed as percentage change in health  
14 effect per unit of exposure. This is an established approach when quantifying health impacts  
15 mediated by air pollution (O'Connell et al., 2009).  
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### 21 *2.1. Air pollution scenarios: 2007-2014*

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24 We defined a reference scenario corresponding to 2007, based on data drawn from the official  
25 National Emission Inventory for Spain (MARM, 2010), and designed a projected scenario to  
26 simulate air pollution distribution in 2014 in a case where air quality control measures planned in  
27 2007 proved successful. This projected scenario was based on the reference scenario defined  
28 for Spain using emission projection methodology (Lumbreras et al., 2008), and assumed  
29 significantly decreased emissions of fine particle precursors (e.g., 51% reduction in primary fine  
30 particle emissions) resulting from technological measures targeting the road transport sector,  
31 industry and power generation (Table 1). The projected scenario reflected the most likely future  
32 situation, since it included expected outcomes from official plans and specific legislation (see  
33 Supplementary Material, Table 1). Accordingly, the emissions and, by extension, the changes in  
34 air quality reported in this paper may be regarded as the most feasible evolution over the period  
35 considered. These measures affect a wide number of pollutants, with reduction in fine particle  
36 concentrations being chosen as an overall indicator of the health benefits to be obtained as a  
37 result of an improvement in air quality.  
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47 For both scenarios, emissions were initially processed using the Sparse Matrix Operator Kernel  
48 Emissions (SMOKE) modelling system (Borge et al., 2008). The US Environmental Protection  
49 Agency's (US EPA) Community Multiscale Air Quality model (CMAQ v4.6) was then applied  
50 (Byun et al., 2006) to simulate fine particle ( $\mu\text{g}/\text{m}^3$ ) concentration levels for the entire Iberian  
51 Peninsula, Balearic Islands, Ceuta and Melilla, using a grid with a spatial resolution of  $16 \times 16$   
52  $\text{km}^2$  (4,500 cells). Since the SERCA modelling domain was centred on the Iberian Peninsula,  
53 the Canary Islands were not included for estimation purposes. The Community Multiscale Air  
54 Quality (CMAQ) model is a next-generation 3D Eulerian Chemical-transport model which  
55 provides a comprehensive picture of air pollutants in the atmosphere under an holistic  
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1 approach. Interactions among pollutants and processes are taken into account (emissions,  
2 physical transport and deposition phenomena, photochemical reactions, gas-particle  
3 interactions, secondary aerosols, etc.). Detailed information regarding the working principles  
4 and model formulation can be found elsewhere (Byun et al., 2006; Byun et al., 1999). The  
5 CMAQ modelling results provided the basis for the health impact estimates. Using the  
6 Environmental Benefits Mapping and Analysis Programme (BenMAP:  
7 <http://www.epa.gov/air/benmap/>), a health impact assessment tool designed by the US EPA, air  
8 pollution changes in each cell were calculated by subtracting air pollution levels resulting from  
9 CMAQ models (projected minus reference).

## 14 *2.2. Study population and mortality rates for the reference scenario*

17 For each town in Spain (8,109 municipalities), the Spanish National Statistics Institute furnished  
18 population data and the number of deaths corresponding to all-cause mortality, including  
19 external causes (International Classification of Diseases, 10<sup>th</sup> revision (ICD-10), codes A00-  
20 Y98), all non-accidental causes (ICD-10 codes A00-R99), ischemic heart disease (ICD-10  
21 codes I20-I25) and lung cancer (ICD-10 code C33-C34), broken down by 5-year age groups, for  
22 the period 2005-2007, to make for more stable estimates. Lung cancer deaths included deaths  
23 due to malignant neoplasm of the trachea, bronchus, and lung. Mortality and municipal  
24 population data were used to calculate the mortality rates for each town. In addition, we also  
25 used municipal population data for year 2012 to consider the effect of the Spanish demographic  
26 shift on this health impact assessment.

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

## 59 *2.3. Selection of concentration-response functions*

1 We estimated attributable deaths using health impact functions based on studies of long-term  
2 exposure to fine particles conducted on large cohorts in Europe (Cesaroni et al., 2013;  
3 Raaschou-Nielsen et al., 2013a) and North America (Crouse et al., 2012; Krewski et al., 2009;  
4 Lepeule et al., 2012; Pope et al., 2004; Pope et al., 2002). We calculated the mortality impact of  
5 a reduction in fine particles for all-causes (Krewski et al., 2009; Lepeule et al., 2012; Pope et al.,  
6 2002), all non-accidental causes (Cesaroni et al., 2013; Crouse et al., 2012), ischemic heart  
7 disease (Cesaroni et al., 2013; Crouse et al., 2012; Krewski et al., 2009; Pope et al., 2004) and  
8 lung cancer (Cesaroni et al., 2013; Krewski et al., 2009; Lepeule et al., 2012; Pope et al., 2002;  
9 Raaschou-Nielsen et al., 2013a). The concentration-response function relates a change in fine  
10 particle concentration to a change in mortality. In order to be consistent with the selected  
11 concentration-response functions, all mortality analysis targeted the age group examined in  
12 each cohort study. Table 2 summarizes the main characteristics of these cohort studies and  
13 their concentration-response functions, expressed as hazard ratios per 10 µg/m<sup>3</sup> increase in fine  
14 particles.  
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24 Several concentration-response functions used for this health impact assessment analysis were  
25 not included in the BenMAP. In these cases, the values of the regression coefficients (β), which  
26 is the natural logarithm of the hazard ratio for an increase in concentrations of fine particles of 1  
27 µg/m<sup>3</sup>, and their standard errors were calculated on the basis of the published confidence  
28 interval of concentration-response functions for specific causes (Abt Associates Inc, 2010a) and  
29 were then introduced into the BenMAP software.  
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#### 34 *2.4. Estimation of attributable fine particle health impact*

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37 The BenMAP tool is compatible with the US EPA's Community Multiscale Air Quality model.  
38 Following the application of Community Multiscale Air Quality software, the model's outputs  
39 were processed and introduced into the BenMAP, in order to estimate crude figures of all-  
40 cause, all non-accidental cause, ischemic heart disease and lung cancer mortality attributable to  
41 the changes in air quality. For each grid cell within Spain's territorial boundaries, we therefore  
42 supplied average population figures for the period 2005-2007, mortality rates broken down by 5-  
43 year age group, and estimated fine particle levels for 2007 and 2014. We repeated the analyses  
44 using the Spanish population in 2012.  
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51 Assuming that the entire population was exposed to fine particle air pollution, attributable deaths  
52 were calculated in absolute and relative numbers on a grid cell-by-cell basis in Spain. The  
53 following equation was used to calculate the change in the mortality rate based on differences in  
54 CMAQ-derived fine particle concentrations between the two simulations:  
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$$59 \Delta Y = Y_0 (1 - 1/HR^{\Delta Q}) * P$$

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1 where  $Y_0$  is the mortality rate at the reference scenario; HR, the hazard ratio for an increase in  
2 concentrations of fine particles of  $1 \mu\text{g}/\text{m}^3$ , as derived from the selected cohort studies (Table 2);  
3  $\Delta Q$ , the change in estimated air pollutant concentration between the reference and projected  
4 scenario; and P, the potentially affected population at the reference scenario.  
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8 The BenMAP software calculates a distribution of point estimates in each grid cell of the number  
9 of attributable deaths associated with changes in fine particles between the two scenarios  
10 considered. For each grid cell, we selected the median, and the 5<sup>th</sup> and 95<sup>th</sup> percentiles of this  
11 distribution to provide a range of uncertainty for health impact assessment results. National  
12 figures of deaths attributable to fine particle reduction were obtained by adding up all the cell  
13 estimates. When the lower estimate of the concentration-response function was below 1, as  
14 was the case for the effect of fine particles on lung cancer mortality in the framework of the  
15 European Study of Cohorts for Air Pollution Effects (Raaschou-Nielsen et al., 2013a), we  
16 considered that the minimum health benefits of reducing air pollution would be null, and set the  
17 lower limit of the range to 0. The methodology used in this study is described in detail elsewhere  
18 (Abt Associates Inc, 2010a; Abt Associates Inc, 2010b; Fann et al., 2009).  
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### 27 **3. Results**

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29 In Spain, the main sectors responsible for emissions of primary fine particles in 2007 and 2014  
30 were road transport and other mobile sources, machinery, non-industrial combustion plants, and  
31 combustion in the energy, transformation, and manufacturing industries. The combination of all  
32 these accounted for 94% of emissions of this pollutant in 2007. Among these sectors, note  
33 should be taken of transport (both road and off-road) with 58% of total fine particle emissions in  
34 2007. By implementing air quality control measures, it is precisely these sectors, along with the  
35 combustion sector (in the energy, transformation, and manufacturing industries), that could  
36 most reduce their emissions, i.e., by 69% and 59% respectively (Table 1).  
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44 With regard to the air quality simulation, the national average fine particle concentration in the  
45 reference scenario (2007) was  $6.3 \mu\text{g}/\text{m}^3$ ; the result of modelling for 2014 showed a generalised  
46 improvement throughout the territory, with the average fine particle concentration being reduced  
47 to  $5.4 \mu\text{g}/\text{m}^3$ . The difference between the two scenarios amounts to an overall reduction of  
48 approximately 15% or  $1 \mu\text{g}/\text{m}^3$  (range  $0.3\text{-}4.3 \mu\text{g}/\text{m}^3$ ) in Spain. If air quality control measures  
49 were successfully implemented, reductions would be achieved in especially important fine  
50 particle levels, particularly in large Spanish cities such as Madrid ( $4.3 \mu\text{g}/\text{m}^3$ ), Barcelona and the  
51 Greater Barcelona area ( $3.5 \mu\text{g}/\text{m}^3$ ), and Valencia ( $3 \mu\text{g}/\text{m}^3$ ). Figure 2 displays the difference in  
52 simulated average fine particle concentration ( $\mu\text{g}/\text{m}^3$ ) between the projected (2014) and  
53 reference scenario (2007) for each grid cell.  
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1 Spanish population was heterogeneously distributed across 8,019 towns, though most of these  
2 subjects tend to congregate in large cities (Figure 1). Spain had an annual population over the  
3 age of 30 years of 27,953,825 in 2007, and 30,889,710 in 2012. Table 3 shows the average  
4 annual number of deaths (period 2005-2007) for each selected mortality indicator, as well as  
5 population figures in 2007 and in 2012 according to the specific age range used in each cohort  
6 study.  
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10 Table 3 also summarizes the long-term mortality findings in terms of the total annual number of  
11 attributable deaths (50<sup>th</sup>, 5<sup>th</sup>-95<sup>th</sup> percentiles) and crude annual rates per 100,000 population,  
12 which could be potentially prevented by the fine particle reduction scenario in Spain. Using 2007  
13 population figures and depending on the selected concentration-response functions, our  
14 analysis indicated a number of attributable deaths from all causes ranging from 2,365 to 4,163,  
15 corresponding to crude rates from 8 to 15 deaths delayed per 100,000 population, and it would  
16 account for approximately 0.7-1.1% of the total number of annual deaths in this population. Of  
17 the estimated mortality attributable to all causes, between 186 and 777 annual deaths (1-5  
18 deaths per 100,000 population) were due to lung cancer and between 654 and 1,817 annual  
19 deaths (2-6 deaths per 100,000 population) were due to ischemic heart disease. In relative  
20 terms, the impact of air pollution was greater when cause-specific mortality coefficients were  
21 used, i.e., 1.0-6.5% of annual deaths due to lung cancer and 1.8-5.1% of annual deaths due to  
22 ischemic heart disease.  
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31 On the other hand, we explored the effect of using different estimates from the same cohort  
32 study, i.e. American Cancer Society cohort (Krewski et al., 2009; Pope et al., 2004; Pope et al.,  
33 2002). We found a decrease by 43% for all causes (2,365 deaths, range: 1,306-3,420), by 22%  
34 for lung cancer (389 deaths, range: 180-518), and by 15% for ischemic heart disease (972  
35 deaths, range: 761-1,181), when using the Krewski's concentration-response functions  
36 compared to those of Pope.  
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42 Finally, in relation to the 2012 population figures, our findings in terms of postponed deaths  
43 would increase by 18% for all causes, by 10% for lung cancer, and by 17% for ischemic heart  
44 disease, compared to the values using 2007 population data and Pope's estimates. In contrast,  
45 when we used the Harvard Six Cities concentration-response functions and its younger  
46 population range (Lepeule et al., 2012), the increase was limited to 5% for all-causes and to 7%  
47 for lung cancer.  
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52 Figure 3 depicts the geographical distribution of the absolute number of annual attributable  
53 deaths and the annual crude rate of attributable deaths per 100,000 population expected in  
54 2014 using population in 2007, and estimated using Pope's concentration-response functions  
55 (Pope et al., 2004; Pope et al., 2002). In terms of absolute numbers, the greatest health benefits  
56 resulting from a reduction in air pollution would be observed in large cities and provincial  
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1 capitals, where the highest fine particle reduction concentrations are usually found. This is  
2 because of the wide difference in concentrations between the two scenarios and the great  
3 number of inhabitants that congregate in these population centres. In the country's capital,  
4 Madrid (2,146,146 inhabitants aged over 30 years), a total of 650, 168 and 80 annual deaths  
5 due to all causes, ischemic heart disease and lung cancer respectively (50<sup>th</sup> percentile) was  
6 estimated to be attributable to a 4.3 µg/m<sup>3</sup> reduction in fine particles. Something similar would  
7 occur in Barcelona and its outlying towns (Hospitalet de Llobregat, Prat de Llobregat, Sant Adrià  
8 de Besòs and Venturada) (with 1,346,419 inhabitants aged over 30 years), where there were an  
9 estimated 292, 69 and 37 annual deaths due to all causes, ischemic heart disease and lung  
10 cancer respectively. Other towns situated in the Greater Barcelona area and in Valencia and the  
11 Greater Valencia area also registered a reduction in fine particles of over 3 µg/m<sup>3</sup>, so that they  
12 made a substantial contribution to the number of deaths attributable to air pollution.  
13 Nevertheless, the geographical distribution of the crude mortality rates indicates that the  
14 greatest health benefits in relative terms would be felt in certain areas of the Autonomous  
15 Regions of Galicia, Castile-León, Extremadura and Andalusia, and along the Mediterranean.  
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#### 24 **4. Discussion**

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27 This study reports the mortality impact in Spain expected in 2014, resulting from a mean  
28 reduction of 1 µg/m<sup>3</sup> in fine particle concentrations. Taking into account 2007 population data,  
29 between 8 and 15 all-cause deaths per 100,000 population could be postponed annually by the  
30 expected reduction in fine particle levels. For specific subgroups, estimates varied from 10 to 30  
31 deaths for all non-accidental causes, from 1 to 5 for lung cancer, and from 2 to 6 for ischemic  
32 heart disease. For each mortality indicator, our results varied depending on the selected cohort  
33 studies, which included different age range and provided different hazard ratios.  
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39 If we consider the Spanish population growth occurred from 2007 to 2012 and Pope's  
40 estimates, the mortality impact would increase by 18%, 10% and 17% for all causes, lung  
41 cancer and ischemic heart disease, respectively (Pope et al., 2004; Pope et al., 2002). We  
42 should keep in mind that the American Cancer Society cohort included people over 30, while  
43 the Harvard Six Cities cohort recruited participants between 25 and 74 years old. This age  
44 variation could explain the lower increases -close to 5%- obtained applying the Harvard cohort  
45 risk functions to our data. Differences between both estimates could highlight the relevance of  
46 Spanish population ageing in our health impact assessment.  
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53 The results of this health impact assessment are in line with other previously conducted studies,  
54 both national (Perez et al., 2009) and international in scope (Anenberg et al., 2010; Ballester et  
55 al., 2008; Pascal et al., 2013). Our findings afford new reasons for reviewing the fine-particle-  
56 related provisions envisaged under Directive 2008/50/EC on ambient air quality and cleaner air  
57 for Europe.  
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1 With respect to the methodology, it should be noted that accurate assessment of population  
2 exposure to air pollution is crucial to estimating the health impact. This study used air quality  
3 models with a spatial resolution of 16x16 km<sup>2</sup> and incorporated air pollution control measures  
4 recently implemented in Spain (see Supplementary Material, Table 1). Spatial comparisons of  
5 air pollution patterns are facilitated by the use of maps and are useful in health-based policy-  
6 making. In terms of a reduction in emissions, this would primarily take place in industries,  
7 essentially power plants in the north-western quarter of the country and the ceramics industry in  
8 areas lying along the Mediterranean seaboard. Nonetheless, the most important reductions are  
9 expected in urban settings, and are associated with technological improvements to vehicles  
10 (mainly the fitting of particle filters) and the application of sustainable urban transport and/or air  
11 quality control plans. These measures have already been partially implemented and have  
12 achieved a substantial reduction in fine particle emissions (e.g., at a national level the reduction  
13 in fine particle emissions in the period 2007-2009 was 20% (MARM, 2011).  
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22 Our projections should be valid, since fine particle reduction levels have been described in  
23 European countries in recent years and have been attributed to various causes. On the one  
24 hand, the implementation of pollution-abatement strategies in Europe is having a direct effect on  
25 the levels of fine particles and their various components. A recently published study has stated  
26 that reductions in fine particles were observed across all stations in Spain and Europe to  
27 varying degrees (7-49%) over the period 2002-2010 (Cusack et al., 2012). This reduction has  
28 been gradual and consistent over time, implying the success of cleaner anthropogenic activities.  
29 On the other hand, the influence of the North Atlantic Oscillation has been noted, a large-scale  
30 meteorological phenomenon which is most prevalent during winter and modifies the frequency  
31 of Saharan dust intrusions across the Iberian Peninsula (Vicente-Serrano et al., 2011). As a  
32 result of the negative North Atlantic Oscillation, particulate matter levels have been considerably  
33 lower than in other winters (Pérez et al., 2008). Lastly, the ongoing economic crisis could also  
34 have caused a general fall in fine particle emissions (Cusack et al., 2012) and thus changed  
35 ambient trace element concentrations (Arruti et al., 2011; Santacatalina et al., 2012). Since  
36 2008, many European countries have been in recession, which affects air pollutants through a  
37 reduction in activities associated with a healthy economy (e.g., increased road traffic, industrial  
38 processes and construction) (Cusack et al., 2012).  
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49 Since reductions in air pollution occur gradually after the implementation of environmental  
50 policies, the appearance of any concomitant health benefits could be expected to occur in a  
51 similar manner. Whereas any short-term health impacts might be expected to be seen almost  
52 immediately, in the case of the consequences of air pollution caused by a combination of short-  
53 and long-term causes, it might well take some years before the ensuing health benefits would  
54 be observable. Moreover, risk factors can be competitive, something that could also interfere in  
55 the appearance of any long-term benefits. Hence, greater uncertainty surrounds the nature of  
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1 any possible long-term impacts and benefits than those in the short term (Kunzli et al., 2001).  
2 Intervention studies have been conducted to estimate the reduction in risk following a decrease  
3 in air-pollution levels (Clancy et al., 2002; Pope et al., 1992). Taking these studies into account,  
4 Roosli et al. proposed an exposure-response model to quantify dynamic changes in mortality  
5 following increases or decreases in air-pollution levels (Roosli et al., 2005). According to these  
6 authors, a substantial proportion of the benefit flowing from reducing contamination levels is  
7 seen to occur a few years after the reduction has taken place: in percentage terms, the effect  
8 was estimated as being 40% in the same year and 80% within 5 years (e.g., in our study a  
9 range of 1,892-3,330 attributable deaths). At all events, it should be noted that, while major  
10 benefits are to be expected in terms of public health, the real temporal pattern of such  
11 incremental health benefits is unknown and difficult to assess.  
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18 The choice of a concentration-response function between fine particle exposure and mortality  
19 can generate a considerable difference in the predicted health impact estimate at lower  
20 concentrations. To explore these variations, we used different hazard ratios provided by large  
21 cohort studies conducted in Europe (Cesaroni et al., 2013; Raaschou-Nielsen et al., 2013a) and  
22 North America (Crouse et al., 2012; Krewski et al., 2009; Lepeule et al., 2012; Pope et al., 2004;  
23 Pope et al., 2002), that could be considered the most updated evidence of the effects of long-  
24 term exposure to fine particles on mortality. Table 2 summarizes the main characteristics of the  
25 selected cohort studies for this health impact assessment. These studies reported different  
26 concentration-response functions for fine particles-related health effects. The disparities among  
27 them can be due to a) the variability among different populations, i.e. disparities in susceptibility,  
28 baseline health conditions or lifestyles; b) the environmental conditions, such as study area  
29 characteristics, geographic location or pollutant mixtures; and c) the exposure assessment  
30 methodology.  
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39 In relation to the North American cohort studies, the American Cancer Society cohort (Krewski  
40 et al., 2009; Pope et al., 2004; Pope et al., 2002) is usually regarded as the largest cohort study  
41 available to date on the long-term effects of fine particles on mortality. The estimates furnished  
42 by this cohort are more conservative than those reported by similar studies (Crouse et al., 2012;  
43 Lepeule et al., 2012), and have already been used in other health impact assessment studies  
44 carried out in Europe (Ballester et al., 2008; Pascal et al., 2013). The Extended follow-up of the  
45 American Cancer Society cohort through 2000 (18 years) (Krewski et al., 2009) supported  
46 earlier findings (16 years follow-up) (Pope et al., 2004; Pope et al., 2002) of a positive  
47 association between long-term exposure to fine particles in ambient air and increased mortality  
48 rates in urban centres in the United States. The analysis conducted by Krewski and colleagues  
49 observed a decrease in the concentration-response function estimates for deaths attributable to  
50 fine particles compared with that of the initial follow-up period (Pope et al., 2004; Pope et al.,  
51 2002). According to Krewski and colleagues, the lower risk found could be due to exposure  
52 misclassification increasing over time. They assigned exposure based on residence location at  
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1 the beginning of follow-up and cohort members who moved increased over time. In addition,  
2 fine particles concentrations declined over the follow-up period, so assigning a single exposure  
3 measure would not have fully captured this temporal pattern. Finally, as the cohort ages, air  
4 pollution effects may decline due to the healthy survivor effect (Krewski et al., 2009). The  
5 American Cancer Society cohort results showed how the health effect estimates of fine particles  
6 changed over time. When using hazard ratios from the Updated Analysis of the American  
7 Cancer Society cohort (Pope et al., 2004; Pope et al., 2002), we found that 4,163 annual deaths  
8 could be delayed in 2014, including 500 due to lung cancer and 1,143 deaths due to ischemic  
9 heart disease, in a population of nearly 28 million. These last findings decreased by 43%, 22%  
10 and 15% respectively, when using the estimates from the Extended Analysis of the American  
11 Cancer Society study (Krewski et al., 2009). It is complicated to extrapolate these deviations  
12 when applying their estimates to target populations, and transferability issues can arise (Boldo  
13 et al., 2011).

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21 Several studies undertaken in Europe have also estimated concentration-response functions for  
22 health outcomes attributable to long-term exposure to fine particles. In this report, we have used  
23 the most recent results of European cohort studies (Cesaroni et al., 2013; Raaschou-Nielsen et  
24 al., 2013a). For lung cancer, we used the latest results of European Study of Cohorts for Air  
25 Pollution Effects (Raaschou-Nielsen et al., 2013a), which combined 14 long-term cohort studies  
26 from nine European countries. They identified a hazard ratio of 1.40 (95% CI= 0.92-2.13) for all  
27 lung cancers per 10  $\mu\text{g}/\text{m}^3$  in fine particles (Raaschou-Nielsen et al., 2013a), which is similar to  
28 the Harvard Six Cities estimate (Lepeule et al., 2012) and that from the Canadian study (Crouse  
29 et al., 2012), but higher than the estimate from the American Cancer Society study (Pope et al.,  
30 2002), and from the cohort study in Italy (Cesaroni et al., 2013).

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38 The use of Rome longitudinal study risk estimates (Cesaroni et al., 2013) could be considered a  
39 cautious approach, as they were lower than those reported in other European (Brunekreef et al.,  
40 2009; Naess et al., 2007; Raaschou-Nielsen et al., 2013a) and North American settings (Crouse  
41 et al., 2012; Lepeule et al., 2012; Pope et al., 2002). These Italian risk functions could be more  
42 suitable for our health impact assessment due to the common characteristics between both  
43 countries. Italy and Spain share notable similarities on culture and environmental conditions, i.e.  
44 both are Mediterranean countries located in southern Europe. Additional similarities exist with  
45 respect to crucial socioeconomic indicators, such as labor markets or population educational  
46 attainment (Eurostat, 2013).

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53 The health impact analysis estimated that an overall reduction of 1  $\mu\text{g}/\text{m}^3$  in fine particles by  
54 2014 would succeed in preventing mortality attributable to this environmental risk factor. Taking  
55 into account the basic demographic components (mortality, fertility and migration), Spain is  
56 undergoing an ageing process which is accelerated by the decreasing birth rate and negative  
57 migratory balances. The Spanish National Statistics Institute has estimated that the greatest  
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1 population growth would be concentrated among the higher age groups (INE, 2012). To  
2 incorporate population changes into the analysis, we repeated the calculations using 2012  
3 population figures. Taking into account the population over the age of 30 years in 2012, the  
4 expected number of deaths attributable to fine particles exposure would be 4,901, a figure  
5 substantially higher than the one estimated using the population data in 2007 (4,163 deaths)  
6 (Table 3).  
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10 Our study also incorporated impact analysis for mortality due to specific causes, such as  
11 ischemic heart disease and lung cancer, since European studies on short- and long-term  
12 particulate matter exposure indicate a direct association with mortality in general, and mortality  
13 due to cardiopulmonary disease in particular (Fajersztajn et al., 2013; Hoek et al., 2013; Pope et  
14 al., 2006). Our study focused on mortality because background country-wide rates of other  
15 health outcomes, such as hospital admissions or restricted activity days, were not available. In  
16 any event, further evidence has emerged of the effects of long-term exposure to fine particulate  
17 air pollution on diseases other than cardiovascular and respiratory diseases, such as adverse  
18 birth outcomes (Proietti et al., 2013), diabetes (Andersen et al., 2012; Raaschou-Nielsen et al.,  
19 2013b), neurological development in children and neurological disorders in adults (Ruckerl et  
20 al., 2011). There is a need to consider new health outcomes to be examined in health impact  
21 assessment studies.  
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30 The risk of ischemic heart disease has particularly strong and consistent associations with  
31 exposure to fine particles. Ischemic heart disease ranks as the leading cause of death in Spain,  
32 despite the fact that most of the risk factors (sedentarism, hypertension and dyslipidaemia) are  
33 known and modifiable. The trend in the mortality rate shows that from 1990 to 2007, risk in  
34 Spain fell by almost 30%, owing to improvements in treatment and lower exposure to risk  
35 factors (Bertomeu et al., 2008). Exposure to environmental particulate matter is another risk  
36 factor which potentiates cardiovascular morbidity and mortality due to acute (Peters et al., 2001)  
37 and chronic effects (Pope et al., 2004; Pope et al., 2002), and the mechanisms whereby this  
38 could cause systemic cardiovascular effects are being investigated (Bhaskaran et al., 2011;  
39 Brook et al., 2010). Evidence accumulated during the preceding decade indicates that the most  
40 important part of mortality caused by air pollution is due to cardiovascular disease, such that for  
41 every 10  $\mu\text{g}/\text{m}^3$  increase in fine particles, mortality due to ischemic heart disease increases from  
42 10% (Cesaroni et al., 2013) to 31% (Crouse et al., 2012) in this mortality impact analysis. These  
43 findings have led to the proposal that exposure to these particles should be considered a new  
44 modifiable cardiovascular risk factor. According to our results, Spain could prevent a range of 2-  
45 5% of mortality due to this cause if the implementation of air quality control measures were  
46 effective.  
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57 In the case of lung cancer, smoking is considered the principal risk factor and gives rise to  
58 differences in mortality rate trends between men and women. Although it continues to be the  
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1 tumour with the highest mortality rates, among men in Spain this rate decreased by 1% per  
2 annum from the 1990s, while among women it increased by 3% per annum over the same  
3 period (Cabanés et al., 2010). Epidemiological evidence that links air pollution to mortality from  
4 lung cancer is robust, particularly if only adenocarcinomas of the lung are considered  
5 (Raaschou-Nielsen et al., 2013a). Exposure to fine particulate matter is currently recognised as  
6 another of the principal modifiable risk factors for lung cancer (Fajersztajn et al., 2013; Thacker  
7 et al., 2005). New scientific evidence supports the relationship between exposure to fine  
8 particles and this disease (Fajersztajn et al., 2013), and it is estimated that a 10 µg/m<sup>3</sup> increase  
9 in fine particle concentrations is associated with a 15%-27% increase in lung cancer mortality  
10 (Turner et al., 2011). According to our results, Spain could prevent up to 6% of mortality due to  
11 this cause by reducing airborne fine particulate matter.  
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18 Recently, Pope and colleagues (Pope et al., 2011) assessed the exposure–response  
19 relationship between fine particle exposure and cardiovascular and lung cancer mortality,  
20 reporting that the relationship for lung cancer (almost linear) was qualitatively different to that for  
21 cardiovascular mortality (nonlinear). These results are relevant, in view of the fact that health  
22 impact assessment studies conducted to date have tended to apply concentration-response  
23 functions, on the assumption of linear relationships between fine particle concentrations and the  
24 health effects assessed, something that might lead to the impact of exposure to low fine particle  
25 levels on cardiovascular mortality being underestimated.  
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## 31 **5. Conclusions**

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

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56 Mortality data were supplied by the Spanish National Statistics Institute under a specific  
57 confidentiality protocol. The research findings are the responsibility of the authors.  
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Table 1. Primary fine particle emissions (t) and emission variation (%) in Spain (2007-2014).

<b>Selected Nomenclature for Sources of Air Pollution group<sup>s</sup></b>	<b>Activity</b>	<b>Emissions in 2007 (t)</b>	<b>Emissions in 2014 (t)</b>	<b>Emission variation (%)</b>
01	Combustion in energy and transformation industries	13,808	5,388	-61
02	Non-industrial combustion plants	23,048	22,516	-2
03	Combustion in manufacturing industry	10,770	4,661	-57
04	Production processes	5,086	4,498	-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	2,848	3,951	39
	<b>TOTAL</b>	<b>132,437</b>	<b>65,314</b>	<b>-51</b>

<sup>a</sup> Selected Nomenclature for sources of Air Pollution 11 (Nature) was not included since no variation on natural sources was considered for this period.

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

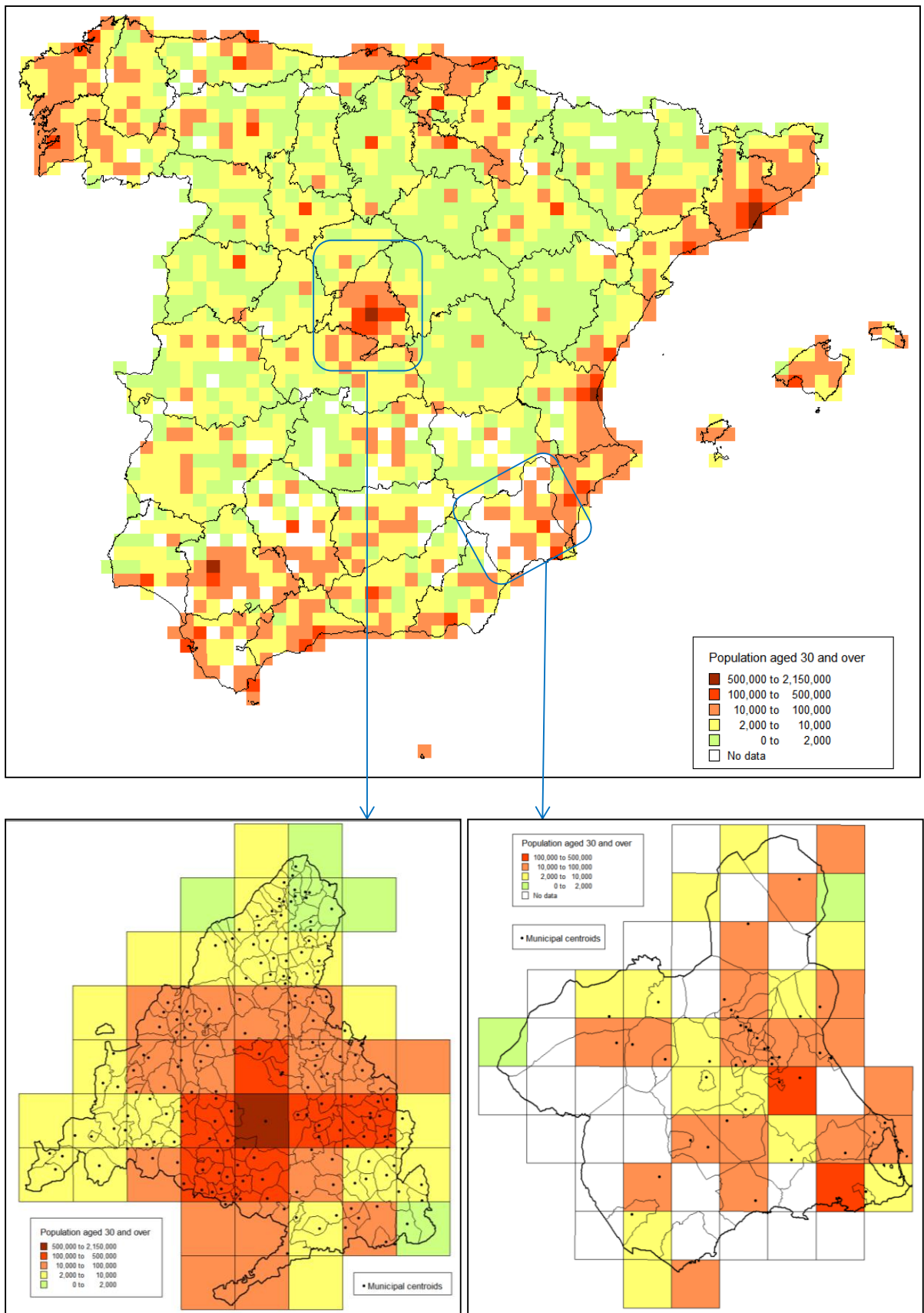
Cohort study	Reference	Study area	Population		Follow-Up		Fine particles exposure assessment	Health outcome (mortality)	Hazard ratio (95%CI) (for 10 µg/m <sup>3</sup> increase in fine particles)
			Number of Participants	Age range	Number of years	Last year			
American Cancer Society	Pope et al., 2002	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	8,096	25-74	35	2009	Central monitoring stations		1.14 (1.07-1.22)
Canadian national cohort	Crouse et al., 2012	Canada	2,145,400	>25	10	2001	Satellite-derived estimates	All non-accidental causes	1.15 (1.13-1.16)
Rome longitudinal study	Cesaroni et al., 2013	Italy	1,265,058	>30	9	2001	Eulerian dispersion model	(ICD-10: A00-R99)	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	8,096	25-74	35	2009	Central monitoring stations		1.37 (1.07-1.75)
ESCAPE Project*	Raaschou-Nielsen et al., 2013	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.

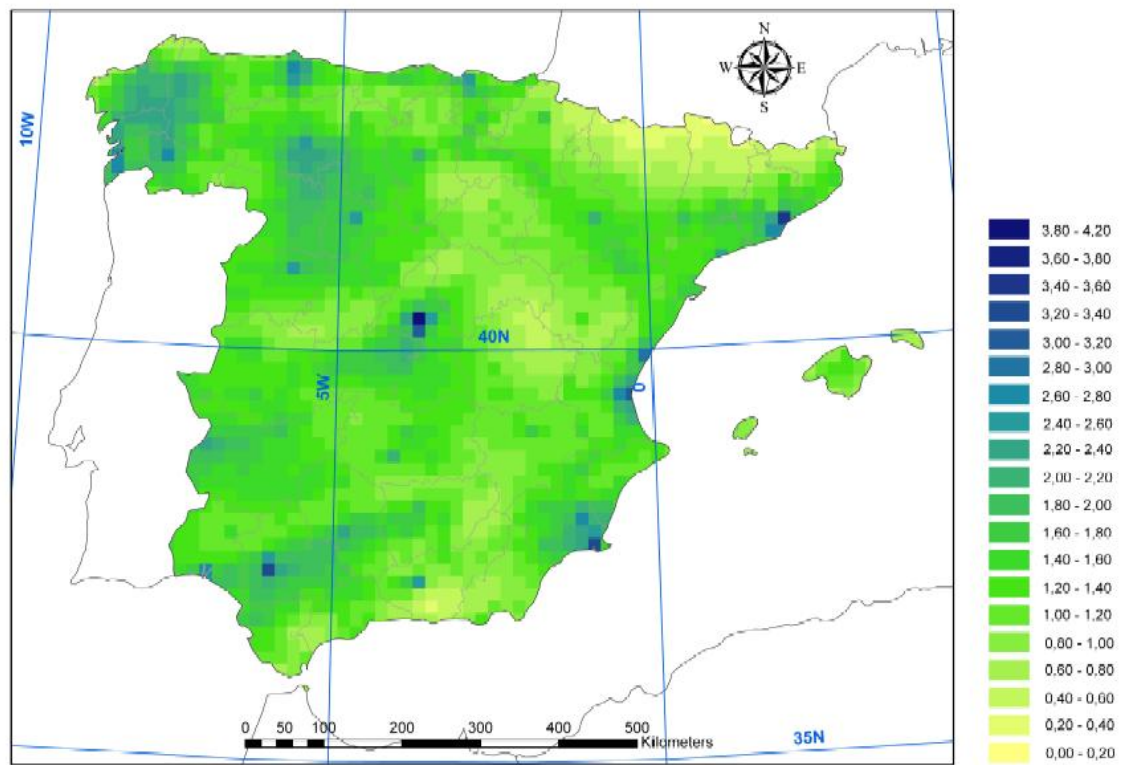
Table 3. Long-term mortality impacts of reducing fine particle concentrations in Spain by 2014 (absolute numbers and numbers per 100,000 population).

Long-term health impact assessment													
Based on the Spanish population in 2007										Based on the Spanish population in 2012			
Mortality indicator	Reference	Age range	Average annual mortality (Period 2005-2007)	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	
<b>All causes</b>													
	Pope et al., 2002	30-99	360,407	27,953,825	4,163	1,635 - 6,669	15	30,889,710	4,901	1,925 - 7,852	16		
	Krewski et al., 2009				2,365	1,306 - 3,420	8		2,821	1,557 - 4,080	9		
	Lepeule et al., 2012	25-74	114,796	28,081,812	2,961	1,729 - 4,178	10	29,724,117	3,108	1,814 - 4,384	10		
<b>All non-accidental causes</b>													
	Crouse et al., 2012	>25	348,330	31,572,075	9,447	8,712 - 10,173	30	33,857,417	11,273	10,400 - 12,14	33		
	Cesaroni et al., 2013	>30	347,661	27,953,825	2,677	2,128 - 3,224	10	30,889,710	3,197	2,542 - 3,851	10		
<b>Lung cancer</b>													
	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 - 1,256	3	29,724,117	833	294 - 1,345	3		
	Raaschou-Nielsen et al., 2013	43-73	8,870	12,279,889	589	0 - 1,157	5	14,054,059	662	0 - 1,300	5		
	Cesaroni et al., 2013	>30	18,848	27,953,825	186	50 - 321	1	30,889,710	207	55 - 357	1		
<b>Ischemic heart disease</b>													
	Pope et al., 2004	30-99	35,672	27,953,825	1,143	922 - 1,362	4	30,889,710	1,343	1,089 - 1,596	4		
	Krewski et al., 2009				972	761 - 1,181	3		1,159	907 - 1,408	4		
	Crouse et al., 2012	>25	35,693	31,572,075	1,817	1,65 - 1,984	6	33,857,417	2,165	1,966 - 2,364	6		
	Cesaroni et al., 2013	>30	35,672	27,953,825	654	472 - 836	2	30,889,710	780	562 - 996	3		

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



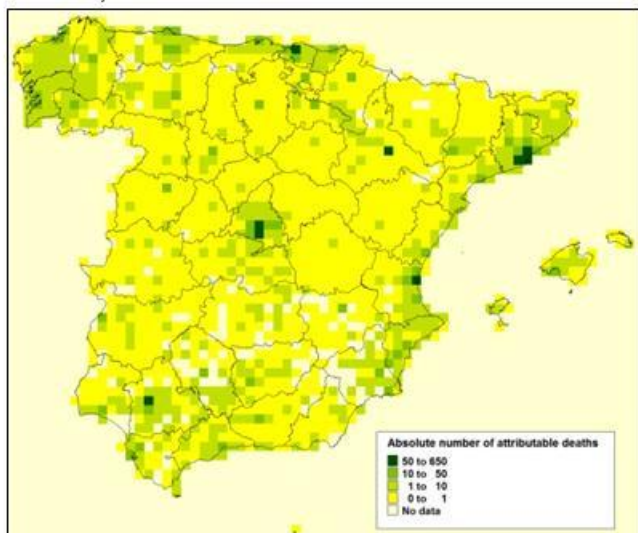
**Figure 2.** Modeled fine particle reduction ( $\mu\text{g}/\text{m}^3$ ) between reference and projected scenarios (2007-2014).



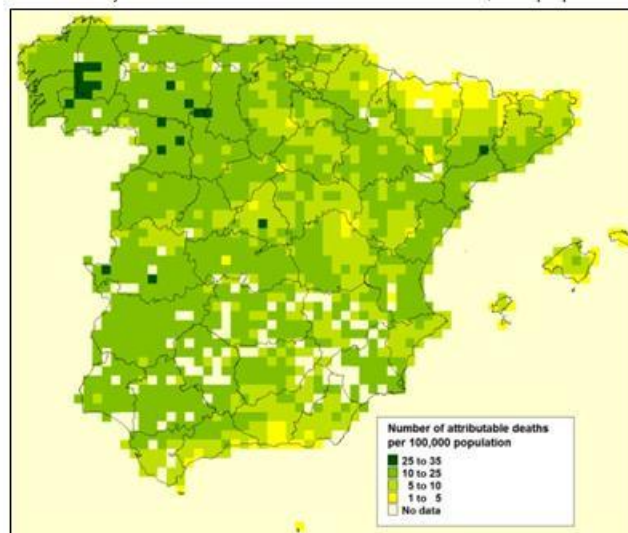
**Figure 3.** Assessment of the annual long-term mortality impact of a reduction in fine particle levels ( $\mu\text{g}/\text{m}^3$ ) in Spain. Air quality scenarios: reference year, 2007; projected year, 2014. Population and mortality rate: period 2005-2007.

a) Estimated health impact assessment for all causes, according to Pope et al., 2002. ICD-10: A00-Y98.

a.1) Absolute number of annual attributable deaths

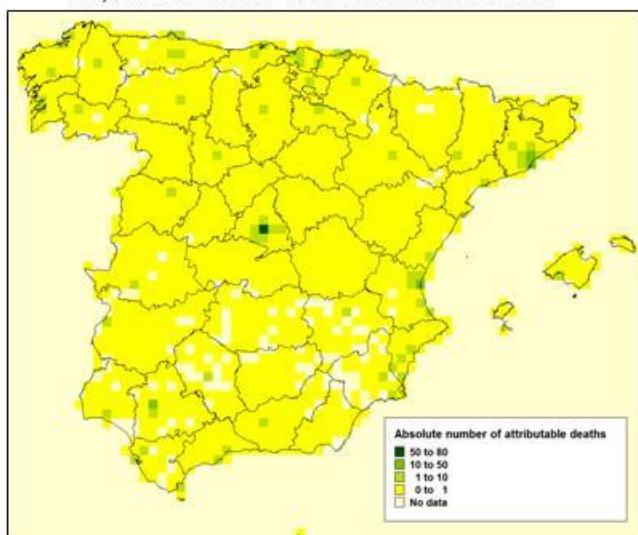


a.2) Crude rates of attributable deaths/100,000 population

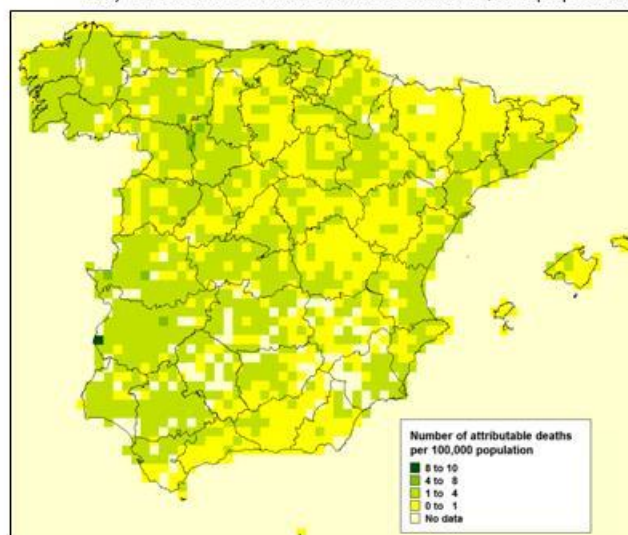


b) Estimated health impact assessment for lung cancer, according to Pope et al., 2002. ICD-10: C33-34.

b.1) Absolute number of annual attributable deaths



b.2) Crude rates of attributable deaths/100,000 population

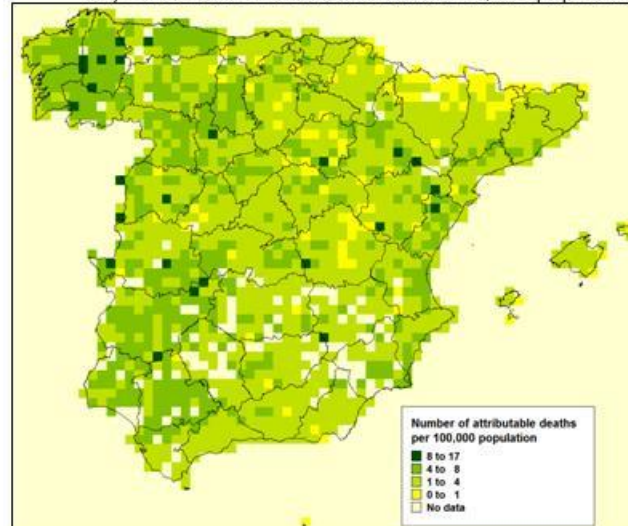


c) Estimated health impact assessment for ischemic heart disease, according to Pope et al., 2004. ICD-10: I20-I25.

c.1) Absolute number of annual attributable deaths



c.2) Crude rates of attributable deaths/100,000 population





**Supplementary Material**

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