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The association of air pollution and greenness with mortality and life expectancy in Spain: A small-area study

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ABSTRACT

Background: Air pollution exposure has been associated with an increase in mortality rates, but few studies have focused on life expectancy, and most studies had restricted spatial coverage. A limited body of evidence is also suggestive for a beneficial association between residential exposure to greenness and mortality, but the evidence for such an association with life expectancy is still very scarce.
Objective: To investigate the association of exposure to air pollution and greenness with mortality and life expectancy in Spain.
Methods: Mortality data from 2148 small areas (average population of 20,750 inhabitants, and median population of 7672 inhabitants) covering Spain for years 2009–2013 were obtained. Average annual levels of PM_{10}, $PM_{2.5}$, NO_2 and O_3 were derived from an air quality forecasting system at 4×4 km resolution. The normalized difference vegetation index (NDVI) was used to assess greenness in each small area. Air pollution and greenness were linked to standardized mortality rates (SMRs) using Poisson regression and to life expectancy using linear regression. The models were adjusted for socioeconomic status and lung cancer mortality rates (as a proxy for smoking), and accounted for spatial autocorrelation.
Results: The increase of 5 $\mu g/m^3$ in PM_{10}, NO_2 and O_3 or of 2 $\mu g/m^3$ in $PM_{2.5}$ concentration resulted in a loss of life in years of 0.90 (95% credibility interval CI: 0.83, 0.98), 0.13 (95% CI: 0.09, 0.17), 0.20 years (95% CI: 0.16, 0.24) and 0.64 (0.59, 0.70), respectively. Similar associations were found in the SMR analysis, with stronger associations for $PM_{2.5}$ and PM_{10}, which were associated with an increased mortality risk of 3.7% (95% CI: 3.5%, 4.0%) and 5.7% (95% CI: 5.4%, 6.1%). For greenness, a protective effect on mortality and longer life expectancy was only found in areas with lower socioeconomic status.
Conclusions: Air pollution concentrations were associated to important reductions in life expectancy. The reduction of air pollution should be a priority for public health.

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1. Introduction

The rapid urbanization the world is experiencing poses various risks to human health (Julien, 2005). Currently, around 50% of the world population is living in urban areas, and this percentage is expected to rise to 70% by 2030 (Martine and Marshall, 2007). Although the harmful effects of air pollution have been reported for years, air pollution continues to be one of the main environmental risk factors contributing to the global burden of disease, with an estimated impact of 5.5 million deaths per year worldwide (Forouzanfar et al., 2015).

Furthermore, residential urban areas are also often characterized by scarce greenness. Urban green spaces can be health-promoting according to several proposed mechanisms, including increasing physical activity levels, reducing stress and improving social cohesion (Jonker et al., 2014; Lee et al., 2015; Maas et al., 2009; Mitchell and Popham, 2008; Nieuwenhuijsen et al., 2014). Through these pathways, exposure to green spaces could decrease morbidity and mortality. However, evidence is limited and only a few studies have investigated the association with mortality (Gascon et al., 2016; Villeneuve et al., 2012). In addition, green spaces are suggested to reduce the heat island effect and exposure to noise and traffic-related air pollutants (Dadvand et al., 2012, 2015). Such an inter-association between air pollution and greenness requires studies of the health effects of greenness to address the role of air pollution as possible mediator in their analyses (Gascon et al., 2016; Hu et al., 2008).

While urban areas are considered to be most at risk for exposure to high levels of air pollution and would benefit the most from increases in green space, currently, rural areas have been underrepresented in research. Population in rural areas may have different characteristics than urban populations (e.g. health behaviors), and the same marker of exposure can mask different exposure characteristics in the two settings. For example, particulate matter (PM) can have a different composition in rural than in urban areas, and measures of total greenness cannot differentiate between types and the diversity of greenness, which can be different in urban and rural areas (e.g. urban park versus grassland, and high versus low variation). For instance, Garcia et al. (2016) found stronger associations between $PM_{2.5}$ and ischemic heart disease mortality in rural areas than in urban areas. Therefore, studies encompassing both rural and urban areas are of great interest. Furthermore, there are calls for complementing studies reporting relative risks (RRs) with other metrics that may be more interpretable and that provide a direct measure of public health impact such as loss of life expectancy (Brunekreef and Holgate, 2002; Gascon et al., 2016). However, the available evidence on the impact of air pollution and greenness on life expectancy is still very scarce (Jonker et al., 2014; Wang et al., 2014).

Therefore, the aim of the present study was to investigate the association of air pollution and greenness with mortality and life expectancy in Spain using a small-area ecological study.

2. Methods

This population-based study was based on data on mortality, life-expectancy, air pollution and greenness for the small areas of entire Spain, except the Canary Islands and the cities of Ceuta and Melilla, during the period 2009–2013. Spain was divided into small geographical areas that were either municipalities, or in case they had <3500 inhabitants, groups of adjacent municipalities with similar social and demographic characteristics. Large cities were included as single areas and not divided into sub-areas. The areas used here were the same as those used in the Atlas of Mortality of Spain (Benach de Rovira and Martínez Martínez, 2013). The average population per area was 20,750 inhabitants (median 7672) and the mean surface was 232 km^2 (Table 1). We considered as urban areas those communities with over 10,000 inhabitants in the year 2011, as defined by the Spanish Statistics Institute (INE) (Gonzalez, 2008).

2.1. Mortality data

Mortality data for natural causes (International Classification of Diseases codes: ICD-9: 001–799, ICD-10:A00–R99) of years 2009–2013 were obtained from the Spanish Mortality Register, provided by the National Institute of Statistics. The data were stratified by sex and five-year age groups, and provided by small area and for the entire Spain. The small areas used in the analyses were the smallest areas for which mortality data could be obtained, owing to confidentiality reasons. Additionally, data on the alive population by sex, five-year age groups and area were obtained from the 2011 Spanish census (Instituto Nacional de Estadística (INE)).

2.2. Exposure to air pollution and greenness

The main exposures were the five-year averages of the air pollution concentrations and the level of greenness in each small area. The air pollutants were PM with an aerodynamic diameter smaller than 10 µm (PM_{10}), PM with a diameter under 2.5 µm ($PM_{2.5}$), nitrogen dioxide (NO_2) and ground-level ozone (O_3). The annual average concentrations of years 2009 to 2013 were obtained from the CALIOPE air quality forecasting system (Baldasano et al., 2011). CALIOPE predicts the air quality in the Iberian Peninsula with a temporal resolution of one hour and a spatial resolution of 4 km by 4 km by combining four models, namely a meteorological model, an emissions model, a chemical transport model and an atmospheric mineral dust model. Annual concentrations in the 4 km by 4 km grid were upscaled to the small areas by overlaying the grid to the small area map and then calculating the weighted average of all grid cells that had some part within the limits of a given small area, using built-up area percentage as weights (Ignaccolo et al., 2013). The resulting area averages of air pollution levels over the study period were used in the analyses. Table S1 presents the results on the air pollution models validation.

The level of greenness at each small area was indicated by the Normalized Difference Vegetation Index (NDVI), a satellite-derived indicator of greenness (i.e. photosynthetically active vegetation) based on land surface reflectance of visible (red) and near-infrared parts of spectrum (Weier and Herring, 2011). It ranges from -1 to $+1$, with higher numbers indicating higher greenness. A total of 44 NDVI images covering all Spain excluding the Canary Islands were obtained from Landsat 8 OLI (Operational Land Imager), which provided NDVI values at 30 m by 30 m resolution. Images were obtained from the April–July season (i.e. the period of peak greenness) of year 2015 for days with the minimum cloud coverage. As greenness is not expected to vary extensively over time, the measurements can be representative for exposure during the study period. Average NDVI was calculated for all small areas.

2.3. Covariate data

To adjust for socioeconomic status (SES), the neighbourhood-level socioeconomic vulnerability index was obtained from the Atlas of Urban Vulnerability of Spain (Hernández Aja et al., 2012). This indicator was based on information from the 2001 Spanish Census and provided values at the census tract level (Spain was divided into around 35,000 census tracts that belonged to 8108 municipalities). A value for each small area was obtained by computing the average of the values of the census tracts belonging to the area, weighted by the population of each tract. The indicator uses information on the percentages of unemployment, unemployment among young people, low education, nonqualified workers, and temporary workers in the census tract. Higher values of this index indicate higher deprivation. The 2011 socioeconomic vulnerability index was not available, but we obtained the 2011 percentage of low education and the 2011 percentage of unemployment. To control for smoking, lung cancer mortality rates from years 2009 to 2013 were used as a proxy, as the percentage of smokers was not available for all municipalities (Hansell et al., 2013).

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Table 1
Description of study variables, stratified by urban and rural areas.a, *

Variable	Mean	Median	Min–max	1st qu[a]–3rd qu	p^*
Population (2011)	20,750	7672	1756–3,199,000	4992–15,120	
Urban	44,680	19,120	10,000–3,199,000	13,270–33,540	<0.001
Rural	5734	5507	1756–9998	4122–7151	
Area in km^2	232.4	131.4	0.4–2929.0	54.4–299.4	<0.001
Urban	282.3	174.9	0.4–2929.0	80.6–386.3	
Rural	152.8	74.8	0.8–1853.0	31.4–186.5	
Number of (observed) deaths (2009–2013)	840.4	377	123–129,400	273.0–589.8	
Urban	1656	701	234–129,400	496–1141	<0.001
Rural	313.1	296	123–850	241–371	
Concentration of PM_{10} in μg/m^3 (2009–2013)	17.26	17.08	12.04–31.34	14.88–19.40	
Urban	18.55	18.56	12.30–31.34	16.56–20.38	<0.001
Rural	16.45	15.97	12.04–22.84	14.50–18.06	
Concentration of $PM_{2.5}$ in μg/m^3 (2009–2013)	8.22	8.01	5.60–15.28	7.12–9.12	
Urban	8.91	8.76	5.95–15.28	7.78–9.68	<0.001
Rural	7.79	7.60	5.60–12.00	6.88–8.57	
Concentration of NO_2 in μg/m^3 (2009–2013)	9.48	7.54	4.97–51.08	6.28–10.30	
Urban	12.57	10.14	5.26–51.08	7.70–14.20	<0.001
Rural	7.54	6.69	4.97–29.32	5.89–8.17	
Concentration of O_3 in μg/m^3 (2009–2013)	80.39	80.80	56.96–90.80	77.80–83.36	
Urban	80.16	81.12	56.96–90.80	76.90–84.65	0.197
Rural	80.53	80.59	65.18–89.90	78.16–82.78	
Greenness indicated by NDVI	0.498	0.467	0.110–0.881	0.367–0.632	
Urban	0.464	0.439	0.112–0.860	0.334–0.576	<0.001
Rural	0.520	0.489	0.110–0.881	0.384–0.666	
Index of vulnerability (2001)	0.631	0.619	0.197–0.997	0.499–0.766	
Urban	0.589	0.578	0.266–0.943	0.481–0.685	<0.001
Rural	0.658	0.655	0.197–0.997	0.521–0.997	
Lung cancer SMR (2009–2013)	0.961	0.948	0.170–2.352	0.7695–1.133	
Urban	0.993	0.990	0.476–1.668	0.8445–1.134	<0.001
Rural	0.940	0.909	0.170–2.352	0.7195–1.131	

[a] Quartile.
[*] P value calculated by the independent 2-group Mann-Whitney *U* test.

2.4. Statistical analysis

Air pollution and greenness were linked to standardized mortality rates (SMRs) using Poisson regression and to life expectancy using linear regression. All analyses were conducted for the entire Spain, and also stratified by urban and rural areas. Results for PM_{10}, NO_2 and O_3 were presented for a 5 μg/m^3 contrast, while the contrast for $PM_{2.5}$ was 2 μg/m^3. These contrasts were chosen as they were very close to the interquartile range (Table 1). For NDVI, results were presented for an interquartile range increase. All models were adjusted for the 2001 index of socioeconomic vulnerability, the 2011 percentage of people with low education and the lung cancer SMRs. The R software was used to conduct all analyses (R Core Team, 2015).

2.4.1. Mortality analysis

The SMRs were calculated for each area as the ratio between observed and expected deaths in that area. The number of expected deaths was computed in each area by applying the age and sex-specific mortality rates of the entire Spain to the population structure of each area (indirect standardization). The following model was fitted,

$$O_i \sim Poisson(E_i * \theta_i)$$
$$\log(\theta_i) = \log(\text{SMR}) = \beta_0 + \beta_0 x_1 + \cdots + \beta_k x_k + \nu_i, \quad (1)$$

where O_i denotes the observed number of deaths in small area i and E_i the expected number of deaths; θ_i is the relative risk (RR) in area i, or equivalently, the SMR; β_j ($j = 1, \ldots k$) is the regression coefficient linking explanatory variable x_j ($j = 1, \ldots k$) with θ_i; and the ν_i are independent and normally distributed random effects. The expected counts were included in the model as an offset. Spatial autocorrelation of residuals was tested using Moran's I statistic. If present, sparse spatial generalized linear mixed models were fitted to account for spatial autocorrelation (Hughes and Haran, 2013; Hughes, 2014). The R package ngspatial was used (Hughes, 2014). Briefly, these models incorporate synthetic predictors to the regression model (1) that are orthogonal to the predictor space and that can account for the positive spatial dependence. Such synthetic predictors are obtained from an expression called the Moran operator, which involves the orthogonal complement of the covariate space and an adjacency matrix defining the neighbours (Hughes and Haran, 2013; Hughes, 2014). We defined areas that shared borders as neighbours. The dimensionality of the model can be reduced by keeping only the first M eigenvectors of the Moran operator. We selected M = 50, which, in our data, guaranteed that there was no residual spatial autocorrelation in any of the models. Other models that include spatial random effects such as the Besag-York-Mollie (BYM) model can induce bias in the regression coefficients in either direction and can produce variance inflation, and are not recommended (Hodges and Reich, 2010; Reich et al., 2006). However, as these models have been commonly used, we report their results in the supplement. Such models were estimated using the Integrated Nested Laplace Approximation method implemented in the R-INLA package (Bivand et al., 2015).

2.4.2. Life expectancy analysis

Life expectancy calculations were restricted to years 2010–2012 to have three years centred at the year of the census, i.e. the years from which the population estimates were obtained, as suggested elsewhere (Toson and Baker, 2003). To obtain stable estimates of life expectancy at birth in each small area, we applied the method developed by Jonker et al. (2012). This Bayesian approach is based on the life table method of Chiang (1972), but it allows smoothing the mortality rates used in the calculations by borrowing information between adjacent age groups, adjacent geographic areas, and sexes to stabilize the life expectancy estimates. We used the same specifications for prior distributions as detailed in Jonker et al. (2012). Life expectancy estimations for each area were estimated in WinBUGS using Markov chain Monte Carlo (MCMC) methods. We used 15,000 iterations for burn-in, followed by

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10,000 iterations with a thinning interval of 10. Additional details on these models are provided in the supplementary material.

Following the methodology of Jonker et al. (2014), life expectancy estimates were used as the response variable in a subsequent linear regression model that assessed the association between life expectancy and exposures while adjusting for confounders. This was implemented in a Bayesian model that accounted for the uncertainty in life expectancy estimations. Spatial autocorrelation of residuals was tested using Moran's I statistic. As in the SMR models, if residual autocorrelation was present, sparse spatial generalized linear mixed models were fitted with the ngspatial package (Hughes and Haran, 2013; Hughes, 2014). For the case of life expectancy, $M = 300$ eigenvectors were retained so that residual spatial autocorrelation disappeared. Additionally, in the supplement we reported the results of the commonly used models that include random effects with a spatial structure, although their use is not recommended (Hodges and Reich, 2010; Reich et al., 2006). Details on these models are provided in the supplement.

2.4.3. Additional analyses

We investigated the interaction between air pollution and greenness by including individual pollutants, greenness and their product in the same model. These interactions were also tested separately for rural and urban areas. Moreover, as the association of green space with mortality is suggested to vary by SES (Gascon et al., 2016), we stratified the analysis of the association between greenness and mortality and life expectancy by the median of the index of vulnerability. Additionally, we conducted the following sensitivity analyses: 1) not including lung cancer SMRs as a covariate; 2) not including the 2011 percentage of low education as a covariate; and 3) including the 2001 vulnerability index, the 2011 percentage of unemployment and the lung cancer SMRs as covariates.

3. Results

3.1. Descriptive analysis

The study included 2148 small-areas encompassing a total population of 44,561,414 people. A total of 828 (38.5%) areas had >10.000 inhabitants and were classified as urban, and 83% of the study population lived in these urban areas. All exposures except ozone showed statistically significant differences between urban and rural areas ($p < 0.001$), with lower values of the air pollutants and higher values of NDVI in rural areas (Table 1). Additionally, the index of vulnerability showed higher values in rural than in urban areas (i.e. lower SES in rural areas). Lastly, the lung cancer SMR had a median of 0.948 in Spain, with a higher value for urban areas than for rural areas ($p < 0.001$).

The geographical distributions of all variables involved in the analysis are described and demonstrated in maps in the supplement (Figs. S1–S10). All variables showed spatial patterns. Furthermore, all air pollutants were moderately correlated with each other, and negatively associated with greenness, except for NO_2 which showed a non-significant correlation with greenness (Table S2). Additionally, NO_2 and O_3 were negatively correlated. Furthermore, all exposures were moderately, positively correlated with the index of vulnerability, except for NO_2 and greenness, which showed a negative correlation. The correlation of lung cancer mortality with the other variables was weak. Lastly, NO_2 demonstrated a strong positive correlation with the population size (number of inhabitants), while greenness and the socioeconomic vulnerability index were negatively correlated to the population size.

3.2. Associations with exposures

The results of single-exposure Poisson regression models of SMRs are shown in Table 2. Table 2 only shows unadjusted models and fully adjusted sparse spatial generalized linear mixed models, as residuals from models with independent random effects showed significant spatial autocorrelation (Moran's $I > 0.27$ for all models), thus violating the independence assumption. Residual autocorrelation was eliminated when sparse spatial generalized linear mixed models were used (Moran's $I < 0.03$ for all models). In the final models, the four air pollutants as well as greenness were significantly associated with increased mortality (Table 2). PM_{10}, $PM_{2.5}$ and O_3 were significantly associated to mortality in both rural and urban areas, although the associations were stronger in rural areas. NO_2 showed opposite effects; it was associated to increased mortality risk in rural areas, but to lower risk in urban areas. Greenness was associated with higher mortality in urban areas, but no significant association was found in rural areas.

The results of the life expectancy modelling are given in Table 3. Table 3 only shows unadjusted models and fully adjusted sparse spatial generalized linear mixed models, as models with independent random effects showed significant spatial autocorrelation of residuals (Moran's $I > 0.5$ for all models). Residual autocorrelation was eliminated when sparse spatial generalized linear mixed models were used (Moran's $I < 0.003$ for all models). In the final models, the four air pollutants were significantly associated with reduced life expectancy, while increased greenness did not show a significant association (Table 3). Similarly to the results for SMRs, PM_{10}, $PM_{2.5}$ and O_3 were significantly associated to shorter life expectancy in both rural and urban areas, although the associations were stronger in rural areas. NO_2 was associated with shorter life expectancy in rural areas, but it was not significantly associated with life expectancy in urban areas. Conversely, higher greenness was associated with reduced life expectancy in urban areas, but it was not associated with life expectancy in rural areas.

In the models with spatial random effects, all associations were strongly reduced, both for SMR and life expectancy (Table S3). When considering all areas, none of the air pollutants had a statistically significant association with SMR, while only $PM_{2.5}$ was associated with life expectancy. The inclusion of spatial random effects did not alter the SMR estimates in rural areas, but it reversed the sign of the association for PM_{10} and $PM_{2.5}$ in urban areas. For life expectancy, inclusion of spatial random effects reduced the strength of the associations in both rural

Table 2
Relative risks (RRs) and 95% credibility intervals (CI) for mortality. Results from single exposure models.

	PM_{10} (5 μg/m^3) RR (95% CI)	$PM_{2.5}$ (2 μg/m^3) RR (95% CI)	NO_2 (5 μg/m^3) RR (95% CI)	O_3 (5 μg/m^3) RR (95% CI)	NDVI (IQR) RR (95% CI)
All					
Unadjusted[a]	1.092 (1.089, 1.095)	1.056 (1.054, 1.059)	0.994 (0.993, 0.995)	1.032 (1.030, 1.033)	0.978 (0.976, 0.981)
Adjusted[b]	1.057 (1.054, 1.061)	1.037 (1.035, 1.040)	1.001 (1.000, 1.002)	1.023 (1.021, 1.024)	1.008 (1.005, 1.011)
Rural					
Unadjusted[a]	1.152 (1.144, 1.160)	1.123 (1.116, 1.129)	1.022 (1.016, 1.028)	1.039 (1.035, 1.044)	0.973 (0.968, 0.978)
Adjusted[b]	1.121 (1.113, 1.130)	1.098 (1.091, 1.104)	1.046 (1.040, 1.053)	1.026 (1.022, 1.031)	1.003 (0.998, 1.008)
Urban					
Unadjusted[a]	1.082 (1.079, 1.086)	1.040 (1.037, 1.043)	0.992 (0.991, 0.994)	1.028 (1.026, 1.029)	0.986 (0.983, 0.990)
Adjusted[b]	1.033 (1.029, 1.037)	1.019 (1.016, 1.022)	0.997 (0.996, 0.999)	1.016 (1.014, 1.017)	1.015 (1.011, 1.018)

[a] Unadjusted model including only exposure and independent random effects.
[b] Results from sparse spatial generalized linear mixed models to account for spatial autocorrelation. Models were adjusted for 2001 socioeconomic vulnerability index, 2011 percentage of low education, and lung cancer SMR.

Table 3
Change in life expectancy in years (β) and 95% credibility intervals (CI). Results from single exposure models.

	PM_{10} (5 μg/m^3) β (95% CI)	$PM_{2.5}$ (2 μg/m^3) β (95% CI)	NO_2 (5 μg/m^3) β (95% CI)	O_3 (5 μg/m^3) β (95% CI)	NDVI (IQR) β (95% CI)
All					
Unadjusted[a]	−1.23 (−1.30, −1.16)	−0.80 (−0.86, −0.75)	−0.07 (−0.02, 0.03)	−0.33 (−0.38, −0.29)	0.29 (0.23, 0.35)
Adjusted[b]	−0.90 (−0.98, −0.83)	−0.64 (−0.70, −0.59)	−0.13 (−0.17, −0.09)	−0.20 (−0.24, −0.16)	−0.03 (−0.10, 0.03)
Rural					
Unadjusted[a]	−1.71 (−1.82, −1.60)	−1.39 (−1.49, −1.29)	−0.24 (−0.35, −0.15)	−0.52 (−0.59, −0.44)	0.33 (0.24, 0.41)
Adjusted[b]	−1.39 (−1.50–1.28)	−1.13 (−1.23, −1.04)	−0.57 (−0.67, −0.46)	−0.36 (−0.43, −0.28)	−0.03 (−0.12, 0.05)
Urban					
Unadjusted[a]	−0.80 (−0.92, −0.68)	−0.38 (−0.47, −0.29)	0.12 (0.07, 0.17)	−0.23 (−0.29, −0.18)	0.13 (0.02, 0.23)
Adjusted[b]	−0.34 (−0.46, −0.22)	−0.24 (−0.32, −0.15)	0.02 (−0.03, 0.07)	−0.09 (−0.15, −0.04)	−0.17 (−0.27, −0.07)

Models were adjusted for 2001 socioeconomic vulnerability index, 2011 percentage of low education, and lung cancer SMR.
[a] Unadjusted model including only exposure and independent random effects.
[b] Results from sparse spatial generalized linear mixed models to account for spatial autocorrelation.

and urban areas. Lastly, higher greenness was associated with increased mortality risk and lower life expectancy in all adjusted models.

3.3. Additional results

We found interactions between greenness and the air pollutants (Table S4). In Table S5, we show the estimated effects of air pollutants at the 5th and 95th percentiles of greenness. The effect of PM_{10}, $PM_{2.5}$ and O_3 in rural areas was stronger in areas with lower levels of greenness, while in urban areas, the effect was stronger in the areas with high levels of greenness. For NO_2 the effect was stronger in areas with high levels of greenness in both urban and rural areas.

Furthermore, the association between greenness and mortality and life expectancy was tested stratified by the index of vulnerability (Table S6). Results showed protective associations of greenness with mortality and loss of life within areas with lower SES, while higher greenness was associated with higher mortality and lower life expectancy in areas with a higher SES.

Lastly, the sensitivity analyses did not change the results notably (Table S7). Excluding the adjustment for the lung cancer SMR did not change the associations (Table S7.1), and neither did not adjusting for the percentage of people with low education (2011) (Table S7.2). When the unemployment rates of 2011 were used instead of the 2011 percentage of people with low education, NO_2 showed a protective association with mortality, and the association linking higher greenness to increased mortality became stronger (Table S7.3).

4. Discussion

The association between long-term exposure to air pollution and greenness and two different measures of mortality (i.e. SMR and life expectancy) over a large study area (i.e. entire Spain) was investigated. The air pollutants PM_{10}, $PM_{2.5}$, NO_2 and O_3 were identified as risk factors for all-cause mortality and associated with loss of years of life. The strongest association was found for PM_{10}, with a reduction of ten months of life for an increase of a size almost equivalent to the interquartile range of PM_{10} concentrations (5 μg/m^3). The results were similar for both metrics, but slightly stronger for the life expectancy analysis. The findings for greenness were not conclusive; an increase in greenness was only associated with lower mortality and higher life expectancy in areas with lower SES.

The air pollution results seem to be in line with findings of previous research, although there were some differences. To compare different studies, all risk estimates in the following section are given for a 10 μg/m^3 increase in air pollutant concentrations, except when otherwise mentioned. Table S8 shows the equivalence of the associations in the different metrics. The risk estimates for $PM_{2.5}$ were larger in our study than in most previous studies. For instance, while we found a RR of 1.18 (95% CI: 1.17, 1.20), others reported a RR of 1.06 (Beelen et al., 2008; Hoek et al., 2013) or a hazard ratio for all-cause mortality of 1.10 (Carey et al., 2013). For PM_{10}, a systematic review and meta-analysis by Hoek et al. (2013) found that the mortality risk increased by 3.5% (95% CI: 0.4, 6.6%), which is lower than our findings of an excess risk of 11.4% (95% CI: 10.8, 12.2%). In terms of O_3, a recent study found positive significant associations between O_3 with all-cause mortality, which persisted after adjusting for $PM_{2.5}$ and NO_2 (HR 1.01, CI: 1.00, 1.02) (Turner et al., 2016). This association was smaller than the RR found in this study of 1.04 (95% CI: 1.04, 1.05).

However, our study found inconsistent results for NO_2. Previous research has reported associations between long-term exposure to NO_2 and mortality, for instance, an excess of risk of 5% (95% CI: 3, 8%) (Hoek et al., 2013) or 2.7% (95% CI: 1.0, 5.0%) (Beelen et al., 2008). In the present study, the results in rural areas were similar (RR: 4.6%, 95% CI: 4.0, 5.3%), but were smaller when considering all areas. In urban areas, NO_2 showed no association with life expectancy and a protective association with mortality.

Contrary to our expectations, we found a positive association between greenness and mortality. Only in areas with lower SES, greenness was a protective factor for mortality with a RR of 0.97 (95% CI: 0.96, 0.98) for an interquartile range increase in NDVI. Although previous research has not yet been conclusive, this estimate is less strong than, for instance, the RR for non-accidental mortality of 0.95 (95% CI: 0.94, 0.96) for an interquartile range change in NDVI, reported in a cohort in Canada (Villeneuve et al., 2012). Moreover, a RR for all-cause mortality of 0.92 (95% CI: 0.87, 0.97) was found in a meta-analysis that compared the highest and the lowest categories of green space exposure (Gascon et al., 2016).

Studies associating life expectancy with air pollution are scarce and have generally reported weaker associations compared to our study. Pope et al. (2009b) found a potential gain in life of 0.77 years associated with a decrease of 10 μg/m^3 of $PM_{2.5}$ concentration, while our study found a gain of 3.20 (95% CI: 2.95, 3.50) years for the same decrease. For greenness, research is also limited, but Jonker et al. (2014) found that an increase of one standard deviation in the percentage of urban green could increase life expectancy by 0.10 to 0.14 years. In comparison, our study found no significant association with life expectancy when including all areas. However, an increase of 0.34 years (95% CI: 0.27, 0.41) was associated to an interquartile range increase in NDVI in areas with lower SES, but in contrast, higher greenness was associated with lower life expectancy when only including urban areas in the analysis.

Our observed associations were significantly smaller in urban than in rural areas. Several recent papers have reported larger health effects at lower exposure levels than at higher levels (Crouse et al., 2012; Garcia et al., 2016; Marshall et al., 2015; Pope et al., 2009a, 2011). A suggested explanation is a phenomenon of saturation of the underlying biological processes (Pope et al., 2011). In the present study, there were additional factors that could explain the differences between urban and rural areas. First, air quality models often underestimate concentrations in big cities (Baldasano et al., 2011; Schaap et al., 2015). In our study, NO_2 was the pollutant showing the strongest underestimation in cities compared to rural areas. Second, within-area variation of exposure could not be considered in our study and it is expected to be greater in cities. When there are high and low exposure locations in one area, the effect of exposure could be concealed. This may be especially the case for NO_2, because its concentrations vary mainly with traffic, while $PM_{2.5}$ or PM_{10} have more homogeneous distributions (REVIHAAP, 2013). Third, urban areas may have a more complex within-area distribution of SES that could not be accounted for in our study. Within large cities, pollution levels are often associated to SES (Fernandez-Somoano et al., 2013).

In our study, greenness was identified as a statistically significant risk factor for increased natural-cause mortality within urban areas. Similar findings were observed by Richardson et al. (2012), who also found that the potential benefits of green space could be compromised by other accompanying conditions (such as car dependency) and lifestyles that are prevalent in the greener cities. It is also noteworthy that greenness and NO_2, the two factors for which we observed results in the unexpected direction, were the only two factors negatively associated with socioeconomic vulnerability. Thus, residual confounding by SES could explain those associations. This is supported by the fact that the associations with NO_2 and greenness were the ones that suffered more changes when models were adjusted for unemployment. Additionally, greenness showed a protective effect for mortality within areas with lower SES, which supports the suggestion that populations with lower SES may benefit more from green space than those of higher SES (Mitchell and Popham, 2008; Nieuwenhuijsen et al., 2014). The results on greenness could also have been influenced by the exposure assessment, as the quality, size and accessibility, and diversity of green space could not be taken into account (Gascon et al., 2016; Jonker et al., 2014). Finally, we cannot preclude that there is a selection process in which sicker populations move to cleaner areas.

We have used recently developed models to account for residual spatial autocorrelation (Hughes and Haran, 2013; Hughes, 2014). Models that include spatial random effects, such as the Besag-York-Mollie model, have been commonly used in such settings, but its use has been recently questioned. In particular, it has been shown that when both the response and the exposure variables show a strong trend along the long axis of the map, adding spatially correlated errors will nullify the observed associations between the response and the exposures (Hodges and Reich, 2010). This was precisely what we observed in our data.

Our results are limited by its ecological design, which always carries the risk of falling into the ecological fallacy. However, this design enabled the inclusion of entire Spain without any selection, and allowed the comparison between rural and urban areas. Although we include commonly used confounders in studies of air pollution (i.e. age, sex, a deprivation index and a surrogate for smoking prevalence) (Beelen et al., 2015; Hoek et al., 2013; Pelucchi et al., 2009), in this study only area-level measures were available, which neglects individual variation and the distribution of these variables within areas. Additionally, the socioeconomic indicator was a deprivation index from 2001, which precedes the study period. However, we adjusted for the 2011 percentage of low education or unemployment rate to take into account current conditions. Furthermore, the use of lung cancer mortality as a surrogate for smoking has its limitations as air pollution is also a risk factor for lung cancer (Raaschou-Nielsen et al., 2013), and adjustment for this variable could remove not only the effects of smoking, but also part of the effects of air pollution. However, in our analysis, not adjusting for lung cancer rate did not change the main conclusions.

5. Conclusions

This study suggests an association between long-term air pollution exposure and a reduction of life expectancy. Despite the ecological nature of the study, results are in line with previous studies. As a large proportion of the population is exposed to air pollution (and due to continuing urbanization, this proportion will only grow), and no safe level of exposure has been identified yet (Kelly and Fussell, 2015), the reduction of air pollution could have large health benefits. For greenness, conflicting results were found, but this could have been due to limitations of the study such as unmeasured confounders, exposure assessment solely by NDVI, and a complex association with SES. However, apart from increasing life expectancy, greenness could pose major benefits to urban residents by protecting them from environmental exposures present in cities such as heat, noise and high air pollution levels. Therefore, further investigations on the effects of greenness with longitudinal study designs including more individual variables are highly encouraged.

Declaration of interests

We have no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.envint.2016.11.009.

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