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Long term effects of traffic noise on mortality in the city of Barcelona, 2004–2007



Maria Antònia Barceló^{a,b}, Diego Varga^a, Aurelio Tobias^{a,c}, Julio Diaz^d, Cristina Linares^d, Marc Saez^{a,b,*}

^a Research Group on Statistics, Econometrics and Health (GRECS), University of Girona, Girona, Spain

^b CIBER of Epidemiology and Public Health (CIBERESP), Spain

^c Institute of Environmental Assessment and Water Research (IDAEA), Spanish Council for Scientific Research (CSIC), Barcelona, Spain

^d National School of Health, Instituto de Salud Carlos III, Madrid, Spain

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ABSTRACT

Numerous studies showing statistically significant associations between environmental noise and adverse health effects already exist for short-term (over one day at most) and long-term (over a year or more) noise exposure, both for morbidity and (albeit to a lesser extent) mortality. Recently, several studies have shown this association to be independent from confounders, mainly those of air pollutants. However, what has not been addressed is the problem of misalignment (i.e. the exposure data locations and health outcomes have different spatial locations). Without any explicit control of such misalignment inference is seriously compromised.

Our objective is to assess the long-term effects of traffic noise on mortality in the city of Barcelona (Spain) during 2004–2007. We take into account the control of confounding, for both air pollution and socioeconomic factors at a contextual level and, in particular, we explicitly address the problem of misalignment.

We employed a case-control design with individual data. We used deaths resulting from myocardial infarction, hypertension, or Type II diabetes mellitus in Barcelona between 2004 and 2007 as cases for the study, while for controls we used deaths (likewise in Barcelona and over the same period of time) resulting from AIDS or external causes (e.g. accidental falls, accidental poisoning by psychotropic drugs, drugs of abuse, suicide and self-harm, or injuries resulting from motor vehicle accidents). The controls were matched with the cases by sex and age.

We used the annual average equivalent A-weighted sound pressure levels for daytime (7–21 h), evening-time (21–23 h) and night-time (23–7 h), and controlled for the following confounders: i) air pollutants (NO₂, PM₁₀ and benzene), ii) material deprivation (at a census tract level) and iii) land use and other spatial variables. We explicitly controlled for heterogeneity (uneven distribution of both response and environmental exposures within an area), spatial dependency (of the observations of the response variables), temporal trends (long-term behaviour of the response variables) and spatial misalignment (between response and environmental exposure locations). We used a fully Bayesian method, through the Integrated Nested Laplace Approximation (INLA). Specifically, we plugged the whole model for the exposure into the health model and obtained a linear predictor defined on the entire spatial domain. Separate analyses were carried out for men and for women.

After adjusting for confounders, we found that traffic noise was associated with myocardial infarction mortality along with Type II diabetes mellitus in men (in both cases, odds ratios (OR) were around 1.02) and mortality from hypertension in women (ORs around 1.01). Nevertheless, only in the case of hypertension in women, does the association remain statistically significant for all age groups considered (all ages, ≥ 65 years and ≥ 75 years).

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* Correspondence to: Research Group on Statistics, Econometrics and Health (GRECS), University of Girona, Carrer de la Universitat de Girona 10, Campus de Montilivi, 17071 Girona, Spain.

E-mail address: marc.saez@udg.edu (M. Saez).

URL: <http://www.udg.edu/grecs.htm> (M. Saez).

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1. Introduction

Environmental noise poses a very significant risk to human health and road traffic has been identified as the major source of noise exposure. It is estimated that every year in Europe there are

at least 10,000 premature deaths due to exposure to noise (European Environmental Agency (EEA), 2015). In fact, the European Union's Environmental Noise Directive (European Union, 2002) defines a threshold of 55 decibels (dB) for day, evening and night periods (in order to reduce 'annoyance') and of 50 dB for night periods (in order to reduce sleep disturbance). However, the levels at which adverse effects occur could be even lower. According to the World Health Organization (WHO) (World Health Organization, 2009), there is a night noise guideline (NNG) threshold of 40 decibels (dB) which, when exceeded, is considered as having an adverse effect on health. The European Environmental Agency (EEA) points out that over 83 million Europeans are exposed to levels of noise greater than 50 dB at night, mainly as a consequence of road traffic (European Environmental Agency (EEA), 2014). This traffic-related noise in Western Europe has resulted in the loss of, at least, one million healthy life years every year (WHO (World Health Organization), 2011). A recent meta-analysis indicates traffic noise to be among the four environmental factors that have the greatest impact on health, causing between 400 and 1500 disability-adjusted life years (DALY) per million in Europe (Hänninen et al., 2014).

There are already numerous studies showing statistically significant associations between environmental noise and adverse health effects, both for morbidity (World Health Organization, 2009; WHO (World Health Organization), 2011; Hänninen et al., 2014; Perron et al., 2012; Ising and Braun, 2000; van Kempen et al., 2002; Schwela et al., 2005; Stansfeld et al., 2005; Niemann et al., 2006; Babisch, 2008, 2006; Selander et al., 2009a; de Kluizenaar et al., 2007; Babisch and van Kamp, 2009; Sørensen et al., 2011a, 2011b, 2014, 2013; van Kempen and Babisch, 2012; Babisch et al., 2014a, 2014b; Foraster et al., 2014; Fuks et al., 2011; Dratva et al., 2012; Ising et al., 2003, 2004a, 2004b; Linares et al., 2006; Tobias et al., 2001; Eriksson et al., 2014; Schell et al., 2006; Dadvand et al., 2014; De Roos et al., 2014; Halonen et al., 2015) and (to a lesser extent) mortality (Halonen et al., 2015; Gan et al., 2012; Kihal-Talantikite et al., 2013; Tobias et al., 2015a, 2015b, 2014). These health effects not only include sleep disturbance, (World Health Organization, 2009; WHO (World Health Organization), 2011; Perron et al., 2012) and/or psychological stress (Hänninen et al., 2014), but also other adverse health effects including cardiovascular disease (WHO (World Health Organization), 2011; van Kempen et al., 2002; Babisch, 2008, 2006; Selander et al., 2009a, 2014; Tobias et al., 2001; Sørensen et al., 2011, 2014; Halonen et al., 2015) or mortality (Halonen et al., 2015; Gan et al., 2012; Tobias et al., 2015b) as well as an increase in cardiovascular risk factors such as hypertension (de Kluizenaar et al., 2007; Babisch and van Kamp, 2009; Sørensen et al., 2011; van Kempen and Babisch, 2012; Babisch et al., 2014a, 2014b; Foraster et al., 2014; Fuks et al., 2011; Dratva et al., 2012). Furthermore, respiratory diseases (Ising et al., 2003, 2004a, 2004b; Linares et al., 2006; Tobias et al., 2001) and mortality (Tobias et al., 2014), along with Type II diabetes, morbidity (Sørensen et al., 2013; Eriksson et al., 2014) and mortality (Tobias et al., 2015a) and adverse pregnancy outcomes such as low birth weight (Schell et al., 2006; Dadvand et al., 2014).

There is increasing evidence of a significant association between ambient noise and serious cardiovascular events such as ischaemic heart disease (World Health Organization, 2009; Stansfeld et al., 2005; Babisch, 2008; Selander et al., 2009a; Gan et al., 2012) and stroke (Sørensen et al., 2011, 2014; Halonen et al., 2015). Furthermore, recent meta-analyses suggest a very likely causal relationship between hypertension and aircraft (de Kluizenaar et al., 2007; Babisch and van Kamp, 2009) and/or road traffic noise (van Kempen and Babisch, 2012).

The pathophysiological mechanisms explaining such associations could well be related to the response to environmental noise. This response is forwarded to the hypothalamus through the

limbic system in an endocrine process culminating in the release of adrenaline, norepinephrine and, more importantly, cortisol in the adrenal cortex. Exposure to noise causes disruptions to night sleep and awakens electroencephalogram effects, causing a shortage of deep and restful SWS (slow-wave sleep) sleep and disrupting REM (rapid eye movement) sleep (Belojevic et al., 1997). Decreased restful sleep time results in an increase in cortisol levels the following day (Belojevic et al., 1997; Vgontzas et al., 1999; Ising et al., 2004a). All of the studies observed individuals' general maladjustment to long-term night noise, which may lead to chronicity in an overproduction of cortisol (Ising and Ising, 2002; Maschke et al., 2002, 2003).

Hypercortisolemia is associated with the development of atherosclerosis. In response to stress, cortisol activates the metabolism of adipose tissue in order to increase the available energy in the body. Lipolysis of triglycerides increases the amount of fatty acids in the arteries, favouring the irreversible accumulation of plaques that, in turn, increase the risk of a cardiovascular event through ischaemia or thrombosis (Samra et al., 1998; Spreng, 2000a, 2000b). It is also well known that hyperglycaemia resulting from the overproduction of cortisol can lead to insulin resistance and thus increase the risk of developing Type II diabetes (Sørensen et al., 2013; Eriksson et al., 2014; Tobias et al., 2015a). High noise levels activate the body's sympathetic nervous system, increasing blood pressure, blood viscosity and vasoconstriction, all of which leads to increased heart rate and blood lipids (Haralabidis et al., 2008; DKV, 2012). Furthermore, it has been reported that, in children, an increase of cortisol concentration activates the hypothalamus–pituitary–adrenal axis, leading, in the long term, to an aggravation of respiratory diseases (Ising et al., 2003, 2004a, 2004b).

For almost all of these adverse health events, close to 50% of the studies made have focused on the effects of short-term (essentially exposure over a day maximum) and the other fifty centred on the long-term (exposure over a year or more) effects (Niemann et al., 2006; Selander et al., 2009a; Sørensen et al., 2011a, 2011b, 2014, 2013; Babisch et al., 2014a, 2014b; Foraster et al., 2014; Fuks et al., 2011; Dratva et al., 2012; Ising et al., 2003, 2004a, 2004b; Eriksson et al., 2014; Schell et al., 2006; Halonen et al., 2015; Gan et al., 2012; Kihal-Talantikite et al., 2013) of high noise levels.

However, the independent association between traffic noise and adverse health effects has been questioned by the occurrence of confounding, mainly by air pollutants (Beelen et al., 2009; Hart et al., 2013; Schwela et al., 2005). Traffic not only contributes to 80% of the environmental noise in a large city, but it is also the main source of air pollution (Díaz et al., 2003). In Babisch et al. (2014a, 2014b), for instance, mutual adjustment for PM_{2.5} and traffic noise led to associations (with hypertension) which, although positive, could no longer be considered statistically significant. Likewise, Foraster et al. (2014) found inconsistent associations (with hypertension and high blood pressure) when considering outdoor traffic noise, which is probably due to a high degree of collinearity with NO₂. Sørensen et al. (2014) found indications of a combined effect of both road traffic and air pollution (NO₂) on the risk of stroke. Nevertheless, several recent studies have shown an association between adverse health events, including mortality, and environmental noise (Ising and Braun, 2000), independent of the effect of the air pollutants that are routinely measured. Niemann et al. (2006), for instance, argued that the risk of respiratory diseases in children could actually be caused by environmental noise rather than air pollution. Adverse health events include cardiovascular events such as hypertension (de Kluizenaar et al., 2007; Sørensen et al., 2011; Babisch et al., 2014a, 2014b), high blood pressure (Fuks et al., 2011; Dratva et al., 2012) and stroke (Halonen et al., 2015), respiratory diseases (Niemann et al., 2006), as well as cause-specific mortality such as cardiovascular disease (Halonen et al., 2015).

On the other hand, it is also argued that an individual's acceptance of environmental noise is determined by demographic aspects, such as the length of time that an individual has lived in their place of residence, as well as psychosocial factors such as the level of sensitivity, and/or the individual's attitude and personality (Guski, 1999; Paunovic et al., 2009).

While individuals may become accustomed to a noisy environment, it would seem that this habituation can not be extended to actually having an effect on the cardiovascular system of the individuals during night-time exposure (Muzet, 2002; Holzman, 2014). Clearly the longer the time an individual spends in a noisy environment, the more accustomed they become to its noise levels. In addition, becoming accustomed to a certain level of noise depends on how adequate the level of acoustic insulation of the home is and exactly what the noise level of the surrounding environment is. Both of these aspects are related to socioeconomic factors, either individually or contextually. In fact, socioeconomic variables in general and deprivation in particular, could aggravate, modify or even confound the effect of environmental noise on adverse health outcomes (Kihal-Talantikite et al., 2013).

There is also a significant statistical problem that has not been taken into account by epidemiological studies. Studies examining the effects of environmental irritants on health (either air pollution or noise) face the challenge of attempting to assess the level of exposure experienced. Ideally, measurements of personal exposure could be used, but data of this type are limited. Niemann et al. (2006) and Ising et al. (2003) used questionnaires to assess noise exposure on the individual level. In both questionnaires, the study subjects (or their parents in the case of Niemann et al. (2006)) answered specific questions regarding noise exposure. These questions were then transformed into (ordinal) categorical variables, rated from 'none' (i.e. no (Niemann et al., 2006) or low (Ising et al., 2003) noise annoyance) to 'extremely' (i.e. extreme (Niemann et al., 2006) or high exposure to noise (Ising et al., 2003)). However, all the other studies assessing the long-term effects of environmental noise have relied on spatial data designs (Selander et al., 2009a; Sørensen et al., 2011a, 2011b, 2014, 2013; Babisch et al., 2014a, 2014b; Foraster et al., 2014; Fuks et al., 2011; Dratva et al., 2012; Ising et al., 2004a, 2004b, 2011, 2014, 2013; Eriksson et al., 2014; Schell et al., 2006; Halonen et al., 2015; Gan et al., 2012; Kihal-Talantikite et al., 2013). That is to say, measurements from the geographical region of the study are used to assess environmental nuisance levels. Hence, exposure data and health outcomes often have different spatial locations, so they are 'misaligned' (Gelfand, 2010) (also known as the 'modifiable areal unit' or the 'change of support' problem (Gotway and Young, 2002; Gelfand, 2010)). As with most air pollution studies, those assessing the long-term effects of noise address the misalignment problem (albeit only implicitly) using a two-stage modelling procedure, or a plug-in approach, where predictions from an exposure model (first stage) are used as covariates in a health effect model (second stage). Although predictions in a few cases are obtained from exposure models that explicitly incorporate spatial structure, even in these cases the plug-in approach does not take into account the uncertainty in the exposure predictions. This leads to a complex form of measurement error, resulting in bias of the health effect (Wannemuehler et al., 2009; Ingebrigtsen et al., 2015).

Our objective is to assess the long-term effects of traffic noise on mortality in the city of Barcelona (Spain) during 2004–2007. As methodological challenges, we take into account the control of confounding, both air pollution and socioeconomic factors at contextual level and, in particular, we explicitly address the misalignment problem by using a method that provides consistent and efficient estimates of the effects of traffic noise.

2. 2. Methods

2.1. Design

We used a case-control design with individual data. As cases, we used deaths from myocardial infarction (ICD-10: I21-I22), hypertension (ICD-10: I10-I15), and Type II diabetes mellitus (ICD-10: E10-E14) which occurred in Barcelona between 2004 and 2007. As controls, we used deaths that had occurred in the city over the same period from AIDS (ICD-10: B20-B24, R75) or external causes (accidental falls – ICD-10: W00-W19-; accidental poisoning by psychotropic drugs and drugs of abuse – ICD-10: X41-X45, F11-F12, F14-F16, F19-; suicide and self-harm – ICD-10: X60-X84; injury by motor vehicle accident – multiple ICD-10 codes).

Finally, our sample sizes were as follows: myocardial infarction (6439 deaths), hypertension (4412 deaths) and Type II diabetes mellitus (2670 deaths). The total number of controls was 6560. Controls were matched 1:1 with cases by sex and age, choosing them at random when the number of cases were fewer than the total number of controls.

The information was obtained from death certificates collected by the Catalan Mortality Register. We only considered the death certificates of Barcelona city residents who died in the city between 2004 and 2007. Each certificate included the age, sex, the (last) residential address and the underlying cause of the individual's death. We georeferenced the residential addresses of all the study subjects (at the side of the residential address).

2.2. Noise exposure

Traffic noise assessment was based on the Barcelona City Council's 2007 official noise map.

The Directive 2002/49/EC (Directive 2002/49/EC) on assessment and management of environmental noise, established the need to make strategic noise maps for agglomerations of more than 250,000 inhabitants. In our case this involved the cities of Barcelona (with an area of 100.4 km², 62 km² of which correspond to urban land) and Sant Adrià del Besos (located on the coast to the north of and surrounded by Barcelona with an area of 3.87 km², all urban land). In Catalonia, strategic noise maps contain, at least, information concerning the situation as to acoustic noise levels, the estimated number of people located in an area exposed to noise, and the map of acoustic capacity (Technical Memory, 2015).

Information on the existing noise situation allows noise sources and levels to be distinguished. Directive 2002/49/EC calls for strategic maps to be made according to the night-time level L_n , and the index of noise immission day-evening-night L_{den} , which, in turn, depends on L_d , the equivalent sound level determined over the 14 h period between 7 am and 21 h (daytime) and over all the day periods of a year; L_e , the equivalent term determined in the range between 21 h and 23 h (evening hours) and over all the evening periods of a year; and L_n , the equivalent term determined in the range between 23 h and 7 a.m. (night time) and over all the night periods of a year (Technical Memory, 2015). The noise taken into account was incident sound i.e. it did not include the noise reflected at the façade of the dwelling under consideration, and the height of the evaluation points was representative of 4 m above the ground.

The estimate of the number of people located in an area exposed to noise was made by allocating the population located at specific addresses to the noise level determined by the stretch of road (in intervals of 100 m) to which the addresses belonged. If there were houses assigned to an address whose façade was most exposed to another street or to an area with a different level of exposure to the actual address, the total population was distributed according to the exposed perimeter of the building

façade. The population at risk was estimated for the L_n indicator in the ranges of noise levels 50–55, 55–60, 60–65, 65–70 and > 70 dB (A), and the population exposed to the L_{den} indicator in 55–60, 60–65, 65–70, 70–75 and > 75 dB (A).

Two methods of analysis, simulation and measurement of actual levels were simultaneously applied to plot the cities' noise levels and mark them onto the map of the city itself. The simulation method was used because of the traffic levels from the major road and rail infrastructures and the plot of the cities' main roads. The calculations were carried out as recommended by the methods contained in the European Directive 2002/49/EC (Directive 2002/49/EC). After obtaining the results of the modelling, they were then compared with those obtained with sound level measurements in situ. Thus, the model was fed back with real data and it was possible to calibrate some of the parameters of the model in order to increase representativeness (Technical Memory, 2015). In Barcelona not all houses have façades that directly face the street, rather a considerable part of the population is exposed to noise from the interior patios their homes are built around. In these cases, the actual level of noise exposure was also estimated by the simulation method. When not enough information concerning vehicle transit was available to use simulation, or when there was a great diversity of street types and activities, the actual noise levels were measured. In order to obtain measurements of the levels that could be representative of all the streets in the agglomeration, the number and location of measuring points were chosen by their representativeness in relation to the characteristics of the urban plot (Technical Memory, 2015). In addition, the measurements were made according to the different types of noise sources: road traffic, entertainment, shopping areas, industry and trams.

In summary, a total of 2309 short (with a minimum duration of 15 min, only during the day) and 109 long (for at least 24 h, including morning, evening and night) duration periods, both based on the two methods (simulation and measurement), are included on the map (Plan to reduce noise pollution in the city of Barcelona, 2015) Data were mapped as isolines, drawn every 5 dB (A). Annual average equivalent A-weighted sound pressure levels were calculated for daytime (7–21 h), evening-time (21–23 h) and night-time (23–7 h).

2.3. Air pollution

Annual average daily levels of particulates (PM_{10}) nitrogen dioxide (NO_2) and benzene for 2001–2007 were obtained from the 10 monitoring stations in the Catalan Atmospheric Pollution Surveillance and Control Network (XVPCA), located within the city of Barcelona. In fact, Barcelona is part of an Air Quality Area (ZQA, acronym in Catalan). Within each ZQA, the geographical distribution of the monitoring stations is optimal in the sense that areas of the same type (defined by the degree of land use and the type of emission sources) fall within the same area and thus a similar level of immissions are covered by the monitoring station (Air Quality, 2015). In this case, data were collected as point processes located at each of the stations.

To build the database (always before the analyses), we 'assigned' each study subject with the median of the annual levels of air pollution at each of the monitoring stations from 2001 until the year before his/her death. That is, for example, for an individual who died in 2003 we 'attached' the median of the levels (annual averages) of 2001 and 2002 for each of the three air pollutants from each of the ten monitoring stations. Therefore, for this individual, we will have ten variables (each for each of the monitoring stations) for each of the three air pollutants. Each of these variables has associated location coordinates of the corresponding station.

2.4. Socioeconomic variables

As we did not have individual-level socioeconomic data we used the contextual variable of disposable household income for 2007 (in fact, a deprivation index). Data were obtained from the OpenDataBCN website (Territorial distribution of household income in Barcelona). The Barcelona City Council has divided Barcelona into 73 neighbourhoods (Calvo et al., 2007) for administrative and statistical purposes, thus the index was constructed for each one using five socioeconomic indicators: i) unemployment rate (computed as unemployed over resident population aged 16–65 years), ii) the percentage of resident population aged 25 years or more with a university degree, iii) cars per 1000 over total resident population, iv) cars more than 16 horsepower (hp) but less than two years old over the total number of cars less than two years old and v) private home resale prices (Calvo et al., 2007).

We assigned study subjects to one disposable household income quartile based on the neighbourhood they resided in.

2.5. Additional controls for environmental nuisance exposures

We tried to control for other types of environmental nuisance exposures (i.e. other air pollutants, environmental noise not related to traffic, etc), through land use variables and other spatial variables (see Fig. 1). We believe that these variables, along with the data obtained from the XVPCA air pollution network, would approximate traffic related air pollution more efficiently.

The Cartographic Institute of Catalonia (ICC) provided the cover map of Catalonia (scale 1:250,000) for 2002 from which the land use variable was obtained using classification techniques according to legend and land use from the CORINE Land Cover project and based on the visual interpretation of images from the Thematic Mapper (TM) sensor installed on the LANDSAT-5 satellite (Chuvieco et al., 2010). In the city itself, only five categories of the initial 22 occur: road infrastructure, residential, commercial and service areas, industrial and mixed urban or built-up land.

We assigned the study subjects to one or other of the land use categories according to their residential address.

Moreover, we included other variables, also with a spatial distribution (spatial variables hereinafter) that could have explained some of the residual confounding not captured by the air pollutants or the land use variables. These spatial variables include density (of population) of the census tract where the study subject lived, the altitude of their residential address, and the distances (in metres) from the study subject's residential address to: i) streets with high density traffic (on average more than 19,000 vehicles per day during the week), ii) petrol stations, iii) green areas (parks and gardens) and iv) industrial estates. Distances were constructed by considering a geographical layer corresponding to 2002 for each variable. The urban area and road layers were obtained from the ICC through the Catalan Government's Department of Territory and Sustainability. To obtain the new raster layers we used the Euclidean distance function, included in the ArcGis10 Spatial Analyst application. Then, we used the merge function of the ArcGis10 Geoprocessing module, to combine these layers into one single layer. The layers were continuous and defined as raster layers. We allowed the relationships between the response variables and spatial variables to be nonlinear. For this reason, all of the spatial variables were categorized into quartiles.

Since distance to possible sources of noise (i.e. roads, industrial sites, etc.) could act as an over fitting, we also checked if not adjusting for these distances would have changed the results in any way.

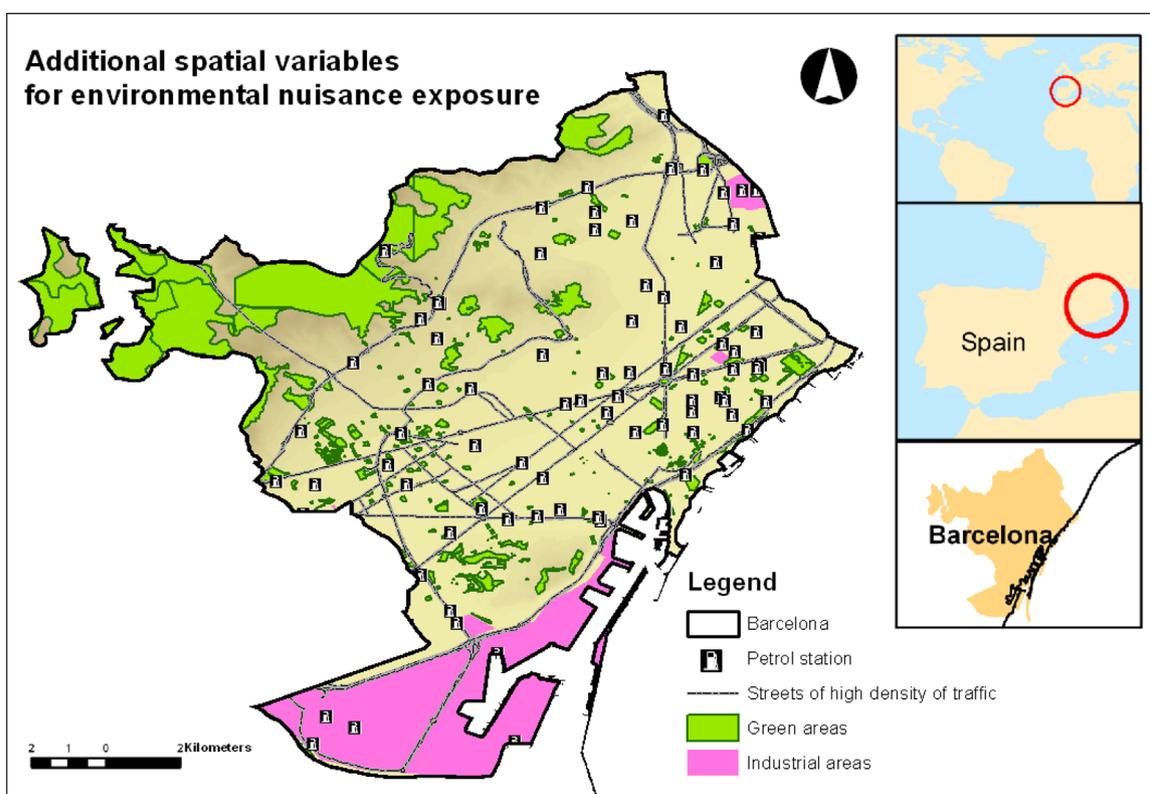


Fig. 1. Additional spatial variables for environmental nuisance exposure.

2.6. Statistical analyses

For each of the specific causes of mortality, we specified generalised linear mixed models with binomial response (case or control) and a logistic link,

$$\log\left(\frac{\text{Prob}(Y_i = 1)}{1 - \text{Prob}(Y_i = 1)}\right) = \eta_i$$

where Y denoted each of the response variables, myocardial infarction, hypertension, and Type II diabetes mellitus. The subscript i denoted the study subject (0 for a control, 1 for a case, i.e. death for each of the response variables) and η a linear predictor for subject i .

For each subject, the linear predictor included those variables that might explain the probability of being case: noise levels, air pollutants (PM_{10} , NO_2 and benzene), disposable household income, land use, spatial variables (density, altitude and the four distance variables) and the year in which the study subject died (aiming to control temporal trends, if any). While noise levels were introduced into the different models (that is to say, for each response variable, one model for a daytime noise level, another for the evening and a third for night-time), air pollution (NO_2 , PM_{10} and benzene) levels along with all the other covariates were introduced into each of the models.

Analyses for men and women were made separately, with and without stratifying by age (under 65, 65 years and over; 75 and over). There are several reasons for such stratification. First, there is some evidence from previous literature of stronger associations between noise exposure and adverse health effects among women (Selander et al., 2009b), particularly for metabolic outcomes such as Type II diabetes (Sørensen et al., 2013; Eriksson et al., 2014). Second, we do not have any exposure measures individually. In fact, the measure of exposure is ecological. Therefore, the exposure will be different for individuals who are more sedentary

individuals and those who are more mobile. In general, given the low rate of activity compared with that of other European countries, women are more sedentary (at least on the neighbourhood level), than men. Furthermore, older people are more sedentary than younger ones.

2.7. Addressing the misalignment problem

In our case, health data (i.e. the response variables) observed at point locations (the residential addresses of the individuals) were misaligned with the two main explanatory variables, air pollution and noise levels, along with some of the confounders. In fact, there are different types of misalignment depending on the spatial scale and/or locations of the data: misalignment between point locations, between point locations and areal units, and between the areal units themselves (Gelfand, 2010). Air pollution levels were also collected at point locations, specifically at each one of the air pollution monitoring stations. However, these locations did not necessarily coincide with those of the response variables (in this case, misalignment was between point locations). Noise levels were recorded using a different spatial resolution (i.e. isolines drawn every 5 dB (A)) to that of the response variables (in this case, misalignment was between point locations and areal units). As regards to confounders, socioeconomic variables were recorded at a neighbourhood level, while density (of population) corresponded to the census tract where the study subject lived and land use variables were obtained from a cover map of Catalonia (scale 1:250,000). All of these were misaligned between the point locations and areal units.

Wannemuehler et al. (2009) find that when environmental nuisance levels (in our case, noise and air pollution levels) exhibit spatial variation across the study region, using exposure point estimators such as, for instance, the arithmetic or inverse-distance weighted average of several monitors or even estimates based on one centrally located monitor or the nearest monitor, can lead to

bias and the underestimation of the health effect of interest. However, as we noted earlier, most studies do not use those point estimators but rather a two-stage strategy, or a plug-in approach, where, in the first stage, an 'exposure' model is used to predict environmental nuisance levels at points where the response is observed. Typically, predictions are obtained from exposure models that explicitly incorporate spatial structure (e.g. deterministic interpolation, Kriging, or land use regressions). In the second stage, these predictions (of the environmental nuisance levels) are used as covariates in a 'health' model, the model of interest.

The problem with the plug-in approach is that, unless the exposure model is perfectly specified (which almost never happens) measurement error committed in the estimation of the parameters is not random. This error is 'drawn' to the second stage via the predictions. If the measurement error was random, then the estimators of the parameters of interest in the 'health' model (relative risks, for example) would be unbiased but inefficient. That is to say, their standard errors would be inflated and would result in few statistically significant associations being obtained (Barceló et al., 2009). However, the measurement error is systematic and can be decomposed into a Berkson-like component and a classical-like component (Gryparis et al., 2009; Szpiro et al., 2011; Szpiro and Paciorek, 2013). The Berkson-like component is associated with predicting the exposure. Generally, the predictions come from a smoothed exposure surface, implying that the predicted values are less variable than the unobserved truth. The classical-like component is associated with the uncertainty in estimating exposure model parameters. Classical error induces biased parameter estimates, while Berkson error inflates their standard errors (Szpiro et al., 2011). Thus, this complex form of measurement error leads to biased and inconsistent (i.e. asymptotically biased) estimates and erroneous standard errors in the estimates of the parameters. This results in the inference being greatly compromised. Therefore, in order to obtain correct health effect estimates, this measurement error needs to be taken into consideration (Gryparis et al., 2009; Szpiro et al., 2011; Szpiro and Paciorek, 2013; Ingebrigtsen et al., 2015).

Different methods for correcting the measurement error have been proposed. First, if it were possible to correctly specify the exposure model, the measurement error could be corrected by using parametric bootstrapping (Madsen et al., 2008; Lopiano et al., 2011; Szpiro et al., 2011). However, a correct representation of the data generating mechanism for the true exposure is unrealistic. More recently, Szpiro and Paciorek (2013) suggested a non-parametric bootstrap method to account for the extra variability induced by using predicted exposures as covariates in the health model. They point out that the proposed error correction method is robust for the misspecification of the exposure model and yields valid inference for the health effect parameter. The exposure simulation approach (Gryparis et al., 2009) uses simulated exposures in an attempt to correct the variance of the plug-in estimator. However, this approach (based on the classical measurement structure) produces biased estimates. The size of the bias depends on the size of the variance in the measurement error. Another error correction method is regression calibration (Carroll and Stefanski, 1990; Carroll et al., 2006) where external validation data (e.g. personal measurements) are used to adjust for measurement error (Gryparis et al., 2009; Szpiro et al., 2011; Szpiro and Paciorek, 2013; Spiegelman, 2010, 2013). Gryparis et al. (2009) point out that the regression calibration approach performed relatively well in a simulation study where they used different exposure scenarios and so they advocate for such a method because it is convenient to implement. However, in terms of statistical efficiency, Bayesian methods (two-stage and fully Bayesian) are better than the out-of-sample regression calibration. In a two-stage Bayesian method, the interim posterior from the exposure

model is used as a prior distribution for the exposure in the health model (Barceló et al., 2009; Gryparis et al., 2009). This accounts for the extra uncertainty associated with predicting exposure at the missing locations. A fully Bayesian method uses a joint modelling approach for exposure and health data (Gryparis et al., 2009; Mollitor et al., 2006; Kim et al., 2010). The joint Bayesian model adjusts automatically for any measurement error caused by misalignment. Gryparis et al. (2009) found that the Bayesian methods performed well for continuous health outcomes and expected a similar performance for binary data, but because of the time-consuming computations and the poor mixing of the Markov chain Monte Carlo (MCMC) scheme, they did not pursue the Bayesian methods in their simulation study with non-Gaussian health outcomes.

In this paper we used a consistent and efficient method (Ingebrigtsen et al., 2015). We also used a fully Bayesian method, however, as a result of computational problems, we did not use MCMC but rather the Integrated Nested Laplace Approximation (INLA) (Rue et al., 2009; Blangiardo et al., 2013), which is a computationally efficient alternative to MCMC. Specifically, instead of modelling exposure (i.e. noise and air pollutants) and health variables in separate steps and plugging estimated exposures into the health model, we plugged the whole model for the exposure into the health model and obtained a linear predictor defined on the entire spatial domain. In the joint model uncertainty is propagated into the health model automatically (Ingebrigtsen et al., 2015). Further detail can be found in the appendix.

2.8. Spatial adjustment

With spatial data, as is our case, it is necessary to distinguish between two sources of extra variability, 'spatial dependence' or clustering, and non-spatial heterogeneity (Barceló et al., 2009). To take into account this extra-variability, we introduced some structure into the model. Heterogeneity was captured by using a random effect associated with the intercept. As before for spatial dependency, we followed the work of Lindgren et al. (2011), and specified a Matérn structure explicitly constructed through the Stochastic Partial Differential Equation INLA approach (SPDE INLA) (Lindgren et al., 2011).

2.9. Control for temporal trends

Temporal trends were controlled by including in the linear predictor the year of the death of the study subject. This variable was not introduced linearly, but nonparametrically through a random effect associated with the trend and structured according to a random walk of order one (The R INLA Project, 2015).

All analyses were made with the INLA library (R-INLA Project, 2015; Rue et al., 2009) available through the free software R (version 3.1.0) (R Development Core Team, 2012).

3. Results

In 2004, the population of Barcelona stood at 1,578,546 inhabitants – 746,045 (47.26%) men and 832,501 (52.74%) women (Statistical Institute of Catalonia, 2015). Those aged over 65 represented 17.28% or 128,917 men and 24.49% or 203,877 women. Among those aged 75 or more, 7.47% were men and 12.99% were women.

According to the Technical Memory of the Strategic Noise Map of the Barcelonès I (Barcelona and Sant Adrià del Besòs) (Technical Memory, 2015), 44.9% of the population are exposed to noise levels below 65 dB (A), while of the remaining 55.1%, 27% are exposed to levels between 65 and 70 dB (A), 22.8% to levels between 70–75 dB (a) and 5.2% to levels above 75 dB (a).

Table 1
Unadjusted comparison of cases and controls for noise exposure, air pollutants and deprivation index.

	Myocardial infarction			Hypertension			Type II diabetes Mellitus		
	Case	Control	p-value ^a	Case	Control	p-value ^a	Case	Control	p-value ^a
Men									
Noise levels (dB)^b									
Day (7–21 h)	65.85	64.36	0.013	64.75	64.58	0.303	64.77	64.36	0.107
Evening (21–23 h)	62.18	61.64	0.012	62.08	61.92	0.374	62.11	61.64	0.087
Night (23–7 h)	56.12	55.51	0.008	55.98	55.98	0.517	56.06	55.51	0.057
Air pollution levels (µg/m³)^b									
PM ₁₀	29.91	28.02	0.051	33.13	31.24	0.003	30.14	29.02	0.062
NO ₂	17.84	17.83	0.989	19.60	19.11	0.472	18.85	17.83	0.120
Benzene	0.329	0.309	0.220	0.372	0.356	0.515	0.354	0.309	0.036
Deprivation index ^c (Barcelona = 100)	100.57	98.89	0.232	101.59	103.20	0.271	102.04	99.89	0.077
Women									
Noise levels (dB)^b									
Day (7–21 h)	65.02	64.95	0.773	64.72	64.38	0.090	64.95	64.72	0.398
Evening (21–23 h)	62.35	62.30	0.837	62.07	61.67	0.065	62.30	62.00	0.309
Night (23–7 h)	56.32	56.25	0.788	56.00	55.56	0.058	56.25	55.93	0.318
Air pollution levels (µg/m³)^b									
PM ₁₀	29.71	29.69	0.967	32.70	30.77	0.015	30.23	29.71	0.420
NO ₂	17.50	16.89	0.315	20.51	19.15	0.116	18.60	16.89	0.016
Benzene	0.312	0.262	0.008	0.453	0.342	< 0.001	0.336	0.262	0.001
Deprivation index ^c (Barcelona = 100)	101.54	101.91	0.834	101.75	105.00	0.088	101.91	100.17	0.367

^a p-value of the test of mean differences (values at case locations vs. values at control locations), Student's t (bilateral).

^b For purely descriptive purposes, and always before the analyses, noise and air pollution levels were assigned to the study subject's residential address using ordinary Kriging.

^c Disposable household income (Barcelona=100) of the neighbourhood of the study subject's residential address.

In 2008, the age-standardized mortality rate per 100,000 inhabitants was 1307 (men) and 709 (women). The mortality rates for diseases of the circulatory system were 341.3 for men and 219.6 for women. The rates for endocrine, nutritional and metabolic diseases reached 35.7 for men and 24.8 for women (Agència de Salut Pública de Barcelona, 2015).

We show some descriptive results in Tables 1 and 2. For purely descriptive purposes, and always before the analyses, noise and air pollution levels were assigned to the study subject's residential address using ordinary Kriging. In all cases, noise levels were higher in the location of cases than in the location of controls (Table 1). However, only in the case of men who died from myocardial infarction was the difference clearly statistically significant ($p < 0.05$). In men who died from Type II diabetes mellitus and in women who died from hypertension, the differences in the noise levels between cases and controls were only marginally statistically significant ($p < 0.1$). The levels of PM₁₀ were higher in the cases' locations than in those of the controls in the case of hypertension (both sexes) and only marginally statistically significant in the cases of myocardial infarction and Type II diabetes mellitus

for men. The levels of benzene were always higher and statistically significant at the locations of female cases and at the locations of those men who died from Type II diabetes mellitus. The levels of NO₂ were only statistically different between locations of cases and controls in the case of women who died from Type II diabetes mellitus. Finally, disposable household income was larger, although marginally significant ($p < 0.1$), in the neighbourhoods with the cases of Type II diabetes mellitus in men and of the female controls with hypertension.

We show in Table 2, the correlations between the (explanatory) variables of interest (i.e. noise and air pollution levels). Correlations between noise levels were very high (always above 0.9). In fact, as depicted in Table 1, the average levels of noise (and standard deviations) are very similar between day, evening and night. Noise, therefore, would seem to be very persistent in the city. As regards to air pollutants, although all of them were statistically different from zero, (at 95% confidence level) they were small between the air pollutants themselves and between the air pollutants and noise levels. There was one notable exception, the levels of NO₂ and benzene.

Spatial distribution of traffic noise levels was similar for daytime, evening-time and night-time (Fig. 2). The highest levels were concentrated, as expected, in areas with more traffic, namely the city centre and the peripheral and interior ring roads.

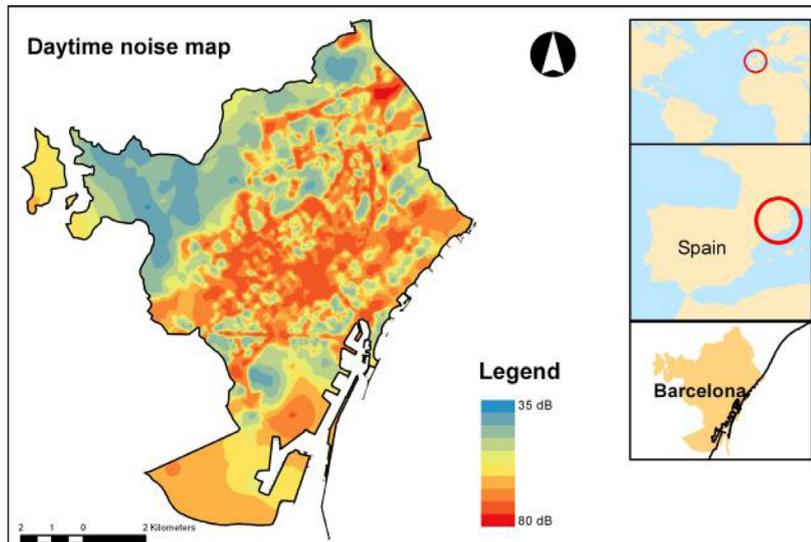
The results of the estimation are shown in Tables 3–5. Our results were robust to various sensitivity analyses (for instance, including and excluding distances to: i) streets with high density traffic, ii) petrol stations, iii) green areas and iv) industrial estates). Noise levels were found to be statistically significantly associated with myocardial infarction in the case of men of all ages (Table 3). No statistically significant associations were found for men under 65 years old. In men aged 65 years and older, the noise levels in the evening lost significance and in men aged 75 years and older only daytime noise levels were statistically significantly associated, although only at 90% of confidence. Note that the odds ratios (OR) appeared to follow a gradient (although credibility intervals CrI hereinafter overlapped), higher during the daytime (for men of any age, OR=1.020, per 1 dB, 95% CrI: 1.010–1.042), somewhat

Table 2
Pearson correlation between and within noise exposure and air pollution variables.

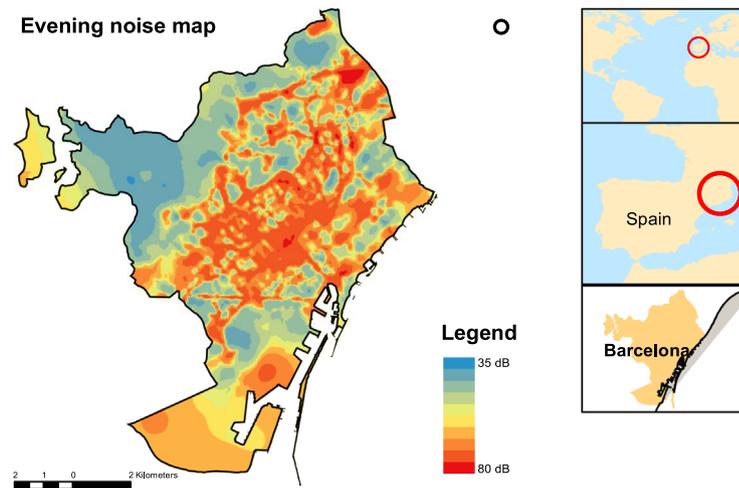
	Noise levels			Air pollution levels		
	Day (7–21 h)	Evening (21–23 h)	Night (23–7 h)	PM ₁₀	NO ₂	Benzene
Noise levels						
Day (7–21 h)	1	0.976	0.983	0.024	0.160	0.108
Evening (21–23 h)	0.976	1	0.977	0.014	0.175	0.094
Night (23–7 h)	0.983	0.977	1	0.013	0.171	0.115
Air pollution levels						
PM ₁₀	0.024	0.014	0.013	1	0.277	0.229
NO ₂	0.160	0.175	0.171	0.277	1	0.719
Benzene	0.108	0.094	0.115	0.229	0.719	1

All the correlation coefficients were statistically significant ($p < 0.05$). Student's t (bilateral).

a.- Spatial distribution of noise levels in Barcelona, 2007. Daytime (7h-21h)



b.- Spatial distribution of noise levels in Barcelona, 2007. Evening time (21h-23h)



c.- Spatial distribution of noise levels in Barcelona, 2007. Night-time (23h-7h)

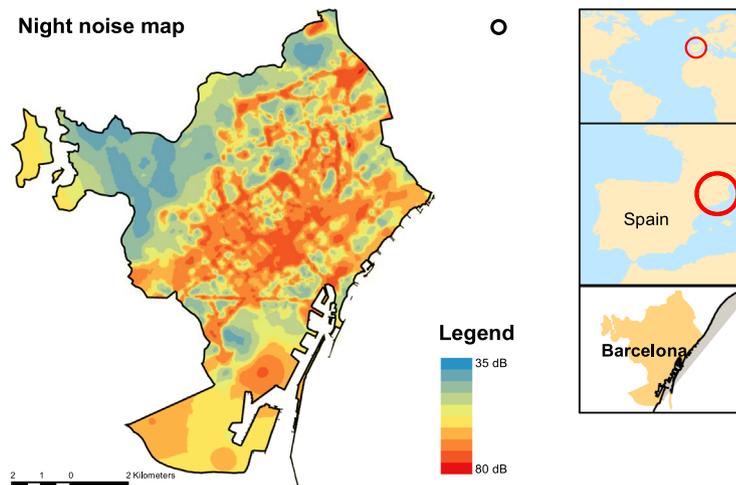


Fig. 2. (a) Spatial distribution of noise levels in Barcelona, 2007. Daytime (7–21 h). (b) Spatial distribution of noise levels in Barcelona, 2007. Evening time (21–23 h). (c) Spatial distribution of noise levels in Barcelona, 2007. Night-time (23–7 h).

Table 3
Results of the estimates of odds ratio and 95% credibility intervals. Myocardial infarction mortality.

Myocardial infarction (ICD-10: I21-I22)	Males				Females			
	All	<65 years	≥ 65 years	≥ 75 years	All	<65 years	≥ 65 years	≥ 75 years
Noise levels (dB)								
Day (7h-21)	1.020 (1.010,1.042)	1.005 (0.971, 1.040)	1.033 (1.008,1.070)	1.033 (0.991,1.077)	1.007 (0.980,1.035)	1.002 (0.825, 1.038)	1.006 (0.973,1.039)	0.987 (0.952,1.022)
Evening (21h-23h)	1.019 (1.009,1.039)	1.010 (0.978,1.043)	1.024 (0.991,1.058)	1.023 (0.984,1.064)	1.001 (0.976,1.027)	0.946 (0.847, 1.045)	1.000 (0.970,1.031)	0.981 (0.948,1.014)
Night (23h-7h)	1.018 (1.010,1.037)	1.007 (0.978,1.037)	1.026 (1.010,1.057)	1.021 (0.985,1.059)	1.006 (0.983,1.030)	0.958 (0.864,1.051)	1.003 (0.974,1.032)	0.986 (0.956,1.017)
Air pollution levels (µg/m³)								
PM₁₀	0.982 (0.973,1.992)	0.979 (0.964,1.994)	0.983 (0.968,1.969)	0.979 (0.962,1.996)	0.976 (0.965,1.987)	0.998 (0.957, 1.041)	0.962 (0.949,1.975)	0.964 (0.950,1.769)
NO₂	0.983 (0.969,1.998)	0.996 (0.974, 1.020)	0.965 (0.944,1.988)	0.965 (0.940,1.991)	0.986 (0.970,1.002)	0.929 (0.861, 1.013)	0.994 (0.974,1.015)	0.988 (0.967,1.009)
Benzene	1.184 (0.700,1.998)	1.190 (0.227, 1.872)	4.735 (2.002,11.334)	5.661 (1.938,17.638)	1.796 (0.884,3.589)	1.197 (0.397, 1.503)	3.259 (1.452,7.336)	3.783 (1.662,8.732)
Deprivation [First quartile]¹								
Second quartile	0.838 (0.584,1.203)	0.840 (0.466, 1.507)	0.841 (0.505,1.415)	0.906 (0.503,1.654)	0.605 (0.389,0.939)	0.631 (0.218, 1.368)	0.616 (0.364,1.045)	0.772 (0.418,1.359)
Third quartile	0.831 (0.580,1.191)	0.867 (0.510, 1.471)	0.746 (0.446,1.258)	0.922 (0.497,1.725)	0.913 (0.567,1.474)	0.844 (0.121, 1.594)	0.903 (0.509, 1.615)	0.980 (0.540,1.795)
Fourth quartile	1.097 (0.732,1.653)	0.721 (0.383, 1.356)	2.368 (1.200,4.896)	3.095 (1.408,7.237)	0.810 (0.508,1.297)	1.106 (0.106, 1.316)	0.864 (0.498,1.514)	1.143 (0.634,2.083)

Also adjusted for land use, spatial variables (density, altitude and distance to: i) streets with high density traffic, ii) petrol stations, iii) green areas and iv) industrial estates), for spatial dependence (heterogeneity and spatial dependence), and temporal trends.

¹ Reference category: First quartile

Odds ratio for noise levels per 1 dB; for air pollutants per 1 µg/m³. Interquartile range for PM₁₀ 10 µg/m³, for NO₂ 15 µg/m³, Benzene 1.400 µg/m³

In bold, the 90% credibility interval did not contain the unity (i.e. statistical significant at 90%); Shaded and in bold, the 95% credibility interval did not contain the unity (i.e. statistical significant at 95%).

Table 4
Results of the estimates of odds ratio and 95% credibility intervals. Hypertension mortality.

Hypertension (ICD-10: I10-I15)	Males				Females			
	All	<65 years	≥ 65 years	≥ 75 years	All	<65 years	≥ 65 years	≥ 75 years
Noise levels (dB)								
Day (7h-21)	1.003 (0.992,1.015)	1.002 (0.991, 1.014)	1.004 (0.993,1.015)	1.002 (0.992,1.014)	1.013 (1.004,1.023)	1.010 (1.001, 1.020)	1.013 (1.004,1.023)	1.010 (1.001,1.020)
Evening (21h-23h)	1.004 (0.993,1.016)	1.003 (0.992,1.016)	1.005 (0.994,1.017)	1.004 (0.992,1.016)	1.014 (1.005,1.024)	1.011 (1.001,1.021)	1.014 (1.005,1.024)	1.011 (1.001,1.021)
Night (23h-7h)	1.005 (0.994,1.018)		1.006 (0.994,1.0183)	1.004 (0.993,1.017)	1.016 (1.006,1.026)	1.012 (1.002,1.022)	1.016 (1.006,1.026)	1.012 (1.002,1.023)
Air pollution levels (µg/m³)								
PM₁₀	1.006 (1.001,1.012)	1.006 (1.001, 1.012)	1.006 (1.001,1.012)	1.006 (1.001,1.012)	1.007 (1.002,1.012)	1.007 (1.002, 1.011)	1.007 (1.003,1.013)	1.006 (1.003,1.011)
NO₂	1.003 (0.994,1.012)	1.003 (0.994, 1.012)	1.004 (0.996,1.013)	1.003 (0.995,1.012)	1.000 (0.993,1.008)	1.000 (0.993, 1.008)	0.999 (0.993,1.007)	1.000 (0.993,1.008)
Benzene	0.811 (0.636,1.031)	0.857 (0.661, 1.106)	0.791 (0.618,1.011)	0.837 (0.650,1.073)	0.737 (0.575,1.943)	0.772 (0.595, 1.003)	0.737 (0.579,1.939)	0.775 (0.602,0.995)
Deprivation [First quartile]¹								
Second quartile	1.492 (1.173,1.892)	1.122 (0.877, 1.411)	1.483 (1.162,1.888)	1.215 (0.963,1.530)	1.509 (1.221,1.864)	1.227 (1.006, 1.497)	1.656 (1.347,2.036)	1.306 (1.072,1.591)
Third quartile	1.173 (0.879,1.563)	1.113 (0.187, 1.594)	1.160 (0.866,1.552)	0.903 (0.684,1.192)	1.250 (1.068,1.613)	0.880 (0.705, 1.200)	1.390 (1.086,1.780)	0.947 (0.758,1.183)
Fourth quartile	1.730 (1.248,2.442)	1.577 (1.028, 1.828)	1.657 (1.187,2.359)	1.098 (0.827,1.479)	1.414 (1.034,1.939)	0.878 (0.682, 1.135)	1.814 (1.340,2.463)	1.047 (0.812,1.352)

Also adjusted for land use, spatial variables (density, altitude and distance to: i) streets with high density traffic, ii) petrol stations, iii) green areas and iv) industrial estates), for spatial dependence (heterogeneity and spatial dependence), and temporal trends.

¹ Reference category: First quartile

Odds ratio for noise levels per 1 dB; for air pollutants per 1 µg/m³. Interquartile range for PM₁₀ 10 µg/m³, for NO₂ 15 µg/m³, Benzene 1.400 µg/m³

In bold, the 90% credibility interval did not contain the unity (i.e. statistical significant at 90%); Shaded and in bold, the 95% credibility interval did not contain the unity (i.e. statistical significant at 95%).

Table 5
Results of the estimates of odds ratio and 95% credibility intervals. Diabetes Mellitus type II mortality.

Diabetes Mellitus (ICD-10: E10-E14)	Males				Females			
	All	<65 years	≥ 65 years	≥ 75 years	All	<65 years	≥ 65 years	≥ 75 years
Noise levels (dB)								
Day (7h-21)	1.023 (0.995,1.052)	1.008 (0.950, 1.070)	1.039 (1.009,1.085)	1.043 (0.991,1.099)	1.000 (0.970,1.031)	0.995 (0.123, 1.061)	0.995 (0.960,1.032)	0.982 (0.945,1.021)
Evening (21h-23h)	1.022 (1.010,1.050)	1.009 (0.956,1.067)	1.032 (0.991,1.076)	1.036 (0.987,1.089)	0.994 (0.966,1.023)	0.996 (0.866,1.106)	0.989 (0.956,1.022)	0.977 (0.941,1.013)
Night (23h-7h)	1.023 (1.010,1.048)	1.008 (0.958,1.062)	1.036 (1.010,1.078)	1.033 (0.987,1.081)	0.998 (0.971,1.025)	0.981 (0.917,1.052)	0.990 (0.959,1.022)	0.979 (0.946,1.013)
Air pollution levels (µg/m³)								
PM₁₀	0.977 (0.965,1.988)	0.965 (0.938,1.991)	0.976 (0.959,1.924)	0.971 (0.951,1.909)	0.977 (0.964,1.990)	1.234 (0.873, 1.702)	0.965 (0.949,1.980)	1.019 (0.676,1.557)
NO₂	0.994 (0.975,1.013)	0.938 (0.886, 1.077)	0.981 (0.955,1.007)	0.982 (0.953,1.013)	0.995 (0.977,1.014)	0.979 (0.706, 1.343)	1.007 (0.984,1.032)	0.966 (0.949,1.982)
Benzene	1.376 (0.744,2.543)	0.997 (0.345,11.98)	5.296 (2.018,14.074)	5.514 (1.610,2.055)	0.997 (0.449,2.250)	1.245 (0.783, 2.485)	1.084 (0.360,3.276)	1.003 (0.979,1.027)
Deprivation [First quartile]¹								
Second quartile	1.172 (0.760,1.808)	1.107 (0.310, 2.612)	1.240 (0.697,2.226)	1.317 (0.677,2.617)	0.664 (0.537,1.087)	0.759 (0.423, 1.491)	0.798 (0.440,1.454)	0.803 (0.424,1.530)
Third quartile	0.843 (0.532,1.340)	0.843 (0.151, 1.245)	0.766 (0.412,1.430)	0.895 (0.433,1.867)	1.487 (0.898,2.477)	1.317 (0.865, 2.257)	1.708 (1.009,3.178)	1.679 (0.889,3.208)
Fourth quartile	1.370 (0.812,2.313)	1.282 (0.826,1.375)	2.953 (1.370,6.578)	4.333 (1.753,11.315)	1.195 (0.880,1.716)	1.116 (0.837, 1.013)	1.308 (0.894,2.496)	1.604 (0.816,3.201)

Also adjusted for land use, spatial variables (density, altitude and distance to: i) streets with high density traffic, ii) petrol stations, iii) green areas and iv) industrial estates), for spatial dependence (heterogeneity and spatial dependence), and temporal trends.

¹ Reference category: First quartile

Odds ratio for noise levels per 1 dB; for air pollutants per 1 µg/m³. Interquartile range for PM₁₀ 10 µg/m³, for NO₂ 15 µg/m³, Benzene 1.400 µg/m³

In bold, the 90% credibility interval did not contain the unity (i.e. statistical significant at 90%); Shaded and in bold, the 95% credibility interval did not contain the unity (i.e. statistical significant at 95%).

lower in the evening (OR=1.019, per 1 dB, 95% CrI: 1.010–1.039) and the lowest being at night-time (OR=1.018, per 1 dB, 95% CrI:1.010–1.037). For women, noise levels were not found to be statistically significantly associated with mortality from myocardial infarction.

Mortality from hypertension was only found to be associated with noise levels (day, evening and night) in the case of women in all of the three age strata we considered. (Table 4). The odds ratios for women of any age were quite similar. The odds ratios for women aged 75 years or older were somewhat smaller, but credibility intervals overlapped in all cases. In this case there was also a gradient in the ORs, but this time it was inverted, being higher at night (OR: 1.016, per 1 dB, 95% CrI: 1.006–1.026, all ages; OR: 1.012, per 1 dB, 95% CrI: 1.002–1.023, 75 years and older), followed by evening (OR:1.014, per 1 dB, 95% CrI: 1.005–1.024, all ages; OR: 1.011, per 1 dB, 95% CrI: 1.001–1.021, 75 years and older) and lower in the day (OR: 1.013, per 1 dB, 95% CrI: 1.004–1.023, all ages; OR: 1.010, per 1 dB, 95% CrI: 1.001–1.020, 75 years and older).

However, mortality from Type II diabetes mellitus was only found to be associated with noise levels in the case of men (Table 5). The association was statistically significant during the daytime for men aged 65 years or older, during the evening for men of any age and at night for men of any age and also in the strata of those aged 65 and older. In other cases (in men), the associations were only marginally significant. The gradient with decreasing OR from daytime to night-time only occurred for men 75 years or more, although it was marginally significant.

Note that in all cases where we found statistically significant associations, noise levels increased the risk of death after adjustment for air pollutants and economic deprivation. In the case of mortality from hypertension the air pollutant that was statistically and significantly associated was PM₁₀. The lack of association between NO₂ and the response variables could be related to the high correlation between NO₂ and benzene.

Deprivation was associated (also after adjustment for other variables) with mortality, with the exception of mortality from myocardial infarction in women and in men younger than 65

years. Note, however, as this association was not linear and not all quartiles were statistically significant. In all cases, the greater the deprivation, the greater the increased risk of death. The ORs corresponding to deprivation were particularly high for men 65 years or older who died from myocardial infarction or Type II diabetes mellitus. In these cases, the ORs corresponding to the fourth quartile (most deprived neighbourhoods) were two or three times higher than the rest of ORs associated with deprivation (statistically significant).

4. Discussion

After adjusting for confounders, we found that traffic noise was associated with myocardial infarction mortality, with Type II diabetes mellitus in men and with mortality from hypertension in women. Note, however, this association only occurred 'consistently' in the case of mortality from hypertension in women.

In this sense, not all subjects are exposed to the same levels of environmental noise. In fact, only those with lower mobility, that is to say, those who spend more time at home or in any case around their home, suffered. Our guess is that this group of people could correspond to older women, particularly those aged 75 or more. Furthermore, if there really was an adverse effect caused by environmental noise, after adjustment for its confounders, it was higher at night, a time when individuals are less accustomed to noisy environments (Muzet, 2002; Holzman, 2014). To be more precise, these two conditions only appeared in the association between mortality from hypertension and environmental noise. In the other cases, associations occurred in men under 75 years although they can be more mobile than older males and therefore exposed to fewer episodes of environmental noise in their homes.

As mentioned above, recent meta-analyses suggested a very likely causal relationship between road traffic (van Kempen and Babisch, 2012) and/or aircraft noise (de Kluienaar et al., 2007; Babisch and van Kamp, 2009) and hypertension. In van Kempen and Babisch (2012) the combined odds ratio was 1.034 [95%

confidence interval (CI) 1.011–1.056] per 5 dB (A) increase of the 16 h average road traffic noise level. Compare our estimates for women aged 75 years and older, expressed by 5 dB (A) increases, OR night-time (8 h, range 18.91–73.76 dB (A)): 1.062 (95% CrI:1.012–1.114); OR evening time (2 h, range 25.83–76.53 dB (A)): 1.056 (95% CrI:1.007–1.106); OR daytime (14 h, range 35.86–78.26 dB (A)): 1.052 (95% CrI:1.005–1.102).

Although there is less evidence, the estimates provided by the literature on the association between environmental noise and the incidence of Type II diabetes mellitus and myocardial infarction, practically coincide with ours. Compare our ORs for the association of environmental noise and Type II diabetes around 1.020, with a relative risk equal to 1.011 per 1 dB increase in Sørensen et al. (2013), and a cumulative incidence of diabetes of 3% in Eriksson et al. (2014). In the same way, Selander et al. (2009a), for instance, found an odds ratio of 1.01 for the association between noise and myocardial infarction.

It is also worth noting that the effect of noise on mortality was slightly higher than that of PM₁₀. These results coincide with those other studies found for the city of Madrid (Spain) which reveal that the effects of both PM₁₀ and environmental noise on mortality are quite similar (Tobías et al., 2015c).

As the main limitation to our work, we had no explanatory variables, apart from sex, age and the address of the subjects, at the individual level. In particular, we cannot control for factors, such as individual socioeconomic data, lifestyles and comorbidities that may differ between cases and controls and also be related to noise and air pollution. These factors may also act as confounders or effect modifiers. Some of these factors could have been controlled by adjusting confounders we had, in particular by introducing the deprivation index, but also through the spatial variables. However, it is likely that there was still some residual confounding.

Among the uncontrolled confounders, we would like to point out, as a second limitation, some meteorological variables particularly in temperature and atmospheric pressure. However, there are three reasons we were unable to obtain them. First and foremost, we did not know the exact date of death of the cases, rather we only knew the year of the death. Ascertaining this would have involved using an annual average of these meteorological variables, which certainly made little sense. Second, in Barcelona there are only four meteorological stations and two of them are located on the outskirts of the city. Finally, there was little variability in these variables in 2004–2007.

Nevertheless, we believe that the residual confounding was controlled, at least to a large extent, by the spatial adjustment. In fact, by introducing random effects we controlled both the heterogeneity (owing to unobserved confounders without a spatial structure) and the spatial dependence (because of unobserved confounders with a spatial structure).

As a third limitation, some of the causes of death taken as controls may be indirectly related to exposure to environmental noise. For instance, stress and aggression levels could be higher with higher noise levels. This could lead to a greater number of accidents. In this regard, there may be some bias (albeit small) in the estimation of the health effects of high noise levels.

A fourth limitation is related to the data of the variable noise. Studies in Madrid (Spain) (Tobías et al., 2015c) indicate that during the period 2001–2010 a slightly downward trend was maintained, so using 2007 data, as in our case, the worst case scenario would be underestimating the exposure of the population.

As a fifth limitation, the association between environmental exposures and mortality is subject to (non-differential) misclassification for several reasons including, i) we do not know how many hours per day, if at all, the person stayed at their official address, ii) we do not know how long they resided at this last

address, iii) we have no information as to which floor the person lived on, iv) neither do we know if the windows of their flat faced the street or were located at the back of the house, v) we have only very indirect information about the building's noise insulation and vi) although we have traffic noise data at our disposal, we do not have information concerning noise from other sources.

The sixth and final limitation, as in any Bayesian analysis, was that the choice of the prior distributions of model parameters (i.e. priors) may have had a considerable impact on the results. However, we performed sensitivity analyses to assess how the prior on the hyperparameters influenced the estimation results. First, by increasing the precision (lowering the variance) and second, by testing other priors different to those used by default in R INLA, that is, log gamma with different shape and inverse-scales; uniform, centered half-normal and priors that penalise the complexity (Martins et al., 2015). In any case, we found no significant differences.

Despite the limitations, we can conclude that our results on the long-term effects of traffic noise on daily mortality, along the lines of those of Hänninen et al. (2014), and our recent results for the city of Madrid (Tobías et al., 2015a, 2015b, 2014), show that environmental noise should be considered a major pollutant. Hence, traffic noise control should be a priority in public health policy and environmental decision-making. Some preventive measures would be fairly easy to implement, i.e. a decrease in 0.5 dB (A) could be achieved if 12% of the cars were electric vehicles (Warburg et al., 2014).

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Appendix

The exposure field was modelled as the spatial surface,

$$z(s) = \alpha + x(s) \quad s \in D$$

where s denoted the spatial locations (of the exposures), D the spatial domain, α was an intercept and $x(\cdot)$ a zero mean Gaussian random field with Matérn covariance function $C(\cdot, \cdot)$. In particular, for the covariance between locations u and v (in R^2), we used the parameterisation.

$$C(u, v) = \sigma^2(\kappa\|v - u\|)K_1(\kappa\|v - u\|)$$

where $\|\cdot\|$ is the Euclidean distance; K_1 is the modified Bessel function of the second kind and first order; κ is a positive scaling parameter related to the spatial correlation range ρ ; and σ^2 is the marginal variance (Ingebrigtsen et al., 2015).

For the health model, we specified:

$$E(Y_i^h) = \mu_i^h$$

$$g(\mu_i^h) = \beta_0 + \beta_z z_i^h$$

where the superscript h denoted the values at locations without exposure observations; Y_i^h corresponded to the i -th observation of the response variable; μ_i^h was the expected mean (conditional to the explanatory variables); $g(\cdot)$ denoted a link function; β_0 and β_z were unknown parameters; and z_i^h was an exposure measurement at the location s_i^h .

Now, the joint linear predictor is defined on the entire spatial domain.

$$\eta(s) = \beta + \beta_z x(s) \quad s \in D$$

Here, the intercept was $\beta = \beta_0 + \beta_z \alpha$, a combination of the health model parameters β_0 and β_z , and the intercept in the exposure model α .

The two parts of the joint model were estimated simultaneously from the data. We used the Stochastic Partial Differential Equation INLA approach (SPDE INLA) (Lindgren et al., 2011).

First, we used a discretisation of the spatial domain D into a triangulated mesh by means of piecewise linear basis functions and created a mapping of A from the mesh node locations to any location $s \in D$. In particular, we created two mapping matrices: i) one between the mesh and the health observation locations, $A_{ik}^h = \varphi_k(s_i^h)$ (the superscript h referred to the health component) and ii) the other between the mesh and the exposure measurement locations, $A_{ik}^e = \varphi_k(s_i^e)$ (the superscript e referred to the exposure component). In vector form the linear predictors can now be written as,

$$\eta^{h,jo \text{ int}} = \beta 1 + \beta_z A^h w$$

$$\eta^e = \alpha 1 + A^e w$$

which in the latent Gaussian Markov Random Field (GMRF) model framework translated into observations $y^* = (y, z^e)$, linear predictions $\eta^* = (\eta^{h,jo \text{ int}}, \eta^e)$, and latent field $x^* = (\beta, \alpha, w)$. Now, the hyperparameters are β_z , σ^2 and ρ . We used, as an initial choice for the priors of the hyperparameters, those used by default in R INLA (log gamma with shape equal to 1 and inverse-scale equal to $5e-05$). However, we did conduct a sensitivity analysis as well, choosing different priors and different parameters for them.

Conflicts of interest

There are no conflicts of interest for any of the authors. All authors will disclose any actual or potential conflict of interest including any financial, personal or other relationships with other people or organisations within three years of beginning the submitted work that could inappropriately influence or be perceived to influence their work.

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