

RESEARCH ARTICLE

Neighbourhood Characteristics and Long-Term Air Pollution Levels Modify the Association between the Short-Term Nitrogen Dioxide Concentrations and All-Cause Mortality in Paris

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Abstract

Background

While a great number of papers have been published on the short-term effects of air pollution on mortality, few have tried to assess whether this association varies according to the neighbourhood socioeconomic level and long-term ambient air concentrations measured at the place of residence. We explored the effect modification of 1) socioeconomic status, 2) long-term NO₂ ambient air concentrations, and 3) both combined, on the association between short-term exposure to NO₂ and all-cause mortality in Paris (France).

Methods

A time-stratified case-crossover analysis was performed to evaluate the effect of short-term NO₂ variations on mortality, based on 79,107 deaths having occurred among subjects aged over 35 years, from 2004 to 2009, in the city of Paris. Simple and double interactions were statistically tested in order to analyse effect modification by neighbourhood characteristics on the association between mortality and short-term NO₂ exposure. The data was estimated at the census block scale (n=866).

Results

The mean of the NO₂ concentrations during the five days prior to deaths were associated with an increased risk of all-cause mortality: overall Excess Risk (ER) was 0.94% (95%CI=[0.08;1.80]). A higher risk was revealed for subjects living in the most deprived census blocks in comparison with higher socioeconomic level areas (ER=3.14% (95%CI=[1.41-4.90]), p<0.001). Among these deprived census blocks, excess risk was even higher where

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long-term average NO₂ concentrations were above 55.8 µg/m³ (the top tercile of distribution): ER=4.84% (95%CI=[1.56;8.24], p for interaction=0.02).

Conclusion

Our results show that people living in census blocks characterized by low socioeconomic status are more vulnerable to air pollution episodes. There is also an indication that people living in these disadvantaged census blocks might experience even higher risk following short-term air pollution episodes, when they are also chronically exposed to higher NO₂ levels.

Introduction

The association between ambient air pollution and mortality is widely documented in the literature [1,2]. Various pollutants were studied, including Particulate Matter (PM) and nitrogen dioxide (NO₂). Times-series and case-crossover studies were the most frequently used study designs for assessment of the short-term effects of exposure to air pollution, whereas cohort studies were most commonly performed to evaluate long-term effects. Long-term exposures have greater effects than short-term variation of pollutants' concentrations [3–5]. In the APHENA multi-city study, the combined effect of PM₁₀ on all-cause mortality across all-ages for cities with daily air pollution data ranged from 0.2% to 0.6% for a 10 µg/m³ increase in ambient PM₁₀ concentrations [5]. However, the public health significance of these results is still a matter of debate because of the harvesting (or death displacement) effect [6–8]. People at high risk of dying at any given point in time may die prematurely due to an air pollution episode, but these precipitated deaths are followed by a short period of decline in mortality—during which the pool of people at high risk of dying is reconstituted. The reconstitution of this pool is influenced by many factors such as age, smoking, pre-existing diseases, poor socioeconomic conditions, and chronic exposure to air pollution. Little research has been undertaken to explore the joint impact of short-term variations in air pollution and of chronic exposure. Such research as there is makes an underlying assumption that the effect of short-term variations in exposure is constant over the range of long-term exposures [5]. However, acute outcomes associated with short-term variations in air quality build up upon chronic conditions that have been shown to be linked with long-term exposures—in particular such cardiovascular conditions as haemostasis impairment, atherosclerosis or hypertension [9, 10].

Besides, deprived populations are reported to be more affected by exposure to air pollution [11–13] via two main pathways: differential exposure (disadvantaged groups may be more intensely exposed to pollution than affluent groups) and differential vulnerability (disadvantaged people may be more likely to manifest the adverse effects of air pollution because, in general, they already experience poorer health status due to social determinants). However, though several studies have assessed whether socioeconomic status (SES) modifies the risk of all-cause mortality in relation to short-term variations in air pollution, the results remain inconsistent: some studies have observed higher risk among subjects with a low SES [14–18] whereas others did not [19–22]. The variety of indicators defining socioeconomic status could partially explain the difference in results observed: income [22], education level [15–17, 21], housing characteristics [19], occupational activities [16, 17, 19], and sometimes a global socioeconomic index encompassing an array of variables [18, 22, 23]. Moreover, these SES measures were assessed at different levels across studies, using either individual [16, 19, 21] or area-based measures [17, 18, 22, 23].

In this context, the main objective of the present study was to explore how a combination of neighbourhood characteristics (socioeconomic profile and long-term exposure to ambient air NO₂ levels) might modify the short-term association between variations in NO₂ and all-cause mortality in Paris (France). Paris is characterized by long-term average NO₂ concentrations that vary substantially across the city according to traffic density (the main determinant of NO₂ levels) as well as by a variety of districts hosting populations with contrasting socioeconomic profiles.

Material and Methods

Study setting and small-area level

The city of Paris has a population of about 2,250,000. The small-area level used was the IRIS (a French acronym for 'blocks for incorporating statistical information'). Designed by the French National Census Bureau (INSEE), the IRIS constitutes the smallest census unit area whose aggregate data can be used on a routine basis. The city of Paris is subdivided into 992 IRIS—named "census blocks" hereafter—with a mean population of 2,199 inhabitants and a mean area of 0.11 km² (range from 0.009 to 5.4 km²).

Health data

We considered all deaths that occurred in the city of Paris for residents older than 35 years old from January 2004 to December 2009. All-cause mortality data were provided by the death registry of the city of Paris. Individual information on age, sex, date of death, and census block of residence was available for each case. For confidentiality reasons it was not possible to distinguish causes of mortality, thus external causes of deaths could not be excluded. The analysis included only subjects older than 35 years at the time of death to minimize this bias since accidental causes of death are dominant in subjects under 35 years old [24]. We obtained the population size in each stratum from the INSEE. Ethical approval was obtained from the French commission on data privacy and public liberties (CNIL—Commission Nationale de l'Informatique et des Libertés).

Air pollution data

NO₂ was selected as the exposure indicator because it is recognized to be a good tracer of the air pollution generated by traffic, the main source of air pollution in Paris, and to present a small scale spatial heterogeneity greater than other pollutants.

- Estimation of long-term NO₂ concentrations at the census blocks level: Annual NO₂ concentrations were modelled from a grid of 25x25m resolution throughout the period 2002–2009 by engineers at AirParif (the regional association for the surveillance of air quality: <http://www.airparif.asso.fr/>). The ESMERALDA inter-regional platform for air quality mapping and forecasting (www.esmeralda-web.fr) provided background pollution data, while the STREET dispersion model [25] was used for traffic-related pollution. To compute annual NO₂ concentrations at a fine spatial resolution (25x25m), these models incorporated several input data types: emission inventories, meteorological data and background pollution measurements—supplied respectively by the industry, by regional environmental administration, by Météo-France (the French meteorological agency) and by the regional network monitoring stations, alongside building and traffic parameters. Air pollutant concentrations were then aggregated at census block scale in order to obtain annual mean NO₂ concentration for each census block. Long-term NO₂ concentrations at census block scale were computed as the mean of daily NO₂ concentrations from 2002 to 2009. The small spatial

heterogeneity of the long-term NO₂ concentrations lead us to categorize the exposure into tertiles of the distribution (limits for each interval are shown in [Table 1](#))

- Estimation of short-term NO₂ concentrations and exposures: To reconstitute census-block-specific NO₂ daily variability within each census block, we combined the annual NO₂ concentrations estimated by the dispersion models described in the previous section with the daily NO₂ concentrations measured by fixed monitoring stations located within the city of Paris. In total, Paris City counts 12 fixed monitoring stations measuring NO₂, including 6 background stations and 6 traffic stations. To achieve this NO₂ daily variability reconstitution, we followed a series of three steps. Firstly, each census block was assigned by AirParif to the monitoring station (named the 'index' monitor) best representing overall NO₂ air quality within the census block, using clustering methods. Secondly, the ratio between daily NO₂ concentrations for the 'index' monitor and its annual mean was computed for each 'index' monitor, so as to derive temporal series centred on 1. Thirdly, the annual concentration of NO₂ modelled for each census block was multiplied by the daily variability ratio (obtained at the second step) for the associated 'index' monitor to compute daily concentration of NO₂ for each census block. In this step, we hypothesized that daily variations of NO₂ concentrations in a given census block would be similar to the daily variation of its 'index' monitor. Over the whole period of study, missing daily NO₂ concentrations amounted to between 5% and 12%. Linear regression was used to substitute missing daily concentrations for each monitoring station using predicted values for the same day, based on mean daily concentrations for the available stations (separately for background and traffic stations).

Socioeconomic index

To characterize socioeconomic status, we used an index developed at the census block scale for Paris, which is described elsewhere [26]. Briefly, a Principal Component Analysis (PCA) was used to select variables among 41 socioeconomic and demographic variables provided by the 2006 national census at census block level. According to the results of this Principal Component Analysis, 15 variables were most correlated with the first component, and thus selected to carry out a final Principal Component Analysis, where the reduced first component was used to calculate the socioeconomic index. Finally, hierarchical ascendant clustering was performed to gather census blocks into homogenous socioeconomic categories. Hierarchical clustering is an unsupervised clustering method which creates a hierarchy of classes (i.e. clusters), frequently used following a PCA or other data mining techniques. The purpose is to find a partition in *N* classes that either maximizes between-classes inertia or minimizes within-classes inertia. This inertia-based clustering criterion allows the creation of classes that are homogeneous in their composition and heterogeneous between one another. In our work, hierarchical

Table 1. Descriptive statistics of NO₂ concentrations (short and long term) across the study period (2004–2009).

Short term concentrations	Mean [CV% [†]]	Long term concentrations	Mean [CV% [‡]]
All blocks	52.59 [26.47%]	All blocks	53.21 [11.43%]
Least deprived blocks	52.78 [25.29%]	Least exposed blocks	47.48 [4.76%]
Intermediate blocks	52.33 [26.66%]	Intermediate blocks	53.15 [2.92%]
Most deprived blocks	53.01 [26.99%]	Most exposed blocks	60.61 [7.18%]

[†]: expressed in µg/m³

[‡]CV% = coefficient of variation in %

clustering revealed 3 homogeneous socioeconomic categories numbered 1 (most privileged) to 3 (most deprived). The characterization of census blocks for these 3 categories is presented in [S1 Table](#). About 13% (n = 126) of census blocks remained unassigned to a socioeconomic category because of being poorly inhabited (parks, recreation facilities, business and commercial districts, etc.). We did not, therefore, take these unclassified census blocks into account in the model (variables distributions were not modified: results not shown). In total, 866 IRIS (79,107 deaths) were analysed for the present study.

Proven or likely confounders

Following the literature [[20,27–31](#)] dealing with the health effects of air pollution, several confounders were considered in our study.

- Daily temperature (maximum, mean and minimum), daily relative humidity (maximum, mean and minimum) and daily mean atmospheric pressure; the data were obtained from the Météo-France Montsouris station in Paris.
- Incidence rate of the weekly influenza case counts. Information on weekly influenza case counts in the Ile-de-France region (which includes the city of Paris as well as the whole surrounding metropolitan area) was obtained from the Inserm *Sentinelles* network (<http://websenti.u707.jussieu.fr/sentiweb/>).
- Holidays.

Statistical analyses

Associations between daily NO₂ concentrations and all-cause mortality were investigated using a case-crossover design [[32](#)]. Control days were selected using a monthly time-stratified approach: the study period was divided into monthly strata and control days were chosen from the same day of the week as the case day within each stratum [[33](#)]. For example, for a death occurring on a given weekday (e.g., a Monday), control days were the same days of the week throughout the rest of the month (thus, three or four days; here, all other Mondays of the same month). This control selection strategy takes account of time trends, seasonality, day of the week, temporal autocorrelation in exposure time-series, while avoiding overlap biases [[33](#)].

The statistical strategy was structured in 3 successive steps.

Firstly, associations between death events and ambient air pollution concentrations modeled by census block were estimated, adjusting for holidays, meteorological variables (the cubic B-spline function of the maximum daily temperature, the inverse of the humidity mean of the previous five days' deaths), and influenza epidemics, following the approach exposed below. Regarding temperature, we used a Cubic B-spline function of the maximum daily value which is recognised by the literature to have a strong short-term effect on mortality counts in comparison with the simple function of temperature [[34–36](#)]. Regarding humidity, we used the inverse of the mean of the previous five days' deaths (lag period 5 noted lag 0–5) [[37](#)] rather than the simple arithmetic mean, because it is a better fit. Finally, atmospheric pressure was not retained in the model because it was not significant, and AIC was not improved (see details in [S2, S3](#) and [S4](#) Tables).

In the second step, we tested the influence of the various lag periods between NO₂ treated as a continuous variable, and short term mortality, by computing the mean of NO₂ concentrations across the four to seven days prior to deaths (lag0-4 to lag0-7). Whatever the lag period of exposure we considered in the adjusted model, the short term effect of NO₂ concentrations on

mortality was statistically significant. However, we chose the 0–5 lag period which both gave a low AIC criteria and a low correlation with long-term NO₂ exposure estimates.

Finally, in the third step, we assessed effect modification by age, sex, census block level socioeconomic status and long-term NO₂ concentrations by testing interactions in the models.

Effect estimates of air pollution on the 0–5 lag period were expressed as the percent increase in risk of mortality (excess risk) associated with a 10 µg/m³ short-term increase in NO₂, with corresponding 95% confidence intervals. All statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC).

Results

The study included a total of 79,107 deaths among subjects above 35 years of age from 2004 to 2009. A majority (65%) occurred after the age of 75 and 38% beyond age 85; 53% of cases were female deaths.

[Table 1](#) gives descriptive statistics of air quality, for both short-term NO₂ concentrations (average of 5 days preceding death events) and long-term (average values over the study-period). Average NO₂ concentration was 52.6 µg/m³ on the 5 days preceding death events (short-term exposure) and 53.2 µg/m³ over the study period (long-term exposure).

Socioeconomic categories: About 20% of subjects resided in socioeconomic category 1 census blocks (the most privileged), 55% in category 2, and 25% in category 3 (the most deprived). [Fig 1](#) shows the residential distribution of these three socioeconomic categories in the city of Paris. The most deprived census blocks (category 3) are mainly located in the eastern and northern fringe of the city, i.e. along the *périphérique* (ring road), while census blocks characterized by a higher SES (categories 1 and 2) are found in the centre and western part of Paris. There was no evidence of differences in the short-term NO₂ concentrations across the census blocks in three socioeconomic categories ([Table 1](#)).

NO₂ long-term concentration: [Fig 2](#) represents spatial distribution, at census block level, of long-term NO₂ concentrations in the city of Paris. The most polluted areas are observed along the *périphérique* and the Seine river (next to major thoroughfares with high traffic volume) and in the north-western part of Paris.

All-cause mortality associated with short-term variations in NO₂: The overall Excess Risk (ER) of all-cause mortality is equal to 0.94% (95%CI = [0.08;1.80]; p = 0.03) for a 10 µg/m³ increase in short-term NO₂ concentrations ([Table 2](#)). Stratified analyses by individual characteristics revealed subgroups exhibiting a higher risk in relation with short-term NO₂ concentrations ([Table 2](#)): elderly people (>85 years) and males. We also demonstrate that neighbourhood characteristics modify the effect of short term exposure to NO₂. Subjects living in the lower socioeconomic category census blocks experience a higher NO₂-related mortality (ER = 3.14%; 95%CI = [1.41, 4.90]) than in the most privileged ones (the interaction p-value is borderline significant = 0.07). When the privileged and middle socioeconomic categories were grouped, based on the similarity of their excess risk values, interaction between the short-term exposure to NO₂ and SES became statistically significant (interaction p-value = 0.028).

People living in census blocks exhibiting the highest long-term exposure to NO₂ had a higher risk of mortality in relation with short-term NO₂ concentrations (ER = 1.92%; 95%CI = [0.28;3.59]) than the less-exposed census block (interaction p-value is borderline significant = 0.09). Further, [Fig 3](#) shows the results of the combined effects of SES and long-term exposure to NO₂, and reveals that the effect modification due to SES (the way SES affects the effect of short-term exposure on mortality) is significantly influenced by long-term NO₂ values (the Chi-Square homogeneity-test which compared the 6 excess risks was borderline significant: p-value = 0.06). When the census blocks in the 1st and 2nd tertiles of long-term NO₂

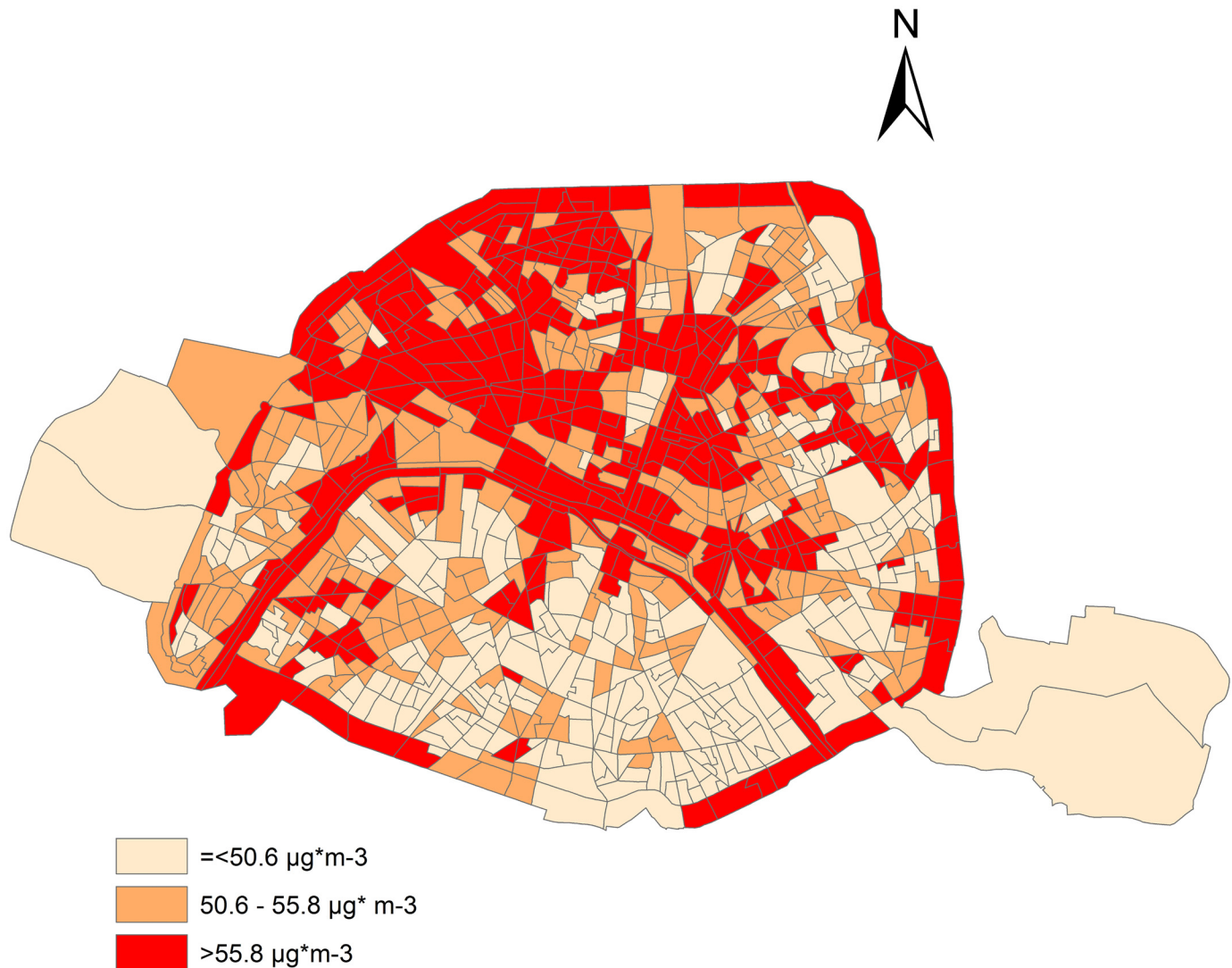


Fig 1. Socioeconomic categories in census block areas in Paris.

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concentrations were grouped (because they had similar excess risks), the combined effect of SES and long-term NO₂ concentrations became clearly significant (interaction $p = 0.02$), suggesting a higher risk of all-cause mortality related to changes in short-term NO₂ concentrations in those census blocks that are both most deprived and have the highest long-term NO₂ values (ER = 4.84%; 95%CI = [1.56; 8.24]).

Discussion

We investigated the association between short-term variations of NO₂ concentrations and all-cause mortality in the city of Paris between 2004 and 2009, with the aim of assessing whether this association was modified by population socioeconomic characteristics and/or long-term concentrations measured at census block level. We found an increase in all-cause mortality with a short-term 10-µg/m³ increase in NO₂ during the 0–5 day lag period. Stronger associations were observed for subjects living in areas having low socioeconomic status. Our results also show an effect modification according to the combination of SES and long-term exposure

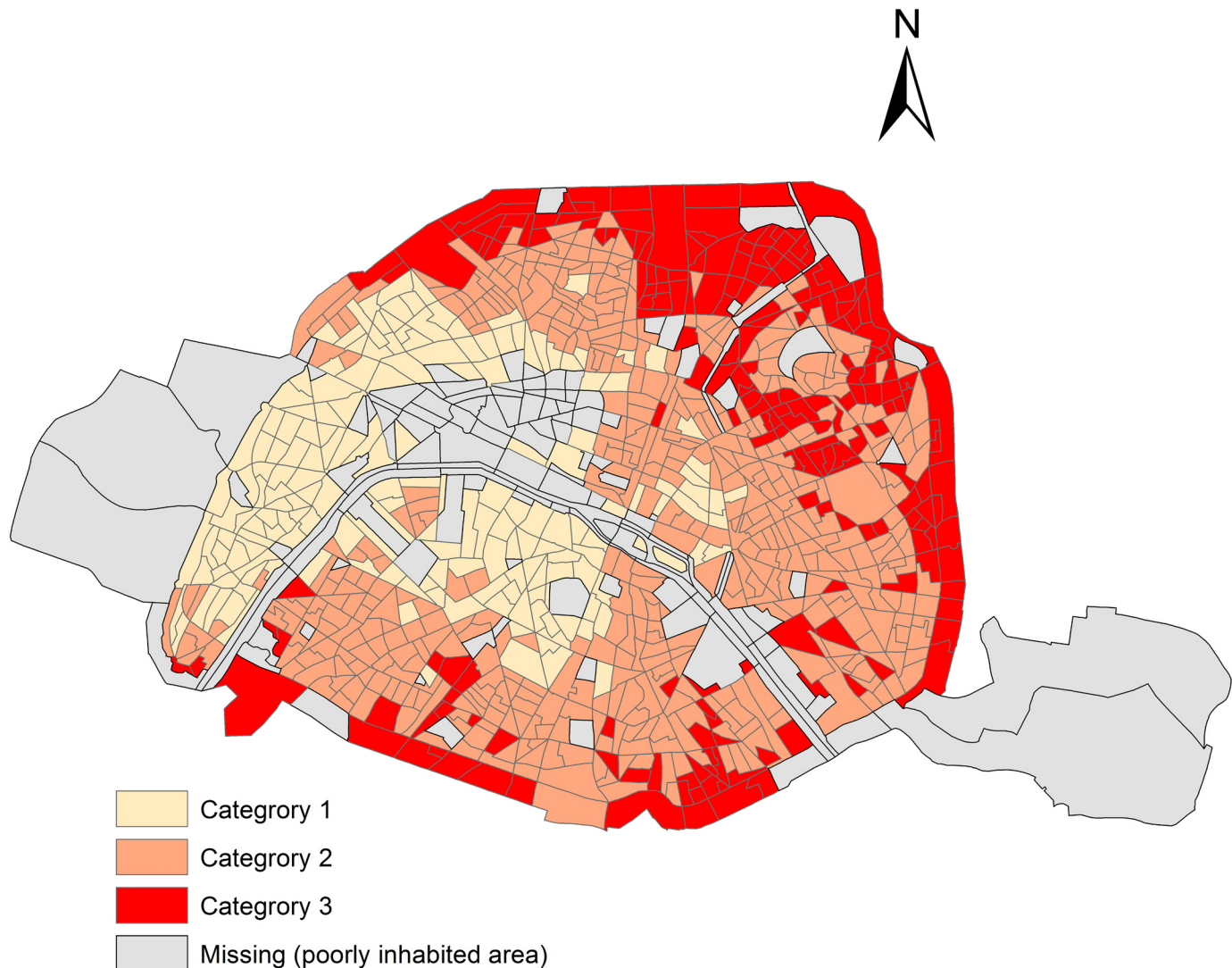


Fig 2. NO₂ concentrations from 2002 to 2009, in census block areas within Paris.

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to NO₂: among the most deprived census blocks, excess risk is 4.84% (95%CI = [1.56;8.24]) when long-term average NO₂ values are above 55.8 $\mu\text{g}/\text{m}^3$ (the top tercile of the distribution) versus 2.56% (95%CI = [0.53;4.64]) when long-term average NO₂ values are lower; corresponding figures in less deprived census blocks are 0.86% (95%CI = [-1.05;2.81]) and 0.12% (95%CI = [-1.02;1.26]).

Regarding the effect of socioeconomic status, our results are consistent with previous findings. Higher risks of all-cause mortality related to short-term exposure to NO₂ or particulate matter (PM) have already been described among adults with poor socioeconomic characteristics such as: less qualified occupational activities [13, 17, 19], poor housing characteristics [19], low educational level [13, 17], and low socioeconomic index [13, 18].

Two main hypotheses may explain the increased health effect of air pollution among people in lower socioeconomic categories. Firstly, poorer subjects may be more exposed to higher levels of air pollutants due to their residential and/or occupational proximity to emitting sources. While this was described in the majority of studies [38, 39], some did report opposite findings

Table 2. Excess risk of all-cause mortality associated with a 10-µg/m³ short-term NO₂ increase, Paris, France, 2004–2009.

Variables	n (%)	Excess risk(%) [†]	95% CI	p value [‡]
Total	79,107 (100)	0.94	0.08, 1.80	0.032
Age (year)				
35–84	49,353 (62)	0.36	-0.72, 1.44	0.51
≥ 85	29,754 (38)	1.86	0.50, 3.24	0.01
Sex				
Female	41,774 (53)	0.22	-0.94, 1.38	0.71
Male	37,333 (47)	1.75	0.51, 3.00	0.01
Census block socioeconomic categories				
Category 1 (most privileged)	16,101 (20)	0.81	-1.01, 2.66	0.38
Category 2	43,582 (55)	0.04	-1.09, 1.18	0.95
Category 3 (most deprived)	19,424 (25)	3.14	1.41, 4.90	0.00
Level of long-term NO₂ exposure				
1 st tertile: ≤ 50.6 µg/m ³	29,894 (38)	0.06	-1.34, 1.47	0.94
2 nd tertile: 50.6–55.8 µg/m ³	25,864 (33)	1.07	-0.30, 2.45	0.13
3 rd tertile: > 55.8 µg/m ³	23,349 (30)	1.92	0.28, 3.59	0.02

[†]: Adjusted for maximum temperature (spline function), mean from lag 0 to 5 relative humidity (inverse function), incidence rate of influenza case counts, and holidays

[‡]: significant p-value in bold (p<5%)

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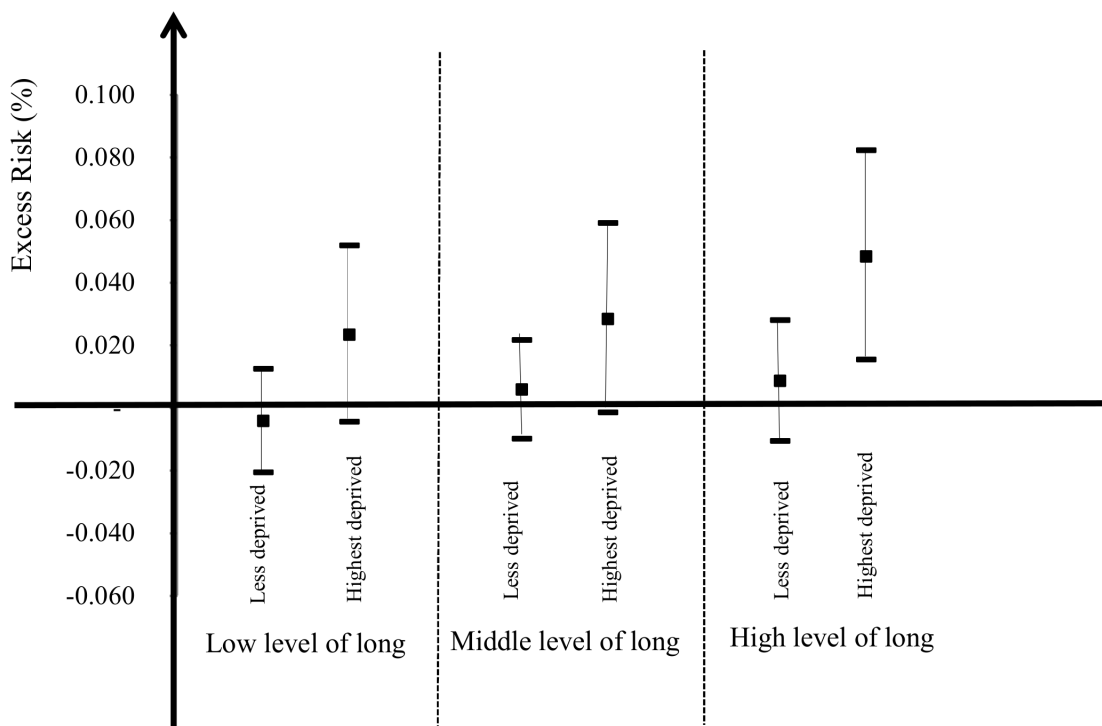


Fig 3. Excess risk of mortality associated with a 10-µg/m³ short-term NO₂ increase and 95% confidence Interval, stratified by SES and long-term NO₂ concentrations- Paris, France, 2004–2009.

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[18, 40]. Within the city of Paris, we did not observe differences in annual mean NO₂ between census blocks by socioeconomic category (Fig 1). Were there any such difference, it would be more in the direction of higher average values in better-off census blocks than in more deprived areas. As we showed elsewhere, such disparities are highly dependent on the historical social and urban make-up of each city [14, 41]. In our study, we assessed exposure to air pollution according to place of residence, which does yield some exposure misclassification. In their daily lives, individuals also encounter several micro-environments (at home, while commuting, at the workplace, etc.) and these do contribute substantially to their total exposure. Thus, exposure differential between socioeconomic categories could still be a reasonable hypothesis to explain our findings; indeed, indoor exposure at home varies across socioeconomic categories, with elevated concentrations of multiple pollutants in lower SES households [42]. Within the P.A.R.I.S. (Pollution and Asthma Risk: an Infant Study) infant cohort [43], a survey of indoor NO₂ concentrations over a period of 7 days was undertaken in 196 homes. Concentrations measured in the homes of parents from low socioeconomic categories were, on average, higher than in homes from high socioeconomic categories (33.1 [13.3] µg/m³ vs. 25.9 [8.4] µg/m³) (C Roda, unpublished data, 2012). Furthermore, total exposure depends not only on ambient or indoor air concentrations, but also on the amount of time spent in these environments. Because they are much more likely to spend weekends and holiday periods away from Paris (e.g. at a second home in the countryside, or travelling), the time-weighted exposure of wealthier families to Parisian ambient air is likely to be lower than for deprived families, who take fewer holidays, less often and for shorter periods [44] as was noted in Rome [18]

Finally, the workplace micro-environment may also differentiate socioeconomic groups, and blue-collar workers and other modest social categories are more likely to be exposed to specific occupational exposures [45].

A second hypothesis invoked to explain the increased health effect of air pollution among lower socioeconomic categories is that groups with lower SES may be more vulnerable to the health effects of certain exposures because they experience poorer health for reasons directly related to their disadvantaged socioeconomic and psychosocial conditions [12]. Such populations, because of their limited economic and educational resources, may accumulate risk factors for chronic diseases. By this process, these populations would present 'a predisposition' to the development of health conditions as a result of any additional environmental insult. Such conditions may also hamper the continuation of occupational activities, a situation that will eventually lead to reduced income and, in turn, possibly to deteriorated health—and greater vulnerability to air pollution.

To our knowledge, no study has looked at whether the effect of short-term changes in air pollution on mortality differs according to the combination of long-term exposure to NO₂ and socioeconomic status. The piecewise-constant proportional hazards model used in the New England study was successful in capturing both acute and chronic effects of PM_{2.5} [46]; however, it did not explore whether short-term effect estimates were influenced by long-term air pollution. An indication of a higher risk of mortality in association with short-term air quality variations in NO₂ was observed, in our study, among the specific group composed of people living in the census blocks that were both most deprived and having higher long-term NO₂ concentrations. A number of authors have shown that changes in air pollution levels increases mortality through a short-term harvesting effect, characterized by the precipitated death of frail subjects [7, 8]. This manifests as an increase in mortality within a few days of a pollution episode, followed by a period of decline in mortality during which the pool of people at highest risk of dying is reconstituted. Long-term exposure to air pollution has been described as a factor in reconstituting the frail subjects' pool [8, 11]. Our results support the hypothesis that the rate at which this pool of at risk subjects is reconstituted may be higher in lower socioeconomic

groups, where strong risk factors for mortality are more prevalent (smoking, pre-existing diseases, poorer access to health care). Moreover, long-term exposure to higher pollution is a cause of frailty through the development of chronic conditions—in particular such cardiovascular conditions as haemostasis alterations, atherosclerosis or hypertension [9, 47]. Further, SES might be associated with cumulative exposure to air pollutants—not only in ambient air but also indoors, both at home and in the workplace, as well as while commuting.

One limitation of our study is that socioeconomic status was assessed ecologically, at census block (rather than individual) level. The French census block is the smallest administrative unit for which socioeconomic and demographic information from the national census is available. The division of neighbourhoods into census blocks by the national statistical institute aims to maximize their homogeneity in terms of population size, socioeconomic characteristics, land use and zoning, thus reducing the risk of ecological bias. According to Krieger et al. [48], the census block is an adequate geographical scale for the assessment of social inequalities.

Our results should not be interpreted in causal terms. Rather, nitrogen dioxide levels are indicators of proximity to emission sources associated with industrial combustion processes, urban heating and petrol or diesel powered traffic [31]. In the city of Paris, and in general in the Ile-de-France region (whose economy shifted, over the last three decades of the 20th century, from industry to services) NO_x emissions are mainly associated with traffic—as clearly illustrated in Fig 1B, where higher annual NO₂ levels match areas of dense traffic. We cannot rule out the possibility that the associations observed could be explained by other air pollutants having the same sources. Several studies have shown a strong correlation between traffic soot/ultrafine particles and NO₂ [33, 38]. For those Paris city monitoring stations having PM₁₀ and PM_{2.5} concentrations available for the 2002–2009 period, we computed the correlation between NO₂ and PM, with no data on ultrafine particles. This correlation ranged from 0.45 to 0.74 for PM₁₀ and between 0.51 and 0.66 PM_{2.5}, by monitoring site.

Our findings suggest a higher risk of short-term all-cause mortality among men than among women. A few studies have looked at gender as a potential effect-modifier for the association between NO₂ or PM and mortality, reaching partially inconsistent conclusions [13, 20, 23, 49]. These results need further investigation, in particular to better understand whether the effect modification by gender could be explained by socially-derived gendered exposures and/or by biological differences (e.g. hormonal status).

Conclusions

In conclusion, the present study provides evidence that socioeconomic status has an effect on the association between short-term exposure to ambient air NO₂ and all-cause mortality in the city of Paris, and interacts with long-term exposures. Because there is not wide variation between NO₂ concentrations across the census blocks in the three socioeconomic categories, differential vulnerability is likely to be the most probable explanation of our finding. Other studies should be conducted to further explore these complex processes.

Supporting Information

S1 Table. Description of socioeconomic categories.
(DOCX)

S2 Table. Model parameters for confounders.
(DOCX)

S3 Table. Knots for spline effect of maximum daily temperature.
(DOCX)

S4 Table. Basics details for spline effect of maximum daily temperature. (DOCX)

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Author Contributions

Conceived and designed the experiments: SD DZN WK C. Padilla TB. Performed the experiments: AL PC SD C. Petit. Analyzed the data: SD C. Petit AD TB. Contributed reagents/materials/analysis tools: SD C. Petit WK C. Padilla DZN. Wrote the paper: SD C. Petit AD DZN TB. Read and approved final manuscript: SD C. Petit AD WK C. Padilla TB AL PC DZN.

References

1. ERS (European Respiratory Society). Air Quality and Health. Available: <http://www.ersnet.org/publications/air-quality-and-health.html>.
2. Chen B, Kan H: Air pollution and population health: a global challenge. *Environ Health Prev Med* 2008, 13(2):94–101. doi: [10.1007/s12199-007-0018-5](https://doi.org/10.1007/s12199-007-0018-5) PMID: [19568887](https://pubmed.ncbi.nlm.nih.gov/19568887/)
3. Ren C, Tong S: Health effects of ambient air pollution—recent research development and contemporary methodological challenges. *Environ Health* 2008, 7:56. doi: [10.1186/1476-069X-7-56](https://doi.org/10.1186/1476-069X-7-56) PMID: [18990231](https://pubmed.ncbi.nlm.nih.gov/18990231/)
4. Samoli E, Aga E, Touloumi G, Nisiotis K, Forsberg B, Lefranc A, et al. Short-term effects of nitrogen dioxide on mortality: an analysis within the APHEA project. *Eur Respir J* 2006, 27(6):1129–38. PMID: [16540496](https://pubmed.ncbi.nlm.nih.gov/16540496/)
5. Kloog Coull BA, Zanobetti A, Koutrakis P, Schwartz JD. Acute and Chronic Effects of Particles on Hospital Admissions in New-England. *PLoS ONE*, 2012, 7(4): e34664. doi: [10.1371/journal.pone.0034664](https://doi.org/10.1371/journal.pone.0034664) PMID: [22529923](https://pubmed.ncbi.nlm.nih.gov/22529923/)
6. Samoli E, Peng R, Ramsay T, Pipikou M, Touloumi G, Dominici F, et al. Acute effects of ambient particulate matter on mortality in Europe and North America: results from the APHENA study. *Environ Health Perspect* 2008, 116(11):1480–6. doi: [10.1289/ehp.11345](https://doi.org/10.1289/ehp.11345) PMID: [19057700](https://pubmed.ncbi.nlm.nih.gov/19057700/)
7. Zanobetti A, Schwartz J, Samoli E, Gryparis A, Touloumi G, Atkinson R, et al. The temporal pattern of mortality responses to air pollution: a multicity assessment of mortality displacement. *Epidemiology* 2002, 13(1):87–93. PMID: [11805591](https://pubmed.ncbi.nlm.nih.gov/11805591/)
8. Schwartz J: Is there harvesting in the association of airborne particles with daily deaths and hospital admissions? *Epidemiology* 2001, 12(1):55–61. PMID: [11138820](https://pubmed.ncbi.nlm.nih.gov/11138820/)
9. Sun Q, Hong X, Wold LE. Cardiovascular Effects of Ambient Particulate Air Pollution Exposure. *Circulation*. 2010; 121:2755–2765 doi: [10.1161/CIRCULATIONAHA.109.893461](https://doi.org/10.1161/CIRCULATIONAHA.109.893461) PMID: [20585020](https://pubmed.ncbi.nlm.nih.gov/20585020/)
10. Zanobetti A, Canner MJ, Stone PH, Schwartz J, Sher D, Eagan-Bengston E, et al. Ambient pollution and blood pressure in cardiac rehabilitation patients. *Circulation*. 2004; 110:2184–2189. PMID: [15466639](https://pubmed.ncbi.nlm.nih.gov/15466639/)
11. Anderson HR, Atkinson RW, Bremner SA, Marston L: Particulate air pollution and hospital admissions for cardiorespiratory diseases: are the elderly at greater risk? *Eur Respir J* 2003, Suppl 40: :39s–46s.
12. Marmot M: Social determinants of health inequalities. *Lancet* 2005, 365(9464):1099–104. PMID: [15781105](https://pubmed.ncbi.nlm.nih.gov/15781105/)
13. Bell ML, Zanobetti A, Dominici F. Evidence on Vulnerability and Susceptibility to Health Risks Associated With Short-Term Exposure to Particulate Matter: A Systematic Review and Meta-Analysis. *Am J Epidemiol*. 2013; 178(6):865–876 doi: [10.1093/aje/kwt090](https://doi.org/10.1093/aje/kwt090) PMID: [23887042](https://pubmed.ncbi.nlm.nih.gov/23887042/)
14. Deguen S, Zmirou-Navier D: Social inequalities resulting from health risks related to ambient air quality—A European review. *Eur J Public Health* 2010, 20(1):27–35. doi: [10.1093/eurpub/ckp220](https://doi.org/10.1093/eurpub/ckp220) PMID: [20081212](https://pubmed.ncbi.nlm.nih.gov/20081212/)
15. Wojtyniak B, Rabczenko D, Stokwizewski J: Does air pollution have respect for socio-economic status of people? [Abstract]. *Epidemiology* 2001, 12:S64.
16. Filleul L, Rondeau V, Cantagrel A, Dartigues JF, Tessier JF: Do subject characteristics modify the effects of particulate air pollution on daily mortality among the elderly? *J Occup Environ Med* 2004, 46(11):1115–22. PMID: [15534498](https://pubmed.ncbi.nlm.nih.gov/15534498/)

17. Jerrett M, Burnett RT, Brook J, Kanaroglou P, Giovis C, Finkelstein N, et al. Do socioeconomic characteristics modify the short term association between air pollution and mortality? Evidence from a zonal time series in Hamilton, Canada. *J Epidemiol Community Health* 2004, 58(1):31–40. PMID: [14684724](#)
18. Forastiere F, Stafoggia M, Tasco C, Picciotto S, Agabiti N, Cesaroni G, et al. Socioeconomic status, particulate air pollution, and daily mortality: differential exposure or differential susceptibility. *Am J Ind Med* 2007, 50(3):208–16. PMID: [16847936](#)
19. Ou CQ, Hedley AJ, Chung RY, Thach TQ, Chau YK, Chan KP, et al. Socioeconomic disparities in air pollution-associated mortality. *Environ Res* 2008, 107(2):237–44. doi: [10.1016/j.envres.2008.02.002](#) PMID: [18396271](#)
20. Bateson TF, Schwartz J: Who is sensitive to the effects of particulate air pollution on mortality? A case-crossover analysis of effect modifiers. *Epidemiology* 2004, 15(2):143–9. PMID: [15127905](#)
21. Zeka A, Zanobetti A, Schwartz J: Individual-level modifiers of the effects of particulate matter on daily mortality. *Am J Epidemiol* 2006, 163(9):849–59. PMID: [16554348](#)
22. Wong CM, Ou CQ, Chan KP, Chau YK, Thach TQ, Yang L, et al. The effects of air pollution on mortality in socially deprived urban areas in Hong Kong, China. *Environ Health Perspect* 2008, 116(9):1189–94. doi: [10.1289/ehp.10850](#) PMID: [18795162](#)
23. Chiusolo M, Cadum E, Stafoggia M, Galassi C, Berti G, Faustini A, et al. Short Term Effects of nitrogen dioxide on mortality and susceptibility factors in ten Italian cities: the EpiAir study. *Environ Health Perspect* 2011, 119:1233–1238. doi: [10.1289/ehp.1002904](#) PMID: [21586369](#)
24. Meslé F, Vallin J: Reconstructing long-term series of causes of death: the case of France. *J Quant Interdiscip Hist* 1996, 29:72–87.
25. Vardoulakis S, Fisher BEA, Pericleous K, Gonzalez-Flesca N: Modelling air quality in street canyons: a review. *Atmospheric Environment* 2003, 37:155–182.
26. Lalloué B, Monnez JM, Padilla C, Kihal W, Le Meur N, Zmirou-Navier Det al. A statistical procedure to create a neighbourhood socioeconomic index for health inequalities analysis. *Int J Equity Health* 2013, 12:21. doi: [10.1186/1475-9276-12-21](#) PMID: [23537275](#)
27. Bateson TF, Schwartz J. Selection bias and confounding in case—crossover analyses of environmental time-series data. *Epidemiology*. 2001; 12(6):654–61. PMID: [11679793](#)
28. Chardon B, Host S, Pedrono G, Gremy I. Contribution of case-crossover design to the analysis of short-term health effects of air pollution: Reanalysis of air pollution and health data. *Rev Epidemiol Sante Publique*. 2008 Feb; 56(1):31–40. doi: [10.1016/j.respe.2007.11.002](#) PMID: [18262376](#)
29. Danet S, Richard F, Montaye M, Beauchant S, Lemaire B, Graux C, et al. Unhealthy effects of atmospheric temperature and pressure on the occurrence of myocardial infarction and coronary deaths. A 10-year survey: the Lille-World Health Organization MONICA project (Monitoring trends and determinants in cardiovascular disease). *Circulation* 1999, 100(1):E1–7. PMID: [10393689](#)
30. Montero JC, Mirón IJ, Criado-Álvarez JJ, Linares C, Díaz J: Influence of local factors in the relationship between mortality and heat waves: Castile-La Mancha (1975–2003). *Sci Total Environ* 2012, 414:73–80 doi: [10.1016/j.scitotenv.2011.10.009](#) PMID: [22154213](#)
31. Hajat S, Armstrong BG, Gouveia N, Wilkinson P. Mortality displacement of heat-related deaths: a comparison of Delhi, São Paulo, and London. *Epidemiology*. 2005 Sep; 16(5):613–20. PMID: [16135936](#)
32. Maclure M: The case-crossover design: a method for studying transient effects on the risk of acute events. *Am J Epidemiol* 1991, 133(2):144–53. PMID: [1985444](#)
33. Janes H, Sheppard L, Lumley T: Case-crossover analyses of air pollution exposure data: referent selection strategies and their implications for bias. *Epidemiology* 2005, 16:717–26. PMID: [16222160](#)
34. Breitner S, Wolf K, Devlin RB, Diaz-Sanchez D, Peters A, Schneider A. Short-term effects of air temperature on mortality and effect modification by air pollution in three cities of Bavaria, Germany: a time-series analysis. *Sci Total Environ*. 2014 Jul 1; 485–486:49–61. doi: [10.1016/j.scitotenv.2014.03.048](#) PMID: [24704956](#)
35. Goldberg MS, Gasparrini A, Armstrong B, Valois MF. The short-term influence of temperature on daily mortality in the temperate climate of Montreal, Canada. *Environ Research*. 2011 Aug; 111(6):853–60.
36. Deschenes O. “Temperature, human health, and adaptation: A review of the empirical literature,” NBER Working Papers 18345, National Bureau of Economic Research, Inc.
37. Lepeule J, Rondeau V, Filleul L, Dartigues JF: Survival analysis to estimate association between short-term mortality and air pollution. *Environ Health Perspect* 2006, 114(2):242–7. PMID: [16451861](#)
38. Brochu PJ, Yanosky JD, Paciorek CJ, Schwartz J, Chen JT, Herrick RF, et al. Particulate air pollution and socioeconomic position in rural and urban areas of the Northeastern United States. *Am J Public Health* 2011, 101(Suppl 1):S224–30. doi: [10.2105/AJPH.2011.300232](#) PMID: [21836114](#)

39. Kruize H, Driessen PP, Glasbergen P, van Egmond KN: Environmental equity and the role of public policy: experiences in the Rijnmond region. *Environ Manage* 2007, 40(4):578–95. PMID: [17879127](#)
40. McLeod H, Langford IH, Jones AP, Stedman JR, Day RJ, Lorenzoni I, et al. The relationship between socio-economic indicators and air pollution in England and Wales: implications for environmental justice. *Reg Environ Change* 2000, 1:18–85.
41. Padilla CM, Kihal W, Vieira VM, Rosselo P, Le Nir G, Zmirou-Navier D, et al. Air quality and social deprivation in four French metropolitan areas— A spatio-temporal environmental inequality analysis conducted at a small geographical level. *Environ. Research*, 2014, 34, 315–324
42. Adamkiewicz G, Zota AR, Fabian MP, Chahine T, Julien R, Spengler JD, et al. Moving environmental justice indoors: understanding structural influences on residential exposure patterns in low-income communities. *Am J Public Health* 2011, 101(Suppl 1):S238–45. doi: [10.2105/AJPH.2011.300119](#) PMID: [21836112](#)
43. Clarisse B, Nikasinovic L, Poinard R, Just J, Momas I: The Paris prospective birth cohort study: which design and who participates? *Eur J Epidemiol* 2007, 22(3):203–210. PMID: [17279453](#)
44. Hoibian S.. Les catégories défavorisées, de plus en plus sur le bord de la route des vacances. Crédoc, Note de synthèse N 4; S3916—Juillet 2012
45. Niedhammer I, Chastang JF, David S, Kelleher C: The contribution of occupational factors to social inequalities in health: findings from the national French SUMER survey. *Soc Sci Med* 2008, 67(11):1870–81. doi: [10.1016/j.socscimed.2008.09.007](#) PMID: [18851892](#)
46. Kloog, Coull BA, Zanobetti A, Koutrakis P, Schwartz JD. Acute and Chronic Effects of Particles on Hospital Admissions in New-England. *PLoS ONE*, 2012, 7(4): e34664. doi: [10.1371/journal.pone.0034664](#)
47. Zanobetti A, Canner MJ, Stone PH, Schwartz J, Sher D, Eagan-Bengston E, et al. Ambient pollution and blood pressure in cardiac rehabilitation patients. *Circulation*. 2004; 110:2184–2189. PMID: [15466639](#)
48. Krieger N, Chen JT, Waterman PD, Soobader MJ, Subramanian SV, Carson R: Choosing area based socioeconomic measures to monitor social inequalities in low birth weight and childhood lead poisoning: The Public Health Disparities Geocoding Project (US). *J Epidemiol Community Health* 2003, 57(3):186–99. PMID: [12594195](#)
49. Zanobetti A, Schwartz J: Race, sex, and social status as modifiers of the effects of PM₁₀ on mortality. *J Occup Environ Med* 2000, 42:469–74. PMID: [10824299](#)