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# Long-term exposure to traffic pollution and hospital admissions in London

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ABSTRACT

Evidence on the effects of long-term exposure to traffic pollution on health is inconsistent. In Greater London we examined associations between traffic pollution and emergency hospital admissions for cardio-respiratory diseases by applying linear and piecewise linear Poisson regression models in a small-area analysis. For both models the results for children and adults were close to unity. In the elderly, linear models found negative associations whereas piecewise models found non-linear associations characterized by positive risks in the lowest and negative risks in the highest exposure category. An increased risk was observed among those living in areas with the highest socioeconomic deprivation. Estimates were not affected by adjustment for traffic noise. The lack of convincing positive linear associations between primary traffic pollution and hospital admissions agrees with a number of other reports, but may reflect residual confounding. The relatively greater vulnerability of the most deprived populations has important implications for public health.



## 1. Introduction

A large body of evidence from daily time-series studies has found short-term associations between a range of ambient air pollutants, including those of primary traffic origin, and emergency hospital admissions for cardiovascular and respiratory conditions (WHO, 2013). Evidence for associations with long-term exposure to traffic pollutants, in contrast, is rather mixed (HEI, 2010; WHO, 2013). A systematic review on studies published between 1950 and 2007 found none reporting positive associations between chronic exposure to nitrogen dioxide ($NO_2$) or nitrogen oxides ($NO_x$) and cardiovascular or respiratory morbidity and concluded that, due to the small number of studies, evidence on these pollutants was insufficient to make solid conclusions (Chen et al., 2008). In 2010, a report on traffic-related air pollution and health also concluded that the epidemiologic evidence relating to the associations between long-term exposure to primary traffic exposures, for example nitrogen oxides, and health was largely inconclusive (HEI, 2010).

To address this question studies of traffic-related pollution within cities are needed. Population-wide small-area studies which use routinely collected register data have the relative advantage over most cohort studies of individuals of having a larger sample size and greater representativeness, although they are likely to be more vulnerable to residual confounding from unmeasured area and individual-level factors. Previous ecological studies of environmental exposures in London, however, have successfully used small-area methods (Halonen et al., 2015a, 2015b; Hansell et al., 2013).

Therefore, as part of a research programme into the health effects of traffic pollution in London (TRAFFIC study (King's College London, 2014)), we conducted a within-city small-area study of the associations between long-term exposure to primary traffic pollution and hospital admissions for cardiovascular and respiratory diseases for the whole of London between 2003 and 2010. We hypothesized that long-term average pollution contributes to

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exacerbations of existing health conditions resulting in additional hospital admissions observable at the small-area. We used a dispersion model to estimate at a fine spatial scale long-term exposure to six primary traffic pollutants including metrics for exhaust and non-exhaust related primary particles that have rarely been used in previous studies. In addition to the commonly used linear models we used piecewise linear models that relax the assumption of linearity across the whole exposure range.

## 2. Methods

### 2.1. Study area

Our study area comprised all postcode areas within the M25 motorway with over nine million inhabitants. Each postcode is nested within a Census Output Area (COA) that was the spatial unit of analysis (n = 27,731). Mean population of COAs is 300 (>40 households) (Office for National Statistics, 2014). We included 27,686 COAs with complete information for the exposures, health outcomes, and possible area-level confounders.

### 2.2. Health outcomes

We selected the first emergency hospital episode in each of the years 2003–2010 recorded in the Hospital Episode Statistics provided by the Health and Social Care Information Centre (HSCIC). We used emergency rather than all (including elective) admissions to better capture exacerbations of disease as opposed to planned visits due to existing diseases. The outcome groups were (ICD-10): all cardiovascular diseases (I00-I99), coronary heart disease (I20-I25), heart failure (I50), stroke (I61, I63, I64), all respiratory diseases (J00-J99), obstructive respiratory diseases (J12-J18 and J20-J22) and infections of the lower respiratory tract (J40-J46). Cardiovascular outcomes were analysed in two age groups: 45–74 and ≥ 75 years old, and respiratory outcomes in three age groups: 0–14, 15–64, and ≥65 years old. We used the sum of admissions across 2003–2010 within each COA. Of all HES admission records in England from 2003 to 2010, 4.2% did not have a valid postcode and were excluded. Annual mid-year population estimates at COA-level by sex and 5-year age band from the Office for National Statistics (ONS) were used to calculate admission rates. The study uses SAHSU data, supplied from ONS; data use was covered by approvals from the National Research Ethics Service - reference 12/LO/0566 and 12/LO/0567 - and by Health Research Authority Confidentially Advisory Group (HRA-CAG) for Section 251 support (HRA - 14/CAG/1039); superseding National Information Governance Board and Ethics and Confidentiality Committee approval (NIGB - ECC 2-06(a)/2009).

### 2.3. Exposures

We used the KCL urban dispersion model (Beevers et al., 2013; Kelly et al., 2011) to estimate average annual concentrations (2003–2010), as follows: 1) six primary traffic pollutants: nitrogen oxides ($NO_x$), nitrogen dioxide ($NO_2$), as well as exhaust (tailpipe emissions) and non-exhaust (brake and tyre wear and re-suspension) related primary $PM_{2.5}$ and $PM_{10}$ (aerodynamic diameter <2.5 and < 10 μm, respectively); and 2) five pollutants reflecting the contribution of regional/urban background pollution: $PM_{2.5}$, $PM_{10}$ and ozone ($O_3$) from which we calculated coarse fraction of $PM_{10}$ ($PM_{10-2.5}$) and oxidative gases ($O_x$, i.e. $NO_2+O_3$) (Williams et al., 2014) The modelling was based on Atmospheric Dispersion Modelling System (ADMS) v.4 and road source model v.2.3, which incorporates hourly meteorological measurements, empirically derived $NO–NO_2–O_3$ and PM relationships, and information on source emissions from the London Atmospheric Emissions Inventory (LAEI) (Greater London Authority, 2008). For NOx and $NO_2$, modelled data have been evaluated against measurement data from monitoring sites with an annual data capture of >75%. Minimum number of sites was 62 in 2003, and maximum number was 100 in 2008. The model performed well when validated against measurements: a comparison of observed vs. modelled concentrations provided high spearman correlation coefficients (r): for NOx r varied between 0.79 and 0.92, and for $NO_2$ between 0.85 and 0.93. More detailed information about the modelling procedure and model validation can be found elsewhere (Beevers and Dajnak, 2015). Spatial resolution of the model was 20 × 20 m; estimates for each postcode address centroid were based on interpolation between model grid points. COA-level exposure was calculated as the mean of: 1) annual mean concentrations at all postcode address centroids within a COA, and 2) overall study years.

### 2.4. Statistical analyses

Adjacent small areas tend to be more alike than those further apart. To model these spatial dependencies we used ecological Poisson regression specified in a Bayesian framework that was implemented through the Integrated Nested Laplace Approximation (INLA) approach (Rue et al., 2009) using R 3.1.0 package R-INLA (www.r-inla.org) (Martino and Rue, 2010; R Core Team, 2014). We included age and sex standardised expected numbers of admissions as offsets in the models and accounted for (i) spatial residuals through a conditional autoregressive structure which assumes dependencies between neighbouring areas, and (ii) spatially unstructured variability through an area specific random effect. Minimally informative priors were specified on all the parameters in the model: Gaussian distributions centred on zero and characterised by a precision (1/variance) equal to 0.00001 for the regression coefficients; Gaussian distributions on the two random effects, both centred on zero and characterised by a lognormal (0.5, 0.00005) on the logarithm of the precision.

First we used linear Poisson regression models to determine associations between pollutants and cause-specific hospital admissions. Linear models are most commonly used and thus results can be more reliably compared with prior findings. However, the associations between air pollutants and health outcomes are not necessarily linear. To overcome this issue, categorical variables based on percentiles of the exposure are often used that do not account for changes in the estimates of epidemiological risk (RR/OR) within each category. As a compromise between the two approaches we used piecewise linear models that relax the assumption of linearity of any association across the whole range of exposures. These models use pre-defined exposure categories (here characterised by approximately equal exposure range in each) and assume a (potentially different) linear effect within each category. Models were adjusted for COA-level confounders: quintiles of socioeconomic deprivation; tertiles of proportion of COA population of black and South Asian ethnicities; proxy for smoking (annual smoothed age and sex standardised relative risk of lung cancer mortality (ICD-10: C33-C34)) (Hansell et al., 2013); and daytime road traffic noise ($L_{Aeq,\ 16\ h}$). The Carstairs index (Morgan and Baker, 2006) was used as small-area level composite measure of socioeconomic deprivation. Deprivation and ethnicity data were derived from the UK Census 2011, provided by the ONS, and cancer data are derived from national cancer registries and were supplied by the ONS. Annual daytime (from 7:00 to 22:59) road traffic noise levels were modelled at geometric centroids of ~190,000 postcode locations in London using the TRAffic Noise EXposure (TRANEX) (Gulliver et al., 2015) model with 0.1 dB(A)

**Table 1**
Distribution of hospital admissions for cardiovascular and respiratory diseases across 27,686 Census Output Areas, London, 2003–2010.

| Outcome | Mean | SD[a] | Minimum | P25[b] | Median | P75[c] | Maximum | Total n |
|---|---|---|---|---|---|---|---|---|
| **Cardiovascular** | | | | | | | | |
| All 45-74 | 6.8 | 4.3 | 0 | 4 | 6 | 9 | 69 | 187,395 |
| All ≥75 | 6.5 | 6.3 | 0 | 2 | 5 | 9 | 135 | 179,099 |
| IHD[d] 45-74 | 2.8 | 2.4 | 0 | 1 | 2 | 4 | 30 | 77,019 |
| IHD ≥75 | 1.8 | 2.1 | 0 | 0 | 1 | 3 | 32 | 48,522 |
| Heart failure 45-74 | 0.6 | 1.0 | 0 | 0 | 0 | 1 | 10 | 16,786 |
| Heart failure ≥75 | 1.3 | 1.7 | 0 | 0 | 1 | 2 | 49 | 34,951 |
| Stroke 45-74 | 0.9 | 1.1 | 0 | 0 | 1 | 1 | 12 | 24,458 |
| Stroke ≥75 | 1.3 | 1.8 | 0 | 0 | 1 | 2 | 30 | 35,697 |
| **Respiratory** | | | | | | | | |
| All 0-14 | 4.1 | 3.5 | 0 | 2 | 3 | 6 | 48 | 113,163 |
| All 15-64 | 5.4 | 3.9 | 0 | 3 | 5 | 7 | 113 | 149,308 |
| All ≥65 | 7.2 | 8.6 | 0 | 3 | 5 | 9 | 179 | 198,899 |
| Infections 0-14 | 1.7 | 1.8 | 0 | 0 | 1 | 2 | 20 | 46,217 |
| Infections 15-64 | 2.0 | 2.0 | 0 | 1 | 2 | 3 | 73 | 56,595 |
| Infections ≥65 | 4.2 | 6.3 | 0 | 1 | 3 | 5 | 126 | 116,292 |
| Obstructive 0-14 | 0.9 | 1.3 | 0 | 0 | 0 | 1 | 19 | 25,108 |
| Obstructive 15-64 | 1.8 | 2.1 | 0 | 0 | 1 | 3 | 22 | 50,253 |
| Obstructive ≥65 | 2.4 | 3.0 | 0 | 0 | 1 | 3 | 32 | 66,979 |

[a] Standard deviation.
[b] 25th percentile.
[c] 75th percentile.
[d] Ischaemic heart disease.

**Table 2**
Distribution of average air pollution concentrations and potential confounding variables across 27,686 Census Output Areas, London, 2003–2010.

| Variable | Mean | SD[a] | Minimum | P25[b] | Median | P75[c] | Maximum | IQR[d] |
|---|---|---|---|---|---|---|---|---|
| **Primary traffic pollutant** ($\mu g/m^3$) | | | | | | | | |
| $NO_x$ | 66.2 | 16.2 | 34.8 | 54.4 | 64.0 | 75.7 | 178.9 | 21.3 |
| $NO_2$ | 39.0 | 6.50 | 25.4 | 34.3 | 38.4 | 43.0 | 73.4 | 8.7 |
| Exhaust related primary $PM_{2.5}$ | 0.72 | 0.28 | 0.28 | 0.52 | 0.66 | 0.85 | 3.33 | 0.33 |
| Non-exhaust related primary $PM_{2.5}$ | 0.73 | 0.24 | 0.27 | 0.55 | 0.70 | 0.86 | 3.17 | 0.31 |
| Exhaust related primary $PM_{10}$ | 0.80 | 0.32 | 0.30 | 0.58 | 0.74 | 0.95 | 3.74 | 0.37 |
| Non-exhaust related primary $PM_{10}$ | 2.46 | 0.80 | 0.98 | 1.88 | 2.37 | 2.91 | 10.5 | 1.03 |
| **Regional/urban background pollutant** ($\mu g/m^3$) | | | | | | | | |
| $PM_{2.5}$ | 15.3 | 0.86 | 13.7 | 14.7 | 15.2 | 15.8 | 20.0 | 1.1 |
| $PM_{10}$ | 24.0 | 1.50 | 21.3 | 22.9 | 23.8 | 24.9 | 36.5 | 2.0 |
| $PM_{10\text{-}2.5}$ | 8.7 | 0.71 | 0.00 | 8.25 | 8.66 | 9.11 | 19.8 | 0.86 |
| $O_3$ | 38.7 | 3.80 | 24.6 | 36.0 | 38.8 | 41.4 | 48.3 | 5.4 |
| $O_x$ ($NO_2$+$O_3$) | 77.7 | 2.78 | 73.4 | 75.7 | 77.1 | 79.1 | 98.7 | 3.4 |
| **Area-level covariates** | | | | | | | | |
| Noise, $L_{Aeq,16hr}$ (dB) | 58.5 | 3.58 | 54.8 | 55.4 | 57.4 | 60.6 | 78.2 | 5.2 |
| Deprivation score | 0.00 | 3.18 | −5.99 | −2.62 | −0.45 | 2.22 | 13.7 | 4.5 |
| Black ethnicity (%) | 12.0 | 12.2 | 0.00 | 2.86 | 7.69 | 17.6 | 73.2 | 14.7 |
| South Asian ethnicity (%) | 10.2 | 13.2 | 0.00 | 2.41 | 5.26 | 11.7 | 90.8 | 9.3 |
| Smoking[e] | 1.00 | 0.28 | 0.29 | 0.79 | 0.96 | 1.16 | 3.15 | 0.40 |

[a] Standard deviation.
[b] 25th percentile.
[c] 75th percentile.
[d] Interquartile range.
[e] Smoothed age and sex standardised relative risk for lung cancer mortality.

noise level resolution. For the analyses mean noise levels were aggregated to COA-level.

We tested interactions between continuous exposure and quintiles of socioeconomic deprivation, and ran sensitivity analyses: 1) adjusting models for an "inner-outer London" dummy (13 inner and 20 outer London boroughs) (London Councils, 2014); 2) using different prior distributions in the models; and 3) using 95th percentiles (instead of means) of the air pollution concentrations within the COAs. Because the correlations between pollutants were high (Supplemental Table 1) we confined these sensitivity analyses to associations between $NO_x$ and all cardiovascular and all respiratory admissions. All results are presented as relative risks (RR) with 95% credible intervals (CI) per "half a range increase" that is based on each pollutant's exposure categories used for the piecewise models, for example, per 7.5 $\mu g/m^3$ for $NO_x$.

## 3. Results

### 3.1. Descriptive statistics

Total numbers and distributions of all outcomes by age groups across COAs are shown in Table 1. Table 2 presents the distributions of average air pollutant concentrations across the COAs. Area-level variation was larger for the primary traffic pollutants (coefficient of variation range 0.17–0.40) compared to the regional/urban background pollutants (coefficient of variation range 0.04–0.10). In Fig. 1 spatial distribution of modelled NOx levels over the study area is shown. Correlations between pollutant concentrations were high; for $NO_x$ in relation to PM concentrations Spearman r ranged from 0.94 to 0.98, and for $O_3$ the range was from −0.92 to −0.99 (Supplemental Table 1). Correlations between pollutants and

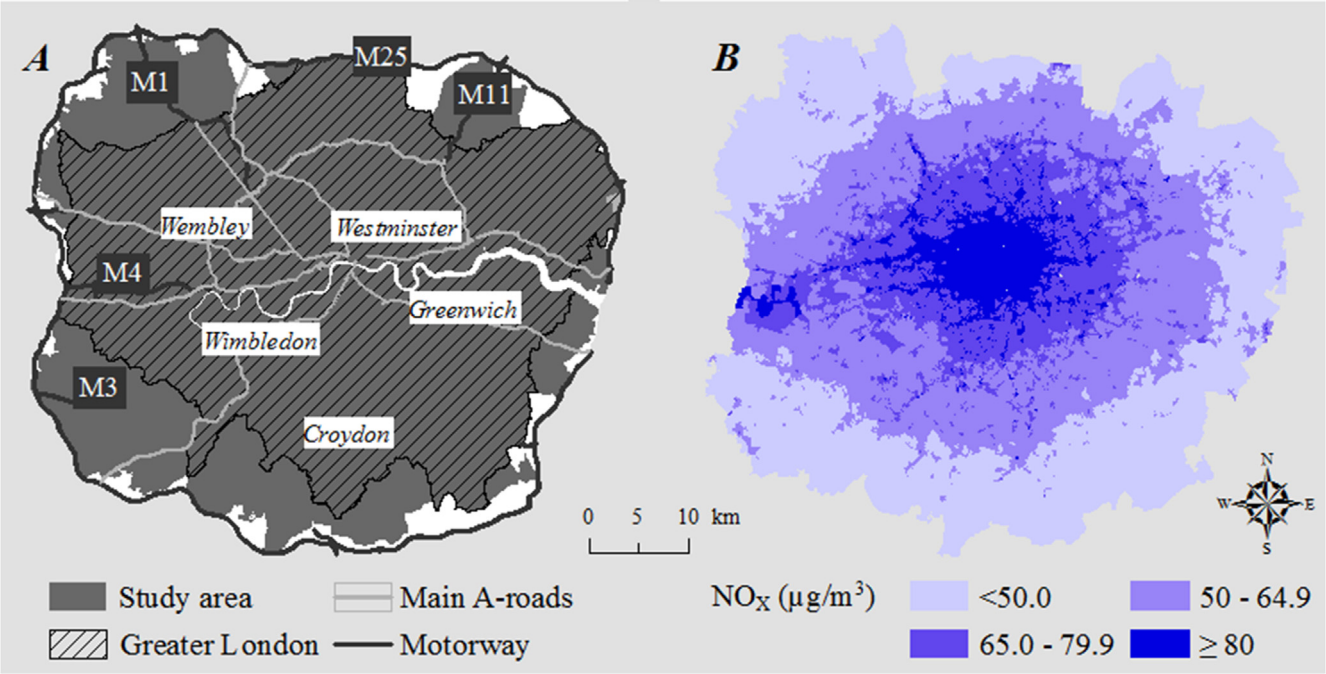


**Fig. 1.** Map of A) the study area and B) distribution of nitrogen oxide (NOx) concentrations.

**Table 3**
Adjusted[a] relative risks (RR, 95% credible intervals, CI) for all cardiovascular admissions in association with traffic and regional/urban background pollutants.

| Pollutant | | All cardiovascular admissions | | | | | |
|---|---|---|---|---|---|---|---|
| | | 45-74 yr (n = 187,395) | | | ≥75 yr (n = 179,099) | | |
| Primary traffic | Increment µg/m$^3$ | RR | 95% CI | | RR | 95% CI | |
| $NO_x$ | 7.5 | 1.00 | 0.99 | 1.01 | 0.99 | 0.98 | 1.00 |
| $NO_2$ | 4.0 | 1.00 | 0.99 | 1.02 | 0.98 | 0.97 | 1.00 |
| Exhaust related primary $PM_{2.5}$ | 0.15 | 1.00 | 0.99 | 1.01 | 0.98 | 0.97 | 0.99 |
| Non-exhaust related primary $PM_{2.5}$ | 0.10 | 1.00 | 0.99 | 1.01 | 1.00 | 0.99 | 1.00 |
| Exhaust related primary $PM_{10}$ | 0.15 | 1.00 | 0.99 | 1.01 | 0.99 | 0.98 | 1.00 |
| Non-exhaust related primary $PM_{10}$ | 0.50 | 1.00 | 0.99 | 1.01 | 0.99 | 0.98 | 1.00 |
| **Regional/urban background** | | | | | | | |
| $PM_{2.5}$ | 0.60 | 1.00 | 0.98 | 1.02 | 0.98 | 0.96 | 1.00 |
| $PM_{10}$ | 1.0 | 1.00 | 0.99 | 1.01 | 0.99 | 0.97 | 1.00 |
| $PM_{10-2.5}$ | 0.35 | 1.00 | 0.99 | 1.01 | 0.99 | 0.98 | 1.00 |
| $O_3$ | 2.5 | 0.99 | 0.98 | 1.01 | 1.02 | 1.00 | 1.04 |
| $O_x$ | 1.5 | 1.00 | 0.99 | 1.01 | 0.99 | 0.98 | 1.00 |

[a] Models adjusted for age, sex, area-level socioeconomic deprivation, ethnicity, smoking, and daytime road traffic noise.

deprivation index varied by exposure category; correlations between NOx and deprivation by increasing NOx exposure category were: 0.12 (when NOx <50 µg/m$^3$), 0.31 (50–64.9 µg/m$^3$), 0.10 (65–79.9 µg/m$^3$), and −0.06 (≥80 µg/m$^3$).

### 3.2. Results from linear models

Linear associations between pollutants and all cardiovascular hospital admissions were close to unity among adults (45–74 years) and the elderly (≥75 years) (Table 3). Effect estimates for all respiratory admissions among children (≤14 years) and adults (15–64 years) were close to one (Table 4). Among the elderly (≥65 years), nearly all effect estimates for all respiratory admissions were slightly below one.

### 3.3. Results from piecewise models for cardiovascular outcomes

Partially and fully adjusted relative risks for all cardiovascular admissions and NOx from the piecewise analyses are presented in Table 5. Estimates adjusted only for age and sex indicated a clear pattern of higher relative risks at low exposures compared to high exposures. Increasing adjustment for confounders partially attenuated this pattern among adults (45–74 years), but less so among the elderly (≥75 years). Adjustment for smoking, ethnicity, and road noise accounted for the majority of the attenuation in the effect estimates at the lowest exposure range whereas effect estimates at the highest exposure range remained unchanged. Additional adjustment for area-level deprivation had a minor effect. Results from the fully adjusted piecewise analyses for the other primary traffic and all regional/background pollutants are in Supplemental Table 2. Similar to the results for NOx, there was no evidence of an association between any of the pollutants and cardiovascular admissions among adults. Among the elderly, results were similar to NOx with positive associations, i.e. increased risks, in the lowest exposure categories and negative associations, i.e. “protective effects”, in the highest exposure categories.

In association with $NO_x$, the fully adjusted results from

**Table 4**
Adjusted[a] relative risks (RR, 95% credible intervals, CI) for all respiratory admissions in association with traffic and regional/urban background pollutants.

| Pollutant | | All respiratory admissions | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 0–14 yr (n = 113,163) | | | 15–64 yr (n = 149, 308) | | | ≥65 yr (n = 198, 899) | | |
| Primary traffic | Increment μg/m$^3$ | RR | 95% CI | | RR | 95% CI | | RR | 9% CI | |
| $NO_x$ | 7.5 | 1.01 | 1.00 | 1.02 | 1.00 | 0.99 | 1.01 | 0.99 | 0.97 | 1.00 |
| $NO_2$ | 4.0 | 1.01 | 0.99 | 1.03 | 0.99 | 0.98 | 1.01 | 0.98 | 0.96 | 1.00 |
| Exhaust related primary $PM_{2.5}$ | 0.15 | 1.01 | 0.99 | 1.02 | 1.00 | 0.99 | 1.01 | 0.98 | 0.97 | 0.99 |
| Non-exhaust related primary $PM_{2.5}$ | 0.10 | 1.00 | 0.99 | 1.01 | 1.00 | 0.99 | 1.01 | 0.99 | 0.98 | 1.00 |
| Exhaust related primary $PM_{10}$ | 0.15 | 1.00 | 0.99 | 1.02 | 1.00 | 0.99 | 1.01 | 0.98 | 0.97 | 0.99 |
| Non-exhaust related primary $PM_{10}$ | 0.50 | 1.00 | 0.99 | 1.02 | 1.00 | 0.98 | 1.01 | 0.99 | 0.97 | 1.00 |
| **Regional/urban background** | | | | | | | | | | |
| $PM_{2.5}$ | 0.60 | 1.01 | 0.99 | 1.04 | 0.99 | 0.97 | 1.01 | 0.98 | 0.96 | 1.00 |
| $PM_{10}$ | 1.0 | 1.01 | 0.99 | 1.03 | 0.99 | 0.98 | 1.01 | 0.98 | 0.96 | 1.00 |
| $PM_{10\text{-}2.5}$ | 0.35 | 1.00 | 0.99 | 1.01 | 1.00 | 0.99 | 1.01 | 0.99 | 0.98 | 1.00 |
| $O_3$ | 2.5 | 0.99 | 0.97 | 1.02 | 1.01 | 0.99 | 1.03 | 1.02 | 1.00 | 1.05 |
| $O_x$ | 1.5 | 1.01 | 0.99 | 1.02 | 1.00 | 0.99 | 1.01 | 0.99 | 0.97 | 1.00 |

[a] Models adjusted for age, sex, area-level socioeconomic deprivation, ethnicity, smoking, and daytime road traffic noise.

**Table 5**
Partially and fully adjusted relative risks for all cardiovascular hospital admissions in association with 7.5 μg/m$^3$ increase in nitrogen oxide.

| $NO_x$ | n COAs | All cardiovascular admissions | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Mean n of admissions | 45-74 yr (n = 187,395) | | | Mean n of admissions | ≥75 yr (n = 179,099) | | |
| Increment 7.5 μg/m$^3$ | | | RR | 95% CI | | | RR | 95% CI | |
| **Partially adjusted 1**[a] | | | | | | | | | |
| <50.0 | 4991 | 7 | 1.07 | 1.01 | 1.12 | 9 | 1.04 | 0.99 | 1.08 |
| 50–64.9 | 13,062 | 7 | 1.06 | 1.04 | 1.09 | 7 | 1.03 | 1.00 | 1.05 |
| 65–79.9 | 2316 | 6 | 1.03 | 1.01 | 1.05 | 5 | 1.00 | 0.98 | 1.02 |
| ≥80.0 | 8115 | 6 | 1.02 | 1.01 | 1.03 | 4 | 0.98 | 0.96 | 1.00 |
| **Partially adjusted 2**[b] | | | | | | | | | |
| <50.0 | 4991 | 7 | 1.03 | 0.99 | 1.09 | 9 | 1.03 | 0.98 | 1.07 |
| 50–64.9 | 13,062 | 7 | 1.03 | 1.01 | 1.06 | 7 | 1.02 | 0.99 | 1.04 |
| 65–79.9 | 2316 | 6 | 1.02 | 1.00 | 1.04 | 5 | 1.00 | 0.98 | 1.02 |
| ≥80.0 | 8115 | 6 | 1.02 | 1.01 | 1.03 | 4 | 0.98 | 0.97 | 0.99 |
| **Fully adjusted**[c] | | | | | | | | | |
| <50.0 | 4991 | 7 | 1.03 | 0.98 | 1.07 | 9 | 1.03 | 0.98 | 1.07 |
| 50–64.9 | 13,062 | 7 | 0.99 | 0.97 | 1.01 | 7 | 1.00 | 0.98 | 1.03 |
| 65–79.9 | 2316 | 6 | 0.99 | 0.97 | 1.01 | 5 | 0.99 | 0.97 | 1.01 |
| ≥80.0 | 8115 | 6 | 1.01 | 1.00 | 1.02 | 4 | 0.98 | 0.96 | 1.00 |

[a] Models adjusted for age and sex.
[b] Models adjusted for age and sex, ethnicity, smoking and daytime road traffic noise.
[c] Models adjusted for age and sex, ethnicity, smoking and daytime road traffic noise and area-level socioeconomic deprivation.

piecewise models for heart failure and stroke were similar to those for all cardiovascular diseases, but associations for ischaemic heart disease were close to unity (Supplemental Table 3).

### 3.4. Results from piecewise models for respiratory outcomes

Partially and fully adjusted results for NOx in association with all respiratory admissions from the piecewise analyses are in Table 6. Confounder adjustment had relatively little impact on the estimates among children. In adults and the elderly, the additional confounder adjustment particularly for smoking, ethnicity, and road noise had clear impact on the effect estimates at the low compared to high exposure range.

Fully adjusted results for the other primary traffic and all regional/background pollutants with respiratory admissions from piecewise linear models were similar to those for NOx (Supplemental Table 4). Associations between $NO_x$ and obstructive diseases were similar to those for all respiratory diseases in all age groups (Supplemental Table 5). Associations between $NO_x$ and lower respiratory tract infections among the elderly shared the same non-linear pattern as all respiratory admissions, but we observed no associations in children or adults (Supplemental Table 5).

### 3.5. Effect modification and sensitivity analyses

Interactions between $NO_x$ and deprivation in the lowest vs. highest quintile had posterior probabilities (of having an increased risk of hospital admissions with increasing exposure) > 0.95 suggesting effect modification by deprivation. For all cardiovascular admissions the relative risks among adults increased slightly with increasing deprivation; relative risk in the area of lowest deprivation was 0.99 (95% CI 0.97–1.00 per 7.5 μg/m$^3$ increase in $NO_x$) and 1.01 (95% CI 1.00-1.03) in the area of highest deprivation. While differences are small, the finding supports effect modification as the credibility intervals did not overlap. Smaller differences across deprivation quintiles were observed for the elderly (Fig. 2). In associations between $NO_x$ and all respiratory admissions in children, we also observed this increasing trend by deprivation (Fig. 3). In areas of lowest deprivation relative risk was 0.98 (95% CI 0.96-1.00 per 7.5 μg/m$^3$ increase in $NO_x$) but in areas of highest deprivation the corresponding RR was 1.02 (95% CI 1.01-1.04), which also supports effect modification as the credibility intervals did not overlap. Sensitivity analyses adjusting for the inner-outer London borough, using different priors, or using the 95th percentile of the exposure range had a minor effect on the results (Supplemental Tables 6 and 7).

**Table 6**
Partial and fully adjusted relative risks for all respiratory disease hospital admissions in association with 7.5 μg/m$^3$ increase in nitrogen oxide.

| $NO_x$ | n COAs | All respiratory admissions | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Mean n of admissions | 0-14 yr (n = 113,163) | | | Mean n of admissions | 15-64 yr (n = 149,308) | | | Mean n of admissions | ≥65 yr (n = 198,899) | | |
| Increment 7.5 μg/m$^3$ | | | RR | 95% CI | | | RR | 95% CI | | | RR | 95% CI | |
| **Partially adjusted 1**[a] | | | | | | | | | | | | | |
| <50.0 | 4193 | 4 | 1.04 | 0.98 | 1.10 | 5 | 1.12 | 1.05 | 1.20 | 8 | 1.13 | 1.06 | 1.20 |
| 50–64.9 | 10,374 | 4 | 1.02 | 0.99 | 1.05 | 5 | 1.06 | 1.03 | 1.10 | 8 | 1.08 | 1.05 | 1.11 |
| 65–79.9 | 8035 | 4 | 1.01 | 0.99 | 1.03 | 6 | 1.04 | 1.01 | 1.06 | 7 | 1.01 | 0.99 | 1.03 |
| ≥80.0 | 5084 | 4 | 1.01 | 1.00 | 1.02 | 6 | 1.00 | 0.99 | 1.02 | 6 | 0.99 | 0.97 | 1.00 |
| **Partially adjusted 2**[b] | | | | | | | | | | | | | |
| <0.50 | 4193 | 4 | 1.02 | 0.96 | 1.08 | 5 | 1.06 | 1.00 | 1.13 | 8 | 1.09 | 1.03 | 1.15 |
| 0.5–0.79 | 10,374 | 4 | 1.01 | 0.98 | 1.05 | 5 | 1.04 | 1.00 | 1.07 | 8 | 1.05 | 1.02 | 1.08 |
| 0.8–1.09 | 8035 | 4 | 1.01 | 0.99 | 1.04 | 6 | 1.04 | 1.01 | 1.06 | 7 | 1.00 | 0.97 | 1.03 |
| ≥1.1 | 5084 | 4 | 1.02 | 1.00 | 1.03 | 6 | 1.01 | 1.00 | 1.03 | 6 | 0.99 | 0.98 | 1.01 |
| **Fully adjusted**[c] | | | | | | | | | | | | | |
| <0.50 | 4193 | 4 | 1.02 | 0.96 | 1.08 | 5 | 1.04 | 0.99 | 1.10 | 8 | 1.08 | 1.02 | 1.14 |
| 0.5–0.79 | 10,374 | 4 | 1.00 | 0.97 | 1.03 | 5 | 0.98 | 0.95 | 1.00 | 8 | 1.01 | 0.98 | 1.04 |
| 0.8–1.09 | 8035 | 4 | 1.00 | 0.98 | 1.03 | 6 | 1.00 | 0.98 | 1.02 | 7 | 0.98 | 0.95 | 1.00 |
| ≥1.1 | 5084 | 4 | 1.01 | 1.00 | 1.03 | 6 | 1.00 | 0.99 | 1.01 | 6 | 0.98 | 0.97 | 0.99 |

[a] Models adjusted for age and sex,
[b] Models adjusted for age and sex, ethnicity, smoking and daytime road traffic noise
[c] Models adjusted for age and sex, ethnicity, smoking and daytime road traffic noise and area-level socioeconomic deprivation

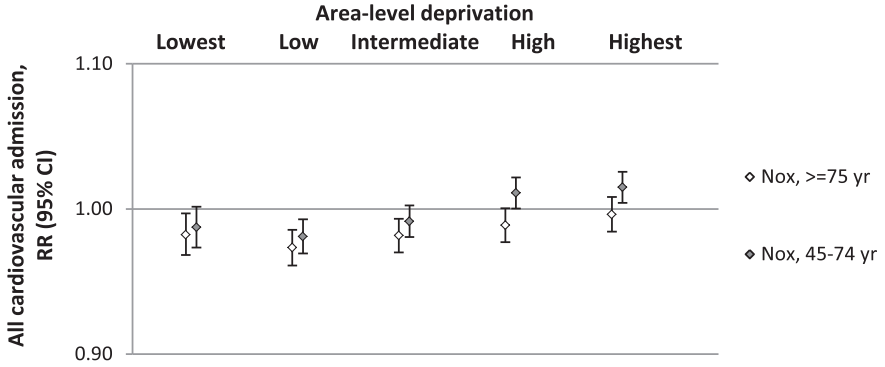


**Fig. 2.** Adjusted[a] associations between an interquartile range increase in nitrogen oxides ($NO_x$) concentration and all cardiovascular hospital admissions among adults and the elderly by quintiles of area-level deprivation. [a]Models adjusted for age, sex, ethnicity, smoking and daytime road traffic noise.

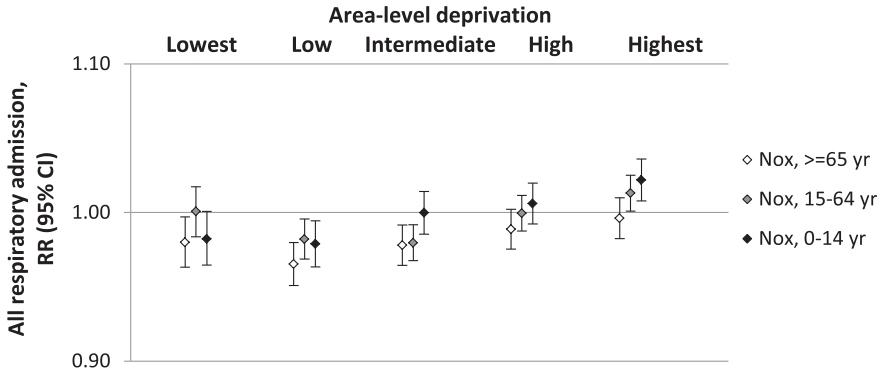


**Fig. 3.** Adjusted[a] associations between an interquartile range increase in nitrogen oxides ($NO_x$) concentration and all respiratory hospital admissions among children, adults and the elderly by quintiles of area-level deprivation. [a]Models adjusted for age, sex, ethnicity, smoking and daytime road traffic noise.

## 4. Discussion

Our comprehensive and statistically powerful analysis of air pollution and hospital admissions for cardiovascular and respiratory diseases in the whole population of London found little evidence of positive associations. Some non-linear associations were observed, especially in the elderly, which took the form of inverse J-shaped dose response. For some outcomes there was evidence of effect modification by area-level socioeconomic deprivation, with an increasing trend across deprivation quintiles and small but significant positive associations in the highest deprivation group.

### 4.1. Methodological issues

Our hypothesis was that increased long-term exposure to air pollutants, especially those from traffic sources, increases the risk of exacerbation of cardiovascular and respiratory diseases and that this is reflected in emergency hospital admissions for these conditions. It is already known from many time-series studies, including some from London, that short-term exposure to a range of gaseous and particulate pollutants measured at city monitors is associated with increased hospital admissions (Atkinson et al., 1999; WHO, 2013). The postulated mechanism is acute exacerbation of disease in an individual already on the brink of admission. It is not known to what extent such increases in risk represent the bringing forward in time of an inevitable admission, or cause an additional admission that would not have otherwise occurred. It is only in the latter scenario that there would be an increase in admission rates detectable in a small-area analysis with disease counts aggregated over many years.

Whereas time-series analyses control by design spatial confounding factors that are relatively stable over time, small-area analyses such as ours are vulnerable to spatial confounding. This is especially the case for hospital admissions which reflect not only aetiological factors responsible for the development of disease and the incidence of exacerbating factors, but complex organisational and behavioural factors (Anderson, 1978) which do not relate to the severity of disease and which cannot be accounted for by crude measures of deprivation. At the outset we were aware of the potential for spatial confounding and had planned a change on change analysis at postcode level which would be more robust to spatial confounding. However, temporal changes over the period 2003–2010 were very similar spatially and too small for this approach to be adopted and we therefore chose to use a small-area approach which had been applied successfully in previous studies (Halonen et al., 2015a, 2015b; Hansell et al., 2013). Our analytic approach using conditional autoregressive models will have captured some unmeasured spatial confounders, and in addition to age and sex, we controlled for area-level smoking, ethnicity, road traffic noise and socioeconomic deprivation. Nevertheless, we cannot exclude the possibility of residual confounding. For example, the piecewise model found lower risks in areas of highest exposures and some of the highest exposures are in extremely wealthy areas of central London. Thus, use of the Carstairs index, may not have been sufficient to adequately adjust for socioeconomic status because one of its components (car ownership) is likely to represent different social status in the inner (more affluent) parts of the city than elsewhere.

The fine scale dispersion model employed to estimate long-term exposures has been used extensively for traffic planning in London (Greater London Authority, 2010) and performed well when validated against measurements. However, due to lack of covariate data and low numbers of admissions at postcode level, the aggregation of postcodes to COAs was associated with a loss of variability in exposure estimates for the pollutants. Nevertheless, the variability of primary traffic pollutants remained clearly greater than that of urban background pollutants such as $PM_{2.5}$.

### 4.2. Comparison with literature

Overall, we found little evidence for positive linear associations between air pollution and hospital admissions in London. Our estimates were characterised by narrow confidence intervals; thus the lack of associations could not be explained by a lack of statistical power. Our results are generally in line with the available literature which comprises few if any studies of equivalent power. Several recent studies, many of which are based on cohort data, have examined the effects long-term exposure to markers of traffic exposure: $NO_2$ and $NO_x$. A summary of these studies (Table 7) shows that nearly half of the studies reported positive and statistically significant associations, a few others reported positive non-significant associations, and the rest reported no associations. Positive associations were more common for respiratory than cardiovascular outcomes, and the respiratory effects were often observed either among older population groups or in children. We also observed the strongest positive associations for respiratory outcomes among the elderly although only at the lowest exposures.

As the associations between air pollutants and health outcomes are not necessarily linear we used piecewise linear models that can identify non-linear relationships and are more easily interpreted than more flexible and complex models like cubic splines. That the strongest positive associations were observed in the lowest exposure category particularly for some outcomes among the elderly is likely due to differential residual confounding, as adjustment for area-level confounders had a greater impact on the effect estimates in the low than high exposure category. However, it should be noted that concentration response functions relating air pollution to health outcomes are not infrequently observed to be steeper at low concentrations and flatten out at higher concentrations. This is illustrated by the integrated exposure response curves derived from combining cohort results for various sources of pollution that are much steeper at low concentrations (Burnett et al., 2014). This pattern has also been reported, for example, for ambient $PM_{2.5}$ concentration in association with cardiovascular mortality (Pope et al., 2011), and for $NO_2$ and $PM_{2.5}$ with IHD mortality (Cesaroni et al., 2013; Crouse et al., 2012). However, none of these studies observed a decline in association at higher exposure as we did. Due to different study methods, previous findings are not directly comparable to ours and further research using similar piecewise regression methods are needed to make solid conclusions.

Few studies have examined the modifying role of area-level deprivation on the associations between traffic pollution and health. No effect modification by area deprivation was observed by Atkinson et al., 2015 in their study that examining first COPD admissions in an English cohort (Atkinson et al., 2015). However, in their earlier work, associations between $NO_2$ and heart failure incidence were stronger in the least versus most deprived areas (Atkinson et al., 2013). In our study, area-level socioeconomic deprivation seemed to slightly modify the associations for traffic pollutants with all cardiovascular admissions among adults, and with all respiratory admissions among children, with small but significant positive associations in the highest deprivation group observed.

### 4.3. Strengths and limitations

Our study of all London residents' benefits from the large number of events included, its representativeness, and consistency of characterisation of outcomes, exposure, and confounding factors. This is in contrast to cohort studies, which are often underpowered for the investigation of major events, subject to attrition, and unrepresentative of the population. Conversely, cohort studies are not prone to the ecological fallacy whereby observed risks for small areas may not apply to all individuals in that area. Both cohort studies and the present study design are prone to problems of exposure characterisation (e.g. lack of time-activity patterns), but have to a variable extent the advantage of using individual-level confounding data such as smoking habit, residential history and exposure earlier in life. Many cohort studies to date have lacked data on neighbourhood-level socioeconomic indicators (de Kluizenaar et al., 2013; Katsoulis et al., 2014; Miller et al., 2007; Molter et al., 2014; Neupane et al., 2010) which can be a source of

**Table 7**
Summary table on the literature on associations between traffic related air pollution and morbidity from year 2005.

| Author, year | Study design | Location | Population, n (age year) | Traffic exposure | Outcome | Finding[a] |
|---|---|---|---|---|---|---|
| | | | | | **Cardiovascular** | |
| Maheswaran et al., 2005b | Ecological | England | 308,841 (≥45) | $NO_x$ | CHD[b] admission | − |
| Maheswaran et al., 2005a | Ecological | England | 199,682 (≥45) | $NO_x$ | Stroke admission | + |
| Johnson et al., 2010 | Ecological | Canada | 1,034,945 | $NO_2$ | Stroke admission | − |
| Miller et al., 2007 | Cohort | USA, 36 MSA[d] | 65,893 women (50–70 at baseline) | $NO_2$ | All CVD[c] events | − |
| Cesaroni et al., 2014 | Cohort | 11 ESCAPE | 100,166 (44–74 at baseline) | $NO_2$, $NO_x$, $PM_{2.5}$ abs[e] | Acute coronary events | − |
| Rosenlund et al., 2008 | Cohort | Italy | Residents of Rome (35–84) | $NO_2$ | First coronary event | + |
| Katsoulis et al., 2014 | Cohort | Greece | 1504 women | $NO_2$ | CHD[b] incidence | + |
| Atkinson et al., 2013 | Cohort | England | 836,557 (40–89 at baseline) | $NO_2$ | Heart failure | + |
| Atkinson et al., 2013 | Cohort | England | 836,557 (40–89 at baseline) | $NO_2$ | MI, arrhythmia, stroke incidence | − |
| Lipsett et al., 2011 | Cohort | CA, USA | 12,172–15,149 (postmenopausal women) | $NO_x$, $NO_2$ | MI, stroke, incidence | − |
| de Kluizenaar et al., 2013 | Cohort | Netherlands | 18,213 (≥65) | $NO_2$, EC | CHD[b], cerebrovascular admission | − |
| Katsoulis et al., 2014 | Cohort | Greece | 2752 (47 at baseline) | $NO_2$ | All CVD[c], stroke incidence | − |
| Stafoggia et al., 2014 | Cohort | 11 ESCAPE | 99,446 (44–74 at baseline) | $NO_2$, $NO_x$, $PM_{2.5}$ abs[e] | Cerebrovascular, incident | − |
| Sorensen et al., 2014 | Cohort | Denmark | 57,053 (50–64 at baseline) | $NO_2$ | Stroke, incident | − |
| Andersen et al., 2012b | Cohort | Denmark | 57,053 (56 at follow-up) | $NO_2$ | Stroke, incident | weak |
| Rosenlund et al., 2006 | case–control | Sweden | 1379 + 1870 (45–70) | $NO_2$ | MI, overall | − |
| | | | | | **Respiratory** | |
| Rushworth et al., 2014 | Ecological | England | Residents of Greater London | $NO_2$, $NO_x$ | All respiratory admissions | weak |
| Andersen et al., 2011 | Cohort | Denmark | 57,053 (56 at baseline) | $NO_2/NO_x$ | COPD[f] admission | +/weak |
| Schikowski et al., 2014 | Cohort | 3 ESCAPE | 6550 (34–54 at baseline) | $NO_2$, $NO_x$, $PM_{2.5}$ abs[e] | COPD[f] incidence | − |
| Atkinson et al., 2015 | Cohort | England | 812,063 (40–89 at baseline) | $NO_2$ | COPD[f] admission | weak |
| MacIntyre et al., 2014 | Cohort | 10 ESCAPE | 16,059 (up to 3) | $NO_2$, $NO_x$ | Diagnosed pneumonia | + |
| Andersen et al., 2012a | Cohort | Denmark | 50-65 at baseline | $NO_2$ | Asthma admission | + |
| Young et al., 2014 | Cohort | USA | 39,350 (55, women) | $NO_2$ | Asthma, incident | − |
| Modig et al., 2009 | Cohort | Sweden | 3609 (39 at baseline) | $NO_2$ | Asthma, onset/incident self-reported | + |
| Yamazaki et al., 2014 | Cohort | Japan | 10,069 (6–9 at baseline) | EC[g]/$NO_x$ | Asthma, incident | +/weak |
| Oftedal et al., 2009 | Cohort | Norway | 2871 (9–10) | $NO_2$ (lifetime) | Asthma, onset | − |
| Jerrett et al., 2008 | Cohort | CA, USA | 217 (10–18 at baseline) | $NO_2$ | Asthma, onset | + |
| McConnell et al., 2010 | cohort | CA, USA | 2497 (5–9 at baseline) | $NO_2$ | Asthma, incidence | + |
| Molter et al., 2014 | (brith) cohort | England | 1158 (3–11) | $NO_2$ | Asthma prevalence | − |
| Gruzieva, 2013 | (birth) cohort | Sweden | 4089 (0–12) | $NO_x$ | Asthma, incident at 12 yr | + |
| Neupane et al., 2010 | case–control | Canada | 345 + 494 (≥65) | $NO_2$ | Pneumonia | + |
| Modig et al., 2006 | case–control | Sweden | 203 + 203 (20–60) | $NO_2$ | Asthma, incident | weak |
| Clark et al., 2010 | Nested case–control | British Columbia | 37,401 | $NO_2$ | Asthma, incidence | + |
| Anderson et al., 2013 | Meta-analysis | | | $NO_2$ | Asthma | + |

[a] Finding: "−" means no or negative association, "+" means positive statistically significant association, and "weak" means positive statistically non-significant association.
[b] Coronary heart disease.
[c] All cardiovascular diseases.
[d] Metropolitan Statistical Areas.
[e] $PM_{2.5}$ absorbance.
[f] Chronic obstructive pulmonary disease.
[g] Elemental carbon.

additional confounding, whereas our study did not have data on individual-level confounders nor residential mobility. Having secondary housing outside London, for example, where air pollution exposure is likely to be lower, may be more common among the more affluent residents of the more polluted inner boroughs (City of London, Westminster, and Kensington and Chelsea (Office for National Statistics, 2012)) than in outer London boroughs. This may have added to the exposure misclassification and masked some positive associations in the high exposure group. It may also, in part, help to explain the observed effect modification by deprivation, with lowest risks in lowest deprivation quintiles. We did not know the spatial distribution of the excluded admission records without valid geographical information, and thus cannot say how many would have been in London (the study area) or whether their spatial distribution was non-random. However, when we mapped the hospital admissions they did not suggest missing data corresponding to particular areas. Also, as the percentage was rather small, we suspect this factor is unlikely to bias our results. Finally, some significant associations may also have occurred due to chance due to multiple testing of different outcomes and exposures.

### 4.4. Conclusions

Overall, in this large and statistically powerful study within London we found no convincing positive linear associations, which is in line with much of the existing literature generally based on smaller studies. The piecewise analyses revealed positive associations in the low and negative associations in the high exposure categories potentially due to differential residual confounding, but this finding needs to be replicated in other studies. There was evidence of effect modification with area-level socioeconomic

deprivation, with those living in areas of higher deprivation having the greatest risk of hospital admission. Increased vulnerability of the most deprived groups in urban centres, chronically exposed to air pollution over the long-term, will have important implications for public health.

## Conflicts of interest

The authors declare no conflicts of interest.

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## Contributions

JIH contributed to the study design, statistical script, and data analyses, and drafted the report. MB contributed to the study design and statistical script. DF, JG, SDB, DD, HRA and FJK contributed to exposure assessment. MBT, JG, HRA, SDB, FJK and CT contributed to the funding and study design. All authors contributed to critical reading of, and commented on the report, helped to interpret the data, and approved the final draft.

## Submission declaration

The authors that the work described has not been published previously, that it is not under consideration for publication elsewhere, that its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere including electronically in the same form, in English or in any other language, without the written consent of the copyright-holder.

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## Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.envpol.2015.09.051.

## References

Andersen, Z.J., Hvidberg, M., Jensen, S.S., et al., 2011. Chronic obstructive pulmonary disease and long-term exposure to traffic-related air pollution: a cohort study. Am. J. Respir. Crit. Care Med. 183, 455–461.
Andersen, Z.J., Bonnelykke, K., Hvidberg, M., et al., 2012a. Long-term exposure to air pollution and asthma hospitalisations in older adults: a cohort study. Thorax 67, 6–11.
Andersen, Z.J., Kristiansen, L.C., Andersen, K.K., et al., 2012b. Stroke and long-term exposure to outdoor air pollution from nitrogen dioxide: a cohort study. Stroke 43, 320–325.
Anderson, H.R., 1978. Increase in hospitalisation for childhood asthma. Arch. Dis. Child. 53, 295–300.
Anderson, H.R., Favarato, G., Atkinson, R.W., 2013. Long-term exposure to air pollution and the incidence of asthma: meta-analysis of cohort studies. Air Qual. Atmos. Health 6, 47–56.
Atkinson, R.W., Anderson, H.R., Strachan, D.P., et al., 1999. Short-term associations between outdoor air pollution and visits to accident and emergency departments in London for respiratory complaints. Eur. Respir. J. 13, 257–265.
Atkinson, R.W., Carey, I.M., Kent, A.J., et al., 2013. Long-term exposure to outdoor air pollution and incidence of cardiovascular diseases. Epidemiology 24, 44–53.
Atkinson, R.W., Carey, I.M., Kent, A.J., et al., 2015. Long-term exposure to outdoor air pollution and the incidence of chronic obstructive pulmonary disease in a national English cohort. Occup. Environ. Med. 72, 42–48.
Beevers, S., Dajnak, D., 2015. Traffic Project Supplementary Files. Air Pollution Model. KCLurban Model Description, Evaluation and Outputs. London. http://www.kcl.ac.uk/lsm/research/divisions/aes/research/ERG/research-projects/traffic/index.aspx.
Beevers, S.D., Kitwiroon, N., Williams, M.L., et al., 2013. Air pollution dispersion models for human exposure predictions in London. J. Expo. Sci. Environ. Epidemiol. 23, 647–653.
Burnett, R.T., Pope 3rd, C.A., Ezzati, M., et al., 2014. An integrated risk function for estimating the global burden of disease attributable to ambient fine particulate matter exposure. Environ. Health Perspect. 122, 397–403.
Cesaroni, G., Badaloni, C., Gariazzo, C., et al., 2013. Long-term exposure to urban air pollution and mortality in a cohort of more than a million adults in Rome. Environ. Health Perspect. 121, 324–331.
Cesaroni, G., Forastiere, F., Stafoggia, M., et al., 2014. Long term exposure to ambient air pollution and incidence of acute coronary events: prospective cohort study and meta-analysis in 11 european cohorts from the ESCAPE project. BMJ, 21: f7412.
Chen, H., Goldberg, M.S., Villeneuve, P.J., 2008. A systematic review of the relation between long-term exposure to ambient air pollution and chronic diseases. Rev. Environ. Health 23, 243–297.
Clark, N.A., Demers, P.A., Karr, C.J., et al., 2010. Effect of early life exposure to air pollution on development of childhood asthma. Environ. Health Perspect. 118, 284–290.
Core R Team, 2014. R: a Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria.
Crouse, D.L., Peters, P.A., van Donkelaar, A., et al., 2012. Risk of nonaccidental and cardiovascular mortality in relation to long-term exposure to low concentrations of fine particulate matter: a Canadian national-level cohort study. Environ. Health Perspect. 120, 708–714.
de Kluizenaar, Y., van Lenthe, F.J., Visschedijk, A.J., et al., 2013. Road traffic noise, air pollution components and cardiovascular events. Noise Health 15, 388–397.
Greater London Authority, 2008. London Atmospheric Emissions Inventory 2008. London. http://data.london.gov.uk/dataset/laei-2008.
Greater London Authority, 2010. Mayor's Air Quality Strategy. London, UK. http://www.london.gov.uk/priorities/environment/publications/mayors-air-quality-strategy.
Gruzieva, O., Bergstrom, A., Hulchiy, O., et al., 2013. Exposure to air pollution from traffic and childhood asthma until 12 years of age. Epidemiology 24, 54–61.
Gulliver, J., Morley, D., Vienneau, D., et al., 2015. Development of an Open-source Road Traffic Noise Model for Exposure Assessment. Environmental Modelling & Software (Epub ahead of print).
Halonen, J.I., Blangiardo, M., Toledano, M.B., et al., 2015a Jul 6. Is long-term exposure to traffic pollution associated with mortality? A small-area study in London. Environ. Pollut. 208, 25–32. http://dx.doi.org/10.1016/j.envpol.2015.06.036 pii: S0269-7491(15)00329-2. (Barking, Essex: 1987). (Epub ahead of print).
Halonen, J.I., Hansell, A.L., Gulliver, J., et al., 2015b Jun 23. Road traffic noise is associated with increased cardiovascular morbidity and mortality and all-cause mortality in London. Eur. Heart J. pii: ehv216 (Epub ahead of print).
Hansell, A.L., Blangiardo, M., Fortunato, L., et al., 2013 Oct 8. Aircraft noise and cardiovascular disease near heathrow airport in London: small area study. BMJ. http://dx.doi.org/10.1136/bmj.f5432, 347:f5432.
HEI, 2010. Traffic-related Air Pollution: a Critical Review of the Literature on Emissions, Exposure, and Health Effects. Special Report. Health Effects Institute, Boston.
Jerrett, M., Shankardass, K., Berhane, K., et al., 2008. Traffic-related air pollution and asthma onset in children: a prospective cohort study with individual exposure measurement. Environ. Health Perspect. 116, 1433–1438.
Johnson, J.Y., Rowe, B.H., Villeneuve, P.J., 2010. Ecological analysis of long-term exposure to ambient air pollution and the incidence of stroke in Edmonton, Alberta, Canada. Stroke 41, 1319–1325.
Katsoulis, M., Dimakopoulou, K., Pedeli, X., et al., 2014. Long-term exposure to traffic-related air pollution and cardiovascular health in a Greek cohort study. Sci. Total Environ. 490, 934–940.
Kelly, F., Armstrong, B., Atkinson, R., et al., 2011. The London low emission zone baseline study. Investigator's report. Res. Rep. Health Eff. Inst. 10–11.
King's College London, 2014. Traffic Project. http://www.kcl.ac.uk/lsm/research/divisions/aes/research/ERG/research-projects/traffic/index.aspx.
Lipsett, M.J., Ostro, B.D., Reynolds, P., et al., 2011. Long-term exposure to air pollution and cardiorespiratory disease in the California teachers study cohort. Am. J. Respir. Crit. Care Med. 184, 828–835.
London Councils, 2014. List of Inner/Outer London Boroughs. http://www.londoncouncils.gov.uk/node/1938.
MacIntyre, E.A., Gehring, U., Molter, A., et al., 2014. Air pollution and respiratory

infections during early childhood: an analysis of 10 European birth cohorts within the ESCAPE Project. Environ. Health Perspect. 122, 107–113.
Maheswaran, R., Haining, R.P., Brindley, P., et al., 2005a. Outdoor air pollution and stroke in Sheffield, United Kingdom: a small-area level geographical study. Stroke 36, 239–243.
Maheswaran, R., Haining, R.P., Brindley, P., et al., 2005b. Outdoor air pollution, mortality, and hospital admissions from coronary heart disease in Sheffield, UK: a small-area level ecological study. Eur. Heart J. 26, 2543–2549.
Martino, S., Rue, H., 2010. Implementing Approximate Bayesian Inference Using Integrated Nested Laplace Approximation: a Manual for the Inla Program. http://www.math.ntnu.no/~hrue/GMRFsim/manual.pdf.
McConnell, R., Islam, T., Shankardass, K., et al., 2010. Childhood incident asthma and traffic-related air pollution at home and school. Environ. Health Perspect. 118, 1021–1026.
Miller, K.A., Siscovick, D.S., Sheppard, L., et al., 2007. Long-term exposure to air pollution and incidence of cardiovascular events in women. N. Engl. J. Med. 356, 447–458.
Modig, L., Jarvholm, B., Ronnmark, E., et al., 2006. Vehicle exhaust exposure in an incident case-control study of adult asthma. Eur. Respir. J. 28, 75–81.
Modig, L., Toren, K., Janson, C., et al., 2009. Vehicle exhaust outside the home and onset of asthma among adults. Eur. Respir. J. 33, 1261–1267.
Molter, A., Agius, R., de Vocht, F., et al., 2014. Effects of long-term exposure to PM10 and NO2 on asthma and wheeze in a prospective birth cohort. J. Epidemiol. Commun. Health 68, 21–28.
Morgan, O., Baker, A., 2006. Measuring deprivation in England and Wales using 2001 carstairs scores. Health Stat. Q. 31, 28–33.
Neupane, B., Jerrett, M., Burnett, R.T., et al., 2010. Long-term exposure to ambient air pollution and risk of hospitalization with community-acquired pneumonia in older adults. Am. J. Respir. Crit. Care Med. 181, 47–53.
Office for National Statistics, 2012. 2011 Census, Second Address Estimates for Local Authorities in England and Wales. http://www.ons.gov.uk/ons/rel/census/2011-census/second-address-estimates-for-local-authorities-in-england-and-wales/index.html.
Office for National Statistics, 2014. Output Areas (OAs). http://www.ons.gov.uk/ons/guide-method/geography/beginner-s-guide/census/output-area–oas-/index.html.
Oftedal, B., Nystad, W., Brunekreef, B., et al., 2009. Long-term traffic-related exposures and asthma onset in schoolchildren in oslo, norway. Environ. Health Perspect. 117, 839–844.
Pope 3rd, C.A., Burnett, R.T., Turner, M.C., et al., 2011. Lung cancer and cardiovascular disease mortality associated with ambient air pollution and cigarette smoke: shape of the exposure-response relationships. Environ. Health Perspect. 119, 1616–1621.
Rosenlund, M., Berglind, N., Pershagen, G., et al., 2006. Long-term exposure to urban air pollution and myocardial infarction. Epidemiology 17, 383–390.
Rosenlund, M., Picciotto, S., Forastiere, F., et al., 2008. Traffic-related air pollution in relation to incidence and prognosis of coronary heart disease. Epidemiology 19, 121–128.
Rue, H., Martino, S., Chopin, N., 2009. Approximate Bayesian inference for latent Gaussian models by using integrated nested laplace approximations. J. R. Stat. Soc. Ser. B 71, 319–392.
Rushworth, A., Lee, D., Mitchell, R., 2014. A spatio-temporal model for estimating the long-term effects of air pollution on respiratory hospital admissions in greater London. Spat. Spatiotemporal Epidemiol. 10, 29–38.
Schikowski, T., Adam, M., Marcon, A., et al., 2014. Association of ambient air pollution with the prevalence and incidence of COPD. Eur. Respir. J. 44, 614–626.
Sorensen, M., Luhdorf, P., Ketzel, M., et al., 2014. Combined effects of road traffic noise and ambient air pollution in relation to risk for stroke? Environ. Res. 133, 49–55.
Stafoggia, M., Cesaroni, G., Peters, A., et al., 2014. Long-term exposure to ambient air pollution and incidence of cerebrovascular events: results from 11 European cohorts within the ESCAPE project. Environ. Health Perspect. 122, 919–925.
WHO, 2013. Review of Evidence on Health Aspects of Air Pollution – REVIHAAP Project: Final Technical Report Bonn: WHO/Europe.
Williams, M.L., Atkinson, R.W., Anderson, H.R., et al., 2014. Associations between daily mortality in London and combined oxidant capacity, ozone and nitrogen dioxide. Air Qual. Atmos. Health 7, 407–414.
Yamazaki, S., Shima, M., Nakadate, T., et al., 2014. Association between traffic-related air pollution and development of asthma in school children: cohort study in Japan. J. Expo. Sci. Environ. Epidemiol. 24, 372–379.
Young, M.T., Sandler, D.P., DeRoo, L.A., et al., 2014. Ambient air pollution exposure and incident adult asthma in a nationwide cohort of U.S. Women. Am. J. Respir. Crit. Care Med. 190, 914–921.