



Is long-term exposure to traffic pollution associated with mortality? A small-area study in London



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ABSTRACT

Long-term exposure to primary traffic pollutants may be harmful for health but few studies have investigated effects on mortality. We examined associations for six primary traffic pollutants with all-cause and cause-specific mortality in 2003–2010 at small-area level using linear and piecewise linear Poisson regression models. In linear models most pollutants showed negative or null association with all-cause, cardiovascular or respiratory mortality. In the piecewise models we observed positive associations in the lowest exposure range (e.g. relative risk (RR) for all-cause mortality 1.07 (95% credible interval (CI) = 1.00–1.15) per 0.15 $\mu\text{g}/\text{m}^3$ increase in exhaust related primary particulate matter $\leq 2.5 \mu\text{m}$ ($\text{PM}_{2.5}$)) whereas associations in the highest exposure range were negative (corresponding RR 0.93, 95% CI: 0.91–0.96). Overall, there was only weak evidence of positive associations with mortality. That we found the strongest positive associations in the lowest exposure group may reflect residual confounding by unmeasured confounders that varies by exposure group.

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1. Introduction

There is concern over the effect of traffic pollution on health (HEI, 2010; WHO, 2013). This relates both to the increased concentrations present near roads and to the possibility that primary traffic pollutants might be more toxic than those comprising the regional/urban background such as total particulate mass with aerodynamic diameter $< 2.5 \mu\text{m}$ ($\text{PM}_{2.5}$). Investigating this question using epidemiological methods is challenging because variations in air pollution concentrations due to primary traffic emissions occur in addition to considerable regional/urban background pollutant concentrations (Kunzli, 2014). Further, there is considerable potential for confounding of pollution effects by socioeconomic factors when conducting small-area analyses within cities. Although the association between $\text{PM}_{2.5}$ or PM_{10} and mortality is well

established (Beelen et al., 2014a; Carey et al., 2013; Cesaroni et al., 2013; Jerrett et al., 2013; Krewski et al., 2005, 2009; Maheswaran et al., 2005), these tend to be more influenced by urban/regional background concentrations and to date, there is less evidence associating mortality with long-term exposure to the primary traffic pollutants such as nitrogen oxides (NO_x) or particles related specifically to vehicle emissions (Beelen et al., 2008, 2014b; Cesaroni et al., 2013; Dimakopoulou et al., 2014; Jerrett et al., 2013; Maheswaran et al., 2005). The majority of epidemiological studies of air pollution and mortality have been based on comparisons between cities, which vary in regional/urban background pollutants as well as in traffic related pollution. In contrast, the investigation of health effects of near-traffic pollution requires analyses at a fine spatial scale within a city.

Reviews of epidemiological studies indicate that socioeconomic deprivation may, in addition to being associated with greater exposure, also adversely modify the effect of air pollution exposure on health (Deguen and Zmirou-Navier, 2010; Sacks et al., 2011). However, few long-term exposure studies have investigated whether deprivation might modify associations for primary traffic

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pollutants (Atkinson et al., 2013; Carey et al., 2013).

As part of a research programme into the health effects of traffic pollution (TRAFFIC study) (King's College London, 2014) we investigated the association between primary traffic pollution and mortality in London, a city of approximately nine million inhabitants. We conducted a small-area ecological study of mortality using spatially resolved estimates of exposure to six primary traffic pollutants as well as five pollutants, such as PM_{2.5}, which tend to be more influenced by regional/urban background concentrations. Traffic noise was treated as a potential confounder (Tetreault et al., 2013); a substantive paper on road traffic noise, mortality and hospital admissions is published elsewhere (Halonen et al., 2015). In this paper we address two questions: 1) is long-term exposure to primary traffic pollutants associated with increased risk of all-cause or cause-specific mortality? and 2) are these associations modified by socioeconomic deprivation?

2. Materials and methods

2.1. Study area and population

Our study area comprised all of London within the M25 motorway (~2,156 km²) (Supplemental Fig. 1), with a population of over eight million. The spatial unit for our analysis was the census geographical unit Lower Layer Super Output Area (LSOA, n = 5482) with a mean population of 1500 (range 1000–3000) (Office for National Statistics, 2014). The analysis comprised 5358 LSOAs with complete information for the exposures, health outcomes and area-level confounders.

2.2. Outcomes

We included mortality data for the population aged 25 years or over. The underlying cause of death was classified using the 10th revision of the International Classification of Diseases (ICD10): all natural (A00–R99); cardiovascular (I00–I99) and respiratory (J00–J99) causes. In addition to the cause of death, these data included the person's age, sex and postcode of residential address at registration of death. We also obtained annual mid-year population estimates at Census Output Area (COA) level (with a mean population of 300 (range 100–1200) by age and sex for 2003–2010. Annual death counts and population estimates were aggregated to LSOAs, the smallest unit with sufficient deaths for the cross-sectional analysis, by sex and 5-year age bands to calculate mortality rates. The mortality and population data were supplied by the Office for National Statistics (ONS), derived from the national mortality registrations and the Census. Data are held by the UK Small Area Health Statistics Unit (SAHSU) at Imperial College London. Data use was covered by approval from the National Research Ethics Service – reference 12/LO/0566 and 12/LO/0567 – and by National Information Governance Board and Ethics and Confidentiality Committee approval for section 251 support (NIGB – ECC 2–06(a)/2009).

2.3. Pollution concentrations

We used a dispersion model to estimate average annual concentrations of six primary traffic pollutants; nitrogen oxides (NO_x), nitrogen dioxide (NO₂), as well as exhaust (tailpipe emissions) and non-exhaust (brake and tyre wear and re-suspension) related primary PM_{2.5} and PM₁₀, for ~190,000 postcode address centroids in London for each year between 2003 and 2010. This model provided corresponding estimates for regional/urban background pollutants PM_{2.5}, PM₁₀ (aerodynamic diameter less than 2.5 μm and 10 μm, respectively) and ozone (O₃), and from these we calculated coarse

fraction of PM₁₀ (PM_{10-2.5}) and oxidative gases (O_x, i.e. combined oxidant NO₂ + O₃) (Clapp and Jenkin, 2001; Williams et al., 2014). The model includes regional/urban background PM_{2.5}, PM₁₀, and O₃ from outside London, which is predominantly secondary in nature, having longer atmospheric lifetimes and being more homogeneously distributed. All “background” emission sources from London are represented as volume sources of dimension 1 × 1 km and between 2 m and 50 m high. Very close to the address centroids, then, we represent traffic emissions road by road, which results in model predictions that are highly detailed close to road sources where concentration gradients are steepest. By using dispersion models and detailed emissions we were able to estimate the contribution to pollutant concentrations from London's road traffic alone. We used the KCLurban dispersion modelling system based on Atmospheric Dispersion Modelling System (ADMS) v.4 and road source model v.2.3, which incorporates hourly meteorological measurements, empirically derived NO–NO₂–O₃ and PM relationships, and information on source emissions from the London Atmospheric Emissions Inventory (LAEI) (Greater London Authority, 2008). The model was not adjusted in any way and performed well when validated against measurements: a comparison of observed vs. modelled concentrations provided high spearman correlation coefficients (r). The values of r for monthly NO_x and NO₂ varied across a relatively small range giving an average (and standard deviation) of 0.82 (0.049) and 0.84 (0.033), respectively. More detailed information about the modelling procedure and model validation can be found elsewhere (Beevers and Dajnak, 2015; Beevers et al., 2013). Whilst industrial sources in the UK and Europe are important contributors to regional scale particulate matter concentrations and locally can contribute to short periods of high pollutant concentrations, in London emission sources are dominated by road traffic, whose effects on human exposure are multiplied by being released at ground level. The combination of the small scale of industrial emissions in London, their emissions released at height, and the use of annual mean concentrations in this study means that London's industrial sources play a minor role in human exposure. We aggregated all exposure data to LSOAs by 1) calculating the mean of all postcode address centroid annual averages within a LSOA, and 2) calculating the mean across all study years within a LSOA.

2.4. Confounders

Exposure to traffic-related air pollution (Goodman et al., 2011) and risk of mortality (Halonen et al., 2013; Meijer et al., 2012) have been shown to vary by area-level socioeconomic deprivation. We therefore used the Carstairs deprivation index (a composite measure based on unemployment, overcrowding, car ownership and low social class) (Morgan and Baker, 2006) standardized to the study area as a marker of LSOA-level deprivation with higher values indicating more deprived areas. We adjusted for ethnic differences between LSOAs using the percentage of black ethnicity and South Asian ethnicity. The Carstairs and ethnicity data were derived from the UK Census 2011 provided by the Office for National Statistics.

Because no individual- or area-level smoking data were available, we used annual smoothed age and sex standardised relative risk of lung cancer mortality (ICD-10: C33–C34) at the LSOA level as a proxy for smoking as in a previous study in London (Hansell et al., 2013). Because of variations in population structure and higher pollution levels in the London city centre we constructed a dummy variable for inner (n = 13) and outer (n = 20) London boroughs (London Councils, 2014) for inclusion in sensitivity analyses.

To control for possible confounding by road traffic noise (Tetreault et al., 2013) we included daytime A-weighted equivalent continuous sound pressure level (L_{Aeq16, road}) in all models. We

modelled annual road traffic noise levels for years 2003–2010 for each of the ~190,000 postcode locations in London placed 1 m from the facade of the nearest residential dwelling, with 0.1 dB(A) noise level resolution using the TRAffic Noise EXposure (TRANEX) model in open-source GIS (Gulliver et al., 2015). This model uses information on road traffic flows and speeds attributed to road geography, land cover, road geography, and building heights. We aggregated annual postcode level noise estimates to LSOAs by using the mean across all annual postcode centroid averages within a LSOA, and averaged these over 2003–2010.

2.5. Statistical analyses

Geographical data have a degree of spatial dependency, as adjacent areas tend to be more similar to each other than areas further apart. In order to model this, we used ecological Poisson regression specified in a Bayesian framework implemented through the Integrated Nested Laplace Approximation (INLA) (Rue et al., 2009) approach. We calculated the age and sex standardised expected numbers of deaths for each LSOA using mortality rates for the study area and period and included these as offsets in the models. Following the Besag–York–Mollie (BYM) specification we modelled the spatial dependence (spatially structured residual) through an intrinsic conditional autoregressive structure assuming that areas which share boundaries are correlated, and non-spatial heterogeneity (unstructured residual), which is due to the unobserved non-spatial variables, through a random effect (Blangiardo et al., 2013). Default prior distributions were specified on the variance parameters for the spatially structured and unstructured residuals.

We used linear and piecewise linear Poisson regression models to determine associations for each pollutant with all-cause and cause-specific mortality. We fitted a cubic spline to a scatter plot on primary traffic pollutant concentrations and standardized mortality ratios for all-cause mortality to examine the linearity of these relationships. While linear models are commonly used in small-area studies, the piecewise model relaxes the assumption of linearity of any association across the whole range of exposures. These models use defined exposure categories and assume a (potentially different) linear effect within each of these categories which provides clearer interpretation of the results when compared to models using cubic splines, for example. We chose exposure cut points for each pollutant that resulted in four categories characterised by approximately equal exposure range in each category (e.g. ~15 $\mu\text{g}/\text{m}^3$ for each NO_x and ~0.3 $\mu\text{g}/\text{m}^3$ for each exhaust related primary $\text{PM}_{2.5}$ category). For a sub-set of pollutants we also ran models where exposure categories were based on quartiles ensuring the same number of LSOAs in each category, but allowing for differences in exposure ranges across categories. All models were adjusted for the following area level confounders: quintiles of socioeconomic deprivation; tertiles of both black and South Asian ethnicities; proxy for continuous smoking and daytime road traffic noise.

To examine effect modification by deprivation, we added an interaction term “continuous exposure \times deprivation” to the regression models. Due to high correlations between the exposures (Supplemental Table 1), and to limit the number of analyses, interactions were tested for all-cause mortality in a sub-set of three primary traffic pollutants: NO_x (commonly used indicator of local traffic-related pollution), exhaust related primary $\text{PM}_{2.5}$ (most tailpipe emission particles are likely to be in the $\text{PM}_{2.5}$ size fraction) and non-exhaust related primary PM_{10} (most particles from brake and tyre wear are likely to be in the PM_{10} size fraction).

We performed several sensitivity analyses for the above-mentioned sub-set of primary traffic pollutants in association

with all-cause mortality. First, we used the Index of Multiple Deprivation (IMD) instead of the Carstairs index to control for area-level deprivation. IMD was not our primary measure of deprivation because it was not standardised for the study area and includes information on outdoor pollution levels in the “living environment” domain. Second, we adjusted models for the “inner-outer London” dummy. Third, we used different prior distributions in the models. Fourth, we used annual medians and 95th percentiles (instead of means) of air pollution concentrations at postcode centroids to calculate LSOA level concentrations across years.

All analyses were run in R 3.1.0 (R Core Team, 2014) using the package R-INLA (www.r-inla.org) (Martino and Rue, 2010). For comparability, 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 (e.g. per 7.5 $\mu\text{g}/\text{m}^3$ for NO_x and per 0.15 $\mu\text{g}/\text{m}^3$ for exhaust related primary $\text{PM}_{2.5}$).

3. Results

From 2003 to 2010 there were a total of 442,560 deaths from natural causes among adults ≥ 25 years old in London with a mean of 83 (SD = 48) per LSOA. Of these deaths, 151,585 were for cardiovascular diseases (per LSOA mean = 28, SD = 18), and 63,141 for respiratory diseases (per LSOA mean = 12, SD = 9). Mortality rates, particularly for cardiovascular and respiratory causes, were lower in inner than outer London (Supplemental Fig. 1). Within the 13 inner London boroughs 35% of LSOAs belonged to the lowest cardiovascular mortality category (standardised mortality ratio < 0.8) versus 25% within the outer London boroughs.

Descriptive statistics of the air pollution concentrations are presented in Table 1. The greatest variation was in the primary traffic pollutants (coefficient of variation ranging between 0.16 and 0.38) as would be expected whereas those pollutants dominated by regional/urban background concentration displayed less variation between LSOAs (coefficient of variation 0.03–0.10). NO_x concentrations generally increased with decreasing distance to Central London (Supplemental Fig. 2). Correlations between pollutant concentrations were high; for example, for NO_x in relation to PM metrics Pearson’s r ranged from 0.96 to 0.98, and for O_3 from $r = -0.92$ to -0.96 (Supplemental Table 1). For daytime road traffic noise the highest correlations were with non-exhaust related primary $\text{PM}_{2.5}$ and PM_{10} (for both $r = 0.62$). Correlations between primary traffic pollutants and deprivation varied according to exposure levels. For example, correlations between exhaust related primary $\text{PM}_{2.5}$ and continuous deprivation were 0.16, 0.24, 0.12 and -0.17 according to increasing exposure category.

When using the linear models, associations between primary traffic pollutants and mortality outcomes were negative or close to unity (Table 2). For example, exhaust related primary particulates were negatively associated with all-cause, cardiovascular and respiratory mortality (RR for all-cause mortality 0.96, 95% CI: 0.94–0.97 for 0.15 $\mu\text{g}/\text{m}^3$ increase in exhaust related primary $\text{PM}_{2.5}$). Ozone was positively associated with all outcomes (Table 2). Fitting a cubic spline to a scatter plot of exhaust related primary $\text{PM}_{2.5}$ concentrations and standardized mortality ratios for all-causes indicated non-linear relationship (Supplemental Fig. 3).

Adjusting the piecewise linear models for the area-level confounders changed the effect estimates most in the lower exposure categories (partially adjusted results for all-cause mortality are shown in Supplemental Table 2). The confounder adjusted results for traffic pollutants based on the piecewise linear models are shown in Table 3. The effect estimates for all-cause mortality varied with exposure category being positive in the lowest and negative in the higher exposure categories. Across the traffic related primary

Table 1
Distribution of average air pollutant concentrations across Lower Layer Super Output Areas (LSOA) in London (2003–2010).

Pollutant ($\mu\text{g}/\text{m}^3$)	Mean	SD	Min	P25	Median	P75	Max	IQR
Primary traffic								
NO _x	65.9	15.5	35.4	54.7	64.2	75.4	132.6	20.7
NO ₂	38.9	6.21	25.8	34.3	38.4	42.9	64.2	8.6
Exhaust related primary PM _{2.5}	0.71	0.26	0.28	0.52	0.66	0.84	2.19	0.32
Non-exhaust related primary PM _{2.5}	0.73	0.22	0.28	0.57	0.71	0.87	1.71	0.30
Exhaust related primary PM ₁₀	0.80	0.30	0.31	0.59	0.74	0.95	2.45	0.36
Non-exhaust related primary PM ₁₀	2.46	0.73	0.99	1.90	2.39	2.92	5.71	1.02
Regional/urban background								
PM _{2.5}	15.3	0.83	13.7	14.7	15.1	15.8	19.2	1.1
PM ₁₀	24.0	1.42	21.3	22.9	23.8	24.9	29.8	2.0
PM _{10-2.5}	8.73	0.60	7.54	8.27	8.67	9.11	11.4	0.84
O ₃	38.8	3.72	27.5	36.2	38.8	41.5	48.1	5.3
O _x (NO ₂ + O ₃)	77.7	2.60	73.4	75.8	77.2	79.1	92.0	3.3
Covariates								
L _{Aeq16} (dB)	58.7	2.36	54.8	56.9	58.4	60.1	70.0	3.2
Deprivation score	0.00	3.37	-6.46	-2.80	-0.39	2.39	11.3	5.2
Black ethnicity (%)	11.8	10.9	0.00	3.40	8.13	17.2	63.7	13.8
South Asian ethnicity (%)	10.7	12.9	0.07	3.03	5.54	12.2	74.7	9.2
Proxy for smoking rate ^a	1.02	0.28	0.00	0.81	0.98	1.19	2.38	-

^a Smoothed standardised relative risk of lung cancer mortality.

Table 2
Adjusted^a relative risks for mortality (95% credible intervals) in association with air pollutants using linear models.

Pollutant	Per ($\mu\text{g}/\text{m}^3$)	All-cause (n = 442,560)		All cardiovascular (n = 151,585)		All respiratory (n = 63,141)	
		RR	(95% CI)	RR	(95% CI)	RR	(95% CI)
Primary traffic							
NO _x	7.5	0.99	0.98–1.00	0.98	0.96–0.99	0.95	0.93–0.97
NO ₂	4.0	0.99	0.97–1.00	0.97	0.94–0.99	0.93	0.90–0.96
Exhaust related primary PM _{2.5}	0.15	0.98	0.97–1.00	0.96	0.94–0.97	0.92	0.90–0.94
Non-exhaust related primary PM _{2.5}	0.10	0.99	0.98–1.00	0.99	0.98–1.01	0.96	0.95–0.98
Exhaust related primary PM ₁₀	0.15	0.99	0.9–1.00	0.96	0.95–0.98	0.93	0.91–0.95
Non-exhaust related primary PM ₁₀	0.50	0.99	0.97–1.00	0.98	0.96–1.00	0.94	0.92–0.97
Regional/urban background							
PM _{2.5}	0.60	0.98	0.96–1.00	0.95	0.92–0.97	0.90	0.87–0.94
PM ₁₀	1.0	0.98	0.96–1.00	0.96	0.94–0.99	0.91	0.88–0.95
PM _{10-2.5}	0.35	0.99	0.97–1.00	0.98	0.96–1.00	0.95	0.92–0.97
O ₃	2.5	1.02	1.00–1.04	1.03	1.00–1.05	1.07	1.04–1.11
O _x (NO ₂ + O ₃)	1.5	0.99	0.98–1.01	0.97	0.95–0.99	0.94	0.92–0.96

^a All models adjusted for age, sex, area-level socioeconomic deprivation, ethnicity, smoking and daytime road traffic noise.

particulates, the strongest association with all-cause mortality was seen in the lowest category of exhaust related primary PM_{2.5} (RR = 1.04, 95% CI: 0.99–1.10 per 0.15 $\mu\text{g}/\text{m}^3$ increase), but in the highest category the corresponding RR was 0.98 (95% CI: 0.96–1.00). Similar piecewise linear associations across the exposure ranges were observed for cardiovascular mortality with slightly larger effect estimates (Table 3). With all respiratory mortality the effect estimates were mainly below unity in all exposure categories (Table 3). When we used quartiles of LSOAs for the exposure categorisation the patterns were similar to those using the chosen cut points (Supplemental Table 3).

Associations between regional/urban background pollutants and all-cause mortality remained weak in piecewise models (Supplemental Table 4). Moreover, PM_{2.5}, PM₁₀ and PM_{10-2.5} were also associated with increased risk of cardiovascular mortality in the lowest exposure category while the associations were negative in the highest exposure category. The positive association between O₃ and mortality remained with the slopes flattening in the higher exposure groups (Supplemental Table 4).

Fig. 1 shows effect modification by area-level deprivation in the associations for NO_x and exhaust-related particulates with all-cause mortality when using linear models with the interaction term. There was a negative association between exhaust related

primary PM_{2.5} and all-cause mortality in the lowest quintile of deprivation, and slightly increasing effects estimates with increasing deprivation. The trend was similar for NO_x and non-exhaust related primary PM₁₀. Relative risks for all-cause mortality in association with 0.15 $\mu\text{g}/\text{m}^3$ increase in exhaust related primary PM_{2.5} were 0.97 (95% CI: 0.95–0.99) in the lowest, and 0.99 (95% CI: 0.98–1.01) in the highest deprivation group.

Results from the sensitivity analyses using IMD as a measure for area-level deprivation, adjustment for inner-outer London borough, models with different priors, or using median or 95th percentile air pollution concentrations did not materially alter the patterns of results (Supplemental Table 5).

4. Discussion

Overall, there was only weak evidence of positive associations between primary traffic pollutants and mortality. Our results suggest that the area-level relationship for several pollutants and mortality is non-linear across the exposure range, with generally positive associations at the lowest and negative associations at the highest exposure levels. Piecewise linear models can identify such non-linear relationships and are more easily interpretable than more flexible and complex models like cubic splines. Due to the

Table 3
Adjusted^a relative risks for mortality (95% credible intervals) in association with half a range increase in traffic pollutants using piecewise linear models.

Pollutant (per $\mu\text{g}/\text{m}^3$)	n LSOAs	Mean n of deaths	All-cause (n = 442,560)		Mean n of deaths	All cardiovascular (n = 151,585)		Mean n of deaths	All respiratory (n = 63,141)	
			RR	(95% CI)		RR	(95% CI)		RR	(95% CI)
NO_x (7.5)										
<50.0	802	105	1.02	0.98–1.07	36	1.04	0.99–1.10	16	1.00	0.93–1.01
50.0–64.9	2004	89	1.00	0.97–1.02	32	1.01	0.98–1.04	13	0.98	0.94–1.00
65.0–79.9	1606	73	0.98	0.96–1.00	25	0.98	0.96–1.01	10	0.96	0.92–1.00
≥80.0	946	66	0.99	0.98–1.01	19	0.95	0.93–0.97	7	0.91	0.88–0.99
NO₂ (4.0)										
<33.0	969	105	1.03	0.98–1.08	36	1.06	0.99–1.13	16	1.00	0.92–1.02
33.0–40.9	2565	85	0.99	0.96–1.02	31	1.00	0.96–1.04	13	0.99	0.93–1.01
41.0–47.9	1508	68	0.98	0.95–1.00	22	0.96	0.93–1.00	9	0.89	0.85–0.99
≥48.0	316	64	0.98	0.95–1.02	17	0.89	0.84–0.93	6	0.83	0.77–0.97
Exhaust related primary PM_{2.5} (0.15)										
<0.50	1132	101	1.04	0.99–1.10	35	1.07	1.00–1.15	15	0.97	0.89–1.89
0.50–0.79	2614	84	0.98	0.96–1.01	30	0.98	0.95–1.01	13	0.97	0.93–1.11
0.80–1.09	1204	68	0.99	0.96–1.01	22	0.96	0.93–1.00	9	0.92	0.88–0.81
≥1.1	403	63	0.98	0.96–1.00	17	0.93	0.91–0.96	6	0.89	0.86–0.74
Non-exhaust related primary PM_{2.5} (0.10)										
<0.55	1218	100	1.02	0.99–1.05	35	1.04	1.00–1.07	15	0.99	0.94–1.64
0.55–0.74	1791	86	1.00	0.98–1.02	31	1.01	0.99–1.04	13	1.00	0.96–1.56
0.75–0.94	1529	74	0.98	0.96–1.00	25	0.98	0.96–1.01	10	0.96	0.93–1.00
≥0.95	820	65	0.99	0.98–1.01	19	0.97	0.95–1.00	7	0.93	0.90–0.78
Exhaust related primary PM₁₀ (0.15)										
<0.60	1480	99	1.02	0.98–1.07	35	1.05	1.00–1.11	15	0.98	0.91–1.45
0.60–0.89	2283	83	0.98	0.96–1.00	30	0.98	0.95–1.01	12	0.97	0.93–1.11
0.90–1.19	1123	67	0.99	0.96–1.01	22	0.97	0.94–1.00	9	0.92	0.88–0.83
≥1.2	472	65	0.97	0.97–1.00	17	0.94	0.92–0.96	7	0.90	0.88–0.75
Non-exhaust related primary PM₁₀ (0.50)										
<2.0	1593	98	1.02	0.99–1.06	34	1.06	1.01–1.11	15	0.98	0.93–1.11
2.0–2.9	2571	80	0.98	0.98–1.01	28	0.99	0.96–1.02	12	0.97	0.93–1.03
3.0–3.9	1030	69	0.99	0.99–1.02	21	0.98	0.95–1.02	8	0.87	0.88–0.96
≥4	164	54	0.97	0.92–1.02	14	0.91	0.85–0.97	5	0.83	0.74–0.88

^a All models adjusted for age, sex, area-level socioeconomic deprivation, ethnicity, smoking and daytime road traffic noise.

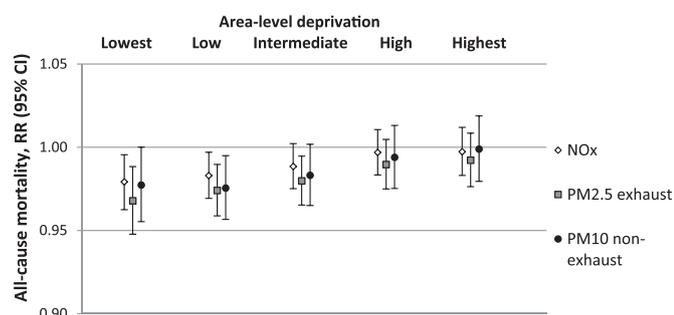


Fig. 1. Adjusted^a relative risks for all-cause mortality in association with half a range increase in nitrogen oxides (NO_x), exhaust related primary PM_{2.5} and non-exhaust related primary PM₁₀ by quintiles of area-level socioeconomic deprivation. (^aModels adjusted for age, sex, area level ethnicity, smoking, and daytime road traffic noise.)

area level study design, however, we cannot omit the possibility that unmeasured confounding, that may vary by exposure groups, has affected the findings.

Effects of long-term exposure to air pollutants have been studied in several different settings although few studies have focused on primary traffic pollutants. One ecological study from the UK has reported a positive association between long-term exposure to NO_x and coronary heart disease mortality at the census enumeration district level (with an average of 450 residents) (Maheswaran et al., 2005). In cohort studies based in Rome and California positive associations were reported for NO₂ with non-accidental and cardiovascular mortality (Cesaroni et al., 2013; Jerrett et al., 2013). In a Dutch cohort, on the other hand, no associations were observed between NO₂ and all-cause, cardiovascular or respiratory mortality after adjusting for individual-level confounders (Beelen et al.,

2008). The results of the European ESCAPE project were similar to those of the present study in that there were no linear associations for NO_x or NO₂ with all-cause and cardiovascular mortality (Beelen et al., 2014a, 2014b). Moreover, the ESCAPE reported a negative association between PM_{2.5} absorbance (i.e. particulate marker for traffic emissions) and respiratory mortality (Dimakopoulou et al., 2014) that is in line with the linear model results of this study. Our piecewise models, however, revealed that these associations may be non-linear across the exposure range. Concentration response functions that are steeper at low concentrations and flatten out at higher concentrations are not infrequently reported. This pattern has been shown in cohort studies, for example, for ambient PM_{2.5} and NO₂ concentrations in association with cardiovascular mortality (Cesaroni et al., 2013; Crouse et al., 2012). As we are not aware of prior small-area studies using piecewise linear models our findings cannot be directly compared with other studies or study areas and should be confirmed in further studies.

We observed no linear association between total PM_{2.5} or PM₁₀ and mortality which agrees with findings from a Dutch cohort study (Beelen et al., 2008) and the ESCAPE results for cardiovascular and respiratory mortality (Beelen et al., 2014b; Dimakopoulou et al., 2014). Most prior individual-level studies, including the ESCAPE analyses for all-cause mortality (Beelen et al., 2014a) and the nationwide analyses using the American Cancer Society (ACS) cohorts (Krewski et al., 2005, 2009), have reported positive associations between PM_{2.5} and mortality. However, in the city-specific analyses of the ACS Cancer Prevention Study II for Los Angeles and New York City, marked differences by region were observed (Krewski et al., 2009). In the Los Angeles region spatial variability in PM_{2.5} concentrations was high, and the associations between PM_{2.5}

and all-cause mortality were strong whereas, similar to our study, small spatial variation in PM_{2.5} and no association for all-cause mortality was observed in the New York City region. The inconsistent findings underline the importance of large within-city studies instead of those comparing effects between cities.

We also observed that the association between primary traffic pollutants and mortality was the lowest in the least deprived quintile. In London, relatively high exposures to traffic pollutants are present in the least deprived quintile. The finding of different associations in this group using a linear model is consistent with the results from the piecewise linear model showing negative associations in the most exposed category. Other studies investigating effect modification by deprivation have shown mixed findings, likely due to differences in study designs (cohort, ecological, between or within-city), populations (e.g. age and sex distributions), exposure assessment methods (monitoring site measurements, modelled), geographical units as well as epidemiological model forms (linear, non-linear). Carey et al. reported stronger positive associations between NO₂ and mortality in UK areas with high (vs. low) income deprivation (Carey et al., 2013). However, in another cohort from the UK converse effect modification was reported (Atkinson et al., 2013), and no effect modification by deprivation was observed in Scottish cohorts (Yap et al., 2012). We observed a negative association of air pollution in the lowest deprivation group which has been observed in a study of daily mortality in Rome (Forastiere et al., 2007). In that study, the authors speculated that this was due to a differential burden of chronic diseases leading to greater susceptibility among the residents of disadvantaged areas. Data on prevalent disease were not available for our study population; however, greater mortality and admission rates in deprived vs. affluent areas, particularly among women, in England have been reported (Pujades-Rodriguez et al., 2014).

Several limitations should be considered while interpreting these results. Firstly, the ecological study design provides associations at the small-area level, which may not reflect the individual-level association (Morgenstern, 1995). We adjusted for several important potential confounders; however, other area level characteristics that predict area level death rates and are associated with air pollution exposure are likely to exist. The conditional autoregressive model captures some unmeasured spatial confounders; however, some residual confounding is likely still apparent in our results. Furthermore, the Carstairs index might not fully characterise deprivation in London mainly because car ownership in inner London does not mean the same in terms of deprivation compared to sub-urban areas. However, analyses using the IMD resulted in similar findings. The different correlations observed between traffic pollutants and deprivation by exposure categories (positive in the lowest and negative in the highest exposure) also suggest differential confounding patterns between deprived and affluent areas, which may explain, in part, the lower relative risks at higher exposures. Similarly, confounder adjustment had a larger impact on the relative risks in the lower exposure compared to higher exposure categories. If confounders like deprivation were measured with more error in higher exposure categories (low deprivation), adjustment would be less effective resulting in more residual confounding at higher exposures.

Another limitation is that due to low numbers of deaths in smaller geographical areas we averaged air pollution concentrations from postcode to LSOA level, and due to lack of time variant confounder data air pollution concentrations were averaged again annually over the study period which will have reduced the exposure contrast between LSOAs. Averaging over LSOAs of different geographical size may also have led to larger exposure misclassification in the large vs. small LSOAs. Some exposure misclassification is likely to have occurred because we were not

able to take into account residential history or personal time-activities. Indeed, some associations may have been masked because some residents of the inner London boroughs, particularly those of City of London, Westminster, and Kensington and Chelsea have other dwellings outside London (Office for National Statistics, 2012) where the level of exposure is likely to be lower. As these boroughs also have low area-level deprivation (Office for National Statistics, 2013), exposure misclassification due to secondary housing may partly explain the negative associations observed in the low deprivation groups.

This study has a number of strengths including the large general population sample, inclusion of all mortality events in the study region, and a wide range of primary traffic and regional/background air pollutants over the long term, providing sufficient statistical power to detect modest associations. The recently completed ESCAPE project had 29,076 deaths from all causes, 9994 from cardiovascular disease and 1559 from respiratory diseases. These deaths occurred in 16–22 different populations, with likely variation in coding of death across populations. In contrast, this analysis included 442,560 deaths in a single population. We also used a range of exposure measures targeting specific primary traffic exposures that have rarely been used in prior studies, and we adjusted for possible confounding by road traffic noise. In addition, to our knowledge, this was the first small-area study to use a piecewise linear model that relaxes the assumption of linearity over the whole exposure range.

In conclusion, there was only weak overall evidence of positive associations with primary traffic pollutants and mortality. The piecewise linear approach suggested non-linear relationships for most traffic pollutants with all-cause and cardiovascular mortality with weak positive associations at relatively low exposures and weak negative associations at the higher exposures in London. For respiratory mortality associations were close to unity or negative. The observed associations may reflect, at least in part, residual confounding by deprivation and other unmeasured factors that may vary by exposure group.

Conflicts of interest

The authors declare no conflicts of interest.

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Contributors

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

Submission declaration

The authors declare 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, 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.2015.06.036>.

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