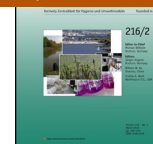




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Long-term traffic air and noise pollution in relation to mortality and hospital readmission among myocardial infarction survivors

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ABSTRACT

Background: There is relatively little evidence of health effects of long-term exposure to traffic-related pollution in susceptible populations. We investigated whether long-term exposure to traffic air and noise pollution was associated with all-cause mortality or hospital readmission for myocardial infarction (MI) among survivors of hospital admission for MI.**Methods:** Patients from the Myocardial Ischaemia National Audit Project database resident in Greater London ($n = 18,138$) were followed for death or readmission for MI. High spatially-resolved annual average air pollution (11 metrics of primary traffic, regional or urban background) derived from a dispersion model (resolution $20\text{ m} \times 20\text{ m}$) and road traffic noise for the years 2003–2010 were used to assign exposure at residence. Hazard ratios (HR, 95% confidence interval (CI)) were estimated using Cox proportional hazards models.**Results:** Most air pollutants were positively associated with all-cause mortality alone and in combination with hospital readmission. The largest associations with mortality per interquartile range (IQR) increase of pollutant were observed for non-exhaust particulate matter (PM_{10}) (HR = 1.05 (95% CI 1.00, 1.10), IQR = $1.1\ \mu\text{g}/\text{m}^3$); oxidant gases (HR = 1.05 (95% CI 1.00, 1.09), IQR = $3.2\ \mu\text{g}/\text{m}^3$); and the coarse fraction of PM (HR = 1.05 (95% CI 1.00, 1.10), IQR = $0.9\ \mu\text{g}/\text{m}^3$). Adjustment for traffic noise only slightly attenuated these associations. The association for a 5 dB increase in road-traffic noise with mortality was HR = 1.02 (95% CI 0.99, 1.06) independent of air pollution.**Conclusions:** These data support a relationship of primary traffic and regional/urban background air pollution with poor prognosis among MI survivors. Although imprecise, traffic noise appeared to have a modest association with prognosis independent of air pollution.© 2015 The Authors. Published by Elsevier GmbH. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Health effects of long-term exposure to air pollution have been primarily examined among general populations (Beelen et al., 2014; Hoek et al., 2013; Carey et al., 2013; Cesaroni et al., 2014).

Abbreviations: MI, myocardial infarction; NO_x , nitrogen oxides; O_3 , oxidant gases; $\text{PM}_{2.5}$, particulate matter with aerodynamic diameter $\leq 2.5\ \mu\text{m}$; PM_{10} , particulate matter with aerodynamic diameter $\leq 10\ \mu\text{m}$; HGV, heavy goods vehicles; MINAP, Myocardial Ischaemia National Audit Project; STEMI, ST-elevation myocardial infarction; IMD, Index of Multiple Deprivation; dB, decibels; $\text{L}_{\text{Aeq}16}$, daytime A-weighted equivalent continuous sound pressure level; ACE, angiotensin-converting-enzyme; PCI, percutaneous coronary intervention.

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However, studies among susceptible sub-groups, such as survivors of myocardial infarction (MI), are scarcer and results have included positive as well as null findings (Zanobetti and Schwartz, 2007; von Klot et al., 2009; Koton et al., 2013; Tonne and Wilkinson, 2013; Rosenlund et al., 2008). In contrast to air pollution, individual-level estimates of road traffic noise in relation to all-cause mortality are not currently available in general populations or among MI survivors.

Prior studies have reported associations mainly between long-term exposure to total particulate mass concentration and post-myocardial infarction mortality and readmission to hospital (Zanobetti and Schwartz, 2007; von Klot et al., 2009; Koton et al., 2013). There is less evidence for particulates from traffic exhaust and non-exhaust (e.g. brake and tyre wear) or for gaseous pollutants (Tonne and Wilkinson, 2013; Rosenlund et al., 2008). Furthermore, exposure in some studies has been based on data

from monitoring stations at national- (Koton et al., 2013) or city-level (Zanobetti and Schwartz, 2007) which may result in relatively large exposure misclassification.

Like air pollution, noise is a pervasive environmental exposure in urban settings. An estimated 50% of the European population living in urban areas is exposed to average road traffic noise above L_{DEN} (Day-Evening-Night-Level, A weighted average sound pressure level over 24 h, with weighting for extra sensitivity to evening and night noise) 55 dB, levels which are thought to pose health risks (WHO, 2011). More than 1 million healthy life years are estimated to be lost annually due to environmental noise in Europe, with the largest burdens attributable to sleep disturbance and annoyance (WHO, 2011). The burden attributable to ischaemic heart disease is also sizeable: 61,000 healthy life years lost (WHO, 2011).

As part of a programme of research investigating the health effects of traffic pollution in Greater London, we used high spatially-resolved exposure estimates for a range of air pollutants (including nitrogen oxides (NO_x), oxidant gases (O_x , i.e. $NO_2 + O_3$), traffic exhaust and non-exhaust related particulate matter (PM), total $PM_{2.5}$ and PM_{10}) as well as for road traffic noise. These detailed exposure data allow for focused investigation of exposure to traffic air and noise pollution in relation to outcome following hospital admission for MI. We used the Myocardial Ischaemia National Audit Project (MINAP) database of individuals admitted to hospital with MI in Greater London to investigate whether long-term exposure to traffic air and noise pollution was associated with all-cause mortality or hospital readmission for MI.

2. Methods

2.1. Study population

The cohort consisted of residents of Greater London admitted to hospital with a final diagnosis of ST-elevation myocardial infarction (STEMI) and non-ST elevation myocardial infarction (non-STEMI) identified through the MINAP (Birkhead et al., 2004; Herrett et al., 2010) database. Greater London was defined as the area within the M25 motorway (population over 8 million, area ~ 2150 km²). Diagnosis of STEMI was based on clinical history, presence in the electrocardiogram of ST elevation consistent with infarction (ST elevation ≥ 2 mm in contiguous chest leads and/or ST elevation ≥ 1 mm in two or more standard leads), and elevated enzyme or troponin levels. Diagnosis of non-STEMI was based on symptoms consistent with cardiac ischaemia, electrocardiographic changes (new ST or T-wave changes except ST elevation), and elevated troponin levels. As in prior studies, participants were excluded from follow-up for the 28 days following the first admission (von Klot et al., 2009; Tonne and Wilkinson, 2013). Participants included in the analysis cohort had hospital admissions recorded in the MINAP database between 1 January 2003 and 31 March 2007 with complete data on postcode of residence (on average 14 addresses and area of 12,400 m²; postcode centroid rounded to nearest 100 m to protect confidentiality), date of admission, age, sex, and vital status at the end of follow-up; were older than 25 and lived inside the geographic range of modelled air pollution for Greater London. Vital status was obtained from the Office of National Statistics. Although 162 hospitals reported admissions meeting these criteria, many reported only a small number. These hospitals may have been outside of Greater London, but admitted individuals with residential postcodes within the study area. We therefore further restricted the analyses to individuals admitted to hospitals that had more than 10 STEMI or non-STEMI admissions between 1 January 2003 and 31 March 2007 ($n = 18,138$) (Supplementary Table 1). A total of 50 hospitals which included 98% of the admissions were included in the final analysis; mean number of admissions per hospital was 363

(SD = 305). For the analysis of mortality, follow-up continued until the date of death or 1 April 2010. For the analysis of mortality or readmission for STEMI or non-STEMI combined, follow-up continued until the date of readmission, death, or 28 February 2010. As the outcome data sources covered slightly different periods, there was one month difference in end of follow-ups. Residence at the time of hospital admission was included in the database; data were not available on complete residential history. Our study was approved by the London School of Hygiene and Tropical Medicine research ethics committee (#6298).

2.2. Covariates

Participants' age, sex, ethnicity, postcode of residence, smoking and medical history, in-hospital treatment, and prescribed medication at discharge were collected from the MINAP database (Birkhead et al., 2004). Area-level deprivation has been found to be associated with survival after cardiac admission (Tonne et al., 2005) and with air pollution concentrations (Havard et al., 2009; Hajat et al., 2013). We therefore used Index of Multiple Deprivation (IMD) 2007 data calculated at the Lower Layer Super Output Area level (on average 1500 residents, area of 402,396 m²). We adjusted models for the income domain of IMD, since the composite IMD measure includes data on air pollution levels (Goodman et al., 2011).

2.3. Air pollution exposure

Annual average air pollution concentrations for the years 2003–2010 were modelled at resolution of 20 m \times 20 m using an approach described in detail elsewhere (Beevers et al., 2013; KCLurban, 2015). In short, KCLurban is a dispersion modelling system based on Atmospheric Dispersion Modelling System model 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 emissions from the London Atmospheric Emissions Inventory (GLA, 2008). Individual-level exposure was defined as the average concentration at model grid points within 100 m of each patient's postcode centroid for each year. We included six primary traffic pollutants including nitrogen dioxide (NO_2); oxides of nitrogen (NO_x); exhaust (tailpipe emissions) and non-exhaust (brake and tyre wear and re-suspension) related primary PM_{10} and $PM_{2.5}$ (aerodynamic diameter ≤ 10 μ m and ≤ 2.5 μ m respectively). For comparison, we also included five pollutants primarily reflecting regional or urban background: ozone (O_3); total oxidant gases (O_x , $NO_2 + O_3$); (Williams et al., 2014) PM_{10} , $PM_{2.5}$ and the coarse fraction of PM_{10} ($PM_{10} - PM_{2.5}$). We also included volume of heavy goods vehicles (HGV) per 1000 total vehicle-km on major roads within 100, 200, and 300 m buffers around each patient's postcode centroid.

2.4. Traffic noise

We included traffic noise as a potential confounder of the associations between air pollution and prognosis, as well as a traffic-related exposure of interest. Noise estimates for the years 2003–2010 were modelled using the open-source TRAffic Noise EXposure (TRANEX) model based on the Calculation of Road Traffic Noise method (Gulliver et al., 2015). This model uses information on the same road traffic flows and speeds used in the air pollution model in this study, road geography, land cover, and building heights. The noise exposure model covered a slightly smaller area compared to the air pollution exposure model; <2% of participants with air pollution exposure were assigned missing noise. We included daytime A-weighted equivalent continuous sound pressure level (L_{Aeq16}) in decibels (dB) modelled at the nearest postcode centroid.

Table 1
Characteristics of participants hospitalized with myocardial infarction in London between 2003 and 2007.

Variable	n (% missing) ^a	
Mean (SD) age (year)	18,138 (0)	68 (14)
Male (%)	18,138 (0)	68
White ethnicity (%)	15,643 (14)	81
Smoking (%)	16,363 (10)	
Never		25
Ex		29
Current		32
Non-current, unknown history		14
Medical history prior to the first admission (%)		
Hypertension	15,936 (12)	52
Diabetes	15,536 (14)	21
Angina	15,792 (13)	26
Cerebrovascular disease	15,172 (16)	7
Heart failure	15,473 (15)	5
Previous AMI	16,036 (12)	21
Final diagnosis (%)	18,138 (0)	
ST elevation		46
Non-ST elevation		54
Reperfusion (%)	18,026 (1)	
None		60
Lysis		29
Primary PCI		11
Discharge drugs (%)		
ACE inhibitor	14,040 (23)	83
Beta-blocker	14,331 (21)	77
Aspirin	14,581 (20)	94
Statin	14,346 (21)	94
Mean (SD) area-level (LSOA) deprivation		
% residents in income deprivation	18,138 (0)	16 (11)

Abbreviations: AMI, acute myocardial infarction; PCI, percutaneous coronary intervention; ACE, angiotensin-converting-enzyme inhibitor; LSOA, lower super output area.

^a Percentage missing based on 18,138 sample size whereas percentage distributions for a given covariate are based on number with complete information for that covariate.

2.5. Statistical analysis

In Cox proportional hazards models, time was modelled as days of follow-up starting 28 days after hospital admission. Each admitting hospital was allowed to have its own baseline hazard rate. Therefore, our analysis investigates the association of within-hospital catchment area variation in exposure and prognosis and takes into account clustering of individuals with similar attributes other than those included in our model within a fairly small area. Air pollution concentrations were included as a time-varying exposure, where the annual average concentration was assigned to the person-time falling within the corresponding calendar year. Exposures to traffic noise and HGV volume were similarly assigned. We adjusted for clinical and individual-level demographic characteristics as well as area-level income deprivation, which were predictors of prognosis and correlated with air pollution concentrations. In the main analysis, we limited covariate adjustment to those with relatively little missing data (Table 1). Covariates were included in the following form: year of follow-up (categorical), age (age, age², and age³), reperfusion (no reperfusion treatment = reference, thrombolysis, or percutaneous coronary intervention (PCI)); STEMI (binary), area-level income deprivation (continuous); and traffic noise (continuous). The same analytical approach was used to investigate deaths and readmissions combined. We assessed violations of the proportional hazard assumption by including an interaction term with follow-up for each covariate in the fully adjusted models. Multi-pollutant analyses were not performed because of the high collinearity of the pollutants resulting in limited statistical power. The results are presented as hazard ratios (HR) for an interquartile range (IQR) increase in air pollutant concentration

with 95% confidence intervals (CI) to enable comparison of exposure metrics in relation to their ranges in the study area. Analyses were done using SAS PROC PHREG (version 9.3, SAS Institute, Cary, NC, USA).

As a sensitivity analysis, we extended confounder adjustment to also include smoking (never smoked = reference, ex-smoker, current, or non-current with unknown history); binary indicators for white ethnicity, history of diabetes, angina, and MI prior to the first admission recorded in MINAP. We also controlled for pre-scribed medication (yes vs. no) for angiotensin-converting-enzyme (ACE) inhibitors, aspirin, beta-blockers, or statins at the time of discharged from hospital. Because of the large extent of missing data in these additional covariates (Table 1), we used multiple imputation to impute missing covariates. This approach assumes data are missing at random, which is reasonable given that the pattern of missing data was mostly dependent on hospital data collection practices rather than the value of the covariate. Imputation was done using PROC MI in the SAS statistical software (version 9.3, SAS Institute, Cary, NC USA) using 10 imputations. The imputation model included all covariates in the analysis model, all air pollutants, noise, censoring, and indicator variables for each hospital. Hazard ratios (HR) were estimated using a Cox proportional hazards model fit to each imputed dataset and combined to get an overall HR using PROC MIANALYZE.

3. Results

Participants had a mean age of 68 years, were mostly white (81%) and male (68%) (Table 1). Of first admissions in the database, 54% were non-STEMI, whereas 80% of readmissions were. There were a total of 5129 deaths and 390 readmissions for STEMI or non-STEMI; the average duration of follow up to death was 4.0 years (SD = 1.9, Min = 0, Max = 7.2). Distributions of air pollution exposure, road traffic noise, and HGV traffic are presented in Table 2. The coefficient of variation was greater for primary traffic pollutants compared to pollutants representing regional and urban background. Correlations between the modelled exposures are provided in Supplemental Table 2. In general, correlations between pollutants were positive ranging from 0.41 (between PM_{2.5} and O_x) to 1.00 (between NO₂ and NO_x), except for correlations between O₃ and the other pollutants, which were negative ranging from -0.75 to -0.92. Correlations were weaker between air pollutants and noise; the strongest correlation was 0.54 between noise and PM non-exhaust fraction.

Associations for air pollutants with all-cause mortality are presented with and without adjustment for road traffic noise in Table 3. Hazard ratios without adjustment for noise were positive ranging between 1.02 and 1.06, except for O₃ which was negatively associated with mortality. Further adjustment for traffic noise slightly attenuated the associations and decreased the precision of the estimates. Noise adjusted associations were largest in magnitude for PM₁₀ from non-exhaust traffic sources and coarse fraction of PM. Additional confounder adjustment (Supplemental Table 3) did not materially change the results from those in Table 3.

Results for analyses combining all-cause mortality and readmission to hospital for STEMI or non-STEMI (Table 4) were broadly similar to those from analyses including mortality only. Adjustment for traffic noise slightly attenuated the associations. Noise adjusted associations were largest in magnitude for PM₁₀ and PM_{2.5}. Results with additional confounder adjustment (Supplemental Table 4) were broadly similar.

Small positive but imprecise associations were observed between road traffic noise and prognosis (Table 5). Associations between HGV traffic near residence and prognosis were also positive, but small in magnitude.

Table 2

Distribution of exposure to air pollution, road traffic noise, and heavy goods vehicle traffic volume within person-time of follow-up to death.

Exposure	Mean (SD)	P25	Median (P50)	P75	IQR	COV
Primary traffic ($\mu\text{g}/\text{m}^3$)						
NO ₂	37.1 (6.4)	32.6	36.3	40.6	7.9	0.17
NO _x	61.8 (16.3)	50.5	59.0	69.7	19.2	0.26
PM ₁₀ exhaust	0.7 (0.3)	0.5	0.6	0.8	0.3	0.43
PM ₁₀ non-exhaust	2.3 (0.9)	1.7	2.2	2.8	1.1	0.39
PM _{2.5} exhaust	0.6 (0.3)	0.4	0.6	0.7	0.3	0.50
PM _{2.5} non-exhaust	0.7 (0.3)	0.5	0.6	0.8	0.3	0.43
Regional/urban background ($\mu\text{g}/\text{m}^3$)						
O ₃	40.3 (4.0)	37.8	40.5	43.1	5.3	0.10
O _x	77.4 (3.6)	75.4	76.7	78.6	3.2	0.05
PM ₁₀	23.2 (1.9)	21.9	22.9	24.1	2.2	0.08
PM _{2.5}	14.6 (1.3)	13.7	14.4	15.2	1.5	0.09
PM coarse	8.6 (0.7)	8.1	8.5	9.0	0.9	0.08
Road traffic Noise (dB)						
L _{Aeq16}	58.1 (5.2)	55.0	55.4	58.8	3.8	0.09
HGV traffic (per 1000 km)						
Within 100 m buffer	84.9 (166.5)	0	0	120.6	120.7	1.96
Within 200 m buffer	358.9 (519.9)	10.6	218.5	487.2	476.6	1.45
Within 300 m buffer	823.27 (1005.3)	201.4	583.4	1057.6	856.1	1.22

Abbreviations: P, percentile; IQR, interquartile range; COV, coefficient of variation; NO₂, nitrogen dioxide; NO_x, nitrogen oxides; PM₁₀, particulate matter <10 μm ; PM_{2.5}, particulate matter <2.5 μm ; PM coarse, PM_{10-2.5}; O₃, ozone; O_x, oxidant gases (NO₂ + O₃); L_{Aeq16}, A-weighted equivalent continuous sound pressure level; HGV, heavy goods vehicle.

4. Discussion

Our analysis resulted in several main findings. First, there was a consistent pattern of modest, positive associations between air pollutants other than O₃ and prognosis. Second, there was no indication that primary traffic pollutants were more strongly associated with prognosis compared to regional or urban background pollutants. Third, traffic noise was only moderately correlated with air pollution and did not fully explain the observed associations with air pollution. Fourth, there was a small, positive association between traffic noise and prognosis independent of air pollution exposure.

Correlations across air pollutants were high, likely explaining the pattern of positive associations with several pollutants. High

correlations between pollutants are largely due to the exposure model which uses similar input data on emission sources and dispersion processes for several of the pollutants. However, the exposure model attempts to reflect observed correlations in measured concentrations. Among primary traffic pollutants, the largest associations with prognosis were for NO₂ and non-exhaust PM, a marker of brake and tyre wear. However, these associations were similar in magnitude to those for several regional pollutants such as PM_{2.5}, PM₁₀, and coarse fraction of PM. Negative associations between annual mean O₃ and mortality, have been observed elsewhere (Carey et al., 2013). Negative associations between O₃ and prognosis in our results are likely explained by the high negative correlations between O₃ and particle concentrations (e.g. PM_{2.5}), for which there is strong evidence of associations with mortality

Table 3Hazard ratios^a and 95% CI for all-cause mortality per interquartile range increase in exposure.

Exposure	IQR ($\mu\text{g}/\text{m}^3$)	Covariate adjusted HR (95% CI) (n = 5104 events)	Covariate + noise adjusted HR (95% CI) (n = 4950 events)
Primary traffic			
NO ₂	8.0	1.04 (0.99, 1.10)	1.04 (0.97, 1.10)
NO _x	19.2	1.03 (0.98, 1.08)	1.02 (0.97, 1.08)
PM ₁₀ exhaust	0.3	1.02 (0.99, 1.06)	1.01 (0.97, 1.06)
PM ₁₀ non-exhaust	1.1	1.05 (1.00, 1.10)	1.05 (0.99, 1.11)
PM _{2.5} exhaust	0.3	1.02 (0.98, 1.07)	1.02 (0.97, 1.06)
PM _{2.5} non-exhaust	0.3	1.04 (1.00, 1.09)	1.04 (0.99, 1.09)
Regional/urban background			
O ₃	5.3	0.97 (0.91, 1.04)	0.98 (0.91, 1.05)
O _x	3.2	1.05 (1.00, 1.09)	1.04 (0.99, 1.09)
PM ₁₀	2.2	1.05 (0.99, 1.12)	1.04 (0.97, 1.12)
PM _{2.5}	1.5	1.06 (0.98, 1.14)	1.04 (0.95, 1.14)
PM coarse	0.9	1.05 (1.00, 1.10)	1.05 (0.99, 1.11)

Abbreviations: IQR, interquartile range; NO₂, nitrogen dioxide; NO_x, nitrogen oxides; O₃, ozone; O_x, oxidant gases (NO₂ + O₃); PM_{2.5}, particulate matter <2.5 μm ; PM₁₀, particulate matter <10 μm ; PM coarse, PM_{10-2.5}.

^a All models stratified by admitting hospital. Covariates modelled as age (age, age², age³), time (year of follow-up, categorical), sex, reperfusion (none, lysis, PCI), STEMI (yes/no), and area-level income deprivation (continuous).

Table 4Hazard ratios^a and 95% CI for combined all-cause mortality and hospital readmission for myocardial infarction per interquartile range increase in exposure.

Exposure	IQR ($\mu\text{g}/\text{m}^3$)	Covariate adjusted HR (95% CI) (n = 5490 events)	Covariate + noise adjusted HR (95% CI) (n = 5326 events)
Primary traffic			
NO ₂	8.0	1.05 (0.99, 1.10)	1.04 (0.98, 1.11)
NO _x	19.2	1.03 (0.99, 1.08)	1.03 (0.98, 1.08)
PM ₁₀ exhaust	0.3	1.02 (0.98, 1.05)	1.01 (0.97, 1.06)
PM ₁₀ non-exhaust	1.1	1.04 (0.99, 1.08)	1.04 (0.99, 1.10)
PM _{2.5} exhaust	0.3	1.02 (0.98, 1.06)	1.02 (0.97, 1.06)
PM _{2.5} non-exhaust	0.3	1.03 (0.99, 1.08)	1.03 (0.98, 1.08)
Regional/urban background			
O ₃	5.3	0.96 (0.90, 1.02)	0.96 (0.89, 1.03)
O _x	3.2	1.04 (1.00, 1.08)	1.04 (0.99, 1.09)
PM ₁₀	2.2	1.05 (0.99, 1.11)	1.05 (0.98, 1.12)
PM _{2.5}	1.5	1.06 (0.98, 1.14)	1.05 (0.97, 1.15)
PM coarse	0.9	1.04 (0.99, 1.09)	1.04 (0.98, 1.10)

Abbreviations: IQR, interquartile range; NO₂, nitrogen dioxide; NO_x, nitrogen oxides; O₃, ozone; O_x, oxidant gases (NO₂ + O₃); PM_{2.5}, particulate matter <2.5 μm ; PM₁₀, particulate matter <10 μm ; PM coarse, PM_{10-2.5}.

^a All models stratified by admitting hospital. Covariates modelled as age (age, age², age³), time (year of follow-up, categorical), sex, reperfusion (none, lysis, PCI), STEMI (yes/no), and area-level income deprivation (continuous).

Table 5
Hazard ratios^a and 95% CI for road traffic noise and HGV volume associated with all-cause mortality and mortality and readmission for myocardial infarction combined.

Exposure	Unit change	HR (95% CI) All-cause mortality	HR (95% CI) All-cause mortality or readmission
L_{Aeq16} ^b	5 dB	1.02 (0.99, 1.06)	1.02 (0.99, 1.05)
HGV traffic within 100 m	120.7 (IQR)	1.02 (1.00, 1.04)	1.01 (0.99, 1.03)
HGV traffic within 200 m	476.6 (IQR)	1.02 (0.99, 1.05)	1.01 (0.98, 1.04)
HGV traffic within 300 m	856.1 (IQR)	1.01 (0.98, 1.04)	1.01 (0.98, 1.03)

Abbreviations: L_{Aeq16} A-weighted equivalent continuous daytime sound pressure level; HGV heavy goods vehicle.

^a All models stratified by admitting hospital. Covariates modelled as age (age, age², age³), time (year of follow-up, categorical), sex, reperfusion (none, lysis, PCI), STEMI (yes/no), and area-level income deprivation (continuous).

^b Further adjustment for PM_{2.5} (continuous).

(HEI, 2000). Because of strong collinearity between pollutants and limited statistical power, we did not fit multi-pollutant models; therefore, we were not able to identify the single pollutant most strongly associated with prognosis.

The majority of deaths among these MI survivors is likely to do be due to cardiovascular causes (Rosenbloom et al., 2012); however, without cause of death data we were not able confirm that air pollution and road traffic noise influenced cardiovascular rather than other causes. Nonetheless, evidence supports biological mechanisms linking particulate air pollution with ischaemic events like MI and cardiovascular death as well as noise exposure with cardiovascular disease. Inhaled particles may stimulate lung nerve reflexes and consequently alter systemic autonomic balance within minutes to hours of elevated exposure, thereby triggering cardiovascular events (Brook et al., 2010; Brook, 2008). Epidemiological evidence indirectly suggests that MI survivors have higher risk of hospital readmission for cardiac causes due to air pollution exposure in the preceding hours compared to the general population (von Klot et al., 2005). Longer term exposures are likely to augment risk of cardiovascular events due to systemic inflammation induced by oxidative stress and inflammation in the lung (Brook et al., 2010; Brook, 2008). Whether MI survivors are also more susceptible compared to the general population for pathways related to longer term exposure is unclear. Evidence from experimental studies provides plausibility for the link between long term exposure to environmental noise and cardiovascular diseases including hypertension, ischaemic heart disease, and stroke (Basner et al., 2014). Potential mechanisms include stress reactions to perceived discomfort, and non-conscious physiological stress from interaction between the auditory and other regions of the central nervous system (Basner et al., 2014; Muenzel et al., 2014). Long term noise exposure can lead to an imbalance in allostatic load, affecting metabolism and subsequently increased cardiovascular risk factors including blood pressure, blood lipid and glucose concentrations, and viscosity (Basner et al., 2014; Muenzel et al., 2014). These risk factors elevate the risk of severe events including MI, stroke, and cardiovascular death.

Our results for all-cause mortality are broadly comparable with similar studies of long-term exposure to air pollution in Europe within general populations (Beelen et al., 2014; Carey et al., 2013; Tonne and Wilkinson, 2013; Cesaroni et al., 2013). Although more imprecise, the magnitude of association for PM_{2.5} in our study (HR 1.06 (95% CI 0.98, 1.14)) is larger than those reported in several comparable studies, none of which adjusted for traffic noise. For the equivalent change in concentration as used in our study (1.5 µg/m³), covariate adjusted HRs for PM_{2.5} and mortality were

1.02 (95% CI 1.01, 1.04) in the ESCAPE study of multiple cohorts (Beelen et al., 2014); 1.02 (95%CI 1.00, 1.04) in the national English cohort (Carey et al., 2013); and 1.01 (95% CI 1.00, 1.01) for a cohort in Rome (Cesaroni et al., 2013). Similarly for NO₂, a better marker of traffic-related pollution, equivalent HRs (per 8 µg/m³) were 1.01 (0.99, 1.02) from ESCAPE; 1.02 (95% CI 1.00, 1.03) for the English national cohort; and 1.02 (1.02, 1.03) for the cohort in Rome compared to 1.04 (95% CI 0.99, 1.10) in our study. Our estimates are also larger in magnitude compared to equivalent estimates in a similar population of MI survivors in England and Wales: 1.03 (95% CI 1.01, 1.05) for PM_{2.5} and 1.01 (95% CI 0.98, 1.03) for NO₂ (Tonne and Wilkinson, 2013). Compared to the study including MI survivors across England and Wales, the larger estimates for London may be a reflection of the higher spatial resolution of the exposure models and reduction in exposure misclassification; however, we also had more limited statistical precision compared to this larger study.

Evidence is limited regarding the health effects of long-term exposure to non-exhaust traffic particles. Nonetheless, this evidence is increasingly important given that these particles may have relatively higher capacity to induce oxidative damage in the lungs compared to exhaust particles (Kelly et al., 2011), and because current emission controls have reduced tailpipe emissions (Hoek et al., 2013). In agreement with our findings among MI survivors, the California Teachers Study reported strong associations between non-tailpipe PM_{2.5} components (namely iron, zinc and silicon that have been related to brake and tyre wear (Kelly et al., 2011) and re-suspended road dust) and ischaemic heart disease mortality (Ostro et al., 2010). Our observed association between coarse particulate matter and mortality can be compared with prior studies in general-population cohorts. Positive non-significant associations have been observed in Europe with natural-cause mortality (Beelen et al., 2014). No clear association was observed between coarse PM and all-cause and coronary heart disease mortality in a large cohort of US women (Puett et al., 2009).

There is relatively little evidence available regarding the link between road traffic noise and mortality, particularly all-cause mortality. The most comparable results to ours are from a cohort study in the Netherlands which reported a positive non-significant association between road noise Lden >65 vs. ≤50 dB(A) and all-cardiovascular mortality after adjustment for air pollution (Beelen et al., 2009). In a London-based small-area study using the same noise exposure model, daytime noise was significantly associated with all-cause mortality in areas with >60 dB relative to those with <55 dB: RR 1.04 (95% CI 1.00–1.07) after adjusting for PM_{2.5} (Halonen et al., 2015). However, we found no prior individual-level studies reporting associations for all-cause mortality in general populations or among MI survivors. Our results, therefore, fill an important gap in the literature. The plausibility of a link with post-MI prognosis is supported by evidence from a meta-analysis of a positive association between road traffic noise and any coronary heart disease event (prevalence, incidence and mortality) (Babisch, 2014).

The strengths of this study include the comprehensive accounting for important differences in case management across hospitals by using detailed clinical data on treatments within the MINAP database and by allowing each hospital to have its own baseline hazard. The highly spatially resolved exposure data for a wide range of air pollutants and noise is another improvement to prior, similar studies. We are aware of no similar study among MI survivors that adjusted air pollution estimates for traffic noise and reported the independent effects of noise on prognosis.

The main limitation of this study was limited statistical power due to relatively little variation in exposure within each hospital catchment area. There were several positive associations between air pollutants and prognosis, even after adjusting for noise; however, precision of the estimates was limited. Large numbers of

events are required for studies of within-city variation in traffic pollution, which even in Europe's largest city varied little. Also, we were not able to examine cause-specific mortality as these data were not available in the MINAP database. Due to low numbers, separate analyses by cause of death would have had even more limited statistical power. Postcode centroid coordinates in MINAP were rounded for purposes of patient confidentiality, resulting in loss of accuracy of the air pollution and noise exposure estimation and likely bias towards the null. Complete data on residential history of participants were not available. However, we explored the stability of residential postcodes over time among individuals who were re-admitted to hospital; only 5% of participants moved between first and second admission in the database. In sensitivity analyses we adjusted for individual-level smoking and clinical history, which are likely to be important mediators of the relationship between an individual's socioeconomic position and prognosis. Several studies have shown that area-level measures of deprivation are more correlated with air pollution exposure than individual-level deprivation, thus, adjustment for area-level socioeconomic factors can essentially remove the correlation between individual-level deprivation and air pollution exposure (Goodman et al., 2011; Naess et al., 2007). Lack of data on individual-level deprivation is therefore not likely to be an important limitation of our analysis. Finally, we adjusted for prescribed medication at discharge, but did not have data on drugs taken during follow-up or other secondary prevention measures, which may have resulted in some residual confounding.

In conclusion, these findings provide additional support that long-term exposure to air pollution is associated with all-cause mortality and hospital readmission for MI among MI survivors. These associations were not fully explained by road traffic noise, which may also have an independent effect on prognosis. There was no evidence that primary traffic pollutants were more strongly associated with prognosis compared to pollutants reflecting regional or urban background. Further investigation using very large studies enabling multi-pollutant models are required to further identify which pollutants and sources are primarily responsible for observed health effects.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.ijheh.2015.09.003>.

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