European Heart Journal (2005) **26**, 2543–2549
doi:10.1093/eurheartj/ehi457

Clinical research

Outdoor air pollution, mortality, and hospital admissions from coronary heart disease in Sheffield, UK: a small-area level ecological study

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Received 8 March 2005; revised 18 July 2005; accepted 22 July 2005; online publish-ahead-of-print 15 September 2005

KEYWORDS
Air pollution;
Coronary disease;
Hospitalization;
Mortality

Aims To examine the hypothesis that coronary heart disease mortality and emergency hospital admission rates are higher in areas with higher outdoor air pollution levels.
Methods and results Modelled nitrogen oxides (NO_x), particulate matter (PM_{10}), and carbon monoxide (CO) levels were interpolated to 1030 census enumeration districts using an ecological study design. Results, based on 6857 deaths and 11 407 admissions from 1994–98 and a population of 199 682 aged ≥45 years, were adjusted for age, sex, deprivation, and smoking prevalence. Mortality rate ratios were 1.17 (95% CI 1.06–1.29), 1.08 (95% CI 0.96–1.20), and 1.05 (95% CI 0.95–1.16) in the highest relative to the lowest NO_x, PM_{10}, and CO quintile categories, respectively. Corresponding admission rate ratios were 1.00 (95% CI 0.90–1.10), 1.01 (95% CI 0.90–1.14), and 0.88 (95% CI 0.79–0.98).
Conclusion The results are consistent with an excess risk of coronary heart disease mortality in areas with high outdoor NO_x, a proxy for traffic-related pollution, but residual confounding cannot be ruled out. If causality were assumed, 6% of coronary heart disease deaths would have been attributable to outdoor NO_x, and targeting pollution reduction measures at high pollution areas would be an option for coronary mortality prevention.

Introduction

Numerous daily time-series studies have found increase in the risk of mortality and hospital admissions from cardiorespiratory disease with increasing levels of outdoor air pollution.[1] A few have specifically examined coronary heart disease, finding evidence for acute effects on mortality and hospital admissions.[2–5] Case-crossover studies suggest that elevated outdoor air pollution levels and exposure to traffic transiently increase the risk of myocardial infarction within 1–48 h of exposure,[6–8] although a further case-crossover study found no evidence of a link with primary cardiac arrest.[9] Medium-term effects of outdoor air pollution on mortality may be larger than short-term effects,[10–12] with one study specifically examining coronary heart disease.[11] Chronic exposure to current outdoor air pollution levels, to which road traffic emissions are a major contributor, may have even larger impacts on mortality than acute exposure.[13] Four cohort studies have examined the effect of chronic exposure to outdoor air pollution on cardiopulmonary mortality,[14–19] with three finding evidence of increased risk[14,15,18] and a cause-specific analysis reporting an association with coronary heart disease.[19] A further cohort study found an increased risk of coronary heart disease mortality with chronic exposure to nitrogen oxides (NO_x).[20]

The evidence suggests that coronary heart disease mortality and hospital admissions should be higher in areas with elevated levels of outdoor air pollution because of its combined acute and chronic exposure effects. Evidence of raised coronary heart disease risk in high pollution areas would support targeting of policy interventions on such areas to reduce pollution levels. Ecological studies carried out using small areal units offer a useful means of examining disease risk at the geographical level. There may be substantial variation in outdoor air pollution levels within a small spatial scale, particularly in relation to road traffic pollution. Ecological studies using small areal units can successfully capture fine grain variation in outdoor air pollution levels, increasingly available through the use of air pollution models.[21] In addition, population characteristics, including exposure levels, are likely to be more homogeneous within small geographical areas. Also, as these areas are usually

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defined at censuses, there will be information on socioeconomic deprivation, allowing adjustment for its confounding effect.

We examined the hypothesis that coronary heart disease mortality and hospital admission rates are higher in areas with higher levels of outdoor air pollution, using a small-area level ecological correlation study.

Methods

We used 1030 census enumeration districts (CEDs) as the unit of analysis. We examined routinely collected data on coronary heart disease deaths [International Classification of Diseases, ninth revision (ICD-9) 410–414] for 1994–98 from the national death registration system and emergency hospital admissions (ICD-10, I20–I25) from April 1994 to March 1999 from the national hospital episode statistics system. We used 1991 census denominator populations corrected for underenumeration[22] and scaled to mid-year estimates for Sheffield Health Authority by age and sex for 1994–98.

Modelled air pollution data for particulate matter (PM_{10}) less than 10 μm in diameter, NO_x and carbon monoxide (CO), generated at a 200 m grid square resolution using an air pollution model (Indic-AirViro, SMHI Inc.), were provided by Sheffield City Council. The pollution model incorporated points (e.g. factories), lines (e.g. roads), and grids (e.g. background emissions from housing estates) as sources of pollution and meteorological data. Models were run for 1994–99 (excluding 1998 owing to incomplete meteorological data) and the 5-year average was calculated. We have reported previously on model validation using visual inspection of pollution maps and comparison with monitored pollution values, and the limitations of these modelled data.[21,23] Essentially, the patterns of pollution on NO_x, CO, and PM_{10} maps appeared valid but there were six circumscribed areas (108 CEDs) with erroneously high levels owing to errors in the emissions database on the PM_{10} map. These CEDs were therefore excluded before any statistical analysis was undertaken. In addition, the model appeared to overestimate absolute levels of NO_x and underestimate absolute levels of CO when compared with monitored levels and therefore we rescaled modelled values to monitored equivalent values using linear regression. We interpolated modelled values to CEDs, taking into account population locations within CEDs using postcodes weighted by the number of domestic delivery points within each postcode, using previously described methodology.[24] We then categorized pollution values by quintile, aiming for an equal number of CEDs within each quintile. In view of the limitations of the modelled data, we decided to carry out the analyses using quintiled categories rather than analyse pollutants as continuous variables and provide rate ratios per unit increase in pollutant. In addition, analysis by quintile does not make assumptions about linearity.

To examine if estimates of the exposure effect would be improved by taking into account daily local population movements with consequent variation in exposure, we also calculated average exposures using a 1 km radius around each postcode centroid and interpolated these spatially averaged values to CEDs.[21] We chose this distance because surveys indicate that 1 km is the average walking journey length.[25] We then categorized these smoothed pollution values by quintile.

We used the Townsend index, a widely used deprivation index in the UK, to adjust for socioeconomic deprivation at the CED level.[26] This is a standardized combination of four 1991 census variables: the proportion of economically active residents who were unemployed; the proportion of households without a car; the proportion of households not owner-occupied; and the proportion of overcrowded households.

To adjust for cigarette smoking prevalence, we used survey data from a random sample of adults (66% response rate) carried out in 2000. Of the 9821 respondents, 2532 with complete smoking information were current smokers (25.8%). Ward level smoking prevalence (there were 29 electoral wards in Sheffield) was attributed to all CEDs within each ward.

Statistical analysis

We used Poisson regression methods in SAS.[27] We grouped CED level data by sex and age band (nine categories from 45–54 to 85+ years) and pollutant category, deprivation category, and smoking prevalence by quintiles. The effect of each of the pollutants was examined in separate analyses adjusted for age, sex, deprivation, and smoking prevalence. We included an age-by-deprivation interaction as this has previously been found to be substantial in magnitude.[28] The results are presented as rate ratios with 95% confidence intervals (CI). Analyses were then rerun, substituting unsmoothed pollution variables with the 1 km radius smoothed variables. *P*-values are two-sided and $P < 0.01$ may be considered significant to take account of the three pollutants examined.

Factors that may affect model assumptions include non-linearity, overdispersion, and spatial autocorrelation. Non-linearity was addressed using quintiled categories. We adjusted 95% CIs for overdispersion (deviance/df = 1.2). We examined for spatial autocorrelation in model residuals between neighbouring areas using a conditional autoregressive spatial model.[29] We found no evidence of spatial autocorrelation after age, sex, and socioeconomic deprivation had been taken into account.

Basic results are presented as rates directly standardized for age and sex, using the population of the study area as the standard. Population attributable risk fraction was calculated using the formula:

$$\sum\left[\frac{p_i(RR_i - 1)}{p_i(RR_i - 1) + 1}\right]$$

where p_i is the proportion of the population in category i; and RR_i the relative risk in category i.

Results

The analysis was based on 6857 deaths and 11 407 emergency hospital admissions from coronary heart disease in people aged ≥45 years in the 5-year period within the study area. The corresponding denominator population was 199 682 (998 408 person-years), giving an average of 194 people aged ≥45 years per CED. Deaths, admissions, and age and sex-specific rates are shown in *Table 1*. Rates were higher for men and increased with age in both sexes, although admission rates tended to level off in the oldest age bands. Correlation coefficients for NO_x with PM_{10} and CO for CEDs were 0.87 and 0.88, respectively, and 0.82 for PM_{10} with CO. *Table 2* shows mean values and category limits by quintiles, age and sex standardized mortality, and admission rates and population counts within categories. Rates generally increased with increasing pollution, socioeconomic deprivation, and smoking prevalence.

Mortality

Table 3 shows the effect of the three pollutants on mortality after adjustment for age and sex, and then further adjustment for socioeconomic deprivation and smoking prevalence. Mortality rate ratios generally rose across pollutant categories, although there was inconsistency across the highest CO categories. Further adjustment for deprivation and smoking prevalence diminished mortality rate ratios.

For NO_x, after adjustment for age, sex, deprivation, and smoking prevalence, there was a significant association with mortality [χ^2 (LR) = 14.6, df = 4, $P = 0.0055$], with a

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Table 1 Deaths, hospital admissions, and population counts and rates by age and sex for coronary heart disease (Sheffield, UK 1994–98)

Age (years)	Deaths (1994–98)	Admissions (1994–98)	Annual mortality per 100 000 (95% CI)	Annual admissions per 100 000 (95% CI)	Population
Women					
85 +	1007	696	2578 (2425–2740)	1782 (1655–1918)	7813
80–84	702	829	1674 (1556–1801)	1977 (1848–2114)	8387
75–79	621	906	1126 (1042–1218)	1643 (1540–1753)	11 027
70–74	437	854	703 (640–771)	1373 (1285–1468)	12 437
65–69	219	645	359 (314–409)	1057 (979–1141)	12 207
60–64	115	503	183 (152–219)	799 (732–871)	12 595
55–59	51	376	76 (58–100)	563 (509–623)	13 351
50–54	20	218	26 (17–41)	286 (251–327)	15 228
45–49	13	144	16 (9–28)	179 (152–210)	16 113
Total	3185	5171	584 (564–604)	947 (922–973)	109 159
Men					
85 +	440	264	3378 (3081–3702)	2027 (1799–2283)	2605
80–84	543	551	2535 (2333–2755)	2573 (2369–2793)	4283
75–79	795	943	2230 (2081–2388)	2645 (2483–2816)	7131
70–74	722	949	1481 (1378–1592)	1947 (1828–2073)	9750
65–69	476	904	893 (817–977)	1696 (1590–1809)	10 659
60–64	318	928	543 (486–605)	1584 (1486–1688)	11 721
55–59	183	776	281 (243–324)	1190 (1109–1276)	13 045
50–54	113	550	150 (125–181)	732 (674–796)	15 027
45–49	82	371	101 (81–125)	455 (411–504)	16 302
Total	3672	6236	811 (786–838)	1378 (1344–1412)	90 523
Total men and women	6857	11 407	687 (671–703)	1143 (1122–1164)	199 682

rate ratio of 1.17 (95% CI 1.06–1.29) in the highest relative to the lowest NO_x category. The trend across categories was also significant [χ^2 (LR) = 10.1, df = 1, $P = 0.0015$]. For PM_{10}, the association and trend were not significant, with an adjusted rate ratio of 1.08 (95% CI 0.96–1.20) in the highest PM_{10} category. Adjustment for deprivation reduced the (age- and sex-adjusted) rate ratio from 1.30 (95% CI 1.19–1.43) to 1.17 (95% CI 1.07–1.29), with further adjustment for smoking prevalence reducing it to 1.08 (95% CI 0.96–1.20). For CO, although the rate ratios were different across categories [χ^2 (LR) = 13.7, df = 4, $P = 0.0084$], the test for trend was of borderline significance [χ^2 (LR) = 4.4, df = 1, $P = 0.037$]. This was because of inconsistency across categories, with an adjusted rate ratio of 1.05 (95% CI 0.95–1.16) in the highest, but 1.16 (95% CI 1.06–1.28) in the second highest CO category.

Table 3 also shows the effect of 1 km spatially smoothed pollution values on rate ratios adjusted for deprivation, smoking, age, and sex. For all three pollutants, the smoothed values generally tended to marginally diminish rate ratios when compared with rate ratios obtained using unsmoothed values.

Hospital admissions

Table 3 shows the effect of the three pollutants on emergency hospital admissions before and after additional adjustment for deprivation and smoking prevalence. Before adjustment for these two confounding variables, rate ratios generally increased with increasing pollution levels. However, adjustment for these confounders appeared to abolish any evidence of association for all three pollutants.

The effect of 1 km spatially smoothed pollution estimates on admission rate ratios, adjusted for age, sex, deprivation, and smoking prevalence, is shown in *Table 3*. These smoothed pollution estimates made little difference to the overall flat pattern in rate ratios observed for all three pollutants.

Discussion

We observed a 17% (95% CI 6–29%) excess risk of coronary heart disease mortality in areas with high levels of outdoor NO_x after adjustment for age, sex, socioeconomic deprivation, and smoking prevalence. We also observed weaker and inconsistent associations between PM_{10} and CO levels and coronary heart disease mortality. There was no evidence of association between all three pollutants and emergency hospital admissions for coronary heart disease after adjustment for confounders. Spatially smoothed pollution estimates using a 1 km radius did not appear to make any substantial difference to observed rate ratios. The results are consistent with an excess risk of coronary heart disease mortality associated with living in areas with high outdoor NO_x levels, a marker for traffic-related pollution.

We are not aware of any published ecological studies on the association between outdoor air pollution levels and coronary heart disease carried out at the small-area level. A cohort study examining chronic exposure to NO_x observed a relative risk of 1.08 (95% CI 1.03–1.12) for coronary heart disease mortality for a 10 $\mu g/m^3$ increase in NO_x levels.[20]

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Table 2 Mean values and category limits for modelled (unsmoothed) NO_x, PM_{10}, and CO levels, socioeconomic deprivation, smoking prevalence, age and sex standardized mortality, hospital admission rates for coronary heart disease, population counts, and number of CEDs within categories (Sheffield, UK, 1994–98)

Category by quintile	Mean value (category limits)	Annual mortality per 100 000 (95% CI)	Annual admissions per 100 000 (95% CI)	Population (CEDs)
NO_x ($\mu g/m^3$)				
5	61.9 (≥57.7)	811 (767–856)	1300 (1244–1357)	31 749 (206)
4	55.8 (≥54.2 to <57.7)	735 (696–773)	1165 (1116–1214)	36 801 (206)
3	53.0 (≥52.0 to 54.2)	657 (623–692)	1144 (1098–1190)	41 333 (207)
2	50.9 (≥49.6 to <52.0)	673 (639–708)	1166 (1121–1211)	44 151 (205)
1	47.6 (<49.6)	601 (568–633)	994 (952–1035)	45 647 (206)
PM_{10} ($\mu g/m^3$)				
5	23.3 (≥20.6)	793 (748–839)	1368 (1309–1428)	29 805 (185)
4	19.8 (≥19.3 to <20.6)	750 (708–792)	1182 (1129–1235)	32 121 (184)
3	18.8 (≥18.2 to <19.3)	677 (639–716)	1124 (1074–1174)	34 711 (186)
2	17.5 (≥16.8 to <18.2)	652 (617–686)	1093 (1048–1137)	42 828 (183)
1	16.0 (<16.8)	613 (577–648)	1010 (965–1 055)	38 843 (184)
CO ($\mu g/m^3$)				
5	482 (≥455)	739 (698–781)	1225 (1171–1280)	31 212 (206)
4	443 (≥433 to <455)	778 (739–818)	1215 (1165–1264)	38 343 (206)
3	426 (≥419 to <433)	689 (653–726)	1173 (1126–1220)	39 893 (206)
2	405 (≥387 to <419)	648 (616–681)	1114 (1071–1157)	45 805 (206)
1	360 (<387)	602 (568–635)	1024 (981–1 067)	44 429 (206)
Socioeconomic deprivation (score)				
5 (most deprived)	6.71 (≥5.44)	777 (737–818)	1449 (1393–1505)	34 381 (207)
4	4.33 (≥3.11 to <5.44)	732 (697–768)	1373 (1323–1422)	41 737 (206)
3	1.56 (≥0.09 to <3.11)	730 (694–766)	1116 (1071–1162)	40 385 (205)
2	−0.94 (≥−2.07 to <0.09)	642 (607–678)	951 (907–994)	39 987 (206)
1 (least deprived)	−3.48 (<−2.07)	538 (504–572)	847 (806–889)	43 192 (206)
Smoking prevalence (%)				
5	36.0 (≥31.0)	809 (769–850)	1449 (1396–1503)	38 343 (229)
4	28.8 (≥27.6 to <31.0)	719 (681–758)	1260 (1209–1311)	36 970 (205)
3	26.5 (≥25.7 to <27.6)	696 (659–733)	1172 (1125–1220)	39 277 (183)
2	21.4 (≥18.7 to <25.7)	633 (599–666)	1030 (988–1 073)	44 534 (213)
1	16.8 (<18.7)	590 (556–624)	834 (794–874)	40 558 (200)

A case–control study found that exposure to the highest tertile of outdoor nitrogen dioxide (NO_2) levels was associated with a relative risk of 1.43 (95% CI 1.07–1.92) for myocardial infarction.[30] Two large cohort studies reported relative risks for cardiopulmonary mortality ranging from 1.26 to 1.37 for the most polluted areas when compared with the least polluted areas.[14,15] Further analysis of one of these cohorts found a relative risk of 1.18 (95% CI 1.14–1.23) for coronary heart disease mortality associated with a 10 $\mu g/m^3$ increase in $PM_{2.5}$.[19] Another cohort study examining traffic-related air pollution observed a relative risk of 1.95 (95% CI 1.09–3.52) for cardiopulmonary mortality associated with living near a major road.[18]

A recent scientific statement from the American Heart Association has described several plausible mechanistic pathways by which air pollution could increase the risk of coronary heart disease, including enhanced coagulation and thrombosis, a propensity for arrhythmias, acute arterial vasoconstriction, systemic inflammatory responses, and the chronic promotion of atherosclerosis.[31] However, relatively few studies have specifically examined NO_x. Peters *et al.*[32] examined whether patients with implanted cardioverter defibrillators experienced potentially life-threatening arrhythmias after air pollution episodes and found that a 26 p.p.b. increase in NO_2 was associated with increased defibrillator discharges 2 days later. Takano *et al.*[33] found that chronic exposure to ambient levels of NO_2 raised triglyceride concentrations and decreased HDL to total cholesterol ratios in obesity-prone rats, suggesting a mechanism through increased atherogenic risk. It has been postulated that fine particulate air pollution provokes alveolar inflammation, causing the release of potentially harmful cytokines which result in increased coagulability.[34] Experiments on healthy non-smoking humans have shown that NO_2 exposure also has an inflammatory effect.[35] If NO_x is viewed as a marker for outdoor pollution, then there is evidence that the complex mix of pollutants may act through other mechanisms including effects on plasma viscosity,[36] fibrinogen,[37] arterial vasoconstriction,[38] and autonomic function.[39] In addition, there is epidemiological evidence for general pathophysiological pathways of disease related to long-term exposure.[19]

The association between NO_x, and to a lesser extent PM_{10} and CO, and coronary heart disease mortality remained after adjustment for socioeconomic deprivation and smoking prevalence, but there was no evidence of any association with emergency admissions after adjustment for these confounders. One potential explanation is that a

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Table 3 Rate ratios for mortality and emergency hospital admissions from coronary heart disease in relation to modelled outdoor air pollution (NO_x, PM_{10}, and CO) quintile categories (Sheffield, UK, 1994–98)

	Rate ratios (95% CI)	
	Mortality	Hospital admissions
NO_x		
Adjusted for sex and age (not spatially smoothed)		
5 (highest)	1.36 (1.24–1.48)	1.31 (1.20–1.44)
4	1.23 (1.13–1.34)	1.18 (1.08–1.29)
3	1.09 (1.00–1.19)	1.15 (1.06–1.26)
2	1.12 (1.03–1.22)	1.17 (1.08–1.28)
1 (lowest)	1	1
Adjusted for sex, age, deprivation, and smoking (not spatially smoothed)		
5 (highest)	1.17 (1.06–1.29)	1.00 (0.90–1.10)
4	1.11 (1.01–1.21)	0.98 (0.89–1.07)
3	1.02 (0.93–1.11)	0.98 (0.90–1.08)
2	1.06 (0.98–1.16)	1.03 (0.95–1.12)
1 (lowest)	1	1
Adjusted for sex, age, deprivation, and smoking (spatially smoothed using a 1 km radius)		
5 (highest)	1.15 (1.04–1.27)	0.94 (0.85–1.05)
4	1.07 (0.97–1.18)	0.99 (0.90–1.09)
3	1.05 (0.95–1.15)	0.99 (0.90–1.09)
2	1.08 (0.99–1.18)	0.98 (0.89–1.07)
1 (lowest)	1	1
PM_{10}		
Adjusted for sex and age (not spatially smoothed)		
5 (highest)	1.30 (1.19–1.43)	1.36 (1.23–1.50)
4	1.23 (1.13–1.35)	1.17 (1.07–1.29)
3	1.10 (1.01–1.21)	1.11 (1.01–1.22)
2	1.06 (0.98–1.16)	1.08 (0.98–1.19)
1 (lowest)	1	1
Adjusted for sex, age, deprivation, and smoking (not spatially smoothed)		
5 (highest)	1.08 (0.96–1.20)	1.01 (0.90–1.14)
4	1.08 (0.98–1.20)	0.97 (0.87–1.08)
3	1.00 (0.90–1.11)	0.96 (0.86–1.07)
2	1.03 (0.94–1.12)	1.03 (0.93–1.13)
1 (lowest)	1	1
Adjusted for sex, age, deprivation, and smoking (spatially smoothed using a 1 km radius)		
5 (highest)	1.07 (0.96–1.21)	1.07 (0.95–1.20)
4	1.03 (0.93–1.15)	0.97 (0.87–1.08)
3	1.00 (0.90–1.10)	1.04 (0.93–1.15)
2	0.97 (0.89–1.07)	1.01 (0.92–1.11)
1 (lowest)	1	1
CO		
Adjusted for sex and age (not spatially smoothed)		
5 (highest)	1.24 (1.14–1.36)	1.20 (1.09–1.32)
4	1.30 (1.19–1.41)	1.19 (1.09–1.30)
3	1.15 (1.05–1.25)	1.15 (1.05–1.26)
2	1.08 (0.99–1.17)	1.09 (1.00–1.19)
1 (lowest)	1	1
Adjusted for sex, age, deprivation, and smoking (not spatially smoothed)		
5 (highest)	1.05 (0.95–1.16)	0.88 (0.79–0.98)
4	1.16 (1.06–1.28)	0.96 (0.87–1.06)
3	1.04 (0.95–1.14)	0.94 (0.86–1.04)
2	1.03 (0.94–1.13)	0.97 (0.89–1.07)
1 (lowest)	1	1
Adjusted for sex, age, deprivation, and smoking (spatially smoothed using a 1 km radius)		
5 (highest)	1.07 (0.96–1.18)	0.90 (0.81–1.00)
4	1.13 (1.03–1.24)	1.02 (0.92–1.13)
3	1.04 (0.95–1.14)	0.96 (0.87–1.06)
2	1.01 (0.92–1.10)	1.01 (0.92–1.11)
1 (lowest)	1	1

range of factors, including medical practice, illness behaviour, and pressure on hospital beds, influences even emergency admissions, and these factors may have masked any underlying association. We have previously reported a similar observation regarding the winter effect, where excess winter mortality at the small-area geographical level was clearly apparent for cardiovascular mortality but not for emergency hospital admissions.[40] Another potential explanation is that air pollution-related coronary heart disease is more likely to be fatal, with events such as fatal arrhythmias occurring before patients can reach hospitals.

The PM_{10} effect appeared less prominent than the NO_x effect on coronary heart disease mortality and there may be a number of explanations. Both deprivation and smoking prevalence contributed to the greater attenuation of the PM_{10} effect. The modelling approach used may have had greater ability to characterize and represent spatial variation in NO_x than PM_{10}. The relative spatial homogeneity of PM_{10} may have been greater than that of NO_x. We did not have data on ultrafine particles, which more closely reflect traffic-related sources than larger particles. $PM_{2.5}$ has been found to be more strongly associated with mortality than coarser particles.[17] It is interesting to note that we found stronger associations between air pollution and stroke, with adjusted rate ratios of 1.37 (95% CI 1.19–1.57), 1.33 (95% CI 1.14–1.56), and 1.26 (95% CI 1.10–1.46) for NO_x, PM_{10}, and CO, respectively, in the highest pollution quintile categories.[23] Adjustment for deprivation and smoking prevalence had relatively less impact on stroke mortality rate ratios. The effects of air pollution on mortality appear to be more pronounced in very elderly people[31] and this might be a potential explanation as stroke is much commoner in the very elderly population.

There are a number of potential limitations to this study. The potential for ecological bias cannot be ruled out. We adjusted for the substantial confounding effects at the small-area level from socioeconomic deprivation and smoking prevalence, but the possibility of residual confounding cannot be ruled out. In view of the limitations regarding absolute values of the modelled exposure data,

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we chose to examine the association in terms of relative levels of pollution within the overall area using categories based on quintiles. Errors in exposure estimation may nevertheless result in exposure misclassification. Daily population movements expose individuals to different outdoor pollution levels. Their activities may be in the immediate neighbourhood or over greater distances related to travel to work. Without individual-level daily activity information, this pattern of exposure would be difficult to model. We attempted to account for exposure variation in the immediate vicinity by using 1 km radius spatial exposure averages but this did not enhance rate ratios. A further potential source of exposure misclassification is long-term population movements. We have previously found that ~20% of the population aged ≥45 years living in Sheffield throughout an 8-year period moved at least once within the city.[21] In general, exposure misclassification tends to dilute the magnitude of the true underlying association, though in some circumstances it might bias associations away from the null.[41]

If we assume causality, then 6% of coronary heart disease deaths would have been attributable to high outdoor NO_x levels, a proxy for traffic-related pollution. Although this population attributable risk fraction may not appear large, outdoor air pollution is important, as it is a potentially modifiable risk factor for coronary heart disease mortality. Our results suggest that pollution reduction measures targeted at high pollution areas may be considered as a feasible option for prevention of mortality from coronary heart disease. However, residual confounding cannot be ruled out and further studies are needed to confirm our findings, including studies with data to adjust for confounding factors at the individual level.

Acknowledgements

This work uses data provided with the support of the ESRC and JISC, and census and boundary material, which are copyright of the Crown, the Post Office, and the ED-LINE Consortium. The study was funded by a grant from the Trent Research Scheme. We would like to thank Sheffield City Council for providing the air pollution data. The views expressed in this publication are those of the authors and not necessarily those of the funding organization or data providers.

Conflict of interest: none declared.

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Clinical vignette

doi:10.1093/eurheartj/ehi520

Salmonella-infected left ventricular thrombus

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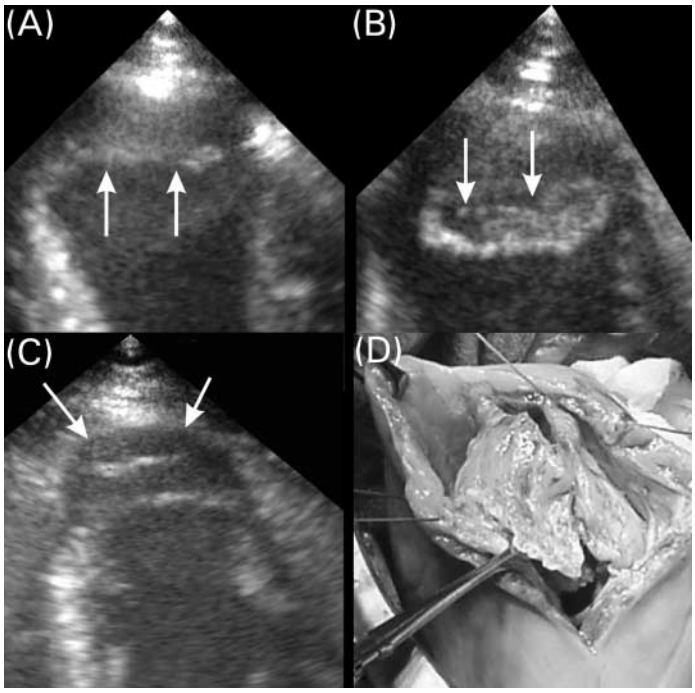

A 64-year-old man had an anterior AMI in 1996 leaving him with an ejection fraction of 40% but symptom free on treatment with ACE-inhibitor. In 2003, he developed *Salmonella enteritidis* infection but remained febrile despite ciprofloxacin. Leucocyte scintigraphy revealed activity in the heart and echocardiography showed apical akinesia covered with a mural thrombus that grew and accumulated cystic material over a week (Panels A and B, arrows). After severe attacks of chills, the thrombus had emptied the majority of its cystic material, but the infection persisted over the following 2 weeks even after replacement of ciprofloxacin by chloramphenicol in maximum dosages. Simultaneously, an echo-weak apical bulge was emerging giving rise to suspicion of impending perforation, a feared complication of Salmonella-infected thrombi (Panel C, arrows). The aneurysm and thrombus were resected with Dor's procedure and the resected myocardium and thrombus were spongious, containing culture negative greyish fluid (Panel D). Ciprofloxacin was administered for another 6 weeks, and at 1-year follow-up, no relapse of the infection had occurred. However, permanent NYHA class III heart failure developed despite treatment with furosemide, ACE-inhibitor, and beta-blocker.

Salmonella-infected thrombi in aortic aneurysms or deep vein thrombosis are well-known complications to salmonelloses, whereas less than 20 cases in the heart are reported. Aneurysmectomy was primarily avoided in our patient because of fear of provoking heart failure but persistent clinical infection and impending myocardial rupture forced surgical treatment. According to the literature, patients appear to succumb on medical treatment alone, although most cardiac thrombi are culture negative when extirpated.

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