Long-Term Exposure to Traffic-Related Air Pollution Associated with Blood Pressure and Self-Reported Hypertension in a Danish Cohort

Mette Sørensen,1 Barbara Hoffmann,2 Martin Hvidberg,3 Matthias Ketzel,3 Steen Solvang Jensen,3 Zorana Jovanovic Andersen,1 Anne Tjønneland,1 Kim Overvad,4,5* and Ole Raaschou-Nielsen1*

1Institute of Cancer Epidemiology, Danish Cancer Society, Copenhagen, Denmark; 2IUF-Leibniz Research Institute for Environmental Medicine and Medical Faculty, Heinrich Heine University of Düsseldorf, Düsseldorf, Germany; 3National Environmental Research Institute, Aarhus University, Roskilde, Denmark; 4Department of Epidemiology, School of Public Health, Aarhus University, Aarhus, Denmark; 5Department of Cardiology, Centre for Cardiovascular Research, Aalborg Hospital, Aarhus University Hospital, Aalborg, Denmark

BACKGROUND: Short-term exposure to air pollution has been associated with changes in blood pressure (BP) and emergency department visits for hypertension, but little is known about the effects of long-term exposure to traffic-related air pollution on BP and hypertension.

OBJECTIVES: We studied whether long-term exposure to air pollution is associated with BP and hypertension.

METHODS: In 1993–1997, 57,053 participants 50–64 years of age were enrolled in a population-based cohort study. Systolic and diastolic BP (SBP and DBP, respectively) were measured at enrollment. Self-reported incident hypertension during a mean follow-up of 5.3 years was assessed by questionnaire. We used a validated dispersion model to estimate residual long-term nitrogen oxides (NOx), a marker of traffic-related air pollution, for the 1- and 5-year periods prior to enrollment and before a diagnosis of hypertension. We conducted a cross-sectional analysis of associations between air pollution and BP at enrollment with linear regression, adjusting for traffic noise, measured short-term NOx, temperature, relative humidity, and potential lifestyle confounders (n = 44,436). We analyzed incident hypertension with Cox regression, adjusting for traffic noise and potential confounders.

RESULTS: A doubling of NOx exposure during 1- and 5-year periods preceding enrollment was associated with 0.53-mmHg decreases (95% confidence interval (CI): –0.88, –0.19 mmHg) and 0.50-mmHg decreases (95% CI: –0.84, –0.16 mmHg) in SBP, respectively. Long-term exposure also was associated with a lower prevalence of baseline self-reported hypertension (per doubling of 5-year mean NOx: odds ratio = 0.96; 95% CI: 0.91, 1.00), whereas long-term NOx exposure was not associated with incident self-reported hypertension during follow-up.

CONCLUSIONS: Long-term exposure to traffic-related air pollution was associated with a slightly lower prevalence of BP at baseline, but was not associated with incident hypertension.

KEY WORDS: air pollution, blood pressure, hypertension, epidemiology, nitrogen oxide. Environ Health Perspect 120:418–424 (2012). http://dx.doi.org/10.1289/ehp.1103631 [Online 3 January 2012]
oxides (NO₂), nitrogen dioxide (NO₂), and nitrogen oxide (NO) concentrations in the air at each address at which the cohort members lived from 5 years prior to baseline until follow-up was completed in 2000–2002. AirGIS calculates air pollution at a location as the sum of local air pollution from street traffic calculated with the Operational Street Pollution Model from input data on traffic (intensity and type), emission factors, street and building geometry, and meteorology (Berkowicz 2000; Kaksimisi et al. 2011); urban background from a simplified area source dispersion model that takes into account urban vehicle emission density, city dimensions (transport distance), and building height (Berkowicz et al. 2008); and regional background estimated from trends at rural monitoring stations and national vehicle emissions. Input data have been described elsewhere (Raaschou-Nielsen et al. 2010). The AirGIS system has been validated in several studies, and the correlation (r) between modeled and measured half-year mean NO₂ concentrations at 204 positions in the greater Copenhagen area was 0.90 (Kettel et al. in press; Raaschou-Nielsen et al. 2000). The AirGIS system calculates air pollution hour by hour, which was summarized as the yearly average concentration at each residential address.

We used NO₃ as a measure of exposure to air pollution from traffic because measured NO₃ correlates strongly with other traffic-related pollutants in Danish streets: r = 0.93 for total particle number concentration (10–700 nm) and r = 0.70 for PM₁₀ (PM ≤ 10 μm in aerodynamic diameter) (Hertel et al. 2001; Kettel et al. 2003). If NO₂, NO₃, and NO could not be calculated because of failed geocoding, we imputed the concentration calculated at the preceding or subsequent residential address of the cohort member as previously described (Raaschou-Nielsen et al. 2011). We then calculated 1-year and 5-year time-weighted average NO₃, NO₂, and NO concentrations before baseline enrollment (cross-sectional study), and 1-year and 5-year time-weighted averages before a new diagnosis of hypertension or the end of follow-up (follow-up study).

Based on the enrollment address and the geographical information system (GIS) road network, we generated two additional traffic variables: a dichotomous indicator for the presence or absence of a street with a traffic density > 10,000 vehicles per day within 50 or 100 m of the residence, and the total number of kilometers driven by vehicles within 200 m of the residence each day (the product of street length and traffic density for all streets within a 200-m radius).

We used hourly measurements at a urban background monitoring station (20 m above ground; chemiluminescence NO/NOₓ model 200A; Teledyne Advanced Pollution Instrumentation, San Diego, CA, USA) to estimate 3-day average exposures to NO₂, NO₃, and NO (on the day of the BP measurement and the 2 preceding days) among participants enrolled by the Copenhagen Center. The monitoring station was located in the center of Copenhagen, with a median residential distance from the monitoring station of 5.5 km (5th–95th percentile, 1.5–14.2 km). We used hourly measures of temperature and relative humidity from three locations (Copenhagen, Aalborg, and Odense) to estimate 3-day average concentrations for all participants. Previous studies on air pollution and BP have found different lags and cumulative exposures to be important (Auchincloss et al. 2008; Dvorch et al. 2009; Harrahi et al. 2006; Zanobetti et al. 2004). We calculated a 3-day mean because this has been suggested to be related to BP (Dvorch et al. 2009; Zanobetti et al. 2004).

We estimated exposure to road traffic noise (Leq) at all enrollment addresses using the computer software SoundPLAN [http://www.soundplan.dk/; see Supplemental Material (http://dx.doi.org/10.1289/ehp.1103631)].

**BP measurement.** At baseline enrollment, trained staff members measured brachial artery BP tomated TAKEDA UA 751 or UA-743 using automated oscillometric sphygmomanometers (model UA 751 or UA-743; Takeda Pharmaceutical Co. Ltd., Osaka, Japan). The measurement was conducted with the subject in the supine position after a minimum of 5 min rest and at least 30 min after tobacco smoking and intake of food, tea, or coffee. If SBP was ≥ 160 mmHg more, or if DBP was ≥ 95 mmHg, the measurement was repeated after an interval of at least 3 min, and the lower of the two measurements was used. We excluded from the present analysis all participants who indicated on the enrollment questionnaire that they were taking or had ever taken medication for hypertension. Height and weight were measured at baseline according to standardized protocols.

**Incidence of hypertension.** Information on hypertension was assessed by questionnaire at enrollment and in the follow-up survey. Specifically, at enrollment participants were asked whether they had ever been hypertensive or were taking or had ever taken hypertension medication, and in the follow-up survey they were asked whether they had ever been diagnosed with hypertension by a medical doctor or were taking or had ever taken hypertension medication. In both the cross-sectional study on hypertension and the follow-up study, we excluded all participants with hypertension at or prior to enrollment and participants with missing or contradictory answers to the hypertension questions.

**Statistical methods.** Cross-sectional analysis of BP and hypertension. We used general linear models to estimate associations between residential exposure to long-term NOₓ, NO₂, and NO (1- and 5-year averages prior to baseline) and systolic and DBP measured at baseline (among participants who did not report use of medications to treat hypertension), and logistic regression models to estimate associations between 1- and 5-year average NOₓ, NO₂, and NO concentrations and the prevalence of self-reported hypertension at baseline (PROC GLM and PROC GENMOD in SAS, version 9.1; SAS Institute Inc., Cary, NC, USA). Exposures were modeled as categorical variables (with cut points based on quartiles) and as continuous variables after logarithmic transformation (log2) to satisfy the assumption of linearity, which we evaluated using linear spline models with boundaries at deciles of exposure for the analytic cohort (BP) or cases (hypertension) (Greenland 1995). In addition, we estimated associations of BP and prevalent hypertension with short-term NOₓ, NO₂, and NO exposures averaged over 3 days (the day of BP measurement and the previous 2 days, log2 transformed and categorical) among Copenhagen residents, and associations with the presence or absence of a major road within 50 m of the baseline residence and traffic density within 200 m of the baseline residence (log2 transformed or categorical) among all participants.

We adjusted analyses for potential confounders: age (continuous), sex, calendar year, center of enrollment (Copenhagen or Aarhus), area (Copenhagen city, Aarhus city, or Copenhagen or Aarhus surroundings defined as residence within 7–25 km of either city center), length of school attendance (< 8, 8–10, > 10 years), body mass index (BMI; kilograms per meter squared, linear), smoking status (never, former, current), alcohol intake (yes/no; grams per day among drinkers, linear), intake of fruit and vegetables (linear splines with a knot at 350 g/day), sport during leisure time (yes/no; hours per week among active, continuous), road traffic noise (Leq; decibels; residential exposure at enrollment), season (winter, spring, summer, and autumn), mean relative humidity (continuous), and ambient temperature during 3 days (the day of BP measurement and the 2 preceding days). Temperature showed a weak inverse association with BP ≤ 11.5°C and a steep inverse association at temperatures > 11.5°C. Therefore, temperature was modeled using linear splines with a knot at 11.5°C. In addition we adjusted for the socioeconomic status (SES) of the participants’ municipality (or district for Copenhagen residents) classified as low, medium, or high based on information on average education, work market affiliation, and income at the time of enrollment. Analysis of associations with short-term NOₓ, NO₂, and NO concentrations were also adjusted by...
the 1-year mean concentration of NOx, NO2, or NO, respectively, in the previous year.

In a secondary analysis restricted to Copenhagen residents (n = 21,507), we adjusted associations between long-term NOx by measured ambient NOx concentrations averaged over the day of the BP measurement and the previous 3 days. In addition, we conducted sensitivity analyses restricted to participants with normal BP (SBP ≤ 140 and/or DBP ≤ 90) or participants with SBP < 160 and/or DBP < 100. In exploratory analyses, we tested for interactions between modeled long-term exposure to NOx and sex, education, smoking, temperature, area, SES, and history of cardiovascular disease by introducing interaction terms into the model.

Graphical presentation of the functional form of association between NOx and SBP adjusted for the potential confounders was estimated with the OLS function in Design Library [R statistical software, version 2.9.0 (http://www.r-project.org)].

**Follow-up for hypertension.** We analyzed data based on Cox proportional hazards model with age as the underlying time metric (Thiebaut and Benichou 2004). We used left truncation at age of enrollment, so that subjects were considered at risk from enrollment into the cohort, and right censoring at age of event (self-reported hypertension) or age at follow-up survey, whichever came first. We stratified all analyses by sex and calendar year. Exposure to long-term air pollution was modeled using time-dependent variables of time-weighted average NOx, NO2, and NO concentrations at each year of age during follow-up (one row of data for each year of age that a participant contributed to follow-up).

We calculated incidence rate ratios (IRRs) for hypertension in association with 1- and 5-year mean NOx, NO2, and NO concentrations at the time of diagnosis compared with 1- and 5-year mean NOx, NO2, and NO concentrations for all cohort members at risk at that point in time. IRRs for the two traffic proxies (major road and traffic load) were calculated using enrollment addresses. Analyses were adjusted for baseline information on smoking status, length of school attendance, alcohol intake, intake of fruit and vegetables, BMI, sport during leisure time, SES, area, and traffic noise. We interpreted a p-value < 0.05 as statistically significant.

**Results**

**BP and baseline hypertension.** Of 57,053 participants, we excluded 571 who had been diagnosed with cancer before baseline, but because of delay in the Danish Cancer Registry, were erroneously included; 2,737 with incomplete residential address information; 63 without BP measurement; and 2,961 with missing information on covariates leaving 50,721 participants for the baseline hypertension analyses. Of these, 6,285 received hypertension medicine at and/or before enrollment, leaving 44,436 participants for the BP analyses.

Table 1 shows the distribution of baseline characteristics in the study population. Long-term exposure to NOx and traffic load at the address at enrollment was correlated, with a Spearman rank coefficient (rS) of 0.95 between the 1- and 5-year mean NOx (p = 0.0001) and 0.51 between traffic load and 1-year NOx mean (p = 0.0001).

![Figure 1. Association [mean (95% CI) between NOx exposure 5 years preceding enrollment (log transformed) and SBP in 44,436 cohort participants, adjusted for age, sex, center, calendar year, area, smoking, BMI, length of school attendance, municipality SES, intake of alcohol, fruit and vegetables, physical activity, traffic noise, season, temperature, and relative humidity.](image-url)
Modeled exposure to NOx, NO2, and NO at the enrollment address was highly correlated: 0.98 between NOx and NO, 0.97 between NOx and NO2, and 0.92 between NO2 and NO (1-year data; \( p < 0.0001 \)). Short- and long-term exposure to NOx were not correlated. There was a significant correlation between long-term exposure to NOx and \( L_{den} \) at enrollment (0.69 and 0.67 for the 1- and 5-year period preceding enrollment; \( p < 0.0001 \)).

The distributions of systolic and DBP were slightly right-skewed. However, similar results were observed for untransformed and log-transformed values, and regression estimates for the untransformed data are presented.

Long-term exposure to NOx was inversely associated with BP (Figure 1, Table 2). Although significant, the estimated changes were rather small. Categorical analyses showed a monotonically inverse dose–response relationship between the 1- and 5-year NOx means and SBP, whereas this was not apparent for the DBP. Corresponding estimates for long-term exposures to NO2 and NO were generally consistent with those shown for NOx (see Supplemental Material, Table 1 [http://dx.doi.org/10.1289/ehp.1103631]).

Adjustment for road traffic noise changed the estimates slightly (data not shown); for example, a doubling in 1-year NOx was associated with a –0.39 mmHg change in SBP before adjustment for traffic noise and a –0.53 mmHg change in SBP after adjustment. Further adjustment by short-term NOx concentrations (among Copenhagen participants only) had little effect on estimates (data not shown).

For example, the estimated changes in SBP per doubling of 1- and 5-year NOx exposures were –0.50 mmHg (95% confidence interval (CI): –0.93, –0.07 mmHg) and –0.51 mmHg (95% CI: –0.94, –0.08 mmHg), respectively, after adjusting for short-term NOx. When restricted to the 23,982 participants who had normal BP at baseline, the estimated changes in SBP per doubling of 1- and 5-year NOx exposures were –0.24 mmHg (95% CI: –0.50, 0.01 mmHg) and –0.20 mmHg (95% CI: –0.45, 0.05 mmHg), respectively. When restricted to the 38,565 participants who had SBP < 160 and/or DBP < 100, the corresponding estimates were –0.27 mmHg (95% CI: –0.55, 0.01 mmHg) and –0.22 mmHg (95% CI: –0.50, 0.05 mmHg), respectively.

Inverse associations between exposure and BP were also estimated for short-term NOx and for the two traffic proxies (Table 2). The categorical analyses for the 3-day NOx mean and traffic load showed no clear dose–response relationship in relation to BP.

Sex, temperature, and a diagnosis of cardiovascular disease appeared to modify the association between NOx and SBP (Table 3).

| Categorical analyses for the 3-day NOx mean and traffic load showed no clear dose–response relationship in relation to BP. |

| Exposure | \( \text{Difference in BP (mmHg)}^a \) |
| --- | --- |
| NOx 5-year mean (µg/m³) \( ^{bc} \) | 11,109 | 0.00 |
| < 16.9 | 11,109 | –0.20 (–0.72, 0.32) |
| 16.9–19.6 | 11,109 | –0.49 (–0.89, 0.09) |
| 19.6–29.2 | 11,109 | –0.62 (–1.35, 0.11) |
| > 29.2 | 44,436 | –0.50 (–0.84, –0.16) |
| Linear trend per doubling | 11,116 | 0.00 |
| NOx 1-year mean (µg/m³) \( ^c \) | 11,109 | 0.00 |
| < 17.0 | 11,109 | –0.32 (–0.86, 0.22) |
| 17.0–20.2 | 11,109 | –0.49 (–1.08, 0.11) |
| > 20.2–27.2 | 11,109 | –0.58 (–1.32, 0.15) |
| Linear trend per doubling | 11,109 | 0.00 |

For example, the estimated changes in SBP per doubling of 1- and 5-year NOx exposures were –0.50 mmHg [95% confidence interval (CI): –0.65, 0.00] –0.41 mmHg (–0.81, 0.00), respectively. When \( NO_2 \) and NO were not correlated, there was a significant correlation between long-term exposure to NOx and \( L_{den} \) at enrollment (0.69 and 0.67 for the 1- and 5-year period preceding enrollment; \( p < 0.0001 \)).

Table 2. Associations between concentrations of NOx and traffic at the residence and systolic and DBP at enrollment [mean (95% CI)].

| Exposure | \( \text{Difference in BP (mmHg)}^a \) |
| --- | --- |
| NOx 5-year mean (µg/m³) \( ^{ab} \) | 11,109 | 0.00 |
| < 16.9 | 11,109 | –0.20 (–0.72, 0.32) |
| 16.9–19.6 | 11,109 | –0.49 (–0.89, 0.09) |
| 19.6–29.2 | 11,109 | –0.62 (–1.35, 0.11) |
| > 29.2 | 44,436 | –0.50 (–0.84, –0.16) |
| Linear trend per doubling | 11,116 | 0.00 |
| NOx 1-year mean (µg/m³) \( ^c \) | 11,109 | 0.00 |
| < 17.0 | 11,109 | –0.32 (–0.86, 0.22) |
| 17.0–20.2 | 11,109 | –0.49 (–1.08, 0.11) |
| > 20.2–27.2 | 11,109 | –0.58 (–1.32, 0.15) |
| Linear trend per doubling | 11,109 | 0.00 |

*Adjusted by age, sex, center, calendar year, area, smoking status, BMI, length of school attendance, municipality SES, alcohol intake, intake of fruit and vegetables, physical activity, traffic noise, season, temperature, and relative humidity.

**The cutoff points between exposure groups were the 25th, 50th, and 75th percentiles.

†Time-weighted average concentration of NOx 1 and 5 years preceding enrollment.

*Based on participants from the Copenhagen center. The analysis of 3-days mean of NOx was also adjusted by the preceding 1-year mean concentration of NOx. More than 10,000 vehicles per day. A diagnosis of myocardial infarction and/or stroke before enrollment.
and BP seemed stronger in women than in men and was only apparent at temperatures below 15°C and among participants without cardiovascular disease, whereas among participants with a history of cardiovascular disease there seemed to be a positive association. Furthermore, for measured short-term NOX (3-day mean) we found changes of −0.27 mmHg (95% CI: −1.73, 1.39 mmHg) and −0.56 mmHg (95% CI: −1.00, −0.11 mmHg) for above and below 15°C, respectively, per doubling in 3-day NOX mean (p for interaction = 0.71).

Of the 50,721 participants included in the analyses of prevalent self-reported hypertension at baseline, 8,201 reported that they had been diagnosed with hypertension. Long-term exposure to NOX was inversely associated with the prevalence of hypertension [evaluated as odds ratios (ORs); Table 4], with similar associations estimated for corresponding exposures to NO2 and NO [see Supplemental Material, Table 2 (http://dx.doi.org/10.1289/ehp.1103631)]. The presence of a major road within 50 or 100 m of the residence seemed to be associated with a lower prevalence of hypertension, whereas there was no evidence of an association with traffic load.

**Follow-up for hypertension.** Of the 45,271 persons that filled out the follow-up questionnaire, we excluded 7,110 with hypertension at or prior to enrollment, 1,841 participants with missing or contradictory answers to the hypertension questions, 2,897 with incomplete residential address information, and 148 with missing information on covariates, leaving a study base of 33,275 participants with an average follow-up period of 5.3 years. Among these, 3,195 participants reported that they had been diagnosed with hypertension within the follow-up period.

Table 1 shows the distribution of baseline characteristics in the study population. The distribution of baseline characteristics among the 33,275 participants followed up for hypertension was very similar to the distributions in the baseline study cohort.

We found no clear associations between exposure to traffic-related air pollution and risk for self-reported hypertension in the subset of participants who responded at the follow-up survey (evaluated as IRRs; Table 4). In analyses of NOX, point estimates were slightly elevated, but CIs included the null. Estimates did not demonstrate monotonic dose–response relations with increasing quantiles of exposure. Participants who lived within 50 m of a major road had a 13% higher risk for hypertension (95% CI: 0.97, 1.32%). Exclusion of participants with a history of myocardial infarction (n = 335) or stroke (n = 206) at baseline resulted in only minor changes in estimated associations (data not shown). Also with regard to exposure to long-term NOX and NO, no clear associations were found between exposure and risk for hypertension [see Supplemental Material, Table 2 (http://dx.doi.org/10.1289/ehp.1103631)].

**Discussion**

Long-term exposure to traffic-related air pollution was inversely associated with systolic and DBP and the prevalence of self-reported hypertension in a cross-sectional design, whereas long-term exposure to traffic-related air pollution was not associated with the risk of self-reported hypertension during approximately 5 years of follow-up.

**Strengths and limitations.** Strengths included the large study population, with detailed information on potential confounders. Furthermore, access to residential address histories improved estimation of long-term air pollution. In addition, we adjusted for exposure to road traffic noise, which potentially is associated with traffic-related air pollution (de Kluizenaar et al. 2007; Sørensen et al. 2011) and has been associated with BP and hypertension (Babisch 2006). However, we cannot rule out residual confounding, for example, by individual SES or intake of sodium or potassium.

Although the dispersion models used to estimate long-term exposures to air pollution in the present study have been successfully validated and applied (Andersen et al. 2011; Berkowicz et al. 2008; Ketzel et al. in press; Raaschou-Nielsen et al. 2000), such estimates are inevitably associated with some degree of uncertainty, which would result in exposure misclassification. However, such misclassification should be nondifferential with respect to BP and hypertension.

A limitation of the study of measured BP at baseline part of this study is the cross-sectional design. Although we have adjusted for many possible confounders, associations should be confirmed using a longitudinal design with repeated measures. Results of previous studies of air pollution and BP measured at different points in time have been inconsistent, with some studies reporting positive associations (de Paula et al. 2005; Dvonch et al. 2009; Zanobetti et al. 2004), and others reporting inverse associations (Brauer et al. 2001; Ebel et al. 2005; Ibald-Mulli et al. 2004) without clear relations between the results observed and the design of the study.

The measurement of systolic and DBP in our study was standardized but did not follow standard clinical protocols for diagnosing hypertension, which require several measurements of BP. We repeated measurements only if SBP was ≥ 160 mmHg or DBP was ≥ 95 mmHg, and used the lower of the two measurements, which may have resulted
in a systematic bias toward lower values in participants with higher BP. This could have biased the BP estimate toward an inverse association. When we restricted the sample to participants with normal BP values, who were less likely to have had repeated BP measurements, inverse associations were less pronounced but still evident between long-term NOx and BP. However, it is not possible to determine whether or how much differences observed after restriction reflect a reduction in misclassification of the BP measurements versus selection bias caused by limiting the analysis to potentially less susceptible participants.

Our prospective study of hypertension also has some limitations. First, information on hypertension was self-reported, and the actual number of hypertensive participants is probably underestimated. Therefore, a number of participants who were actually hypertensive at baseline were falsely included as non-hypertensive. Second, information on hypertension was self-reported and was therefore potentially biased toward an inverse association between air pollution and BP. However, it is not possible to determine how much of this association is due to exposure to air pollution and how much is due to other factors that could influence NO concentrations, such as geography and season.

Similarly, we found that the inverse association between air pollution and BP was present only at temperatures <15°C. The concentration of NOx is rather constant during a year, but during summer the association tended to be negative although not statistically significant. The analysis of the effects of air pollution on blood pressure and vascular function in healthy humans. Hypertension 54:659–667.

Conclusions

Long-term exposure to traffic-related air pollution was associated with a slightly lower BP but was not consistently associated with self-reported hypertension.

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Hoffmann B, Moebus S, Dragano N, Stang A, Mohlenkamp S, et al. 2011. Results of previous studies of short-term exposures and BP have been inconsistent (Brauer et al. 2001; Brook et al. 2009; Chuang et al. 2010; de Paula et al. 2005; Dvoroch et al. 2009; Harrabi et al. 2006; Ibald-Mulli et al. 2004; Urch et al. 2005; Zanobetti et al. 2004). Ibald-Mulli et al. (2004) suggested that a possible mechanism for a decrease in BP caused by exposure to air pollution could be a shift in sympathovagal balance due to an increase in vagal tone. Another explanation could relate to the effect of NO as a potent vasodilator that diffuses freely across membranes. NO is present in exhaust from vehicles and is converted to NO2 through reaction with ozone. Because ozone is generated from oxygen reacting with sunlight, NO is usually present in lowest concentrations during summer. NO, NO2, and their sum, NOx, are highly correlated (Hertel et al. 2001; Ketzel et al. 2003), and it is therefore extremely difficult to disentangle the effects of the three exposures. A closer look at the results reported by Auchincloss et al. (2008) indicates that the positive association between long-term air pollution exposure and BP was evident only in the warmer season (>10°C); whereas at temperatures <10°C, the association tended to be negative although not statistically significant. Similarly, we found that the inverse association between air pollution and BP was present only at temperatures <15°C. The concentration of NOx is rather constant during a year, but during summer the contribution of NO is reduced because of higher ozone concentrations. This and other factors that could influence NO concentrations, such as geography and season, might also explain differences in results among studies of different populations.

Our results suggest that among patients with a previous diagnosis of cardiovascular disease, long-term exposure to NOx might be positively associated with BP, indicating that these patients might be a susceptible group. This analysis was, however, based on relatively few patients with cardiovascular disease.

Hypertension. We found inconsistent associations of long-term air pollution with hypertension. In the cross-sectional analysis of self-reported hypertension at baseline, we saw a small inverse association, consistent with the results of the BP analysis. However, exposure was not inversely associated with incident self-reported hypertension, and results could indicate a slight positive association, although estimates did not indicate a monotonic dose-dependent relationship. Studies using validated hypertension as outcome are necessary to disentangle possible sources of bias.

To our knowledge, this is the first study to estimate effects of long-term air pollution on the incidence of hypertension. A few previous studies have reported that short-term air pollution was associated with emergency department visits for hypertension (Guo et al. 2010a, 2010b) and that long-term air pollution was positively associated with prevalence of self-reported hypertension (Johnson and Parker 2009). Exposure to air pollution has been associated with increased inflammation and oxidative stress, as well as endothelial dysfunction (Brook et al. 2010; Hoffmann et al. 2009), which may contribute to the development and progression of atherosclerosis and risk of hypertension. Because most studies have focused on PM2.5 and not NO and NO2, direct comparisons are difficult. In contrast to well-known vasodilatory effects of NO, PM mixtures are extremely variable and may have very different physiological effects depending on the predominant constituents.
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