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The joint association of air pollution and noise from road traffic with cardiovascular mortality in a cohort study

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Keywords: air pollution, noise, cardiovascular mortality, cohort.
ABSTRACT

Objectives
The authors investigated associations between cardiovascular mortality and air pollution and noise together.

Methods
Data from an ongoing Dutch cohort study on diet and cancer (NLCS, 120,852 subjects; follow-up 1987-1996) were used. Cox proportional hazard analyses were conducted for the association between cardiovascular mortality and exposure to black smoke (BS), traffic intensity on the nearest road and road traffic noise at the home address.

Results
The correlations between traffic noise and background BS, and traffic intensity on the nearest road were moderate at: 0.24 and 0.30 respectively. Traffic intensity was associated with cardiovascular mortality, with highest relative risk (95% confidence interval) for ischemic heart disease (IHD) mortality: 1.11 (1.03 - 1.20) (increment 10,000 mvh/24h). Relative risks for BS concentrations were elevated for cerebrovascular (1.39 (0.99 - 1.94)) and heart failure mortality (1.75 (1.00 - 3.05) (increment 10 $\mu$g/m$^3$). These associations were insensitive to adjustment for traffic noise. There was an excess of cardiovascular mortality in the highest noise category (>65 dB(A)), with elevated risks for IHD (1.15 (0.86 - 1.53) and heart failure mortality (1.99 (1.05 - 3.79). After adjustment for BS and traffic intensity noise risks became unity for IHD mortality and slightly reduced for heart failure mortality.

Conclusions
Associations between BS concentrations and traffic intensity on the nearest road with specific cardiovascular causes of death were not explained by traffic noise in this study.
INTRODUCTION

Cohort studies have shown associations between long-term exposure to particulate matter air pollution and cardiovascular mortality (1-4). Cohort studies which were mostly conducted in Europe have reported associations between traffic-related air pollution and cardiovascular mortality (5-7). Exposure to traffic-related air pollution has been assessed using dispersion modeling (7), measured or modeled air pollution data and traffic variables assessed with geographic information systems (5,6,8,9).

Motorized traffic is not only an important source of air pollution, but also of noise (10,11). Exposure to traffic noise is associated with ischemic heart disease (10). Exposure to traffic noise is usually modeled using traffic intensity, traffic composition, speed, distance to roads, noise barriers and other factors as input variables. The joint association of long-term exposure to air pollution and noise with cardiovascular mortality has not been reported before.

We earlier reported an association between traffic-related air pollution, traffic intensity and mortality in a Dutch cohort (12). In this paper, we study the joint association of long-term exposure to air pollution, traffic intensity and noise with cardiovascular mortality. Because air pollution and noise may be associated with different cardiovascular endpoints (7,9-11,13,14), we studied overall as well as subcategories of cardiovascular mortality.
MATERIALS AND METHODS

Study design

The cohort has been described in detail (15). Briefly, the Netherlands Cohort Study on Diet and Cancer (NLCS) started in September 1986 with 120,852 subjects aged 55-69 years living in 204 municipalities located throughout the country. The NLCS study was designed as a case-cohort study, i.e. cases are derived from the entire cohort, while the person years at risk are estimated from a random subcohort (N ~ 5,000) (16). In our analyses we will however use data from all participants.

At baseline, all participants completed an 11-page questionnaire on risk factors for cancer. For all participants, data from one machine readable page of the questionnaire were entered (with information about age, gender and smoking status). The exact residential address at baseline was also available. The entire cohort was followed up for cancer incidence and mortality (17). For emerging cases and the randomly selected subcohort, the remaining 10 questionnaire pages (not machine readable) were manually entered. As a result, only limited confounder information is available for the full cohort.

Mortality data for the period 1987-1996 were obtained from the Dutch Central Bureau of Genealogy and Statistics Netherlands. Completeness of case ascertainment could be checked by using information from the subcohort. The subcohort (N = 5,000) has been followed biennially. The completeness of mortality follow-up was estimated to be over 99%. Cause of death information from death certificates which were filled in by a physician was available from Statistics Netherlands. For 99.7% of the cases a cause of death was available. The cause of death was coded according to ICD-9 for period 1986-1995 and ICD-10 for 1996. In our analyses we used the primary cause of death. The cause of death was coded according to ICD-9 for period 1986-1995 and ICD-10 for 1996. In our analyses we used the primary cause of death. Cardiovascular mortality was grouped into ischemic heart disease (IHD), cerebrovascular, heart failure, and cardiac dysrhythmia mortality (Table 1).

The NLCS study was approved by institutional review boards from Maastricht University and the Netherlands Organization for Applied Scientific Research (TNO). All cohort members consented to participation by completing the mailed, self-administered questionnaire.

Table 1. Number of deaths during follow-up.*

<table>
<thead>
<tr>
<th>Cause</th>
<th>ICD-9 codes</th>
<th>ICD-10 codes</th>
<th>Number of deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular mortality</td>
<td>400–440</td>
<td>110–170</td>
<td>6,137</td>
</tr>
<tr>
<td>Ischemic heart disease mortality</td>
<td>410–414</td>
<td>120–125</td>
<td>3,521</td>
</tr>
<tr>
<td>Cerebrovascular mortality</td>
<td>430–438</td>
<td>160–169</td>
<td>1,175</td>
</tr>
<tr>
<td>Heart failure mortality</td>
<td>428</td>
<td>150</td>
<td>422</td>
</tr>
<tr>
<td>Cardiac dysrhythmia mortality</td>
<td>427</td>
<td>144–149</td>
<td>339</td>
</tr>
</tbody>
</table>

* ICD is International Classification of Diseases

Air pollution

The air pollution exposure assessment method has been described previously (18). Long-term exposure to outdoor air pollution was estimated at the 1986 home addresses, which were geocoded into standard Dutch geographic coordinates (Address Coordinates Netherlands (ACN)) using a database with high geographical accuracy from 2000 (12).
Exposure was estimated as the sum of regional, urban and local traffic contributions. Regional background concentrations were estimated using interpolation of data from regional background sites in the national monitoring network. The interpolation method was validated using cross-validation (18). The urban component was estimated using regression models relating measured urban concentrations to the number of inhabitants around a monitoring site. The sum of the regional and urban contributions was defined as background concentration. Average background concentrations for the period 1987-1996 were estimated for black smoke, nitrogen dioxide (NO₂), and fine particles less than 2.5 μm in diameter (PM₂.₅). Average background concentrations were assigned to the 1986 home address. In this paper we used Black Smoke (BS) concentrations, as it is a measure of the traffic-related component of particles.

Local traffic contributions were characterized by traffic variables which were assessed using a Geographic Information System (GIS) and a digital road network (from the year 2001) with linked traffic intensities for 1986 (18). To roads without traffic intensities a background traffic intensity value of 1,225 mvh/24h was assigned assuming that these roads are not major. This was done to avoid underestimation of local traffic contributions for example when calculating traffic intensity in a buffer. A value of 1,225 mvh/24h was used, because this was half of the value of 2,450 mvh/24h that was used in the Dutch Environmental Traffic Maps to distinguish between roads for which air pollution assessments were and were not made. Approximately 80% of the participants had an assigned traffic intensity on the nearest road of 1,225 mvh/24h (18). Assessed traffic variables were the traffic intensity on the nearest road, sum of traffic intensity in a 100m buffer around a residential address, and an indicator variable for living near a major road (i.e. living within 100 m of a motorway and/or within 50 m of a local road with traffic intensity > 10,000 mvh/24h). In this paper we used traffic intensity on the nearest road as indicator for local traffic contributions, because it had the strongest association with cardiovascular mortality (12). In addition, studies have shown that there are important variations in the concentrations close to busy roads (18). Other studies have also used traffic variables as indicator for proximity to busy roads (5,6,8,9). Because addresses were geocoded with a database from 2000 and the digital road network was from 2001, coordinates and road network are compatible.

Urban background BS concentration and traffic intensity were separately analyzed to identify separate effects of living near a busy road.

Traffic noise

Road traffic noise at the 1986 home address was estimated for all subjects using EMPARA, a state-of-the-art model for noise mapping in the Netherlands (resolution 25x25m). Traffic noise was modeled as equivalent A-weighted yearly average sound pressure levels (dB(A)) (19). The model is based upon standard noise calculation methods in the Netherlands (20). Input variables for the model are traffic intensity, traffic composition and traffic speed (determining noise emission), distance to roads, land use (hard versus soft surface; density of built-up area), location of noise barriers and quiet asphalt (determining transmission) (19). Input data were collected for the period 2000-2001, because not all required data for 1986 were available. Traffic intensities are a major input variable in these models. We documented that while absolute traffic intensities increased during the follow-up period (1987- 1996), traffic intensity data for 1986 and
1996 were highly correlated (>0.9) (18). Other important factors such as distance to roads and density of the built-up area were likely stable as well.

The validity of EMPARA has been evaluated for both rural and urban locations using measured data and calculations with more detailed noise models. Both the measured and calculated values differed on average less than 2-3 dB(A) from the EMPARA results (19). The range in modeled noise levels was 29-75 dB(A).

As noise exposure indicator, we used the standard measure for noise exposure in the Netherlands before the implementation of the European Noise Directive (21). This was defined as the maximum of the annual average noise level during the day (7 to 19h), or the evening (19 to 23 h) or the night (23 to 7 h). The levels during the evening and during the night receive a penalty of respectively 5 and 10 dB(A) (19). No information was available for other noise indicators like background noise or the number of noise events.

**Statistical analysis**

We conducted analyses in the full cohort using Cox proportional hazards models. Person-years were calculated for all participants from baseline until death or end of follow-up. Person-years for subjects who died from causes other than those being analyzed were defined censored at the time of death in cause-specific analyses.

We added urban background BS concentration and traffic intensity on the nearest road as continuous variables, to assess the potential confounding effects of adding traffic noise to especially the traffic intensity variables.

Effects of traffic noise exposure were analyzed with noise classified into categories of 5 dB(A), from ≤50 dB(A) to >65 dB(A). These categories were chosen to address thresholds which have been observed in previous studies (10).

Effects of air pollution and noise were investigated separately and in conjunction. Relative risks (RR) were calculated for black smoke concentration and traffic intensity differences between the 5th and the 95th percentile: this was rounded to 10 μg/m³ and 10,000 motor vehicles/24h (mvh/24h), respectively. Relative risks for noise were calculated with ≤50 dB(A) as reference category.

We adjusted for gender, age at baseline, and smoking status coded as never, ex, and current smoking separately for cigarette, cigar and pipe smoking. We further adjusted for indicators of socioeconomic status at the neighborhood (average size 3.6 km²) and COROP scale (40 areas; average size ~1,000 km²) as in our previous paper (Table 2) (12).

Because we conducted analyses in the full cohort, only a limited number of confounders was available. Comparing this limited set of confounders with the full confounder set in case-cohort analyses gave evidence that this limited set of confounders was sufficient to adjust for confounding in the air pollution analyses in this cohort (12).

We did not adjust for spatial clustering as it was previously not found to be important (12).

Data management was done using SPSS 12.0 (SPSS Inc, Chicago, US), and statistical analyses were conducted using STATA statistical software 8 (STATA Corporation, College Station, US). GIS calculations were conducted using ArcInfo (ESRI, Redlands, US).
Additional analyses
As sensitivity analyses we investigated traffic intensity on the nearest road as categorical variable (≤1,225 mvh/24h (reference category); 1,225 – 10,000 mvh/24h; and >10,000 mvh/24h).
Further, we conducted analyses with NO$_2$ and PM$_{2.5}$ background concentrations and with other traffic variables (living near a major road and traffic intensity in a 100 m buffer).
We investigated traffic noise as continuous variable in a linear model.
Sensitivity analyses with exclusion of observations with traffic noise above 65 dB(A) were conducted. We also conducted sensitivity analyses with exclusion of subjects for which no traffic data were available.
We conducted separate analyses for men and women because most previous studies investigated the noise effects in men only (10). We investigated effect modification by age (age < 62 years and age > 62 years), cigarette smoking status (never/ex/current) and percentage of persons with low income at the neighborhood scale (in tertiles). Heterogeneity in relative risk estimates between different subgroups was tested using Cochran’s Q test (22).

Table 2. Descriptive characteristics of cardiovascular mortality cases and non-cases according to various baseline characteristics (among subjects for which geographical coordinates of the home address were available (N = 117,528)). Values are number (percentage) or median (Inter Quartile Range).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cases</th>
<th>Non-cases in full cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N = 6,137)</td>
<td>(N = 111,391)</td>
</tr>
<tr>
<td>Gender (men)</td>
<td>4,243 (69.1 %)</td>
<td>52,558 (47.2 %)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>64 (61 – 67)</td>
<td>62 (58 – 65)</td>
</tr>
<tr>
<td>Cigarette smoking status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>1,620 (28.6 %)</td>
<td>43,281 (41.3 %)</td>
</tr>
<tr>
<td>Ex</td>
<td>1,859 (32.8 %)</td>
<td>33,103 (31.6 %)</td>
</tr>
<tr>
<td>Current</td>
<td>2,182 (38.5 %)</td>
<td>28,350 (27.1 %)</td>
</tr>
<tr>
<td>Cigar smoking status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>4,822 (82.4%)</td>
<td>93,776 (87.8%)</td>
</tr>
<tr>
<td>Ex</td>
<td>552 (9.4%)</td>
<td>7,271 (6.8%)</td>
</tr>
<tr>
<td>Current</td>
<td>475 (8.1%)</td>
<td>5,807 (5.4%)</td>
</tr>
<tr>
<td>Pipe smoking status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>5,381 (91.3%)</td>
<td>100,197 (93.4%)</td>
</tr>
<tr>
<td>Ex</td>
<td>318 (5.4%)</td>
<td>4,747 (4.4%)</td>
</tr>
<tr>
<td>Current</td>
<td>194 (3.3%)</td>
<td>2,305 (2.2%)</td>
</tr>
<tr>
<td>Percentage persons with low income in neighborhood</td>
<td>41 (36 – 47)</td>
<td>41 (36 – 46)</td>
</tr>
<tr>
<td>Percentage persons with high income in neighborhood</td>
<td>18 (12 – 24)</td>
<td>19 (13 – 25)</td>
</tr>
<tr>
<td>Percentage persons with low income in a COROP area*</td>
<td>41 (36 – 45)</td>
<td>41 (36 – 45)</td>
</tr>
<tr>
<td>Percentage persons with high income in a COROP area*</td>
<td>19 (18 – 23)</td>
<td>19 (18 – 23)</td>
</tr>
</tbody>
</table>

* COROP areas consist of a central point (e.g. a city) and the surrounding economic and social region. The Netherlands is divided in 40 COROP areas.
RESULTS

For 97 percent of the subjects we were able to estimate air pollution and noise at the home address (N = 117,528). About 57 percent of all cardiovascular deaths was caused by IHD (Table 1). Cardiovascular mortality cases were older and more likely to be male or current smoker compared to non-cases (Table 2).

Air pollution and traffic noise
Background BS, traffic intensity on the nearest road and noise varied substantially within the cohort (Figure 1). 7.5 percent of the subjects were exposed to traffic noise between 60 and 65 dB(A), and 1.6 percent to more than 65 dB(A). For 4.5 percent of the subjects traffic intensity on the nearest road was >10,000 mvh/24h.

Traffic noise exposure was higher for subjects who had a traffic intensity >10,000 mvh/24h on the nearest road (mean 60 dB(A)) compared to subjects who had a traffic intensity ≤10,000 mvh/24h on the nearest road (mean 52 dB(A)).

The correlations between traffic noise and background BS, and traffic intensity on the nearest road were moderate at: 0.24 and 0.30 respectively. The correlation between traffic noise and traffic intensity for subjects with noise levels above 65 dB(A) was slightly lower: 0.22.

Association of air pollution and traffic noise with cardiovascular mortality
Table 3 shows the associations between background BS, traffic intensity on the nearest road and traffic noise with cardiovascular mortality. Traffic intensity on the nearest road was associated with cardiovascular mortality, with the highest relative risk for IHD mortality. Relative risks for background BS concentrations were elevated for cerebrovascular and heart failure mortality. The associations for background BS concentrations and traffic intensity were insensitive to adjustment for traffic noise.

There was an excess of cardiovascular mortality in the highest noise category (>65 dB(A)), which was concentrated in especially heart failure mortality (RR 1.99 (95% confidence interval (CI): 1.05 - 3.79). This relative risk was based on only 10 cases, which is reflected in the wide confidence intervals. The number of cases in the highest noise category was for the other mortality outcomes: 94 for cardiovascular mortality, 49 for IHD mortality, 14 for stroke mortality, 10 for heart failure mortality and 6 for cardiac dysrhythmia mortality.

After adjustment for BS concentrations and traffic intensity the association for IHD mortality reduced to unity and the association for heart failure mortality was slightly reduced to 1.90.

Crude estimates (only age and gender adjusted) did only slightly differ from the adjusted estimates with RRs for cardiovascular mortality of 1.15 (95% CI 1.03 – 1.29) for background BS, 1.07 (95% CI 1.01 – 1.14) for traffic intensity on nearest road, and 1.13 (95% CI 0.92 – 1.39) for the highest noise category.

Additional analyses
When traffic intensity on the nearest road was modeled as a categorical variable, elevated relative risks were found for the category >10,000 mvh/24h for cardiovascular (1.12
(95% CI: 0.99 - 1.28)) and IHD mortality (1.24 (95% CI: 1.05 - 1.46)) (Table 4). The associations for traffic intensity on the nearest road as a categorical variable were insensitive to adjustment for traffic noise. After adjustment for background BS and traffic intensity as a categorical variable, relative risks for traffic noise showed a similar pattern as when traffic intensity was modeled as a continuous variable.

Relative risks for IHD mortality were somewhat elevated for living near a major road (1.15 (95% CI: 0.99 – 1.34)) and for traffic intensity in a 100m buffer (1.05 (95% CI: 0.95 – 1.16)) (Table 4).

Relative risks for background NO$_2$ and PM$_{2.5}$ concentrations were elevated for cerebrovascular and heart failure mortality (Table 4), which is comparable with the results for background black smoke.

The relative risks of traffic noise were essentially unity when traffic noise was included as a continuous exposure variable. Relative risks for background BS and traffic intensity on the nearest road were not affected (data not shown).

After excluding the subjects with noise exposure >65 dB(A), effect estimates for cardiovascular mortality for background BS did not change whereas they slightly increased for traffic intensity on the nearest road from 1.05 (95% CI: 0.99 - 1.12) to 1.09 (95% CI: 1.02 - 1.17). These analyses were conducted to evaluate the independent air pollution effects in subjects with traffic noise levels for which no noise effects have been found.

After excluding the subjects without traffic intensities (~80% of the subjects) the multivariate RRs changed slightly, with RRs for cardiovascular mortality of 1.08 (95% CI 1.00 – 1.17) for traffic intensity on the nearest road, and 1.21 (95% CI 0.89 – 1.66) for the highest noise category. Similar to the main analyses, the RR for the highest noise category decreased when background BS and traffic intensity were included in the model: from 1.34 (95% CI 0.99 – 1.80) to 1.21 (95% CI 0.89 – 1.66).

Effect estimates of background BS, traffic intensity and noise for cardiovascular mortality did not differ between men and women, between subjects aged < 62 years and subjects aged > 62 years, between never, ex and current cigarette smokers, and between groups with different percentages of persons with a low income in a neighborhood (results not shown).
Table 3. Adjusted Relative Risks (95% Confidence Intervals) for association between overall cardiovascular mortality and more specific cardiovascular mortality causes, and background black smoke (continuous), traffic intensity on the nearest road (continuous) and traffic noise exposure (in categories) which are assessed separately and in conjunction.*

<table>
<thead>
<tr>
<th>Model</th>
<th>Exposure</th>
<th>Cardiovascular (N = 6,137)</th>
<th>Ischemic heart disease (N = 3,521)</th>
<th>Cerebrovascular (N = 1,175)</th>
<th>Heart failure (N = 422)</th>
<th>Cardiac dysrhythmia (N = 339)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td>Air pollution indicators</td>
<td>Background black smoke</td>
<td>1.11 (0.96 - 1.28)</td>
<td>1.01 (0.83 - 1.22)</td>
<td>1.39 (0.99 - 1.94)</td>
<td>1.75 (1.00 - 3.05)</td>
<td>0.96 (0.51 - 1.79)</td>
</tr>
<tr>
<td></td>
<td>Traffic intensity on nearest road</td>
<td>1.05 (0.99 - 1.12)</td>
<td>1.11 (1.03 - 1.20)</td>
<td>0.82 (0.68 - 1.00)</td>
<td>1.07 (0.86 - 1.34)</td>
<td>1.04 (0.79 - 1.36)</td>
</tr>
<tr>
<td>Traffic noise exposure</td>
<td>Traffic noise 50 – 55 dB(A)</td>
<td>1.00 (0.94 - 1.07)</td>
<td>1.00 (0.92 - 1.09)</td>
<td>0.90 (0.78 - 1.04)</td>
<td>1.08 (0.85 - 1.38)</td>
<td>1.03 (0.78 - 1.36)</td>
</tr>
<tr>
<td></td>
<td>Traffic noise 55 – 60 dB(A)</td>
<td>1.00 (0.93 - 1.08)</td>
<td>1.02 (0.93 - 1.12)</td>
<td>0.89 (0.76 - 1.05)</td>
<td>1.00 (0.76 - 1.32)</td>
<td>1.08 (0.80 - 1.46)</td>
</tr>
<tr>
<td></td>
<td>Traffic noise 60 – 65 dB(A)</td>
<td>0.91 (0.81 - 1.03)</td>
<td>0.95 (0.82 - 1.11)</td>
<td>0.59 (0.43 - 0.80)</td>
<td>1.04 (0.67 - 1.61)</td>
<td>1.08 (0.67 - 1.72)</td>
</tr>
<tr>
<td></td>
<td>Traffic noise &gt; 65 dB(A)</td>
<td>1.25 (1.01 - 1.53)</td>
<td>1.15 (0.86 - 1.53)</td>
<td>0.88 (0.52 - 1.50)</td>
<td>1.99 (1.05 - 3.79)</td>
<td>1.23 (0.50 - 3.01)</td>
</tr>
<tr>
<td>Both air pollution indicators and traffic noise exposure</td>
<td>Background black smoke</td>
<td>1.11 (0.95 - 1.28)</td>
<td>1.01 (0.83 - 1.22)</td>
<td>1.41 (1.01 - 1.97)</td>
<td>1.76 (1.01 - 3.08)</td>
<td>0.94 (0.50 - 1.76)</td>
</tr>
<tr>
<td></td>
<td>Traffic intensity on nearest road</td>
<td>1.06 (0.99 - 1.13)</td>
<td>1.12 (1.04 - 1.21)</td>
<td>0.90 (0.74 - 1.10)</td>
<td>1.02 (0.79 - 1.32)</td>
<td>1.01 (0.75 - 1.36)</td>
</tr>
<tr>
<td></td>
<td>Traffic noise 50 – 55 dB(A)</td>
<td>1.00 (0.94 - 1.07)</td>
<td>1.00 (0.91 - 1.09)</td>
<td>0.90 (0.78 - 1.04)</td>
<td>1.07 (0.83 - 1.37)</td>
<td>1.03 (0.78 - 1.36)</td>
</tr>
<tr>
<td></td>
<td>Traffic noise 55 – 60 dB(A)</td>
<td>0.99 (0.92 - 1.06)</td>
<td>1.00 (0.91 - 1.10)</td>
<td>0.89 (0.76 - 1.05)</td>
<td>0.97 (0.73 - 1.29)</td>
<td>1.09 (0.80 - 1.47)</td>
</tr>
<tr>
<td></td>
<td>Traffic noise 60 – 65 dB(A)</td>
<td>0.88 (0.78 - 1.00)</td>
<td>0.90 (0.76 - 1.06)</td>
<td>0.61 (0.44 - 0.84)</td>
<td>1.01 (0.64 - 1.59)</td>
<td>1.07 (0.66 - 1.76)</td>
</tr>
<tr>
<td></td>
<td>Traffic noise &gt; 65 dB(A)</td>
<td>1.17 (0.94 - 1.45)</td>
<td>1.01 (0.74 - 1.36)</td>
<td>0.95 (0.55 - 1.66)</td>
<td>1.90 (0.96 - 3.78)</td>
<td>1.23 (0.48 - 3.13)</td>
</tr>
</tbody>
</table>

* Adjusted for age, gender, smoking status, and area level indicators of socio-economic status.

Relative risks for continuous variables were calculated for changes from the 5th to the 95th percentile; for black smoke 10 μg/m³, and for the traffic intensity on the nearest road 10,000 mvh/24h. RRs for traffic noise in categories were calculated with category ≤ 50 dB(A) as reference category. N is number of cases. dB(A) is A-weighted average sound pressure decibel levels.
Table 4. Adjusted Relative Risks (95% Confidence Intervals) for association between overall cardiovascular mortality and more specific cardiovascular mortality causes, with background NO$_2$ and PM$_{2.5}$, and traffic variables: traffic intensity on nearest road in categories, indicator variable for living near a major road and traffic intensity in a 100 m buffer.*

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Cardiovascular (N = 6,137) RR (95% CI)</th>
<th>Ischemic heart disease (N = 3,521) RR (95% CI)</th>
<th>Cerebrovascular (N = 1,175) RR (95% CI)</th>
<th>Heart failure (N = 422) RR (95% CI)</th>
<th>Cardiac dysrhythmia (N = 339) RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Background concentrations</strong></td>
<td></td>
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</tr>
<tr>
<td>Background NO$_2$</td>
<td>1.08 (0.94 – 1.26)</td>
<td>0.97 (0.80 – 1.18)</td>
<td>1.51 (1.07 – 2.12)</td>
<td>1.96 (1.11 – 3.46)</td>
<td>1.05 (0.56 – 1.95)</td>
</tr>
<tr>
<td>Background PM$_{2.5}$</td>
<td>1.11 (0.93 – 1.33)</td>
<td>0.96 (0.75 – 1.22)</td>
<td>1.62 (1.07 – 2.44)</td>
<td>2.69 (1.37 – 5.27)</td>
<td>0.66 (0.30 – 1.45)</td>
</tr>
<tr>
<td><strong>Traffic variables</strong></td>
<td></td>
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<td></td>
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<tr>
<td>Traffic intensity on nearest road</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1,225 – 10,000 mvh/24h</td>
<td>0.96 (0.88 – 1.03)</td>
<td>0.98 (0.89 – 1.09)</td>
<td>0.90 (0.75 – 1.07)</td>
<td>0.92 (0.69 – 1.24)</td>
<td>1.03 (0.75 – 1.41)</td>
</tr>
<tr>
<td>&gt; 10,000 mvh/24h</td>
<td>1.11 (0.99 – 1.25)</td>
<td>1.21 (1.04 – 1.42)</td>
<td>0.75 (0.55 – 1.03)</td>
<td>1.36 (0.90 – 2.05)</td>
<td>1.10 (0.66 – 1.84)</td>
</tr>
<tr>
<td>Living near a major road</td>
<td>1.05 (0.93 – 1.18)</td>
<td>1.15 (0.99 – 1.34)</td>
<td>0.70 (0.51 – 0.96)</td>
<td>0.94 (0.59 – 1.49)</td>
<td>1.13 (0.70 – 1.82)</td>
</tr>
<tr>
<td>Traffic intensity in 100m buffer</td>
<td>1.00 (0.92 – 1.08)</td>
<td>1.05 (0.95 – 1.16)</td>
<td>0.81 (0.67 – 0.99)</td>
<td>0.97 (0.72 – 1.32)</td>
<td>1.07 (0.77 – 1.48)</td>
</tr>
</tbody>
</table>

* Adjusted for age, gender, smoking status, and area level indicators of socio-economic status. Relative risks were calculated for changes from the 5th to the 95th percentile: for NO$_2$ 30 μg/m$^3$, for PM$_{2.5}$ 10 μg/m$^3$, and for traffic intensity in a 100m buffer 335,000 mvh/24h. RRs for traffic intensity on nearest road in categories were calculated with as reference category ≤ 1,225 mvh/24h. RRs for living near a major road were calculated with as reference category not living near a major road. Models for traffic variables included background black smoke (1987-1996). N is number of cases.
DISCUSSION

For the first time, the joint association between long-term exposure to air pollution, traffic intensity and road traffic noise with cardiovascular mortality has been reported. Background BS concentrations, traffic intensity on the nearest road and traffic noise above 65 dB(A) were associated with specific cardiovascular causes of death. Associations with background BS and traffic intensity were insensitive to noise adjustment. Exclusion of observations with traffic noise above 65 dB(A), the only noise category for which some effect was found, did slightly increase the effect estimate for traffic intensity. After adjustment for BS concentrations and traffic intensity, traffic noise risks estimates became unity for IHD mortality, while the noise risk for heart failure mortality was more robust and only slightly reduced.

Traffic noise and air pollution
The moderate correlation of modeled traffic noise with background BS (0.24) and traffic intensity on the nearest road (0.30) allowed an assessment of their independent effects. Traffic on other nearby roads was included in the noise model. However, the correlation between traffic intensity in a 100 meter circle around the home and noise was only slightly larger (0.38). The observed correlations between modeled traffic noise and air pollution were only slightly lower than in Oslo between modeled noise and air pollution: 0.46 for NO$_2$ and 0.46 for residential traffic intensity (23). In addition, the correlation between measured traffic noise and NO$_2$ was 0.35 in Madrid (24), and 0.53 in an urban area in Canada (25). Although traffic intensity is an important input variable for the model, other variables such as road surface, location of noise barriers and traffic speed are also included in the noise model (19). The inclusion of these input variables likely explains the moderate correlation between modeled traffic noise and traffic intensity on the nearest road. Road surface and noise barriers affect noise much more than air pollution (19). Traffic speed also affects air pollution and noise emissions differently. For example, within urban areas, air pollution emissions decrease when speed increases and congestion is less whereas noise emissions increase in the same situation (26,27). The distance decay function used in the noise model differs from air pollution (larger impacted area; beyond first line of buildings). Further, noise levels behave very robust to increases in traffic intensity which may also explain the moderate correlation. Doubling of road traffic intensity results in just a 3 dB(A) higher average noise level (10).

Limitations of the exposure assessment for air pollution and noise have to be considered. Exposure was assessed for the 1986 address. It was estimated that 90 percent of the participants had lived for 10 years or longer, with mean duration of residence 35 years (SD 19.8), at their 1986 address before follow-up (5), and 70 percent of the participants did not move between 1986 and end of follow-up (12). Mean traffic noise levels and the percentage of subjects exposed to the highest noise category did not differ between movers and non-movers, which does not suggest that differential moving due to noise exposure occurred. Information about moving was only available for a subset of the full cohort, and therefore an analysis restricted to non-movers was not possible. We previously showed that relative risks among non-movers increased for the association between black smoke concentrations and mortality (12). Further, concentrations for the
periods 1976-1985 and 1987-1996 were highly correlated (> 0.9) (18). These results support the use of our exposure estimate as a proxy for other time periods.

Traffic noise was estimated using traffic data from 2000-2001 whereas exposure was estimated for the 1986 address. This is likely not a major problem because traffic intensities for the period 1986-1996 were highly correlated (>0.9) (18). Correlations between traffic intensities for 1986 and 1997-2001 were high as well (> 0.87). Traffic intensities have increased over this period, mainly on motorways and in new urban areas (18). The increase on motorways had in general been compensated by measures to reduce (additional) noise. Therefore, we use the assumption that while absolute traffic intensities may have changed, relative differences are likely to be stable and busy roads with high traffic noise levels stayed busy during this time period. Further, we focused mainly on busy roads that have likely been in place between 1987 and 2001 (18).

We had no information about the time people spend at home or information about the work address. However, approximately 85 percent of the population had no paid job at baseline. This percentage resulted from the fact that most women did not have a job at baseline and because part of the men younger than 65 years also had no job at baseline.

Traffic noise exposure was estimated as the maximum level of the yearly average equivalent noise levels during the day, or evening or night. The levels during the evening and during the night receive a penalty of respectively 5 and 10 dB(A). Other studies analyzed daytime or 24-hours exposures and our modeled noise levels may on average be 1 to 5 dB(A) higher. Correlations between indicators for long-term exposure to equivalent noise levels from road traffic are however high (10), since traffic flows during day, evening and night are highly correlated. So the use of different indicators affects the risk observed at a certain noise level, but is unlikely to influence the associations. Due to the high correlation, it is difficult to distinguish the separate effects on mortality of noise exposure during the day, evening and night when information on room orientation is not available. Information about other characteristics of the noise exposure, like the number of events was not available in our study.

We did not have information about mediating factors like bedroom location, window opening habits or sound isolation. Studies have shown that noise effects were larger when such mediating factors were considered in the analyses (10). The implication is that the effect of true noise exposure (indoors) may be underestimated. However, for the population studied the associations with traffic intensity remained and are unlikely due to environmental noise levels possibly due to the exposure reduction strategies listed above. The difference between noise exposure and noise environmental levels may be different in other cities or populations.

Elevated risks of traffic noise on cardiovascular mortality were restricted to the highest noise category (>65 dB(A)), but only 1.6 percent of our participants were exposed to such noise levels. Subjects lived on average for a long period at their baseline address and have therefore been exposed to similar noise levels. From a biological point of view one would expect a continuous increase in risk with increasing noise level. Other studies that assessed exposure-effect relationships of noise on cardiovascular effects showed however also a threshold of effect (10). Physiological adaptation and coping may be reasons for an empirical threshold of effect (10).
A recent Dutch study investigated road traffic noise and hypertension, adjusting for fine particles (PM$_{10}$) exposure (28). Variation in exposure to PM$_{10}$ was however limited and this might be one of the explanations why there was no significant contribution to the relative risk for PM$_{10}$.

**Specific causes of cardiovascular death**

A few cohort studies evaluated the effects of long-term exposure to air pollution on specific causes of cardiovascular mortality, which can be compared with our results for the background black smoke concentration. Pope et al. found an elevated relative risk of 1.12 (95% CI: 1.08 - 1.15) for all cardiovascular diseases plus diabetes for a 10 μg/m$^3$ increase in PM$_{2.5}$ concentrations. Relative risks were 1.18 (95% CI: 1.14 - 1.23) for IHD and 1.13 (95% CI: 1.05 - 1.21) for dysrhythmia, heart failure and cardiac arrest. No elevated risk was found for cerebrovascular disease (13). A large cohort study among U.S. women found increased risks for overall cardiovascular mortality (RR 1.76; 95% CI: 1.25 - 2.47) and for coronary heart disease (RR 2.21; 95% CI: 1.17 - 4.16) for a 10 μg/m$^3$ increase in PM$_{2.5}$ exposure (4). In contrast with the Pope et al. study (13), cerebrovascular mortality was also significantly associated with exposure to PM$_{2.5}$ in this study (4) as in our study. In a small cohort of Norwegian men no association between cerebrovascular mortality and NO$_x$ was found whereas IHD mortality was significantly associated with a 10 μg/m$^3$ increase in NO$_x$ concentrations (RR 1.08; 95% CI 1.03 - 1.12) (7). In general, an association with overall cardiovascular mortality was found. However, results for more specific cardiovascular causes varied between studies. Varying results between studies may be explained by differences in used exposure assessment methods (average concentration for a city versus individual-level traffic-related exposure) and in the air pollutants used (traffic-related pollutants versus less traffic-related pollutants). Different types of air pollution may have different mechanisms of effect. In none of these studies were the results for air pollution adjusted for noise from road traffic.

Recent epidemiologic studies have increased the understanding of the linkage between air pollution and cardiovascular diseases, with a multitude of plausible mechanistic explanations having been demonstrated experimentally during the past few years (29). The physical and chemical characteristics of fresh vehicle exhaust particles are different from those of background particles influenced by atmospheric transformation and coagulation. This may affect the mechanisms of effect. The proposed biological mechanisms linking air pollution to cardiovascular disease involve direct effects of pollutants on the cardiovascular system, blood, and lung receptors, and/or indirect effects mediated through oxidative stress and inflammation (30). A cascade of physiological responses may follow including alterations in blood rheology, cardiac dysrhythmias, and development of atherosclerosis (30). Studies have shown associations between air pollution exposure and ST-depression, which possibly represents myocardial ischemia or inflammation (31,32). These findings suggest that ischemic mechanisms may explain the specific association between traffic exposure and IHD. Cerebrovascular mortality is more likely due to a thrombotic process (33), and possibly components of the background mixture are more related to thrombosis. The mechanisms of effect are however not exactly known yet and all of the mechanisms are likely inter-related.
Traffic intensity near the home address was associated with only IHD mortality in our study. Sensitivity analyses showed that the association was restricted to the highest traffic intensity category (>10,000 mvh/24h). A recent study by Tonne et al. found an association between cumulative traffic near the home and acute myocardial infarction (9). Peters et al. found also an association between exposure to traffic and acute myocardial infarction (14). A German cross-sectional study found that living within 150 m of a major road was associated with the prevalence of coronary heart disease (odds ratio 1.85; 95% CI: 1.21 - 2.84) (8). The results of a study by Rosenlund et al. suggested also that residential traffic-related air pollution increases the risk of coronary heart disease, in particular fatal outcomes (34). The results of these studies suggest that traffic intensity is associated especially with IHD. Our results also suggested an association between IHD and traffic intensity.

Several epidemiological studies investigated the effects of road traffic noise exposure on different cardiovascular endpoints. Inconsistent effects were found for blood pressure and hypertension, but the evidence for IHD is much stronger (10). Cohort and case-control studies in Caerphilly, Speedwell and Berlin found relative risks for IHD ranging from 1.1 to 1.4, although non-significant, at traffic noise levels above 60 dB(A) (35-37). Our IHD risk estimate is in line with these results. Strongest noise effects in our study were found for heart failure mortality, but this association was based upon a small number of cases and has not been evaluated in previous studies. The suggested effect mechanism of noise is based on the general stress concept and works ‘directly’ through synaptic nervous interactions and ‘indirectly’ through the emotional and the cognitive perception of noise. Stress can result in changes in physiological functions and metabolism, including blood pressure, cardiac output, blood lipids, carbohydrates, electrolytes, blood clotting factors, leukocyte count and others. These can be acute changes, but in the long term functional changes and dysregulation may occur, thus increasing the risk of manifest diseases. Since many of these factors are known classical cardiovascular risk factors, chronic noise exposure can increase the risk of cardiovascular disease such as IHD (10,11).

Death certificates may not be a perfect source of information for cause of mortality (38). There may be a convergence towards the most common cardiovascular causes of death and the utility of death certificates may decrease when death occurs at a higher age (39). No recent information was found about the validity of death certification in The Netherlands. It is possible that misclassification of specific cardiovascular causes on death certificates contributes to inconsistency of results between different studies.

Both individual and area-level socioeconomic characteristics have been shown to be predictors of cardiovascular health (40). We adjusted for area-level socioeconomic characteristics, but not at the individual level which was only available for the case-cohort dataset. Analyses in the case-cohort dataset showed however that individual level socioeconomic characteristics did not confound the association (12). Of the area-level indicators of socioeconomic status, especially the percentages of persons with low and high income in a neighborhood were significantly associated with mortality. As air pollution is one mechanism through which low neighborhood socioeconomic status may affect mortality, we may have been over adjusting the effects of air pollution. We cannot
exclude the possibility that traffic intensity is associated with other unmeasured risk factors other than air pollution and noise.

In conclusion, background BS concentrations, traffic intensity on the nearest road and traffic noise above 65 dB(A) were associated with specific cardiovascular causes of death. Associations with background BS and traffic intensity were insensitive to noise adjustment. Associations with traffic noise became unity for IHD mortality and slightly reduced for heart failure mortality after adjustment for background BS and traffic intensity on the nearest road. As this is the first study that reported the effects of long-term exposure to air pollution, traffic intensity and traffic noise on mortality together in one study, further studies are required to confirm or refute our findings.
Main messages

- Motorized traffic is an important source for both air pollution and noise.
- This study reported for the first time the joint association between long-term exposure to air pollution, traffic intensity and road traffic noise with cardiovascular mortality.
- Background black smoke concentrations, traffic intensity on the nearest road and traffic noise above 65 dB(A) were associated with specific cardiovascular causes of death.
- However, associations between black smoke concentrations and traffic intensity on the nearest road with specific cardiovascular causes of death were insensitive for adjustment by traffic noise and were thus not explained by traffic noise in this study.

Policy implications

- Traffic-related air pollution is associated with cardiovascular mortality, while the independent contribution of exposure to traffic-related noise is less clear.
Acknowledgments
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Competing interests
None declared.

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Figure legends

Figure 1. Distribution of estimated background black smoke concentrations (period 1987-1996), traffic intensity on the nearest road and traffic noise exposure, at the 1986 home address (N = 117,528).*

* dB(A) is A-weighted average sound pressure decibel levels; and Mvh/24h is Motor vehicles/24h
References


Mean 52 dB(A)
Min  29 dB(A)
Max  75 dB(A)
SD   7 dB(A)