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META-ANALYSIS

Long-term exposure to ambient air pollution and traffic noise and incident hypertension in seven cohorts of the European study of cohorts for air pollution effects (ESCAPE)

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Aims We investigated whether traffic-related air pollution and noise are associated with incident hypertension in European cohorts.

Methods and results We included seven cohorts of the European study of cohorts for air pollution effects (ESCAPE). We modelled concentrations of particulate matter with aerodynamic diameter ≤2.5 μm ($PM_{2.5}$), ≤10 μm (PM_{10}), >2.5, and ≤10 μm (PM_{coarse}), soot ($PM_{2.5}$ absorbance), and nitrogen oxides at the addresses of participants with land use regression. Residential exposure to traffic noise was modelled at the facade according to the EU Directive 2002/49/EC. We assessed hypertension as (i) self-reported and (ii) measured (systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg or intake of BP lowering medication (BPLM). We used Poisson regression with robust variance

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estimation to analyse associations of traffic-related exposures with incidence of hypertension, controlling for relevant confounders, and combined the results from individual studies with random-effects meta-analysis.

Among 41 072 participants free of self-reported hypertension at baseline, 6207 (15.1%) incident cases occurred within 5–9 years of follow-up. Incidence of self-reported hypertension was positively associated with $PM_{2.5}$ (relative risk (RR) 1.22 [95%-confidence interval (CI):1.08; 1.37] per 5 $\mu g/m^3$) and $PM_{2.5}$ absorbance (RR 1.13 [95% CI:1.02; 1.24] per $10^{-5}m^{-1}$). These estimates decreased slightly upon adjustment for road traffic noise. Road traffic noise was weakly positively associated with the incidence of self-reported hypertension. Among 10 896 participants at risk, 3549 new cases of measured hypertension occurred. We found no clear associations with measured hypertension.

Conclusion Long-term residential exposures to air pollution and noise are associated with increased incidence of self-reported hypertension.

Keywords Hypertension • Air pollution • Particulate matter • Nitrogen oxides • Road traffic noise • Meta-analysis

Introduction

Exposure to outdoor air pollution is related to higher cardiovascular disease risk.[1] It has been suggested that air pollution exposure might also be linked to hypertension, a major global risk factor for premature morbidity and mortality, thus possibly mediating part of the deleterious effect of air pollution on cardiovascular disease. Short-term increases in air pollution levels can raise blood pressure (BP) rapidly, as reported in observational and experimental studies.[1] In contrast, the evidence on long-term effects of air pollution on BP or hypertension is scarce and heterogeneous, with a clear lack of prospective studies. Long-term exposure to air pollution was associated with an increase in systolic and/or diastolic BP in a few recent cross-sectional studies.[2–7] However, results were inverse in a study with a large Danish cohort.[8] Positive associations of air pollution with incident[9,10] and prevalent[4,11] hypertension were reported in some, but not all studies.[5,6,8,12] In our recent cross-sectional meta-analysis of 15 European cohorts we observed a weak positive association between high residential traffic exposure and BP in participants not taking BP lowering medication (BPLM), and an elevated odds ratio for prevalent hypertension. However, there were no consistent associations of air pollutants and BP.[13]

Long-term noise exposure shares many sources with outdoor air pollution and has the potential to confound air pollution estimates. Positive associations between road traffic noise exposure and hypertension have been reported in a meta-analysis of 27 observational studies.[14] Despite the close relation of ambient noise and air pollution, few studies so far have taken noise exposure into account when investigating the effects of air pollution.[5,6,8,13,15,10]

In the present study, we investigated associations between long-term exposure to ambient air pollution, traffic indicators, and road traffic noise with the incidence of hypertension in seven European cohorts participating in the European study of cohorts for Air Pollution Effects (ESCAPE, http://www.escapeproject.eu; 16 Sept 2016).

Methods

Cohort studies

This analysis was a part of the ESCAPE Project, which investigated the long term effects of exposure to air pollution on human health in Europe. We included seven European cohorts from five countries with information on hypertension status for at least two time points (e.g. baseline and follow-up examination) and the most important potential confounders. The population-based cohorts were: Oslo health study (HUBRO, Norway); Stockholm diabetes preventive program (SDPP; Sweden); the Swedish national study of aging and care in Kungsholmen (SNAC-K; Sweden); the Diet, Cancer, and Health cohort (DCH, Denmark); the Heinz Nixdorf risk factors, evaluation of coronary calcification, and lifestyle study (HNR, Germany); the Cooperative Health Research in the Region of Augsburg (KORA, Germany); and Registre Gironí del Cor—Girona's heart registry (REGICOR, Spain). These cohorts have been described previously.[13] Work in all cohorts was conducted in accordance with the Declaration of Helsinki, and with all local ethical requirements.

Exposure assessment

Ambient air pollution concentrations were assessed according to the standard ESCAPE procedure.[16,17] In short, for each area under study, concentrations of PM_{10}, PM_{coarse} (calculated as PM_{10} minus $PM_{2.5}$), $PM_{2.5}$, and $PM_{2.5}$ absorbance (blackness of the $PM_{2.5}$ exposed filter, determined by measurement of light reflectance, as a marker for soot and black carbon), were measured in 20 sites, and concentrations of nitrogen oxides (NO_2, NO_x) were measured in 40 sites in three separate 2-week periods (to cover different seasons) between 2008 and 2011. Adjusted average annual concentrations were calculated for each site based on continuous measurements taken at one background site over a whole year. Using several traffic and land use variables (e.g. traffic, industry, port activity, residential density), derived from Europe-wide and local Geographic Information System databases, area-specific land use regression models were developed for each pollutant and applied to each participant's residential address.

We obtained the area-specific average daily road traffic noise levels as the A-weighted day-evening-night indicator (L_{den}). It was modelled at the residential façades of the participants addresses according to the EU Directive 2002/49/EC, as described previously.[13]

In addition to modelled air pollution and noise, we assessed traffic indicators for the home addresses of participants, including (i) total traffic load on major road fragments (defined as roads with traffic intensities > 5000 vehicles/day) within a 100 m radius around the residence ('traffic load'); and (ii) traffic intensity on the nearest road ('traffic intensity').

Outcome assessment

We investigated two outcomes in those free of disease at baseline incident self-reported hypertension and incident measured hypertension. *Self-reported hypertension* status was obtained at two time points in all

Table 1 Description of personal characteristics of 7 European cohorts at baseline

Variable	HUBRO	SDPP	SNAC-K	DCH	HNR	KORA	REGICOR
Baseline (years)	2000–2001	1992–1994, 1996–1998	2001–2004	1993–1997	2000–2003	1994–1995, 1999–2001	2003–2006
n (total)[a]	16 430	7535	1945	36 829	4507	5177	1931
Systolic BP (mmHg; mean ± SD)	130.4 ± 17.9	122.8 ± 15.9	142.3 ± 19.7	140.4 ± 20.6	133.1 ± 20.8	129.4 ± 18.6	125.3 ± 19.0
Diastolic BP (mmHg; mean ± SD)	75.0 ± 11.3	77.0 ± 10.0	81.9 ± 10.4	83.4 ± 10.6	81.4 ± 10.9	80.6 ± 10.7	78.3 ± 10.3
BPLM intake (%)	12.1%	5.8%	24.5%	13.0%	35.4%	16.0%	21.0%
Self-reported hypertension (%)	–	–	26.9%	17.1%	42.8%	33.3%	30.8%
Measured hypertension (%)	32.5%	24.0%	69.3%	55.2%	56.9%	37.2%	36.0%
Men (%)	44.4%	38.5%	41.6%	47.1%	50.1%	48.2%	48.2%
Age (years; mean ± SD)	48.0 ± 15.2	47.1 ± 4.9	71.1 ± 9.5	56.68 ± 4.3	59.6 ± 7.8	49.4 ± 12.8	55.3 ± 11.5
BMI (kg/m^2; mean ± SD)	25.6 ± 4.1	25.7 ± 4.0	25.7 ± 3.9	26.0 ± 4.1	27.9 ± 4.6	27.1 ± 4.4	26.6 ± 4.1
Area-level SES (%; mean ± SD)	1.8 ± 0.7	21.4 ± 2.9	2.1 ± 0.2	2.3 ± 0.9	12.5 ± 3.5	27.9 ± 18.3	7.9 ± 3.2
Current smoker (%)	25.9%	26.1%	13.6%	37.0%	23.2%	22.3%	20.7%
Passive smoking (%)	24.6%	–	65.8%	82.1%	36.2%	41.0%	–
High alcohol consumption[b] (%)	6.8%	48.0%	60.1%	62.1%	23.0%	46.6%	42.3%
Low education[c] (%)	16.9%	25.9%	20.7%	30.2%	10.7%	10.0%	31.7%
Employed (%)	74.2%	91.7%	29.8%	79.0%	40.5%	61.7%	63.2%
Type 2 diabetes mellitus (%)	3.7%	1.6%	8.4%	2.2%	13.5%	4.1%	13.5%
Coronary heart disease[d] (%)	4.1%	0.4%	4.9%	4.0%	10.5%	5.2%	3.6%

SD, standard deviation; BP, blood pressure; BPLM, BP lowering medication; BMI, body mass index; SES, socio-economic status.
[a]Only participants with full information on exposure variables, measured, hypertension and main covariates at baseline are presented. Prevalent hypertension cases included.
[b]More than six drinks/week.
[c]Primary school or less.
[d]Defined as personal history of myocardial infarction or angina pectoris.

seven cohorts. *Measured hypertension* was assessed as either systolic BP ≥140 mmHg, diastolic BP ≥90 mmHg, or current intake of BPLM, as described elsewhere.[13] Information on measured hypertension at baseline and follow-up was available in five cohorts (SNAC-K, SDPP, HNR, KORA, and REGICOR). Intake of BPLM was additionally analysed as a separate outcome. We assessed agreement of incident self-reported and measured hypertension as the number of participants with concordant hypertension status in the subgroup of those participants who were free of self-reported and measured hypertension at baseline.

Statistical analyses in cohorts

The analyses were performed in each cohort separately, using a uniform statistical protocol and centrally developed analysis codes. Cohort-specific results were pooled with a centrally conducted meta-analysis. Since the exact time of hypertension diagnosis was not available, we estimated the association between exposures and incident hypertension with Poisson regression and present the estimates as relative risk (RR). We used robust variance estimation to avoid variance overestimation, as Poisson regression is applied to binary data. Exposures were entered in the analysis as linear predictors. The main adjustment set was defined a priori and included baseline variables for age, sex, education, economic activity (full time employed, part time employed, retired, homemaker, unemployed), body mass index (BMI), smoking status, pack-years of smoking, passive smoking, total alcohol consumption, wine consumption, physical activity, family history of hypertension (if available), and area-level socio-economic status (SES). Two-exposure models with simultaneous inclusion of individual air pollutants and noise were conducted to adjust for mutual confounding. Extensive sensitivity analyses were conducted to examine the robustness of the results towards different model specifications and outcome definitions (see section 'Cohort-specific sensitivity analyses' in Supplemental Material).

Meta-analysis

We performed the random effects meta-analysis of the cohort specific effect estimates based on the DerSimonian and Laird method.[18] Inclusion of cohorts in the meta-analysis was based on data availability. We defined a *P*-value of the Cochran's Q-test <0.05 or I^2 >50% as an indication of heterogeneity. All analyses were conducted with STATA 10.0–12.0 (StataCorp, College Station, TX, USA) and R 2.13.1 (www.r-project.org; 16 Sept 2016).

Results

The baseline characteristics of the study populations including all participants with repeated information on self-reported or measured hypertension are presented in *Table 1*. Mean age ranged from 47 years (SDPP) to 71 years (SNAC-K), percentage of men from 38% to 50% and mean systolic BP from 122.8 mmHg (SDPP) to 142.3 mmHg (SNAC-K). The prevalence of self-reported hypertension ranged from 17.1% (DCH) to 42.8% (HNR). The prevalence of measured hypertension was lowest in SDPP (24.0%) and highest in SNAC-K (69.3%). The baseline characteristics of the sub-cohorts without prevalent hypertension cases, included in the analyses with incident self-reported or measured hypertension, differed from the respective complete cohorts: participants were slightly younger, had lower BP and BMI values, were more highly educated, smoked less and had a

Table 2 Description of study outcomes in cohorts

Variable	HUBRO	SDPP	SNAC-K	DCH	HNR	KORA	REGICOR
Follow-up (years; mean ± SD)	8.8 ± 0.3	8.9 ± 1.1	5.0 ± 1.4	5.4 ± 0.3	5.1 ± 0.3	8.2 ± 1.3	5.7 ± 0.6
Incident self-reported hypertension							
n (population under risk)	4642	4211	1094	24 181	2205	3402	1337
Cumulative crude incidence (%)	8.9%	14.7%	22.9%	13.8%	21.8%	26.8%	15.3%
Crude incidence rate per year (%)	1.0%	1.7%	4.6%	2.6%	4.3%	3.3%	2.7%
Incident measured hypertension							
n (population under risk)	–	4196	457	–	1759	3250	1234
Cumulative crude incidence (%)	–	41.3%	40.0%	–	36.2%	22.8%	20.8%
Crude incidence rate per year (%)	–	4.6%	8.0%	–	7.1%	2.8%	3.6%
Incident intake of blood pressure lowering medication							
n (population under risk)	6149	5167	1119	24 020	2588	4350	1524
Cumulative crude incidence (%)	14.1%	15.1%	21.5%	9.5%	25.9%	21.8%	15.1%
Crude incidence rate per year (%)	1.6%	1.7%	4.3%	1.8%	5.1%	2.7%	2.6%

Table 3 Description of exposure in all cohorts at baseline (mean ± SD, if not indicated otherwise)

Exposure	HUBRO (*n*=16 430)	SDPP (*n*=7535)	SNAC-K (*n*=1945)	DCH (N = 36 829)	HNR (*n*=4507)	KORA (*n*=5177)	REGICOR (*n*=1931)
$PM_{2.5}$ [$\mu g/m^3$]	9.0 ± 1.3	6.6 ± 1.2	8.0 ± 1.3	11.3 ± 0.9	18.4 ± 1.1	13.6 ± 0.9	15.0 ± 1.6
PM_{coarse} [$\mu g/m^3$]	4.0 ± 2.0	6.3 ± 2.4	8.7 ± 4.8	5.6 ± 1.0	10.1 ± 1.6	6.2 ± 1.1	15.1 ± 2.4
PM_{10} [$\mu g/m^3$]	13.5 ± 3.1	13.7 ± 3.2	16.5 ± 6.0	17.1 ± 1.9	27.8 ± 1.9	20.3 ± 2.4	32.3 ± 3.9
$PM_{2.5}$ absorbance [$\mu g/m^3$]	1.2 ± 0.3	0.5 ± 0.1	0.8 ± 0.2	1.2 ± 0.2	1.6 ± 0.4	1.7 ± 0.2	2.3 ± 0.7
NO_2 [$\mu g/m^3$]	20.8 ± 7.9	8.4 ± 1.7	17.4 ± 4.8	16.3 ± 7.0	30.3 ± 4.9	18.7 ± 3.8	37.1 ± 13.3
NO_x [$\mu g/m^3$]	38.1 ± 15.2	14.4 ± 3.3	33.5 ± 12.5	26.6 ± 18.3	50.8 ± 11.9	32.5 ± 7.2	66.2 ± 28.2
Traffic intensity [10^3 vehicles/day]	2.5 ± 5.1	0.9 ± 1.6	3.8 ± 9.4	3.0 ± 7.2	–	1.6 ± 3.4	4.7 ± 6.9
Traffic load[10^6 vehicles × m/day]	0.8 ± 1.8	0.1 ± 0.4	2.3 ± 3.7	1.2 ± 2.3	1.0 ± 2.3	0.4 ± 1.1	1.7 ± 2.3
L_{den} [dB], median (interquartile range)	55.7 (10)	Not available	66.5 (9.0)	57.6 (9.3)	52.5 (14.3)	53.9 (8.2)	66.9 (6.2)

Only participants with full information on exposure variables, measured, hypertension and main covariates at baseline are presented. Prevalent hypertension cases included.

lower prevalence of coronary heart disease (CHD) and type 2 diabetes mellitus (T2DM; see Supplementary material online, *Tables S1 and S2*).

We included 41 072 participants from all seven cohorts in the analysis of incident self-reported hypertension and 10 896 participants from five cohorts (SNAC-K, SDPP, HNR, KORA, REGICOR) in the analysis of incident measured hypertension (*Table 2*). Overall, 6207 (15.1%) incident cases of self-reported hypertension and 3549 (32.6%) incident cases of measured hypertension were identified. We observed a moderate to almost complete agreement (69.6–84.5%) of cases with self-reported and measured hypertension in the different cohorts. 74 to 98.6% of incident cases of self-reported hypertension were also identified as new cases of BPLM intake (see Supplementary material online, *Table S3*).

We found higher average levels of air pollution in the central and southern European study areas (HNR, KORA, and REGICOR) than in the Scandinavian study areas (HUBRO, SDPP, SNAC-K, DCH; *Table 3*). Traffic and noise exposures were highest in SNAC-K and REGICOR. The distribution of exposures in the sub-cohorts was similar to that in the total study populations at baseline (see Supplementary material online, *Tables S4* and *S5*).

Air pollutants correlated weakly (Spearman's ρ 0.3–0.5) with traffic indicators, except for SNAC-K and DCH, where moderate correlations up to 0.65 were observed (see Supplementary material online, *Table S6*). Air pollutants and traffic indicators correlated weakly to moderately (Spearman's ρ 0.5–0.7) with road traffic noise, except for REGICOR which had higher correlations (Spearman's $\rho > 0.7$).

Several air pollutants were associated with incidence of self-reported hypertension (*Figure 1*). The RR estimates in the meta-analysis of seven studies were 1.22 [95%-confidence interval (CI): 1.08;1.37] per 5 $\mu g/m^3$ $PM_{2.5}$ and 1.13 [1.02;1.24] per $10^{-5}m^{-1}$ $PM_{2.5}$ absorbance (*Table 4*). We also found non-significantly elevated point estimates for PM_{10}, PM_{coarse}, NO_2, NO_x, traffic load, and L_{DEN} with incidence of self-reported hypertension (*Table 4*, *Figure 1*, and see Supplementary material online, *Figures S1–S5*). The association of $PM_{2.5}$ with incident self-reported hypertension was robust to the inclusion of a random intercept for area, additional covariates, short-term air pollution exposure, and to the exclusion of participants who changed their address during follow-up (see Supplementary material online, *Figure S6*). The association of $PM_{2.5}$ absorbance was weaker after adjustment for area-level SES, stronger after adjustment for short-term air pollution, and unchanged with other

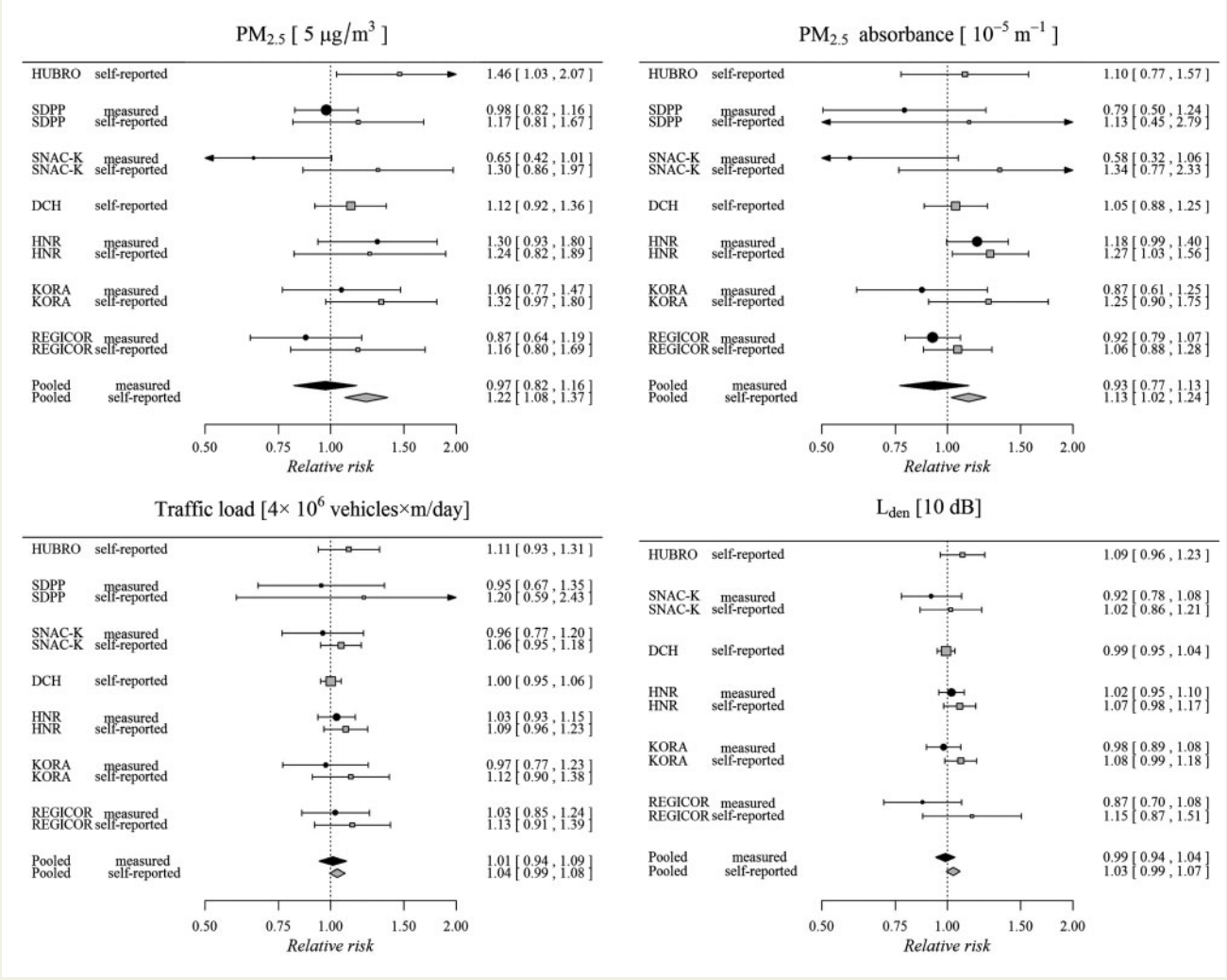

Figure 1 Random-effects meta-analysis of the associations of $PM_{2.5}$, $PM_{2.5}$ absorbance, traffic load and L_{den} at baseline with measured and self-reported incidence of hypertension at follow-up.

Filled marks = incident measured hypertension as outcome; open marks = incident self-reported hypertension. Relative risk (with 95% confidence interval) per given increase in exposure concentration is presented. Estimates were adjusted for age, sex, education, economic activity, body mass index, smoking status, pack-years of smoking, passive smoking, total alcohol consumption, wine consumption, physical activity, family history of hypertension, and area-level SES.

model specifications. Observed effect estimates did not change materially when we restricted the meta-analysis to studies with available data on measured hypertension, which restricted the analysis to 12 249 participants (see Supplementary material online, *Table S7*).

Measured incident hypertension was not related to long-term exposure to air pollution, traffic indicators, or road traffic noise. Heterogeneity of effects between studies was only apparent for $PM_{2.5}$ absorbance (*Table 4* and *Figure 1*). Similarly to the main analyses, we found no associations when using alternative definitions of measured hypertension in sensitivity analyses, although a few RRs were elevated when the 160 mmHg cut-off value was used to define hypertension (see Supplementary material online, *Table S8*).

We observed elevated RRs for the associations between the following pollutants and incident intake of BPLM: 1.15 [0.99; 1.34] per 5 $\mu g/m^3$ of $PM_{2.5}$, 1.08 [0.96, 1.22] per 10^{-5} m^{-1} of $PM_{2.5}$ absorbance, 1.08 [1.01; 1.15] per 4×10^6 vehicles × m/day traffic load, and 1.05 [0.99; 1.10] per 10 dB(A) road traffic noise (*Table 4*).

In two-exposure models, in which an air pollutant and noise exposure were included simultaneously, the estimated RRs for self-reported hypertension only slightly decreased for the PM pollutants (e.g. to 1.20 [1.05, 1.37] for $PM_{2.5}$ and 1.10 [0.98, 1.24] for $PM_{2.5}$ absorbance; see Supplementary material online, *Figure S7*). The estimates for nitrogen oxides and traffic indicators remained unchanged. For measured hypertension, the estimated RRs for PM exposures increased after adjustment for road traffic noise, while the estimates for nitrogen oxides and traffic indicators were mostly unchanged. After adjustment for $PM_{2.5}$, the estimated RRs for road traffic noise were unchanged for measured hypertension and closer to null for self-reported hypertension (see Supplementary material online, *Figure S7*).

Table 4 Pooled estimates of the association of air pollution, traffic indicators and road traffic noise with incidence of measured and self-reported hypertension, and incident intake of blood pressure lowering medication (BPLM)

Exposure	Incident measured hypertension				Incident self-reported hypertension				Incident BPLM use			
	n	RR (95%-CI)	I^2	$p_{het.}$	*n*	RR (95%-CI)	I^2	$p_{het.}$	*n*	RR (95%-CI)	I^2	$p_{het.}$
$PM_{2.5}$ [5 μg/m^3]	5[a]	0.97 (0.80, 1.17)	42.24	0.14	7[d]	1.22 (1.08, 1.37)	0.00	0.89	5[a]	1.15 (0.99, 1.34)	0.00	0.71
PM_{coarse} [5 μg/m^3]	5	0.97 (0.92, 1.03)	0.00	0.53	7	1.07 (0.98, 1.16)	24.24	0.24	5	1.03 (0.95, 1.13)	16.91	0.31
PM_{10} [10 μg/m^3]	5	0.99 (0.87, 1.12)	34.19	0.19	7	1.07 (0.97, 1.18)	16.55	0.30	5	1.01 (0.91, 1.12)	0.00	0.84
$PM_{2.5}$ absorbance [10^{-5} m^{-1}]	5	0.93 (0.77, 1.13)	57.26	0.05	7	1.13 (1.02, 1.24)	0.00	0.80	5	1.08 (0.96, 1.22)	0.00	0.64
NO_2 [10 μg/m^3]	5	0.97 (0.91, 1.03)	0.00	0.81	7	1.03 (0.99, 1.07)	0.00	0.81	5	1.02 (0.96, 1.09)	0.00	0.58
NO_x [20 μg/m^3]	5	0.96 (0.91, 1.01)	0.00	0.98	7	1.03 (0.98, 1.08)	18.90	0.29	5	0.99 (0.93, 1.07)	17.77	0.30
Traffic load [4×10^6 vehicles × m/day]	5	1.01 (0.94, 1.09)	0.00	0.96	7	1.04 (0.99, 1.08)	0.00	0.68	5	1.08 (1.01, 1.15)	0.00	0.96
Traffic intensity [5000 vehicles/day]	4[b]	0.95 (0.90, 1.00)	0.00	0.71	6[e]	1.01 (0.98, 1.03)	16.54	0.31	4[b]	0.98 (0.92, 1.04)	29.37	0.24
L_{den} [per 10 dB]	4[c]	0.99 (0.94, 1.04)	0.15	0.39	6[f]	1.03 (0.99, 1.07)	6.08	0.38	4[c]	1.05 (0.99, 1.10)	0.00	0.97

Results are presented per given exposure increment. Estimates were adjusted for age, sex, education, economic activity, body mass index, smoking status, pack-years of smoking, passive smoking, total alcohol consumption, wine consumption, physical activity, family history of hypertension, and area-level socio-economic status.
RR, relative risk; CI, confidence interval; $p_{het.}$ *P*-value for test for heterogeneity.
[a]SNAC-K, SDPP, HNR, KORA, REGICOR.
[b]SNAC-K, SDPP, KORA, REGICOR.
[c]SNAC-K, HNR, KORA, REGICOR.
[d]DCH, HUBRO, SNAC-K, SDPP, HNR, KORA, REGICOR.
[e]DCH, HUBRO, SNAC-K, SDPP, KORA, REGICOR.
[f]DCH, HUBRO, SNAC-K, HNR, KORA, REGICOR.

In a subgroup analysis we observed higher RRs with PM2.5 for both self-reported and measured hypertension RRs were elevated in participants with CHD or T2DM, although with high imprecision of the effect estimate in the groups with the disorder. Further, the self-reported hypertension RR was higher in more educated participants (see Supplementary material online, *Figure S8*).

Discussion

In this multicentre study including seven European cohorts, long-term residential exposure to $PM_{2.5}$ air pollution and high traffic load was positively associated with incident self-reported hypertension and incident intake of BPLM. These associations did not change substantially after adjustment for road traffic noise. Road traffic noise itself was weakly associated with incident self-reported hypertension and intake of BPLM, but estimates were attenuated after adjustment for $PM_{2.5}$.

In this large prospective study on environmental exposures and incident hypertension, we estimated an increase in risk for self-reported hypertension of 22% per 5 μg/m^3 increase in $PM_{2.5}$. This is in line with prior findings from Coogan *et al.*[10] in a cohort of 4204 black women living in Los Angeles, but is higher than the finding of Chen *et al.*[9] in a sample of 35 303 Ontario residents. Our results also corroborate the positive longitudinal association of high traffic load at the residence with BPLM intake that we previously observed in our cross-sectional investigation in 15 ESCAPE cohorts.[13] The size of the effect is similar to that associated with having a high BMI (RR 1.24 (95%-CI: 1.12, 1.36) per standard deviation, as reported in a study with normotensive adults), thereby underscoring the importance of the observed association.[19]

In the present study we observed relevant differences in the results, with positive associations found for self-reported hypertension and incident intake of BPLM, but no associations found for measured hypertension using the standard JNCVII cut-off values. Outcome misclassification might be a possible explanation as the overlap of cases of self-reported and measured hypertension varied substantially across cohorts. We defined measured hypertension as a combined outcome based on a one-time BP measurement during the study centre visit and/or a reported intake of BPLM. A one-time office-based BP measurement in the framework of a cohort study is subject to large intra-individual variability. This variability, as well as the potential misclassification of medication as anti-hypertensive, if indeed the indication was otherwise, might have led to a low specificity of the measured hypertension definition with many false positives. Supporting this notion of low specificity, we observed elevated RRs when applying a cut-off value of 160 mmHg. In contrast to measured hypertension, self-reported hypertension or intake of BPLM varies less and will lead to fewer false positive cases. This can potentially explain the positive effects for self-reported hypertension and incident BPLM as well as some of the inconsistencies between prior studies, some of which have reported positive associations with hypertension,[4,9–11] while others found null effects.[5,6,8,12]

The effects of $PM_{2.5}$ air pollution on incident hypertension remained stable after adjustment for road traffic noise. These findings are similar to our previous meta-analysis of 15 ESCAPE cohorts, in which adjustment for road traffic noise did not affect the cross-sectional associations between air pollution or traffic indicators and arterial BP.[13] Adjustment for noise led to no or only minor changes in the associations with hypertension in most studies.[5,8,10,13,15]

However, negative confounding of NO_x associations with BP/hypertension by traffic noise was reported in an analysis of the REGICOR study in Spain.[6]

In contrast, the positive relationship between road traffic noise and self-reported hypertension was attenuated after adjustment for $PM_{2.5}$ in our study. A small decrease and loss of statistical significance for the association between noise and BP/hypertension upon adjustment for $PM_{2.5}$ was reported by Babisch *et al.*[15] in the cross-sectional analysis of the KORA study. Three other European studies have shown positive associations between railway and road traffic noise and hypertension/BP, which were robust to adjustment for ambient nitrogen oxide concentrations, but no information on adjustment for particles is given.[20–22] Our air pollution-sensitive noise findings should be interpreted with caution. First, in contrast to ambient air pollution, noise measured at the façade and indoor exposure to traffic-related noise can vary substantially across and within populations. Window technology, location of bed rooms relative to streets, hearing impairment and personal behaviour like ventilation habits or the use of ear plugs can result in misclassification of noise exposure if the assessment is solely based on outdoor façade values. Foraster *et al.*[20] found that associations between air pollution and traffic noise, and prevalent hypertension and systolic BP were more consistent and less affected by mutual adjustment when noise exposure was estimated as indoor noise levels, taking housing characteristics and coping strategies into account.

The suggested biological mechanisms for the cardiovascular effects of air pollution include the elicitation of local and systemic inflammation and oxidative stress, autonomic imbalance, and endothelial dysfunction.[1] Road traffic noise, on the other hand, is a stressor affecting the endocrine system and the autonomic nervous system,[15] therefore, it is possible that air pollution and noise affect different pathophysiologic pathways, or at least, not completely overlapping ones.

One of the limitations of our study is that study-specific differences in outcome assessment might have led to heterogeneity between individual studies. Moreover, measured hypertension was not available for all studies. We could not validate the cases of measured or self-reported hypertension with physician diagnosis in the individual cohorts. The number of participants in the analysis with measured hypertension was about 10 000 participants, which is four times smaller than in the analysis with self-reported hypertension, and it is possible that we did not have sufficient power to detect an association with measured hypertension given the high variance of BP measurements. Selection bias due to a healthy survivor effect should be considered, as we used follow-up data covering 9 years, and possible losses to follow-up could have included those with incident hypertension. The exposure assessment was conducted in 2008–2011, while cohorts were incepted in 1992–2003. We assume, however, that spatial contrasts were stable over time, as has been shown previously.[23]

Our study has a number of strengths. It is one of the first and up to now the largest study, to investigate prospectively the mutual effect of air pollution and road traffic noise on incidence of hypertension, simultaneously. The large multicentre study, with well characterized prospective cohorts, identical protocols for exposure assessment, outcome definition, and statistical analysis, enabled a high degree of harmonization. We used diverse populations with different baseline risks for hypertension, allowing us to extrapolate the results of our study more widely than most single centre studies can. We were able to investigate incidence of hypertension, using alternative definitions of hypertension and to compare the results.

In conclusion, our results show that long-term exposure to $PM_{2.5}$ air pollution and high traffic load are positively associated with incident self-reported hypertension and incident BPLM intake, respectively, and that these associations are not confounded by road traffic noise. We also found supporting evidence that outdoor road traffic noise is associated with self-reported hypertension and intake of BPLM. Given the ubiquitous presence of air pollution, these results, if confirmed, have important public health consequences and call for more stringent air quality regulations.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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