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Residential Air Pollution, Road Traffic, Greenness and Maternal Hypertension: Results from GINIplus and LISAplus

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Abstract

Background: The public health burden of hypertension is high, but its relationship with long-term residential air pollution, road traffic, and greenness remains unclear.

Objective: To investigate associations between residential air pollution, traffic, greenness, and hypertension among mothers.

Methods: Information on doctor-diagnosed maternal hypertension was collected at the 15-year follow-up of two large population-based multicenter German birth cohorts—GINIplus and LISAplus (n=3063). Residential air pollution was modelled by land use regression models within the ESCAPE and universal kriging within the APMoSPHERE projects. Road traffic was defined as traffic load on major roads within a 100-m buffer around residences. Vegetation level (*ie*, greenness) was defined as the mean Normalized Difference Vegetation Index in a 500-m buffer around residences and was assessed from Landsat 5 TM satellite images. All the exposure variables were averaged over three residential addresses during the last 10 years and categorized into tertiles or dichotomized. The individual associations between each of the exposure variables and hypertension were assessed using logistic regression analysis.

Results: No significant and consistent associations across different levels of adjustment were observed between the exposures of interest and hypertension. The only significant estimate was found with coarse particulate matter concentrations (OR 1.66, 95% CI 1.01 to 2.74; 3rd *vs* 1st tertile) among mothers residing in the Wesel area. No significant associations were observed with traffic load or greenness.

Conclusion: This study does not provide evidence on detrimental effects of air pollution and road traffic or beneficial effects of greenness on hypertension among German adults.

Keywords: Hypertension; Air pollution; Cohort studies; Satellite imagery; Geographic information systems; Remote sensing technology; Risk factors

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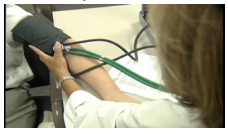

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Introduction

Outdoor air pollution is a major risk factor for global burden of disease[1] causing 3.7 million deaths per year (6.7% of all-cause mortality) worldwide.[2] As outdoor air pollution is a global problem[3] and as no "safe limits" have been identified,[4] even a very modest increase in risk represents an important disease burden. Air pollution is hypothesized to increase the risk of hypertension through systemic oxidative stress and inflammation.[5] Two recent reviews provide evidence for a link between short- and long-term exposure to air pollution and high blood pressure (BP).[6,7] However, many of the studies included into these reviews[8,9] utilized background air pollution data rather than air pollution modelled to residential address. Exposure to residential road traffic could increase BP being a proxy for both traffic-related air pollution and noise.[10] Contrary to that, greenness (*ie*, vegetation level) is hypothesized to decrease BP through stress reduction.[11,12] One study has found an inverse association between residential greenness and BP in children regardless of air pollution.[13]

In this study, we hypothesized that chronic exposure to higher levels of residential air pollution and traffic could increase the risk of hypertension among mothers while higher vegetation levels could have protective effects.

Materials and Methods

Study Population

Data on doctor-diagnosed hypertension in mothers were collected at 15-year follow-up periods; potential confounders were collected mainly at 6-, 10-, and 15-year follow-up periods through self-administrated questionnaires within two ongoing multicenter population-based prospective birth cohorts—GINIplus[14,15] and LISAplus[16]. GINIplus families were recruited in Munich (n=2949) and Wesel (n=3042) between 1995 and 1998, while LISAplus families were recruited in Munich (n=1467), Leipzig (n=976), Wesel (n=348), and Bad Honnef (n=306) between 1997 and 1999. Data from the two cohorts were pooled for this analysis, as the study design for later follow-ups was very similar.[14]

The present analysis was restricted to the families residing in the Munich area (city of Munich and the adjacent regions of Upper Bavaria and Swabia, a predominantly urban area; Fig 1) and in the Wesel area (city of Wesel and the adjacent areas of Münster and Düsseldorf, a predominantly rural area; Fig 1). No exposure data were available for Leipzig and Bad Honnef. The GINIplus and LISAplus studies have been approved by their local ethics committees, and informed consent was obtained from all families.

Exposure Assessment

Long-term (annual average) estimates of the particulate matter (PM; $PM_{2.5}$, PM_{coarse} and PM_{10}) and nitrogen oxides (NO_x [$NO + NO_2$] and NO_2) exposures were calculated using data from the ESCAPE project (European Study of Cohorts for Air Pollution Effects; *www.escapeproject.eu*) which developed area-specific land use regression (LUR) models to assess long-term air pollution in 2009. Detailed descriptions of the ESCAPE LUR models can be found elsewhere.[17-19] Table S1 (online) shows which predictors were included in the LUR models for Munich and Wesel study areas. Several publications have shown the extent of within-city variation of air pollution and the relevance of including these for air pollution estimates and highlighted the importance of higher resolution information on air pollutants.[20,21] LUR models can explain the within-city spatial contrasts in air pollution.[21] Ozone (O_3) concentration

estimates were obtained from the APMoSPHERE (Air Pollution Modeling for Support to Policy on Health and Environmental Risk in Europe) project.[22] This project estimated ozone concentrations for 2001 to a one square kilometer resolution by universal kriging modelling using Airbase, a European database of air quality.

The "traffic load" was calculated based on traffic load on major roads within a 100-m circular buffer around the home residence as the product of number of vehicles per day and length of the major roads (with traffic intensity >5000 vehicles per day).[10]

Residential greenness was assessed using the Normalized Difference Vegetation Index (NDVI) and was based on Landsat 5 Thematic Mapper (TM) satellite images at a resolution of 30 m (Fig 2). The NDVI reflects level of total green vegetation and has been frequently employed for the purpose of measuring greenness in epidemiological studies.[23] As there were no cloud-free images from the same month around the GINIplus/LISAplus 15-year follow-up period (2011–2014, which corresponds to the time of collection of the hypertension data) for both of the study areas, images from 2003 were used under explicit assumption that spatial contrasts of greenness remained similar. This assumption has been proven valid (also for our study areas) in several studies.[24,25] The mean NDVI was calculated for a 500-m circular buffer around the home residence (500 m corresponds to a ten-minutes walking distance, adopting the buffer size used by many other studies).[13,24,26-28] NDVI in a 100-m buffer was also calculated for a sen-

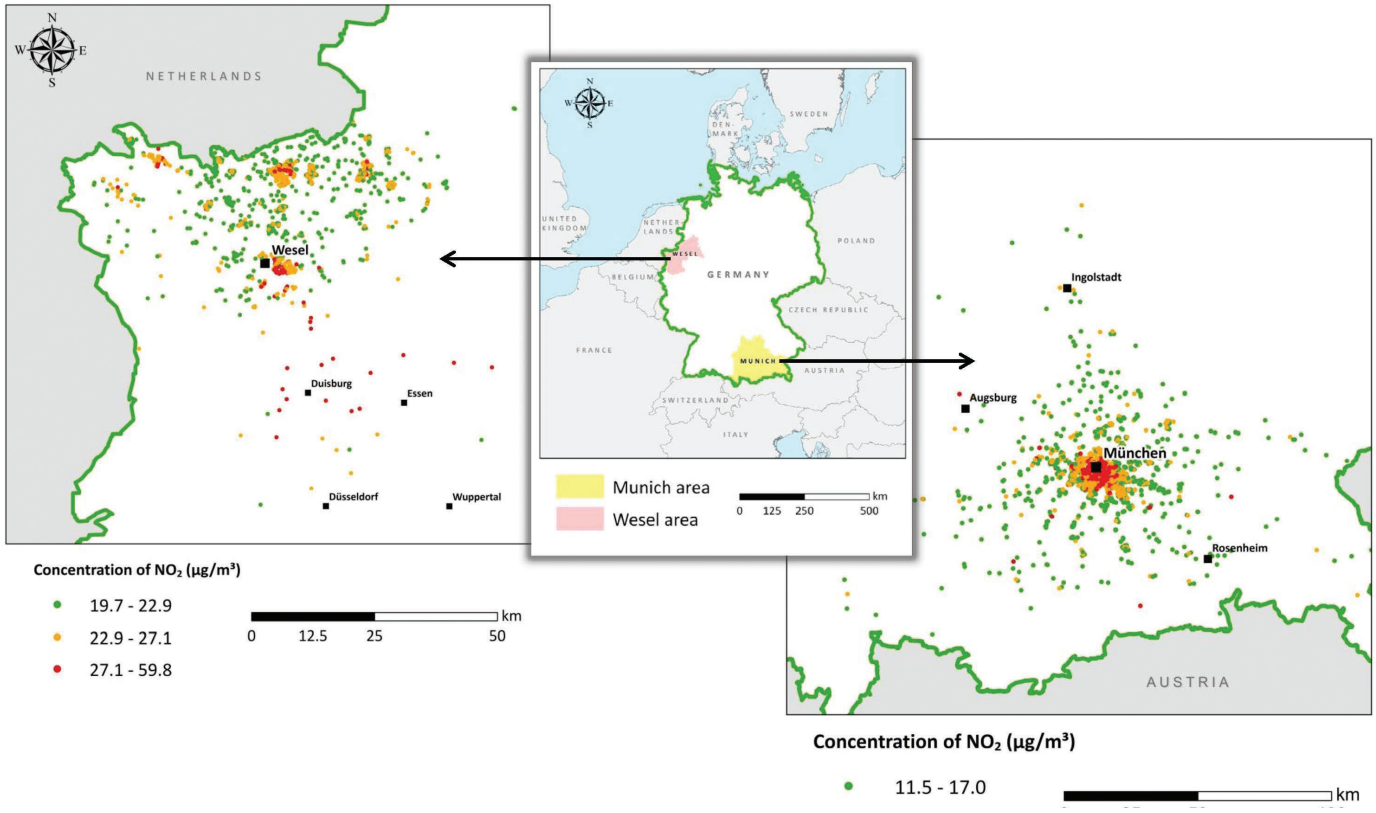

Figure 1: Location of the study areas in Germany and spatial distribution of area-specific NO_2 tertiles in Wesel and Munich study areas

Figure 2: Greenness (NDVI) map of the city of Munich and surroundings based on July 2003 Landsat 5 TM satellite images.

sitivity analysis. A more detailed description of the NDVI calculations used in this study is available elsewhere.[13,26]

The air pollution, greenness, and road traffic exposure variables were averaged for the residential addresses from the 6-, 10-, and 15-year follow-up periods of GINIplus and LISAplus cohorts, thus representing long-term exposures.

Geographic data management and calculations were conducted using the ArcGIS 10.1 Geographical Information System (GIS) (ESRI, Redlands, CA, USA) and Geospatial Modelling Environment (GME) (Spatial Ecology LLC) software programs.

Statistical Analysis

Study area-specific logistic regression models were used in order to model a binary outcome variable—self-report of doctor-diagnosed hypertension. As there was evidence for non-linearity of relationships of the air pollution and greenness variables with hypertension (identified by GAM-plots), we categorized these variables into area-specific tertiles to capture the pattern of exposure-response relationships while maintaining a sufficient number of observations in each category, as was done before.[13,29] Also, due to the high positive skewness of the traffic load variable, a binary traffic variable based on residing within 100-m from a major road ("Yes" *vs* "No") was constructed for the analysis. Results from the regression analyses are presented as odds ratios (ORs) with corresponding 95% CIs. As a sensitivity analysis, the models were run for exposures as continuous variables. These were carried out to test whether findings were subject to decisions made during data analysis. In additional sensitivity analysis, we excluded mothers who changed place of residence during ten years.

Three levels of adjustment were used—crude (non-adjusted), main, and full. Main models were adjusted for current age (yrs), study (GINIplus observation, GINIplus intervention, and LISAplus), socioeconomic status based on education (<10 years, 10 years, and >10 years, according to the German educational system), current body mass index (BMI, kg/m^2) and current active smoking status (smoker, ex-smoker, and non-smoker). Fully adjusted models included the main adjustment set and parental hypertension ("Yes" *vs* "No"), passive smoking ("Ever" *vs* "Never"), and noise annoyance ("Low," "Medium," and "High"). Noise annoyance was originally reported on the 11-category scale (from 0 to 10) and further recoded into three-categorical scale—Low: categories 0 and 1 (no annoyance at all when the window is open); Medium: categories 2 to 5; and High: categories 6 to 10 (strong or unbearable annoyance).[30] All confounders were identified *a priori* based on literature. We additionally verified whether there was effect modification by age, change of residence during the last ten years, and education by stratifying the models by each of these factors.

Table 1: Characteristics of the study population

Variable	Munich (n=1753)	Wesel (n=1310)	p value
Prevalence of hypertension (%)	8.4	9.5	0.325
Mean (SD) age, yrs	47.6 (4.6)	45.7 (3.6)	<0.0001
Study (%)			
GINIplus intervention	34.2	58.2	<0.0001
GINIplus observation	27.7	32.2	
LISAplus	38.2	9.5	
School education (%)			
Low (<10 yrs)	8.0	14.9	<0.0001
Middle (10 yrs)	29.6	49.6	
High (>10 yrs)	62.4	35.5	
Active smoking during last 10 years (%)			
Never	92.4	87.4	<0.0001
Ex-smoker	4.3	6.2	
Current	3.3	6.4	
Mean (SD) BMI, kg/m^2	23.7 (4.1)	24.7 (4.3)	<0.0001
Hypertension among parents (%)			
No	32.4	33.9	<0.044
Yes	57.7	53.9	
NA	9.9	12.2	
Passive smoking during last 10 years (%)	16.9	34.4	<0.0001
Noise annoyance during last 10 years* (%)			
Low	55.2	59.4	0.05
Medium	39.9	36.0	
High	5.0	4.4	
Change of residence during last 10 years (%)	15.4	11.5	0.002
Presence of major road (100-m buffer) (%)	27.3	16.9	<0.0001

*Noise annoyance was originally reported on the 11-category scale (from 0 to 10) and further recoded into three-categorical scale—Low: categories 0 and 1 (no annoyance at all when the window is open); Medium: categories 2 to 5; and High: categories 6 to 10 (strong or unbearable annoyance)[30].

Statistical analyses were conducted using SAS ver 9.2 (SAS Institute Inc, Cary, NC, USA) and R ver 3.3.0 (R Core Team, Vienna, Austria). Running of statistical analyses was simplified by using the *manyregs* package (*https://github.com/*

Table 2: Area-specific exposure distributions

Exposure	Range	Median	T_1*	T_2*	T_3*	p value
$PM_{2.5}$ (μg/m³)						
Munich	10.7 to 18.8	13.3	13.0	13.6	18.8	<0.0001
Wesel	15.8 to 21.4	17.2	17.1	17.6	21.4	
PM_{10} (μg/m³)						
Munich	14.8 to 30.2	20.4	19.3	20.9	30.2	<0.0001
Wesel	23.9 to 33.1	25.2	24.8	25.7	33.1	
PM_{coarse} (μg/m³)						
Munich	4.1 to 13.5	6.1	5.7	6.6	13.5	<0.0001
Wesel	1.9 to 13.8	8.4	8.2	8.6	13.8	
NO_2 (μg/m³)						
Munich	11.5 to 55.7	18.8	17.0	21.0	55.7	<0.0001
Wesel	19.7 to 59.8	23.2	22.3	24.2	59.8	
NO_x (μg/m³)						
Munich	19.7 to 110.0	32.0	29.1	35.1	110.0	<0.0001
Wesel	23.9 to 136.6	33.1	30.8	35.5	136.6	
Ozone (μg/m³)						
Munich	37.9 to 59.3	45.0	44.6	47.1	59.3	<0.0001
Wesel	33.2 to 47.1	38.7	36.3	40.3	47.1	
Residential traffic load, (100 000 vehicles/day)						
Munich	0.0 to 543.0	0.0	0.0	0.0	54.3	<0.0001
Wesel	0.0 to 112.7	0.0	0.0	0.0	11.3	
$NDVI_{500}$						
Munich	0.09 to 0.62	0.34	0.31	0.38	0.62	<0.0001
Wesel	0.21 to 0.65	0.43	0.39	0.46	0.64	

*Upper bounds of the first, second and third tertiles

cbaumbach /manyregs) in R.

Results

After excluding Leipzig and Bad Honnef residents and those with missing data in exposures, outcome or main confounders, 3063 mothers (44.9% from GINIplus observation, 29.2% from GINIplus intervention, and 25.9% from the LISAplus study) were included in the analysis. Baseline characteristics of the study population are shown in Table 1. There was considerable heterogeneity in the distribution of personal characteristics between the areas. In particular, Munich mothers had on average higher education level, smoked less, were older, and had a lower BMI than Wesel mothers. Nevertheless, the prevalence of hypertension was comparable across the two study areas (8.4% in the Munich and 9.5% in the Wesel study areas, p=0.325).

Exposure characteristics (air pollution, greenness, and traffic load) differed strongly between the two study areas with all p values <0.001 (Table 2). All exposure levels, apart from ozone, were higher in the Wesel area. Within the Munich area, PM_{coarse} was strongly correlated with NO_2 and NO_x with Spearman's ρ >0.85. In addition, NO_2 and NOx were strongly correlated (ρ>0.90). Within the Wesel region, there were strong correlations between PM_{10} and $PM_{2.5}$, NO_x and NO_2 (all ρ=0.75) as well as between NO_2 and NOx (ρ=0.97).

No overall consistent associations of long-term exposure to air pollution, greenness, or traffic volume with hypertension were found (Table 3). Firstly, differential effect estimates were observed across study areas (*ie*, ORs frequently indicated effects in opposite directions). Secondly, the size and statistical significance of the effect estimates differed across the levels of adjustment, indicating the presence of confounding. Considering the crude relationships between air pollution, greenness, and traffic load with hypertension, no statistically significant associations were detected across the two study areas. However, in mothers from the Wesel area, there was weak evidence for an association with PM_{coarse} (OR 1.67, 95% CIs 1.02 to 2.73), with increased odds of hypertension within the second tertile compared to the

Table 3: ORs and corresponding 95% CIs of air pollution, traffic load, and greenness and self-report of doctor-diagnosed hypertension estimated by logistic regression analysis

Exposure	Level*	Adjustment†	Munich	Wesel
PM_{10}	Medium *vs* Low	Crude	0.798 (0.529 to 1.205)	1.180 (0.744 to 1.872)
		Main	0.850 (0.567 to 1.275)	1.134 (0.717 to 1.794)
		Full	0.817 (0.528 to 1.264)	1.376 (0.846 to 2.239)
	High *vs* Low	Crude	0.888 (0.578 to 1.363)	1.086 (0.668 to 1.768)
		Main	0.856 (0.549 to 1.336)	1.385 (0.844 to 2.274)
		Full	0.962 (0.618 to 1.497)	1.079 (0.654 to 1.781)
$PM_{2.5}$	Medium *vs* Low	Crude	1.002 (0.672 to 1.494)	0.746 (0.466 to 1.194)
		Main	0.787 (0.516 to 1.120)	1.039 (0.671 to 1.607)
		Full	1.098 (0.718to 1.679)	0.753 (0.461 to 1.229)
	High *vs* Low	Crude	0.806 (0.516 to 1.261)	0.935 (0.585 to 1.496)
		Main	1.126 (0.731 to 1.735)	0.707 (0.429 to 1.167)
		Full	0.835 (0.523 to 1.332)	0.884 (0.545 to 1.435)
PM_{coarse}	Medium *vs* Low	Crude	1.060 (0.707 to 1.589)	1.402 (0.881 to 2.232)
		Main	0.885 (0.581 to 1.347)	1.275(0.798 to 2.037)
		Full	1.061 (0.693 to 1.624)	1.673 (1.024 to 2.732)
	High *vs* Low	Crude	0.894 (0.570 to 1.340)	1.281 (0.781 to 2.101)
		Main	1.051 (0.680 to 1.625)	1.663 (1.008 to 2.743)
		Full	0.895 (0.559 to 1.434)	1.238 (0.744 to 2.060)
NO_2	Medium *vs* Low	Crude	0.790 (0.523 to 1.192)	1.523 (0.953 to 2.434)
		Main	0.855 (0.567 to 1.282)	1.351 (0.839 to 2.175)
		Full	0.803 (0.520 to 1.240)	1.604 (0.985 to 2.613)
	High *vs* Low	Crude	0.860 (0.558 to 1.326)	1.311 (0.791 to 2.170)
		Main	0.828 (0.531 to 1.292)	1.523 (0.925 to 2.508)
		Full	0.902 (0.572 to 1.424)	1.261 (0.750 to 2.118)
NO_x	Medium *vs* Low	Crude	0.761 (0.504 to 1.150)	1.504 (0.941 to 2.403)
		Main	0.851 (0.568 to 1.274)	1.348 (0.837 to 2.169)
		Full	0.764 (0.494 to 1.180)	1.620 (0.993 to 2.640)
	High *vs* Low	Crude	0.849 (0.553 to 1.305)	1.349 (0.814 to 2.235)
		Main	0.733 (0.471 to 1.142)	1.581 (0.960 to 2.604)
		Full	0.872 (0.553 to 1.374)	1.287 (0.767 to 2.158)

Continued

Table 3: ORs and corresponding 95% CIs of air pollution, traffic load, and greenness and self-report of doctor-diagnosed hypertension estimated by logistic regression analysis

Exposure	Level*	Adjustment†	Munich	Wesel
O_3	Medium *vs* Low	Crude	0.826 (0.545 to 1.251)	1.330 (0.844 to 2.096)
		Main	0.934 (0.628 to 1.406)	1.174 (0.737 to 1.869)
		Full	0.810 (0.520 to 1.261)	1.422 (0.878 to 2.303)
	High *vs* Low	Crude	0.992 (0.645 to 1.526)	1.251 (0.764 to 2.048)
		Main	0.797 (0.508 to 1.252)	1.391 (0.852 to 2.273)
		Full	0.944 (0.607 to 1.466)	1.265 (0.764 to 2.095)
$NDVI_{500}$	Medium *vs* Low	Crude	1.011 (0.678 to 1.508)	1.064 (0.687 to 1.650)
		Main	0.779 (0.512 to 1.189)	0.810 (0.507 to 1.293)
		Full	1.101 (0.718 to 1.688)	1.065 (0.671 to 1.691)
	High *vs* Low	Crude	0.894 (0.572 to 1.398)	0.786 (0.479 to 1.289)
		Main	1.134 (0.733 to 1.755)	1.103 (0.688 to 1.769)
		Full	0.889 (0.561 to 1.409)	0.788 (0.474 to 1.311)
Traffic	Yes *vs* No	Crude	0.915 (0.623 to 1.344)	1.129 (0.701 to 1.821)
		Main	0.888 (0.590 to 1.336)	1.041 (0.622 to 1.742)
		Full	0.939 (0.598 to 1.473)	1.123 (0.648 to 1.948)

*Compares tertile 2 to tertile 1 and tertile 3 to tertile 1. The upper bounds of tertiles are shown in Table 2.
†Crude: No adjustment; Main adjustment: adjusted for age, study, active smoking, education and BMI; and Fully adjusted: Main adjustment and additional adjustment for noise annoyance, passive smoking, and parental hypertension

first tertile in the fully adjusted analysis, as well as with PM_{coarse} (OR 1.66, 95% CI 1.01 to 2.74) in the third tertile compared to the first tertile in the main models. The analysis with continuous exposure measures gave way to similar (but no statistically significant) results (Table S2, online). There was no evidence for effect modification by age, education, or changing residence within the last 10 years.

TAKE-HOME MESSAGE

- The public health burden of hypertension is high.
- Environmental factors could be detrimental or protective for hypertension but evidence for that is mixed and limited.
- Residential air pollution and greenness were not associated with hypertension in mothers residing in two German regions.

Discussion

No evidence of an association between long-term residential air pollution, traffic, or greenness and hypertension was detected. A few statistically significant estimates in Wesel mothers suggested some evidence for an association between PM_{coarse} and hypertension in this area. However, since it could not be ruled out that these results

might be due to chance, they should be interpreted with caution.

While it is well established that short-term air pollution increases risk of hypertension in adults, fewer studies investigated the effects of long-term exposure to air pollution and hypertension, and the results are heterogenous.[6,10] In particular, one study has found that long-term exposure confers higher risks of BP elevations than short-term exposure.[31] Amongst others, a recent meta-analysis by Cai, *et al*, found evidence for increased rate of hypertension among persons exposed to PM_{10}.[7] However, the meta-analysis by Fuks, *et al*, on 15 European population-based cohorts, which was omitted from the Cai, *et al*'s review,[7] failed to detect a clear overall association of long-term air pollution and BP.[10] In the present study, long-term exposure to PM was not a significant risk factor for hypertension, except for PM_{coarse} in Wesel. The aforementioned meta-analysis by Cai, *et al*, also concluded that there is evidence for increased risk of hypertension among persons exposed to NO_2.[7] On the other hand, a study of a Danish cohort found an inverse association between NO_x and the rate of hypertension.[32] In the present analysis, NO_2 and NO_x were no significant risk factors for hypertension. Concerning O_3, the studies of Chuang, *et al*, and Dong, *et al*, have found a positive association between long-term exposure and BP levels.[8,33] Our study failed to detect O_3 as a risk factor for hypertension. One of the potential explanations of why we did not detect any associations between the rate of hypertension and air pollution could be that compared to the European guidelines[34] and some highly polluted areas in China,[35,36] air pollution levels in our study areas were very low. Nevertheless, they are consistent with air pollution levels observed in Germany and throughout Europe.[37,38] Moreover, the observed PM levels exceeded the WHO guidelines.[39]

Exposure to residential road traffic has been linked to increased BP in several previous studies.[40,41] Finally, exposure to greenness was demonstrated to decrease risk for cardiovascular mortality and morbidity in several studies.[23] One study has found an association between greenness and BP in children, regardless of air pollution.[13] In our study, residential greenness and road traffic were not associated with hypertension and could therefore not contribute to the evidence cited.

This study has several strengths. Firstly, land use regression models were used to assign address-specific air pollution estimates to all study participants. Compared to studies that have used a single measurement site, our study allowed capturing within-city variations in air pollution and reducing measurement error in the exposure assessment. Secondly, we objectively assessed residential greenness from satellite images. To the best of our knowledge, this is the first study that investigated potential impact of residential greenness on hypertension. However, the authors of the present analysis are aware of several important limitations of this study. Cross-sectional design of the current study does not allow establishing causality. Moreover, the generalizability of the findings may be limited as socio-economically disadvantaged groups are frequently underrepresented in birth cohorts.[42] Loss to follow-up and incomplete exposure, outcome and confounding data further limit the generalizability. In order to investigate the impact of missing data, we compared the original study population to that currently included, and found only minor differences. Furthermore, in this study, air pollution and greenness were estimated only at the residential address. There was no information on air pollution levels at the work place, on the way to work, or during leisure activities. Greenness was assessed using images from 2003 and its levels might have

For more information on hypertension in bus drivers in Colombo, Sri Lanka see http://www.theijoem.com/ijoem/index.php/ijoem/article/view/986

changed over the follow-up period so that some measurement error might be present. However, it has been shown that spatial contrasts in greenness tend to be stable over time.[24,27] Next, there was likely some misclassification of the outcome measure. Hypertension in this study was assessed as a self-reported doctor-diagnosed hypertension. However, hypertension is often underdiagnosed so that many persons unknowingly misreport their outcome status.[43] As study participants were not aware of this study hypothesis as well as of their exposure status, we assumed that misclassification of outcome was non-differential. Measurement error in the covariates might be important, as the information for the mothers had to be assessed indirectly. The smoking status of study participants was, for instance, extrapolated from the variable on whether children experienced smoking by parents at home. Measurement error in the covariates could lead to residual confounding. Finally, missing information on several potential confounders such as physical activity or alcohol consumption might also lead to unmeasured confounding.

In conclusion, this study does not provide evidence on detrimental effects of residential air pollution and road traffic or beneficial effects of greenness on maternal hypertension in two areas in Germany.

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