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The Urban Exposome during Pregnancy and Its Socioeconomic Determinants

Oliver Robinson,[1,2,3,4] Ibon Tamayo,[2,3,4] Montserrat de Castro,[2,3,4] Antonia Valentin,[2,3,4] Lise Giorgis-Allemand,[5] Norun Hjertager Krog,[6] Gunn Marit Aasvang,[6] Albert Ambros,[2,3,4] Ferran Ballester,[4,15] Pippa Bird,[7] Leda Chatzi,[8,9,10] Marta Cirach,[2,3,4] Audrius Dėdelė,[11] David Donaire-Gonzalez,[2,3,4] Regina Gražulevičiene,[11] Minas Iakovidis,[16] Jesus Ibarluzea,[4,12,13,14] Mariza Kampouri,[8] Johanna Lepeule,[5] Léa Maitre,[2,3,4] Rosie McEachan,[7] Bente Oftedal,[6] Valerie Siroux,[5] Remy Slama,[5] Euripides G. Stephanou,[16] Jordi Sunyer,[2,3,4] Jose Urquiza,[2,3,4] Kjell Vegard Weyde,[6] John Wright,[7] Martine Vrijheid,[2,3,4] Mark Nieuwenhuijsen,[2,3,4] and Xavier Basagaña[2,3,4]

[1]MRC-PHE Centre for Environment and Health, School of Public Health, Imperial College London, UK
[2]ISGlobal, Barcelona, Spain
[3]Universitat Pompeu Fabra (UPF), Barcelona, Spain
[4]CIBER Epidemiología y Salud Pública (CIBERESP), Spain
[5]Team of Environmental Epidemiology applied to Reproduction and Respiratory Health, Institut national de la santé et de la recherche médicale (Inserm), Institute for Advanced Biosciences (IAB), Inserm, CNRS, University Grenoble-Alpes, Grenoble, France
[6]Norwegian Institute of Public Health (NIPH), Oslo, Norway
[7]Bradford Teaching Hospitals NHS Foundation Trust (BTHFT), Bradford Institute for Health Research, Bradford, UK
[8]Department of Social Medicine, Faculty of Medicine, University of Crete, Heraklion, Crete, Greece
[9]Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California, USA
[10]Department of Genetics & Cell Biology, Faculty of Health, Medicine, and Life Sciences, Maastricht University, Maastricht, Netherlands
[11]Department of Environmental Sciences, Vytautas Magnus University, Kaunus, Lithuania
[12]Health Research Institute (BIODONOSTIA), San Sebastian, Spain
[13]School of Psychology, University of the Basque Country, San Sebastián, Spain
[14]Public Health Department, Basque Government, San Sebastian, Spain
[15]Epidemiology and Environmental Health Joint Research Unit, FISABIO–Universitat Jaume I–Universitat de Valencia, Valencia, Spain
[16]Environmental Chemical Processes Laboratory (ECPL), Chemistry Department, University of Crete, Heraklion, Crete, Greece

Background: The urban exposome is the set of environmental factors that are experienced in the outdoor urban environment and that may influence child development.

Objective: The authors' goal was to describe the urban exposome among European pregnant women and understand its socioeconomic determinants.

Methods: Using geographic information systems, remote sensing and spatio-temporal modeling we estimated exposure during pregnancy to 28 environmental indicators in almost 30,000 women from six population-based birth cohorts, in nine urban areas from across Europe. Exposures included meteorological factors, air pollutants, traffic noise, traffic indicators, natural space, the built environment, public transport, facilities, and walkability. Socioeconomic position (SEP), assessed at both the area and individual level, was related to the exposome through an exposome-wide association study and principal component (PC) analysis.

Results: Mean±standard deviation (SD) NO_2 levels ranged from $13.6 \pm 5.1\ \mu g/m^3$ (in Heraklion, Crete) to $43.2 \pm 11\ \mu g/m^3$ (in Sabadell, Spain), mean ± SD walkability score ranged from 0.22 ± 0.04 (Kaunas, Lithuania) to 0.32 ± 0.07 (Valencia, Spain) and mean ± SD Normalized Difference Vegetation Index ranged from 0.21 ± 0.05 in Heraklion to 0.51 ± 0.1 in Oslo, Norway. Four PCs explained more than half of variation in the urban exposome. There was considerable heterogeneity in social patterning of the urban exposome across cities. For example, high-SEP (based on family education) women lived in greener, less noisy, and less polluted areas in Bradford, UK (0.39 higher PC1 score, 95% confidence interval (CI): 0.31, 0.47), but the reverse was observed in Oslo (−0.57 PC1 score, 95% CI: −0.73, −0.41). For most cities, effects were stronger when SEP was assessed at the area level: In Bradford, women living in high SEP areas had a 1.34 higher average PC1 score (95% CI: 1.21, 1.48).

Conclusions: The urban exposome showed considerable variability across Europe. Pregnant women of low SEP were exposed to higher levels of environmental hazards in some cities, but not others, which may contribute to inequities in child health and development. https://doi.org/10.1289/EHP2862

Introduction

The majority of the European population now live in an urban environment, and although city living confers many benefits to health, such as increased economic opportunity and access to health facilities, it also brings increased levels of environmental hazards and reduced access to green spaces (Nieuwenhuijsen 2016). These environmental factors have been associated with adverse health outcomes, particularly during vulnerable periods, such as early life (Gascon et al. 2016). For instance, exposure to air pollution has been associated with reduced birth weight (Pedersen et al. 2013) and decreased lung function in children (Gasana et al. 2012), noise has been associated with increased blood pressure in children (van Kamp and Davies 2013), whereas green spaces have been reported to have beneficial effects on birth outcomes (Agay-Shay et al. 2014; Dadvand et al. 2014) and child cognitive development (Dadvand et al. 2015). Furthermore, individuals are exposed simultaneously to a multitude of different factors, which may jointly affect health. The exposome concept, analogous to the genome, has been advanced to describe the totality of lifetime human environmental exposures, with the pregnancy period a key period for exposome assessment (Robinson and Vrijheid 2015).

Although a variety of ways to operationalize the exposome have been proposed (Juarez et al. 2014; Rappaport and Smith 2010; Robinson et al. 2015; Wild 2012), the different conceptions share an approach that considers sets of exposures together. We define the urban exposome as the set of air pollutants, noise,

Address correspondence to O. Robinson, MRC-PHE Centre for Environment and Health, School of Public Health, Imperial College London, St Mary's Campus, Norfolk Place London, UK, W2 1PG. Telephone: 020-75942067. Email: o.robinson@imperial.ac.uk

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meteorological factors, green spaces, and built environment characteristics that an individual is exposed to in the outdoor urban environment and that may be assessed through common geospatial methods. Due to the importance of determinants such as urban form and place, exposures within the urban exposome can be highly correlated to each other, relative to other parts of the exposome (Robinson et al. 2015). Although every individual has a personal exposome, many parts of the exposome, including exposure levels and correlations, are shared between groups due to shared determinants. For instance, individuals may live in the same or similar type of urban environment, which in turn may be conditioned on their nationality, ethnicity, or social class. Environmental inequality, which is the differential exposure to pollution or healthy environments between groups within a population, beyond issues of fairness, may have important health implications. The triple jeopardy hypothesis states that low socioeconomic position (SEP) communities are (i) more highly exposed to environmental hazards and (ii) more susceptible to poor health due to psychosocial stressors and fewer opportunities to choose healthy behaviors, resulting in (iii) experiencing health disparities driven by environmental factors (Brulle and Pellow 2006; O'Neill et al. 2003). However, it is not clear whether all parts of the urban exposome are similarly associated with socioeconomic factors or how these associations differ by geographical setting. Although in some cities, hazards such as air pollutants are associated with lower SEP, in other cities, the reverse is true (Hajat et al. 2015). Furthermore, little is known about the relationship between SEP and other outdoor exposures and the urban exposome as a whole.

In this paper, we aim to describe the urban exposome of pregnant women across nine European cities or urban areas, including exposure levels and correlation structure, and to evaluate the socioeconomic determinants of the urban exposome both within and between cities.

Methods

Study Population

The study was part of the Human Early Life Exposome (HELIX) project (Vrijheid et al. 2014), which aims to characterize the exposome during early life and its relationship to child health and development. Nine urban areas from six existing longitudinal population-based birth cohort studies from across Europe were included: BiB (Born in Bradford) based in Bradford, United Kingdom (Wright et al. 2013); EDEN (Étude des Déterminants pré et postnatals du développement et de la santé de l'ENfant), based in Poitiers and Nancy, France (Heude et al. 2016): INMA (INfancia y Medio Ambiente), based in Sabadell, Valencia, and Gipuzkoa in Spain (Guxens et al. 2012); KANC (Kaunus Cohort), based in Kaunas, Lithuania (Grazuleviciene et al. 2009); MoBa (Norwegian Mother and Child Cohort Study), based in Oslo, Norway (Magnus et al. 2016); and Rhea, based in Heraklion in Greece (Chatzi et al. 2017). Eligibility criteria were applied in each cohort (Table S1). Overall, the study population included 28,710 women who had singleton deliveries between 1999 and 2010 and for whom the home address and the data sources (Table S2) necessary for calculation of NO_2 levels and building density at their homes during pregnancy were available. Information from each study participant was obtained in each cohort by questionnaire or medical records. Approval was obtained from the ethics committees in every site. All participating women provided informed written consent.

Exposure Assessment

For each woman, assessment of exposure during pregnancy at the geocoded residential address at recruitment was made in the PostgreSQL (© 1996–2017, The PostgreSQL Global Development Group), PostGIS (Creative Commons Attribution-Share Alike 3.0 License http://postgis.net), and QGIS (QGIS Development Team, 2016; QGIS Geographic Information System) platforms for the following groups of environmental factors: air pollutants, vehicular traffic, road traffic noise, built environment indicators, natural environment indicators, and meteorological measures, including exposure to ultraviolet (UV) radiation. The pregnancy period was calculated from date of last menstruation or ultrasound measurement.

Daily measurements of temperature, humidity and pressure were obtained from a local weather station in each study area and averaged over the pregnancy period. Daily measurements of UV radiation (as erythemal UV and DNA-damaging UV) at 0.5×0.5-degree resolution was obtained from the Global Ozone Monitoring Experiment onboard the ERS-2 (European Remote Sensing) satellite (Temis 2016) and averaged over the pregnancy period.

For assessment of air pollutants, including particulate matter (PM) with an aerodynamic diameter of less than 2.5 μm ($PM_{2.5}$) and of less than 10 μm (PM_{10}), nitrogen dioxide (NO_2), and nitrogen oxides (NO_X), we used land use regression (LUR) or dispersion models, temporally adjusted to measurements made in local background monitoring stations and averaged over the whole pregnancy period. For most cities, we used site-specific LUR models developed in the context of the ESCAPE project (Beelen et al. 2013; Eeftens et al. 2012). In Bradford, assessment for $PM_{2.5}$ and PM_{10} was made based on the ESCAPE LUR model developed in the Thames Valley region of the United Kingdom and adjusted for background PM levels from monitoring stations in Bradford (Schembari et al. 2015). The ESCAPE European-wide LUR model was applied for $PM_{2.5}$ in Nancy, Poitiers, Gipuzkoa, and Valencia and corrected for local background monitoring data (Wang et al. 2014). In Gipuzkoa and Valencia, PM_{10} estimates were made based on local ratios to $PM_{2.5}$ estimates. In Nancy and Poitiers, dispersion models were used to assess NO_2 and PM_{10} exposure (Rahmalia et al. 2012).

Noise levels Lden (average sound pressure level over all days, evenings, and nights in a year, where the evening value gets a penalty of 5 dB and the night value of 10 dB) were derived from noise maps produced in each local municipality under the European Noise Directive [European Commission and Working Group Assessment of Exposure to Noise (WG-AEN, 2010)]. To improve comparability between centers, the values were categorized into six categories (<55; 55–59.9; 60–64.9; 65–69.9; 70–74.9; >80 dB) for analysis. In Heraklion, estimates on noise were newly modeled following a new fieldwork campaign to assess multiple exposures conducted at 160 monitoring points around the city (van Nunen et al. 2017). Briefly, in addition to air pollutant and meteorological variables, measurements of noise averaged over 30 min monitoring (Sonometer SC160, CESVA monitors), and manual traffic counts of light and heavy vehicles over 15 min were made at each monitoring point. Sites were chosen representing multiple types (e.g., traffic, urban background, urban green) and the campaign conducted during 2015, measuring each monitoring site three times in different seasons (summer, winter, and autumn). We applied the LUR modeling methods and GIS predictor variables used in the ESCAPE project (Eeftens et al. 2012) to develop LUR models of traffic count and noise. The two models are described in Table S3.

We followed the PHENOTYPE protocol (Nieuwenhuijsen et al. 2014) to measure the surrounding vegetation, i.e., trees, shrubs, and parkland, and applied the Normalized Difference Vegetation Index (NDVI) (Weier 2011) derived from the Landsat 4–5 Thematic Mapper (TM) satellite images at 30 m × 30 m resolution (https://lpdaac.usgs.gov/data_access/glovis). NDVI is an indicator of greenness based on land surface reflectance of visible (red) and near-infrared parts of the spectrum and ranges between −1 and 1, with higher numbers indicating more greenness. To achieve maximum exposure contrast, we looked for available cloud-free Landsat TM images during the period between May and August for years relevant to our period of study and calculated greenness within 100-, 300-, and 500-m buffers around each address. We calculated access to major green spaces (parks or countryside) and blue spaces (bodies of water) as the straight-line distance from the home to nearest blue or green space with an area greater than $5{,}000\,m^2$ from topographical maps (Urban Atlas 2006 or local sources, see Table S2).

Topological maps for the following built environment indicators were obtained from local authorities or from Europe-wide sources (Table S2). Traffic-density indicators (traffic density on nearest street, traffic load on major road within 100 m and inverse distance to nearest major road) were calculated from road network maps following the ESCAPE protocol (Beelen et al. 2013; Eeftens et al. 2012). Building density was calculated within 100- and 300-m buffers by dividing the area of building cover (km^2) by the area of buffer (km^2). Population density was calculated as the number of inhabitants per square kilometer surrounding the home address. Street connectivity was calculated as the number of intersections inside 100-m and 300-m buffers, divided by the area (km^2) of each buffer. Access to public transport was assessed through the number of bus stops inside 300-m and 500-m buffers. Facility richness index was calculated as the number of different facility types (Business, Community Services, Educational Institutions, Entertainment, Financial Institutions, Hospitals, Parks and Recreation, Restaurants, Shopping, Transportation Hubs and Travel Destinations) present divided by the maximum potential number of facility types specified, in a buffer of 300 m, giving a score ranging from 0 to 1. Land use Shannon's Evenness Index (SEI) was calculated to provide the proportional abundance of each land use (such as residential, commercial, entertainment, and office development) in a buffer of 300 m, giving a score ranging from 0 to 1. It was calculated by multiplying each proportion of land use type by its logarithm and dividing the sum of all land-use–type products by the logarithm of the total possible land use types. We developed an indicator of walkability, adapted from the previous walkability indexes (Duncan et al. 2011; Frank et al. 2006), calculated as the mean of the deciles of population density, street connectivity, facility richness index, and land use SEI within 300-m buffers, giving a walkability score ranging from 0 to 1.

Socio-Economic and Demographic Variables

Predominant country ethnicity was defined for all cohorts except the BiB as whether the participant was born in the country of cohort or elsewhere. In BiB, predominant country ethnicity was defined as whether the participant self-identified as "white British" or not. We analyzed four indicators of SEP: family education, occupation, family income, and area-based SEP. Indicators were constructed as follows:

Family education. This was considered the primary individual-level SEP indicator because it was available for all cohorts. Family education was defined as the highest level of education reported for either the participants or their partners. It was categorized according to the International Standard Classification of Education (ISCED) (Eurostat 2016) as three levels: Less than primary, primary and lower secondary education; upper secondary and postsecondary nontertiary education; tertiary (university level) education.

Area-level SEP. Area level SEP was defined for all cohorts based on area-level measures of deprivation or socioeconomic indicators for the home address of the participant. For the INMA cities, we used the Spanish Urban Vulnerability Index (Department of Architecture, Housing and Land 2001) at census-area level (average population $(\text{pop.}) = 1{,}500$), for the EDEN cities, we used the French European Deprivation Index score (Pornet et al. 2012) at the IRIS census level ($\text{pop.} = 2{,}000$). For Bradford, we used the UK Index of Multiple Deprivation (Department for Communities and Local Government 2010) at the lower layer super output area ($\text{pop.} = 1{,}500$). For Oslo, we used tertiles of average personal income of the "grunnkrets" area ($\text{pop.} = 1{,}000$) (Statistics Norway 2013). In Kaunas (Smith et al. 2017) and Heraklion (Hellenic Statistical Authority 2001), we used the proportion with tertiary (university-level) education of the voting district ($\text{pop.} = 3{,}400$) and aggregated lower census area ($\text{pop.} = 2{,}000$), respectively. The measures were used to class participants as low, medium, or high SEP, based on tertiles of their distribution at the country level (INMA, BIB, and Eden) or cohort level (Oslo, Heraklion, and Kaunas).

Occupational SEP. The last reported occupation of participating women (available as ISCO88 codes in MoBa, INMA, Rhea, and KANC cohorts), was converted into low, medium, and high SEP, based on the European Socioeconomic Classification (ESEC) (Institute for Social and Economic Research 2006).

Family income. Family income was available in the EDEN, MoBa, BiB, and KANC cohorts. In the EDEN and MoBa cohorts, self-reported family income was converted into low, medium, and high family income based on cohort-specific tertiles. In BiB, we used the responses to the question, "How well would you say you or you and your husband/partner are managing financially these days?" We classed those who responded "Living comfortably" as high family income, those who responded "Doing alright" as medium family income, and those who responded "Just about getting by," "Finding it quite difficult," or "Finding it very difficult" as low family income. In Kaunas, participants were asked directly to class their family income as low, medium, or high.

Statistical Analysis

Pearson's correlations were first calculated and heat maps were drawn [corrplot R package (version 0.84; R Development Core Team)] to display the correlations between continuous exposures.

To evaluate the SEP determinants of the exposome within each urban area, we focused on a reduced exposome dataset of 18 variables, where we removed meteorological variables (which have no within-city spatial variation) and those indicators that were correlated by more than 0.8 to other indicators to improve interpretability of spatial patterns. For some types of exposure, such as traffic and green spaces, the selection included multiple indicators that, as evidenced by their moderate correlations, were considered independent entities that all contribute to proper characterization of urban exposomes. We first performed a separate linear regression between the SEP indicator and each exposure, using the exposure as the dependent variable. All models compared the high SEP group to the reference group, a combined category of medium- and low-SEP participants. Models were adjusted for participant ethnicity (predominant country ethnicity or not), age (continuous variable, years), and marital status (living with partner or not), chosen *a priori* as potential confounders of the SEP-exposure associations. We drew volcano plots by city to display the associations, with each exposure scaled by standard deviation (SD) within city to allow comparability between exposures and city. To allow comparison between SEP indicators, we have presented associations with a further subset of nine exposures (chosen based on expert knowledge as the most representative exposure(s) of each exposure group) as beta coefficients [with 95% confidence intervals (CI)] in the original exposure units.

To evaluate SEP associations with the urban exposome overall, we performed a principal component analysis (PCA) on the reduced exposome dataset of 18 variables, using the "prcomp" command in the base R package. Exposures were first centered by the mean within each city to remove between city variation, and unit variance scaled. The singular value decomposition was then calculated, which defines a rotation of the exposome matrix so that the first derived direction (i.e., the first principal component) is chosen to maximize the SD of the derived variable, the second to maximize the SD among directions uncorrelated with the first, and so on for each subsequent component. The first principal components that cumulatively explained over 50% of variance in the data were retained for analysis with SEP. The scores of these principal components were regressed against SEP in models adjusted for participant ethnicity, age, and marital status as described above.

City-specific effects in the both the single exposure-SEP and PCA-SEP analyses were combined using random effect meta-analyses using the metafor R package (version 2.0-0; R Development Core Team) (Viechtbauer 2010). All analyses were performed in R (version 3.4.4; R Development Core Team).

Missing values (Table S4) of variables were imputed using the method of chained equations (White et al. 2011) for all analyses, using the mice R package (version 3.1.0; R Development Core team) (van Buuren and Groothuis-Oudshoorn 2011). Prior to imputation, skewed exposure variables were transformed to achieve normality. The distributions of all transformed variables were examined to make sure that transformations did not lead to extreme or influential observations. In cases of variables with zeros that required a log transformation, a constant value was added to the variable as the log of zero is minus infinity. The constant value was chosen to minimize the skewness of the resulting variable. (Transformations used are shown in Table S5). All variables were used as potential predictors of missing data, unless they introduced collinearity problems in the imputation process, in which case they were excluded from the imputing equation that gave problems. In addition, we forced the cohort variable into all the imputation models. The method of predictive mean matching was used for all continuous exposures.

Variables that were missing for an entire cohort were also imputed for the PCA analysis only. This includes NO_X (missing in Nancy and Poitiers), PM_{abs} (missing in missing in Nancy, Poitiers, Gipuzkoa, and Valencia), atmospheric pressure (missing in Kaunas), traffic load (missing in Oslo), and noise (missing in Gipuzkoa and Valencia). This option has been shown to be superior to excluding the cohort or excluding the exposure (Held et al. 2016; Jolani et al. 2015).

Results

Participant Demographics

A total of 28,045 women were included in this study (Table 1). The study area with the most participants was Oslo with 10,559, and the area with the least was Sabadell with 547. There was a wide range of education levels between study centers, with the highest proportion of women from highly educated families in the MoBa Oslo cohort (88%) and the lowest in the INMA Valencia cohort (29%). Participating women in Kaunas were the least ethnically diverse, with 97% of women reporting being born in Lithuania, and the Born in Bradford cohort the most ethnically diverse, with 36% of participating women reporting being "white British." Figure 1 shows the geographic spread of the study areas.

Exposure Levels

Table 2 shows levels of environmental exposure by city. Average noise levels (Lden) during the day were lowest in Kaunas (mean 49.6 dB) and highest in Heraklion (mean 64.1 dB). NO_2 levels were highest in Sabadell (mean 43.2 μg/m^3) and lowest in Heraklion (mean 13.6 μg/m^3). $PM_{2.5}$ levels were highest in Nancy

Table 1. Sociodemographic information of study participants, by city.

	MoBa Oslo	KANC Kaunas	BiB Bradford	EDEN Nancy	EDEN Poitiers	INMA Gipuzkoa	INMA Sabadell	INMA Valencia	Rhea Heraklion
N	10559	3625	10008	669	574	594	575	695	746
Mean age, years ± *SD*	31.39 ± 3.98	28.34 ± 5.05	27.81 ± 5.57	29.03 ± 4.87	28.85 ± 5.01	32.58 ± 3.6	31.54 ± 4.29	31.04 ± 4.6	30.41 ± 4.79
N of predominant country ethnicity (%)[a]	8954 (84.8)	3516 (97)	3594 (35.9)	634 (94.8)	531 (92.5)	569 (95.8)	510 (88.7)	607 (87.3)	683 (91.6)
N living with partner (%)	10241 (97)	2894 (79.8)	8395 (83.9)	623 (93.1)	539 (93.9)	590 (99.3)	568 (98.8)	675 (97.1)	730 (97.9)
N working during pregnancy (%)	9894 (93.7)	3032 (83.6)	4202 (42)	526 (78.6)	415 (72.3)	527 (88.7)	509 (88.5)	580 (83.5)	403 (54)
N active smokers (%)	471 (4.5)	279 (7.7)	1625 (16.2)	172 (25.7)	172 (30)	142 (23.9)	175 (30.4)	281 (40.4)	164 (22)
N Area level SEP (low) (%)	3530 (33.4)	779 (21.5)	5620 (56.2)	301 (45)	193 (33.6)	2 (0.3)	115 (20)	127 (18.3)	174 (23)
N Area level SEP (medium) (%)	3576 (33.9)	1857 (51.2)	3525 (35.2)	171 (25.6)	95 (16.6)	90 (15.2)	253 (44)	405 (58.3)	290 (39)
N Area level SEP (high) (%)	3559 (33.7)	989 (27.3)	863 (8.6)	197 (29.4)	286 (49.8)	502 (84.5)	207 (36)	163 (23.5)	282 (38)
N highest education level of family (primary) (%)	47 (0.4)	91 (2.5)	4403 (44)	16 (2.4)	22 (3.8)	29 (4.9)	108 (18.8)	157 (22.6)	27 (3.6)
N highest education level of family (secondary) (%)	1258 (11.9)	1333 (36.8)	1665 (16.6)	214 (32)	232 (40.4)	215 (36.2)	265 (46.1)	336 (48.3)	371 (49.7)
N highest education level of family (tertiary) (%)	9254 (87.6)	2201 (60.7)	3940 (39.4)	439 (65.6)	320 (55.7)	350 (58.9)	202 (35.1)	202 (29.1)	348 (46.6)
N social class by occupation (low) (%)	1610 (15.2)	1199 (33.1)	NA	NA	NA	300 (50.5)	359 (62.4)	444 (63.9)	307 (41.2)
N social class by occupation (medium) (%)	483 (4.6)	65 (1.8)	NA	NA	NA	22 (3.7)	26 (4.5)	22 (3.2)	97 (13)
N social class by occupation (high) (%)	8466 (80.2)	2361 (65.1)	NA	NA	NA	272 (45.8)	190 (33)	229 (32.9)	342 (45.8)
N self-reported family income (low) (%)	3610 (34.6)	1202 (33.2)	3182 (31.8)	277 (41.6)	304 (53.1)	NA	NA	NA	NA
N self-reported family income (medium) (%)	3643 (34.9)	1908 (52.6)	4188 (41.8)	152 (22.8)	156 (27.3)	NA	NA	NA	NA
N self-reported family income (high) (%)	3185 (30.5)	515 (14.2)	2638 (26.4)	237 (35.6)	112 (19.6)	NA	NA	NA	NA

[a]Defined as whether the participant was born in the country of cohort or elsewhere, except in Bradford where it was defined as whether the participant self-identified as "white British."

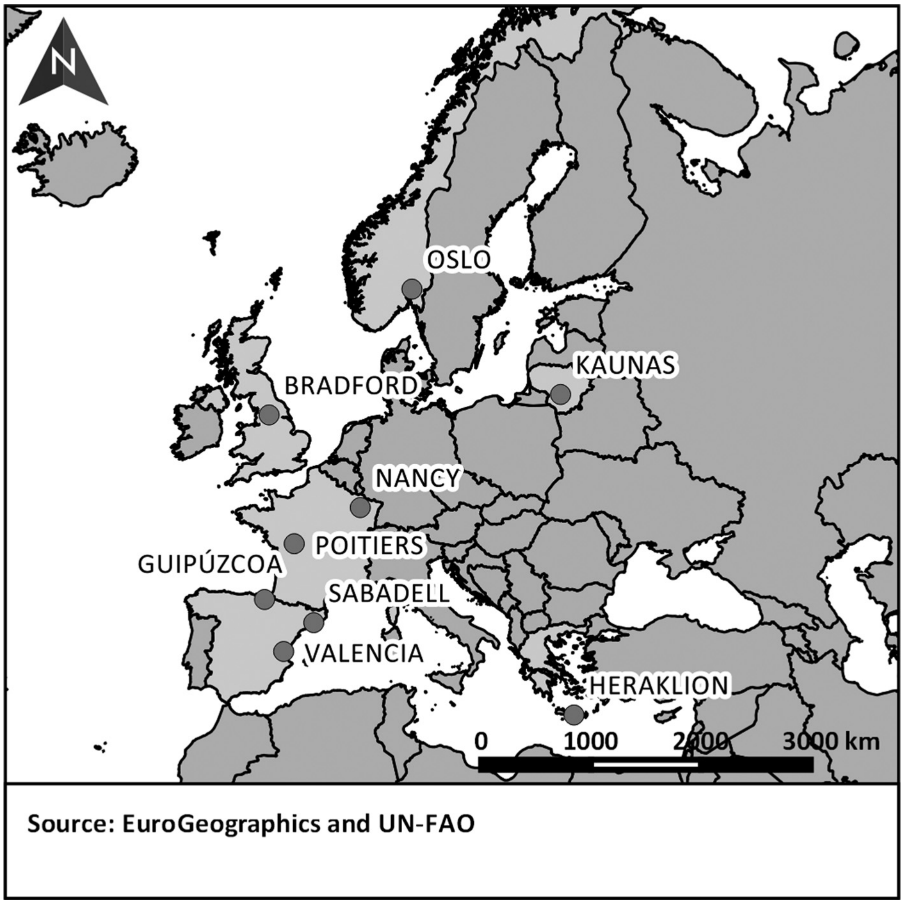

Figure 1. Overview of area locations.

(mean 23.8 $\mu g/m^3$) and lowest in Oslo (mean 10.9 $\mu g/m^3$), whereas PM_{10} levels were highest in Heraklion (mean 37.4 $\mu g/m^3$) and lowest in Oslo (mean 14.1 $\mu g/m^3$). In addition, UV dose levels mirrored the latitude of cities with lowest levels in the most northerly city, Oslo (mean DNA damaging spectrum irradiance: 0.48 kJ/m^2) and the highest in Heraklion (mean 1.71 kJ/m^2). Valencia was the most building dense area (mean 0.37 km^2/km^2 within 300-m buffer) and Kaunas (mean 0.12 km^2/km^2) the least. Mean connectivity was similar in each center, with the exception of Kaunas, which had the lowest street connectivity with a mean of 41 street intersections per km^2, within 300 m from the home address. The most densely populated city was Sabadell (mean 18,700 inhabitants$/km^2$), and the least was Poitiers (mean 2,100 inhabitants$/m^2$). Mean walkability was highest in Valencia (0.32) and lowest in Kaunas (0.22). The southern cities had the least surrounding greenness with the lowest mean NDVI of 0.19 in a 100-m buffer in Heraklion. When green spaces were assessed by distance to major green space, the difference between southern and northern cities was less pronounced. Heraklion had the lowest percentage of women living within 300 m from major green space (61%), whereas Gipuzkoa had the highest (97%). In Gipuzkoa, 76% of women lived within 300 m of a major blue space, but only 1.6% of participants did in Valencia.

Exposure Correlations

Correlations between all 28 included environmental factors across all areas are shown in Figure 2. Noise showed weak correlation (r) with NO_2 (0.18) and NO_X (0.26) but less so with the other air pollutants and was more highly correlated to traffic load (within 100-m buffer, 0.53). The road-traffic indicators showed only weak-to-moderate correlations with the air pollutants (range: 0.01 to 0.34). Building density, particularly assessed in the larger 300-m buffer, correlated most strongly with population density (0.54), NO_2 (0.51), street connectivity (0.48), and inverse distance to major green space (−0.32) and weaker with PM absorbance (0.16). Surrounding greenness (NDVI in 300-m buffer) was negatively correlated with many environmental factors, including noise (−0.26), air pollutants (−0.23 to −0.42), temperature (−0.43), UV radiation (−0.38), and all built environment factors, particularly building density (−0.74). Inverse distance to major blue space was weakly correlated with humidity (−0.19) and green space (0.08 to 0.24). Walkability correlated strongly with building density (0.60), moderately with NO_2 (0.38) and noise (0.30), weaker with traffic load (0.23) and number of bus stops (0.25) and correlated negatively with green space measures (−0.34 to −0.53). Temperature and UV radiation showed moderate correlations with PM_{10} (0.45 and 0.46, respectively).

The pattern of correlations between environmental indicators was broadly similar within each area (Figure 3), although there were some differences. For instance, we observed a range of correlations between population density with noise (−0.19 in Poitiers to 0.15 in Oslo), NO_2 (0.07 in Kaunas to 0.59 in Poitiers), $PM_{2.5}$ (0.10 in Poitiers to 0.52 in Heraklion), surrounding greenness (NDVI 100, −0.64 in Oslo to −0.15 in Kaunas), and walkability (0.1 in Kaunas to 0.72 in Sabadell and Valencia).

Socioeconomic Determinants of Individual Urban Exposures

Figure 4 shows the SD difference in individual exposures by family education level for each study area. The extent of social

Table 2. Exposure levels, by city.

Exposure short name	Description	MoBa Oslo	KANC Kaunas	BiB Bradford	EDEN Nancy	EDEN Poitiers	INMA Gipuzkoa	INMA Sabadell	INMA Valencia	Rhea Heraklion
temperature	Mean Temperature, °C ± SD	7.28 ± 2.37	8.03 ± 2.53	8.57 ± 1.45	10.03 ± 2.19	12.06 ± 2.23	13.85 ± 1.47	13.37 ± 2.47	18.86 ± 1.88	19.28 ± 1.88
humidity	Mean % Humidity ± SD	72.17 ± 3.6	85.52 ± 3	86.62 ± 2.25	77.27 ± 2.56	76.33 ± 3.62	76.54 ± 1.07	75.51 ± 3.17	60.37 ± 0.72	59.24 ± 1.95
pressure	Mean Atmospheric pressure, mb ± SD	999.55 ± 1.83	NA	981.99 ± 1.28	992.24 ± 0.72	1003.27 ± 1.13	988.54 ± 0.75	976.71 ± 0.67	1014.34 ± 1.31	1013.12 ± 1.38
uv (ddf)	Mean UV irradiance DNA damaging dose, kJ/m^2 ± SD	0.48 ± 0.12	0.67 ± 0.23	0.67 ± 0.2	0.77 ± 0.24	0.91 ± 0.26	1.06 ± 0.29	1.14 ± 0.31	1.34 ± 0.29	1.71 ± 0.37
NO_2	Mean NO_2, $\mu g/m^3$ ± SD	22.09 ± 8.2	18.67 ± 3.57	21.55 ± 3.96	30.34 ± 10.29	15.9 ± 5.22	18.89 ± 4.55	43.15 ± 11.02	25.42 ± 10.24	13.62 ± 5.13
NO_x	Mean NO_X, $\mu g/m^3$ ± SD	39.91 ± 16.37	28.98 ± 6.96	36.23 ± 8.37	NA	NA	44.35 ± 11.3	84.23 ± 29.59	41.66 ± 20.31	22.02 ± 11.55
$PM_{2.5}$	Mean $PM_{2.5}$, $\mu g/m^3$ ± SD	10.91 ± 2.1	17.52 ± 2.46	12.83 ± 2.14	23.78 ± 1.77	17.81 ± 1.83	14.24 ± 0.75	15.09 ± 1.76	14.62 ± 1.4	15.11 ± 1.23
PM_{10}	Mean PM_{10}, $\mu g/m^3$ ± SD	14.13 ± 3.52	24.71 ± 2.28	18.69 ± 2.87	23.55 ± 2.19	15.46 ± 1.54	23.73 ± 1.25	27.96 ± 3.9	24.37 ± 2.34	37.44 ± 3.87
PMabs	Mean PM absorbance, $\mu g/m^3$ ± SD	1.20 ± 0.33	2.27 ± 0.26	1.28 ± 0.19	NA	NA	NA	2.62 ± 0.66	NA	1.16 ± 0.3
noise (Lden)	Mean Noise level (Lden) dB(A) ± SD	54.79 ± 6.01	49.55 ± 6.47	58.25 ± 4.1	60.14 ± 6.24	59.01 ± 7.61	NA	61.53 ± 5.81	NA	64.07 ± 3.31
NDVI100	Mean NDVI values within a buffer of 100 m ± SD	0.50 ± 0.12	0.50 ± 0.07	0.40 ± 0.11	0.44 ± 0.11	0.47 ± 0.1	0.38 ± 0.13	0.2 ± 0.06	0.21 ± 0.07	0.19 ± 0.05
NDVI300	Mean NDVI values within a buffer of 300 m ± SD	0.51 ± 0.1	0.50 ± 0.06	0.42 ± 0.1	0.48 ± 0.11	0.50 ± 0.09	0.46 ± 0.12	0.24 ± 0.07	0.24 ± 0.06	0.21 ± 0.05
NDVI500	Mean NDVI values within a buffer of 500 m ± SD	0.52 ± 0.09	0.5 ± 0.06	0.44 ± 0.1	0.5 ± 0.12	0.52 ± 0.09	0.52 ± 0.11	0.26 ± 0.08	0.26 ± 0.06	0.21 ± 0.06
green_dist	Mean Distance to nearest large green space, m ± SD	286 ± 256	180 ± 139	207 ± 155	168 ± 140	137 ± 150	97 ± 77	244 ± 213	144 ± 109	259 ± 176
greenYN	N with major green space within 300 m (%)	6626 (62.8)	2920 (80.6)	7482 (74.8)	552 (82.5)	502 (87.5)	578 (97.3)	403 (70.1)	619 (89.1)	454 (60.9)
blue_dist	Mean Distance to nearest large blue space, m ± SD	873 (440)	1042 (589)	1946 (1194)	1285 (1107)	1341 (1026)	280 (406)	1103 (621)	3156 (1856)	2099 (2557)
blueyn	N with major blue space within 300 m (%)	940 (8.9)	333 (9.2)	237 (2.4)	151 (22.6)	54 (9.4)	450 (75.8)	34 (5.9)	11 (1.6)	64 (8.6)
traffic_load	Mean traffic load of all roads in 100 m buffer, 1000 veh/d m ± SD	NA	1207 ± 1710	1001 ± 1491	1116 ± 1566	607 ± 1127	1369 ± 1427	2478 ± 4682	2860 ± 3243	3759 ± 3522
traffic_near	Mean traffic density on nearest road, veh/d ± SD	2338 ± 4628	8471 ± 8646	2138 ± 5410	11409 ± 13326	6642 ± 7740	1526 ± 2640	6344 ± 10117	3436 ± 5208	3024 ± 6033
road_dist_inv	Mean inverse distance to the nearest road (m^{-1}) ± SD	0.05 ± 0.03	0.03 ± 0.02	0.07 ± 0.38	0.11 ± 0.88	0.12 ± 0.74	0.12 ± 0.35	0.24 ± 0.62	0.5 ± 2.61	0.81 ± 3.51
popdens	Mean Population density, Inhabitants/km^2 ± SD	9800 ± 7922	6569 ± 2252	5442 ± 2049	5032 ± 3946	2074 ± 1787	8105 ± 8205	18745 ± 1393	13701 ± 13462	7904 ± 4345
build_dens100	Mean Building density (area of building cover (km^2) / area of buffer (km^2) within buffer of 100 m ± SD	0.23 ± 0.11	0.15 ± 0.07	0.19 ± 0.07	0.24 ± 0.12	0.16 ± 0.10	0.22 ± 0.01	0.41 ± 0.17	0.44 ± 0.20	0.31 ± 0.14
build_dens300	Mean Building density (area of building cover (km^2) / area of buffer (km^2) within buffer of 300 m ± SD	0.20 ± 0.01	0.12 ± 0.06	0.16 ± 0.06	0.19 ± 0.11	0.12 ± 0.08	0.16 ± 0.07	0.36 ± 0.14	0.37 ± 0.15	0.27 ± 0.12
connect100	Mean Connectivity density (number of intersections/ km^2) within a buffer of 100 m ± SD	290 ± 224	60 ± 39	250 ± 150	211 ± 144	227 ± 172	228 ± 133	225 ± 112	238 ± 130	250 ± 180
connect300	Mean Connectivity density (number of intersections/ km^2) within a buffer of 300 m ± SD	281 ± 150	41 ± 25	200 ± 88	176 ± 84	180 ± 116	170 ± 69	202 ± 57	191 ± 84	210 ± 148
bus_stops300	Mean bus stops within 300 m buffer ± SD	8.95 ± 4.49	7.06 ± 5.67	25.6 ± 12.51	19.94 ± 11.56	21.59 ± 14.87	71.91 ± 74.29	23.86 ± 9.64	33.28 ± 57.74	1.94 ± 3.63
bus_stops500	Mean bus stops within 500 m buffer ± SD	8.12 ± 3.34	6.58 ± 3.56	24.19 ± 8.49	18.16 ± 8.53	21.42 ± 10.21	50.18 ± 42.44	21.09 ± 5.7	30.39 ± 38.2	1.93 ± 2.48
feat_rich300	Mean facility richness within 300 m buffer ± SD	0.1 ± 0.09	0.09 ± 0.06	0.11 ± 0.07	0.08 ± 0.09	0.05 ± 0.08	0.09 ± 0.09	0.1 ± 0.06	0.1 ± 0.09	0.14 ± 0.09
landuseshan300	Mean Land use SEI within 300 m buffer ± SD	0.38 ± 0.2	0.39 ± 0.09	0.47 ± 0.09	0.47 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.42 ± 0.13	0.51 ± 0.11	0.43 ± 0.1
walkability	Mean walkability within 300 m buffer ± SD	0.29 ± 0.09	0.22 ± 0.04	0.28 ± 0.06	0.27 ± 0.05	0.26 ± 0.06	0.29 ± 0.06	0.3 ± 0.05	0.32 ± 0.07	0.31 ± 0.07

Note: NA indicates that exposure was not available.

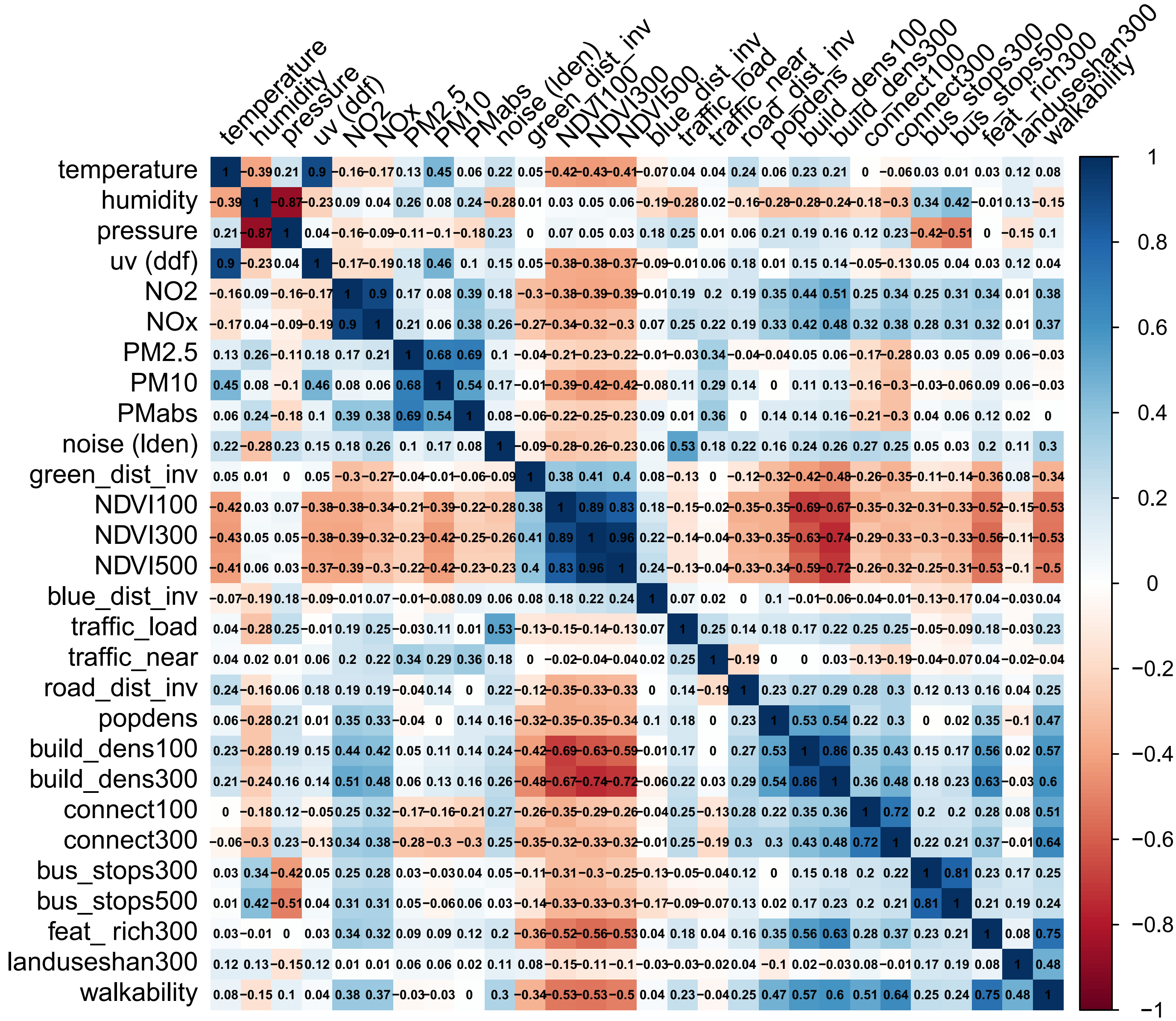

Figure 2. Heatmap showing Pearson's correlation of environmental indicators measured as part of the urban exposome. See Table 2 for exposure short names. Distance to nearest road, major green and blue spaces presented as inverse for interpretability.

patterning of the urban exposome differed considerably among areas. The smallest differences in exposure levels between women by family education level were observed in Gipuzkoa (maximum difference: 0.14 SDs higher traffic load among high-family-education women) and the largest differences in Sabadell (maximum difference: 0.34 SDs lower land use SEI among women of high family education). For area-level SEP (Figure S1), the smallest differences in exposure levels between women were observed in Oslo (maximum difference: 0.18 SDs greater distance to major green space among area SEP women) and the largest differences in Poitiers (maximum difference: 1.26 SDs lower population density among high area SEP women). For all cities except Oslo, associations were stronger with the area SEP indicator than for family education level.

Table 3 displays associations for nine key exposures with area-level SEP and individual-level SEP indicators. We describe associations in the following section with a p value <0.05. Due to the heterogeneity across cities, no significant associations were observed in overall meta-analyses, except for the association between higher family income and lower levels of traffic at the nearest road (based on five cities).

In Oslo, women of high family education were exposed to higher levels of NO_2 (at greater magnitude than for other indicators), lower levels of surrounding greenness and major green space, and higher building density and walkability. A similar pattern was observed with the occupational SEP indicator, although there was no significant association with walkability. Women with high family income were also exposed to higher NO_2 but slightly lower $PM_{2.5}$ and lived in areas with fewer bus stops and lower walkability. Women living in areas of high SEP were exposed to slightly higher levels of $PM_{2.5}$, lower levels of surrounding greenness and major green space, and higher building density and walkability.

In Kaunas, women of high family education were exposed to less average noise but greater building density. Women living in areas of high SEP were exposed to higher levels of air pollutants

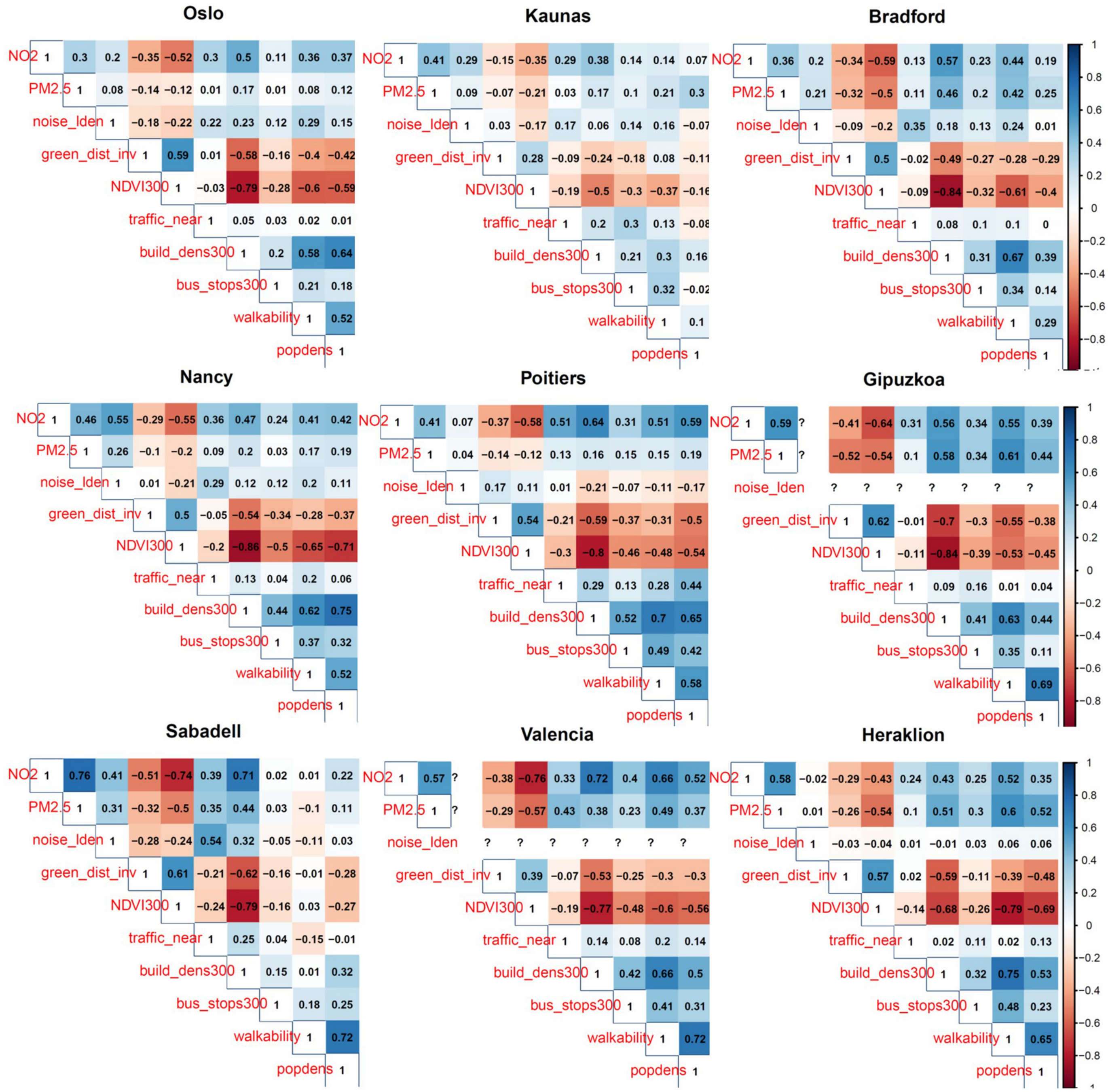

Figure 3. Heatmaps showing Pearson's correlation of environmental indicators, within each city. See Table 2 for exposure short names. Questions marks are shown for noise in Gipuzkoa and Valencia since this exposure was not available for these cities. Distance to major green spaces presented as inverse for interpretability.

and noise (in contrast with the family education indicator); to significantly lower levels of surrounding greenness and major green space; and to higher levels of traffic, building density, and walkability. Among the other two individual-level indicators, only high occupational SEP was significantly associated with higher building density.

In Bradford, women with high family education and high family income were exposed to lower levels of air pollutants; higher levels of surrounding greenness and major green space; and lower levels of building density, access to bus stops, and walkability. The pattern was similar for women living in areas of high SEP, although they were also exposed to significantly less noise.

In the French cities of Nancy and Poitiers, similar associations with area SEP were observed, with women living in areas of high SEP exposed to less air pollution; higher levels of surrounding greenness and major green space; and lower levels of traffic, building density, and walkability. Only in Nancy were women living in high SEP areas exposed to less noise. Associations were weaker with the individual-level indicators: In Nancy, high-education women were exposed to greater building density, and higher-income women were exposed to lower NO_2.

In the Spanish cities, there were contrasting patterns. In Sabadell, women of high family education were exposed to higher levels of NO_2, traffic, and building density. Women of high occupational SEP were exposed to higher levels of NO_2,

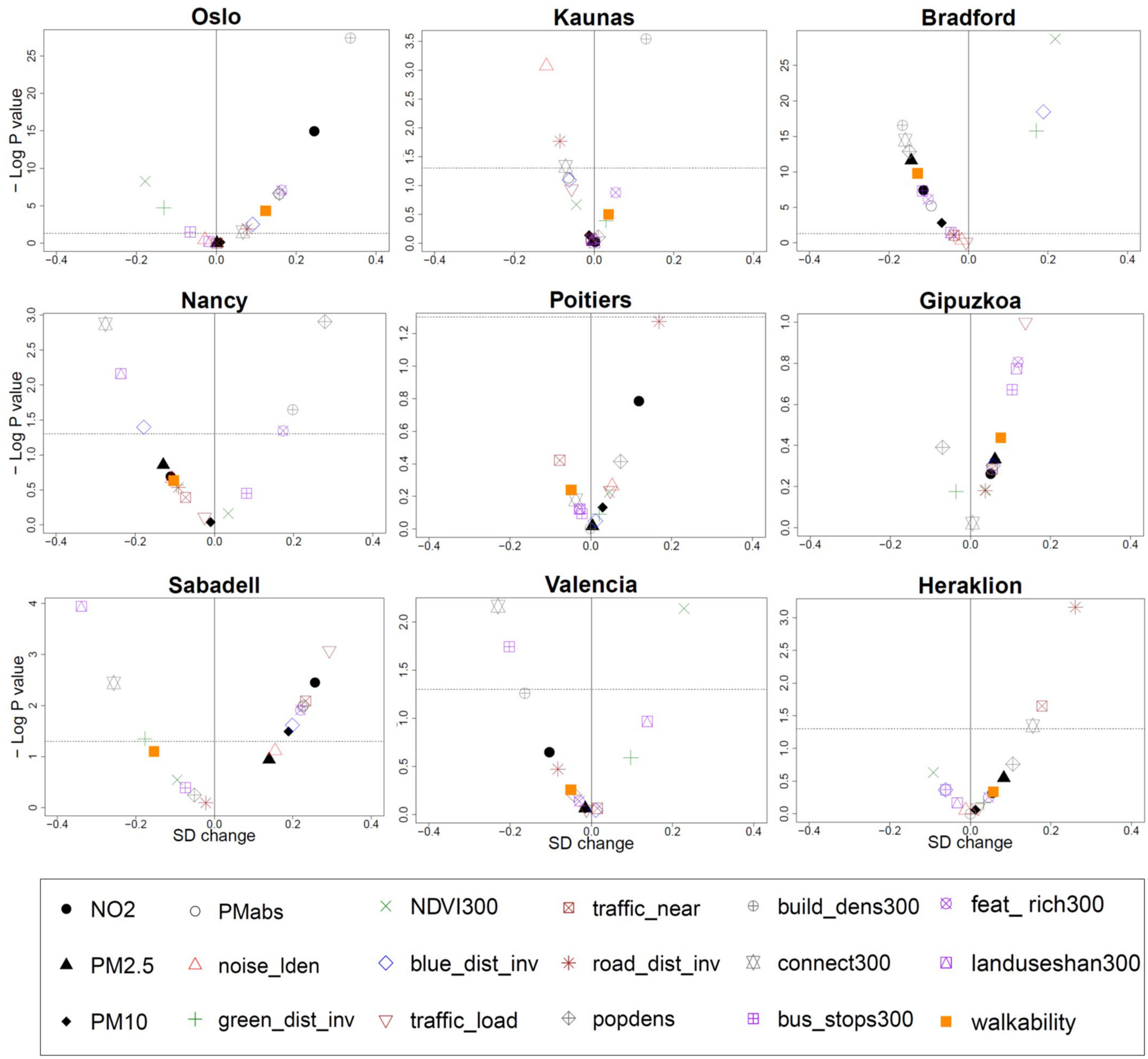

Figure 4. Volcano plots showing exposome-wide associations with family education level, by city. Y-axis shows strength of association (−log p value) and x-axis shows effect size, presented as difference in standard deviation (SD) of each exposure (for that city) between high SEP women (based on family education level) and lower SEP women, adjusted for age, ethnicity and marital status. Positive SD scores indicated higher exposure levels in high SEP women. Dotted horizontal black line shows p value = 0.05. Y-axis differs between city depending on range of p values observed. See Table 2 for exposure short names. Distance to nearest road, major green and blue spaces presented as inverse for interpretability.

lived further from major green space and were exposed to greater levels of traffic and building density. In Sabadell, high area-level SEP was associated with higher levels of air pollutants and noise, lower levels of surrounding greenness and major green space, and higher traffic and building density.

In Valencia the opposite pattern to Sabadell was observed, with lower levels of air pollution, and higher levels of surrounding greenness and major green space, and higher traffic, building density, bus stop access, and walkability among women living in high SEP areas. Women of high family education lived in areas of significantly greater surrounding greenness. Women with high occupational SEP also lived in areas of significantly greater surrounding greenness but less access to bus stops.

In Gipuzkoa, little social patterning was observed for any of the indicators: There was a small but significantly lower exposure to $PM_{2.5}$ and a greater access to bus stops among women living in areas of high SEP. Women of high occupational SEP also had greater access to bus stops.

In Heraklion, there was little social patterning with the two individual-level indicators, family education and occupational SEP, except for positive associations between traffic levels and high SEP (both indicators), and women of high occupational SEP also lived closer to major green space. However, women living in high SEP areas were exposed to higher levels of NO_2; lower levels of surrounding greenness and major green space; and higher traffic, building density, and walkability.

Table 3. Associations between SEP indicators and urban exposures.

SEP indicator	NO_2 (μg/m^3)	$PM_{2.5}$ (μg/m^3)	Noise (Lden, dB(A))	Distance to major green space (m)	NDVI score (300 m buffer)	Traffic at nearest road (vehicles/day)	Building density (300 buffer)	Bus stops (300 buffer)	Walkability (300 buffer)
Family education									
Oslo	2.05 (1.56, 2.54)	0.00 (−0.12, 0.13)	−0.09 (−0.49, 0.31)	34.42 (19.06, 49.79)	−0.017 (−0.023, −0.012)	32 (−247, 310)	0.030 (0.025, 0.035)	−0.24 (−0.51, 0.03)	0.011 (0.006, 0.017)
Kaunas	0.01 (−0.24, 0.26)	−0.01 (−0.18, 0.17)	−0.34 (−0.54, −0.14)	−4.15 (−13.92, 5.61)	−0.003 (−0.007, 0.002)	−68 (−676, 540)	0.008 (0.003, 0.012)	0.01 (−0.39, 0.4)	0.001 (−0.001, 0.004)
Bradford	−0.51 (−0.67, −0.35)	−0.32 (−0.41, −0.23)	−0.11 (−0.28, 0.06)	−26.87 (−33.2, −20.55)	0.024 (0.020, 0.027)	−166 (−393, 60)	−0.010 (−0.012, −0.008)	−1.44 (−1.96, −0.92)	−0.009 (−0.011, −0.007)
Nancy	−1.22 (−2.97, 0.53)	−0.26 (−0.56, 0.05)	−0.67 (−1.79, 0.44)	14.17 (−9.71, 38.05)	0.003 (−0.017, 0.022)	−533 (−2812, 1747)	0.022 (0.004, 0.039)	0.9 (−1.08, 2.87)	−0.005 (−0.014, 0.004)
Poitiers	0.70 (−0.18, 1.58)	0.03 (−0.29, 0.34)	0.33 (−0.78, 1.43)	−0.60 (−26.37, 25.16)	0.003 (−0.013, 0.019)	−474 (−1795, 847)	0.000 (−0.014, 0.015)	−0.3 (−2.86, 2.26)	−0.003 (−0.013, 0.007)
Gipuzkoa	0.33 (−0.42, 1.08)	0.05 (−0.07, 0.18)	NA	3.71 (−8.97, 16.39)	0.003 (−0.018, 0.023)	152 (−283, 587)	0.005 (−0.007, 0.017)	9.01 (−3.21, 21.23)	0.005 (−0.005, 0.015)
Sabadell	2.77 (0.87, 4.66)	0.24 (−0.06, 0.55)	0.88 (−0.11, 1.88)	34.47 (−2.36, 71.3)	−0.005 (−0.018, 0.008)	2244 (503, 3986)	0.029 (0.005, 0.054)	−0.83 (−2.5, 0.84)	−0.008 (−0.017, 0.001)
Valencia	−1.06 (−2.77, 0.65)	−0.02 (−0.26, 0.21)	NA	−10.58 (−28.88, 7.71)	0.014 (0.004, 0.025)	79 (−794, 952)	−0.025 (−0.051, 0.001)	−11.65 (−21.3, −2)	−0.004 (−0.016, 0.009)
Heraklion	0.26 (−0.52, 1.04)	0.10 (−0.08, 0.29)	−0.04 (−0.65, 0.57)	−7.54 (−34.51, 19.44)	−0.004 (−0.012, 0.004)	1130 (213, 2048)	−0.001 (−0.019, 0.017)	−0.23 (−0.78, 0.32)	0.004 (−0.007, 0.014)
meta-analysis	0.38 (−0.37, 1.12)	−0.03 (−0.15, 0.09)	−0.15 (−0.32, 0.02)	2.23 (−11.38, 15.84)	0.002 (−0.007, 0.011)	48 (−164, 259)	0.007 (−0.004, 0.018)	−0.42 (−0.95, 0.11)	−0.001 (−0.006, 0.004)
SEP indicator									
Area Level SEP									
Oslo	0.15 (−0.19, 0.48)	0.14 (0.06, 0.23)	0.17 (−0.1, 0.44)	46.3 (36.01, 56.59)	−0.014 (−0.018, −0.01)	115 (−73, 302)	0.006 (0.002, 0.009)	0.64 (0.46, 0.82)	0.008 (0.004, 0.012)
Kaunas	1.26 (1.01, 1.52)	0.74 (0.56, 0.92)	0.74 (0.53, 0.94)	25.19 (15.04, 35.34)	−0.015 (−0.02, −0.011)	−1385 (−2017, −753)	0.028 (0.024, 0.032)	0.38 (−0.04, 0.79)	0.017 (0.014, 0.019)
Bradford	−1.96 (−2.24, −1.69)	−0.86 (−1.01, −0.71)	−0.37 (−0.67, −0.07)	−71.48 (−82.38, −60.59)	0.069 (0.062, 0.075)	18 (−374, 410)	−0.029 (−0.033, −0.025)	−7.1 (−7.99, −6.2)	−0.03 (−0.034, −0.026)
Nancy	−8.75 (−10.35, −7.16)	−0.57 (−0.86, −0.27)	−1.57 (−2.66, −0.47)	−72.86 (−95.77, −49.95)	0.117 (0.1, 0.133)	−6935 (−9120, −4750)	−0.087 (−0.104, −0.071)	−5.44 (−7.34, −3.53)	−0.046 (−0.054, −0.038)
Poitiers	−6.14 (−6.85, −5.44)	−0.74 (−1.05, −0.44)	0.86 (−0.24, 1.95)	−121.49 (−144.93, −98.05)	0.109 (0.096, 0.122)	−6162 (−7367, −4957)	−0.099 (−0.111, −0.088)	−5.83 (−8.31, −3.34)	−0.051 (−0.06, −0.042)
Gipuzkoa	−0.99 (−2.01, 0.03)	−0.22 (−0.39, −0.05)	NA	10.74 (−6.54, 28.02)	0.003 (−0.025, 0.03)	183 (−410, 776)	0.012 (−0.005, 0.028)	54.52 (38.42, 70.63)	0.003 (−0.011, 0.017)
Sabadell	10.33 (8.64, 12.02)	0.89 (0.59, 1.18)	3.51 (2.56, 4.45)	145.5 (110.94, 180.07)	−0.052 (−0.064, −0.04)	4878 (3191, 6565)	0.12 (0.098, 0.142)	−1.05 (−2.71, 0.6)	−0.014 (−0.023, −0.004)
Valencia	−8.94 (−10.62, −7.26)	−0.95 (−1.18, −0.71)	NA	−58.44 (−77.28, −39.6)	0.074 (0.064, 0.083)	−1582 (−2497, −668)	−0.172 (−0.196, −0.148)	−37 (−46.85, −27.14)	−0.061 (−0.073, −0.049)
Heraklion	0.53 (−0.24, 1.29)	0.19 (0.01, 0.37)	0.07 (−0.52, 0.67)	51.43 (25.23, 77.64)	−0.020 (−0.028, −0.012)	1730 (835, 2625)	0.017 (0.000, 0.035)	0.33 (−0.21, 0.87)	0.026 (0.016, 0.036)
meta-analysis	−1.62 (−5.48, 2.23)	−0.15 (−0.6, 0.29)	0.17 (−0.82, 1.16)	−5.68 (−59.53, 48.17)	0.030 (−0.011, 0.071)	−979 (−3305, 1347)	−0.023 (−0.078, 0.033)	−0.64 (−14.79, 13.52)	−0.016 (−0.037, 0.004)
SEP indicator									
Occupational SEP									
Oslo	0.61 (0.21, 1.00)	0.01 (−0.10, 0.11)	−0.17 (−0.50, 0.15)	19.05 (6.7, 31.41)	−0.004 (−0.009, 0.000)	−208 (−431, 16)	0.009 (0.005, 0.014)	−0.12 (−0.34, 0.10)	0.001 (−0.003, 0.006)
Kaunas	−0.16 (−0.42, 0.09)	−0.04 (−0.21, 0.14)	−0.16 (−0.36, 0.04)	−7.04 (−16.95, 2.87)	−0.001 (−0.006, 0.003)	−105 (−722, 512)	0.006 (0.002, 0.010)	−0.26 (−0.66, 0.14)	0.001 (−0.002, 0.003)
Gipuzkoa	0.28 (−0.47, 1.02)	0.07 (−0.05, 0.19)	NA	−2.54 (−15.16, 10.09)	0.001 (−0.019, 0.021)	−140 (−573, 292)	0.002 (−0.01, 0.014)	12.34 (0.19, 24.48)	0.005 (−0.005, 0.015)
Sabadell	2.61 (0.66, 4.55)	0.09 (−0.22, 0.41)	1.31 (0.30, 2.32)	46.43 (8.71, 84.14)	−0.009 (−0.022, 0.005)	1895 (105, 3685)	0.030 (0.005, 0.055)	0.14 (−1.58, 1.86)	−0.010 (−0.020, 0.000)
Valencia	−0.77 (−2.43, 0.88)	−0.12 (−0.35, 0.11)	NA	−13.47 (−31.2, 4.27)	0.014 (0.004, 0.024)	−180 (−1027, 667)	−0.024 (−0.049, 0.001)	−17.45 (−26.76, −8.14)	−0.005 (−0.017, 0.007)
Heraklion	−0.06 (−0.83, 0.71)	0.11 (−0.08, 0.29)	−0.63 (−1.24, −0.03)	−13.76 (−40.27, 12.76)	−0.005 (−0.013, 0.003)	1607 (708, 2506)	0.001 (−0.017, 0.018)	−0.33 (−0.87, 0.21)	0.006 (−0.004, 0.016)
meta-analysis	0.22 (−0.22, 0.67)	0.02 (−0.04, 0.09)	−0.02 (−0.67, 0.62)	1.81 (−12.3, 15.93)	−0.001 (−0.007, 0.005)	284 (−361, 928)	0.006 (0.000, 0.011)	−1.04 (−6.09, 4.01)	0.000 (−0.004, 0.004)
SEP indicator									
Family income									
Oslo	0.49 (0.13, 0.85)	−0.16 (−0.25, −0.07)	−0.07 (−0.36, 0.22)	−8.74 (−19.87, 2.38)	0.003 (−0.001, 0.007)	−124 (−325, 78)	0.007 (0.003, 0.011)	−0.37 (−0.57, −0.18)	−0.006 (−0.010, −0.002)
Kaunas	0.24 (−0.10, 0.57)	0.13 (−0.1, 0.36)	0.02 (−0.25, 0.28)	−5.64 (−18.73, 7.46)	−0.005 (−0.011, 0.001)	−578 (−1393, 237)	0.004 (−0.001, 0.01)	−0.13 (−0.67, 0.4)	0.003 (−0.001, 0.007)
Bradford	−0.48 (−0.66, −0.31)	−0.05 (−0.14, 0.04)	−0.16 (−0.34, 0.03)	−14.47 (−21.23, −7.71)	0.013 (0.009, 0.017)	−198 (−439, 44)	−0.007 (−0.009, −0.004)	−1.3 (−1.86, −0.74)	−0.004 (−0.006, −0.002)
Nancy	−1.75 (−3.48, −0.03)	−0.11 (−0.4, 0.19)	−0.95 (−2.04, 0.15)	−1.39 (−24.98, 22.2)	0.009 (−0.01, 0.028)	−2227 (−4470, 16)	0.011 (−0.007, 0.029)	0.24 (−1.71, 2.18)	−0.006 (−0.014, 0.003)
Poitiers	0.89 (−0.23, 2.01)	0.04 (−0.36, 0.45)	−0.09 (−1.51, 1.32)	25.68 (−7.07, 58.43)	−0.008 (−0.029, 0.012)	−300 (−1991, 1392)	0.018 (−0.001, 0.036)	0.18 (−3.1, 3.45)	0.007 (−0.006, 0.020)
meta-analysis	0.03 (−0.57, 0.63)	−0.06 (−0.17, 0.04)	−0.11 (−0.24, 0.03)	−8.39 (−15.49, −1.29)	0.003 (−0.005, 0.011)	−179 (−330, −28)	0.004 (−0.003, 0.012)	−0.50 (−1.08, 0.08)	−0.002 (−0.006, 0.002)

Note: Table shows β coefficients and 95% confidence intervals from models comparing the high-SEP group with the reference category, a combined low- and medium-SEP group. Positive values indicate higher exposure among high-SEP women. Models adjusted for age, living with partner or not, and predominant country ethnicity or not. NA indicates that exposure was not available.

Socioeconomic Determinants of the Overall Urban Exposome

Figure 5 shows associations for family education level (Figure 5b) and area SEP (Figure 5c) with the urban exposome summarized by PCA that was performed on the reduced set of 18 indicators, from which between-city differences had been removed. Four components explained 56% of total variance in the dataset. PC1 (explaining 30% of variance) described greener, less urban and less polluted areas and was associated with both indicators of high SEP (family education and area SEP) in Bradford and Valencia and negatively associated in Oslo and Sabadell. High area SEP was positively associated with PC1 only in the French cities and negatively associated in Kaunas and Heraklion. PC2 (explaining 11% of variance) described high-traffic, polluted but less populous areas, and was significantly associated with high SEP in Sabadell, with only small associations observed for the other cohorts. PC3 (explaining 8% of variance) described noisy, walkable areas, and low air pollution areas, and was significantly associated with high SEP in Gipuzkoa (with family education), Bradford (both indicators), Poitiers and Valencia (with area SEP), and negatively associated in Oslo, Nancy (with family education), Sabadell and Heraklion (both with area SEP). PC4 (explaining 7% of variance) described low-traffic areas with access to natural spaces and higher PM levels and was associated with high SEP in Kaunas, Poitiers, Heraklion (all with area SEP), and Bradford (both indicators), and was negatively associated with high SEP in Nancy (family education), Gipuzkoa (areas SEP), and Sabadell. Due to the heterogeneity across cities, no significant associations were observed in overall meta-analyses. PC

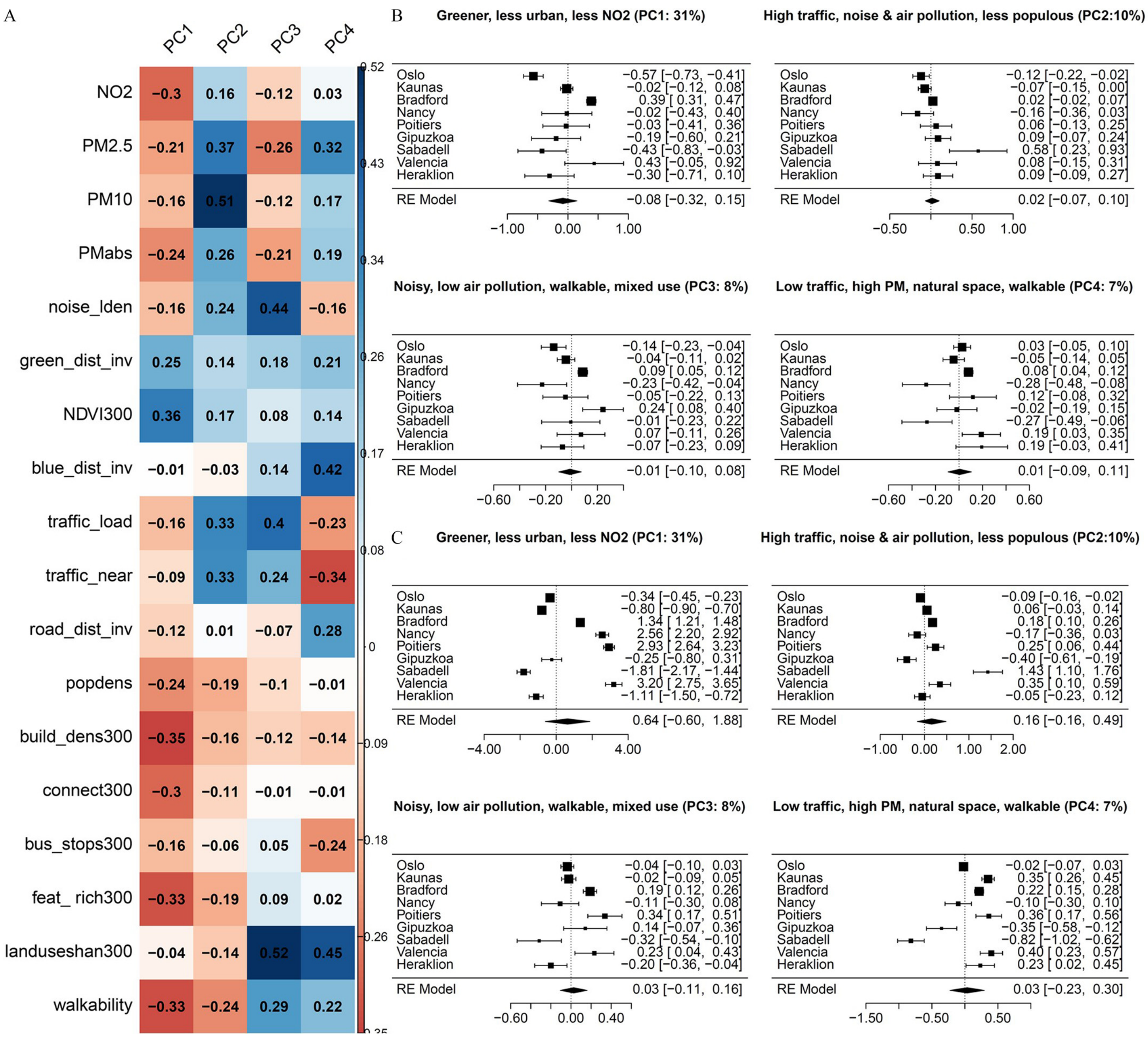

Figure 5. Associations by city between SEP and first four components of PCA, on 18 exposures mean-centerd within each city. (*A*): Heatmap showing exposure loadings of first four components. See Table 2 for exposure short names. Distance to nearest road, major green and blue spaces presented as inverse for interpretability. (*B*): Forest plots, showing associations with family education level by city and overall meta-analysis. (*C*): Forest plots, showing associations with area level SEP by city and overall meta-analysis Models compared high SEP women and lower SEP women, adjusted for age, ethnicity and marital status.

associations with the other indicators are given in Supplementary Table S6.

We also examined associations with ethnicity (Table S6, Figure S2), observing in some cases stronger associations than for the SEP indicators. For instance, in Bradford, scores for PC1 were 1.60 higher (95% CI: 1.52, 1.68) among women of white British ethnicity.

Sensitivity Analysis

We tested the potential impact of the imputation procedure by re-running the single-exposure associations and found very similar results between the imputed and complete case datasets (Table S7). We also examined the stability of the principal component analysis by re-running the analysis with a different city excluded each time (including the handful that were missing exposures such as noise) and found similar loading patterns, whichever city was excluded (Figure S3).

Discussion

We have described, in nine cities and urban areas from across Europe, the urban exposome, which we define as the set of environmental exposures experienced in the outdoor environment, of pregnant women. We observed considerable variability in the urban exposome both within and between areas. Among the air pollutants, average levels of NO_2, $PM_{2.5}$, and PM_{10} were highest in Sabadell, Nancy, and Heraklion, respectively. Average noise levels were highest in Heraklion, whereas surrounding greenness was highest in Kaunas and Oslo. Gipuzkoa had the highest proportion of women living within walking distance of major blue and green space and the most bus stops close to participants' homes. Valencia was the most walkable area, closely followed by the other Mediterranean cities of Sabadell and Heraklion. Although there are few comparable studies of these indicators at the individual level in other cities, the levels we observed for noise and air pollution appear representative of the range of exposure reported in other European cities, although air pollution levels remain considerably higher in cities in many low- and middle-income countries (WHO 2016). We found that the urban exposome of European pregnant women, including exposure to air pollutants, noise, and access to green space, was to varying extents socially determined, with considerable differences among cities.

Higher levels of air pollutants, in particular NO_2, were observed among pregnant women of low SEP in Bradford, Nancy, and Valencia, whereas the reverse was observed in Oslo, Poitiers, and Sabadell. This heterogeneity has been observed in a study of the general population in Western European cities (Temam et al. 2017). Other studies have looked at associations with indictors of SEP at the small area level. Fecht et al. noted consistently higher exposure to PM_{10} and NO_2 among more deprived neighbors in England but an opposite pattern in a national-level analysis in the Netherlands (Fecht et al. 2015). An analysis at the block level in the French city of Strasbourg observed lower NO_2 levels only in the highest quintile of SEP, with similar levels in the other quintiles (Havard et al. 2009). In France, among pregnant women, Ouidir et al. observed an increase in air pollutant ($PM_{2.5}$, NO_2) levels with area-level social deprivation in urban areas (Ouidir et al. 2017). In analysis of exposure of children in the Swedish city of Malmo by mean income of the residential building, Chaix et al. observed higher NO_2 exposure with decreasing income (Chaix et al. 2006). However, Fernandez-Somoano et al. found no association between SEP and NO_2 in Asturias, Spain (Fernández-Somoano and Tardon 2014). In the United States, a more consistent relationship between lower SEP and higher air pollution levels is found (Hajat et al. 2015), although the reverse is reported in some larger metropolitan areas, such as New York (Hajat et al. 2013). We also observed a mixed picture of associations between noise and SEP. Similarly, although some studies in Germany (Hoffmann et al. 2003), and Canada (Dale et al. 2015) showed that increased noise levels are associated with decreased SEP, others in Paris, France (Havard et al. 2011) and in the Netherlands (Kruize and Buowman 2004) associated higher noise with higher SEP. Mixed or inconclusive results were observed in Marseilles, France (Bocquier et al. 2013) and in Birmingham, UK (Brainard et al. 2004). We found higher surrounding greenness around homes of high-SEP women in Bradford and Valencia. This finding is consistent with the few studies regarding green space and social disadvantage in the Netherlands (Kruize et al. 2007), France (Padilla et al. 2016), and the United Kingdom (Mitchell and Popham 2008). However, in the northern, greener cities of Kaunas and Oslo, higher-SEP women lived in areas of lower surrounding greenness.

We observed strong correlation levels between many urban exposome indicators, highlighting the need to consider these exposures jointly in epidemiological studies. We employed PCA to reduce and describe the covariance of the urban exposome, and although other multivariate techniques are available, such as confirmatory factor analysis or model-based clustering, we found PCA to provide interpretable results that captured a considerable portion of the variance of the dataset. Almost a third of the variability of the urban exposome (after removing variability due to between-city differences) was described by a principal component that defined greener, less densely built areas, lower in levels of environmental hazards. Our results support the triple jeopardy hypothesis (Brulle and Pellow 2006) of greater exposure to environmental hazards driving health inequalities only in some cities in Europe. In Bradford and Valencia, lower-SEP women tended to live in more environmentally hazardous areas described by the first component, whereas in Oslo, Sabadell, and Heraklion, the reverse was true. In the other cities, there was little evidence of social patterning along this component. The next most important source of variability was the component describing high-traffic, high-pollution areas that were relatively green and less populated. This component, which by definition describes a type of urban area that is different from the first component, showed little relationship to SEP, except in Sabadell, where high-SEP women tended to live in this type of area. The third and fourth components both described more populous areas with high facility richness, with the third component driven by higher noise and lower air pollution levels, whereas the fourth component was driven by lower traffic levels but also greater access to recreational natural space. Both components showed different social patterning across the cities. The effects of these types of urban exposome during pregnancy on child development should be investigated to fully assess their contributions to health inequalities. However, it should be noted that even in areas such as Bradford, where low-SEP women are exposed to higher levels of environmental hazards, the differences remain relatively small (particularly when assessing individual-level SEP indicators) and are likely to explain only a small proportion of health disparities among SEP groups.

These results will assist in the interpretation of environmental epidemiological studies, where confounding of associations with exposure by sociodemographic factors is a concern. In cities such as Bradford, these factors need to be carefully adjusted for; in others, it is less necessary. Furthermore, in cities such as Oslo, negative confounding may even mask true effects. It is important that the heterogeneity of the effects of exposures and confounders in pooled analyses is assessed and accommodated into models when significant. This process can be done by including interactions of cohort with the exposures or confounders that show heterogeneity by cohort, or by including random slopes by cohort when using mixed-effects models. However, despite the complexity of conducting large pooled analyses across multiple populations, a varying confounder structure has the advantage of increasing casual inference when a consistent association is observed (Richmond et al. 2014).

SEP is a multidimensional construct that can be represented by different indicators in epidemiological research, each providing different information regarding position in society and access to resources. Social class (location in the social division of labor), social status (social honor and prestige), and material circumstances (income, wealth) are independent but correlated dimensions of SEP, each with potentially separate paths to health. Both education and area-level SEP measures are probabilistic indicators, in the sense that people of diverse social classes, status groups, and levels of personal affluence are found in the same education group and residential area. We have used education as our main SEP indicator primarily because it was available and comparable across all cohorts. Although education is strongly related to other SEP indicators (Davey Smith et al. 1998; Oakes and Rossi 2003), we observed large differences in educational level by cohort, suggesting access to education may vary by country and represent SEP differently. We therefore incorporated other indicators where available, finding generally similar associations with the different individual-level indicators. For most cities, we were able classify SEP at the area of residence level using multidimensional deprivation scores. Generally, we found stronger associations with the area-level indicators of SEP, as has been previously reported (Hajat et al. 2013). This finding may be expected because the environmental characteristics of an area may directly affect its level of affluence by making the area a more or less desirable place to live. Also, exposures were estimated at the address level through geospatial methods that, like area-based measures of SEP, rely on area-level characteristics. Although area-level SEP measures may suffer from ecological bias, the deprivation level of the area of residence may involve additional stressors over individual-level SEP, such as fear of crime and access to health care, altering susceptibility to environmental pollutants (Chi et al. 2016). In Oslo, Kaunas, and Heraklion, deprivation scores were unavailable so we characterized the area of residence with only a single area-level indicator (average income or education level). These indicators may insufficiently capture area-level deprivation and may limit comparability with the other cohorts. Indeed, in Oslo, we observed stronger associations with the individual-level indicator, family education. Furthermore, the size of the areas assessed differed somewhat among cities, potentially introducing differing levels of ecological bias.

This study had some further limitations. Although every effort was made to standardize exposure assessment across cohorts, there were some differences in generating exposures, due to differences in availability of data sources. For instance, air pollutant exposures were estimated with various models, and although these are all validated methods, exposure misclassification may vary among cities. Differences in data quality between cities may also be greater for exposures such as noise. Levels of measurement error will also vary among exposures, and our analysis did not attempt to correct for these differences. Although this error will be of the Berkson type and so should not affect the effect estimates themselves, comparability may be reduced due to reductions in power. The larger sample sizes of the northern cohorts also reduce comparability, and these populations may exert greater influence on meta-analyses. For some exposures, including noise and PM absorbance, we were unable to produce estimates in certain urban areas, and we therefore adopted an imputation approach based on the correlation structure for these exposures for the PCA. Exposures were assessed at home address only, which does not take into account exposure experienced at work and during commuting. Personal behaviors that may affect exposure levels were not taken into account. For meteorological factors, fine-scale spatial assessment was not feasible. This factor may be relevant in southern cities where heat-island effects may affect health. Finally, the population of the participating cohorts may not be completely representative of the host population due to issues of under-recruitment of low-SEP women. However, the strengths of the study included the breadth of urban locations and type from across Europe and the large sample size, which increase the generalizability of the study. The common assessment protocol adopted across cohorts and similar age of cohorts increased comparability between cities. Furthermore, the use of detailed questionnaires at recruitment on sociodemographic indicators and fine-scale exposure assessment allowed a unique individual-level analysis, in addition to area-level analysis.

The urban exposome may be both harmful to child development through, for instance, the impact of air pollution and noise, and beneficial, through the promotion of active transport and play. Although more densely built areas were correlated with potentially harmful aspects of the urban environment such as NO_2 and reduced green space, they had certain environmental characteristics that may have health benefits in terms of improving walkability (Grasser et al. 2013) and associated reductions in overweight condition and obesity (Duncan et al. 2014). We adapted a measure of walkability that was developed and validated in the American context, and this study constitutes the first time it has been systematically applied across Europe. Future work will investigate the impact of this indicator on physical activity and child development. With more people than ever living in urban environments (UNFPA 2007), it is vital to improve the harm-to-health balance of the urban environment so as not to exacerbate environmentally driven health inequalities. We observed that the link between population density and potentially beneficial and harmful factors varied to a certain extent across cities. Urban planners should examine the features of urban design contributing to these differences to improve the health of European citizens.

Conclusions

Using an exposome approach to systematically assess multiple exposures experienced in the outdoor environment, we have described the urban exposome of pregnant women, a particularly important subgroup, across nine European cities and urban areas. We found considerable heterogeneity in associations with more socially disadvantaged women living in less healthy environments in cities such as Bradford, and the opposite association observed in Oslo. It is incumbent on local authorities and planners to understand the nature of environmental inequalities in their cities so as to mitigate their effects and reduce health inequities.

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References

Agay-Shay K, Peled A, Crespo AV, Peretz C, Amitai Y, Linn S. 2014. Green spaces and adverse pregnancy outcomes. Occup Environ Med 71(8):562–569, PMID: 24759971, https://doi.org/10.1136/oemed-2013-101961.

Beelen R, Hoek G, Vienneau D, Eeftens M, Dimakopoulou K, Pedeli X, et al. 2013. Development of NO_2 and NO_x land use regression models for estimating air pollution exposure in 36 study areas in Europe - the ESCAPE project. Atmospheric Environment 72:10–23, https://doi.org/10.1016/j.atmosenv.2013.02.037.

Bocquier A, Cortaredona S, Boutin C, David A, Bigot A, Chaix B, et al. 2013. Small-area analysis of social inequalities in residential exposure to road traffic noise in Marseilles, France. Eur J Public Health 23(4):540–546, PMID: 22645238, https://doi.org/10.1093/eurpub/cks059.

Brainard JS, Jones AP, Bateman IJ, Lovett AA. 2004. Exposure to environmental urban noise pollution in Birmingham, UK. Urban Studies 41(13):2581–2600, https://doi.org/10.1080/0042098042000294574.

Brulle RJ, Pellow DN. 2006. Environmental justice: human health and environmental inequalities. Annu Rev Public Health 27:103–124, PMID: 16533111, https://doi.org/10.1146/annurev.publhealth.27.021405.102124.

Chaix B, Gustafsson S, Jerrett M, Kristersson H, Lithman T, Boalt A, et al. 2006. Children's exposure to nitrogen dioxide in Sweden: investigating environmental injustice in an egalitarian country. J Epidemiol Community Health 60(3):234–241, https://doi.org/10.1136/jech.2005.038190.

Chatzi L, Leventakou V, Vafeiadi M, Koutra K, Roumeliotaki T, Chalkiadaki G, et al. 2017. Cohort profile: the mother-child cohort in Crete, Greece (Rhea study). Int J Epidemiol 46(5):1392–1393, PMID: 29040580.

Chi GC, Hajat A, Bird CE, Cullen MR, Griffin BA, Miller KA, et al. 2016. Individual and neighborhood socioeconomic status and the association between air pollution and cardiovascular disease. Environ Health Perspect 124(12):1840–1847, PMID: 27138533, https://doi.org/10.1289/EHP199.

Dadvand P, Wright J, Martinez D, Basagaña X, McEachan RR, Cirach M, et al. 2014. Inequality, green spaces, and pregnant women: roles of ethnicity and individual and neighbourhood socioeconomic status. Environ Int 71:101–108, PMID: 24997306, https://doi.org/10.1016/j.envint.2014.06.010.

Dadvand P, Nieuwenhuijsen MJ, Esnaola M, Forns J, Basagaña X, Alvarez-Pedrerol M, et al. 2015. Green spaces and cognitive development in primary schoolchildren. Proc Natl Acad Sci USA 112(26):7937–7942, PMID: 26080420, https://doi.org/10.1073/pnas.1503402112.

Dale LM, Goudreau S, Perron S, Ragettli MS, Hatzopoulou M, Smargiassi A. 2015. Socioeconomic status and environmental noise exposure in Montreal, Canada. BMC public health 15:205, PMID: 25885357, https://doi.org/10.1186/s12889-015-1571-2.

Davey Smith G, Hart C, Hole D, MacKinnon P, Gillis C, Watt G, et al. 1998. Education and occupational social class: which is the more important indicator of mortality risk? J Epidemiol Community Health 52(3):153–160, PMID: 9616419.

Department of Architecture Housing and Land. 2001. The atlas of urban vulnerability in Spain. http://www.fomento.gob.es/MFOM/LANG_CASTELLANO/_ESPECIALES/SIU/ [accessed 1 June 2012].

Department for Communities and Local Government. 2010. English indices of deprivation. https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015 [accessed 1 January 2014].

Duncan DT, Aldstadt J, Whalen J, Melly SJ, Gortmaker SL. 2011. Validation of Walk Score® for estimating neighborhood walkability: an analysis of four US metropolitan areas. Int J Environ Res Public Health 8(11):4160–4179, PMID: 22163200, https://doi.org/10.3390/ijerph8114160.

Duncan DT, Sharifi M, Melly SJ, Marshall R, Sequist TD, Rifas-Shiman SL, et al. 2014. Characteristics of walkable built environments and BMI z-scores in children: evidence from a large electronic health record database. Environ Health Perspect 122(12):1359–1365, PMID: 25248212, https://doi.org/10.1289/ehp.1307704.

Eeftens M, Beelen R, de Hoogh K, Bellander T, Cesaroni G, Cirach M, et al. 2012. Development of land use regression models for PM(2.5), PM(2.5)absorbance, PM(10) and PM(coarse) in 20 European study areas; results of the ESCAPE project. Environ Sci Technol 46:11195–11205.

European Commission, Working Group Assessment of Exposure to Noise (WG-AEN). 2010. "Good practice guide on noise exposure and potential health effects." EEA technical report no 11/2010. Copenhagen: European Environment Agency

Eurostat. 2016. International standard classification of education (ISCED).

Fecht D, Fischer P, Fortunato L, Hoek G, de Hoogh K, Marra M, et al. 2015. Associations between air pollution and socioeconomic characteristics, ethnicity and age profile of neighbourhoods in England and the Netherlands. Environ Pollut 198:201–210, PMID: 25622242, https://doi.org/10.1016/j.envpol.2014.12.014.

Fernández-Somoano A, Tardon A. 2014. Socioeconomic status and exposure to outdoor NO2 and benzene in the Asturias INMA birth cohort, Spain. J Epidemiol Community Health 68(1):29–36, PMID: 23999377, https://doi.org/10.1136/jech-2013-202722.

Frank LD, Sallis JF, Conway TL, Chapman JE, Saelens BE, Bachman W. 2006. Many pathways from land use to health: associations between neighborhood walkability and active transportation, body mass index, and air quality. Journal of the American Planning Association 72(1):75–87, https://doi.org/10.1080/01944360608976725.

Gasana J, Dillikar D, Mendy A, Forno E, Ramos Vieira E. 2012. Motor vehicle air pollution and asthma in children: a meta-analysis. Environ Res 117:36–45, PMID: 22683007, https://doi.org/10.1016/j.envres.2012.05.001.

Gascon M, Vrijheid M, Nieuwenhuijsen MJ. 2016. "The built environment and child health: An overview of current evidence." Current Environmental Health Reports, 1–8.

Grasser G, Van Dyck D, Titze S, Stronegger W. 2013. Objectively measured walkability and active transport and weight-related outcomes in adults: a systematic review. Int J Public Health 58(4):615–625, PMID: 23224518, https://doi.org/10.1007/s00038-012-0435-0.

Grazuleviciene R, Danileviciute A, Nadisauskiene R, Vencloviene J. 2009. Maternal smoking, GSTM1 and GSTT1 polymorphism and susceptibility to adverse pregnancy outcomes. Int J Environ Res Public Health 6(3):1282–1297, PMID: 19440446, https://doi.org/10.3390/ijerph6031282.

Guxens M, Ballester F, Espada M, Fernández MF, Grimalt JO, Ibarluzea J, et al. 2012. Cohort profile: the INMA–INfancia y Medio Ambiente–(Environment and Childhood) Project. Int J Epidemiol 41(4):930–940, https://doi.org/10.1093/ije/dyr054.

Hajat A, Diez-Roux AV, Adar SD, Auchincloss AH, Lovasi GS, O'Neill MS, et al. 2013. Air pollution and individual and neighborhood socioeconomic status: evidence from the Multi-Ethnic Study of Atherosclerosis (MESA). Environ Health Perspect 121:1325–1333.

Hajat A, Hsia C, O'Neill MS. 2015. Socioeconomic disparities and air pollution exposure: a global review. Curr Environ Health Rep : 2(4):440–450, PMID: 26381684, https://doi.org/10.1007/s40572-015-0069-5.

Havard S, Deguen S, Zmirou-Navier D, Schillinger C, Bard D. 2009. Traffic-related air pollution and socioeconomic status: a spatial autocorrelation study to assess environmental equity on a small-area scale. Epidemiology 20(2):223–230, https://doi.org/10.1097/EDE.0b013e31819464e1.

Havard S, Reich BJ, Bean K, Chaix B. 2011. Social inequalities in residential exposure to road traffic noise: an environmental justice analysis based on the RECORD Cohort Study. Occup Environ Med 68(5):366–374, PMID: 21273211, https://doi.org/10.1136/oem.2010.060640.

Held U, Kessels A, Garcia Aymerich J, Basagaña X, Ter Riet G, Moons KGM, et al. 2016. Methods for handling missing variables in risk prediction models. Am J Epidemiol 184(7):545–551, PMID: 27630143, https://doi.org/10.1093/aje/kwv346.

Hellenic Statistical Authority. 2001. Population Housing Census - Demographic Characteristics. http://www.statistics.gr/en/home.

Heude B, Forhan A, Slama R, Douhaud L, Bedel S, Saurel-Cubizolles MJ, et al. 2016. Cohort profile: The EDEN mother-child cohort on the prenatal and early postnatal determinants of child health and development. Int J Epidemiol 45(2):353–363, PMID: 26283636, https://doi.org/10.1093/ije/dyv151.

Hoffmann B, Robra BP, Swart E. 2003. [Social inequality and noise pollution by traffic in the living environment–an analysis by the German Federal Health Survey (Bundesgesundheitssurvey)]. Gesundheitswesen 65:393–401.

Institute for Social and Economic Research. 2006. European socio-economic classification (ESEC). https://www.iser.essex.ac.uk/archives/esec [accessed 15 September 2016].

Jolani S, Debray TP, Koffijberg H, van Buuren S, Moons KG. 2015. Imputation of systematically missing predictors in an individual participant data meta-analysis: a generalized approach using mice. Statist Med 34(11):1841–1863, https://doi.org/10.1002/sim.6451.

Juarez PD, Matthews-Juarez P, Hood DB, Im W, Levine RS, Kilbourne BJ, et al. 2014. The public health exposome: a population-based, exposure science approach to health disparities research. Int J Environ Res Public Health 11(12):12866–12895, PMID: 25514145, https://doi.org/10.3390/ijerph111212866.

Kruize H, Buowman A. 2004. "Environmental (in)equity in the Netherlands - A case study on the distribution of environmental quality in the Rijnmond region." Bilthoven, Netherlands. RIVM Report 550012003/2004. https://www.rivm.nl/en/Documents_and_publications/Scientific/Reports/2004/september/Environmental_in_equity_in_the_Netherlands_A_case_study_on_the_distribution_of_environmental_quality_in_the_Rijnmond_region?sp=cml2bXE9ZmFsc2U7c2VhcmNoYmFzZT0yMjcxMDtyaXZtcT1mYWxzZTs=&pagenr=2272 [accessed 7 July 2016].

Kruize H, Driessen PPJ, Glasbergen P, Van Egmond K. 2007. Environmental equity and the role of public policy: experiences in the Rijnmond region. Environ Manage 40(4):578–595, PMID: 17879127, https://doi.org/10.1007/s00267-005-0378-9.

Magnus P, Birke C, Vejrup K, Haugan A, Alsaker E, Daltveit AK, et al. 2016. Cohort profile update: The Norwegian mother and child cohort study (MoBa). Int J Epidemiol 45(2):382–388, PMID: 27063603, https://doi.org/10.1093/ije/dyw029.

Mitchell R, Popham F. 2008. Effect of exposure to natural environment on health inequalities: an observational population study. Lancet 372(9650):1655–1660, PMID: 18994663, https://doi.org/10.1016/S0140-6736(08)61689-X.

Nieuwenhuijsen MJ, Kruize H, Gidlow C, Andrusaityte S, Antó JM, Basagaña X, et al. 2014. Positive health effects of the natural outdoor environment in typical populations in different regions in Europe (PHENOTYPE): a study programme protocol. BMJ Open 4(4):e004951, https://doi.org/10.1136/bmjopen-2014-004951.

Nieuwenhuijsen MJ. 2016. Urban and transport planning, environmental exposures and health- new concepts, methods and tools to improve health in cities. Environ Health 15(S1):1–11, https://doi.org/10.1186/s12940-016-0108-1.

O'Neill MS, Jerrett M, Kawachi I, Levy JI, Cohen AJ, Gouveia N, et al. 2003. Health, wealth, and air pollution: advancing theory and methods. Environ Health Perspect 111(16):1861–1870, PMID: 14644658, https://doi.org/10.1289/ehp.6334.

Oakes JM, Rossi PH. 2003. The measurement of SES in health research: current practice and steps toward a new approach. Soc Sci Med 56(4):769–784, PMID: 12560010, https://doi.org/10.1016/S0277-9536(02)00073-4.

Ouidir M, Lepeule J, Siroux V, Malherbe L, Meleux F, Rivière E, et al. 2017. Is atmospheric pollution exposure during pregnancy associated with individual and contextual characteristics? A nationwide study in France. J Epidemiol Community Health 71(10):1026–1036, PMID: 28830952, https://doi.org/10.1136/jech-2016-208674.

Padilla CM, Kihal-Talantikit W, Perez S, Deguen S. 2016. Use of geographic indicators of healthcare, environment and socioeconomic factors to characterize environmental health disparities. Environ Health 15(1):79, PMID: 27449640, https://doi.org/10.1186/s12940-016-0163-7.

Pedersen M, Giorgis-Allemand L, Bernard C, Aguilera I, Andersen AMN, Ballester F, et al. 2013. Ambient air pollution and low birthweight: a European Cohort Study (ESCAPE). Lancet Respir Med 1(9):695–704, PMID: 24429273, https://doi.org/10.1016/S2213-2600(13)70192-9.

Pornet C, Delpierre C, Dejardin O, Grosclaude P, Launay L, Guittet L, et al. 2012. Construction of an adaptable European transnational ecological deprivation index: the French version. J Epidemiol Community Health 66(11):982–989.

Rahmalia A, Giorgis-Allemand L, Lepeule J, Philippat C, Galineau J, Hulin A, et al. 2012. Pregnancy exposure to atmospheric pollutants and placental weight: an approach relying on a dispersion model. Environ Int 48:47–55, PMID: 22836169, https://doi.org/10.1016/j.envint.2012.06.013.

Rappaport SM, Smith MT. 2010. Epidemiology. Environment and disease risks. Science 330(6003):460–461, PMID: 20966241, https://doi.org/10.1126/science.1192603.

Richmond RC, Al-Amin A, Smith GD, Relton CL. 2014. Approaches for drawing causal inferences from epidemiological birth cohorts: a review. Early Hum Dev 90(11):769–780, PMID: 25260961, https://doi.org/10.1016/j.earlhumdev.2014.08.023.

Robinson O, Basagaña X, Agier L, de Castro M, Hernandez-Ferrer C, et al. 2015. The pregnancy exposome: multiple environmental exposures in the INMA-Sabadell Birth Cohort. Environ Sci Technol 49(17):10632–10641.

Robinson O, Vrijheid M. 2015. The pregnancy exposome. Curr Envir Health Rpt 2(2):204, https://doi.org/10.1007/s40572-015-0043-2.

Schembari A, De Hoogh K, Pedersen M, Dadvand P, Martinez D, Hoek G, et al. 2015. Ambient air pollution and newborn size and adiposity at birth: differences by maternal ethnicity (the Born in Bradford Study Cohort). Environ Health Perspect 123(11):1208–1215, PMID: 25978617, https://doi.org/10.1289/ehp.1408675.

Smith G, Cirach M, Swart W, Dėdelė A, Gidlow C, van Kempen E, et al. 2017. Characterisation of the natural environment: quantitative indicators across Europe. Int J Health Geogr 16(1):16, PMID: 28446187, https://doi.org/10.1186/s12942-017-0090-z.

Statistics Norway. 2013. Personal income database.

Temam S, Burte E, Adam M, Anto JM, Basagaña X, Bousquet J, et al. 2017. Socioeconomic position and outdoor nitrogen dioxide (NO_2) exposure in western Europe: a multi-city analysis. Environ Int 101:117–124, PMID: 28159394, https://doi.org/10.1016/j.envint.2016.12.026.

Temis. 2016. UV radiation archives. http://www.temis.nl/uvradiation/UVdose.html [accessed 5 August 2013].

UNFPA (United Nations Fund for Population Activities). 2007. "State of World Population 2007: Unleashing the potential of urban growth."

van Buuren S, Groothuis-Oudshoorn K. 2011. Mice: multivariate imputation by chained equations in R. J Stat Soft 45(3):67, https://doi.org/10.18637/jss.v045.i03.

van Kamp I, Davies H. 2013. Noise and health in vulnerable groups: a review. Noise Health 15(64):153–159, PMID: 23689296, https://doi.org/10.4103/1463-1741.112361.

van Nunen E, Vermeulen R, Tsai MY, Probst-Hensch N, Ineichen A, Davey M, et al. 2017. Land use regression models for ultrafine particles in six European areas. Environ Sci Technol 51(6):3336–3345, PMID: 28244744, https://doi.org/10.1021/acs.est.6b05920.

Viechtbauer W. 2010. Conducting meta-analyses in R with the metafor package. J Stat Soft 36(3):48, https://doi.org/10.18637/jss.v036.i03.

Vrijheid M, Slama R, Robinson O, Chatzi L, Coen M, van den Hazel P, et al. 2014. The human early-life exposome (HELIX): project rationale and design. Environ Health Perspect 122(6):535–544, PMID: 24610234, https://doi.org/10.1289/ehp.1307204.

Wang M, Beelen R, Bellander T, Birk M, Cesaroni G, Cirach M, et al. 2014. Performance of multi-city land use regression models for nitrogen dioxide and fine particles. Environ Health Perspect 122(8):843–849, PMID: 24787034.

Weier JDH. 2011. Measuring vegetation (NDVI & EVI). http://earthobservatory.nasa.gov/Features/MeasuringVegetation/ [accessed 17 November 2013].

White IR, Royston P, Wood AM. 2011. Multiple imputation using chained equations: issues and guidance for practice. Stat Med 30(4):377–399, PMID: 21225900, https://doi.org/10.1002/sim.4067.

WHO (World Health Organization). 2016. WHO global urban ambient air pollution database (update 2016).

Wild CP. 2012. The exposome: from concept to utility. Int J Epidemiol 41(1):24–32, PMID: 22296988, https://doi.org/10.1093/ije/dyr236.

Wright J, Small N, Raynor P, Tuffnell D, Bhopal R, Cameron N, et al. 2013. Cohort profile: The Born in Bradford multi-ethnic family cohort study. Int J Epidemiol 42(4):978–991, PMID: 23064411, https://doi.org/10.1093/ije/dys112.