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Associations between modeled residential outdoor and measured personal exposure to ultrafine particles in four European study areas

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HIGHLIGHTS

- Ultrafine Particle (UFP) land use regression (LUR) models used in health studies.
- Unknown how well LUR models predict long-term personal exposure to UFP.
- LUR modeled UFP compared to measured personal exposure of 154 adults in four cities.
- LUR modeled UFP significantly associated with median but not mean personal exposure.
- LUR models explained personal exposure less than residential outdoor exposure.

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ABSTRACT

Land use regression (LUR) models for Ultrafine Particles (UFP) have been developed to assess health effects of long-term average UFP exposure in epidemiological studies. Associations between LUR modeled residential outdoor and measured long-term personal exposure to UFP have never been evaluated, adding uncertainty in interpretation of epidemiological studies of UFP. Our aim was to assess how predictions of recently developed LUR models for UFP compared to measured average personal UFP exposure in four European areas.

Personal UFP exposure was measured in 154 adults from Basel (Switzerland), Amsterdam and Utrecht (the Netherlands), Norwich (United Kingdom), and Turin (Italy). Subjects performed three 24-h exposure measurements by carrying a real-time monitor measuring particles between 10 and 300 nm (MiniDisc). Subjects reported whereabouts and indoor sources of UFP in questionnaires. In Basel and the Netherlands contemporaneously residential outdoor UFP concentrations were monitored. Area-specific LUR models were applied to model residential outdoor UFP concentrations. Associations between modeled and measured UFP concentrations were assessed with linear regression.

LUR model predictions were significantly associated with median but not mean personal UFP exposures, likely because of the high impact of indoor peaks on mean personal exposures. Regression slopes (±se) combined for

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the four areas were 0.12 ± 0.04 for median and −0.06 ± 0.17 for mean personal exposure. The LUR model explained variance of the median personal exposure less than variance of residential outdoor measurements. Associations did not change when personal exposure was calculated for the time spent at home or when presence of indoor sources was incorporated in the regression models. Regression slopes for measured residential outdoor versus personal exposure were smaller for UFP (0.16 ± 0.04) than for simultaneously measured $PM_{2.5}$ and soot (0.32 ± 0.10 and 0.43 ± 0.06).

Our findings provide some support for the use of LUR models to estimate long-term exposure to ambient generated UFP in epidemiological studies.

1. Introduction

Long-term exposure to ultrafine particles (UFP), particles smaller than 0.1 μm, is hypothesized to be associated with adverse health events because of the potential to penetrate deep into the lungs, high biological reactivity per surface area, and potential uptake in the bloodstream (Oberdörster et al., 2005; Kumar et al., 2013). Very few epidemiological studies on health effects of long-term exposure to UFP have been performed, because of the lack of spatially resolved UFP exposure estimates. Recently multiple Land Use Regression (LUR) models have been developed using long-term (Hoek et al., 2011; Eeftens et al., 2016), short-term (Rivera et al., 2012; Abernethy et al., 2013; Montagne et al., 2015; van Nunen et al., 2017) or mobile monitoring (Saraswat et al., 2013; Patton et al., 2015; Ragettli et al., 2013; Kerckhoffs et al., 2016; Hankey and Marshall, 2015; Weichenthal et al., 2016), allowing prediction of long-term UFP exposure at a fine spatial scale using variables from Geographic Information Systems (GIS). These LUR models predict outdoor concentrations, typically at the residential address of participants of an epidemiological study. The modeled outdoor concentration at the residential address is used as a surrogate for the long-term personal exposure. However, associations between modeled residential outdoor and measured personal exposure have not been evaluated for UFP, adding uncertainty to the interpretation of epidemiological analyses based upon UFP LUR models.

Motorized traffic is a major source of UFP in urban areas (Kumar et al., 2013; Health Effects Institute., 2010). Associations between modeled residential and measured personal exposures to other traffic-related air pollutants, such as particles smaller than 2.5 μm ($PM_{2.5}$), soot ($PM_{2.5}$ absorbance, a surrogate measure for Black Carbon and Elemental Carbon (Cyrys et al., 2003; Janssen et al., 2001; Brunekreef et al., 2005)) and nitrogen oxides (NOx), have been evaluated in previous work. Sahsuvaroglu et al. found no correlation between modeled residential and measured personal NO and NO_2 concentrations (Sahsuvaroglu et al., 2009). Nethery et al. showed a significant correlation for these components (Nethery et al., 2008), but not for $PM_{2.5}$ and soot. Montagne et al. found a consistent correlation for soot, but not for $PM_{2.5}$, NO_2 and NO_x (Montagne et al., 2013). Associations in all studies were weak, attributed to a combination of methodological issues including the difficulty to measure long-term average personal exposure and the difficulty to separate contributions from indoor and outdoor sources, in addition to factors such as time spent away from home and infiltration of outdoor pollution to the indoor environment (Montagne et al., 2013).

We recently developed LUR models for UFP for six European study areas in the framework of the EXPOsOMICS project (Vineis et al., 2016). Study-area specific models were developed based upon harmonized monitoring and modelling procedures (van Nunen et al., 2017) In the current study, we conducted repeated personal exposure measurements of UFP from adult volunteers in four of these study areas. Our main aim was to quantify associations between LUR modeled residential outdoor and measured average personal UFP exposures.

2. Materials & methods

2.1. Study design

Personal exposure to UFP was measured during three 24-h Personal Exposure Monitoring (PEM) sessions as part of the EXPOsOMICS project (Vineis et al., 2016). Healthy non-smoking subjects were recruited from Basel (Switzerland), Norwich (United Kingdom), Amsterdam and Utrecht (the Netherlands, both cities referred to as 'the Netherlands'), and Turin (Italy). The aim was to recruit 40 subjects per area from ongoing cohort studies, because an additional goal was to assess the stability over time of biological markers of exposure in blood samples (Vineis et al., 2016). Contemporaneously with personal measurements, real-time UFP concentrations (Basel and the Netherlands) were measured outdoors at the subject's residential address. Budget constraints did not allow outdoor monitoring in the other cities. Outdoor monitors were located at a central place in the subject's garden, or attached to the façade of the house when the subject was living in an apartment (Montagne et al., 2015; van Nunen et al., 2017). Long-term average modeled residential UFP concentrations were obtained by application of study-area specific LUR models for UFP, developed on short-term monitoring campaigns (van Nunen et al., 2017). We assessed the association between LUR modeled residential and measured median and mean personal UFP exposure using linear regression. To further interpret factors that may have affected associations between LUR predictions and personal exposure, additional analyses were performed. We evaluated personal exposures restricted to time at home and personal exposures corrected for presence of indoor sources. Associations between modeled and measured residential outdoor UFP and measured residential outdoor and personal UFP were assessed. Associations between simultaneously measured residential outdoor and personal $PM_{2.5}$ and $PM_{2.5}$ absorbance (referred to as 'soot') were evaluated to compare specifically the regression slopes with those of the UFP models. Regression slopes reflect infiltration of particles from outdoor to indoors assuming the home outdoor measurements were not influenced by UFP generated indoors.

2.2. Study population and personal exposure monitoring

The inclusion criteria for the study population were age between 50 and 70 years, healthy, no smoking by the subject or in the home of the subject, and availability of a historic blood sample in the framework of an ongoing cohort study (Vineis et al., 2016). To obtain sufficient contrast in ambient UFP at the residential address, the aim was to recruit 20 subjects per area living at a major road (road with >10,000 vehicles/24-h, house at ground floor or first floor) and 20 subjects at a minor road (at least 100 m away from a major road). To assess eligibility, potential subjects completed a screening questionnaire. The health criteria were primarily designed to interpret the biological markers of exposure. At study inclusion, an informed consent form was signed and a baseline questionnaire was completed.

Personal exposure to UFP, $PM_{2.5}$ and soot was measured during three 24-h PEM sessions in different seasons (Summer, Winter and Spring/Autumn) between December 2013 and February 2015. Subjects carried a backpack containing air pollution monitors to measure real-time personal exposure to UFP and 24-h integrated personal exposure to $PM_{2.5}$ and soot. Subjects were asked to perform their daily routine during each PEM session and reported their location and travels in a time-activity diary (TAD). Housing characteristics and presence and use of sources of indoor pollution were recorded in a technician-administered questionnaire. Contemporaneously with personal measurements, real-time UFP (Basel and the Netherlands) and 24-h integrated $PM_{2.5}$ and soot (all areas) were measured outdoor at the subject's residential address. At the exact location of air pollution monitors, the GPS coordinate was collected at each visit.

PEM sessions were performed pairwise, because of availability of monitors. The aim was to monitor one subject at a major and one at a minor road simultaneously, reducing the influence of temporal pollution variability on differences of personal measurements between subjects from major and minor roads. During the entire measurement campaign, real-time UFP and 24-h integrated $PM_{2.5}$ and soot were measured at a reference site in each area. These measurements allowed correction for temporal variability in pollution concentrations (van Nunen et al., 2017). The reference site was an urban background location in the study area. In the larger study area of the Netherlands, the reference site was near Utrecht, located approximately 40 km from Amsterdam. The central reference sites were selected at urban background conditions as the site needed to represent the general pattern over time applicable in large areas in the city. Therefore, a site unaffected by nearby local sources such as major roads was selected. UFP concentrations at the central sites represent concentrations for a large fraction of the population but relatively low compared to air pollution concentrations at major roads.

Recruitment of subjects, pollution monitoring and data processing were standardized across the four study areas. Standardization included a study manual, standard operating procedures for monitoring, identical monitoring instruments and questionnaires, a central laboratory and a 2-day technician training workshop in Utrecht prior to field campaigns.

2.3. Monitoring methods and data processing

Real-time UFP was monitored with a MiniDiSC (Testo AG, Lenzkirch, Germany), operating at a flow of 1 L/min and monitoring particles ranging from 10 to 300 nm at 1 s intervals based on diffusion charging. This monitor does not specifically measure UFP (defined as particles $<$ 100 nm), but UFP typically dominates the particle number in this fraction (HEI Review Panel, 2013). In the remainder of the paper we will use the term UFP to refer to the particle number counts from the MiniDiSC but further discuss the limitations of monitoring a small fraction of larger particles. We prefer not to use the general term particle number counts as this is also used for optical monitoring methods that do not include ultrafine particles. QA/QC included zero checks prior and after measurements and regular colocation of all devices per center at the reference site for at least 3 h, documenting the comparability of the instruments used in each area (van Nunen et al., 2017). All UFP files were cleaned by removal of observations with error codes of the instrument (e.g. deviating flow) and/or in case of a 10-fold increase or decrease in successive UFP observations as performed before (Klompmaker et al., 2015). Measurements were discarded when less than 66.7% of the desired 24-h monitoring time was covered with valid 1-s UFP observations.

24-h $PM_{2.5}$ and soot were sampled on the same 37 mm 2 μm pore size Teflon filter (Andersen Instruments, Fultonville, NY), packed in a Zefon 4-piece filter cassette (Zefon International, Ocala, FL), using a BGI GK 2.05 KTL Cyclone and a BGI 4004-pump (BGI inc, Waltham, MA) operating at a sampling flow of 3.5 L/min. QA/QC for filters included preparation of cassettes in a central laboratory, sealed and cooled transport, and biweekly collection of blanks and duplicates at the reference site alongside the regular reference measurements. The sampling flow of the BGI pump was set at 3.5 L/min before and measured after each session using a calibrated rotameter (Brooks Instruments, Hatfield, PA). The Elapsed Time Counter (ETC) on the BGI pump was reset prior to each measurement, ETC readings after each session were used to record total sampling time. Filters were pre- and post-weighed centrally in a climate-controlled room in IRAS laboratory following 1997 EPA requirements (20–23 degrees Centigrade and 30–40% Relative Humidity) using a microbalance. The 24-h average $PM_{2.5}$ concentration was determined by change in filter weight, corrected with average field blank concentration, following ESCAPE procedures (Montagne et al., 2013; Eeftens et al., 2012). Reflectance of filters was measured using a Smoke Stain Reflectometer (Diffusion Systems Ltd, London, UK). Reflectance was transformed into absorbance according to ISO 9835, corrected with average field blank, following ESCAPE procedures (Montagne et al., 2013; Eeftens et al., 2012). $PM_{2.5}$ and soot measurements were discarded if the ETC showed that the pump operated for less than 66.7% of the desired 24 h and/or the end flow deviated more than 20% from the design value of 3.5 l/min (2.8–4.2 L/min).

GPS coordinates were collected with a high sensitivity handheld GPS device. Coordinates of residential outdoor measurement locations were averaged over three visits and manually corrected for optimal accuracy in position relative to roads on detailed road maps.

2.4. Modeled residential outdoor concentrations

Modeled residential UFP concentrations were obtained centrally by application of 10-fold EXPOsOMICS local LUR models (van Nunen et al., 2017). These models are summarized in Table S1. GIS predictors of each residential outdoor coordinate were generated, and subsequently truncated for the range of predictors that was used at model development to avoid unrealistic predictions. Truncation was applied for 6 of the 154 (4%) sites (one site in Basel, two sites in the Netherlands, and three sites in Norwich). Ten UFP predictions were generated for each subject. Because of the previously documented high agreement in predicted UFP concentrations at the residential address (van Nunen et al., 2017), model predictions were equally weighted to calculate one residential UFP concentration per subject. This prediction was used as modeled residential UFP concentrations in further analysis.

2.5. Time activity and indoor sources

During each PEM session, subjects reported locations and travels per hour with a 5-min accuracy in the Time Activity Diary, available in Fig. S1 in Supplemental Information S2. Location categories covered indoor (Home, Work, and Other indoor), outdoor and in travel (further specified by travel mode). At the end of each PEM session, a technician checked the TAD for completeness and correctness.

Presence of indoor sources in each PEM session were collected as dichotomous variables in the PEM Session Questionnaire. Indoor sources covered were cigarette smoke exposure 'at home', 'somewhere else' and 'overall', home cooking, vacuum cleaning, burning candles, using sprays. Information on home ventilation was collected by recording the opening of windows. Time-invariant presence of gas heating and gas cooking were also recorded each session.

2.6. Data analysis

The overall mean and median UFP concentrations calculated over all valid 1-s personal, residential outdoor, and reference site measurements of the three sessions per subject. Both mean and median personal UFP exposures were calculated because of the typical spiky pattern of 1-s UFP observations, potentially influencing mean concentrations to a large extent (Figs. S2 and S3 for personal exposure and Fig. S4 for residential outdoor concentrations). Linear regression was performed per area to assess the associations between LUR modeled and long-term measured

mean and median personal UFP. In each model, mean reference site UFP levels, contemporaneously observed with measured concentrations, were included for temporal correction. Regression coefficient, standard error, significance level, and the percent explained variation (R^2) of regression models with residential outdoor modeled or measured UFP concentration were used to evaluate associations. A fixed effect meta-analysis of the slopes was performed to assess combined area results.

Additional analyses were performed to get better insight in factors that may affect associations between LUR modeled residential outdoor and measured personal UFP, based upon previous studies. First, the ability of LUR models to predict outdoor concentrations was tested by regressing modeled against measured residential outdoor UFP levels. Second, the association between measured residential outdoor and personal UFP was tested. Third, the association between LUR modeled and measured personal UFP exposure was tested for periods that subjects spent at home according to the time activity diary. As the LUR model predicts residential concentrations, exposures experienced elsewhere are not covered. Concentrations at home could not be determined for Norwich because of incomplete diary data. Fourth, night time (00.00am–8.00am) mean and median UFP concentrations were regressed against modeled UFP levels, since this period likely reflects time without significant indoor source contributions (e.g. cooking). Fifth, models were corrected for session-specific subject-reported exposure to indoor sources, using dichotomous variables for home cooking, vacuum cleaning, burning candles, the use of sprays, opening windows and cigarette smoke exposure 'overall'. Cigarette smoke exposure 'at home' and 'somewhere else' were combined, because of low number of reported individual smoking events. Mixed effect models with random intercepts per subject were fit using session specific mean or median values for these analyses. Lastly, associations between measured residential outdoor and personal $PM_{2.5}$ and Soot exposure were tested, pollutants with a potentially different infiltration in the home and generally lower impact of indoor sources.

For $PM_{2.5}$ and soot, the mean of three observations was used to calculate long-term exposures, since only integrated 24-h average values were available. For a consistency check, the mean of the three 24-h mean levels was also calculated for UFP, showing very high agreement with mean UFP calculations over all 1-s observations ($R^2 = 96\%$, mean difference 86 ± 519 UFP/cm^3). The slight variation between both UFP metrics can be explained by small differences in monitoring duration of individual PEM sessions. Long-term concentrations for all components were calculated when at least two valid PEM sessions were available.

When associations were affected by influential observations (Cook's $D > 1$), associations were further examined without these observations. Furthermore, collinearity of variables (Variance Inflation Factor >3) was evaluated, but not observed in any association. All data cleaning and processing was performed locally. Data analysis was performed centrally, all using the statistical package R (R Core Team, 2008). Cleaning and processing scripts were shared between centers to ensure uniformity in local data handling.

3. Results

3.1. Population characteristics

Population characteristics and distributions of measured average concentrations of air pollution are presented in Table 1. Overall, we included 154 subjects in the study. Successful personal UFP measurements were performed in 142 subjects (89% of the planned 160 subjects). A higher number of subjects and a higher success rate of measurements in Basel, the Netherlands, and Turin was achieved than in Norwich, related to resources allocated to the respective study areas for field work. The proportion of measurements collected on subjects living in a major and a quiet road was almost equal in the Netherlands and Turin, according to the study design. Fewer measurements at major road addresses were performed in Basel and Norwich due to a limited number of eligible subjects, enrolled in recruitment cohorts, living on major roads. Almost half of the subjects had a job and in all areas except Basel gas cooking was customary (80–98% vs 22%). Traffic intensity on the road nearest to the house was highest in the Netherlands. Time spent away from home was highly comparable between all areas (no data for Norwich because diaries were not adequately filled in).

Table 1
Population characteristics and average measured personal and outdoor exposures per area and in combined areas; data presented as Number and [%] or Mean ± SD.

	Basel	The Netherlands	Norwich	Turin	Combined areas
	N = 45	N = 41	N = 26	N = 42	N = 154
Population characteristics	**Number [%]**	**Number [%]**	**Number [%]**	**Number [%]**	**Number [%]**
Male	22 [49]	7 [17]	11 [42]	20 [48]	60 [39]
Works	25 [56]	24 [59]	12 [46]	18 [43]	80 [51]
Lives on major road	10 [21]	20 [48]	8 [26]	20 [48]	58 [38]
Uses gas for cooking	10 [22]	34 [81]	24 [80]	41 [98]	109 [71].
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**
Traffic intensity nearest road	4306 ± 5802	7489 ± 10582	3664 ± 5163	5723 ± 12168	5432 ± 9222
Floor of living room	2.2 ± 1.4	0.6 ± 1.0	0.1 ± 0.4	3.5 ± 2.5	1.7 ± 2.1
Minutes away from home[a]	301 ± 244	320 ± 225	–	301 ± 234	307 ± 235[a]
Measurement success	**Number [%]**	**Number [%]**	**Number [%]**	**Number [%]**	**Number [%]**
Personal UFP	43 [96]	41 [100]	18 [69]	40 [95]	142 [86]
Home Outdoor UFP[b]	42 [93]	41 [100]	–	–	83 [92] [b]
Personal PM2.5 & Soot	45 [96]	40 [98]	23 [89]	42 [100]	150 [91]
Home Outdoor PM2.5 & Soot	45 [96]	41 [100]	18 [69]	42 [100]	146 [88]
Measured exposures	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**
Mean Personal UFP	11685 ± 4791	15462 ± 9880	12297 ± 6096	21071 ± 12770	15497 ± 9933
Median Personal UFP	5398 ± 1374	6059 ± 1850	4455 ± 1500	9883 ± 2796	6733 ± 2850
Mean Home Outdoor UFP[b]	10787 ± 3420	13249 ± 4856	–	–	12003 ± 4346[b]
Personal PM2.5	9.43 ± 3.83	10.30 ± 3.92	12.14 ± 7.02	14.81 ± 6.22	11.58 ± 5.58
Home Outdoor PM2.5	9.59 ± 3.45	13.18 ± 5.62	10.66 ± 6.86	19.51 ± 6.99	13.58 ± 6.91
Personal Soot	0.93 ± 0.56	0.90 ± 0.40	0.76 ± 0.25	2.47 ± 0.87	1.33 ± 0.93
Home Outdoor Soot	1.12 ± 0.45	1.25 ± 0.47	0.94 ± 0.36	3.09 ± 0.94	1.70 ± 1.09

Ultrafine particle (UFP) concentrations in Number/cm^3; $PM_{2.5}$ in μg/m^3; Soot presented as PM2.5 absorbance 10^{-5}/m.
[a] Data not available in Norwich, numbers based on Basel, the Netherlands, and Turin (N = 128).
[b] Collected in Basel and the Netherlands only, percentage/exposures based on these areas (N = 86).

3.2. Air pollution exposure distributions

Distributions of average LUR modeled residential outdoor, measured residential outdoor and personal UFP exposures are presented in Fig. 1, Table 1 and Table S2. In all four areas there was substantial variability of modeled UFP exposure without clear outliers (maximum three times larger than minimum). We note that both modeled and measured UFP include particle number counts above 100 nm. Mean and range of LUR modeled residential outdoor concentrations were close to mean and range of measured mean residential outdoor UFP concentrations (less than 25% difference in mean in Basel and the Netherlands). The average of modeled UFP concentrations was close to the average of measured mean personal UFP exposure, but measured mean personal exposures included more subjects with high exposures. Median personal UFP exposure were a factor two to three lower than personal mean values and showed less variability. Fig. S2 illustrates the presence of very high short-term peaks of personal UFP exposure in the four cities. Peaks occur indoors and outdoors while being away from home, potentially related to local traffic sources. These short peaks affect the mean much more than the median personal exposure. The difference in subject-specific mean and median personal exposure was much larger than the difference in residential mean and median exposure, supporting that a large number of peaks occur indoors and at other locations than the residential address. LUR modeled UFP predictions in the Netherlands and Turin were higher than in Basel and Norwich. Measured personal UFP exposure levels were 30%–40% higher in Turin compared to the three other areas.

Measured concentrations of both $PM_{2.5}$ and soot are presented in Table 1 and Table S2, showing that measured personal exposures were about 80% and 70% of measured residential outdoor exposures. The highest residential and personal concentrations of both components were measured in Turin.

3.3. Modeled residential outdoor vs measured personal concentrations

Modeled residential outdoor UFP concentrations were not associated with measured *mean* personal UFP exposures (Fig. 2 and Table 2). Analyses per area showed a significant association in Norwich only, which became non-significant when one influential observation was excluded from the analysis. A highly significant association with a low regression slope was observed between modeled residential and measured *median* personal UFP concentrations (combined slope 0.12 ± 0.04). Per area, a significant association was observed in Basel only. Standard errors in all models with median personal UFP were 4–5 times lower compared to models with mean personal UFP, illustrating that it is more difficult to detect associations with mean UFP. The larger standard errors likely reflect "noise" due to occasionally encountered very high peak concentrations related to primarily indoor sources and participation in traffic.

Similar associations were found when UFP mean and median personal exposures were calculated only for the time subjects spent at home. There was no association between modeled residential and measured mean personal UFP, but a highly significant association with measured median personal UFP exposure (Table 2). Per area (Norwich excluded), regression slopes and significance levels for these associations were comparable to those obtained over full 24-h observations.

3.4. Prediction of measured residential outdoor UFP by LUR models

LUR models predicted long-term measured mean residential outdoor UFP concentrations moderately well, as previously reported (van Nunen et al., 2017). Explained variability was 48% in Basel and 46% in the Netherlands with regression slopes of 0.73 ± 0.12 and 0.60 ± 0.10 respectively, and the combined slope was 0.65 ± 0.08. These outdoor regression slopes and R^2 are much higher than observed in the regression models with personal exposure as the dependent variable (Table 2), suggesting that measured personal UFP includes sources of variation not accounted for by the outdoor UFP LUR models.

3.5. Measured residential outdoor vs measured personal concentrations

Measured mean residential outdoor UFP levels were not associated with measured mean personal exposure, but significantly associated with measured median personal UFP (regressions slope 0.16 ± 0.04) (Table 3). Associations with measured outdoor were stronger in the Netherlands and similar in Basel compared to modeled outdoor UFP.

Associations between measured residential outdoor and personal $PM_{2.5}$ and soot showed significant regression slopes of 0.32 ± 0.10 and 0.41 ± 0.06 respectively. Although not significant in each area, regression slopes for $PM_{2.5}$ and soot were comparable between the four areas. The regression slopes were substantially higher for $PM_{2.5}$ and soot than for UFP.

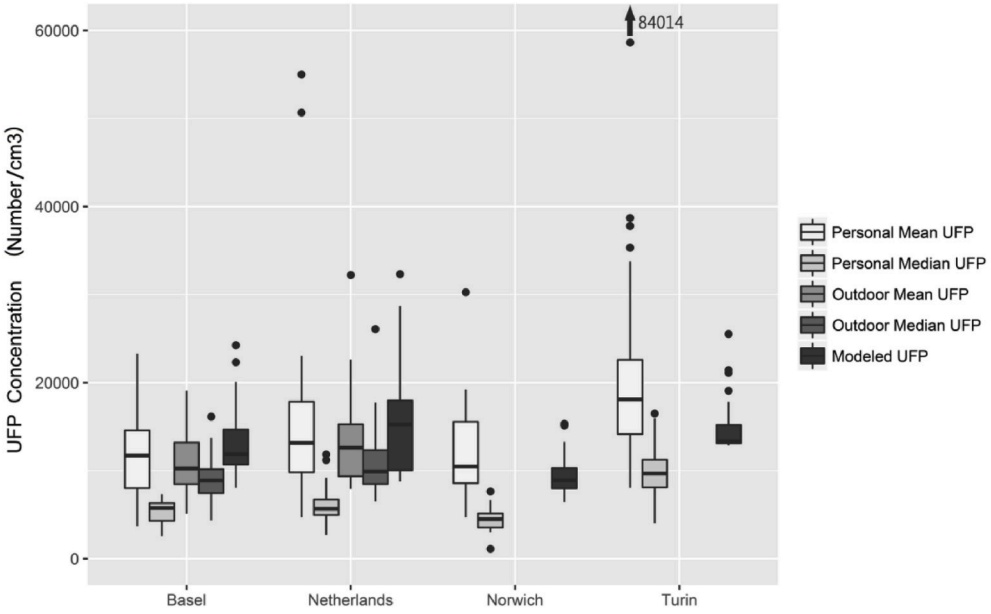

Fig. 1. Distribution of measured personal, measured outdoor and LUR modeled outdoor Ultrafine Particle (UFP) concentrations in Basel (N = 43 Personal, N = 42 Outdoor), the Netherlands (N = 41 Personal, N = 41 Outdoor), Norwich (N = 18 Personal), and Turin (N = 40 Personal). Outdoor measurements were not collected in Norwich and Turin.
Measured concentrations are based on two to three repeated 24-h observations.

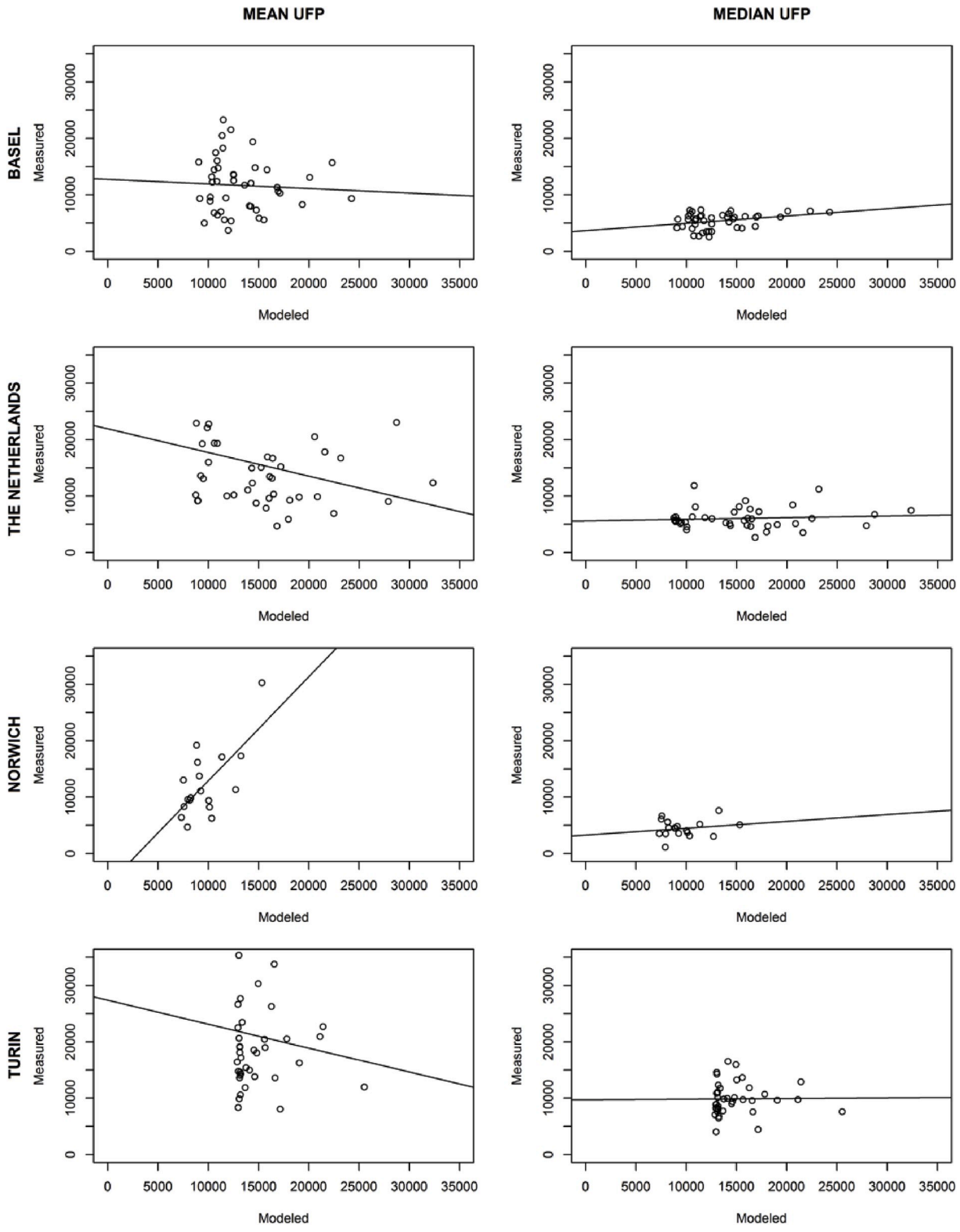

Fig. 2. Associations between modeled residential outdoor and measured subject-specific personal mean/median Ultrafine particle (UFP) exposures (in Number/cm^3) per area. Associations unadjusted for temporal variation are presented.

3.6. Adjustment for indoor sources

An overview of indoor sources used for model correction is presented in Table 4. Over all areas, a low prevalence of cigarette smoke exposure was observed (7%). Little variation between areas was observed in home cooking activities. In Turin, more vacuum cleaning and less bedroom ventilation was reported during PEM sessions. In Basel and the Netherlands, candles were burnt more often. The use of cleaning spray was comparable between areas.

Correction for indoor sources did not consistently affect associations between LUR modeled/measured outdoor and measured mean or median personal exposure (Table 5). Neither regression slopes nor standard

Table 2
Associations between *LUR modeled* home outdoor and average measured personal UFP exposure (Number/cm^3).

Ultrafine Particles	Basel			the Netherlands			Norwich †			Turin			Combined Coefficients †	
Modeled vs	β ± SE	p-value	partial R^2	β ± SE	p-value	partial R^2	β ± SE	p-value	partial R^2	β ± SE	p-value	partial R^2	β ± SE	p-value
Personal Mean	0.022 ± 0.232	0.924	0.00	−0.429 ± 0.273	0.124	0.06	**1.768 ± 0.710**	**0.028***	**0.42**	−0.199 ± 0.732	0.787	0.01	−0.062 ± 0.167	0.712
Personal Mean at home††	−0.120 ± 0.303	0.694	0.02	−0.473 ± 0.305	0.129	0.06	–	–	–	−0.094 ± 0.727	0.898	0.00	−0.279 ± 0.206	0.176
Personal Median	**0.208 ± 0.053**	**<0.001***	**0.14**	0.047 ± 0.051	0.364	0.01	0.155 ± 0.197	0.448	0.11	0.058 ± 0.162	0.722	0.00	**0.122 ± 0.035**	**<0.001***
Personal Median at home††	**0.153 ± 0.055**	**0.008***	**0.07**	0.045 ± 0.054	0.405	0.01	–	–	–	0.074 ± 0.167	0.659	0.00	**0.097 ± 0.037**	**0.009***

Regression slopes (β) ± Standard Error (SE), significance level (p-value) and explained variability (R^2) of model prediction in relation to measured personal Ultrafine Particle (UFP) exposures. Models include contemporaneously measured reference site UFP levels for temporal correction. Combined coefficients are determined by meta-analysis of study area-specific coefficients. * = p-values <0.05.
† = 1 observation with Cook's D > 1 for Personal Mean; When excluded, Norwich association: 0.750 ± 0.775, p = 0.354, R^2 = 11%. Combined associations: 0.126 ± 0.168, p = 0.453.
†† = Mean and median UFP exposure calculated for the time the subject reported to be at home.

Table 3
Associations between *measured* home outdoor and average measured personal UFP exposures (Number/cm^3).

Residential Outdoor vs Personal	Basel †			the Netherlands			Norwich ‡			Turin			Combined Coefficients †‡	
Component	β ± SE	p-value	Partial R^2	β ± SE	p-value	Partial R^2	β ± SE	p-value	Partial R^2	β ± SE	p-value	Partial R^2	β ± SE	p-value
UFP mean	0.117 ± 0.208	0.579	0.00	−0.026 ± 0.330	0.937	0.00	–	–		–	–		0.076 ± 0.176	0.666
UFP median	**0.178 ± 0.054**	**0.002***	**0.17**	**0.147 ± 0.055**	**0.011***	**0.16**	–	–		–	–		**0.163 ± 0.039**	**<0.001***
PM2.5‡‡	0.246 ± 0.236	0.304	0.23	**0.387 ± 0.159**	**0.020***	**0.64**	0.359 ± 0.267	0.199	0.15	0.258 ± 0.164	0.124	0.18	**0.316 ± 0.096**	**0.001***
Soot‡‡	0.301 ± 0.211	0.162	0.04	**0.468 ± 0.106**	**<0.001***	**0.57**	**0.467 ± 0.109**	**<0.001***	**0.55**	**0.374 ± 0.129**	**0.006***	**0.39**	**0.431 ± 0.062**	**<0.001***

Regression slopes (β) ± Standard Error (SE), significance level (p-value), and explained variability (R^2) of long-term measured home outdoor UFP in relation to long-term measured personal Ultrafine particles (UFP), $PM_{2.5}$ and Soot. Models include contemporaneously measured reference site UFP levels for temporal correction Combined coefficients were determined by meta-analysis of study area specific coefficients. *p-values <0.05.
† = 1 observation with Cook's D > 1 for UFP; When excluded, Basel associations: 0.214 ± 0.050, p < 0.001*, R^2 = 0.19; combined associations: 0.184 ± 0.037, p=<0.001*.
‡ = 1 observation with Cook's D > 1 for soot; When excluded, Norwich associations: 0.393 ± 0.140, p < 0.014*, R^2 = 0.56; combined associations: 0.409 ± 0.067, p=<0.001*.
‡‡ = PM2.5 and soot measured as three 24-h integrated averages, hence no median and mean.

errors were affected by adjustment for indoor sources. The unadjusted associations in Table 5 differ numerically from Table 2 because the individual sessions are modeled here.

When restricted to personal measurements at night, associations with modeled UFP were non-significant, despite much lower standard errors of regression slopes. Measured home outdoor UFP was significantly associated with both median and mean personal exposure during night time, related to much lower standard errors and a higher slope (Netherlands, UFP mean only) compared to the full period. Restrictions for night time UFP levels resulted in significant associations due to lower standard errors rather than higher slopes.

4. Discussion

LUR model predictions of mean home outdoor UFP were significantly associated with measured median but not mean personal UFP exposures of adults in four European areas. Regression slopes combined for the four areas were 0.12 ± 0.04 and −0.06 ± 0.17 for median and mean personal exposure respectively. The LUR model explained variance of the median personal exposure less (range 0–14% per area) than variance of residential outdoor measurements (46–48%). Associations did not change when personal exposure was calculated only for the time spent at home or when the presence of indoor sources was incorporated in the regression models. Regression slopes for measured residential outdoor versus personal exposure were smaller for UFP (0.16 ± 0.04) than for $PM_{2.5}$ and soot (0.32 ± 0.10 and 0.43 ± 0.06), consistent with previously reported low infiltration of UFP in indoor environments compared to fine particles.

Table 4
Indoor sources in the 24-h Personal Exposure Monitoring sessions.

	Basel	the Netherlands	Norwich	Turin	Combined areas
	N = 134	N = 123	N = 74	N = 125	N = 456
	Number [%]	Number [%]	Number [%]	Number [%]	Number [%]
Cigarette smoke exposure					
Overall	3 [2]	5 [4]	4 [5]	19 [15]	31 [7]
At home	*2 [1]*	*2 [2]*	*2 [3]*	*8 [6]*	*14 [3]*
Somewhere else	*1 [1]*	*3 [2]*	*2 [3]*	*13 [10]*	*19 [4]*
Meal cooked	105 [78]	101 [82]	42 [57]	118 [94]	366 [80]
Vacuum cleaned	37 [28]	18 [15]	21 [28]	83 [66]	159 [35]
Candle burned	36 [27]	29 [24]	3 [4]	11 [9]	79 [17]
Spray used	25 [19]	26 [21]	14 [19]	22 [18]	85 [19]
Bedroom window open at night	74 [55]	90 [73]	35 [46]	25 [20]	224 [49]

Data on indoor sources was collected in a technician-administered questionnaire after each 24-h session.
'Cigarette smoke exposure – Overall' reflects any cigarette smoke exposure (at home and/or somewhere else).

4.1. Difference in associations of LUR modeled UFP with mean and median personal UFP exposure

EXPOsOMICS LUR models, developed on repeated 30-min mean UFP measurements, were applied to the residential address of the subjects. LUR models only predict outdoor concentrations. The absence of associations between LUR modeled outdoor and mean personal UFP is likely due to the occurrence of high short-term peaks in personal measurements, caused by both indoor sources and exposures on other locations than the residential address. Mean personal exposures were much larger than median personal exposures, reflecting a large impact of short-term peaks on the mean. The implication of the difference in findings for mean and median UFP depends on assumptions regarding toxicity of UFP. If one assumes that toxicity of UFP is not related to composition but only to the number of particles in the ultrafine size range, then the findings for mean UFP are most relevant. The implication is then that average outdoor (modeled and measured) UFP is not a good surrogate for contrast in average personal UFP exposure between subjects. Using the outdoor UFP metrics would result in a very large misclassification of exposure. If, in contrast, we assume that the toxicity of UFP depends on both composition and particle numbers, then we want to distinguish between UFP originating from indoor and outdoor (i.e. traffic) sources. In that case, the findings for median personal UFP (less affected by peak exposures in the house) are more relevant if the interest is in outdoor UFP. For assessment of outdoor generated pollution, we ideally would like to measure personal exposure to ambient-generated particles, but this is currently not feasible (Montagne et al., 2013; Sarnat et al., 2005).

Table 5
Impact of adjustment for indoor sources/restriction to nighttime on association between modeled/measured home outdoor and measured personal UFP exposure.

		Basel		The Netherlands		Norwich †		Turin		Combined Regression †	
	Adjustment/ restriction	β ± SE	p-value	β ± SE	p-value	β ± SE	p-value	β ± SE	p-value	β ± SE	p-value
Modeled home outdoor											
UFP mean	Not adjusted	0.076 ± 0.213	0.722	−0.442 ± 0.224	0.056	**1.440 ± 0.546**	**0.014***	−0.213 ± 0.674	0.753	−0.058 ± 0.145	0.688
	Adjusted for indoor sources	0.332 ± 0.213	0.128	**−0.623 ± 0.232**	**0.011***	0.528 ± 0.679	0.446	−0.275 ± 0.710	0.701	−0.083 ± 0.150	0.580
	Restricted to night hours	0.177 ± 0.109	0.111	0.027 ± 0.343	0.788	**0.595 ± 0.268**	**0.036***	−0.127 ± 0.237	0.600	0.045 ± 0.032	0.158
UFP median	Not adjusted	**0.194 ± 0.051**	**<0.001***	0.049 ± 0.043	0.263	**0.310 ± 0.126**	**0.021***	0.005 ± 0.156	0.976	**0.118 ± 0.031**	**<0.001***
	Adjusted for indoor sources	**0.217 ± 0.054**	**<0.001***	0.063 ± 0.044	0.162	0.184 ± 0.161	0.266	−0.043 ± 0.166	0.797	**0.121 ± 0.033**	**<0.001***
	Restricted to night hours	**0.125 ± 0.058**	**0.036***	0.022 ± 0.033	0.504	0.224 ± 0.166	0.189	−0.018 ± 0.100	0.859	0.047 ± 0.027	0.082
Measured home outdoor		**β ± SE**	**p-value**	**β ± SE**	**p-value**	**β ± SE**	**p-value**	**β ± SE**	**p-value**	**β ± SE**	**p-value**
UFP mean	Not adjusted	0.020 ± 0.163	0.903	−0.044 ± 0.214	0.839	–	–	–	–	−0.003 ± 0.130	0.980
	Adjusted for indoor sources	0.091 ± 0.160	0.571	−0.117 ± 0.212	0.584	–	–	–	–	0.016 ± 0.128	0.920
	Restricted to night hours	0.076 ± 0.069	0.278	**0.081 ± 0.028**	**0.005***	–	–	–	–	**0.081 ± 0.026**	**0.002***
UFP median	Not adjusted	**0.106 ± 0.039**	**0.008***	**0.094 ± 0.034**	**0.008***	–	–	–	–	**0.099 ± 0.026**	**<0.001***
	Adjusted for indoor sources	**0.125 ± 0.039**	**0.002**	**0.085 ± 0.034**	**0.013***	–	–	–	–	**0.102 ± 0.026**	**<0.001***
	Restricted to night hours	**0.087 ± 0.042**	**0.042***	**0.088 ± 0.025**	**<0.001***	–	–	–	–	**0.088 ± 0.021**	**<0.001***

Regression slopes (β) with Standard Error (SE) and significance level (p-value) of modeled or measured home outdoor UFP levels in relation to measured personal levels.
Models are temporal corrected with contemporaneously measured reference site UFP levels. Home outdoor Ultrafine particles (UFP) not measured in Norwich and Turin; Not adjusted = model without correction; Adjusted for indoor sources = model corrected for presence of indoor sources; Restricted to night hours = models using personal night time (00:00–08:00)average UFP concentrations to restrict influence of indoor sources.
Combined coefficients were determined by meta-analysis of local coefficients. *p-values <0.05.
† = 1 observation with Cook's D > 1 for UFP Mean at night. When excluded; Norwich associations: 0.226 ± 0.193, p = 0.252 and combined associations: 0.029 ± 0.024, p = 0.233.

For policy purposes, distinguishing indoor and outdoor contributions to UFP exposure is important as well.

4.2. Factors affecting associations between LUR modeled and measured personal UFP

The associations between LUR modeled and measured personal exposure are overall relatively weak: we only found an association with median personal exposure; the explained variance was low for median personal exposure as well and regression slopes were low. The low regression slopes in associations between modeled and personal UFP may be explained by a combination of factors. The ability of the LUR model to predict outdoor concentrations is only a small component in explaining the association with measured personal exposure. LUR models predicted UFP variability in mean residential outdoor measurements moderately well in both Basel and the Netherlands, consistent with other recent studies showing explained variances between 47% and 88% (Eeftens et al., 2016; van Nunen et al., 2017; Ragettli et al., 2014). LUR models explained variance of measured personal exposure much worse than measured outdoor exposure, suggesting that other factors affect the association (Montagne et al., 2013). First, assessment of long-term personal exposure is challenging, and the inevitably short observation periods lead to highly noisy data to work with. Second, indoor sources may have affected associations. Third, infiltration of UFP in the indoor environment, where subjects spend a large fraction of their time, is low. Fourth, subjects spent time away from home. The possible explanations are explored further below.

4.3. Assessment of long-term personal exposures

Validation of surrogates for long-term exposure to air pollution is challenging because of the general difficulty to obtain measurements of personal exposure of sufficiently long duration in a large group of subjects (Montagne et al., 2013). Measured average personal UFP exposures in our study are affected by this issue. Random error is introduced due to major short-term UFP variability within 24-h observations. Short-term peak UFP exposures can be a factor 200 higher than minimum UFP levels, which largely affects mean personal exposures. In the current study we performed measurements in a larger number of subjects but with a shorter longer monitoring duration per subject compared to previous studies: 142 subjects with 3 × 24 h of measurements per subject. In previous studies, Nethery et al. collected two or three repeated 48-h samples for NO, NO_2, $PM_{2.5}$ and soot in 55 pregnant women (Nethery et al., 2008), Sahsuvaroglu et al. applied two or three repeated 72-h monitoring sessions for NO and NO_2 in 33 elderly adults (Sahsuvaroglu et al., 2009), and Montagne et al. collected six repeated 96-h NO, NO_2, $PM_{2.5}$ and soot measurements in 15 volunteers in both Utrecht, Helsinki and Barcelona (Montagne et al., 2013). Random error in personal exposure (the dependent variable in our linear regression models) does not lead to bias in the estimated regression slope, but it does contribute to a loss in precision (a lower explained variance) of associations with LUR modeled exposures.

4.4. Indoor sources

A large variety of indoor sources affects indoor UFP, extensively described in previous reviews (HEI Review Panel, 2013; Wallace and Ott, 2011). Mean personal UFP levels may have a strong signature of indoor emissions from smoking, gas cooking or candle burning. In the study design we excluded regular smoking in the home, resulting in low overall smoking exposure. Tobacco smoke exposure was low outside the home as well, likely reflecting the reduction of smoking in public spaces. We could not restrict our study population to subjects not using gas for cooking in three of the study areas, given the widespread use of gas for cooking. Gas cooking has been shown to be an important indoor source of UFP (HEI Review Panel, 2013; Wallace and Ott, 2011; Buonanno et al., 2014). The area with the lowest use of gas for cooking (Basel) had the most significant associations between modeled residential outdoor UFP and personal UFP exposure, possibly due to the lower "noise" related to indoor sources. Indoor sources may result in confounding of the association between LUR modeled exposure and personal exposure and in more noise in the dependent variable resulting in lower precision of associations. To rule out confounding by unequal distribution of indoor sources in our current study sample (e.g. less gas cooking in homes along a major road), regression models were specified in which we corrected for subject-reported indoor sources. These corrections resulted in comparable associations to mean or median personal exposures as uncorrected models, suggesting no confounding in our associations. A limitation is that simple questionnaire information may not be enough to characterize the impact of indoor sources (Montagne et al., 2013), e.g. because the impact depends on actual source strength, air exchange rates, and home volume. Therefore, more detailed information on indoor sources of UFP exposures may be desired for future studies, to increase certainty of ruling out confounding in personal exposures. Measured night time exposures, least influenced by indoor sources, were not associated with modeled home outdoor UFP either. The limitation of restriction to the night time period is that there is likely a smaller contrast in exposure from outdoor sources, such as motorized road traffic.

4.5. Infiltration to the indoor environment

Regression slopes between measured residential and measured personal exposures were lower for UFP than for $PM_{2.5}$ and soot. This is consistent with previous studies, illustrating that ultrafine particles infiltrate less to the indoor environment than fine particles, which has been attributed to larger diffusion losses for ultrafine particles compared to fine particles (HEI Review Panel, 2013; Hoek et al., 2008; Long et al., 2001; Rivas et al., 2015). Where precise assessment of long-term average personal exposures and characterization of indoor sources were methodological problems in exposure validation studies, low infiltration describes true environmental processes resulting in lower personal exposure to ambient generated UFP.

For $PM_{2.5}$ and soot, the regression slopes in the current study were in line with previously reported slopes between measured outdoor and personal exposures. Janssen et al. reported regression slopes of 0.46 and 0.48 for $PM_{2.5}$ and 0.95 and 0.61 for soot on 35 and 45 observations in Amsterdam and Helsinki (Janssen et al., 2005), and Hoek et al. found regression slopes of 0.34–0.48 for $PM_{2.5}$ and 0.63 to 0.84 for soot in 152 homes across 4 European cities (Hoek et al., 2008).

$PM_{2.5}$ and soot were measured simultaneously with UFP. The consistent associations between measured outdoor and personal exposure to PM2.5 and soot, suggests the number of observations was sufficient to detect associations.

4.6. Time away from home

Subjects spent on average about 5 h per PEM-session away from home. Exposures in traffic or at locations other than the residential address have been identified as substantial source for UFP exposure (Ragettli et al., 2013; Buonanno et al., 2014). This may have influenced current associations between LUR modeled outdoor at the residence and measured personal UFP levels. However, we found comparable regression coefficients, standard errors and explained variance in associations with 24-h personal exposures and personal exposures restricted to time spent at home. The restriction to time spent at home, clearly increases the impact of indoor sources on mean exposure.

4.7. Study limitations

Our monitoring instrument measured particle number counts between 10 and 300 nm, thus including particles above the cutpoint of 100

nm commonly used to define ultrafine particles. Studies have shown that total particle number counts are dominated by ultrafine particles (HEI Review Panel, 2013), so that our results can mostly be interpreted as associations between modeled and measured UFP. As an example, a study in three European cities including Amsterdam measuring full particle distributions found that 90–93% of the particle number concentration between 10 nm and 1000 nm was within the 10–100 nm size fraction (Hartog et al., 2005). The lack of residential outdoor monitoring in two of the four cities has hampered our interpretation of the associations between modeled and measured personal UFP exposure (our main analysis performed in four cities). It would have been informative to assess whether the pattern observed in Basel and the Netherlands of better associations between modeled UFP with residential outdoor than with personal exposure holds in Turin and Norwich as well. Budget restraints did not allow this. Another limitation is the lack of separating particles from indoor and outdoor sources. The time activity diary in Norwich was not completed well and therefore analyses of associations between modeled and measured exposure for different time periods could be conducted in three of the cities.

5. Conclusion

LUR modeled residential outdoor UFP concentrations were significantly associated with median but not mean measured personal UFP exposure. Median personal exposures are less influenced by home indoor and outdoor peak UFP levels than the mean personal exposure. Regression slopes for measured residential outdoor versus personal exposure were smaller for UFP than for $PM_{2.5}$ and soot, consistent with previously reported low infiltration of UFP in indoor environments compared to fine particles. Our findings provide some support the use of LUR models for estimation of long-term exposure to UFP of outdoor origin in epidemiological studies.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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