Ambient air pollution, traffic noise and adult asthma prevalence: a BioSHaRE approach

Yutong Cai[1], Wilma L Zijlema[2], Dany Doiron[3], Marta Blangiardo[1], Paul R Burton[4,5], Isabel Fortier[3] , Amadou Gaye[6], John Gulliver[1], Kees de Hoogh[1,7,8], Kristian Hveem[9], Stéphane Mbatchou[3], David W Morley[1], Ronald P Stolk[2], Paul Elliott[1], Anna L Hansell[1,10], Susan Hodgson[1]

1: MRC-PHE Centre for Environment and Health, Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK
2: Department of Epidemiology, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands.
3: Research Institute of the McGill University Health Centre and Department of Medicine, McGill University, Montreal, Canada.
4: Data to Knowledge (D2K) Research Group, University of Bristol, Bristol, UK.
5: Public Population Project in Genomics and Society (P^3G), Montreal, Canada.
6: Metabolic, Cardiovascular and Inflammatory Disease Genomics Branch, National Human Genome Research Institute, Bethesda, USA
7: Swiss Tropical and Public Health Institute, Basel, Switzerland
8: University of Basel, Basel, Switzerland.
9: Department of Public Health and General Practice, Norwegian University of Science and Technology, Trondheim, Norway.
10: Directorate of Public Health and Primary Care, Imperial College Healthcare NHS Trust, London, UK.

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Corresponding author:

Yutong Cai, MRC-PHE Centre for Environment and Health, Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, St Mary's Campus, Norfolk Place, London, W2 1PG, UK. E-mail: yutong.cai@imperial.ac.uk Fax: +44 (0) 20 7594 3193 Phone: + 44 (0) 20 7594 2067

"Take-home" message: long-term ambient PM_{10} exposure is associated with asthma prevalence in three European adult cohorts.

ABSTRACT

We investigated effects of both ambient air pollution and traffic noise on adult asthma prevalence, using harmonised data from three European cohort studies established in 2006-2013 (HUNT3, Lifelines, UK Biobank).

Residential exposures to ambient air pollution (PM_{10} and NO_2) were estimated by a pan-European Land Use Regression model for year 2007. Traffic noise for year 2009 was modelled at home address by adapting a standardised noise assessment framework (CNOSSOS-EU). A cross-sectional analysis of 646,731 participants aged ≥20 years was undertaken using DataSHIELD to pool data for individual-level analysis via a 'compute to the data' approach. Multivariate logistic regression models were fitted to assess effects of each exposure on lifetime and current asthma prevalence.

PM_{10} or NO_2 higher by 10 $\mu g/m^3$ was associated with 12.8% (95%CI: 9.5% to 16.3%) and 1.9% (95%CI: 1.1% to 2.8%) higher lifetime asthma prevalence respectively, independent of confounders. Effects were larger in those aged ≥50 years, ever-smokers and less educated groups. Noise exposure was not significantly associated with asthma prevalence.

This study suggests that long-term ambient PM_{10} exposure is associated with asthma prevalence in western European adults. Traffic noise is not associated with asthma prevalence, but its potential to impact on asthma exacerbations needs further investigation.

INTRODUCTION

Asthma is a complex respiratory illness which affects both children and adults. Globally, asthma was the 28th leading cause of disability-adjusted life years in 2010[1] and it was estimated in 2014 that around 334 million people worldwide have asthma[2]. An increasing prevalence of asthma was seen in some parts of the developed world at least until the late 1990s, after which the temporal trend varied across countries[3] ─ in some regions, the asthma epidemic continues to increase in adults[4].

Some potential risk factors have been identified for these prevalence trends. One is exposure to air pollution, which has a role in exacerbations of pre-existing asthma and affects asthma morbidity via various mechanistic pathways, including airway hyper-responsiveness, airway remodelling, oxidative stress and immune response[5]. However, previous studies are inconsistent with respect to the associations between long-term air pollution and asthma prevalence[6] and incidence[7]. In adults, some studies reported positive associations between self-reported traffic intensity and asthma prevalence, though these findings were not supported by analysis of individual modelled exposures to air pollution in the same populations[8,9]. Other studies did not report significant associations of air pollution and adult asthma prevalence[10-15] except one[16]. A few studies investigated the effect of air pollution on adult-onset asthma, with significant associations reported either among all participants[17,18], never-smokers[19] or women only[20]. An analysis of six European cohorts reported positive but non-significant associations of asthma incidence with a range of modelled air pollutants[21].

Another asthma risk factor is chronic psychosocial stress, which may affect asthma morbidity through biological responses and disease management[22]. To our knowledge, there are no studies investigating whether individual exposure to traffic noise, generally seen as an environmental stressor and mostly co-existing with air pollution in road traffic settings, would affect adult asthma morbidity. Only two previous small studies investigated associations between subjective noise exposures and asthma prevalence, with null results reported[23,24].

In this study, we investigated the separate and joint effects of both long-term air pollution and traffic noise exposure on adult prevalent asthma, using a pooled individual-level analysis of harmonised data from three recently established large European cohort studies: HUNT3 (Norway)[25], Lifelines (the Netherlands)[26] and UK Biobank (United Kingdom)[27].

METHODS

Study populations

Three cohort studies participating in BioSHaRE (Biobank Standardisation and Harmonisation for Research Excellence in the European Union-BioSHaRE-EU) were included in this study.

HUNT3 is the third survey of the HUNT (Helseundersøkelsen i Nord-Trøndelag) study, based in Nord-Trøndelag County in Norway[25]. During 2006-2008, data from 50,805 residents aged ≥20 years were collected by trained staff. Lifelines is a multi-disciplinary prospective population-based cohort study examining in a three-generation design the health and health-related behaviours of 167,729 persons living in the North of The Netherlands[26]. During baseline recruitment (2006-2013), residents aged 25-50 years and family members registered in general practices were randomly invited to participate. Quality-checked data on 93,277 Lifelines participants were available within the timeframe of this study. UK Biobank, established during 2006-2010, recruited 502,649 participants aged 40-69 years across the UK[27].

Exposure assessment

Ambient air pollution

Pan-European Land Use Regression (LUR) model at a resolution of 100x100m was used to assign annual air pollution estimates at home addresses for each participant from the three cohorts[28]. Annual mean NO_2 (nitrogen dioxide) and PM_{10} (Particulate Matter with aerodynamic diameter ≤10μm) during 2005-2007 were obtained from over 1500 monitoring sites across Europe; means for 2007 were used in the analyses since data for both pollutants were available for that year for all three cohorts. Only monitoring sites which captured over 75% of the total hours for NO_2 and days for PM_{10} were included. The pan-European LUR model was developed using 80% of these monitored air pollution data, satellite-based ground-level concentrations of NO_2 and $PM_{2.5}$ (Particulate Matter with aerodynamic diameter ≤2.5μm) on a 10-km grid, land-use and traffic variables obtained from GIS (Geographic Information System) (supplement-1). Model performance (explained variance (R^2) between modelled and measured exposures) for PM_{10} and NO_2 estimates was 36-48% and 46-56% respectively, evaluated against the independent subset (20%) of all included monitoring sites[28].

Additional address level annual estimated NO_2 and PM_{10} concentrations for year 2010 were available for Lifelines and UK Biobank, using LUR models for the respective study areas from the ESCAPE (European Study of Cohorts for Air Pollution Effects) project[29,30]. R^2 for PM_{10} and NO_2 ESCAPE LUR models was 60-88% and 81-87% respectively, evaluated using the leave-one-out cross-validation method[29,30].

Traffic noise

We used a simplified version[31], with some lower resolution inputs, of the CNOSSOS-EU (Common noise assessment methods in European Union) noise modelling framework[32] to estimate noise exposures at address level for participants in each study. In brief, noise sound level was estimated for all roads within 500 meters of home address, with consideration of noise propagation due to refraction and diffraction, absorption from buildings, distance and angle of view. Road network geography, hourly vehicle flows, building heights, land cover and meteorological data were obtained for the respective study areas. For participants living on minor roads that were not captured in the national level traffic datasets, we assigned a fixed low-level baseline flow. Traffic data were for the year of 2009 and land cover data were for the year 2006.

For all three cohorts, we modelled annual mean A-weighted sound pressure level in decibels (dB(A)) for day-time noise (Lday, averaged sound level from 07:00 to 19:00) and night-time noise (Lnight, averaged sound level from 23:00 to 07:00).

Harmonisation of covariates and outcomes

Age, sex, Body Mass Index (BMI), education level (primary school or less, secondary school, post-secondary school or above), paid employment (yes or no), smoking (current-, ex- and never-smoker), and years at baseline address were harmonised retrospectively across cohorts (supplement-2), following a validated protocol[33].

Lifetime asthma prevalence ("**ever-had asthma**") was harmonised based on the self-reported answers (yes or no) in study questionnaire (**Table 1**). "**Current-asthma**" was defined as a self-report of ever-had asthma **AND** participant reporting asthma-related medication use, for which data were ascertained differentially in each cohort (**Table 1**).

We did not have information on incident asthma.

Statistical analyses

To overcome the ethico-legal issues associated with physical sharing of data, statistical analyses were performed using DataSHIELD[34], a novel tool which allowed co-analysis of harmonised datasets across the three participating cohorts without physically sharing the individual-level data.

Firstly, we calculated spearman correlations between metrics of air pollution and noise for each cohort. Associations between each metric of air pollution (or noise) and ever and current asthma were analysed using multivariate logistic regression. Both air pollution and noise metrics were analysed on a continuous scale, assuming a linear effect. Additionally, three categories for day-time noise (<55, 55-60, ≥60 dB(A)) and night-time noise (<45, 45-50, ≥50 dB(A)) were used.

The covariates were chosen *a priori* based on current knowledge. The sequence of models was as follow: adjusted for study (Model 1), adjusted for study, age and sex (Model 2), further adjusted for BMI, smoking, education level and employment status (Model 3). Based on Model 3, road traffic noise (or air pollution) were additionally added to the air pollution (or noise) model.

Sensitivity analyses were conducted based on Model 3: a) restricting analyses to those living at the same address ≥10 years; b) using ESCAPE-LUR air pollution metrics (PM_{10} and NO_2) for Lifelines and UK Biobank instead of the pan-European-LUR metrics; c) conducting study-specific analyses and then pooling estimates using meta-analysis methods, in both fixed-effect and random-effect models, to explore heterogeneity[35].

Stratified analyses were conducted based on Model 3 by: i) sex; ii) age <50 or ≥50 years; iii) smoking status; iv) BMI <25, 25-30, ≥30 kg/m^2; v) education level.

Individual-level fixed-effect pooled analyses were done in DataSHIELD v4.1.2. Study-level meta-analyses were done in Stata v12.1, Texas, USA.

RESULTS

Overall, prevalence of ever-had asthma was 11.1% and current-asthma was 4.3% (**Table 2**). Prevalence of ever-had asthma or current-asthma was higher among women, those aged <50 years, with a BMI over 25kg/m^2 and less educated.

Mean(SD) PM_{10} ranged from 11(1.1) (HUNT3) to 24(1.7) (Lifelines) µg/m^3 whilst mean NO_2 ranged from 13(3.9) (HUNT3) to 31(10.7) (UK Biobank) µg/m^3 (supplement-3). Pooling data

for PM_{10} and NO_2 from 606,657 and 608,102 participants respectively, median and inter-quartile range (IQR) PM_{10} was 23 (IQR: 4.3) $\mu g/m^3$; NO_2 29 (IQR: 11.4) $\mu g/m^3$ (supplement-3). In the pooled data, median day-time noise and night-time noise estimates were 59 (IQR: 4.3) and 49 (IQR: 4.2) dB(A) respectively.

Spearman correlations between PM_{10} and daytime noise ranged from r= 0.04 (HUNT3) to 0.38 (Lifelines), and between NO_2 and day time noise ranged from r= -0.05 (HUNT3) to 0.43 (Lifelines) (supplement-4). Correlation between NO_2 and PM_{10} was r=0.8 and between daytime and night-time noise r=0.99 in each of the three cohorts.

In all models, statistically significant associations were found for PM_{10} and NO_2 in relation to prevalence of ever-had asthma (**Table 3**). In the fully adjusted Model 3, PM_{10} higher by 10 $\mu g/m^3$ was associated with 12.8% (95%CI: 9.5% to 16.3%) higher prevalence of ever-had asthma, and 6.4% (95%CI: 1.2% to 11.9%) higher prevalence of current-asthma. NO_2 higher by 10 $\mu g/m^3$ was associated with 1.9% (95%CI: 1.1% to 2.8%) higher prevalence of ever-had asthma, but not current-asthma prevalence. Further adjustments for daytime noise did not change the associations.

No associations between categorical or continuous noise exposures and asthma prevalence were seen (Table 4 and supplement-5).

Significant effect modifications (p-value for interaction<0.01) by age, smoking and education were observed between PM_{10} and ever-had asthma prevalence, with stronger associations seen for those aged≥50 years, ever-smokers and less educated(**Figure 1**). Similar findings were observed for current-asthma (Supplement-6). No significant effect modifications were seen between NO_2 and ever-had or current asthma prevalence by any of the studied variables (supplement-6).

In sensitivity analyses, for participants living at the same address for more than 10 years, associations between PM_{10}, NO_2, and ever-had asthma became slightly stronger (supplement-7). Using ESCAPE-LUR modelled PM_{10} and NO_2 for Lifelines and UK Biobank instead of the pan-European LUR metrics, both ever-had asthma and current-asthma prevalence were significantly associated with both PM_{10} and NO_2 (supplement-7).

Associations between NO_2, PM_{10}, daytime noise and ever-had asthma prevalence in Model 3 assessed via meta-analysis across cohorts (supplementary Figure 1) were similar to those from the individual-level analysis. However, study-specific associations between NO_2, PM_{10}

and current-asthma prevalence were heterogeneous (P<0.05) (supplementary Figure 2) and none of the pooled study estimates in the meta-analyses was significant. The effect size in the meta-analyses was dominated by UK Biobank.

DISCUSSION

In this cross-sectional study involving three large European cohorts, there was a statistically significant positive association between ambient PM_{10} air pollution and both ever-asthma and current-asthma prevalence. NO_2 was significantly associated with ever-asthma but not current-asthma. We found no association between traffic noise exposures and ever or current asthma prevalence.

This study is one of the largest studies of its kind to date. Harmonised exposures and health data of over 600,000 participants from three cohorts were brought together for an integrative pooled individual-level analysis, using DataSHIELD. Both air pollution and noise exposures were modelled at home address, providing an opportunity to investigate health effects of both exposures in the same study.

Previous findings

Only a few studies have investigated the role of air pollution on adult asthma prevalence, with most finding null or weak positive associations. Some used proxy 'traffic intensity' exposures (e.g. living near a busy road, home distance to a major road) in the analyses and reported null associations[11-13,15]. In contrast, two studies found significant associations between self-reported traffic exposures near home and increased adult asthma prevalence[9,10], but not when using individual modelled home outdoor NO_2 or NOx (nitrogen oxides). Neither of these two studies examine NO_2 or NOx effects on a continuous scale. A study of young adult Italians (aged 20-44 years) found that each 18.3 $\mu g/m^3$ increase of NO_2 was non-significantly associated with increased asthma prevalence (OR: 1.13, 95%CI: 0.98 to 1.32)[10]. A national study among 12,177 Australian women reported a null association between 3-year mean annual NO_2 and asthma prevalence[15].

In the SAPALDIA study, long-term exposure to PM_{10} was non-significantly associated with increased prevalence of current asthma (OR: 1.19, 95%CI: 0.83 to 1.70) in current smokers[14]. Recently, a study of 29,459 Canadian women reported that each 10 $\mu g/m^3$ increase of $PM_{2.5}$ was significantly associated with increased ever-diagnosed asthma

prevalence (OR: 1.14, 95%CI: 1.01 to 1.29). Association was stronger among smokers (OR: 1.58, 95%CI: 1.46 to 1.70), compared to non-smokers (OR: 1.16, 95%CI: 0.96 to 1.41)[16].

A review of community-level studies in 2013 concluded that there was no evidence of an effect of long-term air pollution on asthma prevalence[6], though most of the studies included in that review were conducted in children (only two of nine NO_2 estimates and one of nine PM_{10} estimates were for adults).

In contrast to most previous findings, our study suggests that both long-term PM_{10} and NO_2 exposure is associated with increased lifetime asthma prevalence in adults. By pooling individual-level data from three large cohorts, our study has a much larger sample size and statistical power to detect an effect. Also, air pollution at home address was modelled at a fine spatial scale (100m grid) in our study, contributing to the observed robust associations.

Whilst findings in the prevalence studies were not entirely consistent, a positive association is increasingly suggested between ambient air pollution and incident asthma. In a nationwide cohort of U.S women, a borderline significant association between $PM_{2.5}$ and incident asthma was observed (OR: 1.20, 95%CI: 0.99 to 1.46)[20]. However this was not seen in the ESCAPE study (OR: 1.04, 95%CI: 0.88 to 1.23)[21]. Two studies reported significant associations between NO_2 and incident asthma with similar effect sizes[17,18]. In the ESCAPE study, NO_2 was not associated with asthma incidence (OR: 1.10, 95%CI: 0.99 to 1.21)[21].

Effect estimates per 10 $\mu g/m^3$ were much larger for PM_{10} than for NO_2. There are still debates on whether NO_2 on its own causes health effects or merely is a marker of traffic-related, particularly near-road, air pollution[36]. Unlike NO_2, particulate matter (PM) air pollution is more homogeneous over a wider region, and includes sources other than traffic[37]. It was reported that in Europe, $PM_{2.5}$ accounts for 40-80% of PM_{10} mass[29]. $PM_{2.5}$, with various substances attached to it, could travel and deposit deep into the respiratory tract. These substances, including transitions metals and immunogenic substances, could either induce direct airway inflammation or lead to oxidative stress[5], two biological pathways linking to asthma. This may explain in part the relatively larger effect estimates seen for PM_{10}.

A recent review concluded that no clear susceptibility factors could be identified to date for the link between outdoor air pollution and asthma incidence or prevalence[38]. One of the reasons, as the review suggested, may be that most studies lacked statistical power to perform

interaction tests. In our study, due to the large sample size, we were able to investigate interactions among variables selected *a priori*. We found stronger associations among those aged ≥50 years, ever-smokers and less educated, adding evidence to the scant literature. The role of smoking status on the link between air pollution and asthma remains unclear. Some previous studies have reported stronger associations among never- and former-smoker[38] whilst two recent studies, including the ESCAPE study, observed an association only among ever-smokers[16,21]. Different classifications of smoking status were used across previous studies, meaning results are not directly comparable. Smokers may have a higher risk for asthma[39] and it has been suggested that there may exist a synergistic effect of both tobacco smoking and air pollution exposure on asthma[40].

Asthmatics may move to less-polluted areas (e.g. far from a busy road) because of their illness, which could potentially lead to underestimation of the air pollution effects on adult asthma prevalence. However, in our study, mean duration of current residence was similar between asthmatics (16 years) and non-asthmatics (16.7 years) and adjusting for residence years in Model 3 did not change the observed associations, suggesting migration is unlikely to have biased these associations.

Road traffic noise is rarely studied in relation to asthma morbidity. One study found that noise annoyance at night, as subjectively reported by 652 children, was significantly associated with asthma prevalence among girls[23]. Another study of 1383 middle-aged adults reported no association between frequency of intense traffic noise and current asthma prevalence[24]. Our much larger study did not find statistically significant associations between individual modelled noise exposure and ever-asthma or current asthma prevalence, but data were not available to look directly at either asthma incidence or asthma exacerbations. It has been hypothesised that road traffic noise, as a psychological stressor, may induce alternations in the immune system, increase oxidative stress and disturb sleep, which all may potentially result in respiratory exacerbations including asthma[41]. Increasing numbers of studies have linked other environmental stressors (e.g. neighbourhood violence, deprivation) to asthma morbidity[22], but more studies are needed to investigate the role of traffic noise on asthma.

Limitations

This study has a number of limitations. First, we adopted a cross-sectional design, which has limited value in establishing causal associations. Second, our asthma outcome was not strictly

harmonised due to the wording of the original asthma question or variable recording of asthma-related medication data. Third, residual confounding cannot be ruled out as we were unable to harmonise other potential confounders and effect modifiers across the three cohorts, including environmental tobacco smoke, occupational exposures to gases and dust, family history of asthma and area-level socioeconomic status. Finally, the modelled air pollution and noise estimates inevitably had some exposure misclassifications, although this is unlikely to be differential according to the participant's asthmatic status. Given the broad geographic regions that this study covers, we adopted common LUR air pollution and noise models developed for Europe to minimise differences between cohorts that would otherwise be introduced by having different exposure assessment methods. This study is among the first to adapt the CNOSSOS-EU noise framework for epidemiological analysis however traffic flow data were not available for some secondary roads, which will lead to underestimation of noise levels in those areas. As with most air pollution and noise studies, we used home outdoor, but not indoor, air pollution and noise, which may be affected by building type and habits such as window opening, leading to further exposure misclassification.

In conclusion, this large cross-sectional study provides evidence suggesting that long-term ambient particulate air pollution, especially PM_{10}, is associated with asthma prevalence in western European adults. No associations between traffic noise exposures and asthma prevalence were found. Our analyses were conducted using DataSHIELD, a novel 'compute to the data' approach, which could help maximise the scientific potential of established cohorts by pooling personal data robustly yet ethically for research.

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Writing of the paper: YC, PE, ALH, SH

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Air pollution and noise assessment: KdH, DWM, JG.

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Discussion and interpretation of findings: YC, SH, ALH, MB, JG, DWM, KdH, PE

BioSHaRE Coordination Committee: IF, PRB, RS

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Table 1 Information on ever-had asthma and asthma-related medication by each cohort

	Ever-had asthma	**Asthma-related medication**
HUNT3	"*Have you had or do you have any of the following: asthma*?"	"*Have you at any time during the last 5 years taken medicine for asthma, chronic bronchitis, emphysema or COPD*?"
LifeLines	"*Have you ever had asthma*?" "*If you have ever had asthma, was this confirmed by a doctor*?"	Asthma-related medication coded under ATC (Anatomical Therapeutic Chemical) "R03" (drugs for obstructive airway diseases)
UK Biobank	"*Has a doctor ever told you that you have had any of the following conditions*?" *"Asthma?"*	Participants had asthma-related medication if they were currently prescribed an inhaler as ascertained via interviews conducted by research nurses.

Table 2 Prevalence of ever-had asthma and current asthma by each subgroup for each cohort and for the pooled dataset

	Ever-had asthma				**Current-Asthma**			
	HUNT3 (N=50805)	LifeLines (N=93,277)	UK Biobank (N=502,649)	**Pooled**	HUNT3 (N=50805)	LifeLines (N=93,277)	UK Biobank (N=502,649)	**Pooled**
N*	50,783	93,056	500,505	644,344	50,783	93,056	493,157	636,996
Prevalence	5,953 (11.7%)	7,930(8.5%)	57,911 (11.6%)	71,794 (11.1%)	3,900 (7.7%)	3,954 (4.3%)	19,509 (4.0%)	27,363 (4.3%)
Sex								
Men	2,575 (11.2%)	3,178 (8.3%)	24,199 (10.6%)	29,952 (10.4%)	1,604 (7.0%)	1,387 (3.6%)	7,707 (3.4%)	10,698 (3.8%)
Women	3,378 (12.2%)	4,752 (8.7%)	33,712 (12.4%)	41,842 (11.8%)	2,296 (8.3%)	2,567 (4.7%)	11,802 (4.4%)	16,665 (4.7%)
P-value	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00
Age, years								
<50 years	2,563 (12.0%)	5,933 (9.5%)	15,571 (13.3%)	24,127 (12.0%)	1,568 (7.3%)	2,819 (4.5%)	5,150 (4.5%)	9,537 (4.8%)
≥50 years	3,390 (11.5%)	1,937 (6.5%)	42,340 (11.1%)	47,667 (10.8%)	2,332 (8.0%)	1,135 (3.8%)	14,359 (3.8%)	17,826 (4.1%)
P-value	0.11	0.00	0.00	0.00	0.01	0.00	0.00	0.00
BMI, kg/m^2								
<25	1,658 (10.1%)	3,246 (7.7%)	16,961 (10.3%)	21,865 (9.8%)	1,027 (6.2%)	1,497 (3.6%)	5,705 (3.5%)	8,229 (3.7%)
25-30	2,506 (11.2%)	3,039 (8.3%)	23,404 (11.1%)	28,949 (10.7%)	1,600 (7.2%)	1,523 (4.2%)	7,745 (3.7%)	10,868 (4.1%)
≥30	1,734 (15.0%)	1,644 (11.4%)	17,207 (14.1%)	20,585 (13.9%)	1,234 (10.7%)	934 (6.5%)	5,977 (5.0%)	8,145 (5.6%)
P-value	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Smoking								
Never	2,156 (10.2%)	3,599 (9.2%)	31,550 (11.6%)	37,305 (11.2%)	1,291 (6.1%)	1,879 (4.8%)	10,544 (3.9%)	13,714 (4.2%)
Ex	2,098 (13.0%)	2,136 (7.7%)	20,406 (11.8%)	24,640 (11.4%)	1,452 (9.0%)	1,165 (4.2%)	6,832 (4.0%)	9,449 (4.4%)
Current	1,541 (12.6%)	1,606 (8.1%)	5,697 (10.8%)	8,844 (10.4%)	1,052 (8.6%)	629 (3.2%)	2,031 (3.9%)	3,712 (4.4%)
P-value	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00
Education								
Lower	1,447 (12.9%)	248 (11.0%)	9,830 (11.6%)	11,525 (11.7%)	1,039 (9.3%)	145 (6.5%)	3,681 (4.4%)	4,865 (5.0%)
Medium	1,962 (11.7%)	5,225 (8.5%)	11,977 (10.9%)	19,164 (10.2%)	1,247 (7.4%)	2,643 (4.3%)	4,109 (3.8%)	7,999 (4.3%)
Higher	809 (9.9%)	2,265 (8.4%)	35,027 (11.8%)	38,101 (11.5%)	472 (5.8%)	1,075 (4.0%)	11,343 (3.9%)	12,890 (3.9%)
P-value	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

*****Number of participants who had information on asthma. P-value: p-value for chi-square test, significance level at 0.05

Table 3 Associations (Odds ratio, 95%CI) between ambient air pollution (pan-European LUR modelled PM_{10} and NO_2) and asthma prevalence: pooled individual-level analyses from three cohorts

	PM_{10} per 10 µg/m^3				**NO_2 per 10 µg/m^3**			
	N	Ever-had asthma	N	Current asthma	N	Ever-had asthma	N	Current asthma
Model 1	604,414	1.145 (1.112 to 1.179)	597,201	1.063 (1.012 to 1.115)	605,852	1.025 (1.017 to 1.033)	598,627	0.991 (0.978 to 1.004)
Model 2	604,414	1.118 (1.085 to 1.151)	597,201	1.050 (1.000 to 1.102)	605,852	1.019 (1.011 to 1.027)	598,627	0.988 (0.975 to 1.001)
Model 3	566,175	1.128 (1.095 to 1.163)	559,245	1.064 (1.012 to 1.119)	567,485	1.019 (1.011 to 1.028)	560,543	0.988 (0.975 to 1.002)
Model 3 +day-time noise*	562,706	1.131 (1.097 to 1.166)	555,776	1.067 (1.015 to 1.123)	564,014	1.020 (1.011 to 1.028)	557,072	0.988 (0.974 to 1.002)

Model1: adjusted for study; Model 2: adjusted for study, sex, age; Model 3: further adjusted for education, employment status, smoking status and body mass index. *Day-time (07:00-19:00) continuous noise level in dB(A).

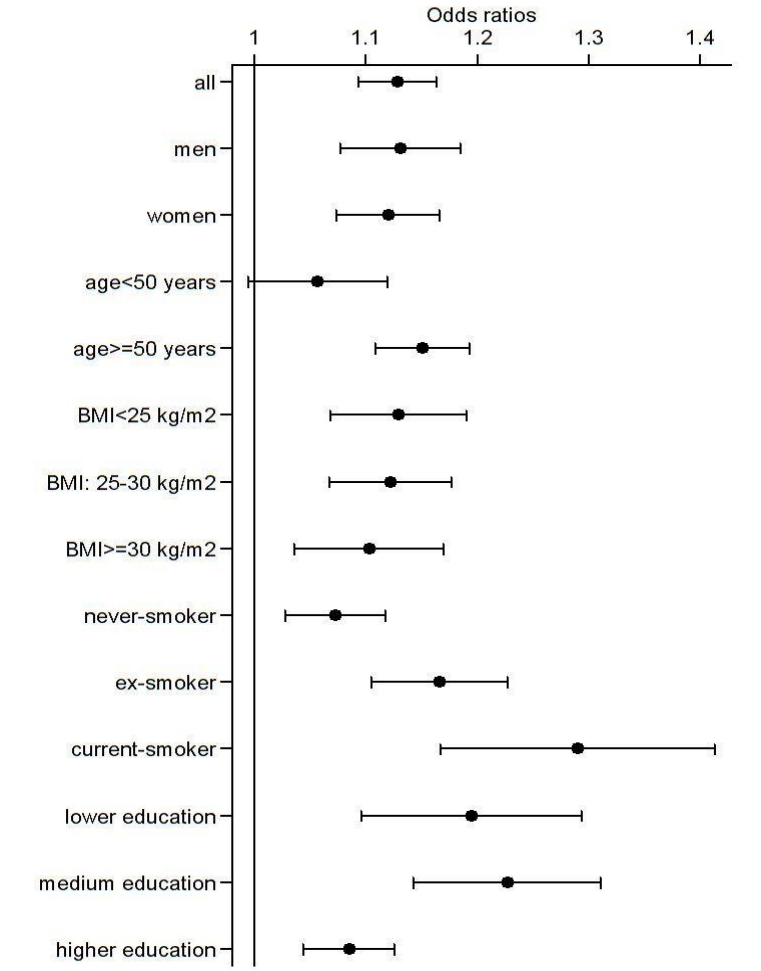
Table 4 Associations (Odds ratio, 95%CI) between categorical day-time noise, night-time noise and asthma prevalence in Model 3: pooled individual-level analyses from three cohorts

		Model 3		**Model 3+PM_{10}**		**Model 3 +NO_2**	
	N#	Ever-had asthma	Current asthma	Ever-had asthma	Current asthma	Ever-had asthma	Current asthma
Day-time noise, dB(A)							
<55*	393,949	1	1	1	1	1	1
55-60	158,700	0.991 (0.972 to 1.011)	0.988 (0.957 to 1.019)	0.988 (0.968 to 1.007)	0.990 (0.959 to 1.021)	0.991 (0.972 to 1.010)	0.994 (0.963 to 1.026)
≥60	63,001	1.013 (0.986 to 1.042)	0.990 (0.947 to 1.036)	1.005 (0.977 to 1.033)	0.985 (0.941 to 1.031)	1.010 (0.982 to 1.038)	0.999 (0.955 to 1.045)
Night-time noise, dB(A)							
<45*	282,647	1	1	1	1	1	1
45-50	254,843	0.991 (0.973 to 1.009)	1.001 (0.973 to 1.031)	0.987 (0.969 to 1.005)	1.002 (0.973 to 1.033)	0.990 (0.972 to 1.008)	1.008 (0.979 to 1.038)
≥50	78,160	1.014 (0.988 to 1.041)	1.010 (0.970 to 1.053)	1.005 (0.979 to 1.032)	1.006 (0.964 to 1.050)	1.010 (0.984 to 1.037)	1.020 (0.977 to 1.065)

*reference category;
#: number of participants in each noise level group included in the main analyses in Model3
Model 3: adjusted for study, sex, age, education, employment status, smoking status and body mass index.
Day-time (07:00-19:00); Night-time (23:00-07:00).

Legend

Figure 1



Associations between pan-European LUR modelled PM_{10} (per 10 µg/m^3) and prevalence of ever-had asthma: subgroup analyses based on Model 3: adjusted for study, age, sex, Body Mass Index (BMI), smoking status, education level and employment status.

Online Supplements

Ambient air pollution, traffic noise and adult asthma prevalence: a BioSHaRE approach

Yutong Cai[1], Wilma L Zijlema[2], Dany Doiron[3], Marta Blangiardo[1], Paul R Burton[4,5], Isabel Fortier[3] , Amadou Gaye[4,6], John Gulliver[1], Kees de Hoogh[1,7,8], Kristian Hveem[9], Stéphane Mbatchou[3], David W Morley[1], Ronald P Stolk[2], Paul Elliott[1], Anna L Hansell[1,10], Susan Hodgson[1]

1: MRC-PHE Centre for Environment and Health, Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK
2: Department of Epidemiology, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands.
3: Research Institute of the McGill University Health Centre and Department of Medicine, McGill University, Montreal, Canada.
4: Data to Knowledge (D2K) Research Group, University of Bristol, Bristol, UK.
5: Public Population Project in Genomics and Society (P^3G), Montreal, Canada.
6: Metabolic, Cardiovascular and Inflammatory Disease Genomics Branch, National Human Genome Research Institute, Bethesda, USA
7: Swiss Tropical and Public Health Institute, Basel, Switzerland
8: University of Basel, Basel, Switzerland.
9: Department of Public Health and General Practice, Norwegian University of Science and Technology, Trondheim, Norway.
10: Directorate of Public Health and Primary Care, Imperial College Healthcare NHS Trust, London, UK.

Corresponding author: Yutong Cai, MRC-PHE Centre for Environment and Health, Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, St Mary's Campus, Norfolk Place, London, W2 1PG, UK.

E-mail: yutong.cai@imperial.ac.uk

Fax: +44 (0) 20 7594 3193

Phone: + 44 (0) 20 7594 2067

Supplement-1

Pan-European LUR model methods

NO_2 and PM_{10} annual estimates for the year 2005-2007 were derived from a pan-European LUR model, which was applied on a 100m grid across Western Europe. Annual mean NO_2 and PM_{10} data during 2005-2007 were obtained from over 1500 monitoring sites across Europe, regulated and reported by EuroAirnet. Only those monitoring sites which captured over 75% of the total hours for NO_2 and days for PM_{10} were included. These monitored air pollution data were served as dependent variables while satellite-based ground-level concentration of NO_2 and $PM_{2.5}$ (both on a 10km grid) and GIS-derived land-use and traffic variables were served as independent variables in the LUR modelling.

- **NO_2**

GIS-derived variables included in the final NO_2 models for 2005, 2006 and 2007 across countries were highly consistent. Table 1 shows the variables included in the final NO_2 model for the year 2007. For variables included in the final models for year 2005 and 2006 as well as the model equations, please refer to the reference paper (Vienneau, D, 2013).

Table 1.1 GIS-variables which were included in the final Satellite-enhanced LUR model for NO_2 (year 2007) for HUNT3, LifeLines and UK Biobank

GIS variable name	Sources	Description
NO_2 (year 2007) Constant		
Minor roads 1500m	Central Road Network: EuroStreets V3.1	Lengths (metre) of all minor roads within 1500 metre
Major roads 100m	Central Road Network: EuroStreets V3.1	Lengths (metre) of all major roads within 100 metre
Semi-natural land 600m	CORINE	Semi-natural land (% of area) within a 600 metre buffer
Minor roads 1500-10000m	Central Road Network: EuroStreets V3.1	Lengths (metre) of all minor roads within 1500-10,000 metre
Total built up land 300m	CORINE	Total built up, % of area (residential, industrial, port, airports, mines, dumps and construction sites)

Satellite-derived surface NO_2 2007	OMI (Ozone Monitoring Instrument)derived from the Aura Satellite	Surface NO_2 concentration: OMI derived NO_2 (ppb) ~10km grid resolution

- **PM_{10}**

Table 2 shows the variables inlcuded in the final PM_{10} model for the year 2007. For model equations, please refer to the reference paper (Vienneau, D, 2013).

Table 1.2 GIS-variables included in the final Satellite-enhanced LUR model for PM_{10} (year 2007) for HUNT3, Lifelines and UK Biobank

GIS variable name	**Sources**	**Description**
PM_{10} (year 2007) Constant		
Minor roads 200-2500m	Central Road Network: EuroStreets V3.1	Lengths (metre) of all minor roads from 200-2500 metre
Minor roads 200m	Central Road Network: EuroStreets V3.1	Lengths (metre) of all minor roads within 200 metre
Major roads*	Central Road Network: EuroStreets V3.1	Lengths (metre) of all major roads
Altitude	SRTM Digital Elevation Database V4.1	Altitude of the geocoded address
Tree canopy 100m	Coarser Global land cover	% of area of tree canopy within 100 metre
Y coordinate	GIS database-ArcGIS10	Y coordinates for 100m cell centroids
Satellite-derived surface $PM_{2.5}$ 2001-2006	Terra Satellite	Surface $PM_{2.5}$ concentration: Terra- derived and humidity-corrected $PM_{2.5}$ aggregated from 2001-2006 ~10km grid resolution

*Buffer not stated in the reference paper

Reference: Vienneau D, de Hoogh K, Bechle MJ, Beelen R, van Donkelaar A, Martin RV, Millet DB, Hoek G, Marshall JD. Western European land use regression incorporating satellite- and ground-based measurements of NO2 and PM10. *Environ Sci Technol* 2013; 47: 13555-13564

Supplement-2

Table 2.1 Harmonised variables used as covariates in the analysis

Harmonised name	Harmonised definition	Unit/Categories
AGE_YRS	Age of the participant in years (continuous) at recruitment	Years
GENDER	Sex of the participant	0: Male; 1:Female
ADM_YRINT	Calendar Year of the interview	calendar year
PM_HEIGHT	Measured height	cm
PM_WEIGHT	Measured weight	kg
PM_BMI_CONTINUOUS	Body Mass Index: calculated using measured or self-reported weight and height (kg/m^2)	kg/m^2
PM_BMI_CATEGORICAL	Body Mass Index calculated using measured or self-reported weight and height (Mass in Kg / (Height in metre)^2) and stratified in 3 categories.	1: less 25 kg/m^2; 2: 25 to 30 kg/m^2; 3: over 30 kg/m^2
SMK_STATUS	Indicator of the participant's current and past smoking status, which includes use of cigarettes, cigars, pipes and other tobacco products.	0: Never-smoker; 1: Ex-smoker; 2: Current-smoker
WORK_STATUS_CURRENT	Indicator of whether the participant is currently in paid employment or is self-employed.	0: No paid employment or not self-employed; 1: Paid employment or self-employed
EDU_HIGHEST_1	Highest level of education completed by the participant. Categories are adapted from the UNESCO Revision of the	0: No education or primary education 1: Secondary education; 2:Vocational/college/university

	International Standard Classification of Education, 2011	

Supplement-3

Table 3.1 Distributions of exposures by cohort and in the pooled data

NO_2, µg/m^3	**N**	**5%**	**10%**	**25%**	**50%**	**75%**	**90%**	**95%**	**Mean(SD)**	**IQR**
HUNT3	50,628	8.2	8.8	10.1	11.9	15.4	18.6	19.5	13.0 (3.9)	5.3
Lifelines	62,212	13.6	14.1	16.6	20.6	25.4	28.9	31.1	21.2 (5.7)	8.8
UK Biobank	495,262	16.7	19.2	23.6	28.9	35	45.1	52.1	30.7 (10.7)	11.4
Pooled	608,102	17	19.2	23.5	28.7	34.9	44.2	50.5	28.3 (9.9)	11.4
PM_{10},µg/m^3	**N**	**5%**	**10%**	**25%**	**50%**	**75%**	**90%**	**95%**	**Mean(SD)**	**IQR**
HUNT3	50,567	9.7	10	10.4	11.2	12	12.6	12.9	11.3 (1.1)	1.6
Lifelines	61,927	21	21.4	22.3	23.6	24.7	25.7	26.5	23.6 (1.7)	2.4
UK Biobank	494,163	17.7	18.7	20.2	21.8	23.6	26	27.5	22.1 (2.9)	3.4
Pooled	606,657	19.3	20.2	21.6	23.3	25	27.2	28.6	21.3 (2.7)	3.4
LDAY, dB(A)	**N**	**5%**	**10%**	**25%**	**50%**	**75%**	**90%**	**95%**	**Mean(SD)**	**IQR**
HUNT3	45,644	39.1	39.5	43.6	47.4	50.3	52.9	54.6	47.0 (4.9)	6.7
Lifelines	74,744	51.3	51.7	52.4	53.9	56.6	60.4	63.9	55.2 (4.0)	4.2
UK Biobank	495,262	51.1	51.4	52.9	54.3	56.4	60.6	66	55.4 (4.3)	3.5
Pooled	615,650	54.7	55.1	56.9	58.8	61.2	65.6	70.8	54.8 (4.3)	4.3
LNIGHT, dB(A)	**N**	**5%**	**10%**	**25%**	**50%**	**75%**	**90%**	**95%**	**Mean(SD)**	**IQR**
HUNT3	45,644	35.1	35.2	37.5	40.2	42.5	44.8	46.4	40.3 (3.7)	5
Lifelines	74,744	42.5	42.8	43.6	45.1	47.8	51.6	55.1	46.4 (4.0)	4.2
UK Biobank	495,262	42.3	42.6	44	45.5	47.5	51.8	57.2	46.6 (4.3)	3.5
Pooled	615,650	45.6	46	47.5	49.3	51.7	56.1	61.2	46.1 (4.2)	4.2

NO_2 AND PM_{10} were estimated based on the pan-European satellite-enhanced LUR model for year 2007 while noise estimates (LDAY and LNIGHT) were for year 2009

Supplement-4

Table 4.1 Spearman correlations between air pollutants and day-time noise (Lday) by cohort

HUNT3 (N=45581)	NO_2	PM_{10}	Lday		
NO_2	-				
PM_{10}	0.80	-			
Lday	**-0.05**	**0.04**	-		
Lifelines (N=62653)	NO_2	PM_{10}	NO_2_ESCAPE	PM_{10}_ESCAPE	Lday
NO_2	-				
PM_{10}	0.78	-			
NO_2_ESCAPE	0.86	0.78	-		
PM_{10}_ESCAPE	0.67	0.54	0.73	-	
Lday	**0.43**	**0.38**	0.56	0.57	-
UK Biobank (N=460,240)	NO_2	PM_{10}	NO_2_ESCAPE	PM_{10}_ESCAPE	Lday
NO_2	-				
PM_{10}	0.77	-			
NO_2_ESCAPE	0.86	0.66	-		
PM_{10}_ESCAPE	0.5	0.42	0.54	-	
Lday	**0.11**	**0.11**	0.23	0.22	-

Correlation between Lday and Lnight (r=0.99) in each cohort.

NO_2: pan-European LUR modelled NO_2 for year 2007

PM_{10}: pan-European LUR modelled PM_{10} for year 2007

NO_2_ESCAPE: ESCAPE LUR modelled NO_2 for year 2010

PM_{10}_ESCAPE: ESCAPE LUR modelled PM_{10} for year 2010

Supplement-5

Table 5.1 Associations (Odds ratio, 95%CI) between traffic noise and asthma prevalence: pooled individual-level analyses from three cohorts

	Day-time noise per 5 dB(A)		Night-time noise per 5 dB(A)	
	Ever-had asthma (n=613,362)	Current asthma (n=606,137)	Ever-had asthma (n=613,362)	Current asthma (n=606,137)
Model 1	1.005 (0.996 to 1.014)	1.000 (0.986 to 1.015)	1.005 (0.996 to 1.015)	1.001 (0.986 to 1.016)
Model 2	1.002 (0.993 to 1.011)	0.999 (0.985 to 1.014)	1.002 (0.993 to 1.012)	1.000 (0.985 to 1.015)
Model 3	0.998 (0.988 to 1.008)	0.994 (0.979 to 1.009)	0.999 (0.989 to 1.009)	0.995 (0.979 to 1.010)
Model 3+NO_2	0.996 (0.987 to 1.006)	0.997 (0.982 to 1.013)	0.997 (0.987 to 1.007)	0.998 (0.983 to 1.014)
Model 3+PM_{10}	0.994 (0.984 to 1.004)	0.992 (0.977 to 1.008)	0.995 (0.985 to 1.005)	0.993 (0.977 to 1.009)

Model1: adjusted for study; Model 2: adjusted for study, sex, age; Model 3: further adjusted for education, employment status, smoking status and body mass index.

Supplement-6

Table 6.1 Subgroup analyses on Model 3: Associations between pan-European LUR NO_2, PM_{10} and ever-asthma prevalence

	NO_2, per 10 µg/m^3		**PM_{10}, per 10 µg/m^3**	
	N	Ever-had asthma	N	Ever-had asthma
Sex				
men	256,230	1.020 (1.007 to 1.033)	255,655	1.131 (1.079 to 1.185)
women	311,255	1.017 (1.006 to 1.029)	310,520	1.120 (1.076 to 1.166)
P (interaction)		0.05		0.18
Age				
<50 years	161,982	0.995 (0.980 to 1.010)	161,636	1.057 (1.000 to 1.119)
>=50 years	405,503	1.028 (1.018 to 1.038)	404,539	1.151 (1.110 to 1.193)
P (interaction)		0.13		0.01
Smoking				
never-smoker	301,380	1.003 (0.991 to 1.014)	300,698	1.073 (1.029 to 1.118)
ex-smoker	195,190	1.032 (1.018 to 1.047)	194,724	1.166 (1.108 to 1.227)
current-smoker	70,915	1.053 (1.028 to 1.078)	70,753	1.290 (1.178 to 1.413)
P (interaction)		0.52		0.00
BMI, kg/m^2				
<25	194,806	1.015 (1.001 to 1.029)	194,412	1.129 (1.071 to 1.190)
25-30	240,402	1.016 (1.002 to 1.029)	239,827	1.122 (1.069 to 1.177)
>=30	132,277	1.021 (1.005 to 1.038)	131,936	1.103 (1.040 to 1.170)
P (interaction)		0.61		0.23
Education				
primary school or less	93,026	1.047 (1.024 to 1.070)	92,814	1.195 (1.106 to 1.294)

secondary school	160,498	1.035 (1.017 to 1.054)	160,085	1.227 (1.147 to 1.311)
post-secondary school or above	313,961	1.009 (0.999 to 1.019)	313,276	1.085 (1.044 to 1.126)
P (interaction)		0.53		0.00

Table 6.2 Subgroup analyses on Model 3: Associations between pan-European LUR NO_2, PM_{10} and current-asthma prevalence

	NO_2, per 10 µg/m^3		**PM_{10}, per 10 µg/m^3**	
	N	Ever-had asthma	N	Ever-had asthma
Sex				
men	252,503	0.992 (0.970 to 1.013)	251,933	1.087 (1.004 to 1.177)
women	308,040	0.984 (0.967 to 1.002)	307,312	1.044 (0.979 to 1.114)
P (interaction)		0.53		0.27
Age				
<50 years	159,102	0.961 (0.937 to 0.986)	158,758	1.016 (0.927 to 1.114)
>=50 years	401,441	0.996 (0.980 to 1.013)	400,487	1.071 (1.009 to 1.137)
P (interaction)		0.50		0.00
Smoking				
never-smoker	297,210	0.956 (0.937 to 0.973)	296,537	0.962 (0.898 to 1.031)
ex-smoker	193,028	1.023 (1.000 to 1.046)	192,575	1.175 (1.080 to 1.278)
current-smoker	70,295	1.022 (0.983 to 1.062)	70,133	1.231 (1.064 to 1.424)
P (interaction)		0.34		0.00
BMI, kg/m^2				
<25	192,194	0.981 (0.958 to 1.005)	191,806	1.036 (0.948 to 1.131)
25-30	237,402	0.972 (0.951 to 0.994)	236,830	1.045 (0.964 to 1.133)

>=30	130,947	1.010 (0.985 to 1.036)	130,609	1.096 (0.998 to 1.203)
P (interaction)		0.33		0.24
Education				
primary school or less	92,476	1.018 (0.983 to 1.055)	92,265	1.118 (0.988 to 1.267)
secondary school	159,132	1.028 (0.998 to 1.058)	158,722	1.205 (1.083 to 1.341)
post-secondary school or above	308,935	0.968 (0.951 to 0.985)	308258	1.004 (0.943 to 1.071)
P (interaction)		0.30		0.00

Supplement-7

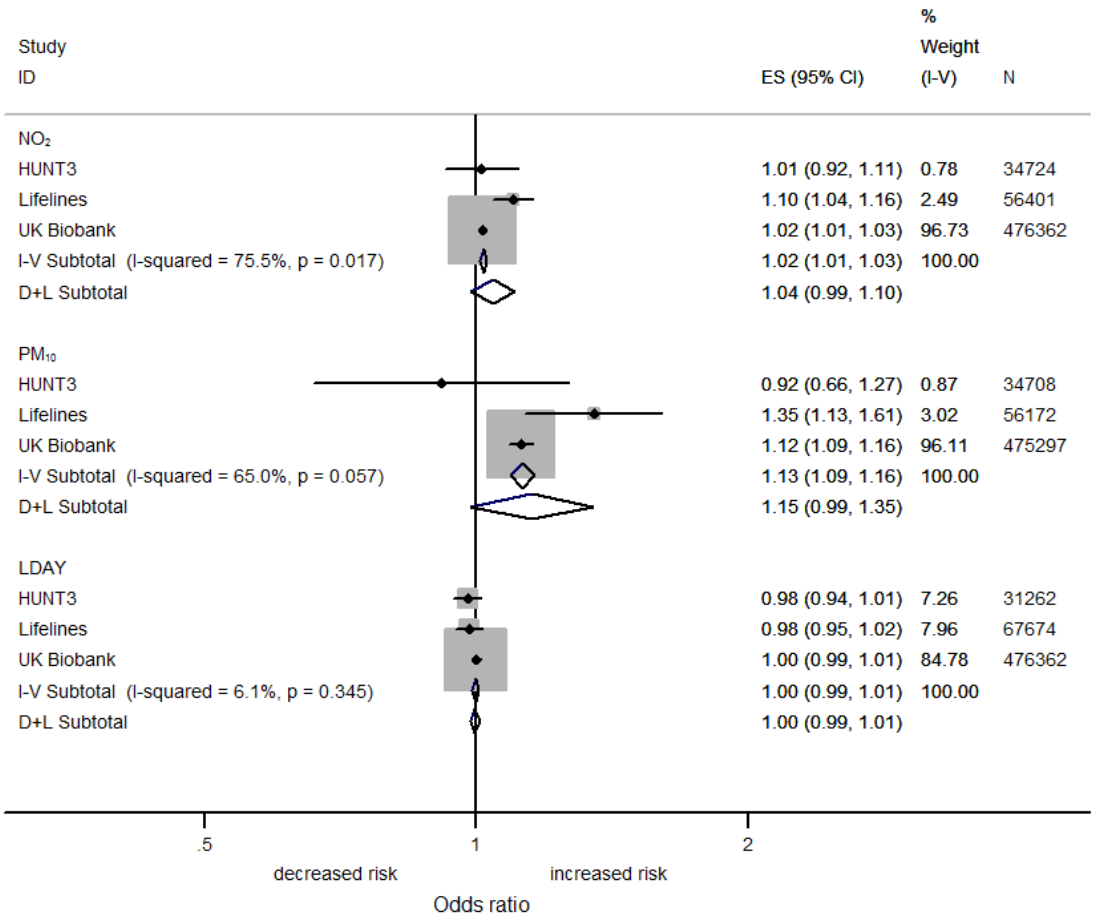
Table 7.1 Sensitivity analyses: restricting analyses to those living at the same address for more than 10 years, adjusting for study, age, sex, BMI, smoking, education, employment status.

NO_2, per 10 µg/m^3				**PM_{10}, per 10 µg/m^3**			
N	Ever-had asthma	N	Current asthma	N	Ever-had asthma	N	Current asthma
376,191	1.026 (1.015 to 1.037)	371,969	0.988 (0.971 to 1.005)	375,387	1.163 (1.120 to 1.208)	371174	1.074 (1.009 to 1.143)
Day-time noise, per 5 dB(A)				**Night-time noise, per 5 dB(A)**			
N	Ever-had asthma	N	Current asthma	N	Ever-had asthma	N	Current asthma
379,794	1.005 (0.993 to 1.018)	375,572	1.007 (0.988 to 1.026)	379,794	1.006 (0.993 to 1.019)	375,572	1.009 (0.988 to 1.028)

Table 7.2 Sensitivity analyses: Using ESCAPE-LUR modelled NO_2 and PM_{10} for LifeLines and UK Biobank and pan-European LUR modelled NO_2 and PM_{10} for HUNT3 in the pooled analyses, adjusting for study, age, sex, BMI, smoking, education, employment status.

NO_2, per 10 µg/m^3				**PM_{10}, per 10 µg/m^3**			
N	Ever-had asthma	N	Current asthma	N	Ever-had asthma	N	Current asthma
567,485	1.023 (1.011 to 1.035)	560,543	1.019 (1.000 to 1.038)	534,347	1.071 (1.021 to 1.123)	527,733	1.114 (1.030 to 1.204)

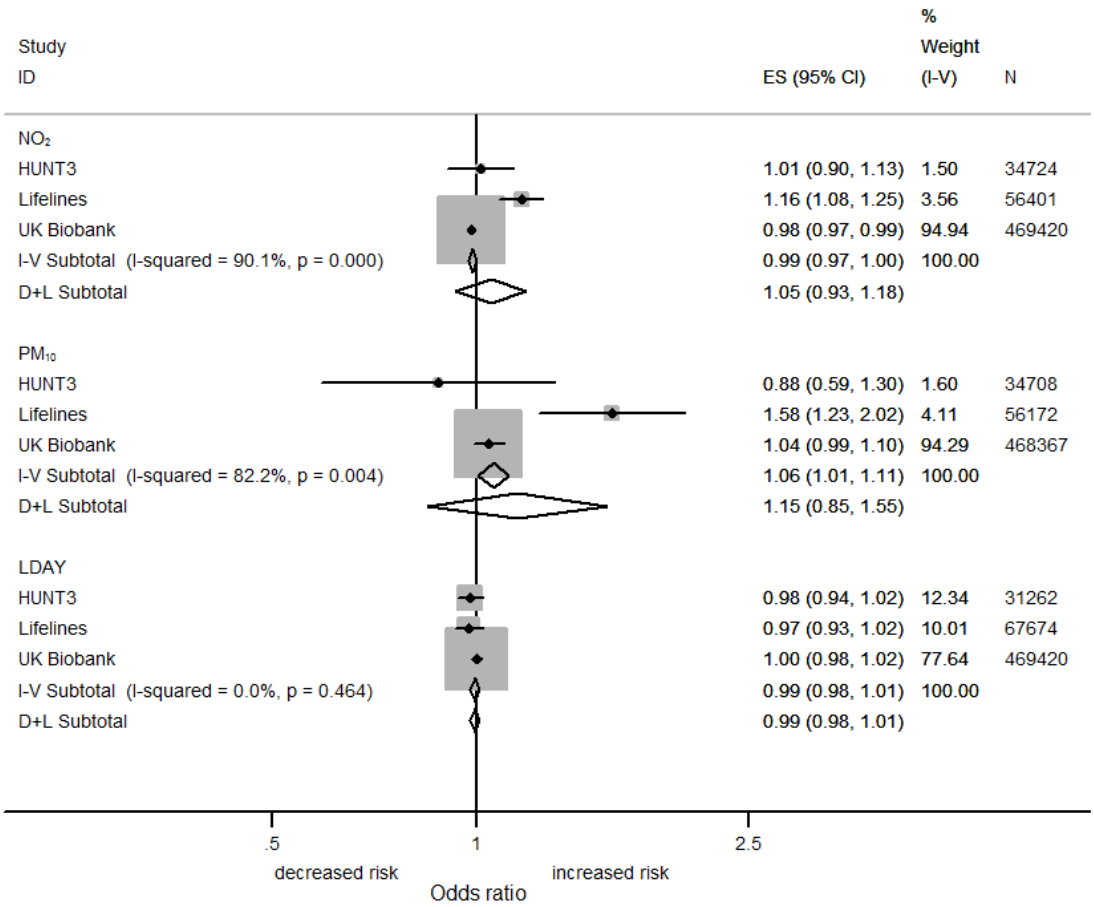
Supplementary Figure 1



Supplementary Figure 1 Associations between pan-European LUR NO_2 (per 10 µg/m^3), PM_{10} (per 10 µg/m^3), daytime noise (LDAY, per 5 dB(A)) and **ever-had asthma prevalence**: study-specific meta-analyses based on model 3 (adjusted for, age, sex, BMI, smoking status, education level and employment status).

ES: Effect estimate
I-squared: variation in estimated effect attributable to heterogeneity
I-V: inverse-variance weighted (fixed effect model)
D+L: DerSimonian and Laird (random effect model)

Supplementary Figure 2



Supplementary Figure 2 Associations between pan-European LUR NO_2 (per 10 µg/m^3), PM_{10} (per 10 µg/m^3), day-time noise (LDAY, per 5 dB(A)) and **current-asthma prevalence**: study-specific meta-analyses based on model 3 (adjusted for age, sex, BMI, smoking status, education level and employment status).

ES: Effect estimate
I-squared: variation in estimated effect attributable to heterogeneity
I-V: inverse-variance weighted (fixed effect model)
D+L: DerSimonian and Laird (random effect model)