



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

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ABSTRACT We investigated the 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 and UK Biobank).

Residential exposures to ambient air pollution (particulate matter with aerodynamic diameter $\leq 10 \mu\text{m}$ (PM₁₀) and nitrogen dioxide (NO₂)) were estimated by a pan-European Land Use Regression model for 2007. Traffic noise for 2009 was modelled at home addresses 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 the effects of each exposure on lifetime and current asthma prevalence.

PM₁₀ or NO₂ higher by $10 \mu\text{g}\cdot\text{m}^{-3}$ was associated with 12.8% (95% CI 9.5–16.3%) and 1.9% (95% CI 1.1–2.8%) higher lifetime asthma prevalence, respectively, independent of confounders. Effects were larger in those aged ≥ 50 years, ever-smokers and less educated. Noise exposure was not significantly associated with asthma prevalence.

This study suggests that long-term ambient PM₁₀ 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.



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Long-term ambient PM₁₀ exposure is associated with asthma prevalence in three European adult cohorts <http://ow.ly/En4b3049S7X>

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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 had 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 hyperresponsiveness, airway remodelling, oxidative stress and immune responses [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, although 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 for 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 females only [20]. An analysis of six European cohorts reported positive but nonsignificant 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 the best of our knowledge, there are no studies investigating whether individual exposure to traffic noise, generally seen as an environmental stressor and mostly coexisting 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 asthma prevalence, 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 (UK) [27].

Methods

Study populations

Three cohort studies participating in BioSHaRE (Biobank Standardisation and Harmonisation for Research Excellence in the European Union) 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 multidisciplinary prospective population-based cohort study

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examining in a three-generation design the health and health-related behaviours of 167 729 individuals 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

A pan-European Land Use Regression (LUR) model at a resolution of 100×100 m was used to assign annual air pollution estimates at the home address for each participant from the three cohorts [28]. Annual mean nitrogen dioxide (NO₂) and particulate matter with aerodynamic diameter ≤10 µm (PM₁₀) concentration data during 2005–2007 were obtained from over 1500 monitoring sites across Europe; means for 2007 were used in the analyses as 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 NO₂ and days for PM₁₀ were included. The pan-European LUR model was developed using 80% of these monitored air pollution data, satellite-based ground-level concentrations of NO₂ and particulate matter with aerodynamic diameter ≤2.5 µm (PM_{2.5}) on a 10-km grid, and land use and traffic variables obtained from a geographical information system (online supplementary material S1). Model performance (explained variance (R²) between modelled and measured exposures) for PM₁₀ and NO₂ 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 NO₂ and PM₁₀ concentrations for 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]. R² for PM₁₀ and NO₂ ESCAPE-LUR models was 60–88% and 81–87%, respectively, as 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 the address level for participants in each study. In brief, noise sound level was estimated for all roads within 500 m of the 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 2009 and land cover data were for 2006.

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

Harmonisation of covariates and outcomes

Age, sex, body mass index (BMI), education level (primary school or less, secondary school, or post-secondary school or above), paid employment (yes or no), smoking (current smoker, ex-smoker or never-smoker) and years at baseline address were harmonised retrospectively across cohorts (online supplementary material S2) following a validated protocol [33].

Lifetime asthma prevalence (“ever-had asthma”) was harmonised based on the self-reported answers (yes or no) in the 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.

First, 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-had asthma 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 and ≥60 dB(A)) and night-time noise (<45, 45–50 and ≥50 dB(A)) were used.

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 Anatomical Therapeutic Chemical classification 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 by interviews conducted by research nurses

COPD: chronic obstructive pulmonary disease.

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

Sensitivity analyses were conducted based on Model 3: 1) restricting analyses to those living at the same address for ≥ 10 years, 2) using ESCAPE-LUR air pollution metrics (PM₁₀ and NO₂) for Lifelines and UK Biobank instead of the pan-European LUR metrics, and 3) 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: 1) sex, 2) age <50 or ≥ 50 years, 3) smoking status, 4) BMI <25, 25–30 or ≥ 30 kg·m⁻² and 5) education level.

Individual-level fixed-effect pooled analyses were performed in DataSHIELD version 4.1.2 (www.datashield.ac.uk). Study-level meta-analyses were performed in Stata version 12.1 (www.stata.com).

Results

Overall, prevalence of ever-had asthma was 11.1% and prevalence of current asthma was 4.3% (table 2). Prevalence of ever-had asthma or current asthma was higher among females, those aged <50 years, with a BMI >25 kg·m⁻² and less educated.

Mean \pm SD PM₁₀ ranged from 11 \pm 1.1 (HUNT3) to 24 \pm 1.7 (Lifelines) $\mu\text{g}\cdot\text{m}^{-3}$, while NO₂ ranged from 13 \pm 3.9 (HUNT3) to 31 \pm 10.7 (UK Biobank) $\mu\text{g}\cdot\text{m}^{-3}$ (online supplementary material S3). Pooling data for PM₁₀ and NO₂ from 606 657 and 608 102 participants, respectively, median (interquartile range (IQR)) PM₁₀ was 23 (4.3) $\mu\text{g}\cdot\text{m}^{-3}$ and NO₂ was 29 (11.4) $\mu\text{g}\cdot\text{m}^{-3}$ (online supplementary material S3). In the pooled data, median (IQR) day-time noise and night-time noise estimates were 59 (4.3) and 49 (4.2) dB(A), respectively.

Spearman correlations between PM₁₀ and day-time noise ranged from $r=0.04$ (HUNT3) to 0.38 (Lifelines), and between NO₂ and day-time noise ranged from $r=-0.05$ (HUNT3) to 0.43 (Lifelines) (online supplementary material S4). Correlation between NO₂ and PM₁₀ was $r=0.8$, and between day-time and night-time noise $r=0.99$ in each of the three cohorts.

In all models, statistically significant associations were found for PM₁₀ and NO₂ in relation to prevalence of ever-had asthma (table 3). In the fully adjusted Model 3, PM₁₀ higher by 10 $\mu\text{g}\cdot\text{m}^{-3}$ was associated with 12.8% (95% CI 9.5–16.3%) higher prevalence of ever-had asthma and 6.4% (95% CI 1.2–11.9%) higher prevalence of current asthma. NO₂ higher by 10 $\mu\text{g}\cdot\text{m}^{-3}$ was associated with 1.9% (95% CI 1.1–2.8%) higher prevalence of ever-had asthma, but not current asthma prevalence. Further adjustments for day-time noise did not change the associations.

No associations between categorical or continuous noise exposures and asthma prevalence were seen (table 4 and online supplementary material S5).

Significant effect modifications (p-value for interaction <0.01) by age, smoking and education were observed between PM₁₀ 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 (online supplementary material S6). No significant effect modifications were seen between NO₂ and ever-had or current asthma prevalence by any of the studied variables (online supplementary material S6).

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	Lifelines	UK Biobank	Pooled	HUNT3	Lifelines	UK Biobank	Pooled
Subjects								
Total	50805	93277	502649	646731	50805	93277	502649	646731
With asthma information	50783	93056	500505	644344	50783	93056	493157	636996
Prevalence	5953 (11.7)	7930 (8.5)	57911 (11.6)	71794 (11.1)	3900 (7.7)	3954 (4.3)	19509 (4.0)	27363 (4.3)
Sex								
Male	2575 (11.2)	3178 (8.3)	24199 (10.6)	29952 (10.4)	1604 (7.0)	1387 (3.6)	7707 (3.4)	10698 (3.8)
Female	3378 (12.2)	4752 (8.7)	33712 (12.4)	41842 (11.8)	2296 (8.3)	2567 (4.7)	11802 (4.4)	16665 (4.7)
p-value [#]	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00
Age years								
<50	2563 (12.0)	5933 (9.5)	15571 (13.3)	24127 (12.0)	1568 (7.3)	2819 (4.5)	5150 (4.5)	9537 (4.8)
≥50	3390 (11.5)	1937 (6.5)	42340 (11.1)	47667 (10.8)	2332 (8.0)	1135 (3.8)	14359 (3.8)	17826 (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	1658 (10.1)	3246 (7.7)	16961 (10.3)	21865 (9.8)	1027 (6.2)	1497 (3.6)	5705 (3.5)	8229 (3.7)
25–30	2506 (11.2)	3039 (8.3)	23404 (11.1)	28949 (10.7)	1600 (7.2)	1523 (4.2)	7745 (3.7)	10868 (4.1)
≥30	1734 (15.0)	1644 (11.4)	17207 (14.1)	20585 (13.9)	1234 (10.7)	934 (6.5)	5977 (5.0)	8145 (5.6)
p-value [#]	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Smoking								
Never-smoker	2156 (10.2)	3599 (9.2)	31550 (11.6)	37305 (11.2)	1291 (6.1)	1879 (4.8)	10544 (3.9)	13714 (4.2)
Ex-smoker	2098 (13.0)	2136 (7.7)	20406 (11.8)	24640 (11.4)	1452 (9.0)	1165 (4.2)	6832 (4.0)	9449 (4.4)
Current smoker	1541 (12.6)	1606 (8.1)	5697 (10.8)	8844 (10.4)	1052 (8.6)	629 (3.2)	2031 (3.9)	3712 (4.4)
p-value [#]	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00
Education								
Lower	1447 (12.9)	248 (11.0)	9830 (11.6)	11525 (11.7)	1039 (9.3)	145 (6.5)	3681 (4.4)	4865 (5.0)
Medium	1962 (11.7)	5225 (8.5)	11977 (10.9)	19164 (10.2)	1247 (7.4)	2643 (4.3)	4109 (3.8)	7999 (4.3)
Higher	809 (9.9)	2265 (8.4)	35027 (11.8)	38101 (11.5)	472 (5.8)	1075 (4.0)	11343 (3.9)	12890 (3.9)
p-value [#]	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Data are presented as n or n (%), unless otherwise stated. BMI: body mass index. [#]: Chi-squared test, significance level at 0.05.

In sensitivity analyses, for participants living at the same address for ≥10 years, associations between PM₁₀, NO₂ and ever-had asthma became slightly stronger (online supplementary material S7). Using ESCAPE-LUR modelled PM₁₀ and NO₂ 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 PM₁₀ and NO₂ (online supplementary material S7).

Associations between NO₂, PM₁₀, day-time noise and ever-had asthma prevalence in Model 3 assessed *via* meta-analysis across cohorts (supplementary figure S1) were similar to those from the individual-level

TABLE 3 Associations between ambient air pollution (pan-European Land Use Regression modelled particulate matter with aerodynamic diameter ≤10 µm (PM₁₀) and nitrogen dioxide (NO₂)) and asthma prevalence: pooled individual-level analyses from three cohorts

	PM ₁₀ per 10 µg·m ⁻³				NO ₂ per 10 µg·m ⁻³			
	Ever-had asthma		Current asthma		Ever-had asthma		Current asthma	
	Subjects	OR (95% CI)	Subjects	OR (95% CI)	Subjects	OR (95% CI)	Subjects	OR (95% CI)
Model 1	604414	1.145 (1.112–1.179)	597201	1.063 (1.012–1.115)	605852	1.025 (1.017–1.033)	598627	0.991 (0.978–1.004)
Model 2	604414	1.118 (1.085–1.151)	597201	1.050 (1.000–1.102)	605852	1.019 (1.011–1.027)	598627	0.988 (0.975–1.001)
Model 3	566175	1.128 (1.095–1.163)	559245	1.064 (1.012–1.119)	567485	1.019 (1.011–1.028)	560543	0.988 (0.975–1.002)
Model 3 + day-time noise[#]	562706	1.131 (1.097–1.166)	555776	1.067 (1.015–1.123)	564014	1.020 (1.011–1.028)	557072	0.988 (0.974–1.002)

Data are presented as n, unless otherwise stated. OR: odds ratio. Model 1: 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 h) continuous noise level in dB(A).

TABLE 4 Associations between categorical day-time noise (07:00–19:00 h), night-time noise (23:00–07:00 h) and asthma prevalence in Model 3: pooled individual-level analyses from three cohorts

	Subjects [#]	Model 3		Model 3+PM ₁₀		Model 3+NO ₂	
		Ever-had asthma OR (95% CI)	Current asthma OR (95% CI)	Ever-had asthma OR (95% CI)	Current asthma OR (95% CI)	Ever-had asthma OR (95% CI)	Current asthma OR (95% CI)
Day-time noise dB(A)							
<55 (reference)	393 949	1	1	1	1	1	1
55–60	158 700	0.991 (0.972–1.011)	0.988 (0.957–1.019)	0.988 (0.968–1.007)	0.990 (0.959–1.021)	0.991 (0.972–1.010)	0.994 (0.963–1.026)
≥60	63 001	1.013 (0.986–1.042)	0.990 (0.947–1.036)	1.005 (0.977–1.033)	0.985 (0.941–1.031)	1.010 (0.982–1.038)	0.999 (0.955–1.045)
Night-time noise dB(A)							
<45 (reference)	282 647	1	1	1	1	1	1
45–50	254 843	0.991 (0.973–1.009)	1.001 (0.973–1.031)	0.987 (0.969–1.005)	1.002 (0.973–1.033)	0.990 (0.972–1.008)	1.008 (0.979–1.038)
≥50	78 160	1.014 (0.988–1.041)	1.010 (0.970–1.053)	1.005 (0.979–1.032)	1.006 (0.964–1.050)	1.010 (0.984–1.037)	1.020 (0.977–1.065)

Data are presented as n, unless otherwise stated. PM₁₀: particulate matter with aerodynamic diameter ≤10 µm; NO₂: nitrogen dioxide; OR: odds ratio. Model 3: adjusted for study, sex, age, education, employment status, smoking status and body mass index. #: participants in each noise level group included in the main analyses in Model 3.

analysis. However, study-specific associations between NO₂, PM₁₀ and current asthma prevalence were heterogeneous (p<0.05) (supplementary figure S2), and none of the pooled study estimates in the meta-analyses were 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 PM₁₀ air pollution and both ever-asthma and current asthma

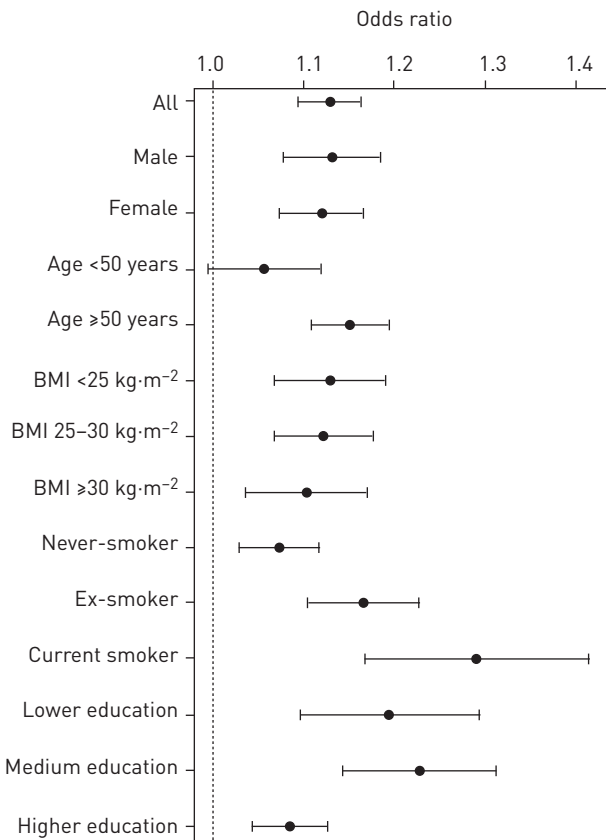


FIGURE 1 Associations between pan-European Land Use Regression modelled particulate matter with aerodynamic diameter ≤10 µm (PM₁₀) (per 10 µg·m⁻³) and prevalence of ever-had asthma: subgroup analyses based on Model 3 (adjusted for study, age, sex, body mass index (BMI), smoking status, education level and employment status). Bars show 95% confidence intervals.

prevalence. NO₂ was significantly associated with ever-asthma but not current asthma. We found no association between traffic noise exposures and ever-had 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 the 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 NO₂ or NO_x (nitrogen oxides). Neither of these two studies examined NO₂ or NO_x effects on a continuous scale. A study of young adult Italians (aged 20–44 years) found that each 18.3 µg·m⁻³ increase of NO₂ was nonsignificantly associated with increased asthma prevalence (OR 1.13, 95% CI 0.98–1.32) [10]. A national study among 12 177 Australian females reported a null association between 3-year mean annual NO₂ and asthma prevalence [15].

In the SAPALDIA study, long-term exposure to PM₁₀ was nonsignificantly associated with increased prevalence of current asthma (OR 1.19, 95% CI 0.83–1.70) in current smokers [14]. Recently, a study of 29 459 Canadian females reported that each 10 µg·m⁻³ increase of PM_{2.5} was significantly associated with increased ever-diagnosed asthma prevalence (OR 1.14, 95% CI 1.01–1.29). Association was stronger among smokers (OR 1.58, 95% CI 1.46–1.70) compared with nonsmokers (OR 1.16, 95% CI 0.96–1.41) [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], although most of the studies included in that review were conducted in children (only two out of nine NO₂ estimates and one out of nine PM₁₀ estimates were for adults).

In contrast to most previous findings, our study suggests that both long-term PM₁₀ and NO₂ 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 the home address was modelled at a fine spatial scale (100 m grid) in our study, contributing to the observed robust associations.

Although 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 US females, a borderline significant association between PM_{2.5} and incident asthma was observed (OR 1.20, 95% CI 0.99–1.46) [20]. However, this was not seen in the ESCAPE study (OR 1.04, 95% CI 0.88–1.23) [21]. Two studies reported significant associations between NO₂ and incident asthma with similar effect sizes [17, 18]. In the ESCAPE study, NO₂ was not associated with asthma incidence (OR 1.10, 95% CI 0.99–1.21) [21].

Effect estimates per 10 µg·m⁻³ were much larger for PM₁₀ than for NO₂. There are still debates on whether NO₂ on its own causes health effects or merely is a marker of traffic-related, particularly near-road, air pollution [36]. Unlike NO₂, particulate matter 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 PM₁₀ mass [29]. PM_{2.5}, with various substances attached to it, could travel and deposit deep into the respiratory tract. These substances, including transition metals and immunogenic substances, could either induce direct airway inflammation or lead to oxidative stress [5], *i.e.* two biological pathways linking to asthma. This may explain in part the relatively larger effect estimates seen for PM₁₀.

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 in the link between air pollution and asthma remains unclear. Some previous studies have reported stronger associations among never- and former-smoker [38] while 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 of 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].

Asthma sufferers 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 subjects with asthma (16 years) and without asthma (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-had 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.

Conclusions

In conclusion, this large cross-sectional study provides evidence suggesting that long-term ambient particulate air pollution, especially PM₁₀, 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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