Air and noise pollution exposure in early life and mental health from adolescence to young adulthood

Joanne B. Newbury PhD,[1*] Jon Heron PhD,[1] James B. Kirkbride PhD,[3] Helen L. Fisher PhD,[2,4] Ioannis Bakolis PhD,[5,6] Andy Boyd BA,[1,7] Richard Thomas MSc,[1,7] Stanley Zammit PhD[1,8]

[1] Population Health Sciences, Bristol Medical School, University of Bristol, UK

[2] Social, Genetic, and Developmental Psychiatry Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK

[3] PsyLife Group, Division of Psychiatry, UCL, London, UK

[4] ESRC Centre for Society and Mental Health, King's College London, London, UK

[5] Department of Biostatistics and Health Informatics, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK

[6] Centre for Implementation Science, Health Service and Population Research Department, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK

[7] UK Longitudinal Linkage Collaboration, University of Bristol, Bristol, UK

[8] MRC Centre for Neuropsychiatric Genetics and Genomics, School of Medicine, Cardiff University, Cardiff, UK

*Corresponding author: Dr J. B. Newbury, Population Health Sciences, Bristol Medical School, Oakfield House, Bristol, BS8 2BN, UK. E-mail: joanne.newbury@bristol.ac.uk.

Telephone: 07853959811.

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Key Points

Question: Is exposure to air and noise pollution in pregnancy, childhood, and adolescence associated with the development of psychotic experiences, depression, and anxiety between ages 13 to 24?

Findings: In this longitudinal birth cohort followed into adulthood (original sample: N>14,000; sample with mental health data: N>9,000), higher $PM_{2.5}$ exposure in pregnancy and childhood was associated with psychotic experiences and depression, and higher noise pollution exposure in childhood and adolescence was associated with anxiety.

Meaning: The findings build on evidence associating air and noise pollution with mental health, by highlighting a role of early-life pollution exposure in youth mental health problems.

Abstract

Importance: Growing evidence associates air pollution exposure with various psychiatric disorders. However, the importance of early-life (e.g., prenatal) exposure to youth mental health is poorly understood. Moreover, few longitudinal studies have investigated the association of noise pollution with youth mental health.

Objectives: To examine the longitudinal associations of air and noise pollution exposure in pregnancy, childhood, and adolescence with psychotic experiences, depression, and anxiety from ages 13-24. We hypothesized that participants exposed to higher air and noise pollution would subsequently have more psychotic experiences, depression, and/or anxiety.

Design: The Avon Longitudinal Study of Parents and Children (ALSPAC) is an ongoing longitudinal birth cohort founded in the 1990s.

Setting: A population-based study in Southwest England, United Kingdom.

Participants: The cohort includes over 14,000 babies with due dates between 1 April 1991 and 31 December 1992; subsequently followed into adulthood.

Exposures: A novel linkage (completed in 2020) was performed to link high-resolution ($100m^2$) estimates of nitrogen dioxide (NO_2), fine particulate matter <2.5 microns ($PM_{2.5}$), and noise pollution to home addresses from pregnancy to age 12.

Main outcomes and measures: Psychotic experiences, depression, and anxiety were measured at ages 13, 18, and 24. Logistic regression models controlled for key individual-, family-, and area-level confounders.

Results: The study included 9,065 participants who had any mental health data, of whom 51.4% (N=4,657) were female, 95.8% (N=7,616) were of White ethnicity, and 19.5% (N=1,544), 11.4% (N=947), and 9.7% (N=811) reported psychotic experiences, depression,

and anxiety, respectively. After covariate adjustment, interquartile range increases ($0.72\mu g/m^3$) in $PM_{2.5}$ during pregnancy and childhood were associated with 11% and 9% elevated odds for psychotic experiences (pregnancy: adjusted [a]OR=1.11, 95% CI=1.04-1.19, p=0.002; childhood: aOR=1.09, 95% CI=1.00-1.10, p=0.04). Pregnancy $PM_{2.5}$ exposure was also associated with depression (aOR=1.10, 95% CI=1.02-1.18, p=0.01). Conversely, higher noise pollution exposure in childhood (aOR=1.19, 95% CI=1.03-1.38, p=0.02) and adolescence (aOR=1.22, 95% CI=1.02-1.45, p=0.03) was associated with elevated odds for anxiety.

Conclusions and relevance: In this longitudinal cohort study, early-life air and noise pollution exposure were prospectively associated with three common mental health problems from adolescence to young adulthood. There was a degree of specificity in terms of pollutant-timing-outcome associations.

Introduction

Childhood, adolescence, and early adulthood are critical periods for the development of psychiatric disorders: worldwide, nearly two-thirds of those affected become unwell by age 25.[1] Identifying early-life risk factors is a crucial research challenge in order to develop preventative interventions and improve lifelong mental health trajectories.

Growing evidence suggests that air pollution exposure may contribute to the onset of psychiatric problems, including mood, affective, and psychotic disorders.[2-6] Air pollution comprises toxic gases and particulate matter (i.e., organic and inorganic solid and liquid aerosols), of mostly anthropogenic origin.[7] Understanding the potential impact of air pollution on mental health is increasingly crucial, given the human and societal cost of poor mental health,[8] given the global shift towards urban living,[9,10] and given the backdrop of emissions-induced climate change.[11]

Air pollution could negatively affect mental health via numerous pathways, including by compromising the blood-brain barrier, promoting neuroinflammation and oxidative stress, and directly entering the brain and damaging tissue therein.[12,13] However, key research gaps remain. First, the relative importance of early-life exposure, including prenatal exposure, is uncertain. Babies and children are thought to be especially vulnerable to air pollution,[14,15] but longitudinal, high-resolution pollution data spanning the early years are scarce. Second, relatively few studies have examined the association of air pollution with youth mental health problems,[16] despite youth being a critical period for intervention. Third, few longitudinal studies have investigated the role of noise pollution in mental health,[17] despite the correlation between noise and air pollution.[18] Finally, studies have often used crude pollution data and lacked adequate controls for potential confounders..

We aimed to advance understanding on this topic by capitalizing on a novel linkage between high-resolution outdoor air and noise pollution data and a cohort of over 14,000 babies born in Southwest England in 1991-1993 and followed into adulthood. We examined the association of air and noise pollution exposure from pregnancy to age 12 with mental health problems from ages 13-24. Based on previous evidence, we focussed on psychotic experiences (e.g., subclinical hallucinations and delusions), depression, and anxiety. These problems are common[1,19-21] and increasing[22] among youth, and strongly predict future psychopathology,[23,24] making them useful and important targets. We hypothesized that participants exposed to higher air and noise pollution would subsequently experience worse mental health.

Methods

Participants

The Avon Longitudinal Study of Parents and Children (ALSPAC) is a UK birth cohort,[25-28] described further in the Supplementary Materials. Briefly, pregnant women residing in and around the City of Bristol (population ~714,000 in 2024) in Southwest England with due dates between 01/04/91 and 31/12/92 were approached to take part in the study. The initial number of pregnancies enrolled was 14,551, resulting in 13,988 children alive at 1 year of age. At age 7, the initial sample was bolstered with additional eligible cases, resulting in 14,901 babies alive at 1 year of age. The catchment area has a mix of urban, suburban, and rural environments.[29] The study website contains details of all the data and a fully searchable data dictionary and variable search tool: http://www.bristol.ac.uk/alspac/researchers/our-data/. Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Informed consent for the use of data

collected via questionnaires and clinics was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time. The present study is reported according to STROBE guidelines.[30]

Psychotic experiences

Psychotic experiences were measured at ages 13, 18, and 24, using a semi-structured interview[31] which consisted of 12 core items about hallucinations, delusions, and thought interference, rated against the Schedule for Clinical Assessment in Neuropsychiatry version 2.0 (SCAN 2.0).[32] Consistent with previous ALSPAC studies,[33,34] psychotic experiences were defined such that 0=none and 1=suspected/definite. The reporting period at each phase was since the participant's 12th birthday. At ages 13, 18, and 24, 13.6% (N=926), 9.2% (N=432), and 12.6% (N=491), reported psychotic experiences, respectively. We summed psychotic experiences across timepoints and dichotomized the variable for analyses, such that participants were scored as 1=suspected/definite psychotic experiences if they reported psychotic experiences at any age.

Depression and anxiety

Depression and anxiety were measured at age 13 via parent-completed Development and Well-being Assessments (DAWBA).[35] Responses were classified into probabilistic bands according to DSM-IV criteria for major depressive disorder (MDD) and generalized anxiety disorder (GAD), and dichotomized for analysis (bands 0-2=0, bands 3-5=1). At ages 18 and 24, depression and anxiety were measured using the Clinical Interview Schedule Revised

147 (CIS-R),[36] a self-administered computerized interview that gave ICD-10 diagnoses of
148 moderate-severe depression and GAD. The reporting period at each phase was the past
149 month, although a 6-month reporting period was used for anxiety at age 13. At ages 13, 18,
150 and 24, 5.6% (N=386), 7.9% (N=359), and 7.7% (N=304) reported depression; and 3.6%
151 (N=254), 5.8% (N=262), and 9.8% (N=386) reported anxiety, respectively. We summed
152 depression and anxiety across timepoints and dichotomized the variables for analysis, such
153 that participants were scored as 1=depression/anxiety if they had depression/anxiety at any
154 age.

155

156 *Air pollution*

157 Air pollutants included nitrogen dioxide (NO_2) and fine particulate matter with a diameter of
158 <2.5 microns ($PM_{2.5}$). Both pollutants have well-established health impacts[10] and more recent
159 associations with psychiatric disorders.[5] These air pollutants were estimated as part of the
160 LifeCycle project[37] using the Effects of Low-Level Air Pollution: A Study in Europe
161 (ELAPSE) model, which is described elsewhere and further in the Supplementary
162 Materials.[38] Briefly, the ELAPSE model is a hybrid land-use regression model for Europe
163 which derived concentrations of NO_2 and $PM_{2.5}$ in 2010. The model produces annualized
164 estimates at $100m^2$ resolution, explaining 59% and 71% of measured spatial variability for
165 NO_2 and $PM_{2.5}$, respectively.[38] Estimates were linked to residential geocodes from pregnancy
166 to age 12 for participants who had lived in the original ALSPAC catchment area[29] up to age
167 12 and provided permission for geospatial linkage. Linkage was completed in 2020.

168

169 *Noise pollution*

Residential noise pollution exposure was also estimated as part of the LifeCycle project,[37] based on the UK Government's Department for Environment, Food & Rural Affairs (DEFRA) 2006 road traffic noise map. Data represent an annualized average of day and night noise pollution, categorized according to low-medium (<55 decibels: the European Environment Agency's threshold[39]), high (55-60 decibels), and very high noise (>60 decibels). eFigure 1 in the Supplementary Materials shows the correlation between noise pollution, NO_2, and $PM_{2.5}$ across timepoints.

Covariates

Potential confounders were informed by the literature and formally selected using a directed acyclic graph (DAG: eFigure 2). We considered individual-/family-level covariates that could be associated with mental health problems and with downward mobility into more polluted neighborhoods. These included ethnicity, family psychiatric history, maternal social class, maternal education, and housing tenure. Area-level covariates included population density, neighborhood deprivation, social fragmentation, and greenspace, and were time-varying, corresponding to the timing of pollution exposure. Covariates are described fully in the Supplementary Materials and briefly below.

Individual-/family-level covariates. Ethnicity of the child was reported by mothers during pregnancy. Family psychiatric was reported by mothers and fathers during pregnancy and defined as the presence of any psychiatric problem affecting the mother, father, or any biological grandparent. Maternal social class was reported by mothers during pregnancy based on occupation. Maternal education was reported by mothers when babies were around 8 months. Home ownership was reported by mothers during pregnancy.

Neighborhood-level covariates. Population density was derived from 1991/2001 census data.[34] Area-level deprivation was based on the 2000 Index of Multiple Deprivation.[40] Social fragmentation was based on a z-scored sum of census data on residential mobility, marital status, single person households, and home ownership.[34] Greenspace was assessed based on the Normalized Difference Vegetation Index.[41]

Statistical analysis

Analyses were performed in Stata v18.0. Code can be found at https://github.com/JBNewbury/bris-phs-pollution-mental-health.git. The characteristics of the sample with versus without mental health data were described according to percentages, means, and standard deviations. Group differences were explored using Chi-square and t-tests. To explore the importance of different exposure periods, we derived exposure estimates for three developmental stages: a) pregnancy, b) childhood (birth to age 9), and c) adolescence (ages 10-12),[42] which were calculated using mean exposure values for NO_2, $PM_{2.5}$, and noise pollution during these age windows. Given that NO_2 and $PM_{2.5}$ had very different absolute ranges, scores were standardized by dividing by the interquartile range (IQR). To aid comparison between air and noise pollution, we treated noise pollution as a continuous variable, assuming a normal distribution underlying the categorical variable. Results treating noise as categorical are reported in the Supplementary Materials.

For main analyses, logistic regression was used to examine the associations of NO_2, $PM_{2.5}$, and noise pollution in pregnancy, childhood, and adolescence with the mental health outcomes. We ran an unadjusted model (Model 1), then adjusted for individual-/family-level covariates (Model 2), and then additionally adjusted for area-level covariates (Model 3). To better understand the independent associations from different exposure periods, we then

adjusted childhood and adolescent exposure for previous exposure (Model 4). However, given that the high correlation between pollutants over time (eFigure 1) could introduce multi-collinearity, we interpret Model 4 with caution. To estimate residual confounding, we also calculated e-values[43] for Models 3 and 4, which indicate the strength of association that an unmeasured confounder would require to nullify associations. All models accounted for potential hierarchy in the data by clustering around the Lower Layer Super Output Area (LSOA's contain ~1,500 residents on average) using the "cluster" command, which provides robust standard errors adjusted for within cluster correlated data.[44] All analyses were conducted following multiple imputation by chained equations,[45] described in the Supplementary Materials.

We conducted three sensitivity analyses. First, we analysed NO_2, $PM_{2.5}$, and noise pollution simultaneously, to control each for the others and address potential co-pollutant confounding. Second, we restricted analyses to participants who did not move house from pregnancy to age 12 (29.8%), to keep pollution levels as consistent over time as possible. Third, we repeated main analyses for those with complete data.

Results

Sample characteristics

The study included 9,065 participants who had any mental health data, of whom 51.4% (N=4,657) were female, 95.8% (N=7,616) were ethnically White, and 19.5% (N=1,544), 11.4% (N=947), and 9.7% (N=811) reported psychotic experiences, depression, and anxiety, respectively (Table 1). Over half the sample (60.8%; N=4,793) had a family psychiatric history; 21.8% (N=1,583) had mothers who worked in manual occupations; 15.7% (N=1,274) had mothers with degrees; and 81.6% (N=6,670) lived in homes owned by their parent(s).

Mean population density was 34 persons per hectare (SD=20.7) and 23.7% (N=1,754) lived in the most deprived neighborhoods. The sample with and without mental health data differed for most variables: those with data were more likely to be female, White, have a family psychiatric history, and have more advantaged characteristics across the other variables. These differences should be borne in mind when interpreting the results.

Air and noise pollution exposure

Figure 1 shows estimated levels of NO_2 and $PM_{2.5}$ for the sample, alongside the World Health Organization's (WHO) 2021 exposure thresholds.[46] Mean levels of NO_2 and $PM_{2.5}$ decreased slightly over time. However, average exposure at age 12 remained above the WHO's thresholds for both pollutants. Additionally, over two-thirds of participants were exposed to high/very high noise pollution,[39] which changed little over time (Figure 1).

Associations of air and noise pollution with mental health

Associations of NO_2, $PM_{2.5}$, and noise pollution with psychotic experiences, depression, and anxiety are shown in Table 2, which shows unadjusted and adjusted results alongside e-values; and Figure 2, which is fully adjusted.

Before covariate adjustment, IQR (4.47μg/m^3) increases in NO_2 during pregnancy were associated with 8% elevated odds for psychotic experiences (OR=1.08, 95% CI=1.00-1.17, p=0.04). However, this was attenuated to the null after adjusting for area-level covariates. In contrast, following covariate adjustment, IQR (0.72μg/m^3**)** increases in $PM_{2.5}$ during pregnancy and childhood were associated with 11% and 9% elevated odds for psychotic experiences, respectively (pregnancy: adjusted [a]OR=1.11, 95% CI=1.04-1.19,

p=0.002); childhood: aOR=1.09, 95% CI=1.00-1.19, p=0.04); although childhood exposure was attenuated to the null after adjusting for pregnancy exposure. There was little evidence of an association between noise pollution and psychotic experiences.

Following covariate adjustment, IQR increases in $PM_{2.5}$ during pregnancy were associated with 10% elevated odds for depression (aOR=1.10, 95% CI=1.02-1.18, p=0.01). There was little evidence of associations between NO_2, noise pollution, and depression.

Before covariate adjustment, IQR increases in NO_2 in pregnancy and childhood were associated with 14% (OR=1.14, 95% CI=1.04-1.26, p=0.006) and 15% (OR=1.15, 95% CI=1.03-1.27, p=0.009) elevated odds for anxiety, respectively, but associations were attenuated to the null after adjusting for area-level covariates. There was little evidence associating $PM_{2.5}$ with anxiety. In contrast, participants exposed to higher noise pollution in childhood and adolescence had 19% and 22% elevated odds for anxiety, respectively (childhood: aOR=1.19, 95% CI=1.03-1.38, p=0.02; adolescence: aOR=1.22, 95% CI=1.02-1.45, p=0.03); although adolescent exposure was attenuated to the null after controlling for pregnancy and childhood exposure. eTable 1 displays results when noise pollution was treated as categorical. This highlighted several dose-response associations, though no difference in model fit compared to the main results.

E-values

In eTables 2 and 3 in the Supplementary Materials, we take as examples the adjusted associations of a) pregnancy $PM_{2.5}$ with psychotic experiences and b) adolescent noise pollution with anxiety; and compare the e-values to the associations from included covariates. E-values were a) 1.46 (lower confidence limit [LCL]=1.24), and b) 1.74 (LCL=1.16), respectively. These were larger in magnitude than the associations of the covariates with the

exposures and outcomes, indicating that an unmeasured confounder would require a relatively strong confounding influence to nullify associations.

Sensitivity analyses

Results from sensitivity analyses are presented in eTables 4-6 and are discussed in the Supplementary Materials. Briefly, point estimates were generally similar after adjusting pollutants for each other; similar (and often higher) for those who did not move house; and similar for complete cases: though confidence intervals were often less precise.

Discussion

In this longitudinal birth cohort study followed up over ~25 years, participants exposed to higher $PM_{2.5}$ during pregnancy and childhood subsequently experienced more psychotic experiences and (for pregnancy exposure only) depression. In contrast, participants exposed to higher noise pollution in childhood and adolescence subsequently experienced more anxiety. These associations were not explained by numerous potential individual-, family-, and area-level confounders.

Our findings suggest an important role of early-life (including prenatal) exposure to air pollution in the development of youth mental health problems. Early-life exposure could be detrimental to mental health given the extensive brain development and epigenetic processes that occur *in utero* and during infancy.[13,15,47,48] Air pollution exposure could also lead to restricted foetal growth[49] and preterm birth,[50] which are both risk factors for psychopathology. Notably, the point estimate for pregnancy $PM_{2.5}$ and depression (10% elevated odds for every 0.72μg/m^3 increase) was considerably greater than a previous meta-

analytic estimate based on exposure in adulthood (10% elevated odds for every 10μg/m^3 increase).[2] These contrasting findings are in keeping with a particularly detrimental role of early-life air pollution exposure. However, our findings could also have arisen if early-life exposure data provide a proxy for cumulative exposure over a longer period, given that families often settle when children are young.

For noise pollution, evidence was strongest for childhood and adolescent exposure. Childhood and adolescent noise pollution exposure could increase anxiety by increasing stress and disrupting sleep; with high noise potentially leading to chronic physiological arousal and disruption to endocrinology.[51] Noise pollution could also impact cognition,[52] which could increase anxiety by impacting concentration during school years. It was interesting that noise pollution was associated with anxiety but not with psychotic experiences or depression. However, our measure of noise pollution estimated only decibels (i.e., intensity) from road sources. Other qualities of noise, such as pitch, could be relevant to mental health.

Study Limitations

We acknowledge several limitations. First, the causality of the findings is uncertain given that data were observational. Despite comprehensive covariate adjustment, residual confounding is inevitable given imperfect selection and measurement of covariates. The relatively large e-values strengthened our confidence in the findings, but future studies should consider other methods to address confounding, such as quasi-experimental designs. Second, ALSPAC families are more affluent and less diverse than the UK population.[53] The extent that our findings generalize to other populations and locations is uncertain. Our findings likely generalize to cities and surrounds in other high-income countries; but may be less

generalizable to urban settings in lower-income countries, which can have more extreme pollution concentrations (https://www.iqair.com/world-air-quality-ranking). Third, modelled pollution data are subject to various sources of measurement error,[38] particularly Berkson-like error whereby estimates are smoother (less variable) than reality, leading to less precise, though unbiased, exposure-outcome estimates.[54,55] For instance, the 100m^2 resolution, though an improvement over many previous studies, would have masked hyperlocal variation (e.g., differences between participants living on adjacent streets), to which NO_2 is especially prone due to its short decay function.[56] Additionally, the model estimated residential exposure, which would have masked variation due to behaviour and time spent away from home. Finer-resolution data, including personal exposure estimates, would enable more precise exposure-outcome estimates, particularly for NO_2. Fourth, we could not apply life-course models to investigate sensitive periods versus cumulative effects, as there was limited within-person variation in exposure over time. Larger datasets (e.g., national registries) and quasi-experimental designs would be required to further tease out this question.

Conclusions

Our study provides novel evidence that early-life exposure to particulate matter is prospectively associated with the development of psychotic experiences and depression in youth. Ours is among only a handful of longitudinal studies investigating the association between noise pollution and mental health, demonstrating an association with anxiety. Our findings suggest a degree of specificity in terms of pollutant-timing-outcome pathways. The opportunity for intervention is potentially enormous. However, though our study addressed various biases affecting observational research, the causality of the findings remains uncertain. Nevertheless, previous post-mortem[57,58] and recent quasi-experimental[3,59] studies

support a causal role of air pollution in mental health problems. Thus, if we assume causality from this triangulating evidence, interventions to reduce population-level exposure (e.g., low emissions zones in cities) could potentially improve youth mental health. There is now a pressing need for further longitudinal research using more precise measures of air and noise pollution; and for replication using quasi-experimental designs.

Corresponding authors: Joanne B. Newbury, PhD (joanne.newbury@bristol.ac.uk), Population Health Sciences, Bristol Medical School, University of Bristol, Oakfield House, Oakfield Grove, Bristol, BS8 2BN, United Kingdom.

Author contributions:

Dr Newbury had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Dr Newbury conceived the study, conducted analyses, and wrote the first draft of the manuscript. Prof Zammit supervised the analyses and write-up and oversaw data collection and assessment scoring in the ALSPAC study. Dr Heron, Dr Bakolis, Prof Kirkbride, and Prof Fisher advised on statistical analyses. Prof Kirkbride oversaw construction of the area-level variables. Mr Boyd and Mr Thomas oversaw the linkage of air and noise pollution data with the ALSPAC study. All authors contributed to the revisions of the manuscript, interpretation of the findings, and approval of the final manuscript.

Conflict of Interest Disclosures:

The authors declare no conflict of interests.

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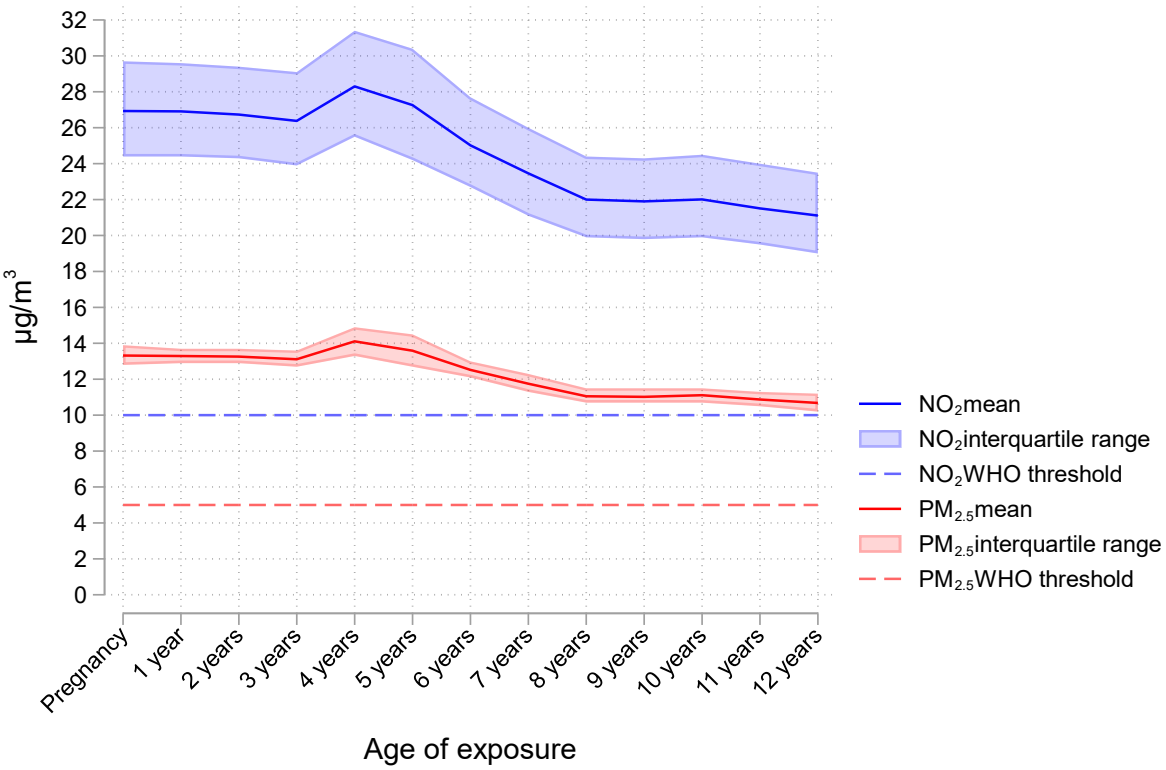
Table 1. Sample characteristics for participants with and without mental health data

Sample characteristics	**Sample with mental health data**		**Sample without mental health data**		X^2 / T	**P-value**
	N/M	%/SD	N/M	%/SD		
Psychotic experiences (ages 13-24)						
No	6,579	83.2	NA	-	-	-
Yes	1,544	19.5	NA	-	-	-
Depression (ages 13-24)						
No	7,397	88.7	NA	-	-	-
Yes	947	11.4	NA	-	-	-
Anxiety (ages 13-24)						
No	7,587	90.3	NA	-	-	-
Yes	811	9.7	NA	-	-	-
Sex						
Male	4,394	48.6	3,295	55.0		
Female	4,657	51.4	2,691	45.0	60.9	<0.001
Ethnicity						
All other ethnicities [a]	338	4.3	275	6.6		
White	7,616	95.8	3,906	93.4	31.0	<0.001
Family psychiatric history						
No	3,093	39.2	2,569	80.81		
Yes	4,793	60.8	610	19.19	1600.0	<0.001
Maternal social class [b]						
1 – Professional	295	4.1	73	1.9		
2 – Managerial and technical	2,302	31.8	849	22.0		
3 – Skilled non-manual	3,068	42.3	1,656	42.9		
4 – Skilled manual	264	3.6	188	4.9		
5 – Partly skilled	1,096	15.1	867	22.4		
6 – Unskilled	223	3.1	230	6.0	258.3	<0.001
Maternal education						
1 – Degree	1,274	15.7	334	7.6		
2 – A level	2,087	25.8	706	16.1		
3 – O level	2,850	35.2	1,472	33.6		
4 – Vocational	730	9.0	499	11.4		
5 – CSE	1,152	14.2	1,373	31.3	693.1	<0.001
House tenure						
Mortgaged/owned	6,670	81.6	3,200	60.3		
Rented	1,506	18.4	2,109	39.7	744.6	<0.001
Population density [c]	33.50	20.7	35.16	19.1	4.3	<0.001
Area-level deprivation						
1 – least deprived	1,419	29.4	596	19.7		
2	830	17.2	456	15.0		
3	785	16.3	515	17.0		
4	864	17.9	529	17.4		
5 – most deprived	933	19.3	937	30.9	179.9	<0.001
Social fragmentation [d]	-0.28	2.9	-0.11	2.8	2.9	0.003
Greenspace [e]	0.41	0.1	0.42	0.1	-3.4	<0.001
NO_2	26.93	4.2	27.08	4.0	2.0	0.047
$PM_{2.5}$	13.32	0.9	13.38	0.8	3.9	<0.001
Noise pollution						
Low (<55 decibels)	1,594	30.5	1,010	30.1		
Medium (55-60 decibels)	2,442	46.8	1,531	45.6		
High (>60 decibels)	1,185	22.7	817	24.3	3.1	0.213

Note: [a] due to small numbers within most ethnicities, all ethnicities other than White were grouped. These ethnicities included Bangladeshi, Black African, Black Caribbean, Chinese, Indian, Pakistani, and other ethnicities; [b] based on maternal occupation; [c] unit is persons per hectare; [d] sum of z-scored census information on population turnover, unmarried people, single person households, and privately rented households; [e] unit is the Normalized Difference Vegetation Index: range -1 to 1; CSE=certificate of secondary education; M=mean; NO_2=nitrogen dioxide; $PM_{2.5}$=particulate matter <2.5microns, unit is micrograms per metre squared; SD=standard deviation; T=t-test statistic; X^2=Chi-square.

a


µg/m3
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
Pregnancy
1 year
2 years
3 years
4 years
5 years
6 years
7 years
8 years
9 years
10 years
11 years
12 years
Age of exposure
NO2mean
NO2interquartile range
NO2WHO threshold
PM2.5mean
PM2.5interquartile range
PM2.5WHO threshold

b

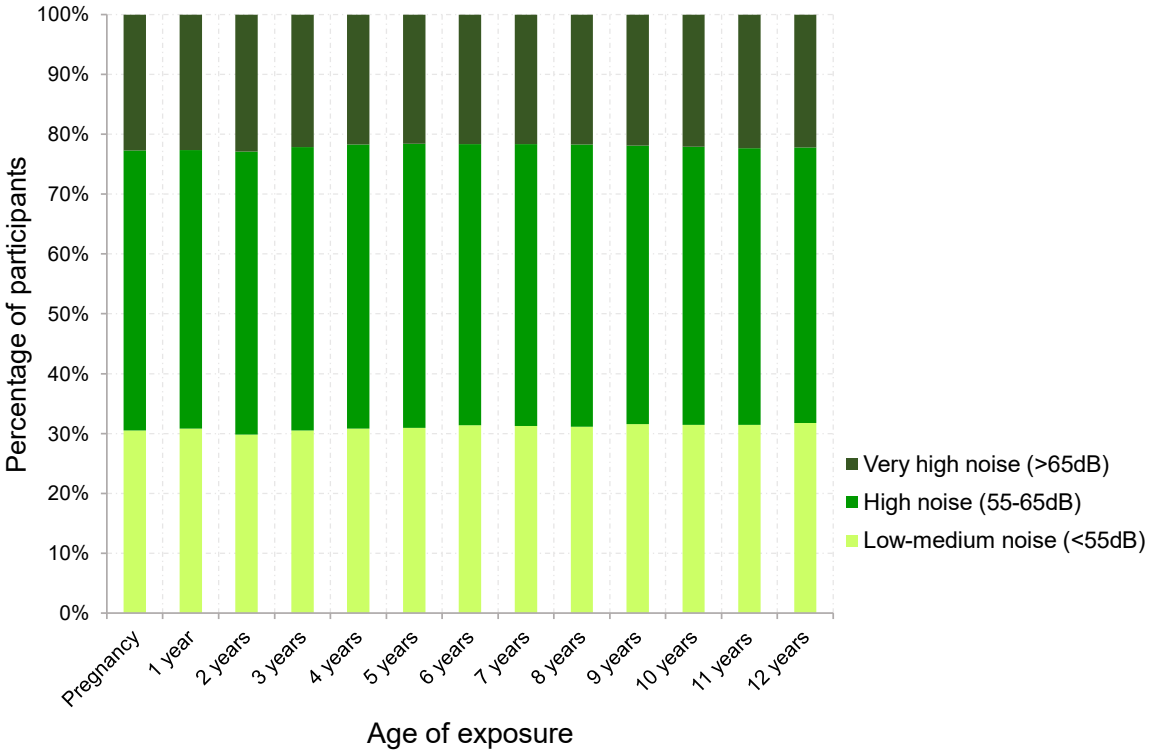

Percentage of participants
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Pregnancy
1 year
2 years
3 years
4 years
5 years
6 years
7 years
8 years
9 years
10 years
11 years
12 years
Age of exposure
Very high noise (>65dB)
High noise (55-65dB)
Low-medium noise (<55dB)

Figure 1. Air and noise pollution exposure in the ALSPAC study sample from pregnancy to age 12

Note: a=air pollution levels; b=noise pollution levels; dB=decibels; NO_2=nitrogen dioxide; $PM_{2.5}$=particulate matter under 2.5 microns; WHO=World Health Organization; $\mu g/m^3$=micrograms per cubic meter

Table 2. Associations of early-life air and noise pollution exposure with youth mental health problems

Outcome	**Pregnancy exposure**			**Childhood exposure**			**Adolescence exposure**		
Pollutant	OR (95% CI)	P-value	E-value (LCL)	OR (95% CI)	P-value	E-value (LCL)	OR (95% CI)	P-value	E-value (LCL)
Model									
Psychotic experiences									
NO_2									
Model 1	1.08 (1.00-1.17)	0.04		1.05 (0.97-1.14)	0.24		1.06 (0.96-1.17)	0.28	
Model 2	1.08 (1.00-1.17)	0.05		1.04 (0.96-1.13)	0.32		1.04 (0.95-1.16)	0.39	
Model 3	1.06 (0.96-1.17)	0.28	1.31 (1.00)	0.97 (0.88-1.07)	0.55	1.21 (1.00)	0.97 (0.85-1.10)	0.58	1.21 (1.00)
Model 4	NA	-	-	0.89 (0.77-1.03)	0.11	1.50 (1.00)	1.02 (0.81-1.28)	0.89	1.16 (1.00)
$PM_{2.5}$									
Model 1	1.11 (1.04-1.18)	0.001		1.11 (1.03-1.19)	0.009		1.09 (0.99-1.21)	0.07	
Model 2	1.11 (1.04-1.18)	0.001		1.10 (1.02-1.19)	0.01		1.09 (0.98-1.20)	0.10	
Model 3	1.11 (1.04-1.19)	0.002	1.46 (1.24)	1.09 (1.00-1.19)	0.04	1.40 (1.00)	1.06 (0.96-1.18)	0.25	1.31 (1.00)
Model 4	NA	-	-	1.00 (0.90-1.12)	0.93	1.00 (1.00)	1.02 (0.84-1.24)	0.82	1.16 (1.00)
Noise									
Model 1	1.06 (0.94-1.20)	0.36		1.04 (0.92-1.17)	0.57		1.01 (0.89-1.15)	0.85	
Model 2	1.06 (0.93-1.20)	0.38		1.03 (0.91-1.17)	0.62		1.00 (0.87-1.14)	0.98	
Model 3	1.04 (0.92-1.18)	0.50	1.24 (1.00)	1.01 (0.89-1.14)	0.88	1.11 (1.00)	1.00 (0.87-1.15)	0.99	1.00 (1.00)
Model 4	NA	-	-	0.95 (0.79-1.15)	0.62	1.29 (1.00)	0.99 (0.81-1.21)	0.90	1.11 (1.00)
Depression									
NO_2									
Model 1	1.06 (0.97-1.15)	0.19		1.09 (0.99-1.20)	0.09		1.09 (0.98-1.22)	0.12	
Model 2	1.06 (0.97-1.15)	0.19		1.08 (0.98-1.19)	0.12		1.08 (0.97-1.20)	0.18	
Model 3	1.10 (0.98-1.24)	0.10	1.43 (1.00)	1.11 (0.98-1.26)	0.09	1.46 (1.00)	1.08 (0.94-1.23)	0.28	1.37 (1.00)
Model 4	NA	-	-	1.09 (0.89-1.33)	0.42	1.40 (1.00)	0.96 (0.72-1.28)	0.77	1.25 (1.00)
$PM_{2.5}$									
Model 1	1.07 (1.00-1.15)	0.04		1.06 (0.97-1.14)	0.18		1.02 (0.93-1.12)	0.66	
Model 2	1.07 (1.00-1.15)	0.04		1.05 (0.97-1.14)	0.25		1.01 (0.92-1.11)	0.82	
Model 3	1.10 (1.02-1.18)	0.01	1.43 (1.16)	1.07 (0.98-1.17)	0.15	1.34 (1.00)	0.99 (0.90-1.10)	0.90	1.11 (1.00)
Model 4	NA	-	-	0.97 (0.86-1.11)	0.69	1.21 (1.00)	0.89 (0.71-1.13)	0.36	1.50 (1.00)

Noise									
Model 1	1.03 (0.90-1.19)	0.66		1.13 (0.97-1.31)	0.12		1.08 (0.92-1.26)	0.35	
Model 2	1.03 (0.90-1.18)	0.69		1.12 (0.96-1.30)	0.15		1.07 (0.91-1.25)	0.41	
Model 3	1.02 (0.89-1.18)	0.74	1.16 (1.00)	1.12 (0.95-1.31)	0.17	1.49 (1.00)	1.05 (0.89-1.23)	0.58	1.28 (1.00)
Model 4	NA	-	-	1.20 (0.97-1.49)	0.09	1.69 (1.00)	1.06 (0.80-1.40)	0.68	1.31 (1.00)
Anxiety									
NO_2									
Model 1	1.14 (1.04-1.26)	0.006		1.15 (1.03-1.27)	0.009		1.05 (0.93-1.19)	0.40	
Model 2	1.14 (1.04-1.26)	0.007		1.14 (1.03-1.27)	0.01		1.05 (0.93-1.19)	0.40	
Model 3	1.08 (0.95-1.23)	0.27	1.37 (1.00)	1.10 (0.97-1.25)	0.15	1.43 (1.00)	0.97 (0.83-1.13)	0.73	1.21 (1.00)
Model 4	NA	-	-	0.97 (0.79-1.21)	0.81	1.21 (1.00)	0.77 (0.57-1.03)	0.08	1.92 (1.00)
$PM_{2.5}$									
Model 1	1.04 (0.97-1.12)	0.22		1.04 (0.96-1.13)	0.34		1.00 (0.91-1.10)	0.98	
Model 2	1.05 (0.98-1.12)	0.19		1.05 (0.96-1.14)	0.30		1.01 (0.91-1.11)	0.90	
Model 3	1.02 (0.95-1.11)	0.55	1.16 (1.00)	1.03 (0.93-1.13)	0.58	1.21 (1.00)	0.98 (0.88-1.09)	0.69	1.16 (1.00)
Model 4	NA	-	-	0.97 (0.84-1.12)	0.67	1.21 (1.00)	0.95 (0.75-1.20)	0.65	1.29 (1.00)
Noise									
Model 1	1.01 (0.88-1.16)	0.86		1.13 (0.98-1.31)	0.09		1.17 (0.98-1.39)	0.08	
Model 2	1.03 (0.90-1.18)	0.67		1.15 (1.00-1.33)	0.06		1.19 (1.00-1.43)	0.05	
Model 3	1.05 (0.91-1.21)	0.51	1.28 (1.00)	1.19 (1.03-1.38)	0.02	1.67 (1.21)	1.22 (1.02-1.45)	0.03	1.74 (1.16)
Model 4	NA	-	-	1.32 (1.04-1.68)	0.02	1.97 (1.24)	0.94 (0.68-1.29)	0.71	1.32 (1.00)

Note: CI=confidence interval; LCL=lower confidence limit. E-values do not include upper confidence limits or p-values; NO_2=nitrogen dioxide; OR=odds ratio; $PM_{2.5}$=particulate matter under 2.5 microns; Model 1-unadjusted; Model 2-adjusted for individual- and family-level covariates; Model 3-additionally adjusted for area-level covariates; Model 4-additional adjusted for earlier exposure. We interpret Model 4 with caution given that high correlations across timepoints could lead to multi-collinearity; Sample sizes of imputed datasets range from N=2,962 (adolescence noise pollution and psychotic experiences) to N=6,180 (pregnancy air pollution and anxiety).

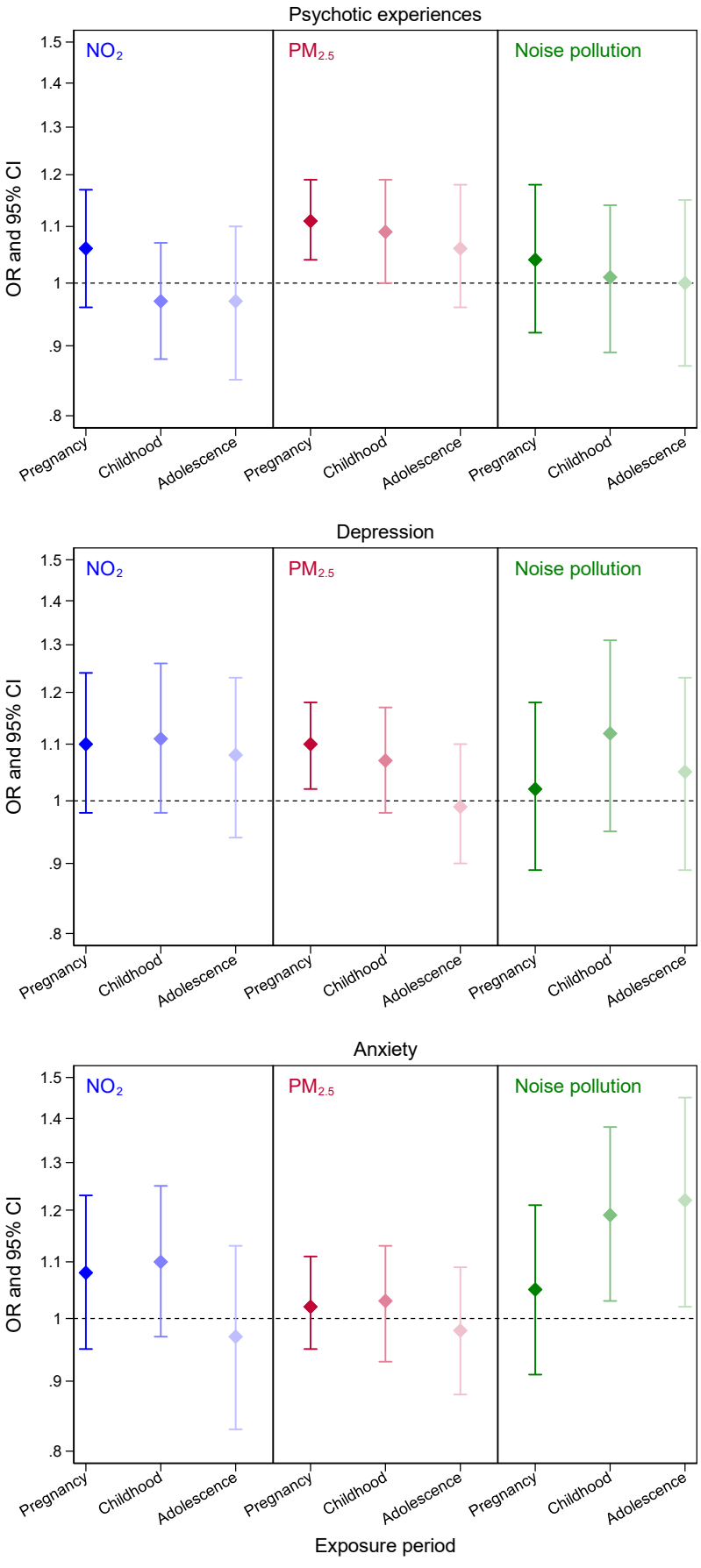

Psychotic experiences
Depression
Anxiety
NO2
PM2.5
Noise pollution
OR and 95% CI
1.5
1.4
1.3
1.2
1.1
1
.9
.8
Pregnancy
Childhood
Adolescence
Exposure period

Figure 2. Adjusted associations of early-life air and noise pollution exposure with youth mental health problems

Note: CI=confidence intervals; NO_2=nitrogen dioxide; OR=odds ratio; $PM_{2.5}$=particulate matter <2.5 microns; Results are from Model 3, which is adjusted for ethnicity, family psychiatric history, maternal social class, maternal education, house tenure, population density, neighborhood deprivation, social fragmentation, and greenspace; Sample sizes of imputed datasets range from N=2,952 (adolescence noise pollution and psychotic experiences) to N=6,154 (pregnancy air pollution and anxiety).

References

1. Solmi M, Radua J, Olivola M, et al. Age at onset of mental disorders worldwide: large-scale meta-analysis of 192 epidemiological studies. *Mol Psychiatry.* 2022; 27(1): 281-295. doi:10.1038/s41380-021-01161-7

2. Braithwaite I, Zhang S, Kirkbride JB, Osborn DP, Hayes JF. Air pollution (particulate matter) exposure and associations with depression, anxiety, bipolar, psychosis and suicide risk: a systematic review and meta-analysis. *Environ Health Perspect.* 2019; 127(12): 126002. doi:10.1289/EHP4595

3. Xue T, Guan T, Zheng Y, et al. Long-term $PM_{2.5}$ exposure and depressive symptoms in China: a quasi-experimental study. *Lancet Reg Health West Pac.* 2021; 6: 100079. doi:10.1016/j.lanwpc.2020.100079

4. Attademo L, Bernardini F. Air pollution and urbanicity: common risk factors for dementia and schizophrenia? *Lancet Planet Health.* 2017; 1(3): e90-e91. doi:10.1016/s2542-5196(17)30042-6

5. Newbury JB, Stewart R, Fisher HL, et al. Association between air pollution exposure and mental health service use among individuals with first presentations of psychotic and mood disorders: retrospective cohort study. *Br J Psychiatry.* 2021; 219: 678-685. doi:10.1192/bjp.2021.119

6. Antonsen S, Mok PL, Webb RT, et al. Exposure to air pollution during childhood and risk of developing schizophrenia: a national cohort study. *Lancet Planet Health.* 2020; 4(2): e64-e73. doi:10.1016/S2542-5196(20)30004-8

7. European Environment Agency. Sources and emissions of air pollutants in Europe. https://www.eea.europa.eu/publications/air-quality-in-europe-2022/sources-and-emissions-of-air. Published 2022. Accessed November 2023.

8. Whiteford HA, Ferrari AJ, Degenhardt L, Feigin V, Vos T. The global burden of mental, neurological and substance use disorders: an analysis from the Global Burden of Disease Study 2010. *PLoS One.* 2015; 10(2): e0116820. doi:10.1371/journal.pone.0116820

9. World Health Organisation. Global Health Observatory. Urban population growth. Geneva, Switzerland: WHO; 2013.

10. World Health Organization. Ambient air pollution: A global assessment of exposure and burden of disease. http://www.who.int/phe/publications/air-pollution-global-assessment/en/. Published 2016. World Health Organization.

11. Lugo-Candelas C. Mental Health in a Changing Planet. *JAMA Psychiatry.* 2023. doi:10.1001/jamapsychiatry.2023.3410

12. Block ML, Calderón-Garcidueñas L. Air pollution: Mechanisms of neuroinflammation and CNS disease. *Trends Neurosci.* 2009; 32(9): 506-516. doi:10.1016/j.tins.2009.05.009

13. de Prado Bert P, Mercader EMH, Pujol J, Sunyer J, Mortamais M. The effects of air pollution on the brain: a review of studies interfacing environmental epidemiology and neuroimaging. *Curr Environ Health Rep.* 2018; 5(3): 351-364. doi:10.1007/s40572-018-0209-9

14. Bateson TF, Schwartz J. Children's response to air pollutants. *Journal of Toxicology and Environmental Health, Part A.* 2007; 71(3): 238-243. doi:10.1080/15287390701598234

15. Silbereis JC, Pochareddy S, Zhu Y, Li M, Sestan N. The cellular and molecular landscapes of the developing human central nervous system. *Neuron.* 2016; 89(2): 248-268. doi:10.1016/j.neuron.2015.12.008

16. Newbury JB, Arseneault L, Beevers S, et al. Association of air pollution exposure with psychotic experiences during adolescence. *JAMA Psychiatry.* 2019; 76(6): 614-623. doi:10.1001/jamapsychiatry.2019.0056

17. Clark C, Paunovic K. WHO environmental noise guidelines for the European region: a systematic review on environmental noise and quality of life, wellbeing and mental health. *Int J Environ Res Public Health.* 2018; 15(11): 2400. doi:10.3390/ijerph15112400

18. Allen RW, Davies H, Cohen MA, et al. The spatial relationship between traffic-generated air pollution and noise in 2 US cities. *Environ Res.* 2009; 109(3): 334-342. doi:10.1016/j.envres.2008.12.006

19. Kelleher I, Connor D, Clarke MC, et al. Prevalence of psychotic symptoms in childhood and adolescence: A systematic review and meta-analysis of population-based studies. *Psychol Med.* 2012; 42(9): 1857-1863. doi:10.1017/S0033291711002960

20. Tiirikainen K, Haravuori H, Ranta K, Kaltiala-Heino R, Marttunen M. Psychometric properties of the 7-item Generalized Anxiety Disorder Scale (GAD-7) in a large representative sample of Finnish adolescents. *Psychiatry Res.* 2019; 272: 30-35. doi:10.1016/j.psychres.2018.12.004

21. Lu W. Adolescent depression: national trends, risk factors, and healthcare disparities. *Am J Health Behav.* 2019; 43(1): 181-194. doi:10.5993/AJHB.43.1.15

22. Dykxhoorn J, Osborn D, Walters K, et al. Temporal patterns in the recorded annual incidence of common mental disorders over two decades in the United Kingdom: a primary care cohort study. *Psychol Med.* 2023: 1-12. doi:10.1017/S0033291723002349

23. Copeland WE, Adair CE, Smetanin P, et al. Diagnostic transitions from childhood to adolescence to early adulthood. *JCPP.* 2013; 54(7): 791-799. doi:10.1111/jcpp.12062

24. Fisher HL, Caspi A, Poulton R, et al. Specificity of childhood psychotic symptoms for predicting schizophrenia by 38 years of age: A birth cohort study. *Psychol Med.* 2013; 43(10): 2077-2086. doi:10.1017/S0033291712003091

25. Boyd A, Golding J, Macleod J, et al. Cohort profile: The 'Children of the 90s'—the index offspring of the Avon Longitudinal Study of Parents and Children. *Int J Epidemiol.* 2013; 42(1): 111-127. doi:doi.org/10.1093/ije/dys064

26. Fraser A, Macdonald-Wallis C, Tilling K, et al. Cohort profile: the Avon Longitudinal Study of Parents and Children: ALSPAC mothers cohort. *Int J Epidemiol.* 2013; 42(1): 97-110. doi:10.1093/ije/dys066

27. Northstone K, Lewcock M, Groom A, et al. The Avon Longitudinal Study of Parents and Children (ALSPAC): an update on the enrolled sample of index children in 2019. *Wellcome Open Res.* 2019; 4. doi:10.12688/wellcomeopenres.15132.1

28. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap) - a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform.* 2009; 42(2): 377-381. doi:10.1016/j.jbi.2008.08.010

29. Boyd A, Thomas R, Hansell AL, et al. Data Resource Profile: The ALSPAC birth cohort as a platform to study the relationship of environment and health and social factors. *Int J Epidemiol.* 2019; 48(4): 1038-1039k. doi:10.1093/ije/dyz063

30. Von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *The Lancet.* 2007; 370(9596): 1453-1457.

31. Horwood J, Salvi G, Thomas K, et al. IQ and non-clinical psychotic symptoms in 12-year-olds: results from the ALSPAC birth cohort. *Br J Psychiatry.* 2008; 193(3): 185-191. doi:10.1192/bjp.bp.108.051904

32. World Health Organization. Schedules for Clinical Assessment in Neuropsychiatry. Published 1994. World Health Organization.

33. Jones HJ, Stergiakouli E, Tansey KE, et al. Phenotypic manifestation of genetic risk for schizophrenia during adolescence in the general population. *JAMA Psychiatry.* 2016. doi:10.1001/jamapsychiatry.2015.3058

34. Solmi F, Lewis G, Zammit S, Kirkbride JB. Neighborhood characteristics at birth and positive and negative psychotic symptoms in adolescence: Findings from the ALSPAC birth cohort. *Schizophr Bull.* 2020; 46(3): 581-591. doi:10.1093/schbul/sbz049

35. Goodman R, Ford T, Richards H, Gatward R, Meltzer H. The Development and Well-Being Assessment: description and initial validation of an integrated assessment of child and adolescent psychopathology. *JCPP.* 2000; 41(5): 645-655. doi:10.1111/j.1469-7610.2000.tb02345.x

36. Lewis G, Pelosi AJ, Araya R, Dunn G. Measuring psychiatric disorder in the community: a standardized assessment for use by lay interviewers. *Psychol Med.* 1992; 22(2): 465-486. doi:10.1017/S0033291700030415

37. de Castro Pascual M, Fossati S, Nieuwenhuijsen M, Vrijheid M. Protocol for integrated urban environment stressors generation in LifeCycle (WP3–Task 3.3). Rotterdam, The Netherlands: Erasmus MC, 2021.

38. De Hoogh K, Chen J, Gulliver J, et al. Spatial $PM_{2.5}$, NO_2, O_3 and BC models for Western Europe–Evaluation of spatiotemporal stability. *Environ Int.* 2018; 120: 81-92. doi:10.1016/j.envint.2018.07.036

39. European Environment Agency. 7th Environment Action Programme. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32013D1386. Published 2013. Accessed November 2023.

40. DETR. Indices of Deprivation 2000. London: Department of the Environment, Transport and the Regions, 2000.

41. Fuertes E, Markevych I, Thomas R, et al. Residential greenspace and lung function up to 24 years of age: The ALSPAC birth cohort. *Environ Int.* 2020; 140: 105749. doi:10.1016/j.envint.2020.105749

42. World Health Organization. Adolescent health. 2022. https://www.who.int/health-topics/adolescent-health#tab=tab_1 (accessed 26/04 2022).

43. VanderWeele TJ, Ding P. Sensitivity analysis in observational research: introducing the E-value. *Ann Intern Med.* 2017; 167(4): 268-274. doi:10.7326/M16-2607

44. Rogers W. Regression standard errors in clustered samples. *STB.* 1994; 3(13): 19-23.

45. StataCorp L. Stata multiple-imputation reference manual: Release 13. *Stata Manual.* 2013; 2013: 1-367.

46. World Health Organization. WHO global air quality guidelines: Particulate matter ($PM_{2.5}$ and PM_{10}), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide. Executive summary. Published 2021. World Health Organization.

47. Mortamais M, Pujol J, Martínez-Vilavella G, et al. Effects of prenatal exposure to particulate matter air pollution on corpus callosum and behavioral problems in children. *Environ Res.* 2019; 178: 108734. doi:10.1016/j.envres.2019.108734

48. Gruzieva O, Xu C-J, Yousefi P, et al. Prenatal particulate air pollution and DNA methylation in newborns: an epigenome-wide meta-analysis. *Environ Health Perspect.* 2019; 127(5): 057012. doi:10.1289/EHP4522

49. Schembari A, De Hoogh K, Pedersen M, et al. Ambient air pollution and newborn size and adiposity at birth: differences by maternal ethnicity (the born in Bradford study cohort). *Environ Health Perspect.* 2015; 123(11): 1208-1215. doi:10.1289/ehp.1408675

50. Bekkar B, Pacheco S, Basu R, DeNicola N. Association of air pollution and heat exposure with preterm birth, low birth weight, and stillbirth in the US: a systematic review. *JAMA Netw Open.* 2020; 3(6): e208243-e208243. doi:10.1001/jamanetworkopen.2020.8243

51. Stansfeld S, Clark C. Health effects of noise exposure in children. *Curr Environ Health Rep.* 2015; 2: 171-178. doi:10.1007/s40572-015-0044-1

52. Hygge S, Evans GW, Bullinger M. A prospective study of some effects of aircraft noise on cognitive performance in schoolchildren. *Psychol Sci.* 2002; 13(5): 469-474. doi:10.1111/1467-9280.00483

53. Golding, Pembrey, Team AS. ALSPAC–The Avon Longitudinal Study of Parents and Children. *Paediatr Perinat Epidemiol.* 2001; 15(1): 74-87. doi:10.1046/j.1365-3016.2001.00325.x

54. Sheppard L, Burnett RT, Szpiro AA, et al. Confounding and exposure measurement error in air pollution epidemiology. *Air quality, atmosphere & health.* 2012; 5: 203-216. doi:10.1007/s11869-011-0140-9

55. Keogh RH, Shaw PA, Gustafson P, et al. STRATOS guidance document on measurement error and misclassification of variables in observational epidemiology: part 1—basic theory and simple methods of adjustment. *Stat Med.* 2020; 39(16): 2197-2231. doi:10.1002/sim.8532

56. Lebret E, Briggs D, Van Reeuwijk H, et al. Small area variations in ambient NO_2 concentrations in four European areas. *Atmos Environ.* 2000; 34(2): 177-185. doi:10.1016/S1352-2310(99)00292-7

57. Calderón-Garcidueñas L, Solt AC, Henríquez-Roldán C, et al. Long-term air pollution exposure is associated with neuroinflammation, an altered innate immune response, disruption of the blood-brain barrier, ultrafine particulate deposition, and accumulation of amyloid β-42 and α-synuclein in children and young adults. *Toxicol Pathol.* 2008; 36(2): 289-310. doi:10.1177/0192623307313011

58. Calderon-Garciduenas L, Reed W, Maronpot RR, et al. Brain inflammation and Alzheimer's-like pathology in individuals exposed to severe air pollution. *Toxicol Pathol.* 2004; 32(6): 650-658.

59. Yao Y, Lv X, Qiu C, et al. The effect of China's Clean Air Act on cognitive function in older adults: a population-based, quasi-experimental study. *Lancet Healthy Longev.* 2022; 3(2): e98-e108. doi:10.1016/S2666-7568(22)00004-6