Maternal exposure to urban environmental stressors and depression in the postnatal period (version 1)

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[1. Background and aims 2](#_Toc39566275)

[2. Exposures 3](#_Toc39566276)

[3. Outcomes 4](#_Toc39566277)

[4. Covariates 6](#_Toc39566278)

[5. Statistical analysis 6](#_Toc39566279)

[6. Data access 9](#_Toc39566280)

[7. Authorship 9](#_Toc39566281)

[8. References 9](#_Toc39566282)

# Background and aims

Maternal postnatal depression (PND) is characterised by symptoms of depressed mood, anxiety and anhedonia in the year following birth and is estimated to affect 6 – 38% of women in high income countries.[1, 2] Not only is it by nature distressing, PND may interfere with the mother’s ability to care for the baby and handle other daily tasks, and is a risk factor for later child mental health problems.[3] It is vital therefore to identify potentially modifiable risk factors to inform policy and interventions.

With an ever-increasing proportion of the world population living in cities, increasing attention is turning to the role of urban environmental stressors such as ambient air pollution, road traffic noise and lack of access to natural spaces in mental health. [4-8] These stressors could impact maternal mental health through different biological mechanism related to e.g. neurotoxic effects of air pollutants, [9] annoyance, poor and disrupted sleep due to noise, and limited ability to natural spaces to relax, exercise and socialise.[10, 11]

Whilst experimental studies provide evidence in support of the mechanisms through which environmental stressors could cause PND, epidemiological evidence is very limited. One small study reported a positive association between exposure to ambient airborne particulate matter (PM) during pregnancy and postnatal depression at 6 months, [12] whilst another reported associations close to null. [13] To our knowledge only one study has examined the association between residential noise and postnatal depression, finding an increased risk of hospitalisation. [14] Evidence for the association between exposure to natural spaces and depression *during* pregnancy is also sparse. Using data from the Born in Bradford cohort, McEachen et al. found an inverse association between access to green space and depression in pregnancy.[15] By contrast, a study, a study in New Zealand reported association between the proportion of greenspace in the local area and PND close to null. McEachen found some evidence for effect modification by socioeconomic position (SEP), with the strongest associations between Normalised Difference Vegetation Index (NDVI) and depression being for mothers of lower education. However, to our knowledge no studies have examined associations between exposure to natural spaces and depression in the postnatal period. Whilst evidence is emerging for the role of the urban environment in depression in other periods of adult life, [16-19] it is relevant to examine specifically at the perinatal period given the heightened vulnerability to stressors at this time.

In this proposal we aim to use the unique data available from up to nine cohorts in the EU Child Cohort Network to study associations between exposure to three indicators of urban environmental stressors in the perinatal period and maternal postnatal depression. Single and joint associations of ambient air pollution, road traffic noise and natural space with PND will be studied, and we will also test for effect modification by SEP. This project will generate new data needed to inform policy aiming to improve maternal and child mental health in urban areas.

# Eligibility

Analysis will be restricted to singleton pregnancies of women giving birth to liveborn children. The following nine cohorts will be invited to participate as they have data on the selected urban environmental exposures and postnatal depression (described below): ALSPAC, BiB, DNBC, EDEN, GenR, INMA, NINFEA, MoBa and RHEA.

Servers have been set up for all cohorts except from ALSPAC and BiB; however these are scheduled to be launched in the next two months. DNBC urban environmental data has not yet been uploaded; however again this will be completed prior to the start of the fellowship.

# Exposures

Three categories of urban environmental stressor will be included: (i) ambient air pollution, (ii) road traffic noise and (iii) access to natural spaces (Table 1). Ambient air pollution will be indicated by average exposure to nitrogen dioxide (NO2) and the inhalable fraction of particulate matter (PM2.5). Road traffic noise will be averaged over the day, evening and night (Lden). Exposure to natural spaces will be captured by NDVI and distance to nearest green and blue spaces >5,000m2. (21)

We have defined three periods of exposure *a priori*: (i) pregnancy, (ii) postnatal (birth to child age 12 months) and (iii) perinatal (both pregnancy and postnatal). However, the accuracy with which urban exposures have been estimated at different time points varies markedly between exposures. This is for two reasons: first, yearly address data was not available for all cohorts. Where there were gaps in the data it was assumed that participants were living at the previously recorded address. Second, for most exposures yearly reference data was not available to estimate the level of the exposure at each specific time point.

The most detailed data is available for ambient air pollution. Average exposure is estimated for both the pregnancy and postnatal period; perinatal exposure will be calculated by taking the time-weighted average of these two values. Add here information on if all cohorts have both NO2 and PM2.5 and that exposures estimated with the ELAPSE LUR modelling for year 2010 if I recall correctly were back-extrapolated using the ratio-methods to the exact pregnancies and the first year after birth. The BiB cohort rely on address at birth, but all other cohorts have data on addresses during pregnancy and after birth.

Move noise section up here – to have same order as in the intro

For NDVI, each period of exposure is estimated based on Landsat data available closest to that time point (Table 1, taken from harmonisation manual). For some cohorts, the estimate of exposure in pregnancy will have been measured prior to pregnancy (ALSPAC, BiB, DNBC, INMA GUIP, INMA VAL); whilst for others it will have been measured during or after pregnancy (EDEN, GEN-R, INMA SBD, MoBa). For example, in BiB the values from pregnancy to 12 months post-birth are based on Landsat data collected a year before pregnancy. As BiB also lacks detailed address data over this period (Table A1), each subject will have the same value from pregnancy to 12 months (based on their address in pregnancy).

**Table 1: Year of Landsat image assigned to each time point for NDVI**

| **cohort, center** | **Period** | **preg** | **birth** | **y1** | **y2** | **y3** | **y4** | **y5** | **y6** | **y7** | **y8** | **y9** | **y10** | **y11** | **y12** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ALSPAC | 1990-2005 | 1990 |  |  |  |  | 1994 |  |  |  |  |  | 2002 |  |  |
| BIB | 2007-2015 | 2006 |  |  | 2011 |  |  |  |  |  |  |  |  |  |  |
| DNBC | 1997-2014 | 1994 |  |  | 2001 |  |  |  |  | 2006 |  |  |  |  |  |
| EDEN NAN | 2003-2010 | 2004 |  |  |  |  | 2010 |  |  |  |  |  |  |  |  |
| EDEN POI | 2003-2013 | 2001-4 |  |  |  | 2007-10 |  |  |  |  |  |  |  |  |  |
| GENR | 2002-2016 | 2005 |  |  |  |  |  |  | 2010 |  |  |  | 2016 |  |  |
| INMA GUIP | 2004-2018 | 2001 |  |  |  | 2010 |  |  |  |  |  |  | 2017 |  |  |
| INMA SBD | 2004-2018 | 2007 |  |  |  |  |  | 2011 |  |  |  |  |  | 2017 |  |
| INMA VAL | 2004-2017 | 2003 |  |  |  |  | 2009 |  |  |  |  | 2015 |  |  |  |
| MOBA | 2004-2015 | 2009 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| RHEA | 2007-2015 | 2008 |  |  |  |  |  |  |  |  |  |  |  |  |  |

Estimates of proximity to natural spaces are based on EU Environment Protection Agency (EUPPA) maps. However, for many cohorts the maps used were produced a considerable time after pregnancy (Table 2). For example, the map used to derive the ALSPAC pregnancy values was produced >10 years after pregnancies in that cohort.

**Table 2: Year of EUPPA map used to estimate distance to green space**

| **cohort** | **period** | **preg** | **birth** | **y1** | **y2** | **y3** | **y4** | **y5** | **y6** | **y7** | **y8** | **y9** | **y10** | **y11** | **y12** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ALSPAC | 1990-2005 | 2006 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| BIB | 2007-2015 | 2006 |  |  |  |  |  | 2012 |  |  |  |  |  |  |  |
| DNBC | 1997-2014 | 2006 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| EDEN NAN | 2003-2010 | 2006 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| EDEN POI | 2003-2013 | 2006 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| GENR | 2002-2016 | 2006 |  |  |  |  |  |  |  |  |  |  | 2012 |  |  |
| INMA GUIP | 2004-2018 | 2009 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| INMA SBD | 2004-2018 | 2006 |  |  |  |  |  |  |  |  | 2012 |  |  |  |  |
| INMA VAL | 2004-2017 | 2006 |  |  |  |  |  |  |  |  | 2012 |  |  |  |  |
| MOBA | 2004-2015 | 2014 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| RHEA | 2007-2015 | 2006 |  |  |  |  |  |  |  |  |  |  |  |  |  |

For almost all cohorts, estimates of road traffic noise are based on measurement at one time point. (Table 3). For some cohorts this was approximately at the time of pregnancy (e.g. BiB), but again for other cohorts it was measured considerably after pregnancy (e.g. ALSPAC, DNBC)

**Table 3: Year of noise data assigned to each time point**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **cohort** | **period** | **preg** | **birth** | **y1** | **y2** | **y3** | **y4** | **y5** | **y6** | **y7** | **y8** | **y9** | **y10** | **y11** | **y12** |
| ALSPAC | 1990-2005 | 2006 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| BIB | 2007-2015 | 2006 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| DNBC | 1997-2014 | 2012 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| EDEN NAN | 2003-2010 | 2005 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| EDEN POI | 2003-2013 | 2009 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| GENR | 2002-2016 | 2012 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| INMA GUIP | 2004-2018 | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| INMA SBD | 2004-2018 | 2006 |  |  |  |  |  |  |  |  | 2012 |  |  |  |  |
| INMA VAL | 2004-2017 | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| MOBA | 2004-2015 | 2006 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| RHEA | 2007-2015 | 2015 |  |  |  |  |  |  |  |  |  |  |  |  |  |

The LifeCycle variables that will be used to derive these exposures are detailed in Table 4. All exposures are continuous variables. A full list of LifeCycle variables required for this study are shown in Table A2.

**Table 4: Details of LifeCycle urban environment exposures**

|  |  |  |  |
| --- | --- | --- | --- |
| **Environmental exposure** | **LifeCycle variable** | **Description** | **Time point of measurement** |
| Ambient air pollution | no2\_preg | Nitrogen dioxide (NO2, ug/m3) | Estimated mean value during pregnancy |
| no2\_1 | Estimated mean value from birth to 12 months |
| pm25\_preg | Inhalable fraction of particulate matter (PM2.5, ug/m3) | Estimated mean value during pregnancy |
| pm25\_1 | Estimated mean value from birth to 12 months |
| Road traffic noise | lden\_preg | Noise from road traffic averaged over day, evening and night (Lden, dB). | Estimated value in pregnancy |
| lden\_0 | Estimated value at birth |
| lden\_1 | Estimated value at 12 months |
| Natural spaces | ndvi300\_preg | Normalised Difference Vegetation Index (NDVI; 300m buffer) | Estimated value in pregnancy |
| ndvi300\_1 | Estimated value at 12 months |
| green\_dist\_preg | Distance to nearest green space (m) | Estimated value in pregnancy |
| green\_dist\_1 | Estimated value at 12 months |
| blue\_dist\_preg | Distance to nearest blue space (m) | Estimated value in pregnancy |
| blue\_dist\_1 | Estimated value at 12 months |

# Outcome

Maternal postnatal depression is captured within LifeCycle by a binary variable (yes/no). It was derived either from questionnaire, self-report or linked registry data. The time point at which depression was measured varies from 2 months (GEN-R) to 18 months (INMA & NINFEA). Table 5 shows the available data based on the LifeCycle catalogue and inquiries with cohorts.

**Table 5: Available data on postnatal depression**

|  |  |  |  |
| --- | --- | --- | --- |
| **Cohort** | **Data available** | **Definition** | **Time point of assessment (period following birth)** |
| ALSPAC | Yes | EPDS score > 12 | 8 months |
| BiB | Yes | GHQ-28 (cut-off TBC) | 6 months |
| DNBC | Yes | Modified GHQ or linked data | 6 months |
| EDEN | Yes | Single self-report question asking whether mother took anti-depressant medication | ??? |
| GenR | Yes | EPDS score > 12 | 2 months |
| INMA | Yes | GHQ-12 | 18 months |
| NINFEA | Yes | Self-report of doctor diagnosis | 18 months |
| MoBa | Yes | EPDS-5 (cut-off TBC) | 6 months |
| RHEA | Yes | EPDS score > 12 | ??? |

EPDS = Edinburgh Postnatal Depression Scale

# Covariates

Whilst many variables are associated with postnatal depression, only some of these are also associated with exposure to environmental stressors. Diagrammatic acyclic graphs (DAGs) for air pollution, traffic noise and natural spaces are shown in Figures 1-3.

*Figure 1: DAG depicting relationships between exposure to ambient air pollution, postnatal depression and covariates*

Diagram

Description automatically generated

*Figure 2: DAG depicting relationships between exposure to road traffic noise, postnatal depression and covariates*

Diagram

Description automatically generated

*Figure 3: DAG depicting relationships between exposure to natural spaces, postnatal depression and covariates*

Diagram

Description automatically generated

We will adjust for maternal socioeconomic position (SEP) as indicated by maternal education, income, area-specific SEP, ethnicity, ~~season of birth~~, maternal age at birth and parity, maybe cohort and year of birth [+finalise list in next meeting]. Where there is evidence of sex differences in associations, we will stratify analyses by sex.

# Statistical analysis

## Overview of analysis

All analyses will be conducted using DataSHIELD. For each cohort, we will first produce descriptive statistics for all urban environmental exposures, PND and the covariates. We will calculate bivariate associations between the urban environmental exposures and the outcome by in single exposure models fitted each exposure one-by-one at each time point seperately. We will test for non-linearity in exposure-outcome associations by binning the exposures into strata (e.g. 5 levels of exposure) and examining associations between these strata and the outcome at each time period. We will examine heterogeneity between cohorts in distributions and associations between study variables.

Logistic regression will be used to estimate associations between (i) each urban environmental exposure and PND, and (ii) all urban environmental exposures together and PND. To determine whether to include multiple indicators of each category of exposure we will first examine correlations between each indicator (NO2 and PM2.5, NDVI and distance to green and blue spaces). If these are highly correlated (R>0.80), only one variable will be included in regression models. We also test for multicollinearity between covariates.

Analyses will first be conducted separately within each cohort. We will then examine the consistency in exposure-outcome associations across cohorts. If there is sufficient homogeneity between results, we will pool effect estimates using study-level meta-analysis with random effects of cohort/study area. You need to add interactions between exposures

As previous research has suggested that SEP may be an effect modifier of the association between environmental exposures and maternal depression we also aim explore this. [15] However, given that our outcome is binary and prevalence is relatively rare we will are unlikely to have power to test this within each cohort.

## Model equations

Equations for the planned models are detailed below. We will initially fit unadjusted models and then models adjusted for covariates described in section 3 (for brevity unadjusted models are not shown here). Three versions of each model will be fitted corresponding to the three time periods of exposure (pregnancy, postnatal, both).

### Separate associations between each exposure and PND

**Ambient air pollution:**

If *N*02 and *PM*2.5 are not highly correlated we will also fit:

**Road traffic noise:**

### **Natural spaces:**

If separate indicators of natural spaces are not highly correlated we will also fit:

### Joint associations between all environmental exposures and PND

### Effect modification of associations by SEP

**Ambient air pollution:**

**Road traffic noise :**

**Natural spaces :**

## Sensitivity / additional analyses

We will repeat analyses restricting the sample to (i) first-time mothers, (ii) pregnancies free of comorbidities (gestational diabetes, hypertensive disorders, and preterm deliveries) and (iii) women reporting no prior history of depression. We will compare results in subsets where PND was measured by questionnaire, self-report or linked registry data.

# Data access

Individual data access agreements are currently being arranged with eligible cohorts.

# Authorship

TC will be listed as first author, MP last author, and all remaining authors from the analysis plan as co-authors. In addition, one to two or more researchers from each participating cohort will be invited as co-authors.

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# Appendices

Table A1: Geocodes assigned to create year by year exposure estimates for traffic noise and green space variables (assumed geocodes in italics).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **cohort** | **preg** | **birth** | **y1** | **y2** | **y3** | **y4** | **y5** | **y6** | **y7** | **y8** | **y9** | **y10** | **y11** | **y12** |
| ABCD | preg | birth | *birth* | *birth* | *y5* | *y5* | y5 | *y5* | *y8* | y8 | *y8* | *y11* | y11 | - |
| ABCDd | preg | birth | *birth* | *birth* | *birth* | *birth* | *y8* | *y8* | *y8* | y8 | *y8* | *y8e* | *y8e* | - |
| ALSPAC | prega | birth | y1 | y2 | y3 | y4 | y5 | y6 | y7 | y8 | y9 | y10 | y11 | y12 |
| BIB | pregb | *preg* | *preg* | *preg* | *y5* | *y5* | y5 |  |  |  |  |  |  |  |
| DNBCe |  |  | y1 | y2 | y3 | y4 | y5 | y6 | y7 | y8 | y9 | y10 | y11 | y12 |
| EDEN | pregb | *preg* | *preg* | *preg* | *y5* | *y5* | y5 | - | - | - | - | - | - | - |
| GASPII | *birth* | birth | m6 | m15 | *m15/y4* | y4 | *y4* | *y7* | y7 | - | - | - | - | - |
| GENR | pregc | birth | y1 | y2 | y3 | y4 | y5 | y6 | y7 | y8 | y9 | y10 | y11 | y12 |
| INMA | pregc | birth | y1 | y2 | y3 | y4 | y5 | y6 | y7 | y8 | y9 | y10 | y11 | y12 |
| KANC | pregc | *preg* | *preg* | *preg/y4* | *y4* | y4 | - | - | - | - | - | - | - | - |
| MOBA | preg | birth | 14\_18m | *14\_18m* | y3 | *y3* | y5 | *y5* | 7\_8y | - | - | - | - | - |
| NINFEA | preg | m6 | m18 | *m18* | *y4* | y4 | *y4* | *y7* | y7 | *y7* | *y10* | y10 | - | - |
| PICCOLIPIÙf | preg | preg | preg | preg | preg | preg | - | - | - | - | - | - | - | - |
| RHEA | preg | *preg* | *preg* | *preg/y4* | *y4* | y4 | y4 |  |  |  |  |  |  |  |

Table A2: LifeCycle variables required for analysis

|  |  |  |
| --- | --- | --- |
| **Variable** | **Opal table** | **Category** |
| area\_ses\_tert\_preg | core non-repeated | covariate |
| area\_ses\_quint\_preg | core non-repeated | covariate |
| mat\_age | core non-repeated | covariate |
| parity\_m | core non-repeated | covariate |
| sex | core non-repeated | covariate |
| birth\_month | core non-repeated | covariate |
| eusilc\_income\_quintiles | core non-repeated | covariate |
| eusilc\_income\_tertiles | core non-repeated | covariate |
| agebirth\_m\_y | core non-repeated | covariate |
| ethn1\_m | core non-repeated | covariate |
| ethn2\_m | core non-repeated | covariate |
| ethn3\_m | core non-repeated | covariate |
| cohort\_country | core non-repeated | covariate |
| preg\_smk | core non-repeated | covariate |
| preg\_alc | core non-repeated | covariate |
| preg\_cig | core non-repeated | covariate |
| preg\_alc\_unit | core non-repeated | covariate |
| breastfed\_any | core non-repeated | covariate |
| breastfed\_ever | core non-repeated | covariate |
| no2\_preg, | core non-repeated | exposure |
| pm25\_preg | core non-repeated | exposure |
| lden\_preg | core non-repeated | exposure |
| ndvi300\_preg | core non-repeated | exposure |
| green\_dist\_preg, | core non-repeated | exposure |
| blue\_dist\_preg, | core non-repeated | exposure |
| cohort\_id | core non-repeated | meta-data |
| pnd | core non-repeated | outcome |
| preg\_dia | core non-repeated | covariate |
| preg\_ht | core non-repeated | covariate |
| ga\_bj | core non-repeated | covariate |
| prepreg\_dep | core non-repeated | covariate |
| child\_id | core non-repeated, core yearly repeated | meta-data |
| edu\_m\_ | core yearly repeated | covariate |
| area\_ses\_tert\_ | core yearly repeated | covariate |
| area\_ses\_quint\_ | core yearly repeated | covariate |
| fam\_split\_up\_ | core yearly repeated | covariate |
| no2\_ | core yearly repeated | exposure |
| pm25\_ | core yearly repeated | exposure |
| lden\_ | core yearly repeated | exposure |
| ndvi300\_ | core yearly repeated | exposure |
| green\_dist\_ | core yearly repeated | exposure |
| blue\_dist\_ | core yearly repeated | exposure |
| age\_years | core yearly repeated | meta-data |
| age\_months | core yearly repeated | meta-data |
| child\_no | core non-repeated | meta-data |
| preg\_no | core non-repeated | meta-data |
| mother\_id | core non-repeated | meta-data |
| outcome | core non-repeated | meta-data |
| con\_anomalies | core non-repeated | covariate |
| cohab\_0 | core non-repeated | covariate |
| cohab\_1 | core non-repeated | covariate |