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

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# 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 EU citizens 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 biological routes (e.g. neurotoxic effects of air pollution), [9] or as psychosocial stressors (e.g. disrupted sleep due to noise, annoyance, and limited 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 airborn 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 mixed: McEachen et al. reported an inverse association between access to green space and depression in pregnancy, [15] whilst Nichani and colleagues reported an association 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 essential to look 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 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 EU policy aiming to improve maternal and child mental health.

# 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 environmental exposures (described below): ALSPAC, BiB, DNBC, EDEN, GenR, INMA, NINFEA, MoBa and RHEA. Of these nine, five cohorts have confirmed data on PND: ALSPAC, EDEN, GEN-R, NINFEA, RHEA. The remaining cohorts will be contacted to confirm if they have data available within LifeCycle.

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 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)

*Table 1: Urban environmental exposures*

|  |  |  |
| --- | --- | --- |
| **Environmental exposure** | **LifeCycle variable name(s)** | **Description** |
| Ambient air pollution | no2\_preg, no2\_1 | Pregnancy mean of nitrogen dioxide (NO2, ug/m3) |
| pm25\_preg, pm25\_1 | Pregnancy mean of inhalable fraction of particulate matter (PM2.5, ug/m3) |
| Road traffic noise | lden\_preg, lden\_0, lden\_1 | Pregnancy mean of noise from road traffic averaged over day, evening and night (Lden, dB) |
| Access to natural spaces | ndvi300\_preg, ndvi300\_0, ndvi300\_1 | Normalised Difference Vegetation Index (cont.? or cat? 300m buffer) |
| green\_dist\_preg, green\_dist\_0, green\_dist\_1 | Distance to nearest green space (m) |
| blue\_dist\_preg, blue\_dist\_0, blue\_dist\_1 | Distance to nearest blue space (m) |

# Outcome

Maternal postnatal depression is captured within LifeCycle by a binary variable (yes/no), derived from either questionnaire, self-report of diagnosis or linked registry data. Table 2 shows the available data based on the LifeCycle catalogue. Cohorts will be contacted to clarify missing information.

*Table 2: Available data on post-natal depression*

|  |  |  |  |
| --- | --- | --- | --- |
| **Cohort** | **Data available** | **Definition** | **Time of measurement** |
| ALSPAC | Yes | EPDS score > 12 | 12 weeks |
| BiB | ??? | GHQ-28? | ??? |
| DNBC | Yes | ??? | ??? |
| EDEN | Yes | Single self-report question asking whether mother took anti-depressant medication | ??? |
| GenR | Yes | EPDS score > 12 | ??? |
| INMA | ??? | ??? | ??? |
| NINFEA | Yes | Self-report of doctor diagnosis | 18 months |
| MoBa | ??? | SCL? | ??? |
| RHEA | Yes | EPDS score > 12 | ??? |

EPDS = Edinburgh Post-natal Depression Scale

# Covariates

Whilst many variables are associated with postnatal depression, only some of these are also associated with exposure to environmental stressors. We will adjust for maternal socioeconomic position (SEP) as indicated by maternal education, area-specific SEP, season of birth, maternal age and parity. We will also adjust for other covariates that are not on the pathway between urban stressors and postnatal depression. We will include child sex as a covariate, and where there is evidence of sex differences in associations we will stratify analyses by sex.

# Statistical analysis

## Overview of analysis

[Checking dose-response, checking consistency across cohorts, across ages, cluster by mothers\_id in case multiple mothers in cohort, include IQR]

Start with descriptives and correlation matrices separately and together for all cohorts

All analyses will be conducted using DataSHIELD. Logistic regression will be used to estimate separate and joint associations between the three environmental exposures within each time period and PND. Results will be pooled via Individual Participant Data (IPD) meta-analysis using the “ds.glm” function within DataSHIELD. Look at all cohorts separately before we decide whether to meta-analyse.

To determine whether to include multiple indicators of each category of exposure we will first examine correlations between each indicator (NO2 and PM2.5, Lden, 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 (for example maternal education and area-level SEP may be highly correlated).

As previous research has suggested that SEP may be an effect modifier of the association between environmental exposures and maternal depression we will also explore this. [15] we will test on the additive scale by calculating whether the odds ratio of PND per unit change in environmental exposure within the stratum of mothers with low education exceeds the sum of separate odds ratios for low maternal education and environmental exposure. [20] [21] ~~Given the number of tests being conducted there is a high probability of false positives, therefore we will interpret interactions cautiously and look for replication of effect modification across cohorts.~~

You need to mention that you first test the shape of the exposure-response for each exposure and each exposure window one-by-one and maybe also do this in each cohort if power?

## Model equations

Equations for the planned models are detailed below. For brevity parameters for covariates are not written out in each model description. Three versions of each model will be fitted (a-c) corresponding to the three time periods of exposure (antenatal, post-natal, both).

### Separate associations between environmental exposures and PND

Models 1a-1c (air pollution):

Models 2a-2c (noise):

Models 3a-3c (natural spaces):

### Combined association between environmental exposures and PND

Models 4a-4c:

### Effect modification of associations by SEP

### Models 5a-5c (pollution):

Models 6a-6c (noise?):

Models 7a-7c (natural spaces):

For models 6a – 7c effect modification will be tested by comparing if:

Findings that joint associations exceed the sum of the separate effects will provide evidence of effect modification.

## Sensitivity / additional analyses

We will repeat analyses restricting the sample to (i) pregnancies free of comorbidities (gestational diabetes, hypertensive disorders, and preterm deliveries) and (ii) 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. Finally, analyses will be repeated using Study Level Meta-Analysis.

# Data access

Individual data access agreements will be arranged with all participating cohorts prior to commencement of the fellowship.

# 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 researchers from each participating cohort will be invited as co-authors.

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# Appendix: 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 |
| preg\_ht | core non-repeated | covariate |
| cohort\_country | core non-repeated | covariate |
| preg\_smk | core non-repeated | covariate |
| preg\_alc | 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 |