Maternal exposure to urban environmental stressors and depression in the postnatal period (version 4)

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# Background and aims

Maternal postnatal depression (PND) is characterised by symptoms of depressed mood, anxiety and anhedonia [1] 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 in New Zealand reported association between the proportion of green space 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 this specifically in 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 stressor 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): Avon Longitudinal Study of Parents and Children (ALSPAC, University of Bristol), Born in Bradford (BiB, Bradford Institute for Health Research), Danish National Birth Cohort (DNBC, University of Copenhagen), Etude sur les Déterminants de la santé de l’Enfant (EDEN, Institut national de la santé et de la recherche médicale ), Generation Rotterdam (GEN-R, Erasmus MC), INfancia y Medio Ambiente (INMA, Barcelona Institute for Global Health), Nascita e INFanzia: gli Effetti dell'Ambiente (NINFEA, University of Turin), Norwegian Mother, Father and Child Cohort (MoBa, Norwegian Institute of Public Health) and The Mother-Child Cohort in Crete (RHEA, University of Crete).

Servers have been set up for all cohorts except from ALSPAC and BiB; however these are anticipated to be launched by May 2021.

# Exposures

Three categories of urban environmental stressor will be included: (i) ambient air pollution, (ii) road traffic noise and (iii) lack of access to natural spaces. 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 two periods of exposure *a priori*: (i) pregnancy and (ii) postnatal (birth to child age 12 months). The accuracy at which urban exposures have been estimated for each cohort at these time points depends on the availability of participant address data (Table A1). Four cohorts have yearly complete address history (ALSPAC, DNBC, GEN-R, INMA), whilst the remaining cohorts (BiB, EDEN, MoBa, NINFEA) have some gaps in address information. For these latter cohorts, at time points where the home address was unavailable it was presumed to be the previously recorded address.

Estimates of exposure to ambient air pollution were based on land use regression (LUR) models developed within the European Study of Cohorts for Air Pollution Effects (ESCAPE) project [20] where available, or models developed within the Effects of Low-Level Air Pollution: A Study in Europe (ELAPSE) project [21] (Table A2). Estimates of exposure during pregnancy and the first year after birth were back-extrapolated using ratio methods. [22] All cohorts had estimated data on N02 and PM2.5, however for cohorts where routine monitoring data for PM2.5 data was not available back-extrapolation was based on recorded N02 (ALSPAC, BiB, EDEN, INMA) or PM10 (RHEA; Table A3).

Estimates of road traffic noise are based on existing European road traffic noise maps, except RHEA where a new map was developed within LifeCycle. One or two maps were selected for each cohort/city to cover the entire study period and assigned to time points of interest (Table A4).

In terms of natural spaces, NDVI was estimated based on Landsat data available at 2-3 timepoints within each cohort (Table A5). Estimates of proximity to natural spaces are based on EU Environment Protection Agency (EUPPA) maps available at 1-2 timepoints for each cohort (Table A6).

The LifeCycle variables that will be used to derive these exposures are detailed in Table 1. All exposures are continuous variables. A full list of LifeCycle variables required for this study is detailed in Table A7.

**Table 1: 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 (Table 2). Two frequently used questionnaires were the Edinburgh Postnatal Depression Scale (EPDS) and the General Health Questionnaire (GHQ). The EPDS is a 10-item questionnaire recording symptoms common in women with depression and anxiety during pregnancy and in the year following the birth. The GHQ is a screening device for identifying minor psychiatric disorders in the general population. The time point at which PND was measured varies from 2 months (GEN-R) to 18 months (INMA & NINFEA). Table 2 shows the available data based on the LifeCycle catalogue and correspondence with cohorts.

**Table 2: Available data on postnatal depression**

|  |  |  |  |
| --- | --- | --- | --- |
| **Cohort** | **Data available** | **Measure** | **Time point of assessment (period following birth)** |
| ALSPAC | Yes | Edinburgh Postnatal Depression Scale | 8 months |
| BiB | Yes | General Health Questionnaire (28 item version) | 6 months |
| DNBC | Yes | Modified GHQ or linked data | 6 months |
| EDEN | Yes | Edinburgh Postnatal Depression Scale | 12 months |
| GenR | Yes | Edinburgh Postnatal Depression Scale | 2 months |
| INMA | Yes | General Health Questionnaire (12 item version) | 18 months |
| NINFEA | Yes | Self-report of doctor diagnosis | 18 months |
| MoBa | Yes | Edinburgh Postnatal Depression Scale (5 item version) | 6 months |
| RHEA | Yes | Edinburgh Postnatal Depression Scale | TBC |

# Covariates

Whilst many variables are associated with postnatal depression, only some of these are also associated with exposure to environmental stressors. A simplified diagrammatic acyclic graph (DAG) depicting potential confounders is shown in Figure 1. We will adjust for maternal socioeconomic position (SEP) as indicated by maternal education, income, area-specific SEP, ethnicity, maternal age at birth, parity, cohort and year of birth. Where there is evidence of sex differences in associations, we will stratify analyses by sex.

**Figure 1: DAG depicting relationships between exposure to urban environmental stressors, postnatal depression and covariates**

A picture containing map, text, outdoor

Description automatically generated

Note: *Simplified version of DAG not depicting all potential relationships between covariates. Potential effect modifiers not shown. Maternal drinking and smoking are potential mediators for some exposures (road traffic noise) but unlikely for others (air pollution, natural spaces).* Air pollution, noise and greenness may also act as confounders or effect modifiers for one another.

# 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 covariates. We will calculate bivariate associations between the urban environmental exposures and the outcome in single exposure models fitted separately for each exposure at each time point. We will test for non-linearity in exposure-outcome associations by fitting models with non-linear transformations of the exposure on a continuous scale (e.g. quadratic). Where there is evidence of non-linearity we will analyse associations with the exposure divided into tertiles or quartiles. We will examine heterogeneity between cohorts in distributions and associations between study variables.

We will first estimate associations between each urban environmental exposure and PND using logistic regression. Odds ratios and 95% confidence intervals for PND will be estimated both in terms of absolute difference in exposure (e.g. 10 μg/m3 increase in NO2) and within-cohort inter quartile range (IQR). Analysis will be conducted unadjusted and with different levels of adjustment for covariates described in section 5. To determine whether to include multiple indicators of each category of exposure we will first examine correlations between each indicator (NO2, 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. If collinearity is not a problem two-exposure models which fit two exposure simultaneously will be used to test the single and joint effects of the exposures on the odds for PND.

We will also estimate the combined effects of multiple categories of environmental exposures and PND. Interactions between exposures (e.g. air pollution and road traffic noise) will be estimated by testing whether the inclusion of a cross-product term between exposures improves model fit.

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.

As previous research has suggested that SEP may be an effect modifier of the association between environmental exposures and maternal depression we will also aim explore this. [15] However, given that our outcome is binary and prevalence is relatively rare we are unlikely to have power to test this within each cohort. We will determine whether exploring interactions is feasible once we have information on prevalence of PND and sample size for each cohort.

## 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, two or more researchers from each participating cohort will be invited as co-authors.

# References

1. Putnam, K.T., et al., *Clinical phenotypes of perinatal depression and time of symptom onset: analysis of data from an international consortium.* The lancet. Psychiatry, 2017. **4**(6): p. 477-485.

2. Howard, L.M., et al., *Non-psychotic mental disorders in the perinatal period.* Lancet, 2014. **384**(9956): p. 1775-88.

3. Stein, A., et al., *Effects of perinatal mental disorders on the fetus and child.* The Lancet, 2014. **384**(9956): p. 1800-1819.

4. Tzivian, L., et al., *Effect of long-term outdoor air pollution and noise on cognitive and psychological functions in adults.* Int J Hyg Environ Health, 2015. **218**(1): p. 1-11.

5. Kotzeva, M.M. and T. Brandmüller, *Urban Europe: statistics on cities, towns and suburbs*. 2016: Publications office of the European Union.

6. Gong, Y., et al., *A systematic review of the relationship between objective measurements of the urban environment and psychological distress.* Environment international, 2016. **96**: p. 48-57.

7. Fan, S.J., et al., *Ambient air pollution and depression: A systematic review with meta-analysis up to 2019.* Sci Total Environ, 2020. **701**: p. 134721.

8. Callaghan, A., et al., *The impact of green spaces on mental health in urban settings: a scoping review.* Journal of Mental Health, 2020: p. 1-15.

9. Amitai, Y., et al., *Neuropsychological Impairment From Acute Low-Level Exposure to Carbon Monoxide.* Archives of Neurology, 1998. **55**(6): p. 845-848.

10. Pirrera, S., E. De Valck, and R. Cluydts, *Nocturnal road traffic noise: A review on its assessment and consequences on sleep and health.* Environment International, 2010. **36**(5): p. 492-498.

11. Hartig, T., et al., *Nature and Health.* Annual Review of Public Health, 2014. **35**(1): p. 207-228.

12. Niedzwiecki, M.M., et al., *Particulate air pollution exposure during pregnancy and postpartum depression symptoms in women in Mexico City.* Environment International, 2020. **134**: p. 105325.

13. Sheffield, P.E., et al., *Association between particulate air pollution exposure during pregnancy and postpartum maternal psychological functioning.* PLoS One, 2018. **13**(4): p. e0195267.

14. He, S., et al., *Residential noise exposure and the longitudinal risk of hospitalization for depression after pregnancy: Postpartum and beyond.* Environ Res, 2019. **170**: p. 26-32.

15. McEachan, R.R., et al., *The association between green space and depressive symptoms in pregnant women: moderating roles of socioeconomic status and physical activity.* J Epidemiol Community Health, 2016. **70**(3): p. 253-9.

16. Cho, J., et al., *Air pollution as a risk factor for depressive episode in patients with cardiovascular disease, diabetes mellitus, or asthma.* J Affect Disord, 2014. **157**: p. 45-51.

17. Zijlema, W.L., et al., *The association of air pollution and depressed mood in 70,928 individuals from four European cohorts.* Int J Hyg Environ Health, 2016. **219**(2): p. 212-9.

18. Lim, Y.-H., et al., *Air Pollution and Symptoms of Depression in Elderly Adults.* Environmental Health Perspectives, 2012. **120**(7): p. 1023-1028.

19. Gascon, M., et al., *Long-term exposure to residential green and blue spaces and anxiety and depression in adults: A cross-sectional study.* Environ Res, 2018. **162**: p. 231-239.

20. Eeftens, M., et al., *Development of Land Use Regression Models for PM2.5, PM2.5 Absorbance, PM10 and PMcoarse in 20 European Study Areas; Results of the ESCAPE Project.* Environmental Science & Technology, 2012. **46**(20): p. 11195-11205.

21. de Hoogh, K., et al., *Spatial PM2.5, NO2, O3 and BC models for Western Europe – Evaluation of spatiotemporal stability.* Environment International, 2018. **120**: p. 81-92.

22. Hoek, G., et al., *A review of land-use regression models to assess spatial variation of outdoor air pollution.* Atmospheric Environment, 2008. **42**(33): p. 7561-7578.

# Appendices

Tables A1 to A6 are taken from WP3.13 harmonisation manual.

**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: Selected models for air pollution data**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Cohort** | **NOX** | **NO2** | **PM2.5** | **PM10** | **PMabs** |
| ALSPAC | - | ELAPSE | ELAPSE | - | - |
| BIB | ESCAPE local LUR | ESCAPE local LUR | ESCAPE local LUR | ESCAPE local LUR | ESCAPE local LUR |
| DNBC | - | ELAPSE | ELAPSE | - | - |
| EDEN NAN | - | ESCAPE local LUR | ELAPSE | Local Dispersion Model (only pregnancy period) | - |
| EDEN POI | - | ESCAPE local LUR | ELAPSE | Local Dispersion Model (only pregnancy period) | - |
| GENR | ESCAPE local LUR | ESCAPE local LUR | ESCAPE local LUR | ESCAPE local LUR | ESCAPE local LUR |
| INMA GUIP | ESCAPE local LUR | ESCAPE local LUR | ELAPSE | - | - |
| INMA SAB | ESCAPE local LUR | ESCAPE local LUR | ESCAPE local LUR | ESCAPE local LUR | ESCAPE local LUR |
| INMA VAL | ESCAPE local LUR | ESCAPE local LUR | ELAPSE | - | - |
| MOBA | ESCAPE local LUR | ESCAPE local LUR | ESCAPE local LUR | ESCAPE local LUR | ESCAPE local LUR |
| RHEA | ESCAPE local LUR | ESCAPE local LUR | ESCAPE local LUR | ESCAPE local LUR | - |

**Table A3: Pollutants used for back-extrapolation when daily values of the specific pollutants were available (ratio method ONLY)**

| **Cohort** | **NO2** | **NOX** | **PM10** | **PM2.5** | **PM2.5abs** | **PMcoarse** | **NO2 (ELAPSE)** | **PM2.5 (ELAPSE)** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ALSPAC |  |  |  |  |  |  | NO2 | NO2 |
| BIB | NO2 | NOX | NO2 | NO2 | NOX | NO2 |  |  |
| DNBC | NO2 |  |  | PM2.5 |  |  |  |  |
| EDEN NAN | NO2 |  |  |  |  |  |  | NO2 |
| EDEN POI | NO2 |  |  |  |  |  |  | NO2 |
| GENRb | NO2 | NOX |  |  |  |  |  |  |
| INMA GUIP | NO2 | NOX |  |  |  |  |  | NO2 |
| INMA SAB | NO2 | NOX | NO2 | NO2 | NOX | NO2 |  |  |
| INMA VAL | NO2 | NOX |  |  |  |  |  | NO2 |
| MOBA | NO2 | NOX | PM10 | PM2.5 | NOX | NO2 |  |  |
| RHEA | PM10 | PM10 | PM10 | PM10 |  | PM10 |  |  |

**Table A4: Year of noise data assigned to each time point**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Cohort** | **preg** | **y1** | **y2** | **y3** | **y4** | **y5** | **y6** | **y7** | **y8** | **y9** | **y10** | **y11** | **y12** |
| ALSPAC | 2006 |  |  |  |  |  |  |  |  |  |  |  |  |
| BIB | 2006 |  |  |  |  |  |  |  |  |  |  |  |  |
| DNBC | 2012 |  |  |  |  |  |  |  |  |  |  |  |  |
| EDEN NAN | 2005 |  |  |  |  |  |  |  |  |  |  |  |  |
| EDEN POI | 2009 |  |  |  |  |  |  |  |  |  |  |  |  |
| GENR | 2012 |  |  |  |  |  |  |  |  |  |  |  |  |
| INMA GUIP | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| INMA SBD | 2006 |  |  |  |  |  |  |  | 2012 |  |  |  |  |
| INMA VAL | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| MOBA | 2006 |  |  |  |  |  |  |  |  |  |  |  |  |
| RHEA | 2015 |  |  |  |  |  |  |  |  |  |  |  |  |

**Table A5: Year of Landsat image assigned to each time point for NDVI**

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

**Table A6: 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 |  |  |  |  |  |  |  |  |  |  |  |  |  |

**Table A7: 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 |