Some Title

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Abstract

Background

Objectives

Methods

Results

Discussion

- Authorship must follow the ICMJE's criteria. Author names should be listed in ScholarOne and author contributions should be detailed in the cover letter ("Author A…"). Neither names nor contributions should appear in the blinded manuscript. Do not include conflicts of interest.
- The use of the word "effect(s)" as a proxy for "association(s)" is discouraged.
- The length of the abstract must be less or equal than 200 words, and should be unstructured, stating the research questions, the methods used, and the results and conclusions of the research.
- The length must be <4,000 words, excluding abstract, references, tables, figure captions, acknowledgments, and Supplementary Material.
  - Use the AMA format.
  - In-text citations: full-sized Arabic numerals in parentheses within the sentence.
- Submission: SER members receive a 10% discount on the fees per page. This should be requested in the cover letter. Also 20% discount for Open Access charges. If uploading a single file (document, tables, figures, SM), designate the file as "Main document - anonymous".

1 Introduction

Do not use "Introduction" as a heading.

1.1 Background and rationale

- Brief review of the literature to summarize current knowledge.
  - Acknowledge inconsistencies.
  - For each study, indicate whether it was observational or experimental, and note key characteristics of study populations or experimental models.
- Explain the scientific background and rationale for the investigation being reported.
  - Identify knowledge gaps addressed by the current study.
- Provide context for the study: include information on exposures and outcomes, and why they are relevant to environmental health.

1.2 Objectives

- Provide a clear description of the study hypotheses/aims/objectives, and eventually an overview of the approach used to address them.

2 Methods

2.1 Study population and design

The Human Early-Life Exposome (HELIX) is an ongoing project which aims to characterize early-life exposures and their potential association with endogenous biomarkers and health outcomes[1]. It consists of six existing population-based birth cohort studies across Europe: BiB (Born in Bradford, UK)[2], EDEN (Study of determinants of pre- and postnatal developmental, France)[3], INMA (Environment and Childhood, Spain)[4], KANC (Kaunas Cohort, Lithuania)[5], MoBa (The Norwegian Mother and Child Cohort Study, Norway)[6], and Rhea (Mother–Child Cohort in Crete, Greece)[7], for a total of 32,000 mother-child pairs. A HELIX subcohort of 1,200 mother-child pairs was fully characterized for the external and internal exposome, including exposure and omics biomarkers during childhood. Eligibility criteria for inclusion in the HELIX subcohort included: a) age 6-11 years, with a preference for 7-9 years; b) availability of sufficient stored pregnancy blood and urine samples; c) availability of complete address history from first to last follow-up; d) no serious health problems, which might affect the results of the clinical testing. Further information can be found in[8].

Ethical permission was obtained from the relevant authorities in the corresponding country.

2.2 Participants

- Cohort study: eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.
- Cross-sectional study: give eligibility criteria, and the sources and methods of selection of participants.
- Describe informed consent protocols.
- Report how and by whom *race* or *ethnicity* was defined, and why this information was included in the study design. Disaggregate race and ethnicity data to the fullest extent possible.

2.3 Variables

- Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers.
- Explain the rationale for treating race as an exposure, confounder, effect modifier, or other type of variable in analyses.
- Units (in `log`):
  - `hitrtse` in `ms`.
  - EDCs in `microg/L`.

  - Cortisol production and cortisone production in `ng/mL`.
  - Cortisol metabolism and 11bHSD in `NA`.

2.3.1 Confounders

- For RQ1 I used creatinine values from HELIX. For RQ3 the ones from the steroids dataset. For RQ2, I included in the model both variables.

2.3.2 Endocrine disrupting chemicals

2.3.3 Corticosteroids

2.3.4 Neurodevelopment

2.4 Data sources and measurement

- For each variable of interest, give sources of data and details of methods of assessment (measurement).

2.5 Bias

- Describe any efforts to address potential sources of bias.

2.6 Study size

- Explain how the study size was arrived at.

2.7 Quantitative variables

- Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why.

2.8 Statistical methods

- In RQ2, I included the logarithm of the denominator in the RHS. In RQ3, I used the logarithm of the ratio in the RHS.
- Methods for selecting potential confounders (provide DAGs).
- Whenever possible, mathematical equations should be written on a single line. For multiplication, use a times sign.
- Describe all statistical methods with assumptions, including those used to control for confounding.
  - Description of outcome model, weighting method, estimand, and balance assessment.
  - Description of method used to estimate effects (e.g., g-computation).
  - Description of method used for SE and CI.
- Describe any methods used to examine subgroups and interactions (sub-group analysis or moderation analysis or analysis of effect-modification).
- Explain how missing data were addressed.
- Cohort study: explain how loss to follow-up was addressed.
- Cross-sectional study: describe analytical methods taking account of sampling strategy.
- Describe any sensitivity analyses.
- When referring to previous publications for methods' details, include a brief description of the approach, key assumptions and limitations, and any deviation.
- Names and version numbers for the used software packages, including non-data arguments if deviating from the default ones.

3 Results

3.1 Participants

- Give reasons for non-participation at each stage.

3.2 Descriptive data

3.3 Outcome data

3.4 Main results

- All results on which study conclusions or inferences are based, including null findings and results of secondary or sensitivity analyses, must be reported. Use of sub-headings that describe the nature of the results (but no declarative statements).
  - Provide a clear and concise description of all findings without extrapolating beyond the study results.
  - Do not limit results to those *statistically significant* or that support the study hypotheses. Avoid using statistical significance testing as the sole or primary criterion for interpreting the obtained results. If significance testing or p-values are used, report numeric p-values, rounded to 1-2 digits, for all results. Use an uppercase italic letter "P", and the values should not be bolded. Indicate whether are 1- or 2-sided.
- Give unadjusted and confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included. Include the number of observations for each analysis after accounting for missing data. Include numeric data within figures (e.g., forest plots), or provide tables with corresponding numeric data for all figures.
  - `marginaleffects` tables.
- Report category boundaries when continuous variables were categorized.

3.5 Other analyses

- Report other analyses done (e.g., analyses of subgroups and interactions, and sensitivity analyses).

4 Discussion

4.1 Key results

- Summarise key results with reference to study objectives.
- Provide a review of the relevant literature to put the study findings into context.
  - It should be complete and balanced, including inconsistent results.

  - It should include, for each source, sufficient details: study design, sample size, population, specific exposures and outcomes.

4.1.1 What does the literature say?

- EDCs and neurodevelopment (ANT).
- EDCs and corticosteroids.
- Corticosteroids and neurodevelopment (ANT).

4.2 Limitations

- Discuss limitations of the study, taking into account sources of potential bias or imprecision.
- Discuss both direction and magnitude of any potential bias.

Some limitations:

- Cross-sectional study.
- Chemicals measured in night and morning samples, whereas metabolites (the outcome) were measured only in night samples.
- Cortisol measured at night, when should be lowest.
- Change of estimand when trimming weights.
- Model misspecification.
- Mixtures effect.
- Residual confounding.
- Some confounders were not used since large percentage of missing values.
- Multiple comparisons.

4.3 Interpretation

- End with a summary of the key findings and their implications for the study hypotheses, future research, and policy.
- Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.

4.4 Generalisability

- Discuss the generalisability (external validity) of the study results.

5 Funding

References

1. Vrijheid M, Slama R, Robinson O, et al. The human early-life exposome (HELIX): Project rationale and design. *Environ Health Perspect.* 2014;122(6):535-544. doi:10.1289/ehp.1307204

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