LifeCycle Analysis Plan: Trajectories of Health Inequalities V1

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# Background and aims

Whilst it is well-established that children from low socio-economic position (SEP) generally have worse mental and physical health outcomes, the majority of this research is from cross-sectional studies. Longitudinal designs are important to establish the age at which inequalities emerge and the course that they take1. Where socio-economic inequalities are present, there are three main trends that can occur: (i) increasing inequality (“Cumulative disadvantage”), (ii) narrowing inequality or (iii) stable inequality2.

Longitudinal research into inequality is most developed for BMI and height, and generally supports the increasing inequality hypothesis. In developed countries lower SEP has been associated with higher BMI from as early as 9 months3, with most studies finding the gap increasing over time4–7. Similarly for height, higher SEP is associated with longer birth length3,8,9 with these differences increasing over time9,10. However, results are not entirely consistent: for example Howe et al. 2013 reported stable trajectories of inequality in fat mass,1 and Howe et al. (2012) reported that the majority of differences in height at age 10 are accounted for by differences in birth-length.8 Child sex is a potentially important modifier, with greater BMI inequalities observed for women in some1,3,7, but not all studies.4

For other outcomes, especially mental health and neurocognitive development longitudinal research is more sparse and findings more varied. Whilst a number of studies have reported higher levels of behavioural/externalising problems in lower SEP children as young as three11,12, to the best of our knowledge only one study has explicity modelled how these differences develop over time, reporting stable inequality1. Socioeconomic differences in internalising symptoms are of smaller magnitude13, but again there is limited research on how these differences develop over time.1,14

In terms of cognitive and language development, discrepent findings have been reported. Whilst higher SEP is associated with superior reading and language development, some studies have reported that these differences remain constant15,16, some to decrease1, or to show a non-linear pattern of first narrowing and then increasing17. These discrepencies may in part be due to the specific cognitive outcome or relate to the education system of the country in which they were conducted. For other outomes, e.g. (respiratory and motor development) there is very limited existing research on the development of inequalities over time18.

The primary aim of this study is to describe trajectories of socioeconomic inequality for key health outcomes across childhood. Specifically, we aim to:

1. Identify the age at which inequalities emerge,
2. Describe the course of these inequalities (increasing, decreasing, stable)

Our secondary aim is to investigate whether inequality trends are moderated by child sex.

# Eligibility and inclusion criteria

To be eligible for inclusion, studies must have data on:

1. At least one of the outcomes described below (Table [[tab:outcomes]](#tab:outcomes)), measured at a minimum of one time point, and
2. Maternal education at birth.

Eligible studies can be from any geographical area and with participants from any ethnic background. A review of the LifeCycle catalogue and work package harmonisation inventories shows that all cohorts have information on the exposure (maternal education) and at least one of the chosen outcomes (details in Table [[tab:outcomes-cohort]](#tab:outcomes-cohort)).

# Analysis plan

## Outcomes

Table [[tab:outcomes]](#tab:outcomes) lists the proposed outcome measures for the study. Outcomes have been chosen to capture key indicators across the following domains of development: (i) Anthropometric, (ii) Cardiometabolic, (iii) Cognitive, (iv) Language, (v) Mental health, (vi) Motor skills. Future projects may wish to focus in more detail on one particular domain (e.g. on more fine-grained aspects of mental health).

[tab:outcomes]Selected outcome measures

|  |  |  |
| --- | --- | --- |
| Outcome | LifeCycle variable name | Unit |
| Height | height\_x | cm |
| Weight | weight\_x | kg |
| Systolic blood pressure | sbp\_x | mm Hg |
| Expiratory volume | TBC | litre |
| Cognitive development | p\_nvi\_x\_x\_st\_a | z-score |
| Language development | p\_lan\_x\_x\_st\_a | z-score |
| Internalising | p\_int\_x\_x\_st\_a | z-score |
| Externalising | p\_ext\_x\_x\_st\_a | z-score |
| Motor skills | p\_gm\_x\_x\_st\_a | z-score |
|  |  |  |
|  |  |  |

Note mental health measures should parent-reported as these are likely to be more ubiquitous and accurate at younger ages.

Note: Systolic vs diastolic blood pressure?

Table [[tab:outcomes-cohort]](#tab:outcomes-cohort) shows our estimation of available outcomes for each cohort:

[tab:outcomes-cohort]Estimated available data by cohort

|  |  |
| --- | --- |
| X1 | X2 |
| ALSPAC | Motor, Internalising, Externalising, Language, Executive function, Memory, Respiratory, Blood pressure, Height, Weight |
| BiB | Blood pressure, Height, Weight |
| CHOP | Internalising, Externalising, Blood pressure, Height, Weight |
| DNBC | Internalising, Externalising, Height, Weight |
| EDEN | Motor, Executive function, Blood pressure, Height, Weight |
| ELFE | Motor, Internalising, Externalising, Language, Height, Weight |
| GECKO | Internalising, Externalising, Blood pressure, Height, Weight |
| GEN-R | Motor, Internalising, Externalising, Respiratory, Height, Weight |
| INMA | Motor, Internalising, Externalising, Language, Executive function, Memory, Respiratory, Blood pressure, Height, Weight |
| MoBa | Motor, Internalising, Externalising, Language, Executive function, Height, Weight |
| NFBC1966 | Motor, Language, Height, Weight |
| NFBC1986 | Motor, Height, Weight |
| RAINE | Motor, Internalising, Externalising, Language, Executive function, Respiratory, Height, Weight |
| RHEA | Respiratory, Blood pressure, Height, Weight |
| SWS | Blood pressure, Height, Weight |

## Exposure

Maternal education at birth will be used as the indicator of socio-economic position (variable edu\_m\_0). Maternal education has been chosen as this information is available for all cohorts, is strongly related to future income and employment, and also reflects non-material family resources (e.g knowledge).19

The harmonised maternal education variable is based on the International Standard Classification of Education 97 (ISCED-97) and consists of three categories:

1. Low (No education to lower secondary; ISCED-97 catergories 0-2)
2. Medium (Upper and post-secondary; ISCED-97 categories 3-4)
3. High (Degree and above; ISCED-97 categories 5-6)

Note: Another option would be to additionally use Serena’s modelled disposal income: add a Word note suggesting this

## Covariates

The primary covariate will be child sex as this has previously been found to moderate the effect of SEP on some health outcomes.1

* Have a look to see what Laura did previously and what other papers did

Add a Word note looking for input on this.

Note: Conversation with Debbie: include proportion university education

Note: Do we also want to include some indicator or urbaness - e.g. likely predictor for some conditions (e.g. FEV), but maybe less likely for others.

Note: Do we want to include things like smoking or are we over-adjusting/getting the causal path wrong? Would we want to test this in future papers by mediation?

## Statistical analysis

In brief, a rank score will be calculated for maternal education and all outcome variables will z-standardised. Multi-level models will be used to estimate (i) socioeconomic differences at baseline and (ii) trajectories of difference over time. Analyses will be conducted separately for each sex, and results will be pooled by meta-analysis. The following sections set out these steps in detail.

### Step 1: Review and prepare available data

Participating cohorts should review available data on the outcomes in table [[tab:outcomes]](#tab:outcomes). Data should be converted into long-form with one variable indicating the child’s age in months at the time of measurement.

### Step 2: Standardise outcome variables

Standardised scores will be used to allow comparison between different outcomes. The WP6 variables (cognitive and language development, internalising, externalising and motor skills) are already standardised so no further transformation is required.

The remaining variables should be standardised for individual j at time point i as follows:

Note: Do we need to do any additional transformations? How do we handle data skew?

### Step 3: Calculate rank score for maternal education

Socioeconomic inequalities will be estimated using the Slope Index of Inequality (SII), an indicator of the difference between the lowest and highest categories of education which also takes into account the education distribution within the sample.20

In order to calculate this, the ordinal maternal education variable should first be converted to a rank score using the following procedure.21 First, the proportion of participants in each of the three educational categories should be calculated. These proportions are then used to calculate the rank range (from 0 - 1) for each educational category, from high to low. The rank mean for each category should be calculated and each level of the original maternal education variable assigned the respective value.

For example, if the proportion of individuals in each educational category from highest to loweest are 20%, 50% & 30%, the rank ranges are:

1. High: 0 - 0.20
2. Medium: 0.20 - 0.70
3. Medium: 0.70 - 1

The mean rank for each category and transformed values for the maternal education variable would therefore be:

1. High = 0.10
2. Medium = 0.45
3. Low = 0.85

### Linear mixed effects model

Linear mixed effect models will then be estimated for each outcome, separately for males and females. The model will contain fixed effects of (i) age, (ii) maternal education rank (calculated as above) and (iii) maternal education rank x age, and random individual-level effects for intercept and slope. The model specification is as follows:

$$Y\_{ij} = (\Beta0 + \mu0\_j) + (\Beta1 + \mu1\_j)(Age\_{ij}) + (\Beta2)(Maternal education\_j) + (\Beta3)(Age\_{ij} \\* Maternal education\_j) + e\_{ij}$$

The regression coefficient $\Beta2$ is the SII, and represents the difference in standard deviations in the outcome between the highest and lowest educational categories. The coefficient $\Beta3$ represents the change in SII for every month increase in age. From these coefficients predicted values of the SII can be calculated for across the age range, and plotted to illustrate the trajectory of inequality for each outcome.

## Output

Model output should contain:

1. Model coefficients and standard errors
2. Sample size used at each time point

In addition cohorts should report the following descriptive information:

1. Percentage of subjects in each education category

Note: what other descriptive info would it be useful to have.

Sample R code is provided at the end of this document to run the models and output the required information to .csv file.

Please send all output to Tim Cadman ([t.cadman@bristol.ac.uk](mailto:t.cadman@bristol.ac.uk)).

For any studies that would prefer to transfer data for the Bristol team to complete analyses please let us know and we can help prepare relevant data transfer forms.

## Meta-analysis

Results from each cohort will then be pooled by meta-analysis, adjusting for the effect of cohort and the proportion of sample in the higher educational category. This latter adjustment is necessary as the SII is sensitive to population distribution.

* Look at McCrory paper about pooling eu cohort studies. Also look

# Code for running models

Note: Once we agree the analysis plan I will run using ALSPAC harmonised lifecycle data, and then add the code which other cohorts can then use to output the results to a .csv

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