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Report on the life course trajectories leading from early internalizing and externalizing indicators to subsequent psychopathology outcomes in childhood

LifeCycle report D6.1

Author(s):

Johanna L. Nader (Norwegian Institute of Public Health)

Jennifer R. Harris (Norwegian Institute of Public Health)

Tim Cadman (University of Bristol)

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LIFECYCLE Project
Coordination and leadership:

Erasmus MC
Generation R (Na-2918)
PO box 2040
3000 CA Rotterdam
The Netherlands

Phone: +31 (0)10 704 3405
Email: lifecycle@erasmusmc.nl
Web: lifecycle-project.eu

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List of Abbreviations

ADBB: Alarme Détresse Bébé

ADHD: Attention deficit hyperactivity disorder

ALSPAC G2: Avon Longitudinal Study of Parents And Children - Generation 2

ALSPAC: Avon Longitudinal Study of Parents And Children

ANT: Attention Network Task

ASD: Autism spectrum disorder

ASQ: Ages and Stages Questionnaire

BAS: Behavioural Approach System

BDI: Becks Depression Inventory

BiB: Born In Bradford Study

BRIEF: Behaviour Rating Inventory of Executive Function

BSID: Bayley Scales of Infant Development

CAST: Childhood Asperger Syndrome Test

CBB: CogState Brief Battery

CBCL: Child Behaviour Checklist

CD: Cognitive disorder

CHOP: Childhood Obesity Programme study

CPRS-R: Revised Conners' Parent Rating Scale

DataSHaPER: DataSchema and Harmonization Platform for Epidemiological Research

DAWBA: Development and Well-Being Assessment

DDST: Denver Developmental Screening Test

DISC-IV: Diagnostic Interview Schedule for Children

DNBC: Danish National Birth Cohort

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, 4th edition

DST: Digit Span Test

EDEN: Étude des Déterminants pré et postnatals du développement et de la santé de l'Enfant

ELFE: Étude Longitudinale Française depuis l'Enfance

FTT: Finger Tapping Test

GECKO: Groningen Expertise Centrum voor Kinderen met Obesitas

GMDS: Griffiths Mental Development scales

GPT: Grooved Pegboard Test

HBCS: Helsinki Birth Cohort Study

INMA: INfancia y Medio Ambiente Project

MB-CDI: MacArthur-Bates Communicative Development Inventories

M-CHAT: Modified Checklist for Autism in Toddlers

MeDALL: Mechanisms of the Development of ALLergy

met Overgewicht

MoBa: Norwegian Mother, Father and Child Cohort Study

N-Back: Working Memory Test

NEPSY-II: Developmental NEuroPSYchological Assessment, Second Edition

NFBC1966/1986: Northern Finland Birth Cohort studies

NINFEA: Nascita e INFanzia, gli Effetti dell'Ambiente

PLIKS: Psychosis-like symptoms measure

Rhea: Mother Child Cohort in Crete

RPM: Raven's Progressive Matrices

SCQ: Social Communication Questionnaire

SDMT: Symbol Digit Modalities Test

SDQ: Strengths and Difficulties Questionnaire

SRS: Social Responsiveness Scale

SWAN: Strengths and Weaknesses of Attention-Deficit/Hyperactivity Disorder Symptoms and Normal Behaviour Scale

SWS: Southampton Women's Survey

TEA-ch: Test of Everyday Attention for Children

TMT: Trail Making Test

TRF: Teacher Report Form

WASI: Wechsler Abbreviated Scale of Intelligence

WP: Work package

WPPSI: Wechsler Preschool and Primary Scale of Intelligence

YRBSS: Youth Risk Behaviour Surveillance System

YSR: Youth Self-Report

Executive summary

The aim of Task 6.1 in the LifeCycle project is to develop and study mental health trajectories leading from early behavioural and cognitive indicators to adverse mental health outcomes in later life. Associations between early-life exposures and longitudinal trajectories are used to construct life course models that account for interactive and cumulative effects on mental health. Stressors in this context include those introduced through socio-economic, migration, urban environment, and lifestyle factors. This report describes fundamental work undertaken in the development of mental health trajectories in the LifeCycle project and presents overviews and findings from our analysis for each step of this work. This includes a comprehensive inventory of the available mental health data resource from 17 cohorts participating in Task 6.1 of the LifeCycle project, and construction of a detailed harmonization plan that was used to achieve equivalence between different assessment instruments and measures. This harmonization was completed to facilitate parallel and meta-analyses of data in the LifeCycle cohorts across mental health domains. In addition, results from preliminary analyses about patterns and trends that characterize these harmonized data between and within cohorts are presented. Finally, preliminary results from ongoing studies utilizing harmonized exposure and outcome data within the context of Task 6.1 are provided. The unique opportunities to perform extensive collaborative mental health life course research through the LifeCycle project are briefly presented and the potential to use epidemiologically relevant findings to address preventative approaches in global public health is considered and discussed.

1. Background

The purpose of task 6.1 in the LifeCycle project is to construct life course trajectories of behavioural and cognitive function, specifically internalizing and externalizing behavioural indicators in early childhood, to study how these are associated with adverse psychopathology (such as ADHD, ASD, CD, anxiety and depression) in later childhood, adolescence and adulthood. Taking into account a range of potential pre-pregnancy, pregnancy, and postnatal environmental influences (collectively defined as the early-life exposome, developed in WP1 of the project), these trajectories will be studied through multi-level models, to identify latent patterns of behavioural measures that predict developmental outcomes and thus can be targeted through early intervention and support strategies.

Life course trajectories have been extensively used to examine how difficulties and challenges at multiple stages in early life are associated with later mental and physical health problems. Studies focused on internalizing and externalizing mental health symptoms in childhood report significant effects of distinctive developmental trajectories on features such as early-adult functioning (Oerlemans et al. 2020), well-being (Kjeldsen et al. 2016), psychotic symptoms (Gin et al. 2021), risky behaviours (Wilson et al. 2015), and ADHD (Millenet et al. 2018). Similar studies have further shown that exposure to environmental features such as poverty (Comeau and Boyle, 2017), parental depression (Mowbray et al. 2018), parental emotional support (Woodman et al. 2016), community violence (Taylor et al. 2018), and parental education (Wang et al. 2018) can significantly impact externalizing and internalizing trajectories, and thus comprise additional risk and protective factors that can influence the degree to which these trajectories are associated with later mental health.

The wealth of literature published to date has repeatedly demonstrated significant associations between deviating early behavioural trajectories and later health problems. However, a large proportion of these studies focused on single cohorts with limited sample sizes, and a restricted combination of mental health indicators and outcomes. WP6 in the LifeCycle project was designed to test and improve upon the wider applicability of such findings, increase statistical power and interpretability, and enhance scientific opportunities to study important factors that shape behavioural trajectories. Co-analysis of data across cohorts is essential to achieve this and data harmonization is a prerequisite for such analyses. However, the mental health and exposure data existing in major European cohorts have never been systematically mapped. A crucial element of such mapping is to determine which data are available longitudinally and at which specific ages so that developmental trajectories can be constructed and compared. Such systematic mapping is also critical for assessing the harmonization potential within the data and provides the foundation for European collaborations to articulate specific and feasible research studies. Detailed descriptive analyses of harmonized data to comparatively explore and illustrate trends across domains and measures further lays the groundwork for assessing equivalence between harmonized variables, which is another key feature emphasized in this report.

Harmonization of mental health data across multiple cohorts helps to maximize the scientific potential of these data through pooled mental health analyses for more than 250,000 pregnancy and birth cohort participants across Europe and Australia. This enables statistically powered studies examining a wide array of exposure and outcome relationships across numerous mental health constructs and domains. Results provide evidence-based insights that can inform and enhance the development of public health strategies across diverse EU populations.

2. Mental health data in the LifeCycle Project

The LifeCycle Project includes 19 cohorts in 13 countries that are contributing with mental health data on offspring: Avon Longitudinal Study of Parents and Children (ALSPAC/ALSPAC G2, United Kingdom), Born in Bradford (BiB, United Kingdom), EU Childhood Obesity Programme (CHOP, Germany/Italy/Spain/Poland/Belgium), Danish National Birth Cohort (DNBC, Denmark), Etude des Déterminants du développement et de la santé de l'Enfant (EDEN, France), Etude Longitudinale Française depuis l'Enfance (ELFE, France), Groningen Expert Center for Kids with Obesity Drenthe cohort (GECKO Drenthe cohort, The Netherlands), the Generation R Study (Generation R/Generation R Next, The Netherlands), Helsinki Birth Cohort Study (HBCS, Finland), Infancia y Medio Ambiente (INMA, Spain), The Norwegian Mother, Father and Child Cohort Study (MoBa, Norway), Northern Finland Birth Cohorts (NFBC1966/1986, Finland), Nascita e INFanzia: gli Effetti dell'Ambiente (NINFEA, Italy), The Raine Study (Australia), Rhea Mother & Child Cohort Study (Rhea, Greece), and the Southampton Women's Survey (SWS, United Kingdom).

In order to map the available data across multiple age groups and illustrate the types of instruments used and domains these covered, a comprehensive inventory was developed. This would also form the basis of developing the project-specific harmonization protocol, as an understanding of the available mental health measures was key to evaluating where equivalence between cohorts could be achieved. The mental health data collectively contain information pertaining to the children from more than 200 measures, covering eight clinical domains across 60 dimensions. A majority of these measures assess domains under a broad banner of ‘mental health’, encompassing psychological functions, cognitive and executive functions and psychological development (67.0%; 136 of 203), covering dimensions such as neurodevelopmental disorders, internalising and externalising symptoms, temperament and mental diagnoses. Further domains include language skills (31.0%; 63 of 203), executive functions (29.1%; 59 of 203), memory (11.3%; 23 of 203) and general intelligence (8.4%; 17 of 203). There are many commonalities between mental health domain-types and significant overlap in the age groups with measures in specific domains (Figure 1). This makes it possible to harmonise the data (Fortier et al. 2010). Most of the cohorts continuously follow up their participants, and the availability of harmonised data will tend to increase with time.

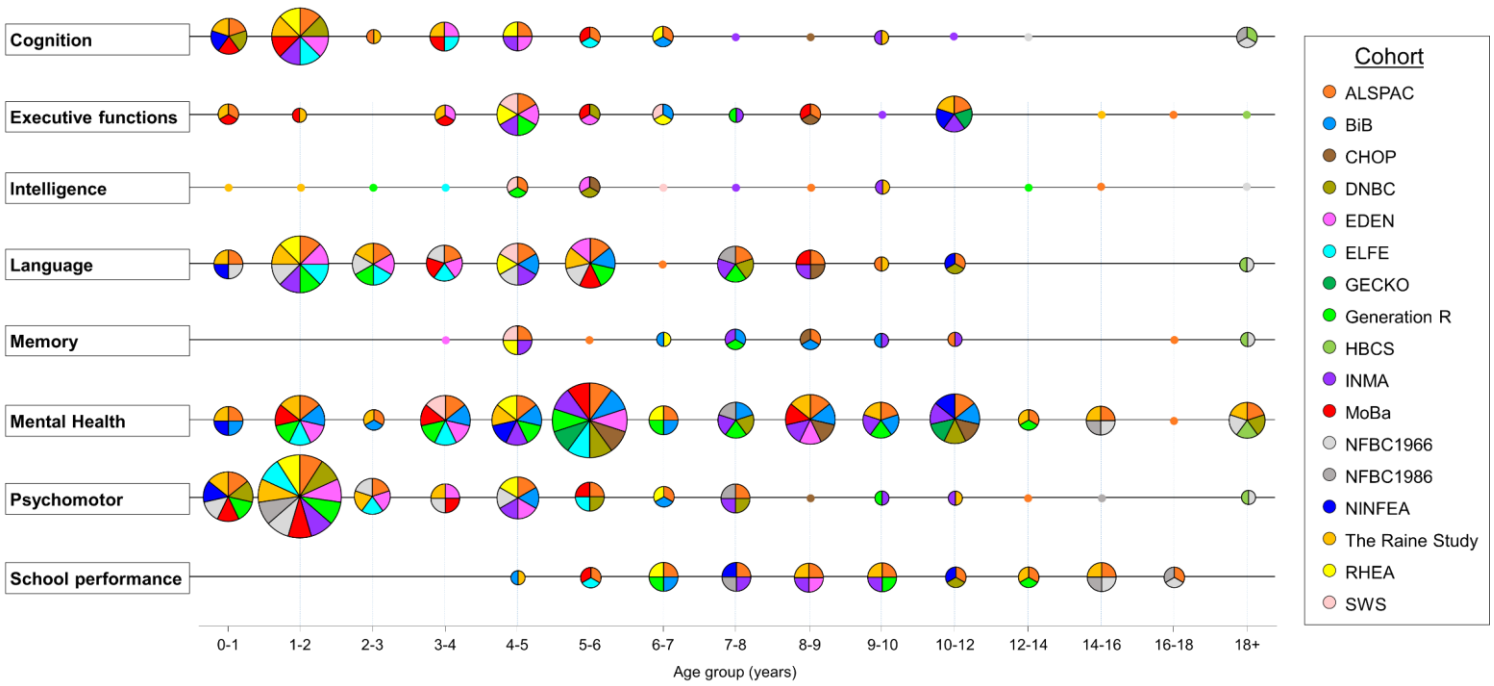


Figure 1. Distribution of mental health measures and cognitive domains across LifeCycle cohorts by age (figure taken from Nader et al.; *under revision*)

Basic illustration of the range of developmental domains of mental health measures and participant ages for cohort data in LifeCycle WP6. Relative pie chart sizes correspond to the number of overlapping cohorts for a given domain category and age range.

In addition to mapping the available data by domains and age groups, it was important to determine we wanted to describe which cohorts had employed items from the same mental health, cognitive and motor function measures, as these data can be pooled or co-analysed more directly without the need for harmonisation (Figure 2). The Child Behaviour Checklist (CBCL) and Strengths and Difficulties Questionnaire (SDQ) are two examples of measures that are often used in epidemiological studies and for which there is a high degree of overlap between the LifeCycle cohorts, and a wide range of age groups for which these measures are available. This presents the opportunity to perform a variety of parallel analyses between cohorts, facilitating informative comparative studies in cases where pooling or co-analysis of data may not be possible. The information displayed in Figure 2 has not been compiled previously and is invaluable on several fronts. It will greatly aid the LifeCycle consortium in developing sub-projects, it can be used by other consortia and researchers to plan new research projects, and it aids European cohorts in building their strategies for further cohort development. For instance, it makes readily available information about where there may be gaps in the availability of important data and where there are new opportunities for collaboration.

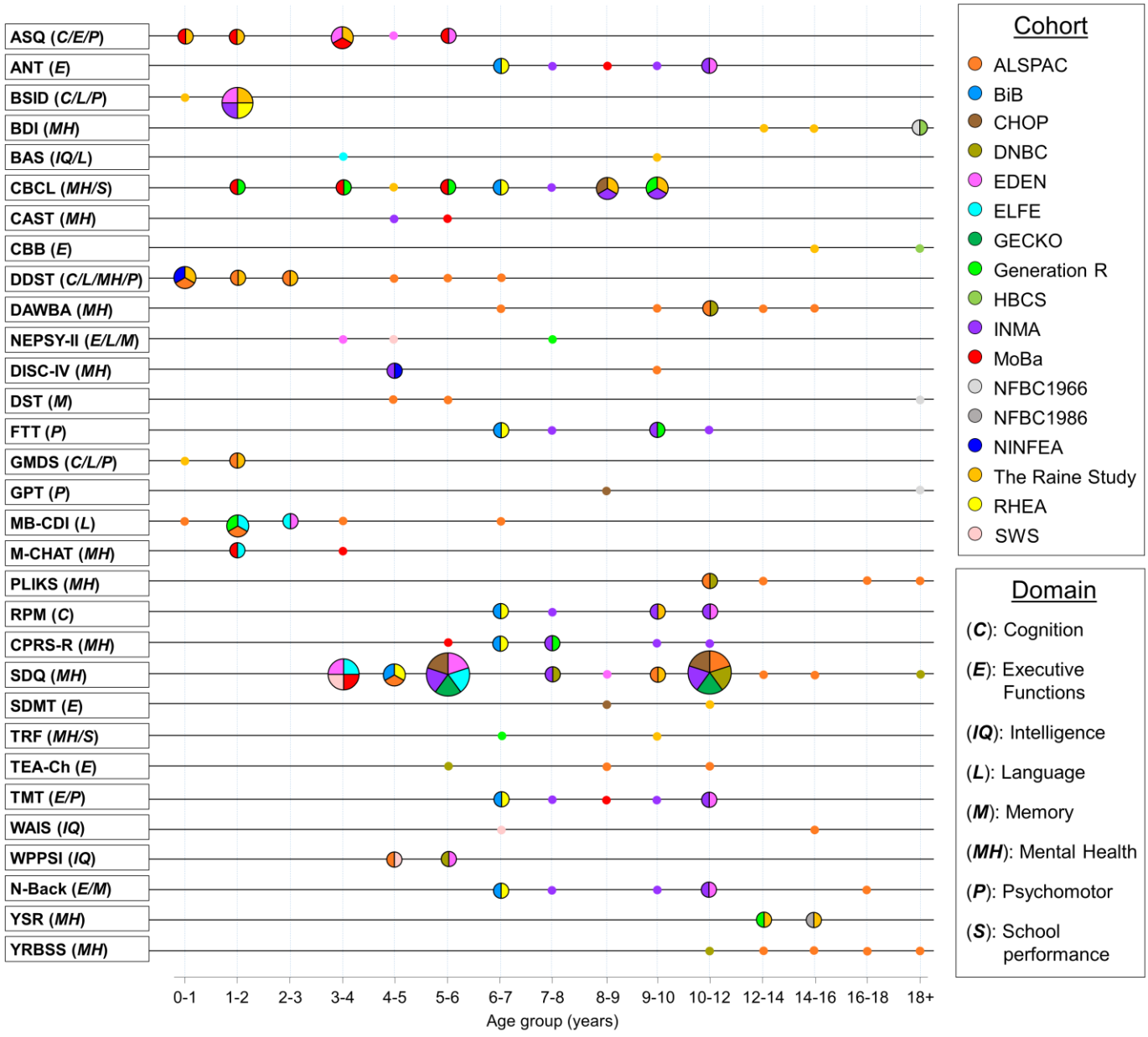


Figure 2. Overview of overlap in mental health and cognitive measures in the LifeCycle cohorts providing mental health data (figure taken from Nader et al.; *under revision*)

Overlap of specific assessment instruments used to collect cognitive and behavioural developmental data in cohorts participating in the LifeCycle project. Relative pie chart sizes correspond to the number of overlapping cohorts for a given domain category and age range.

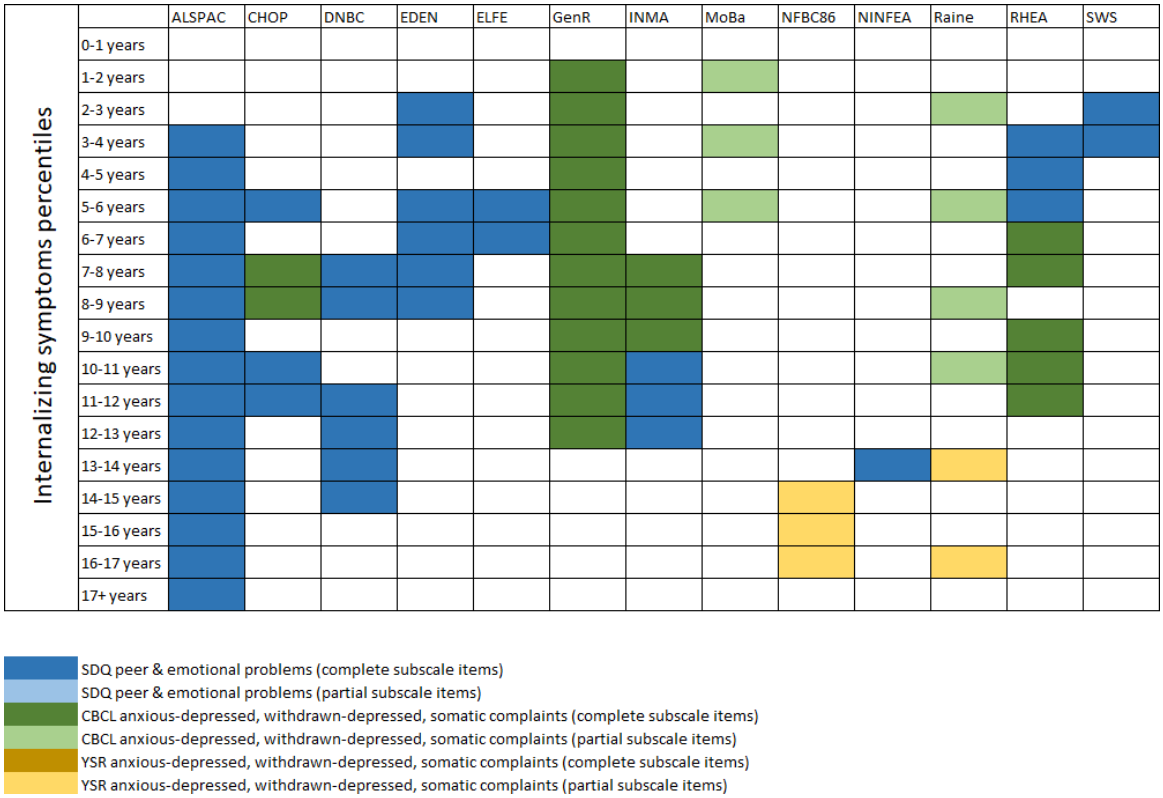
3. Harmonization plan

3.1 Harmonized mental health data in the LifeCycle project

The harmonization protocol developed in WP6 of LifeCycle aimed to generate cognitive and behavioural variables that would facilitate longitudinal meta-analyses across cohorts and measures (Appendix II). The strategy for harmonization was based on an adapted version of the DataSHaPER guidelines (Fortier et al. 2010), and utilized the framework developed in the MeDALL project to perform rigorous, transparent, and effective harmonization (Antó et al. 2012). The procedure used in WP6 is primarily based on statistical harmonization, whereby standardized percentiles derived from prorated scores were calculated across cognitive and behavioural outcomes. This was done to achieve equivalence between cohorts in instances where different instruments and/or scale items were used to derive the same measures.

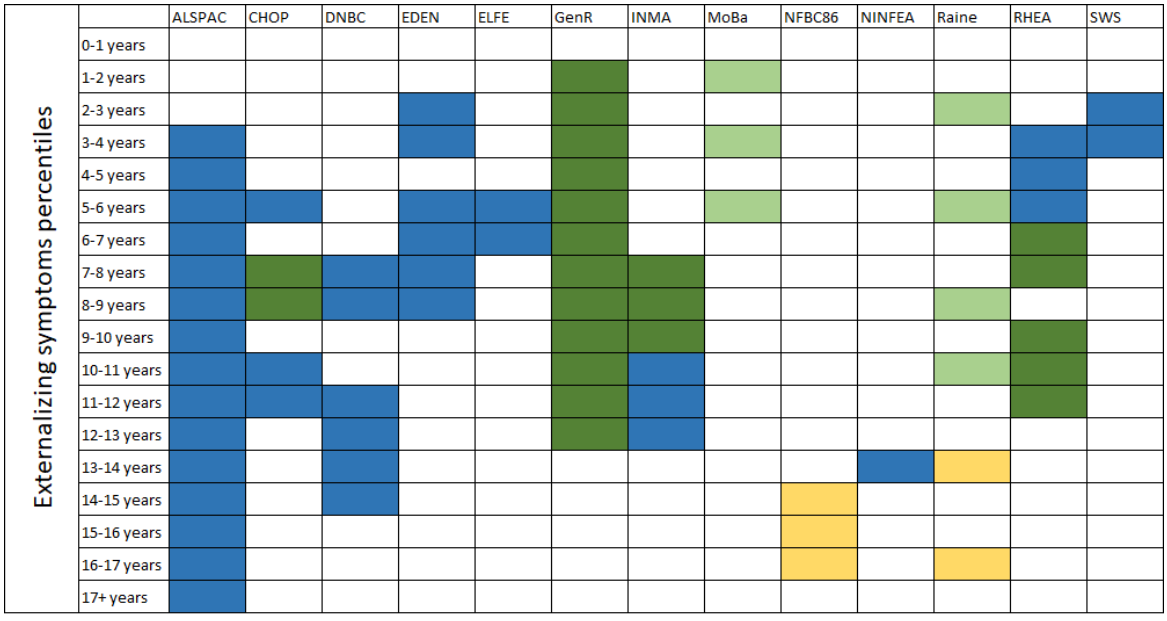
The harmonization in Task 6.1 enables the construction of trajectories that illustrate developmental paths of early behavioural symptoms leading to later adverse psychopathology outcomes. To achieve this, participating cohorts in the LifeCycle project prioritized harmonization of four relevant behavioural areas, focusing on internalizing problems, externalizing problems, ADHD symptoms, and Autism spectrum disorder symptoms. All the measures harmonised thus far in WP6 and in the other work packages can be found in the LifeCycle online catalogue (https://catalogue.lifecycle-project.eu/), which provides an overview of all the measures harmonized for each cohort across age groups, as well as details about the specific harmonization algorithms. Thirteen cohorts have completed harmonization of the four priority behavioural areas, comprising a diverse range of source instruments and data that span all infant, child, and adolescent ages (Figure 3 A-D). A total of three instruments were used to harmonize internalizing and externalizing behaviours (SDQ, CBCL, YSR), while a more diverse range of source instruments were utilized to perform harmonization of ADHD (SDQ, CBCL, CPRS-R, DSM-IV, SWAN) and ASD symptoms (ADBB, M-CHAT, SRS, CAST, SCQ), and cohorts varied in the availability of data from full versus partial scale items. Harmonization in this instance thus made it possible for cohorts that administered only subsets of assessment questionnaires to contribute with variables for meta-analyses, increasing both the potential sample size available for future analyses (and thus statistical power), as well as the range of ages available for modelling mental health trajectories.

(A)



SDQ peer & emotional problems (complete subscale items)
SDQ peer & emotional problems (partial subscale items)
CBCL anxious-depressed, withdrawn-depressed, somatic complaints (complete subscale items)
CBCL anxious-depressed, withdrawn-depressed, somatic complaints (partial subscale items)
YSR anxious-depressed, withdrawn-depressed, somatic complaints (complete subscale items)
YSR anxious-depressed, withdrawn-depressed, somatic complaints (partial subscale items)

(B)



SDQ hyperactivity/inattention and conduct problems (complete subscale items)
SDQ hyperactivity/inattention and conduct problems (partial subscale items)
CBCL rule breaking behaviour, aggressive behaviour (complete subscale items)
CBCL rule breaking behaviour, aggressive behaviour (partial subscale items)
YSR delinquent Behaviour, aggressive behaviour (complete subscale items)
YSR delinquent Behaviour, aggressive behaviour (partial subscale items)

(C)

(D)

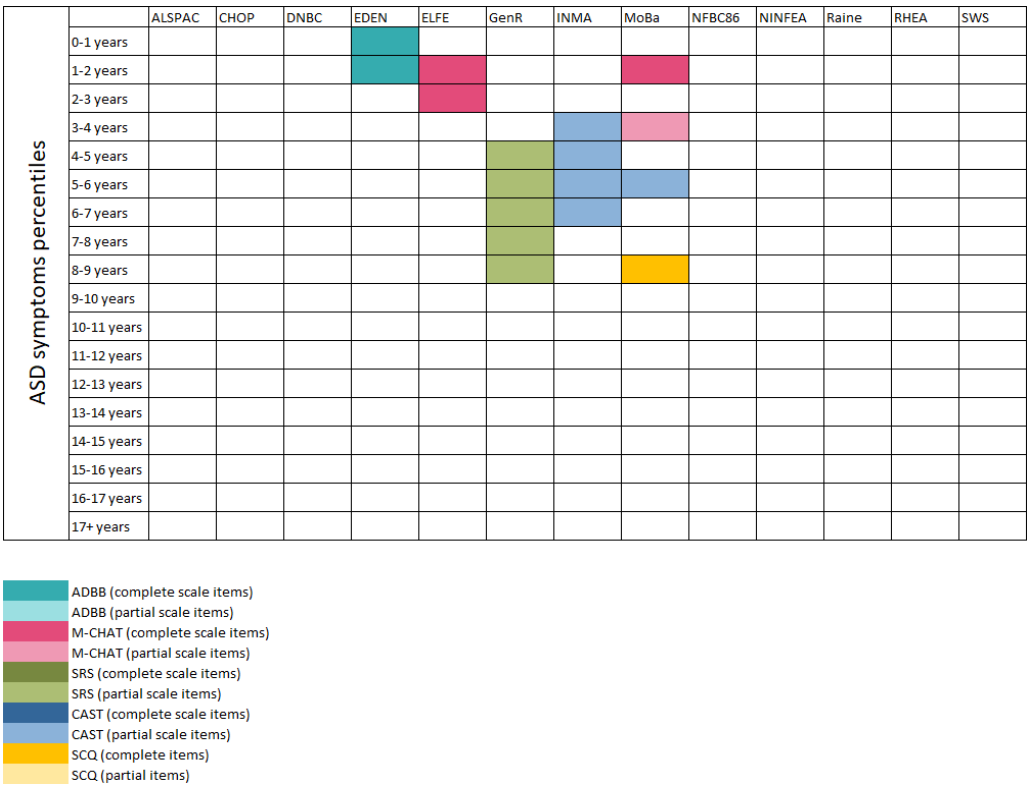


Figure 3 A-D. Overview of cognitive and behavioural data in the LifeCycle project used to harmonize standardized percentiles for internalizing (A), externalizing (B), ADHD (C), and ASD (D) symptoms

3.2 Inspection of trends and patterns

In order to assess how harmonized variables compare across age groups in participating cohorts, mean values for externalizing scores were calculated for participants with high ADHD scores (>50th percentile) and low ADHD scores (<50th percentile). This was done to examine whether the potential to detect differential indicator trajectories exists given a distinct psychopathology outcome. Sample trajectories of harmonized externalizing symptoms in early life leading to later ADHD outcomes illustrate the potential impact these harmonized data can have in causal developmental research (Figure 4). Trends for indicators across age appear largely dissimilar between cohorts, as could be expected for epidemiologically diverse populations such as these, but the consistent divergence between indicator trajectories by ADHD outcome demonstrates one of the important and impactful potential applications of these data in life course research. The combined sample sizes across ages and cohorts in this specific example highlight another significant strength, with total data available ranging from 975 to 42734 child participants in each age group between 0-17+ years. Together with the exhaustive resource of prenatal, pregnancy, and postnatal exposure variables harmonized in work packages 1-3 of the LifeCycle project, these data can thus be used to construct multilevel statistical models to study life course mental health trajectories in a way that accounts for important socioeconomic, urban environment, and lifestyle differences between and within cohort populations.

To address potential equivalence inconsistencies introduced by the use of different assessment instruments for collecting cognitive and behavioural data in individual cohorts, percentiles were additionally calculated for each of the harmonized indicator and outcome measures. This facilitates meta-analysis in cases where heterogeneity of scales compromises the degree to which population-level data can be pooled. Associations between harmonized externalizing symptom percentiles and ADHD symptom percentiles across age were evaluated to explore the potential of this approach for application to research, revealing strong patterns of correlation that hold across inter-cohort comparisons (Figure 5). Based on an inspection of the patterns, there appears to be an improved equivalence compared to raw and prorated scores, which improves the reliability in using these data for pooled analyses. The ability to confidently use and combine these harmonized behavioural and cognitive data to study exposure-outcome relationships of externalizing and internalizing behaviours leading to later psychopathology through trajectories is thus one of the core achievements made through the work done in Task 6.1 of the LifeCycle project.

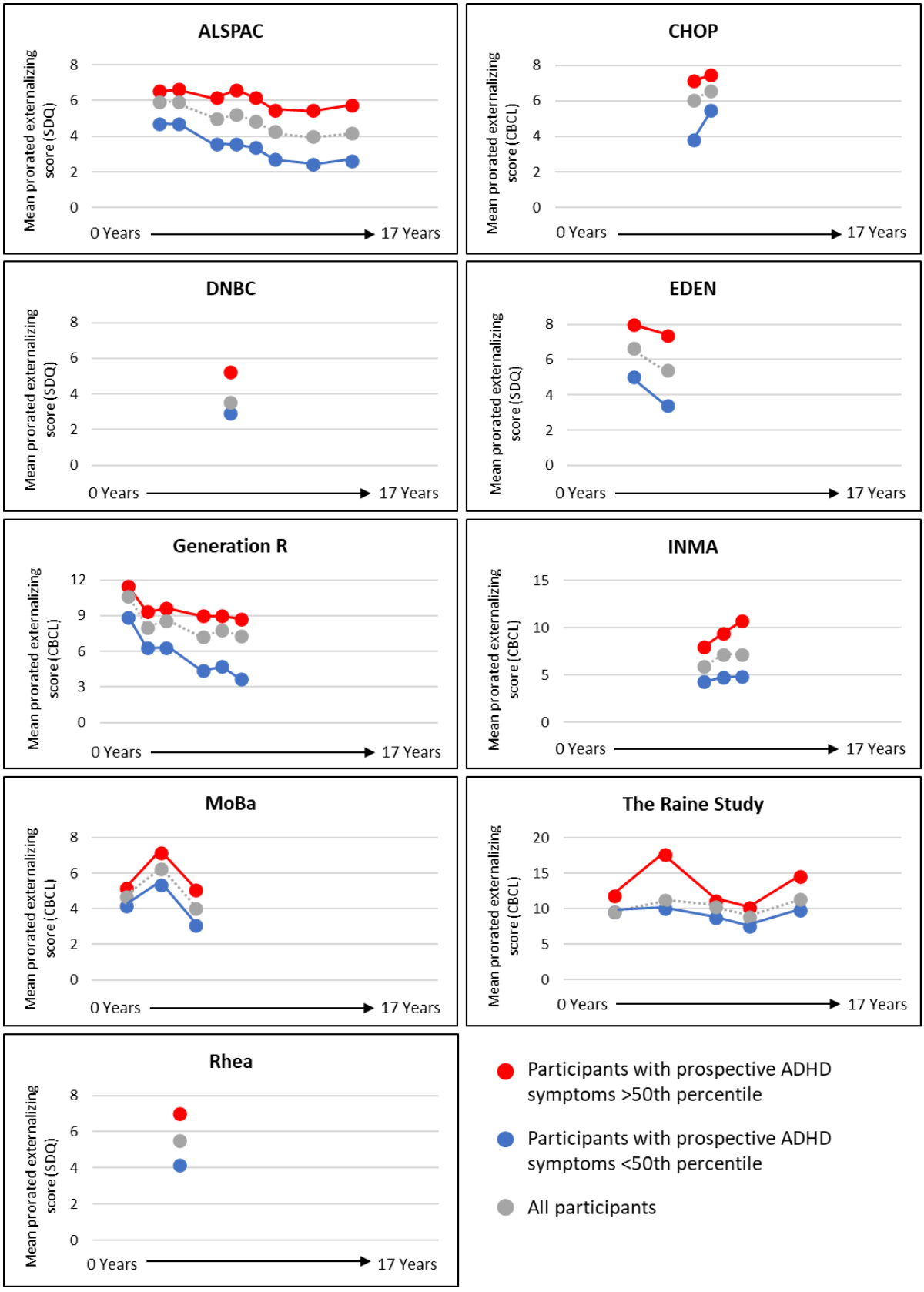
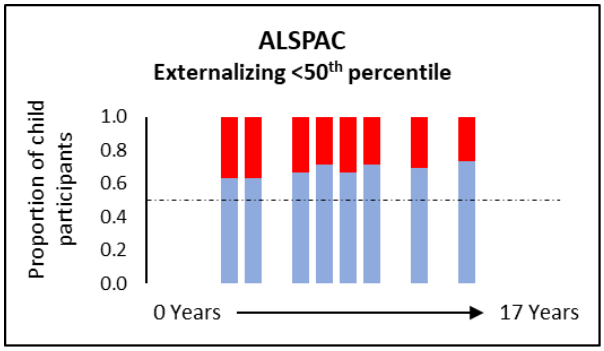
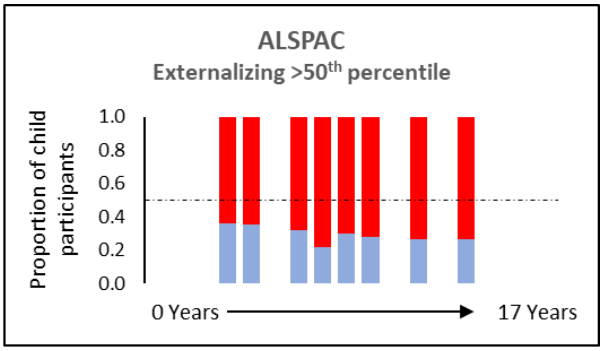


Figure 4. Basic trajectories for mean prorated externalizing symptom scores across childhood and adolescence by ADHD outcome


ALSPAC
Externalizing <50th percentile
Proportion of child participants
1.0
0.8
0.6
0.4
0.2
0.0
0 Years
17 Years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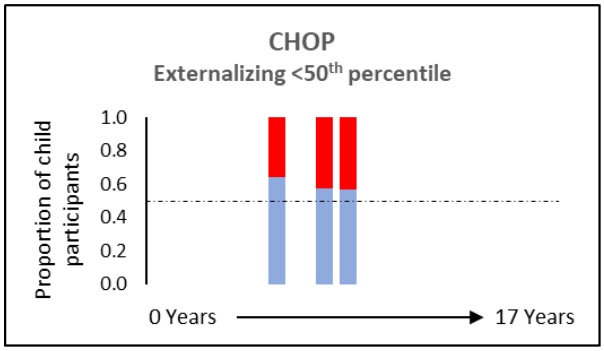
CHOP
Externalizing <50th percentile
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0.6
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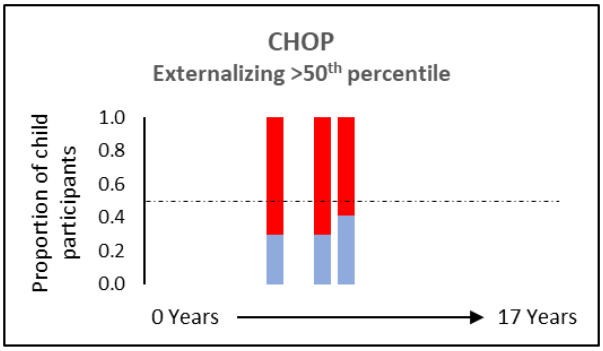
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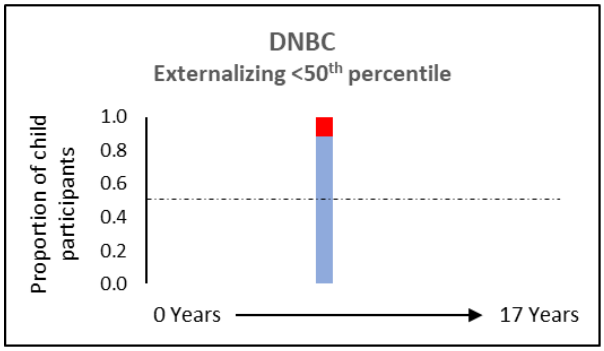
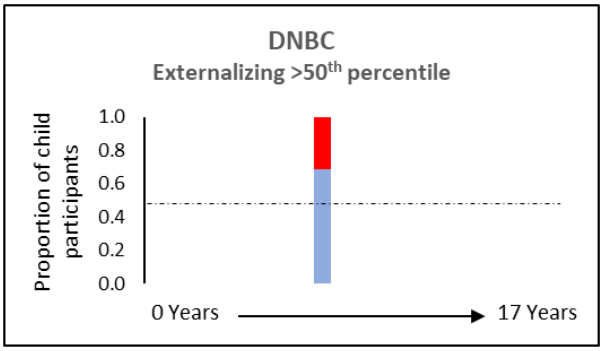

DNBC
Externalizing <50th percentile
Proportion of child participants
1.0
0.8
0.6
0.4
0.2
0.0
0 Years
17 Years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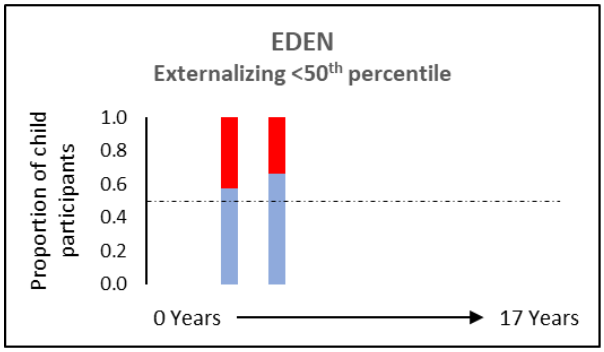
EDEN
Externalizing <50th percentile
Proportion of child participants
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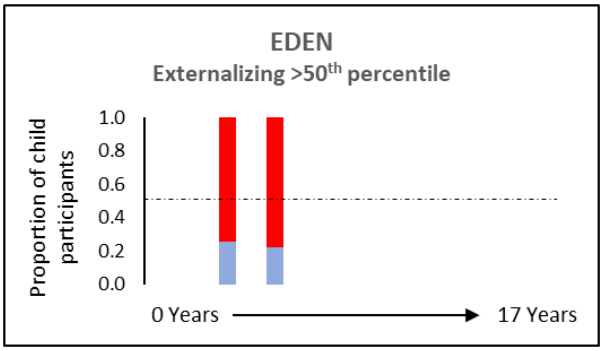
17 Years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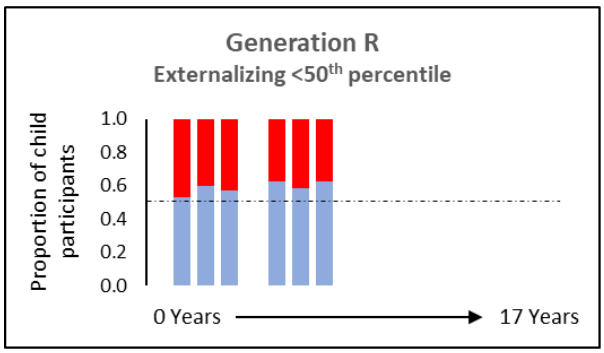
Generation R
Externalizing <50th percentile
Proportion of child participants
1.0
0.8
0.6
0.4
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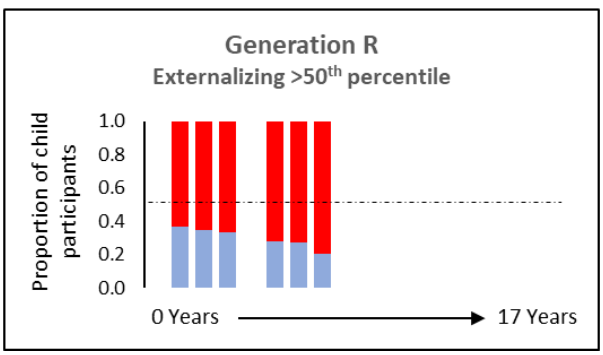
17 Years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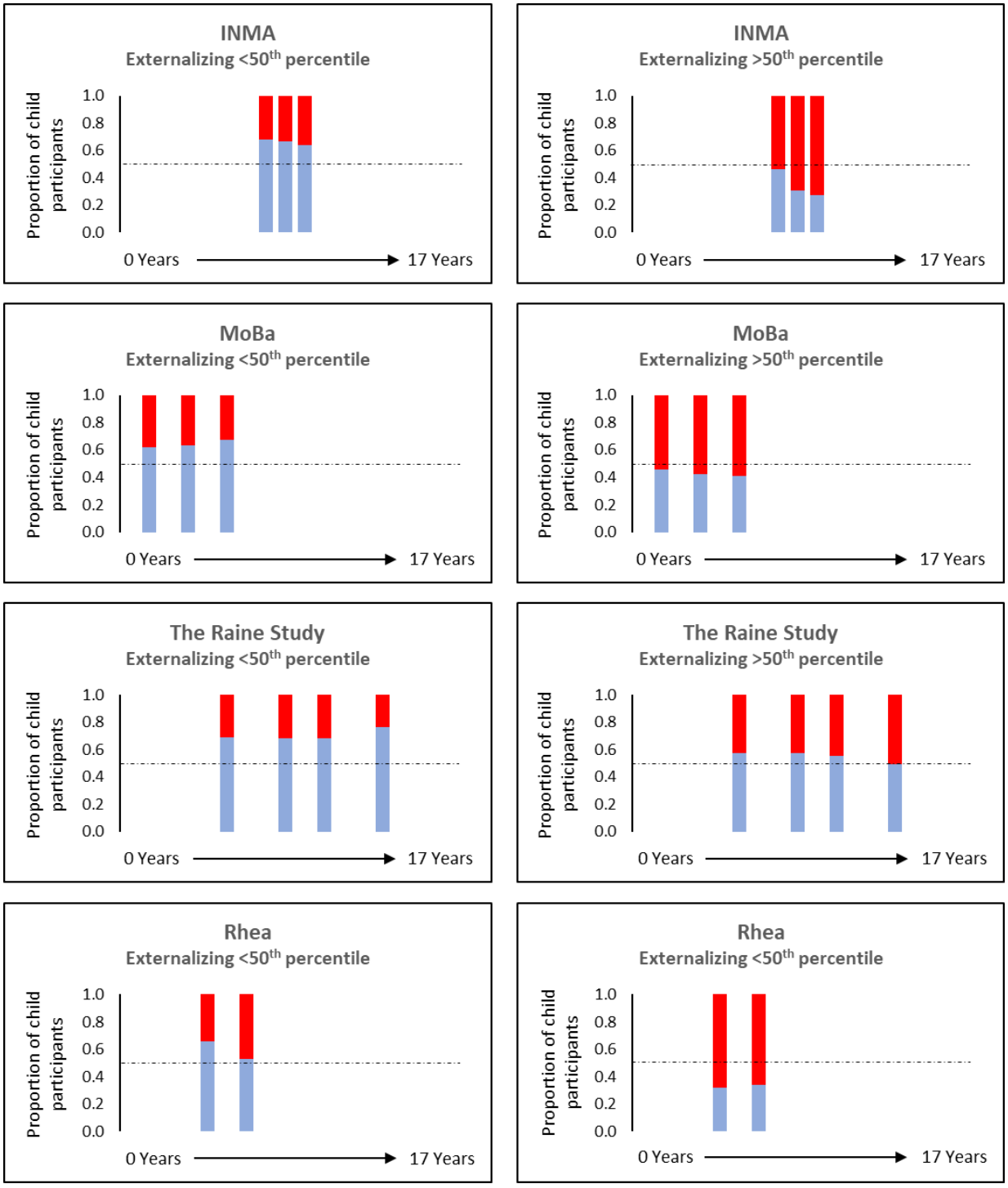


Figure 5. Relative proportion of child participants with ADHD symptoms above or below the 50th percentile by externalizing symptom score percentiles

4. Ongoing Dissemination Activities

4.1 Analyses of mental health trajectories

Methods

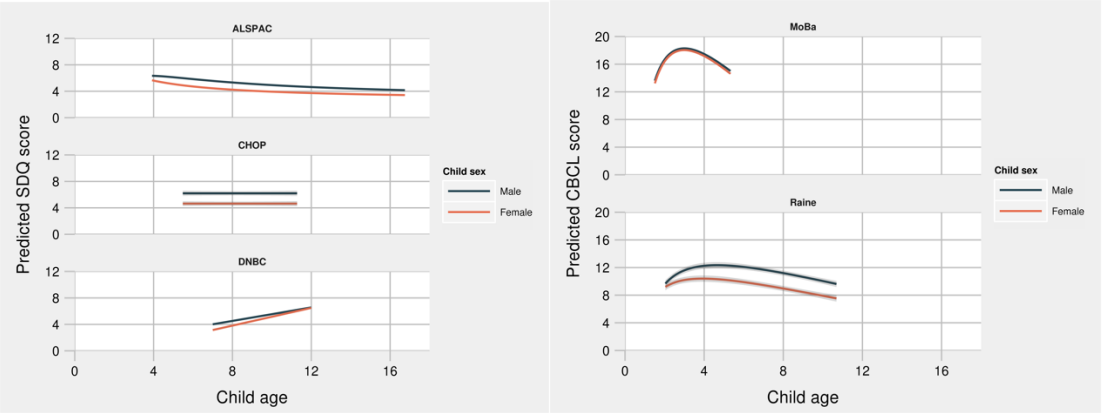
Sample
We included cohorts which had measured externalising at a minimum of 2 time points. This included ALSPAC (n = 10339, 7 measurement occasions), CHOP (n = 700, 3 measurement occasions), DNBC (n = 59413, 2 measurement occasions), MoBa (n = 69871, 3 measurement occasions), The Raine Study (n = 3318, 6 measurement occasions).

Measures
Two different measures of externalising were used: (i) Strengths and Difficulties questionnaire (SDQ; ALSPAC, CHOP, DNBC) and (ii) Child Behaviour Check List (CBCL; MoBa, The Raine Study). As these measures have different scales they were modelled as separate outcomes.

Data analysis
Externalising trajectories were described using multilevel growth curve models using fractional polynomials (Tilling et al. 2014). Multilevel models account for clustering within the data (ie the fact that the same individual contributes multiple observations at different time points). Fractional polynomial models use transformations of the age term to allow non-linear change over time. We include sex as a covariate as there is consistent evidence that males show higher levels of externalising symptoms (Warmuth et al. 2021). All analysis was conducted using DataSHIELD, a software solution that enables remote, non-disclosive federated analysis of data (Budin-Ljøsne et al. 2015).

Results

Figures 6 and 7 show trajectories of externalising using the CBCL and SDQ. Results are largely consistent, showing that symptoms peak around age 4-5 and decrease throughout childhood. The one anomalous finding is with the Danish National Birth Cohort, which appears to show an increase in symptoms over time. For ALSPAC, The Raine Study & CHOP males show higher levels of externalising throughout childhood, whereas differences are minimal for MoBa and DNBC.



Figures 6 & 7: Externalising trajectories measured by SDQ (left) and CBCL (right) (Tim Cadman et al; *unpublished*)

Discussion

Using data from over 130,000 children from five EU birth cohorts, we have described child externalising trajectories. Using data from multiple cohorts (which have collected data at different time periods) allows us to describe trajectories across the whole of childhood. This advances on studies using single cohorts which may only have data over a limited time range.

4.2 Other research underway using WP6 harmonized data

A number of other studies are currently underway that use the harmonized cognitive and behavioural data made available through the harmonization work done in WP6. The work completed thus far has laid the groundwork for multiple mental health studies, many of which are also studying trajectories and longitudinal effects of various early life exposures and experience on later mental health and developmental outcomes.

i.) **Mental health data in LifeCycle (Journal of Epidemiology; *under revision*)**
Lead: Nader and Harris (NIPH)
Cohorts: ALSPAC, BiB, CHOP, DNBC, EDEN, ELFE, GECKO, Generation R, HBCS, INMA, MoBa, NFBC1966, NFBC1986, NINFEA, The Raine Study, RHEA, SWS
Objective: describe child behavioral and mental health data and sample sizes in LifeCycle.

ii.) **Infant feeding and externalizing behaviours**
Lead: Nader and Harris (NIPH)
Cohorts: MoBa, Generation R, The Raine Study
Objective: illustrate and compare infant feeding practices and their association with early childhood externalizing morbidity.

iii.) **Longitudinal association between sleep, behavior and cognition**
Leads: Sabine Plancoulaine, Eve Reynaud, Kathrin Gürlich, Veit Grote
Cohorts: Eden, Elfe, Gecko, Bib, ALSPAC, SWS, INMA
Objective: associate sleep difficulties with behavioural and cognitive difficulties in preschoolers.

iv.) **Nature and Child Cognition and Behavior (study under planning)**
Payam Dadvand, Jordi Julvez, Jordi Sunyer
DNBC, HBC, EDEN, ELFE, CHOP, RHEA, NINFEA, MoBa, REPRO_PL, INMA, Generation R, BiB, ALSPAC, The Raine Study

v.) **Sibling effects and pre-maturity**
Leads: Ninha Silva, Eero Kajantie, Sylvain Sebert (UOULU)
Objective: 1) associate the presence of term-born sibling(s) with the health and social risk of the preterm child; and 2) investigate the impact of prematurity on term-born siblings' physical behavioral and social outcomes.

vi.) **Daycare and emotional and behavioural symptoms**
Leads: Maria Melchior, Barbara Heude, Marie-Aline Charles (INSERM)
Cohorts: EDEN, ELFE
Objective: investigate the relationship between childcare attendance prior to school entry and children's later psychological development.

vii.) **Maternal smoking score and mental health**
Leads: Justiina Ronkainen, Sylvain Sebert, Rae-Chi Huang, Phillip Melton, Ashleigh Lin (UOULU, UWA)
Objective: associate DNA methylation induced by maternal smoking during pregnancy with later behaviour scores in childhood and adolescence.

viii.) **Pregnancy lifestyle and child behavior**
Leads: Jordi Julvez, Raquel Garcia, Sílvia Fernández, Jordi Sunyer
Cohorts: ALSPAC, ERASMUS, MoBa, DNBC, The Raine Study, INMA, GECKO, CHOP, SWS, BiB
Objective: associate a maternal lifestyle score during pregnancy with the trajectories of child internalizing and externalizing problems.

ix.) **Urban exposome during pregnancy and early childhood and child cognitive and motor function**
Leads: Anne-Clair Binter, Monica Guxens (ISGLOBAL)
Cohors: ALSPAC, EDEN, GenR, INMA, MoBa, NINFEA, BiB, RHEA (+WP3 cohorts: ABCD, GASPII, PICCOLOPIÙ)
Objective: assess whether the urban exposome during pregnancy and early childhood is related to cognitive and motor function in children.

x.) **Urban exposome during pregnancy and early childhood and child emotional and behavioural problems**
Leads: Anne-Clair Binter, Monica Guxens (ISGLOBAL)
Cohorts: ALSPAC, EDEN, GenR, INMA, MoBa, NINFEA, BiB, RHEA, ABCD, GASPII, PICCOLOPIÙ
Objective: assess whether the urban exposome during pregnancy and early childhood is related to emotional and behavioural problems in children.

xi.) **Maternal postnatal depression and childhood temperament: insights from the Norwegian Mother and Child Study (MoBa)**
Leads: Johanna L. Nader (NIPH), Jennifer R. Harris (NIPH)
Cohorts: MoBa
Objective: This study uses data from the Norwegian Mother and Child Cohort Study (MoBa) to examine how maternal postnatal depression 6 months after birth predicts symptoms of activity, shyness and emotionality at three stages of preschool age (18 months, 36 months, and 5 years).

4.3 e-Learning Module: *Early Life Exposures in Later Health*

An open access e-Learning module will be launched on the ENeA platform (https://enea.med.lmu.de/) in Fall 2021. The module Early Life Exposures in Later Health consolidates the scientific evidence base and status of recommendations of LifeCycle topics and outcomes. This e-learning module is targeted to international allied healthcare professionals and researchers working in the field. By this means, research findings and WP6 outputs will be directly transferred into practical applications and effectively disseminated in line with current concepts of using digital information sharing with a broad global outreach.

5. Conclusions

The aim of Task 6. 1 was to develop and study mental health trajectories leading from early behavioural and cognitive indicators to adverse mental health outcomes in later life. In the first phase of this work we catalogued, harmonized, and utilized cognitive and behavioural cohort data to study mental health trajectories in child and adolescent participants within the framework of the LifeCycle project. Since the beginning of the LifeCycle project, an inventory of more than 200 mental health measures has been created, from which at least 245 individual harmonized variables were created for internalizing, externalizing, ADHD, and ASD symptom domains. The detailed work done to create an inventory in this task has already been transformed into a peer-review publication (Nader et al. 2021, Journal of Epidemiology; under revision). Analyses of data from more than 130,000 children participating in five LifeCycle cohorts provide comparisons of externalizing trajectories across five LifeCycle cohorts (ongoing study by Tim Cadman et al. described under section 4.1). This work demonstrates how the harmonized data have successfully been used to create longitudinal

mental health trajectories and provides new insights into cross-cohort patterns for these developmental outcomes. The combined resource of harmonized data available through the EU Child Cohort Network created in the LifeCycle project also lays the groundwork for further investigations of more complex developmental trajectories linking early life behavioural indicators with later psychopathology. Examples of such models that are under development and highly relevant to the LifeCycle data are illustrated by other LifeCycle efforts focused on analytic methods (Hughes et al. 2020) for longitudinal analysis in the lifecourse context.

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