Maternal education and cognitive development in 15 European very-preterm birth cohorts from the RECAP Preterm platform

Sentenac, Mariane

2021-12

Sentenac , M , Benhammou , V , Aden , U , Ancel , P-Y , Bakker , L A , Bakoy , H , Barros , H , Baumann , N , Bilsteen , J F , Boerch , K , Croci , I , Cuttini , M , Draper , E , Halvorsen , T , Johnson , S , Kallen , K , Land , T , Lebeer , J , Lehtonen , L , Maier , R F , Marlow , N , Morgan , A , Ni , Y , Räikkönen , K , Rtimi , A , Sarrechia , I , Varendi , H , Vollsaeter , M , Wolke , D , Ylijoki , M & Zeitlin , J 2021 , ' Maternal education and cognitive development in 15 European very-preterm birth cohorts from the RECAP Preterm platform ' , International Journal of Epidemiology , vol. 50 , no. 6 , pp. 1824-1839 . https://doi.org/10.1093/ije/dyab170

http://hdl.handle.net/10138/352125
https://doi.org/10.1093/ije/dyab170

unspecified
acceptedVersion

Maternal education and cognitive development in 15 European very preterm birth cohorts from the RECAP *Preterm* platform

Mariane Sentenac[1*], Valérie Benhammou[1], Ulrika Aden[2], Pierre-Yves Ancel[1], Leonhard A. Bakker[3], Hannah Bakoy[4,5], Henrique Barros[6], Nicole Baumann[7], Josephine Funck Bilsteen[8,9], Klaus Boerch[8], Ileana Croci[10], Marina Cuttini[10], Elizabeth Draper[11], Thomas Halvorsen[4,12], Samantha Johnson[11], Karin Källén[13], Tuuli Land[14], Jo Lebeer[15], Liisa Lehtonen[16,17], Rolf F. Maier[18], Neil Marlow[19], Andrei Morgan[1,19], Yanyan Ni[7,19], Katri Raikkonen[20], Anass Rtimi[1], Iemke Sarrechia[15], Heili Varendi[14], Maria Vollsaeter[4,5], Dieter Wolke[7], Milla Ylijoki[16,21], Jennifer Zeitlin[1]

Affiliations:

1 Université de Paris, CRESS, Obstetrical Perinatal and Pediatric Epidemiology Research Team, EPOPé, INSERM, INRA, F-75004 Paris, France

2 Department of Women's and Children's Health, Karolinska Institute, Stockholm, Sweden

3 Child Health, Netherlands Organization for Applied Scientific Research (TNO), Leiden, Netherlands

4 Department of Clinical Science, University of Bergen, Norway

5 Department of Paediatric and Adolescent Medicine, Haukeland University Hospital, Bergen, Norway.

6 EPIUnit--Instituto de Saúde Pública da Universidade do Porto, Porto, Portugal.

7 Department of Psychology, University of Warwick, Coventry, United Kingdom

8 Department of Pediatrics, Hvidovre University Hospital, Hvidovre, Denmark

9 Section of Epidemiology, Department of Public Health, University of Copenhagen, Copenhagen, Denmark

10 Clinical Care and Management Innovation Research Area, Bambino Gesù Pediatric Hospital, Roma, Lazio, Italy

11 Department of Health Sciences, University of Leicester, Leicester, United Kingdom.

12 Department of Sports Medicine, Norwegian School of Sport Sciences, Oslo, Norway.

13 Dep of Obstetrics and Gynecology, unit of Reproduction Epidemiology, Institution of Clinical Sciences, Lund, University of Lund, Sweden

14 Department of Pediatrics, University of Tartu, Children's Clinic of Tartu University Hospital, Tartu, Estonia
15 Department of Family Medicine & Population Health, Disability Studies, Faculty of Medicine & Health Sciences, University of Antwerp, Antwerp, Belgium
16 Department of Pediatrics and Adolescent Medicine, Turku University Hospital Turku, Finland
17 Department of Clinical Medicine, University of Turku, Turku, Finland
18 Children's Hospital, University Hospital, Philipps University Marburg, Marburg, Germany
19 UCL Elizabeth Garrett Anderson Institute for Women's Health, University College London, London, WC1E 6AU, United Kingdom.
20 Department of Psychology and Logopedics, University Of Helsinki, Helsinki, Finland.
21 Department of Paediatric Neurology, University of Turku and Turku University Hospital, Turku, Finland

Corresponding author
Mariane Sentenac
INSERM 1153
Maternité Port Royal
53 Avenue de l'Observatoire, 75014 Paris
Phone: +33 1 42 34 55 77
E-mail: mariane.sentenac@inserm.fr

Word count (article + abstract) = 3246 words

ABSTRACT

Background

Studies are sparse and inconclusive about the association between maternal education and cognitive development among children born very preterm (VPT). While this association is well-established in the general population, questions remain about its magnitude among children born VPT whose risks of medical and developmental complications are high. We investigated the association of maternal education with cognitive outcomes in European VPT birth cohorts.

Methods

We used harmonised aggregated data from 15 population-based cohorts of children born <32 weeks' gestational age (GA) or <1500g from 1985 to 2013 in 13 countries with information on maternal education and assessments of general development at 2-3 years and/or IQ between 4-15 years. Term-born controls (≥37 weeks' GA) were available in 8 cohorts. Maternal education was classified as: low (primary/lower secondary); medium (upper secondary/short tertiary); high (bachelor's/higher). Pooled standardized mean differences (SMD) in cognitive scores were estimated (reference: high educational level) for children assessed at ages 2-3, 4-7 and 8-15 years.

Results

The study included 10 145 VPT children from 12 cohorts at 2-3 years, 8829 from 12 cohorts at 4-7 years and 1865 children from 6 cohorts at 8-15 years. Children whose mothers had low, compared with high, educational attainment scored lower on cognitive measures (pooled unadjusted SMDs: 2-3y=-0.32 (95%CI: -0.43;-0.21); 4-7y=-0.57 (-0.67;-0.47); 8-15y=-0.54 (-0.72;-0.37)). Analyses by GA subgroups (<27 versus ≥27 weeks), in children without severe neonatal morbidity and term controls yielded similar results.

Conclusions

Across diverse settings and regardless of degree of prematurity, low maternal education was associated with lower cognition.

KEYWORDS

Very preterm births, child development, IQ, intelligence, maternal education, cohort

KEY MESSAGE

- We found lower cognitive scores throughout childhood for children born very preterm whose mothers had low educational levels, with no difference in the effect by degree of prematurity.
- The robust nature of the association in multiple contexts provides good generalizability for our study findings.
- Understanding the association of social factors with cognitive deficit in children born very preterm is essential because these children may benefit most from early intervention

INTRODUCTION

Brain development is complex, involving genetic, physiological, and environmental influences. There is a large body of literature on the neurodevelopment of children born very preterm (VPT) (<32 weeks of gestation) demonstrating a higher risk of cognitive deficits compared to children born at term.[1-3] Brain injury and other neonatal morbidities (e.g. bronchopulmonary dysplasia) are strongly associated with adverse neurodevelopmental outcomes,[3,4] but VPT children without morbidities are also at increased risk for cognitive and other neurodevelopmental impairments.[5]

It is also well established that the social environment in the family and community plays a role in determining cognitive functioning,[6] but there is a lack of comparable evidence regarding the influence of these factors among children born VPT. There are contradictory hypotheses about how social context affects outcomes in VPT children as compared to the general population. Some have posited that social factors would have less effect because of the strong association between biological risk factors and neurodevelopment. For example, a recent study found the effect of maternal education on early language acquisition was attenuated in children with higher clinical risks (e.g. extreme prematurity <28 weeks' gestational age (GA); severe neonatal morbidities).[7] In contrast, others hypothesise that the effect of social factors may be stronger because parental involvement plays a crucial role in enabling children to compensate for potential developmental difficulties, with results suggesting that social factors may modify the effect of preterm birth on cognitive outcomes in children.[8,9] A final possibility is that social factors operate in similar ways regardless of underlying medical risks linked to prematurity or other pregnancy complications. Understanding and quantifying this relationship is particularly important given the impact of VPT

birth on average intelligence quotients (IQs),[2,3] estimated at about 12 points lower than among term-born children, and the long-term consequences on school and employment outcomes.[10,11]

Recent systematic reviews and meta-analyses have shown the complexity of synthesising existing evidence on the relationship between the social environment and cognitive development in children born VPT.[2-4] First, although maternal educational level tends to be the most common indicator of social differences,[3,12-15] other variables are also used (e.g. parental occupation, marital status, family income).[15] Second, even among studies using maternal educational level, international variation in definitions makes it difficult to compare outcomes using common categories. This heterogeneity has prevented meta-analyses from deriving pooled effects of the role of maternal education on childhood cognition. Further variability also results from diversity in ages of assessment[4] and in the domain of cognitive functioning (e.g. executive function, language, general cognition).[7,9,15] A recent Delphi study on priorities for research on the consequences of VPT birth with clinicians, researchers, policy-makers and people with lived-experiences identified the impact of social circumstances as a top-ten theme.[16]

The purpose of this study is to investigate the association of maternal educational level with cognitive outcome in children born VPT, using data from population-based, prospective cohort studies in various European contexts. Based on the heterogeneous conclusions reported in the literature, we hypothesised that the association could vary by country (i.e. higher educational levels could be more protective in certain cultural contexts), key periods in childhood (i.e. with a stronger effect later in childhood), and the degree of prematurity (i.e. with a potentially attenuated effect for children born extremely preterm).

METHODS

Study population and design

This study included 23 European population-based cohorts of children born VPT (<32 weeks of gestation) or with very low birthweight (<1500g) participating in the RECAP Preterm (Research on European Children and Adults Born Preterm) platform which aims to promote research on the consequences of VPT birth.[16] Cohorts were eligible if they could provide 1) information on maternal education at delivery or follow-up, and 2) an assessment of general development at 2-3 years and/or general cognitive ability between 4 and 15 years of age. Some cohorts also comprised a control population of term-born children with measures of maternal education and cognitive outcomes. Fifteen cohorts contributed data.[17-31] The study used aggregated and summary data provided according to a standardised protocol. All cohorts have ethical authorisations and informed consent from families for research on the consequences of VPT birth.

Maternal educational level

Maternal educational level was the primary exposure. The preferred definition was the highest educational level at delivery, although some cohorts only had data on the number of years of schooling. For cohorts that could not provide maternal education at delivery, educational level at follow-up was used. We used the International Standard Classification of Education (ISCED)[32] to create harmonised categories by mapping each cohort's educational variable into one of nine levels, which were then grouped into three categories: (1) low (ISCED 0-2; lower secondary or less), (2) medium (ISCED 3-5; upper secondary/post-secondary/short cycle tertiary), and (3) high (ISCED 6-8, bachelor degree/equivalent or more). We selected this classification, which has been used in analyses of maternal education and preterm birth in Europe,[7,33] to maximise sample sizes in each educational category.

General development and cognitive outcomes

The primary outcome was cognitive functioning in childhood assessed by standardised tests (with normative or control samples) or validated instruments including parent-report questionnaires, which provided continuous scores (standard scores or raw scores, respectively). Cognitive tests or multi-domain tests of child general development were used across the cohorts.

Other variables

To describe the cohorts, we selected social and perinatal variables available in all cohorts and for which harmonised definitions could be specified: maternal age (≥35 years), cohabiting status (living in a couple), maternal country of birth (or if not available maternal nationality or ethnicity), parity, GA, birthweight, child sex, multiple pregnancy, caesarean birth, Apgar score at 5 minutes <7, and breastfeeding at discharge from neonatal care. Neonatal morbidities included necrotizing enterocolitis (stages II-III; NEC-II/III[34]), intraventricular haemorrhage (stages III-IV, IVH-III/IV[35]), cystic periventricular leukomalacia (cPVL), bronchopulmonary dysplasia (supplemental oxygen or ventilation at 36 weeks, BPD) and retinopathy of prematurity (stages III–V, ROP-III/V[36]).

Analysis strategy

Analyses were carried out separately by age group: infancy (2-3 years), early childhood (4-7 years), later childhood (8-15 years). The drop-out rate was computed in each period by dividing the number of participants by the number of survivors at discharge from the neonatal hospitalisation. All analyses were performed on complete cases.

Descriptive tables of perinatal and sociodemographic characteristics were provided on the sample at first follow-up (i.e. two-year follow-up, if followed at two and five).

We used a meta-analytic approach based on aggregate-level data provided by each cohort following a standardised iterative protocol. First, frequencies of selected variables were collected to guide the harmonisation process. Second, harmonised variables were verified and described in summary tables. Third, cohorts provided unadjusted data on cognitive outcomes (i.e. frequencies, mean scores, standard deviations) by maternal educational level for each age group. Lastly, marginal means of cognitive scores were estimated using common multivariable regression models, adjusted for child sex and maternal age as a potential confounder.[4] Random intercept models were specified to account for the correlation within multiple pairs when this was possible at the cohort level and also to account for clustering within countries in the European EPICE/SHIPS study.[29] Differential dropout was accounted for multiple imputation (EPIPAGE 2[37]) or inverse probability weighting (EPICE/SHIPS[7]). Unadjusted and adjusted estimates were provided for children overall, stratified by severity of the VPT birth (<27 weeks, ≥27 weeks), and on the control population of term-born children when available. Estimates were also computed for children born VPT without severe neonatal morbidities (NEC-II/III, IVH-III/IV, cPVL, BPD, ROP-III/V) known to be strong predictors of cognition.[38] We analysed recent cohorts (births≥2000) to allow for more standardised definitions of these morbidities.

The unadjusted and adjusted estimates were pooled by random effects meta-analyses using the DerSimonian and Laird inverse-variance method.[39] The effect measure was expressed as the standardised mean difference (SMD, Hedges g)[39] in cognitive scores between groups defined by maternal educational level (reference group: high education level), making it possible to pool cognitive raw and standardised scores.[39] Pooled SMDs were estimated from both unadjusted and adjusted mean scores,[40] and presented with 95% confidence intervals (CI). The effect size was interpreted as small (SMD=0.2-0.4 of a SD unit), moderate (SMD=0.5-0.8), or large (SMD>0.8).[41]

The unadjusted SMDs were presented as the primary results as this represents the most common meta-analytical approach.[1-3,42] Tests for sub-group differences based on random-effects models were performed. Between-cohort consistency was quantified using I^2 statistics, and we used traditional thresholds of low (I^2<25%), modest (I^2=25-50%) and high (I^2>50%) heterogeneity.[43] Effect modification was investigated using sub-group analyses.

The leave-one-out method was applied in sensitivity analyses in meta-analyses that had high heterogeneity.[43] Pooled risk ratios (RRs) were also computed by random effects meta-analyses to estimate the risk of cognitive deficit (score<1 standard deviation (SD) below the standardised mean or other established cut-offs for unstandardized tests) by maternal education level. Additional sub-group meta-analyses investigated potential biases related to the timing of maternal education measurement (birth vs follow-up), test administration mode (parent vs examiner) and type of test (cognition vs multi-domain) in infancy. The R "meta" package version 4.11-0 was used for pooled analyses.[44,45]

RESULTS

Cohort characteristics

Fifteen cohorts from 13 countries contributed data on 22 528 live VPT births (**Table 1)**. Inclusion criteria were based principally on GA, with cohorts focusing on births <32 weeks or <27 weeks; older cohorts used birthweight thresholds or included births at 32 weeks' GA. Cohorts covered births from 1985-1986 to 2011-2012. Follow-up rates ranged from 51.2% to 98.7%, leading to the participation of 10 145 VPT children at 2-3 years (12 cohorts), 8829 at 4-7 years (12 cohorts), and 1865 at 8-15 years (6 cohorts). In 8 cohorts, data were available for control populations of term-

born children (GA≥37 weeks, n=2642 in infancy and n=1540 in early childhood)(**Supplementary Table S1**).

Maternal educational level was collected at birth in 7 cohorts and at follow-up by the others; the proportion of mothers with high education varied from 6.1% to 47.6% (**Table 2**). In each cohort, one or more cognitive assessments were available in infancy (n=8817 children with complete assessment), early childhood (n=8125), and later childhood (n=1660)(**Supplementary Table S2)**. Missing outcome assessments varied by cohort and period (infancy: 0-19.5%; early childhood: 3.7%-33.2%, later childhood: 9.1%-30.4%)(**Supplementary Table S3**).

Maternal and perinatal characteristics varied between cohorts **(Table 3)**, such as primiparity (31.4% to 66.5%) and multiple births (12.1% to 51.1%).

Results from meta-analyses

Children whose mothers had low, compared with high, educational attainment scored lower on cognitive measures, with a small effect in infancy (SMD=-0.32, 95%CI -0.43 to -0.21, 12 cohorts) and a moderate effect in early (SMD=-0.57, 95%CI -0.67 to -0.47, 12 cohorts) and later childhood (SMD=-0.54, 95%CI -0.72 to -0.37, six cohorts)(**Figure 1)**. Smaller effects were reported for children whose mothers had medium compared to a high educational level. Modest to high heterogeneity was observed. **Table 4** provides adjusted pooled SMDs as well as unadjusted and adjusted pooled SMDs for GA sub-groups (<27 weeks, ≥27 weeks), children without neonatal morbidities and controls, with corresponding forest plots in **Supplementary Figures S1-S11**. The adjusted SMDs for all VPT and by sub-groups were very close to unadjusted SMDs. No statistically significant difference in the effect size was revealed between GA sub-groups, and between VPT

and full-term controls (p>0.1). The SMDs for VPT without neonatal morbidities were similar to SMDs in the group ≥27 weeks.

Sensitivity analyses

The pooled analysis performed using the binary outcome confirmed that a low versus a high maternal educational level was associated with an increased risk of cognitive deficit (RR infancy=1.6, 95%CI 1.3 to 1.8; RR early childhood=2.0, 95%CI 1.6 to 2.5; RR later childhood=1.4, 95%CI 1.0 to 1.9)(**Supplementary Figure S8**). The leave-one-out analysis for groups with high heterogeneity showed that no single cohort had a substantial effect on the pooled estimate **Supplementary Figure** S**11**). The comparison of pooled estimates between sub-groups defined according to the timing of the measure of maternal education and the type of test did not find any difference; however, cohorts using examiner based-tests versus parent-report questionnaires in infancy had larger pooled SMD (p<0.01, **Supplementary Table S4**).

DISCUSSION

This meta-analysis of major population-based European VPT cohorts spanning three decades revealed a consistent positive association between maternal educational level and cognitive test scores among VPT children, with a dose-response effect (between 0.2 and 0.3 SD for mothers with medium education, and 0.3 to 0.6 SD for mothers with low education depending on age at assessment). The effect size was less pronounced in younger children at 2 and 3 years of age, but did not differ by degree of prematurity or between VPT children and term-born controls.

These results confirm the association of maternal educational level with cognitive skills among children born VPT in a wide range of settings, previously only reported in smaller scale or single country studies.[12,13,46-48] While there were some differences across the cohorts in effect sizes, with

modest to high heterogeneity, all but one cohort had negative SMDs for low compared to high maternal education. This cohort, EPICure-1 which included births <27 weeks of GA in the UK and Ireland in 1995, had few children with mothers in the high educational level category (8 to 16 depending on the age group), which may reflect the characteristics of families with extremely preterm children or inadequacy of the classification for describing mothers' education in that time period. In EPICure-2, a similarly defined representative sample from England in 2006, results were very similar to the pooled estimates.

We did not find any differences in the estimated pooled associations between maternal education and cognition according to the level of prematurity, in term-born controls or after excluding neonatal morbidities. Previous studies examining interactions between maternal education and perinatal risk on cognitive outcomes in VPT children have reported mixed results.[7,9,48,49] Several studies hypothesised that disparities in outcome could be more pronounced in VPT populations, as a low educational level may negatively affect a mother's knowledge and access to resources and consequently her ability to mitigate the effects of preterm birth by acting on environmental factors known to affect cognition. These include creating stimulating and enriched learning environments,[50] lowering or managing stress, which is heightened among families with VPT children[51,52] or breastfeeding.[53] Low maternal educational level is also associated with disadvantaged socioeconomic circumstances and adversity which negatively impact brain development and neurocognitive outcomes[54,55] with a stronger detrimental effect for vulnerable children.[9,48] Conversely, some researchers contend that the biological insults leading to poor outcomes among high-risk VPT children (e.g. with lower GA or severe neonatal morbidities) may be less amenable to change in environmental factors.[7] Our results showing similar effect sizes for extremely preterm infants and among term controls suggest that there is not substantial effect

modification. This has been noted in studies of other outcomes after preterm birth (e.g. cerebral palsy).[56]

We found an association between maternal education and cognition in all age groups, with a smaller effect at 2-3 years. At this age, children in some cohorts were assessed using tests of global development which combine an assessment of development in multiple domains, including gross and fine motor development. Moreover, cognitive tests at age 2-3 years are more heavily dependent on motor responses than tests at later ages where task completion relies more on abstract concepts. Motor development, particularly in early years, may be less affected by the social environment and contribute to a lower effect size.[57] The larger effect of maternal education on cognitive outcomes between 4 and 15 years may indicate an accumulation of environmental impact (e.g., less cognitive stimulation or sensitive parenting,[58] uptake and type of early childhood education and care services,[59] differences in school environment).

These results are important for VPT follow-up and intervention policies. First, children born VPT are more often from disadvantaged families because social factors, including maternal education, increase risks of VPT birth.[33,60] Furthermore, lower IQ scores associated with maternal education may have more severe consequences in terms of educational and life opportunities for VPT compared to term children because of the higher baseline risks of impairment. Moreover, some studies have suggested that early intervention programs, including those focusing on parenting education,[51,61] were associated with better cognitive outcomes in children from lower socioeconomic backgrounds only.[61] Finally, given the universal effect of maternal education on cognitive outcomes in childhood suggested by our results, interventions can start early. The neonatal hospitalisation may represent a key window of opportunity for addressing social disparities by reducing financial barriers affecting parental presence,[62] promoting breastfeeding,[62]

and facilitating access to follow-up and early intervention programmes.[63] Study designs that integrate information on the families' social circumstances would ensure that research on the effectiveness of interventions targets health and developmental disparities.

Strengths of this study include pooling data using a standardised protocol from a large number of cohorts in Europe. Harmonising variable definitions, using common inclusion criteria and conducting comparable analyses minimises methodological heterogeneity,[64] which improves the accuracy of pooled estimates. Another strength is the geographic and temporal heterogeneity of the cohorts which adds to the relevance and generalisability of the findings. Study limitations include residual heterogeneity between cohorts due to diverse educational systems and outcome measurements, the small number of cohorts per country limiting investigation of country effects, the lack of some important information because of difficulties harmonising definitions, and potential bias due to attrition or missing outcome data. Countries with higher proportions of immigrants may have less reliable measures of maternal educational achievement. Moreover the underlying mechanisms are complex and some pathways, for instance genetic influences[65] or parental expectation,[66] through which maternal education may impact cognitive development, could not be examined. Lastly, our study is based on VPT cohorts, the principal research design for investigating neurodevelopmental outcomes after VPT birth, which limits causal inference because of potential collider stratification bias. To go beyond our descriptive approach, full birth cohorts are needed to investigate causality and potential mediator-interaction relationships.[67,68]

CONCLUSION

In this meta-analysis of the principal population-based cohorts of children born VPT in Europe, we showed that maternal educational level was a consistent predictor of general development and cognitive outcomes in childhood. Further research is needed on early interventions that can mitigate

these social disparities; more broadly, equity in health and development should be included as a key outcome in all research on VPT birth.

ETHICS APPROVAL

Cohort	Local ethics committee that approved the study cohort
ACTION	Ethical approval was obtained from the Ethics Committees of the regional coordinating institutes in the participating regions.
AYLS	Ethical permission was granted by the Helsinki City Maternity Hospital, Helsinki University Central Hospital and Jorvi Hospital in Finland
BEST-BLS	Ethical approval was obtained from the University of Munich Children's Hospital and the Bavarian Health Council (Landesärztekammer Bayern) in Germany
EPIBEL	Inclusion : no ethics committee involved in 1999-2000, FU 11-15Y : 2012/27
EPICure	NIHR South Central Southampton Research Ethics Committee [05/Q1702/126]
EPICure-2	UCL Research Ethics Committee (reference: 10175/001) and University of Leicester Research Ethics Committee (ref: 10225)
EPIPAGE 1	The EPIPAGE study was approved by the French Data Protection Authority (Commission Nationale de l'Informatique et des Liberte´s)
EPIPAGE 2	Recruitment and follow-up within this study were approved by the national data protection authority (CNIL n° 911 009, 913 020, 916 212) and by the appropriate ethics committees, i.e., the advisory committee on the treatment of personal health data for research purposes (Comité Consultatif sur le Traitement de l'Information en matière de Recherche, CCTIRS reference number 10-626, 12-109 and 16-263) and the committee for the protection of people participating in biomedical research (Comité de Protection des Personnes, CPP SC 2873, CPP 3377).
EPICE/SHIPS	The European study was also approved by the French Advisory Committee on Use of Health Data in Medical Research (CCTIRS, for EPICE, N° 13.020 on 24/01/2013) and the French Expert Committee for Research, Studies and Evaluations in the field of Health (CEREES for SHIPS, TPS12460bis (16/11/2017) as well as the French National Commission for Data Protection and Liberties (CNIL) for both phases (DR-2013-194, on 10/04/2013, DR-2018-098 on 15/05/2018).
EST 02-03	151/T-23, 21.08.2006
EST 07	169/T-18, 24.03.2008 ; 5y Assessment: 214/T-20; 27.04.2012
ETFOL	All eight regional Research Ethics Committees approved the ETFOL study. Use of the data in the ETFOL cohort for this study was approved by the data protection authorities.
EXPRESS	Dnr 42/2004 and 2009/524 (Lund/Sweden)

PEP	Regional Ethics Comittee (REC) Western Norway Health Authority, REC nr. 20.04 and 2009-2271
PIPARI	The PIPARI study protocol was approved by the Ethics Review Committee of the Hospital District of Southwest Finland in December 2000 and again in January 2012

AUTHOR CONTRIBUTIONS

Dr Sentenac conceptualized and designed the study, carried out the analyses at the cohort level, carried out the pooled analyses, interpreted the data, drafted the initial manuscript, and revised the manuscript.

Dr Benhammou contributed to the study concept and design, to the acquisition of cohort data, carried out the analyses at the cohort level, contributed to the interpretation of the data, and revised the manuscript.

Dr Aden, Dr Maier, and Dr Barros contributed to the acquisition of cohort data, interpretation of the data, and revised the manuscript.

Dr Ancel, Dr Boerch, Dr Cuttini, Dr Draper, Dr Halvorsen, Dr Johnson, Dr Lebeer, Pr Lehtonen, Dr Marlow, Dr Raikkonen, Dr Varendi, and Dr Wolke contributed to the acquisition of cohort data, the interpretation of the data, and revised the manuscript.

Mr Bakker and Dr Morgan contributed to conceptualize and design the study, and revised the manuscript.

Mrs Bakoy, Mrs Baumann, Mrs Funck Bilsteen, Mrs Croci, Dr Källén, Dr Land, Dr Ni, Mr Rtimi, Dr Sarrechia, Dr Vollsaeter, and Dr Ylijoki carried out the analyses at the cohort level, contributed to the interpretation of the data, and revised the manuscript.

Dr Kallen contributed to the acquisition of the cohort data, carried out the analyses at the cohort level, contributed to the interpretation of the data, and revised the manuscript.

Dr Zeitlin conceptualized and designed the study, contributed to the acquisition of the cohort data, interpreted the data, contributed to write the initial manuscript, and revised the manuscript.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DATA AVAILABILITY

No individual participant data are available. Data dictionaries are available on the RECAP Preterm platform (https://platform.recap-preterm.eu/pub)

SUPPLEMENTARY DATA

Supplementary Table S1 - Information on geographical coverage. inclusion criteria. and participants of term control groups by cohort and by age group

Supplementary Table S2 - Information on cognitive tests. scores and reference population by cohort and by age group

Supplementary Table S3 - IQ scores and missing data by cohort and by age group

Supplementary Table S4 – Results from sensitivity analysis

Supplementary Figure S1 – Forest plot of standardized mean differences of unadjusted mean IQ scores (SMD and 95% CI) in children born <27 weeks of gestation

Supplementary Figure S2 – Forest plot of standardized mean differences of unadjusted mean IQ scores (SMD and 95% CI) in children born ≥ 27 weeks of gestation

Supplementary Figure S3 – Forest plot of standardized mean differences of adjusted mean IQ scores (SMD and 95% CI) in all VPT children

Supplementary Figure S4 – Forest plot of standardized mean differences of adjusted mean IQ scores (SMD and 95% CI) in children born <27 weeks of gestation

Supplementary Figure S5 – Forest plot of standardized mean differences of adjusted mean IQ scores (SMD and 95% CI) in children born ≥ 27 weeks of gestation

Supplementary Figure S6 – Forest plot of standardized mean differences of unadjusted mean IQ scores (SMD and 95% CI) : subgroup VPT and term controls

Supplementary Figure S7 – Forest plot of standardized mean differences of adjusted mean IQ scores (SMD and 95% CI) in term controls

Supplementary Figure S8 – Forest plot of Relative Risk for cognitive deficit by maternal educational group (and 95% CI) in all VPT children

Supplementary Figure S9 – Forest plot of standardized mean differences of unadjusted mean IQ scores (SMD and 95% CI) in children without neonatal morbidities

Supplementary Figure S10 – Forest plot of standardized mean differences of adjusted mean IQ scores (SMD and 95% CI) in children without neonatal morbidities

Supplementary Figure S11 – Forest plots of the results of the leave-one-out sensitivity analysis (standardized mean differences of unadjusted mean IQ scores) applied when meta-analyses with high heterogeneity (I^2>50%)

FUNDING

This study is part of research on the consequences of very preterm birth for use in developing a research agenda for the RECAP Preterm project, a study to construct a platform combining data from very preterm cohort studies in Europe, which is supported by the European Union's Horizon 2020 research and innovation programme [grant agreement No 733280].

Further funding were received by each cohort:

Data collection for the ACTION follow-up study was funded by the Italian Ministry of Health [RF-2009-1511846] and by two unrestricted grants from Chiesi Farmaceutici S.p.a.

The BEST-BLS was supported by grants PKE24, JUG14, 01EP9504 and 01ER0801 from the German Federal Ministry of Education and Science (BMBF).

The EPICure Study was supported by a programme grant from the Medical Research Council [G0401525 and MR/N024869/1]. Neil Marlow receives part funding from the Department of Health's NIHR Biomedical Research Centre's funding scheme at UCLH/UCL.

The Epipage 1 study was supported by grants from INSERM (national Institute of Health and Medical Research), the Directorate General for Health at the Ministry for Social Affairs, Merck-Sharp and Dohme-Chibret, Medical Research Fondation, and "Hospital Program for Clinical Research 2001 n°AOM01117" of the French Department of Health.

The Epipage 2 cohort relies on several sources of funding, including support from the French National Institute of Public Health Research (IRESP TGIR 2009-01 programme)/Institute of Public Health and its partners (the French Health Ministry, the National Institute of Health and Medical Research [INSERM], the National Institute of Cancer, and the National Solidarity Fund for Autonomy [CNSA]), the National Research Agency through the French EQUIPEX program of investments for the future [grant no. ANR-11-EQPX-0038] and the PremUp Foundation. Additional funding was obtained from the Fondation pour la Recherche Medicale [SPF 20160936356] and Fondation de France [00050329 and R18202KK [Grand Prix]].

The EPICE-SHIPS cohort was funded by the European Union Seventh Framework Programme [FP7/2007-2013, No 259882; Horizon 2020 Research and Innovation Programme, No 633724].

The Estonian cohorts 2002-03 and 2007 was partially funded by Estonian Research Council, grant no ETF7094; Estonian Ministry of Education and Research, grants no SF0182695s05; SF0180004s11.

This EXPRESS study was supported by the Swedish Research Council [grants 2006-3858 and

2009-4250].

The Norwegian Extreme Prematurity Study (PEP) was funded by Western Norway Regional Health Authority and Haukeland University Hospital.

The PIPARI cohort was founded by the C.G. Sundell Foundation, Emil Aaltonen's Foundation, the Finnish Academy of Science, the South-West Finnish Foundation of Neonatal Research.

ACKNOWLEDGEMENTS

The authors acknowledge all members of scientific committees in each participating cohort for their substantial contribution in the acquisition of the data:

The ACTION Study group
Marina Cuttini, Ileana Croci, Simone Piga, Carlo Corchia, Stefano Vicari, Bambino Gesù Pediatric Hospital, IRCCS, Roma, Lazio.
Domenico Di Lallo and Francesco Franco, Lazio Regional Health Authority, Roma, Lazio.

Marco Carrozzi, Mariacristina Fertz and Fabio Uxa, Burlo Garofolo Maternal and Child Hospital, IRCCS,Trieste, Friuli Venezia-Giulia.
Valeria Chiandotto and Franco Macagno, S. Maria della Misericordia Hospital, Udine, Friuli Venezia-Giulia.
Fabio Voller, Monica Da Fré and Franca Rusconi, Regional Agency for Health of Tuscany region, Firenze, Tuscany.
Virgilio Carnielli, Maternal and Child Health Institute, Marche University and Salesi Hospital, Ancona, Marche.
Silvana Miniaci, Pugliese-Ciaccio Hospital, Catanzaro, Calabria.

The EPIBEL Study group
Vicky Hennissen, University of Antwerp, Family Medicine & Population Health
Piet Vanhaesebrouck (emer. Head of NICU) & Koenraad Smets (actual head of NICU) - University Hospital Ghent
Patrick Van Reempts ((emer. Head of NICU), Twan Mulder (actual head of NICU) - Antwerp University Hospital
Gunnar Naulaers, Head of NICU - University Hospital Gasthuisberg Leuven
Filip Cools, Head of NICU - University Hospital, Brussels
Katleen Plaskie & Veronique Demeulemeester, NICU St Augustinus GZA Hospital, Antwerp
Hilde Van de Broek , NICU General Hospital Middelheim
Isabel De Groote, Herbert Roeyers, Liedewij Verhaeghe, Department of Psychology, University of Ghent
Els Bruneel, NICU, General Hospital Zuid-Oost Limburg, Genk
Sabrina Laroche, MD, Department of Neonatology, Antwerp University Hospital

The EPICure Study group
N Marlow, SJ Johnson, ES Draper, KL Costeloe, D. Wolke (Investigators)
T Moore, J Fawke, V Rowell, S Thomas, R Trikic, R Smith, H Palmer, L McCormack (Research Team)

The EPIPAGE 1 Study Group
INSERM U149: B. Larroque (national coordinator), P. Y. Ancel, B. Blondel, G. Breart, M. Dehan, M. Garel, M. Kaminski, F. Maillard, C. du Mazaubrun, P. Missy, F. Sehili, K. Supernant; Alsace: M. Durant, J. Matis, J. Messer, A. Treisser (Hôpital de Hautepierre, Strasbourg); Franche-Comte´: A. Burguet, L. Abraham-Lerat, A. Menget, P. Roth, J-P. Schaal, G. Thiriez (CHU St Jacques, Besançon); Haute-Normandie: C. Leveque, S. Marret, L. Marpeau (Hôpital Charles Nicolle, Rouen); Languedoc-Roussillon: P. Boulot, J-C. Picaud (Hôpital Arnaud de Villeneuve, Montpellier), A-M. Donadio, B. Ledesert (ORS Montpellier); Lorraine: M. André, J-L. Boutroy, J. Fresson, J. M. Hascoet (Maternité Régionale, Nancy); Midi-Pyrénées: C. Arnaud, S. Bourdet-Loubère, H. Grandjean (INSERM U558, Toulouse), M. Rolland (Hôpital des Enfants, Toulouse); Nord-Pas-de-Calais: C. Leignel, P. Lequien, V. Pierrat, F. Puech, D. Subtil, P. Truffert (Hôpital Jeanne de Flandre, Lille); Pays de la Loire: G. Boog, V. Rouger-Bureau, J-C. Roze´ (Hôpital Mère-Enfants, Nantes); Paris-Petite-Couronne: P-Y. Ancel, G. Bréart, M. Kaminski, C. du Mazaubrun (INSERM U149, Paris), M. Dehan, V. Zupan (Hôpital Antoine Béclère, Clamart), M. Vodovar, M. Voyer (Institut de Puériculture, Paris).

The EPIPAGE 2 Study group

Alsace: D Astruc, P Kuhn, B Langer, J Matis, C Ramousset; Aquitaine: X Hernandorena, P Chabanier, L Joly-Pedespan, M Rebola, MJ Costedoat, A Leguen, C Martin; Auvergne: B Lecomte, D Lemery, F Vendittelli, E Rochette; Basse-Normandie: G Beucher, M Dreyfus, B Guillois, Y Toure, D Rots; Bourgogne: A Burguet, S Couvreur, JB Gouyon, P Sagot, N Colas, A Franzin; Bretagne: J Sizun, A Beuchée, P Pladys, F Rouget, RP Dupuy, D Soupre, F Charlot, S Roudaut; Centre: A Favreau , E Saliba, L Reboul, E Aoustin; Champagne-Ardenne: N Bednarek, P Morville, V Verrière; Franche-Comté: G Thiriez, C Balamou, C Ratajczak; Haute-Normandie: L Marpeau , S Marret, C Barbier, N Mestre; Ile-de-France: G Kayem, X Durrmeyer, M Granier, A Lapillonne, M Ayoubi, O Baud, B Carbonne, L Foix L'Hélias, F Goffinet, PH Jarreau, D Mitanchez, P Boileau, C Duffaut, E Lorthe, L Cornu, R Moras, D Salomon, S Medjahed, K Ahmed; Languedoc-Roussillon: P Boulot, G Cambonie, H Daudé, A Badessi, N Tsaoussis, M Poujol; Limousin: A Bédu, F Mons, C Bahans; Lorraine: MH Binet, J Fresson, JM Hascoët, A Milton, O Morel, R Vieux, L Hilpert; Midi-Pyrénées: C Alberge, C Arnaud, C Vayssière, M Baron; Nord-Pas-de-Calais: ML Charkaluk, V Pierrat, D Subtil, P Truffert, S Akowanou, D Roche, M Thibaut; PACA et Corse: C D'Ercole, C Gire, U Simeoni, A Bongain, M Deschamps, M Zahed; Pays de Loire: B Branger, JC Rozé, N Winer, G Gascoin, L Sentilhes, V Rouger, C Dupont, H Martin; Picardie: J Gondry, G Krim, B Baby, I Popov; Rhône-Alpes: M Debeir, O Claris, JC Picaud, S Rubio-Gurung, C Cans, A Ego, T Debillon, H Patural, A Rannaud; Guadeloupe: E Janky, A Poulichet, JM Rosenthal, E Coliné, C Cabrera; Guyane: A Favre, N Joly, Stouvenel A; Martinique: S Châlons, J Pignol, PL Laurence, V Lochelongue; La Réunion : PY Robillard, S Samperiz, D Ramful. Inserm UMR 1153: PY Ancel, H Asadullah, V Benhammou, B Blondel, M Bonet, A Brinis, ML Charkaluk, A Coquelin, V Delormel, M Durox, S Esmiol, M Fériaud, L Foix-L'Hélias, F Goffinet, M Kaminski, G Kayem, K Khemache, B Khoshnood, C Lebeaux, E Lorthe, L Marchand-Martin, L Onestas, V Pierrat, M Quere, J Rousseau, A Rtimi, MJ Saurel-Cubizolles, D Tran, D Sylla, L Vasante-Annamale, J Zeitlin.

The EPICE and SHIPS Research Group

EPICE and SHIPS Research Group : Belgium (J Lebeer, P Van Reempts, E Bruneel, E Cloet, A Oostra, E Ortibus, I Sarrechia); Denmark (K Boerch, L Huusom, P Pedersen, T Weber); Estonia (L Toome, H Varendi, M Männamaa); France (PY Ancel, A Burguet, PH Jarreau, V Pierrat, P Truffert); Germany (RF Maier, M Zemlin, B Misselwitz, S Schmidt, L Wohlers,) Italy (M Cuttini, D Di Lallo, G Ancora, D Baronciani, V Carnielli, I Croci, G Faldella, F Ferrari, F Franco, G Gargano); The Netherlands (A van Heijst, C Koopman-Esseboom); Poland (J Gadzinowski, J Mazela, A Montgomery, T Pikuła) Portugal (H Barros, R Costa, L Mendes Graça, M do Céu Machado, C Rodrigues, T Rodrigues); Sweden (U Aden, AK Edstedt Bonamy, M Norman); United Kingdom (ES Draper, EM Boyle, A Fenton, SJ Johnson, BN Manktelow, DWA Milligan) EFCNI (S Mader, N Thiele, JM Walz); Health Economics team (S Petrou); Inserm Coordination (J Zeitlin, M Bonet, C Bonnet, R El Raffei, A Piedvache, AV Seppanen)

The EST 02-03 Study group

Liis Toome, Tallinn Children's Hospital, Tallinn, Estonia
Külli Muug, Inna Marats, Tartu University Hospital, Tartu, Estonia

The EST 07 Study group

Liis Toome, Birgit Kaasik, Triinu Tänavsuu, Kati Korjus, Tallinn Children's Hospital, Tallinn, Estonia

Ülle Utsal, Mairi Männamaa, Inna Marats, Mari-Anne Vals, Tartu University Hospital, Tartu, Estonia

The ETFOL Study group
We thank the Danish Paediatric Society for establishing the ETFOL study and the parents and the children for their willingness to participate in the ETFOL study.

The EXPRESS Study group
Karin Källén, on behalf of the Express study group

The PEP Study group
Trond Markestad, Department of Clinical Science, University of Bergen, Norway; Department of Paediatric and Adolescent Medicine, Haukeland University Hospital, Bergen, Norway. On behalf of the Norwegian Extreme Prematurity Study Group.

The PIPARI Study group
The PIPARI Study Group includes, Eeva Ekholm, MD, PhD; Linda Grönroos, MD; Leena Haataja, MD, PhD; Nils Holmqvist, MD; Mira Huhtala, MD, PhD; Eveliina Joensuu, MA; Pentti Kero, MD, PhD; Riikka Korja, PhD; Katri Lahti, MD; Helena Lapinleimu, MD, PhD; Liisa Lehtonen, MD, PhD; Tuomo Lehtonen, MD; Marika Leppänen, MD, PhD; Annika Lind, PhD; Petriina Munck PhD; Laura Määttänen, MD; Pekka Niemi, PhD; Anna Nyman, PhD; Riitta Parkkola, MD, PhD; Päivi Rautava, MD, PhD; Katriina Saarinen, Physiotherapist; Tiina Saarinen, MD; Susanna Salomäki, MA; Virva Saunavaara, PhD; Sirkku Setänen, MD, PhD; Matti Sillanpää, MD, PhD; Suvi Stolt, PhD; Päivi Tuomikoski-Koiranen, RN; Karoliina Uusitalo, MD; Milla Ylijoki, MD, PhD.

CONFLICT OF INTEREST STATEMENT

Neil Marlow declares consultancy fees from RSM Consulting, Takeda and Novartis in the past 3 years outside this study.

The other authors have no conflicts of interest relevant to this article to disclose

REFERENCES

1. Allotey J, Zamora J, Cheong-See F, et al. Cognitive, motor, behavioural and academic performances of children born preterm: a meta-analysis and systematic review involving 64 061 children. *BJOG* 2018; **125**: 16-25.
2. Brydges CR, Landes JK, Reid CL, Campbell C, French N, Anderson M. Cognitive outcomes in children and adolescents born very preterm: a meta-analysis. *Dev Med Child Neurol* 2018; **60**: 452-68.
3. Twilhaar E, Wade RM, de Kieviet JF, van Goudoever JB, van Elburg RM, Oosterlaan J. Cognitive outcomes of children born extremely or very preterm since the 1990s and associated risk factors: A meta-analysis and meta-regression. *JAMA Pediatr* 2018; **172**: 361-7.
4. Linsell L, Malouf R, Morris J, Kurinczuk JJ, Marlow N. Prognostic Factors for Poor Cognitive Development in Children Born Very Preterm or With Very Low Birth Weight: A Systematic Review. *JAMA Pediatr* 2015; **169**: 1162-72.
5. Dall'Oglio AM, Rossiello B, Coletti MF, et al. Do healthy preterm children need neuropsychological follow‐up? Preschool outcomes compared with term peers. *Dev Med Child Neurol* 2010; **52**: 955-61.
6. Capron C, Duyme M. Assessment of effects of socio-economic status on IQ in a full cross-fostering study. *Nature* 1989; **340**: 552-4.
7. Sentenac M, Johnson S, Charkaluk ML, et al. Maternal education and language development at 2 years corrected age in children born very preterm: results from a European population-based cohort study. *J Epidemiol Community Health* 2020; **74**: 346-53.
8. Beauregard JL, Drews-Botsch C, Sales JM, Flanders WD, Kramer MR. Does socioeconomic status modify the association between preterm birth and children's early cognitive ability and kindergarten academic achievement in the United States? *Am J Epidemiol* 2018; **187**: 1704-13.
9. Benavente-Fernández I, Synnes A, Grunau RE, et al. Association of socioeconomic status and brain injury with neurodevelopmental outcomes of very preterm children. *JAMA Netw Open* 2019; **2**: e192914-e.
10. Bilsteen JF, Taylor-Robinson D, Børch K, Strandberg-Larsen K, Andersen A-MN. Gestational age and socioeconomic achievements in young adulthood: a Danish population-based study. *JAMA Netw Open* 2018; **1**: e186085-e.
11. Kajantie E, Strang-Karlsson S, Evensen KAI, Haaramo P. Adult outcomes of being born late preterm or early term–What do we know? *Semin Fetal Neonatal Med* 2019; **24**: 66-83.
12. Beaino G, Khoshnood B, Kaminski M, et al. Predictors of the risk of cognitive deficiency in very preterm infants: the EPIPAGE prospective cohort. *Acta Paediatr* 2011; **100**: 370-8.
13. Månsson J, Fellman V, Stjernqvist K, Group ES. Extremely preterm birth affects boys more and socio‐economic and neonatal variables pose sex‐specific risks. *Acta Paediatr* 2015; **104**: 514-21.
14. Nyman A, Korhonen T, Munck P, Parkkola R, Lehtonen L, Haataja L. Factors affecting the cognitive profile of 11-year-old children born very preterm. *Pediatr Res* 2017; **82**: 324-32.
15. Wong HS, Edwards P. Nature or nurture: a systematic review of the effect of socio-economic status on the developmental and cognitive outcomes of children born preterm. *Matern Child Health J* 2013; **17**: 1689-700.
16. Zeitlin J, Sentenac M, Morgan AS, et al. Priorities for collaborative research using very preterm birth cohorts. *Arch Dis Child Fetal Neonatal Ed* 2020; **105**: 538-44.

17. Ancel P-Y, Goffinet F. EPIPAGE 2: a preterm birth cohort in France in 2011. *BMC Pediatr* 2014; **14**: 97.
18. Andrejanova N, Utsal Ü, Männamaa M, et al. *Improvement of the 5-year outcome of live births at <29 gestational weeks with extremely low birth weight (<1000 g) in Estonia.* World Congress of Perinatal Medicine; 2013; Moscow 2013. Available from: https://www.etis.ee/Portal/Publications/Display/f5f115b2-06f4-4f82-9da3-82a1bf5b3e01
19. Cuttini M, Caravale B, Carnielli V, et al. A two-year follow-up study of very preterm infants in Italy: aims and study design. *Paediatr Child Health* 2009; **19**: S145-S52.
20. Fellman V, Hellström-Westas L, Norman M, et al. One-year survival of extremely preterm infants after active perinatal care in Sweden. *Obstet Anesth Dig* 2010; **30**: 22-3.
21. Heinonen K, Räikkönen K, Pesonen A-K, et al. Prenatal and postnatal growth and cognitive abilities at 56 months of age: a longitudinal study of infants born at term. *Pediatrics* 2008; **121**: e1325-e33.
22. Hoff B, Hansen BM, Munck H, Mortensen EL. Behavioral and social development of children born extremely premature: 5‐year follow‐up. *Scand J Psychol* 2004; **45**: 285-92.
23. Larroque B, Ancel P-Y, Marret S, et al. Neurodevelopmental disabilities and special care of 5-year-old children born before 33 weeks of gestation (the EPIPAGE study): a longitudinal cohort study. *Lancet* 2008; **371**: 813-20.
24. Markestad T, Kaaresen PI, Rønnestad A, et al. Early death, morbidity, and need of treatment among extremely premature infants. *Pediatrics* 2005; **115**: 1289-98.
25. Moore T, Hennessy EM, Myles J, et al. Neurological and developmental outcome in extremely preterm children born in England in 1995 and 2006: the EPICure studies. *BMJ* 2012; **345**: e7961.
26. Toome L, Varendi H, Männamaa M, Vals MA, Tänavsuu T, Kolk A. Follow‐up study of 2‐year‐olds born at very low gestational age in E stonia. *Acta Paediatr* 2013; **102**: 300-7.
27. Vanhaesebrouck P, Allegaert K, Bottu J, et al. The EPIBEL study: outcomes to discharge from hospital for extremely preterm infants in Belgium. *Pediatrics* 2004; **114**: 663-75.
28. Wood NS, Marlow N, Costeloe K, Gibson AT, Wilkinson AR. Neurologic and developmental disability after extremely preterm birth. *N Engl J Med* 2000; **343**: 378-84.
29. Zeitlin J, Maier RF, Cuttini M, et al. Cohort profile: Effective Perinatal Intensive Care in Europe (EPICE) very preterm birth cohort. *Int J Epidemiol* 2020; **49**: 372-86.
30. Ylijoki M, Lehtonen L, Lind A, et al. Chorioamnionitis and five-year neurodevelopmental outcome in preterm infants. *Neonatology* 2016; **110**: 286-95.
31. Wolke D, Ratschinski G, Ohrt B, Riegel K. The cognitive outcome of very preterm infants may be poorer than often reported: an empirical investigation of how methodological issues make a big difference. *Eur J Pediatr* 1994; **153**: 906-15.
32. UNESCO Institute for Statistics. *International Standard Classification of Education: ISCED 2011*. Montreal: UNESCO Institute for Statistics; 2012.
33. Poulsen G, Strandberg‐Larsen K, Mortensen L, et al. Exploring Educational Disparities in Risk of Preterm Delivery: A Comparative Study of 12 E uropean Birth Cohorts. *Paediatr Perinat Epidemiol* 2015; **29**: 172-83.
34. Bell MJ, Ternberg JL, Feigin RD, et al. Neonatal necrotizing enterocolitis. Therapeutic decisions based upon clinical staging. *Ann Surg* 1978; **187**: 1-7.
35. Papile L-A, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm. *J Pediatr* 1978; **92**: 529-34.

36. The International Classification of Retinopathy of Prematurity revisited. *Arch Ophthalmol* 2005; **123**: 991-9.
37. Pierrat V, Marchand-Martin L, Arnaud C, et al. Neurodevelopmental outcome at 2 years for preterm children born at 22 to 34 weeks' gestation in France in 2011: EPIPAGE-2 cohort study. *BMJ* 2017; **358**: j3448.
38. Eves R, Mendonça M, Baumann N, et al. Association of Very Preterm Birth or Very Low Birth Weight With Intelligence in Adulthood: An Individual Participant Data Meta-analysis. *JAMA Pediatr* 2021.
39. Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of Interventions version 6.2 (updated February 2021): Cochrane; 2021. Available from: http://www.training.cochrane.org/handbook
40. Lipsey MW, Wilson DB. *Practical Meta-Analysis*: SAGE Publications, Inc; 2001.
41. Cohen J. *Statistical Power Analysis for the Behavioral Sciences* Hillsdale, New Jersey: Lawrence Erlbaum Associates; 1988.
42. Arpi E, D'Amico R, Lucaccioni L, Bedetti L, Berardi A, Ferrari F. Worse global intellectual and worse neuropsychological functioning in preterm-born children at preschool age: a meta-analysis. *Acta Paediatr* 2019; **108**: 1567-79.
43. Patsopoulos NA, Evangelou E, Ioannidis JP. Sensitivity of between-study heterogeneity in meta-analysis: proposed metrics and empirical evaluation. *Int J Epidemiol* 2008; **37**: 1148-57.
44. Balduzzi S, Rücker G, Schwarzer G, . How to perform a meta-analysis with R: a practical tutorial. *Evid Based Ment Health* 2019; **22**: 153-60.
45. R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.r-project.org/. 2020.
46. Leversen KT, Sommerfelt K, Elgen IB, et al. Prediction of outcome at 5 years from assessments at 2 years among extremely preterm children: a Norwegian national cohort study. *Acta Paediatr* 2012; **101**: 264-70.
47. Patra K, Greene MM, Patel AL, Meier P. Maternal education level predicts cognitive, language, and motor outcome in preterm infants in the second year of life. *Am J Perinatol* 2016; **33**: 738-44.
48. Voss W, Jungmann T, Wachtendorf M, Neubauer AP. Long-term cognitive outcomes of extremely low-birth-weight infants: the influence of the maternal educational background. *Acta Paediatr* 2012; **101**: 569-73.
49. Wolke D, Meyer R. Cognitive status, language attainment, and prereading skills of 6‐year‐old very preterm children and their peers: The Bavarian Longitudinal Study. *Dev Med Child Neurol* 1999; **41**: 94-109.
50. Prickett KC, Augustine JM. Maternal Education and Investments in Children's Health. *J Marriage Fam* 2016; **78**: 7-25.
51. Benzies KM, Magill-Evans JE, Hayden KA, Ballantyne M. Key components of early intervention programs for preterm infants and their parents: a systematic review and meta-analysis. *BMC Pregnancy Childbirth* 2013; **13**: S10.
52. Bozkurt O, Eras Z, Sari FN, et al. Does maternal psychological distress affect neurodevelopmental outcomes of preterm infants at a gestational age of≤ 32 weeks. *Early Hum Dev* 2017; **104**: 27-31.
53. LeWinn KZ, Bush NR, Batra A, Tylavsky F, Rehkopf D. Identification of Modifiable Social and Behavioral Factors Associated With Childhood Cognitive Performance. *JAMA Pediatr* 2020; **174**: 1-11.

54. Johnson SB, Riis JL, Noble KG. State of the Art Review: Poverty and the Developing Brain. *Pediatrics* 2016; **137**: e20153075.
55. Najman JM, Hayatbakhsh MR, Heron MA, Bor W, O'Callaghan MJ, Williams GM. The Impact of Episodic and Chronic Poverty on Child Cognitive Development. *J Pediatr* 2009; **154**: 284-9.e1.
56. Forthun I, Strandberg-Larsen K, Wilcox AJ, et al. Parental socioeconomic status and risk of cerebral palsy in the child: evidence from two Nordic population-based cohorts. *Int J Epidemiol* 2018; **47**: 1298-306.
57. Baumann N, Tresilian J, Bartmann P, Wolke D. Early Motor Trajectories Predict Motor but not Cognitive Function in Preterm-and Term-Born Adults without Pre-existing Neurological Conditions. *Int J Environ Res Public Health* 2020; **17**: 3258.
58. Wolke D, Jaekel J, Hall J, Baumann N. Effects of sensitive parenting on the academic resilience of very preterm and very low birth weight adolescents. *J Adolesc Health* 2013; **53**: 642-7.
59. Vandell DL, Belsky J, Burchinal M, Steinberg L, Vandergrift N. Do effects of early child care extend to age 15 years? Results from the NICHD study of early child care and youth development. *Child Dev* 2010; **81**: 737-56.
60. Ruiz M, Goldblatt P, Morrison J, et al. Mother's education and the risk of preterm and small for gestational age birth: a DRIVERS meta-analysis of 12 European cohorts. *J Epidemiol Community Health* 2015; **69**: 826-33.
61. Spittle AJ, Treyvaud K, Lee KJ, Anderson PJ, Doyle LW. The role of social risk in an early preventative care programme for infants born very preterm: a randomized controlled trial. *Dev Med Child Neurol* 2018; **60**: 54-62.
62. Parker MG, Garg A, McConnell MA. Addressing Childhood Poverty in Pediatric Clinical Settings: The Neonatal Intensive Care Unit Is a Missed Opportunity. *JAMA Pediatr* 2020.
63. Baggett KM, Davis B, Landry SH, et al. Understanding the Steps Toward Mobile Early Intervention for Mothers and Their Infants Exiting the Neonatal Intensive Care Unit: Descriptive Examination. *J Med Internet Res* 2020; **22**: e18519.
64. Sentenac M, Boutron I, Draper ES, et al. Defining Very Preterm Populations for Systematic Reviews With Meta-analyses. *JAMA Pediatr* 2020; **174**: 997-9.
65. Sniekers S, Stringer S, Watanabe K, et al. Genome-wide association meta-analysis of 78,308 individuals identifies new loci and genes influencing human intelligence. *Nat Genet* 2017; **49**: 1107-12.
66. Guo X, Lv B, Zhou H, et al. Gender differences in how family income and parental education relate to reading achievement in China: The mediating role of parental expectation and parental involvement. *Front Psychol* 2018; **9**: 783.
67. Cole SR, Platt RW, Schisterman EF, et al. Illustrating bias due to conditioning on a collider. *Int J Epidemiol* 2010; **39**: 417-20.
68. Snowden JM, Basso O. Causal inference in studies of preterm babies: a simulation study. *BJOG* 2018; **125**: 686-92.

Table 1 - Characteristics of the 15 participating cohorts

Cohort	Country, coverage, if not national[a]	Inclusion criteria (GA, BW)	Years of birth	Live birth (N)	Period 1 Age (% FU)[b]	Period 2 Age (% FU)[b]	Period 3 Age (% FU)[b]
ACTION	Italy, 5 regions[c]	<32 wks	2003-2005	2002	2 y (84.6%)	n/a	8-11 y (72.9%)
AYLS	Finland, County of Uusimaa	<32 wks	1985-1986	93	20 m (97.0%)	56 m (93.9%)	n/a
BEST-BLS	Germany, Southern Bavaria	<32 wks	1985-1986	560	20 m (97.5%)	6 y (97.3%)	8 y (97.3%)
EPIBEL	Belgium, Flanders[d]	<27 wks	1999-2000	169	3 y (81.1%)	n/a	11-15 y (55.8%)
EPICure	UK and Ireland	<26 wks	1995	1290	2.5 y (98.1%)	6 y (76.5%)	11 y (69.5%)
EPICure-2	England	<27 wks	2006	2034	2.5 y (55.3%)	n/a	11 y (n/a)[e]
EPIPAGE 1	France, 9 regions[f]	<33 wks	1997	2901	2 y (89.9%)	5 y (75.1%)	n/a
EPIPAGE 2	France, 25 regions	<32 wks[g]	2011	4227	2 y (83.4%)	5 y (70.3%)	n/a
EPICE/SHIPS	10 European countries[h],16 regions	<32 wks	2011-2012	6593	2 y (60.5%)	5 y (51.2%)	n/a
EST 02-03	Estonia	<32 wks (FU <29 wks)	2002-2003	264	n/a	5 y (81.3%)[i]	n/a
EST 07	Estonia	<32 wks (FU 5y: <29 wks)	2007	360	2 y (98.7%)	5 y (38.9%)[i]	n/a
ETFOL	Denmark	<28 wks or <1000g	1994-1995	477	n/a	5 y (90.7%)	n/a
EXPRESS	Sweden	<27 wks	2004-2007	707	2.5 y (77.4%)	6.5 y (76.2%)	n/a

PEP	Norway	<28 wks or <1000g	1999-2000	462	n/a	5 y (81.4%)	n/a
PIPARI	Finland, Turku region	≤ 1500 g[j]	2001-2006	255	2 y (97.3%)	5 y (94.1%)	11 y (89.6%)

Abbreviation: GA= gestational age; BW= birth weight; FU=follow-up; n/a= not available

(a) ACTION (Lazio, Marche,Tuscany, Friuli Venezia-Giulia (FVG) and Calabria) ; EPIPAGE 1 (Alsace, Franche-Comté, Lorraine, Nord-Pas de Calais, Haute Normandie, Pays de Loire, Paris-Petite couronne, Languedoc-Roussillon, Midi-Pyrénées); EPIPAGE 2 (21 regions of the 22 metropolitan regions, and all 4 overseas regions); EPICE/SHIPS (Flanders in Belgium; the Eastern Region of Denmark; Estonia (entire country); Hesse and Saarland in Germany; Emilia- Romagna, Lazio and Marche regions in Italy; the Central and Eastern regions of The Netherlands; Wielkopolska in Poland; the Lisbon and Northern regions of Portugal; and the East Midlands, Northern and Yorkshire and Humber regions in the UK; and the Stockholm region in Sweden)

(b) Number of participants at FU / number of survivors at discharge

(c) Two regions (Calabria and Marche) did not participate at FU at 8-11 years

(d) The original cohort is representative of whole Belgium (total: 322 born alive, of whom 303 were admitted at NICU) but only one region (Flanders) participated at the first follow-up. Non-Dutch speaking parents were excluded from the follow-up

(e) At 11 years, data were collected only among a sub-sample of 200 children

(f) Only 1 region participated at the follow up at 2-3 years

(g) children with cerebral palsy, deafness, blindness, or severe congenital brain malformations were excluded from analyses

(h) The 3 French regions were excluded of this analysis because of the overlap with EPIPAGE 2

(i) FU only among children born before <29 weeks; EST07: follow-up was restricted to specific patient selection (year of birth, birth weight, regional differences) due to financial restriction

(j) Infants with congenital anomalies and malformations were not eligible to this cohort

Table 2 – Definition and distribution of maternal educational level by cohort

Cohort[a]	Measured at[b]	N[c]	Low level (ISCED 0-2)	Intermediate level (ISCED 3-5)	High level (ISCED 6-8)	Missing data
			n (%)	n (%)	n (%)	%
ACTION	Birth	976	290 (30.1)	502 (52.1)	171 (17.8)	1.3
AYLS	Birth	58	23 (40.4)	14 (24.6)	20 (35.1)	1.7
BEST-BLS	Birth	329	108 (33.6)	184 (57.3)	29 (9.0)	2.4
EPIBEL	FU	47	3 (2.4)	19 (45.2)	20 (47.6)	10.6
EPICure	FU	283	62 (23.6)	185 (70.3)	16 (6.1)	7.1
EPICure-2	FU	576	41 (8.0)	295 (57.8)	174 (34.1)	6.3
EPIPAGE 1	Birth	1535	578 (37.6)	288 (18.7)	434 (28.2)	15.3
EPIPAGE 2	Birth	1884	511 (27.2)	780 (41.3)	553 (29.3)	2.1
EPICE/SHIPS	FU	3345	600 (17.9)	1374 (41.1)	1303 (39.0)	2.1
EST 02-03	FU	49	6 (16.7)	23 (63.9)	7 (19.4)	26.5
EST 07	FU	155	20 (13.1)	88 (57.5)	45 (29.4)	1.3
ETFOL	Birth	222	63 (28.8)	110 (50.2)	46 (21.0)	1.4
EXPRESS	FU	398	37 (9.7)	249 (65.5)	94 (24.7)	4.5
PEP	FU	258	19 (7.7)	114 (46.3)	113 (45.9)	4.7
PIPARI	Birth	215	28 (14.2)	87 (44.2)	82 (41.6)	8.4
Total		**10 330**	**2389**	**4382**	**3036**	

Abbreviation: FU=follow-up; ISCED= International Standard Classification of Education
(a) ACTION (Accesso alle Cure e Terapie Intensive Ostetrico Neonatali; Italy) ; AYLS (Arvo Ylppö Longitudinal Study; Finland); BEST-BLS (Bavarian Longitudinal Study Cohort; Germany); EPIBEL (Belgium); EPICure (UK and Ireland); EPICure-2 (England); EPIPAGE 1 and EPIPAGE 2 (Étude épidémiologique sur les petits âges gestationnels; France); EPICE/SHIPS (Effective Perinatal Intensive Care In Europe; Europe); EST 02-03 and EST 07 (Very low gestational age infants born in Estonia; Estonia); ETFOL (Treatment of extremely preterm infants: parents attitudes; Denmark); EXPRESS (Extremely Preterm Infants in Sweden Study; Sweden); PEP (Project Extreme Prematurity; Norway); PIPARI (Development and Functioning of Very Low Birth Weight Infants from Infancy to School Age; Finland).
(b) All cohorts collected data on the highest educational level achieved, except for EXPRESS where was asked about the cumulated years of education received by the mother.
(c) Number of participants at first follow-up available, except for EPIBEL (11-15 years) and EPIPAGE 1 (5 years)

Table 3 – Distribution of maternal, perinatal characteristics and neonatal morbidities by cohort

		Maternal information					Perinatal and child information						Neonatal morbidities				
Cohort (a)	**n (b)**	% mothers ≥ 35 years	% primiparous	% not living in couple (c)	% country-born mother (d)	GA mean/sd (range)	BW mean (sd)	% of male	% multiple births	% Apgar <7	% c-section	% breast milk at dischar	% NEC-II/III	% IVH-III/IV	% cPVL	% BPD	% ROP-III/V
ACTION	976	36.7	66.5	3.3 (2)	82.9 (1)	29.0/1.9 (23-31)	1250 (347)	54.3	28.5	15.2	80.3	63.3	2.2	3.7	1.6	8.9	3.6
AYLS	58	20.7	51.7	5.3 (1)	98.3 (2)	28.7/2.1 (24-31)	1331 (375)	60.3	12.1	33.3	46.6	na	na	10.3	na	6.9	na
BEST-BLS	329	11.9	50.2	7.1 (1)	91.8 (2)	29.6/1.5 (25-31)	1306 (335)	58.4	23.4	23.5	54.4	na	na	9.4	na	60.5	na
EPIBEL	47	6.5	51.1	12.8 (2)	na	25.3/0.8 (23-26)	785 (182)	61.7	51.1	28.3	59.6	38.3	2.1	12.8	6.4	38.3	nc
EPICure	283	16.3	31.4	19.6 (2)	79.1 (3)	24.9/0.7 (22-25)	746 (113)	47.7	21.2	na	16.3	85.4	3.9	17.7	4.6	74.2	nc
EPICure-2	576	28	40.9	14.5 (2)	73.8 (3)	25.6/1.0 (22-26)	802 (149)	50.2	28.6	na	30.3	48.6	na	15.0	4.2	69.3	19.5
EPIPAGE 1	1535	15.5	44.4	7.1 (1)	86.6 (1)	29.9/2.0 (24-32)	1375 (388)	51.3	31.0	11.3	59.7	35.6	3.5	3.1	2.5	12	1.7
EPIPAGE 2	1884	23.5	38.6	6.5 (1)	79.5 (1)	29.8/2.1 (23-32)	1369 (399)	52.6	36.1	19.0	68.6	52.1	3.3	3.1	0.9	11.1	1.4
EPICE/SHIPS	3345	30.7	62.3	8.5 (2)	85.5 (1)	28.8/2.0 (23-31)	1254 (375)	53.0	32.8	14.7	71.6	66.1	4.8	4,0	3.2	14.4	4.6
EST 02-03	49	na	na	38.8 (2)	na	27.1/1.9 (23-30)	996 (228)	53.1	20.4	48.9	38.8	55.1	14.3	8.7	1.0	36.7	22.4
EST 07	155	26.8	45.8	39.4 (2)	na	28.8/2.2 (22-31)	1314 (392)	56.8	26.5	34.2	65.8	35.5	11.6	5.2	1.0	18.7	9.0
ETFOL	219	21.5	63.0	47.9 (1)	92.9 (1)	27.1/1.8 (24-32)	926 (167)	45.7	29.7	13.6	67.2	49.3	3.2	2.7	2.7	nc	3.3
EXPRESS	398	30.2	59.5	na	79.9 (1)	25.4/1.1 (22-26)	783 (169)	55.0	19.3	33.4	57.5	58.2	5.5	10.1	5.0	22.4 (e)	34.4
PEP	258	20.5	na	nc	na	26.5/1.6 (23-31)	854 (172)	55.0	24.8	21.4	67.4	74.4	nc	3.9	5.4	45.3	4.9
PIPARI	215	31.2	51.9	2.5 (1)	na	28.6/2.8 (24-35)	1143 (327)	55.8	31.2	32.7	60.9	na	nc	5.6	2.8	14.0	4.3

Abbreviations: GA= gestational age; BW= birthweight; NEC-II/III=necrotizing enterocolitis stages II-III; IVH-III/IV=intraventricular haemorrhage stages III-IV; cPVL=cystic periventricular leukomalacia; BPD=bronchopulmonary dysplasia; ROP-III/V=retinopathy of prematurity stages III to V; na=not available; nc=not compatible

(a) ACTION (Accesso alle Cure e Terapie Intensive Ostetrico Neonatali; Italy) ; AYLS (Arvo Ylppö Longitudinal Study; Finland); BEST-BLS (Bavarian Longitudinal Study Cohort; Germany); EPIBEL (Belgium); EPICure (UK and Ireland); EPICure-2 (England); EPIPAGE 1 and EPIPAGE 2 (Étude épidémiologique sur les petits âges gestationnels; France); EPICE/SHIPS (Effective Perinatal Intensive Care In Europe; Europe); EST 02-03 and EST 07 (Very low gestational age infants born in Estonia; Estonia); ETFOL (Treatment of extremely preterm infants: parents attitudes; Denmark); EXPRESS (Extremely Preterm Infants in Sweden Study; Sweden); PEP (Project Extreme Prematurity; Norway); PIPARI (Development and Functioning of Very Low Birth Weight Infants from Infancy to School Age; Finland).

(b) Number of participants at first follow-up available, except for EPIBEL (11-15 years) and EPIPAGE 1 (5 years)

(c) living in couple at birth (1) or at follow-up (2)

(d) (1) country-born motherwhen available, or (2) with the nationality of the country, or (3) from not minor ethnicity

(e) For the EXPRESS cohort, the % of severe bronchopulmonary dysplasia was provided

Table 4 – Unadjusted and adjusted pooled standardized mean differences (SMD) of cognitive scores by maternal educational level for all VPT infants, by gestational age sub-group and for control populations

	Infancy (2-3 years old)			Early childhood (4-7 years old)			Later childhood (8-15 years old)		
	N cohorts	Unadjusted SMD 95% CI I^2	Adjusted SMD[a] 95% CI I^2	N cohorts	Unadjusted SMD 95% CI I^2	Adjusted SMD[a] 95% CI I^2	N cohorts	Unadjusted SMD 95% CI I^2	Adjusted SMD[a] 95% CI I^2
All VPT									
medium vs high	11	-0.15 (-0.23; -0.06) I^2=45%	-0.16 (-0.24; -0.08) I^2=33%	12	-0.29 (-0.38; -0.19) I^2=48%	-0.29 (-0.42; -0.16) I^2=68%	6	-0.14 (-0.38; 0.10) I^2=58%	-0.10 (-0.32; 0,11) I^2=47%
Low vs high	12	-0.32 (-0.43; -0.21) I^2=52%	-0.33 (-0.44; -0.22) I^2=52%	12	-0.57 (-0.67;-0.47) I^2=37%	-0.55 (-0.72; -0.39) I^2=71%	6	-0.54 (-0.72; -0.37) I^2=0%	-0.42 (-0.66; -0.18) I^2=24%
< 27 wks							6		
medium vs high	10	-0.08 (-0.20; 0.04) I^2=19%	-0.09 (-0.19; 0.02) I^2=2%	10	-0.26 (-0.48; -0.04) I^2=63%	-0.24 (-0.46; -0.02) I^2=63%	5	0.16 (-0.06; 0.38) I^2=0%	0.13 (-0.09; 0.35) I^2=0%
Low vs high	10	-0.27 (-0.44; -0.10) I^2=23%	-0.27 (-0.42; 0.12) I^2=10%	11	-0.54 (-0.76; -0.33) I^2=33%	-0.57 (-0.79; -0.34) I^2=41%	5	-0.24 (-0.56; 0.08) I^2=0%	-0.23 (-0.55; 0.09) I^2=0%
≥ 27 wks									
medium vs high	8	-0.24 (-0.39; -0.10) I^2=66%	-0.16 (-0.34; 0.02) I^2=77%	10	-0.38 (-0.56; -0.21) I^2=76%	-0.36 (-0.49; -0.22) I^2=62%	3	-0.36 (-0.57; -0.14) I^2=24%	-0.35 (-0.53; -0.17) I^2=0%
Low vs high	8	-0.37 (-0.52; -0.21) I^2=62%	-0.33 (-0.46; -0.19) I^2=51%	10	-0.65 (-0.84; -0.47) I^2=69%	-0.64 (-0.81; -0.48) I^2=61%	3	-0.70 (-1.24; -0.17) I^2=78%	-0.62 (-1.16; -0.09) I^2=78%
Without neonatal morbidities									
medium vs high	8	-0.12 (-0.18; -0.06) I^2=0%	-0.13 (-0.19; -0.07) I^2=0%	6	-0.34 (-0.47; -0.21) I^2=41%	-0.35 (-0.47; -0.22) I^2=39%		na	na
Low vs high	7	-0.35 (-0.53; -0.17) I^2=68%	-0.35 (-0.53; -0.17) I^2=67%	6	-0.67 (-0.91; -0.44) I^2=62%	-0.68 (-0.92; -0.44) I^2=63%		na	na
Control									
medium vs high	6	-0.12 (-0.22; -0.02) I^2=6%	-0.14 (-0.24; -0.04) I^2=5%	5	-0.43 (-0.56; -0.29) I^2=0%	-0.40 (-0.55; -0.26) I^2=0%		na	na
Low vs high	6	-0.22 (-0.44; -0.01) I^2=58%	-0.27 (-0.49; -0.05) I^2=60%	5	-0.55 (-0.77; -0.33) I^2=6%	-0.64 (-0.91; -0.38) I^2=0%		na	na

Abbreviation: na= not available

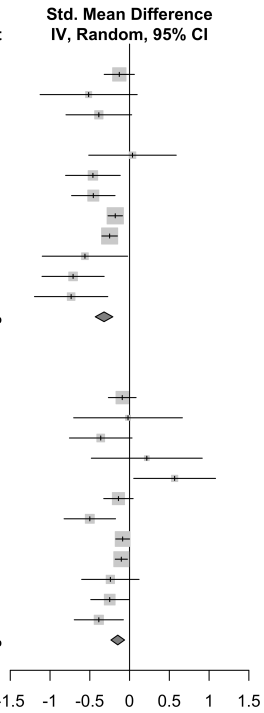
Footnote: the following cohorts took into consideration clustering for multiples in the analyses : ACTION (Italy), AYLS (Finland), BEST-BLS (Germany), EPICure (UK and Ireland), EPICure-2 (England), EPIPAGE 1 (France), EPIPAGE 2 (France), EPICE-SHIPS (Belgium; Denmark; Estonia; Germany; Italy; The Netherlands; Poland; Portugal; UK; Sweden), EST 02-03 (Estonia), EST 07 (Estonia), ETFOL (Denmark), EXPRESS (Sweden), PIPARI (Finland)

(a) adjusted for maternal age and child's sex

Figure 1

a) Infancy childhood (2-3 years old) (12 cohorts)

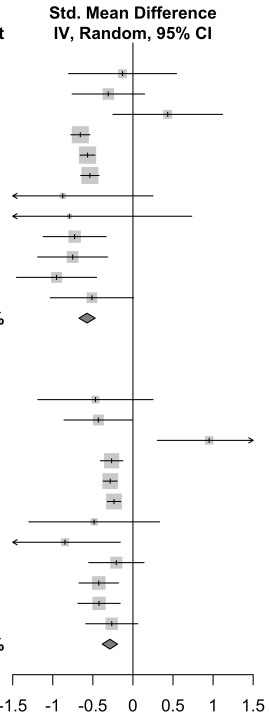
Cohort	Total (Case)	Total (High)	SMD [95% CI]	Weight
Comparison = Low vs high education				
ACTION	290	171	-0.13 [-0.32; 0.06]	14.4%
AYLS	23	20	-0.51 [-1.12; 0.10]	2.9%
BEST	108	29	-0.39 [-0.80; 0.03]	5.5%
EPIBEL	1	15		0.0%
EPICure1	62	16	0.04 [-0.51; 0.59]	3.4%
EPICure2	41	174	-0.46 [-0.80; -0.12]	7.2%
EPIPAGE1	173	76	-0.46 [-0.73; -0.18]	9.8%
EPIPAGE2	1099	840	-0.18 [-0.27; -0.09]	21.5%
EPICE	600	1303	-0.25 [-0.35; -0.15]	21.1%
EST07	20	45	-0.56 [-1.10; -0.03]	3.6%
EXPRESS	37	94	-0.71 [-1.10; -0.32]	6.0%
PIPARI	25	80	-0.73 [-1.20; -0.27]	4.6%
Random effect model	**2479**	**2863**	**-0.32 [-0.43; -0.21]**	**100.0%**
Heterogeneity:Tau^2 = 0.0128; Chi^2 = 20.61, df = 10 (P = 0.02); I^2 = 51%				
Comparison = Interm. vs high education				
ACTION	502	171	-0.09 [-0.27; 0.08]	12.5%
AYLS	14	20	-0.02 [-0.70; 0.66]	1.9%
BEST	184	29	-0.36 [-0.76; 0.03]	4.8%
EPIBEL	17	15	0.22 [-0.48; 0.91]	1.8%
EPICure1	185	16	0.57 [0.05; 1.08]	3.1%
EPICure2	325	174	-0.14 [-0.32; 0.04]	11.9%
EPIPAGE1	76	76	-0.50 [-0.82; -0.18]	6.4%
EPIPAGE2	1315	840	-0.09 [-0.17; 0.00]	17.7%
EPICE	1374	1303	-0.10 [-0.18; -0.03]	18.3%
EST07	88	45	-0.24 [-0.60; 0.12]	5.5%
EXPRESS	249	94	-0.25 [-0.49; -0.01]	9.3%
PIPARI	85	80	-0.39 [-0.69; -0.08]	6.8%
Random effect model	**4414**	**2863**	**-0.15 [-0.23; -0.06]**	**100.0%**
Heterogeneity:Tau^2 = 0.0075; Chi^2 = 19.94, df = 11 (P = 0.05); I^2 = 45%				



Note: ACTION and EPICE/SHIPS (PARCA-R); AYLS and BEST-BLS (Griffiths Mental Development Scale); EPIBEL, EPICure and PIPARI (BSID-II); EPICure-2, EST 07 and EXPRESS (Bayley III); EPIPAGE 1 (Brunet-Lezine); EPIPAGE 2 (ASQ)

b) Early childhood (4-7 years old) (12 cohorts)

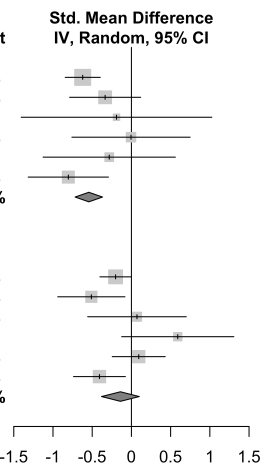
Cohort	Total (Case)	Total (High)	SMD [95% CI]	Weight
Comparison = Low vs high education				
AYLS	17	17	-0.13 [-0.80; 0.54]	4.2%
BEST	80	25	-0.31 [-0.76; 0.14]	7.4%
EPICure1	50	10	0.43 [-0.25; 1.12]	4.1%
EPIPAGE1	689	487	-0.66 [-0.78; -0.54]	17.2%
EPIPAGE2	1099	840	-0.57 [-0.66; -0.47]	17.9%
EPICE	407	1180	-0.54 [-0.65; -0.42]	17.3%
EST0203	6	8	-0.88 [-2.00; 0.25]	1.8%
EST07	2	13	-0.79 [-2.32; 0.73]	1.0%
ETFOL	63	46	-0.73 [-1.12; -0.33]	8.7%
EXPRESS	28	88	-0.75 [-1.19; -0.32]	7.7%
PEP	19	113	-0.95 [-1.45; -0.45]	6.5%
PIPARI	18	76	-0.51 [-1.03; 0.01]	6.2%
Random effect model	**2478**	**2903**	**-0.57 [-0.67; -0.47]**	**100.0%**
Heterogeneity: Tau^2 = 0.0080; Chi^2 = 17.46, df = 11 (P = 0.09); I^2 = 37%				
Comparison = Interm. vs high education				
AYLS	14	17	-0.47 [-1.19; 0.25]	3.1%
BEST	141	25	-0.43 [-0.86; 0.00]	6.5%
EPICure1	160	10	0.95 [0.30; 1.60]	3.7%
EPIPAGE1	331	487	-0.27 [-0.41; -0.13]	13.6%
EPIPAGE2	1315	840	-0.28 [-0.37; -0.20]	14.8%
EPICE	1108	1180	-0.24 [-0.32; -0.15]	14.8%
EST0203	23	8	-0.48 [-1.30; 0.33]	2.6%
EST07	27	13	-0.85 [-1.54; -0.16]	3.3%
ETFOL	110	46	-0.21 [-0.55; 0.14]	8.1%
EXPRESS	240	88	-0.43 [-0.67; -0.18]	10.6%
PEP	114	113	-0.42 [-0.69; -0.16]	10.2%
PIPARI	72	76	-0.26 [-0.59; 0.06]	8.6%
Random effect model	**3655**	**2903**	**-0.29 [-0.38; -0.19]**	**100.0%**
Heterogeneity: Tau^2 = 0.0093; Chi^2 = 21.21, df = 11 (P = 0.03); I^2 = 48%				



Note: AYLS (CMMS, BEERY, and AWST); BEST-BLS, EPICure, EPIPAGE 1 and EST 02-03 (K-ABC); EPIPAGE 2 (WPPSI IV); EPICE/SHIPS (ASQ); EST 07 (K-ABC 2); ETFOL, PEP and PIPARI (WPPSI-R); EXPRESS (WISC-IV)

c) Later childhood (8-15 years old) (6 cohorts)

Cohort	Total (Case)	Total (High)	SMD [95% CI]	Weight
Comparison groups: Low vs high education				
ACTION	214	130	-0.62 [-0.84; -0.40]	33.2%
BEST	79	25	-0.34 [-0.79; 0.12]	21.3%
EPIBEL	3	20	-0.19 [-1.41; 1.02]	5.4%
EPICure1	44	8	-0.00 [-0.76; 0.75]	11.6%
EPICure2	6	57	-0.28 [-1.13; 0.56]	9.8%
PIPARI	20	70	-0.80 [-1.32; -0.29]	18.8%
Random effect model	**366**	**310**	**-0.54 [-0.72; -0.37]**	**100.0%**
Heterogeneity: Tau^2 = 0; Chi^2 = 4.94, df = 5 (P = 0.42); I^2 = 0%				
Comparison groups: Interm. vs high education				
ACTION	381	130	-0.20 [-0.40; 0.00]	24.9%
BEST	144	25	-0.51 [-0.94; -0.08]	16.2%
EPIBEL	19	20	0.07 [-0.56; 0.70]	10.7%
EPICure1	146	8	0.59 [-0.12; 1.31]	9.0%
EPICure2	83	57	0.09 [-0.24; 0.43]	19.5%
PIPARI	74	70	-0.41 [-0.74; -0.08]	19.8%
Random effect model	**847**	**310**	**-0.14 [-0.38; 0.10]**	**100.0%**
Heterogeneity: Tau^2 = 0.0472; Chi^2 = 11.77, df = 5 (P = 0.04); I^2 = 58%				



Note: ACTION and EPICure-2 (K-ABC 2); BEST-BLS and EPICure (K-ABC); EPIBEL (Shortened WISC III); PIPARI (WISC-IV)

Abbreviations: SMD=Standardised mean difference; ASQ= Ages & Stages Questionnaire; ; AWST=Finnish translation of the Aktiver Wortschatztest; BEERY=Beery Developmental Test of Visual-Motor Integration; BSID-II=The Bayley Scales of Infant Development – version 2; CMMS = Columbia Mental Maturity Scale; K-ABC= Kaufman Assessment Battery for Children; K-ABC 2= Kaufman Assessment Battery for Children-second edition; PARCA-R=Parent Report of Children's Abilities-Revised; Shortened WISC III= Wechsler Intelligence Scale for Children-Third edition short form; WISC-IV= Wechsler Intelligence Scale for Children-Fourth Edition; WPPSI IV= Wechsler Preschool & Primary Scale of Intelligence-Fourth edition; WPPSI-R= Wechsler Preschool & Primary Scale of Intelligence-Revised edition

SUPPLEMENTARY ONLINE MATERIALS

Supplementary Table S1 - Information on geographical coverage, inclusion criteria, and participants of term control groups by cohort and by age group

Cohort	Country.coverage. if not national[1]	Inclusion/exclusion criteria	Years of birth	Maternal educational level	Period 1 (2-3 years): IQ test and score / N participants with complete assessment	Period 2 (4-7 years): IQ test and score / N participants with complete assessment
ACTION	FVG, Tuscany, Marche, Lazio and Calabria	Inclusion: term-born Exclusion: foreign mothers	2005-2006	Same measure than for cases	PARCA-R (Non-verbal) / n=380	Not available
AYLS	County of Uusimaa, Finnland	Inclusion: An infant born after every second hospitalized infant and without evidence of neonatal illness was identified from one of the three biggest maternity hospitals in the study area during the same period.	1985/86	Same measure than for cases	Griffiths Mental Development Scale (DQ) / n=658	Not available
BLS	Southern Bavaria, Germany	Inclusion: Healthy infants who were cared for on the normal postnatal wards in the same obstetric hospitals	1985/86	Same measure than for cases	Griffiths Mental Development Scale (DQ) / n=916	K-ABC (MPC) / n=350
EPIPAGE 2	France	Inclusion: selected sample from the Elfe cohort of children born at or near term (>=37 wks)	2011	Same measure than for cases	Not available	WPPSI-IV (FSIQ) / n=592 (1)
EST 07	Whole Estonia	Inclusion: term healthy infant matched with the study group by sex. age and birth hospital Exclusion: Illness and intensive care requirement within 1st week of life.	2007	Same measure than for cases	Bayley-III (cognitive score) / n=153	Not available
ETFOL	All Denmark	Inclusion: 36-43 completed weeks	1994-1995	Same measure than for cases	Not available	WPPSI-R (FSIQ) / n=76

EXPRESS	Whole Sweden	Inclusion: singleton at-term birth with a 5-minute Apgar score greater than 3 with matching of control participants for place of living, sex, GA-adjusted day of birth +/- 14days, and maternal country of birth Exclusion: Women delivering extremely preterm but not residing in Sweden in study period. Terminations of pregnancy and infants born outside of Sweden and transferred to Sweden for neonatal care	2004-2007	Same measure than for cases	Bayley-III (cognitive score) / n=370	WISC-IV (FSIQ) / n=371
PIPARI	Finland/Turku university hospital	The parents of first boy and girl born in each week was asked to take part in the study. If they refused. the parents of next boy/girl were asked. Inclusion criteria were 1) birth weight ≥-2 SD according to age and gender specific Finnish growth charts 2) gestational age ≥37 weeks at birth 3) the family lived inside the hospital catchment area 4) the child was not admitted to neonatal care during the first week of life 5) family was Finnish or Swedish speaking.	2001-2003	Different measure / variable has been changed in the same manner as for cases group	BSID-II (MDI) / n=165	WPPSI-R (FSIQ) / n=151 (2)

(1) Charles MA. Thierry X. Lanoe JL. Bois C. Dufourg MN. Popa R. Cheminat M. Zaros C. Geay B. Int J Epidemiol. 2020 Apr 1;49(2):368-369j. doi: 10.1093/ije/dyz227).

(2) Munck. P. Haataja. L. Maunu. J. Parkkola. R. Rikalainen. H. Lapinleimu. H. & PIPARI Study Group. Cognitive outcome at 2 years of age in Finnish infants with very low birth weight born between 2001 and 2006. Acta paediatrica. 2010; 99(3). 359-366.

Supplementary Table S2 - Information on cognitive tests, scores and reference population by cohort and by age group

Cohort	IQ test	Score (a- Age-based, scaled; b-Raw)*	Reference population (country, birth year)	Definition of cognitive delay	IQ test	Score (a- Age-based, scaled; b-Raw)	Reference population (country, birth year)	Definition of cognitive delay	IQ test	Score (a- Age-based, scaled; b-Raw)	Reference population (country, birth year)	Definition of cognitive delay	Information and references
		Infancy (2 to 3 years)			**Early childhood (4 to 7 years)**				**Later childhood (8 to 15 years)**				
ACTION	PARCA-R	non verbal cognition (0-34) (b)	None	<22 (1)					K-ABC 2	MPI (a)	Norms (Italy. collection in 2007-2011)	<-1SD (<85)	**Infancy:** <2.5th percentile of the term reference group was used : Johnson. S.. Evans. T. A.. Draper. E. S.. Field. D. J.. Manktelow. B. N.. Marlow. N.. ... & Boyle. E. M. (2015). Neurodevelopmental outcomes following late and moderate prematurity: a population-based cohort study. Archives of Disease in Childhood-Fetal and Neonatal Edition. 100(4). F301-F308. **Later childhood:** Valente Torre L. KABC-II. Studio italiano e norme preliminari. Giunti O.S. ed. January 2011).
AYLS	Griffiths Mental Development Scale	DQ (a)	Norms (Finland, 1985)	<-1SD	Multiple tests (CMM,AWST, and BEERY)	IQ composite score (a)	Norms (Finland, 1985)	<-1SD					
BEST-BLS	Griffiths Mental Development Scale	DQ (a)	Norms (Bavaria, 1985)	<-1SD	K-ABC	MPC (a)	Norms (Bavaria, 1985)	<-1SD	K-ABC	MPC (a)	Norms (Bavaria, 1985)	<-1SD	

EPIBEL	BSID-II	MDI (a)	Norms (Netherlands, 1996-1999)	<85(<-1SD)				Shortened WISC III	Intelligence score (a)	Norms (Netherlands; n/a)	<85 (<-1SD)	**Infancy:** van der Meulen BF, Ruiter SA, Spelberg LHC, Smrkovsky ´M. Bayley Scales of Infant Development (BSID) – II. Nederlandse versie. Lisse, The Netherlands: Swets Test Publishers; 2002. **Later childhood:** Kort, W., Schittekatte, M., Dekker, P.H., Verhaeghe, P., Compaan, E.L., Bosmans, M. & Vermeir, G.. (2005). WISC-III NL. Handleiding en Verantwoording. London: The Psychological Corporation. Reference abbreviated IQ score: Reference abbreviated IQ score: Gregoire J (2000) Comparison of three short forms of the Wechsler Intelligence Scale for Children: third edition (WISCIII). Eur Rev Appl Psychol 50:437–441
EPICure	BSID-II	MDI (a)	Norms (USA, -)	<85 (<-1SD)	K-ABC	MPC (a)	Norms (UK. late 1970s) or control	<95 (<-1SD) (controls as reference)	K-ABC	MPC (a)	Control	<93 (<-1SD)	**Infancy:** Bayley N. Manual for the Bayley Scales of Infant Development. 2nd ed. San Antonio, Tex.: Psychological Corporation, 1993
EPICure-2	Bayley III	MDI and predicted MDI (a)	-	<85 (<-1SD)					K-ABC 2	MPI (a)	Control	<91 (<-1SD)	**Infancy:** Bayley III scores were converted to a predicted mental developmental index because of difficulty in interpreting the results of Bayley III assessments as absolute values. See Moore. T.. Johnson. S.. Haider. S.. Hennessy. E.. & Marlow. N. (2012). Relationship between test scores using the second and third editions of the Bayley Scales in extremely preterm children. The Journal of pediatrics. 160(4). 553-558.
EPIPAGE 1	revised Brunet-Lezine	DQ (a)	Norms (France, -)	<85 (<-1SD)	K-ABC	MPC (a)	Norms	<85 (<-1SD)					

EPIPAGE 2	ASQ (5 subscales)	ASQ score (0-300) (b)	None	<-2SD from the mean on any of the five domains (2)	WPPSI IV	FSIQ (a)	Control	<85 (<-1SD)		**Infancy:** Squire J. Twombly E. Bricker D. Potter L. ASQ-3:User's guide. BaltimoreBrookes Publishing: Ages & Stages Questionnaires®. Third Edition (ASQ-3TM). 2009. http://products.brookespublishing.com/Ages-Stages-Questionnaires-Third-Edition-ASQ-3 P569.aspx. Accessed December 28. 2016
EPICE/SHIPS	PARCA-R	non verbal cognition (0-34) (b)	None	<22	ASQ	Problem solving subscale	None	<-2SD		**Infancy:** <2.5th percentile of the term reference group was used : Johnson. S.. Evans. T. A.. Draper. E. S.. Field. D. J.. Manktelow. B. N.. Marlow. N.. ... & Boyle. E. M. (2015). Neurodevelopmental outcomes following late and moderate prematurity: a population-based cohort study. Archives of Disease in Childhood-Fetal and Neonatal Edition. 100(4). F301-F308. **Early childhood**: Squire J. Twombly E. Bricker D. Potter L. ASQ-3:User's guide. BaltimoreBrookes Publishing: Ages & Stages Questionnaires®. Third Edition (ASQ-3TM). 2009. http://products.brookespublishing.com/Ages-Stages-Questionnaires-Third-Edition-ASQ-3 P569.aspx. Accessed December 28. 2016
EST 02-03					K-ABC	MPI (a)	Norms (Estonia, 2002-2003)	<85 (<-1SD)		
EST 07	Bayley III	Cognitive scale (a)	Norms (Estonia. 2007)	<85 (<-1SD)	K-ABC 2	MPI (a)	Norms (Estonia, 2001)	<85 (<-1SD)		

ETFOL					WPPSI-R	FSIQ (a)	Control	<96 (-1SD)					
EXPRESS	Bayley III	Cognitive scale (a)	Controls (Swedish, 2004-2007)	<85 (<-1SD)	WISC-IV	FSIQ (a)	Norms (Scandinavian, n/a)	<85 (<-1SD)					
PEP					WPPSI-R	FSIQ (a)	Norms (Sweden,1999)	<85 (<-1SD)					**Early childhood**: Wechsler D (1999) Wechsler preschool and primary scale of intelligence-revised (Swedish edition). Psykologforlaget AB.Stockholm
PIPARI	BSID-II	MDI (a)	Norms (US, 1993) and controls	<85 (<-1SD)	WPPSI-R	FSIQ (a)	Norms (Finland; 1995) and controls	<85 (<-1SD)	WISC-IV	FSIQ (a)	Norms (Finland; 2011)	<90 (<-0.68 SD)	**Later childhood:** Wechsler D. Wechsler Intelligence Scale for Children -IV. Käsikirja II. Teoriatausta. standardointi ja tulkinta (Handbook II. Theoretical background. standardization and interpretation). Jyväskylä Psykologien Kustannus 2011.

* Tests asked in infancy included cognitive scale (PARCA-R/non verbal cognition; BSID-II/MDI; Bayley-III/cognitive scale) and multidomain scale (Griffiths Mental Development Scale/DQ; ASQ/ASQ score)

(1) <2.5th percentile of the term reference group was used : Johnson, S., Evans, T. A., Draper, E. S., Field, D. J., Manktelow, B. N., Marlow, N., ... & Boyle, E. M. (2015). Neurodevelopmental outcomes following late and moderate prematurity: a population-based cohort study. Archives of Disease in Childhood-Fetal and Neonatal Edition, 100(4), F301-F308.

(2) Squire J, Twombly E, Bricker D, Potter L. ASQ-3:User's guide. BaltimoreBrookes Publishing: Ages & Stages Questionnaires®, Third Edition (ASQ-3TM), 2009. http://products.brookespublishing.com/Ages-Stages-Questionnaires-Third-Edition-ASQ-3 P569.aspx.
Accessed December 28, 2016"

Supplementary Table S3 - IQ scores and missing data by cohort and by age group

Cohort	Infancy (2 to 3 years)			Early childhood (4 to 7 years)			Later childhood (8 to 15 years)		
	Missing data on IQ (%)[1]	Complete assessment (n)	mean IQ (SD)	Missing data on IQ (%)[1]	Complete assessment (n)	mean IQ (SD)	Missing data on IQ (%)[1]	Complete assessment (n)	mean IQ (SD)
ACTION	18.4	976	25.0 (4.0)	n/a	n/a	n/a	9.1	731	98.1 (19.7)
AYLS	9.4	58	93.0 (18.9)	22.6	48	91.7 (15.0)	n/a	n/a	n/a
BEST-BLS	16.1	329	88.9 (24.4)	32.5	264	84.8 (17.3)	30.4	272	87.6 (18.8)
EPIBEL	19.5	62	79.6 (19.8)	n/a	n/a	n/a	11.3	47	80.7 (18.5)
EPICure	8.4	283	81.6 (14.4)	22	241	82.1 (19.2)	28.7	219	83.7 (18.0)
EPICure-2	0	576	93.3 (15.2)	n/a	n/a	n/a	19.5	161	85.3 (18.9)
EPIPAGE 1	16.8	406	92.9 (14.7)	16.8	1535	93.5 (19.2)	n/a	n/a	n/a
EPIPAGE 2	0.3	1884 [3]	223.6 (44.4)	33.2	1968	95.8 (15.2)	n/a	n/a	n/a
EPICE/SHIPS	2.8	3345	25.5 (5.2)	3.7	2799 [4]	72.6 (19.3)	n/a	n/a	n/a
EST 02-03	n/a	n/a	n/a	19.7	49	87.1 (10.9)	n/a	n/a	n/a
EST 07	0.6	155	94.7 (15.5)	16.1	47	91.7 (18.8)	n/a	n/a	n/a
ETFOL	n/a	n/a	n/a	9	222	99.5 (15.5)	n/a	n/a	n/a
EXPRESS	19.4	398	94.3 (12.3)	26.1	359	83.9 (14.6)	n/a	n/a	n/a
PEP	n/a	n/a	n/a	15.7	258	92.8 (15.5)	n/a	n/a	n/a
PIPARI	3.3	208	101.6 (14.6)	13	181	101.1 (16.6)	11.1	176	87.8 (17.5)

Abbreviation: n/a= not available

(1) % of participants with missing data at assessment at FU

(2) only 1 region did participate at the follow up at 2-3 years

(3) exclusion of children with CP, deafness, blindness, or severe congenital brain malformations

(4) ASQ was administrated to the entire sample. The WPPSI was administered to all GA<28 weeks (n=672 with complete assessment; mean: 91.5; SD 18.3)

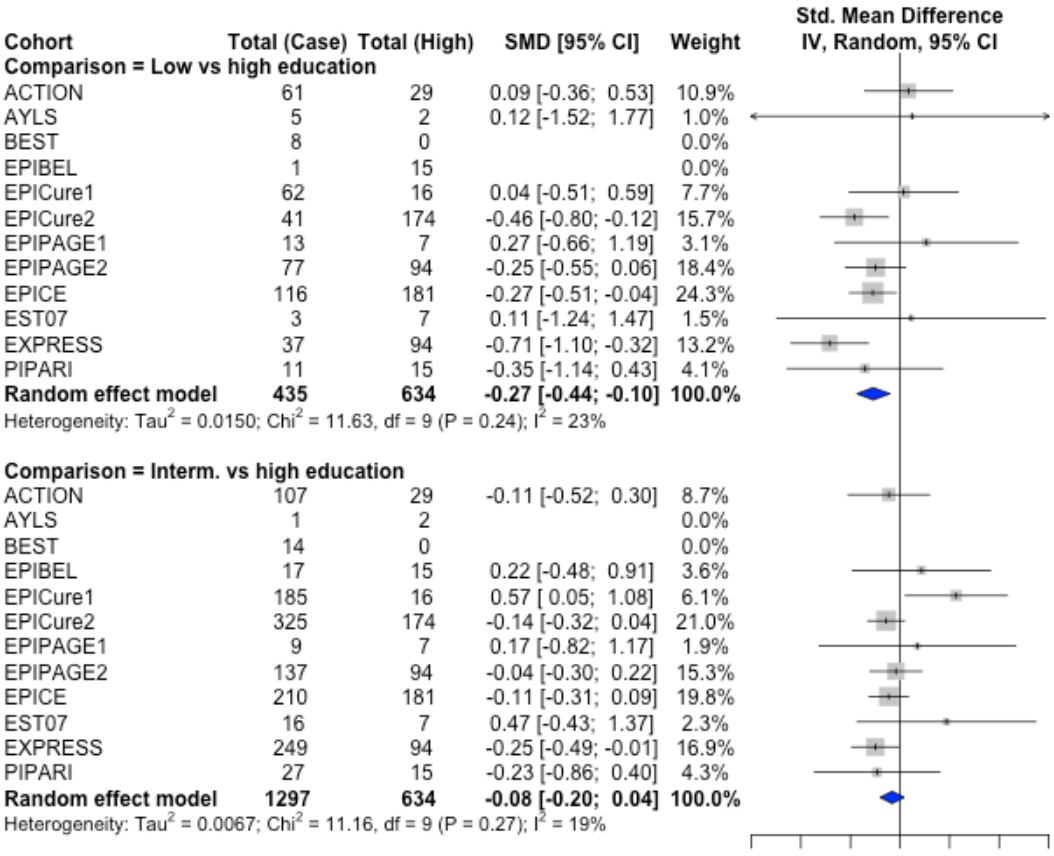
Supplementary Table S4 – Results from sensitivity analysis

Sub-groups	Infancy (2-3 years old)			Early childhood (4-7 years old)		
	N cohorts	**Unadjusted SMD (low vs high) (95% CI)**	**p-value***	**N cohorts**	**Unadjusted SMD (low vs high) (95% CI)**	**p-value***
Measure of maternal educational level						
At birth	6	-0.31 (-0.46 ; -0.15)	0.5951	6	-0.59 (-0.67; -0.51)	0.8749
At follow-up	5	-0.38 (-0.59; -0.16)		6	-0.56 (-0.89; -0.24)	
Type of administration						
Parent report	3	-0.20 (-0.27; -0.14)	0.0004	-	-	
Examiner	8	-0.49 (-0.63; -0.34)		-	-	
Type of test						
Cognitive test	7	-0.36 (-0.53; -0.18)	0.6891	-	-	
Multi-domains test	4	-0.31 (-0.49; -0.13)		-	-	

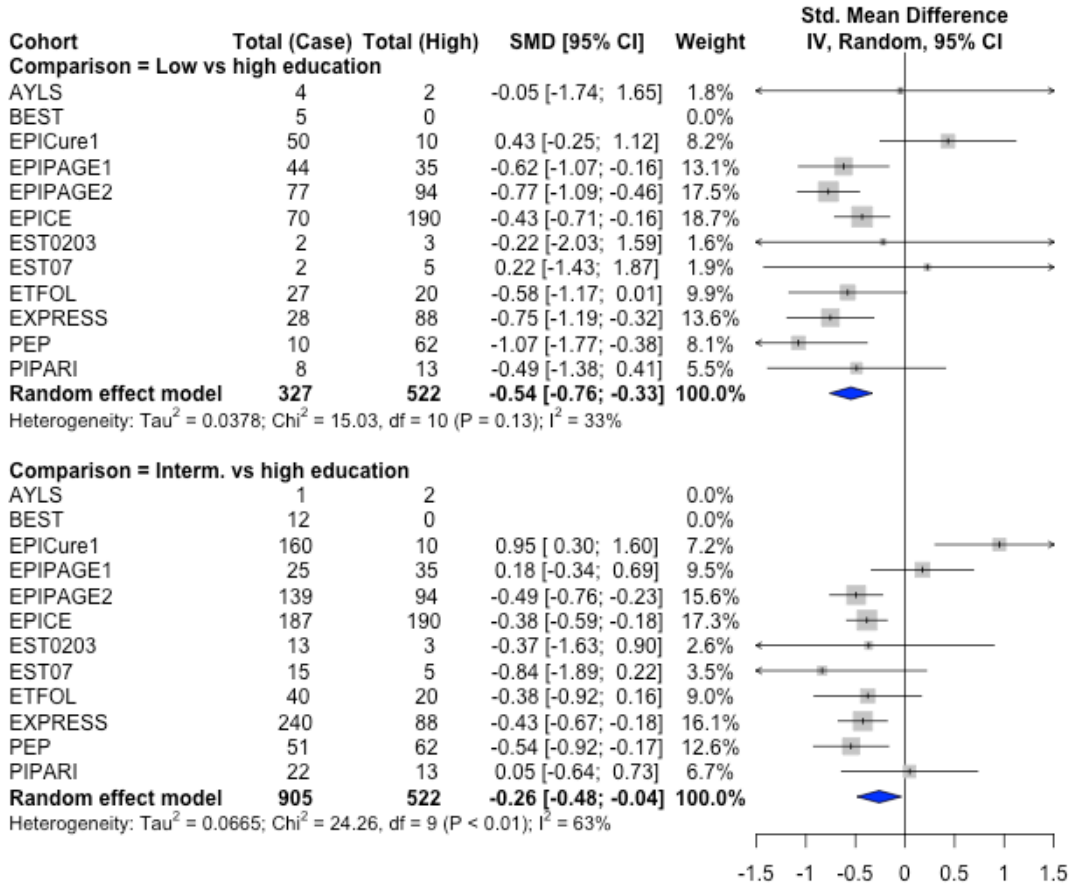
* Test for subgroup differences (random effects model)

Supplementary Figure S1 – Forest plot of standardized mean differences of unadjusted mean IQ scores (SMD and 95% CI) in children born <27 weeks of gestation

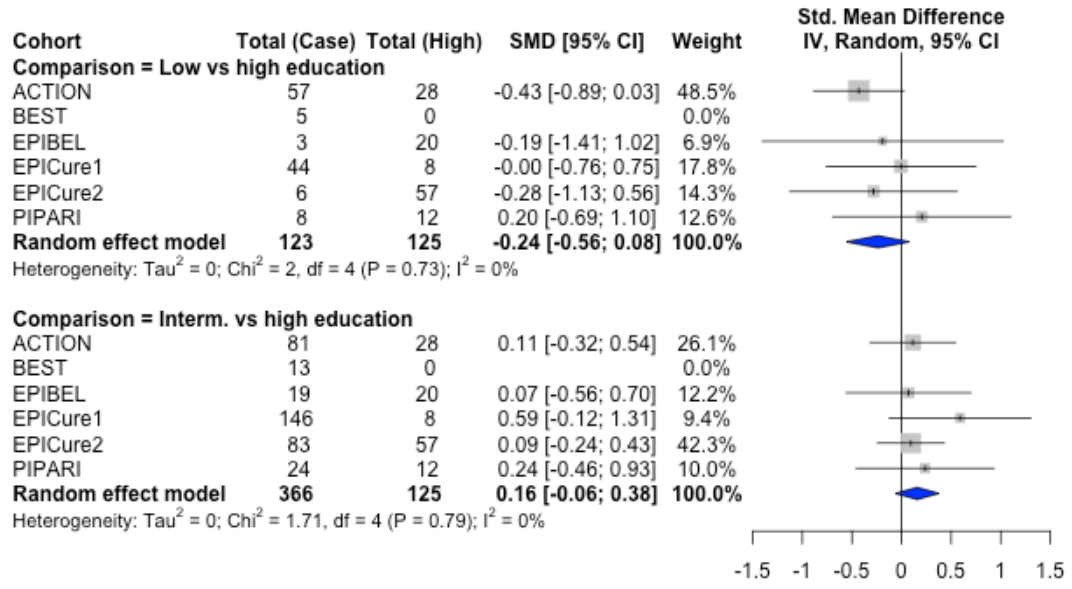
a- Infancy (2-3 years old)



b- Early childhood (4-7 years old)

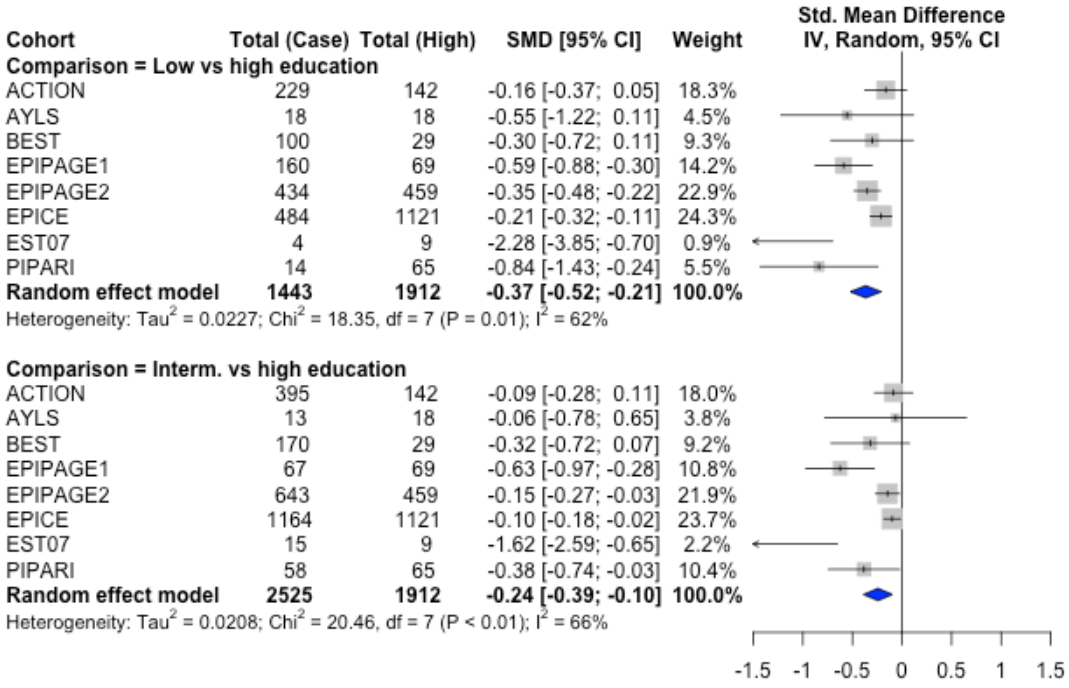


c- Later childhood (8-15 years old)

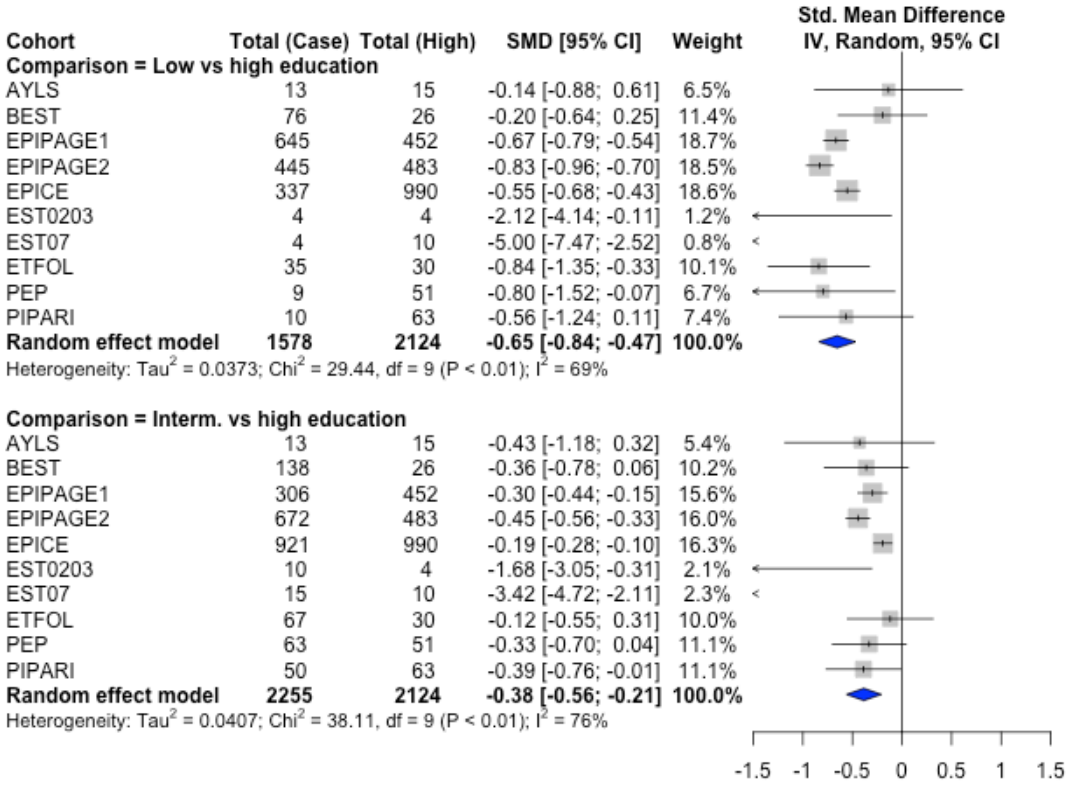


Supplementary Figure S2 – Forest plot of standardized mean differences of unadjusted mean IQ scores (SMD and 95% CI) in children born ≥ 27 weeks of gestation

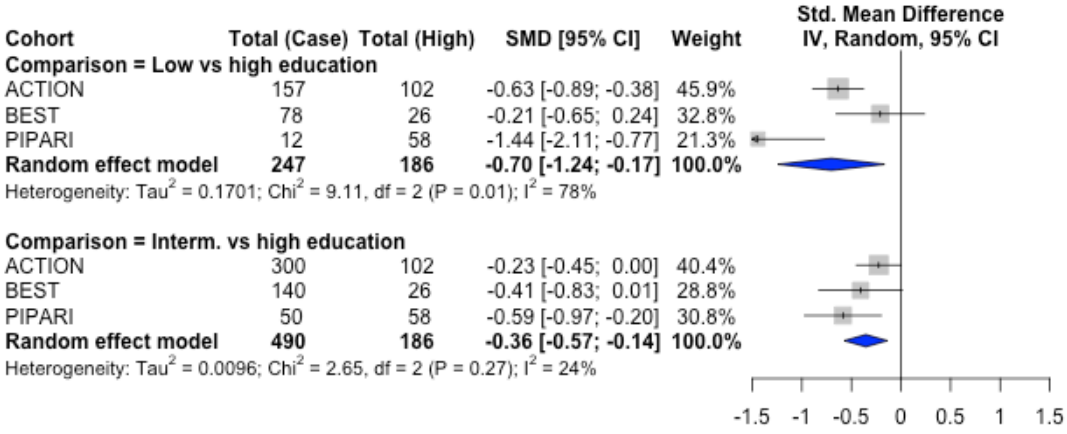
a- Infancy (2-3 years old)



b- Early childhood (4-7 years old)

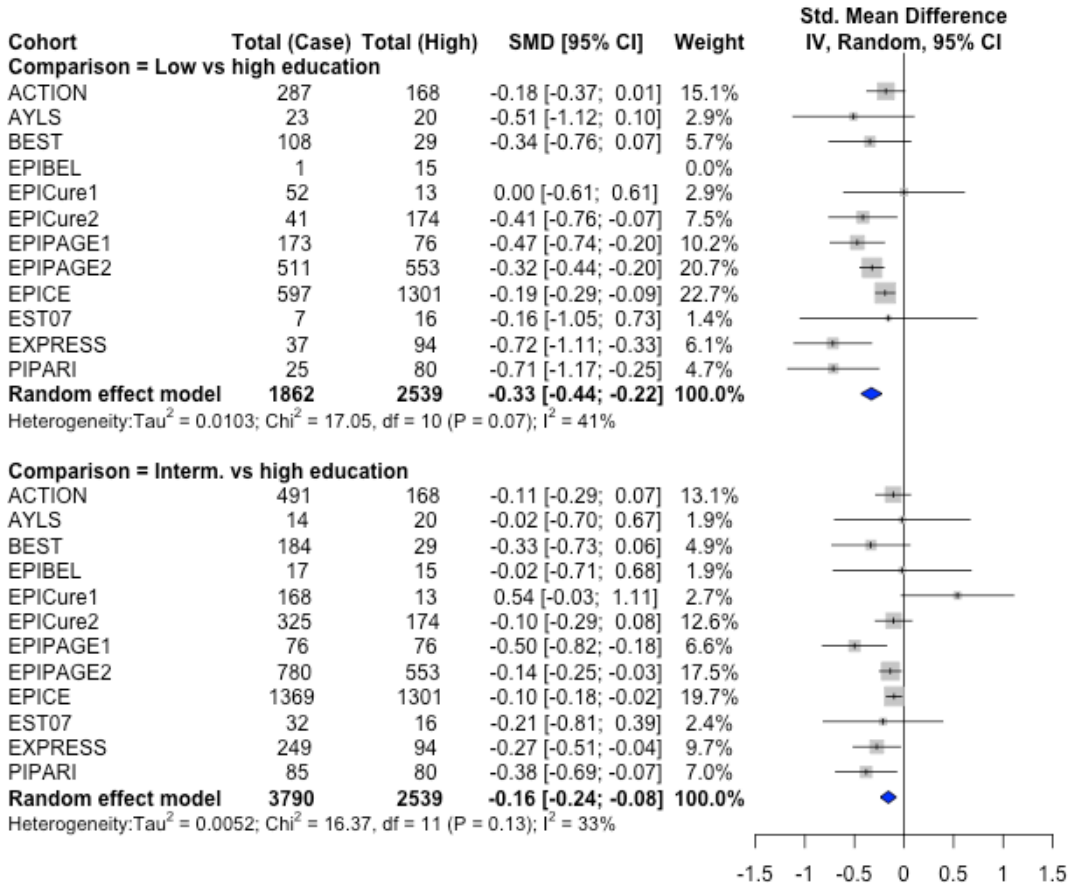


c- Later childhood (8-15 years old)

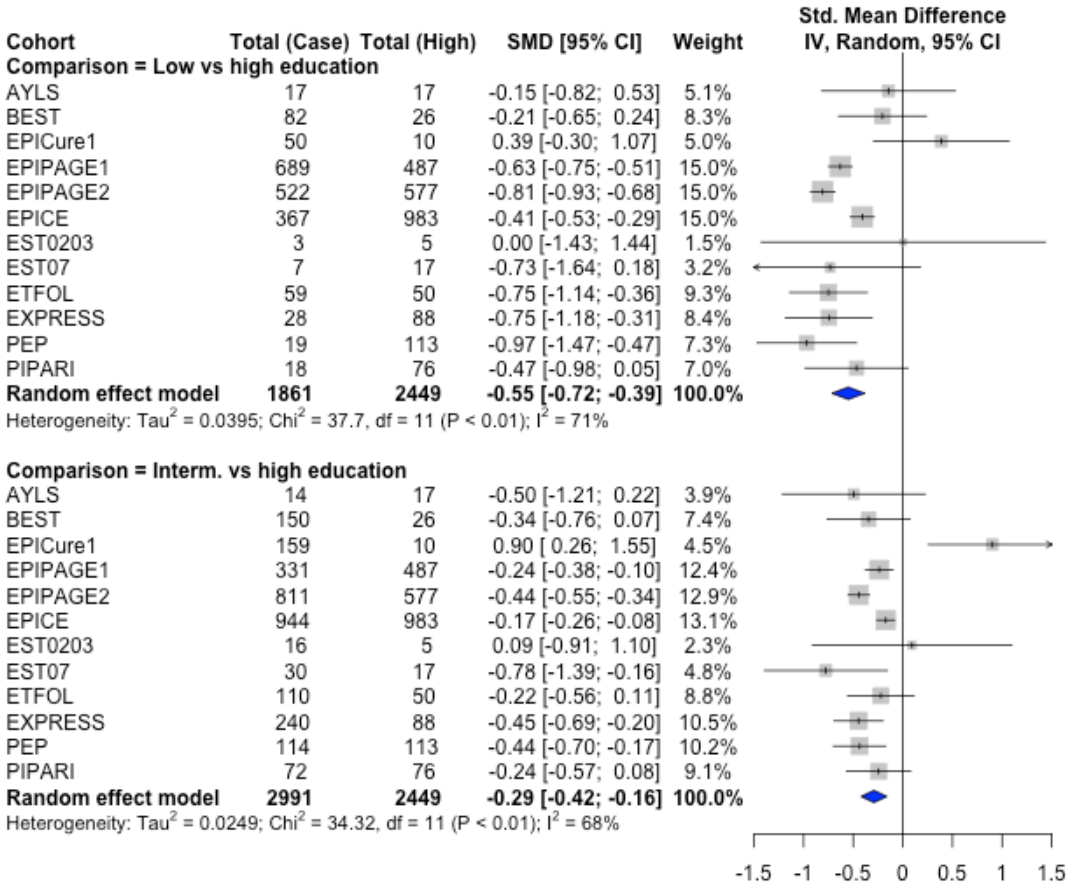


Supplementary Figure S3 – Forest plot of standardized mean differences of adjusted mean IQ scores (SMD and 95% CI) in all VPT children

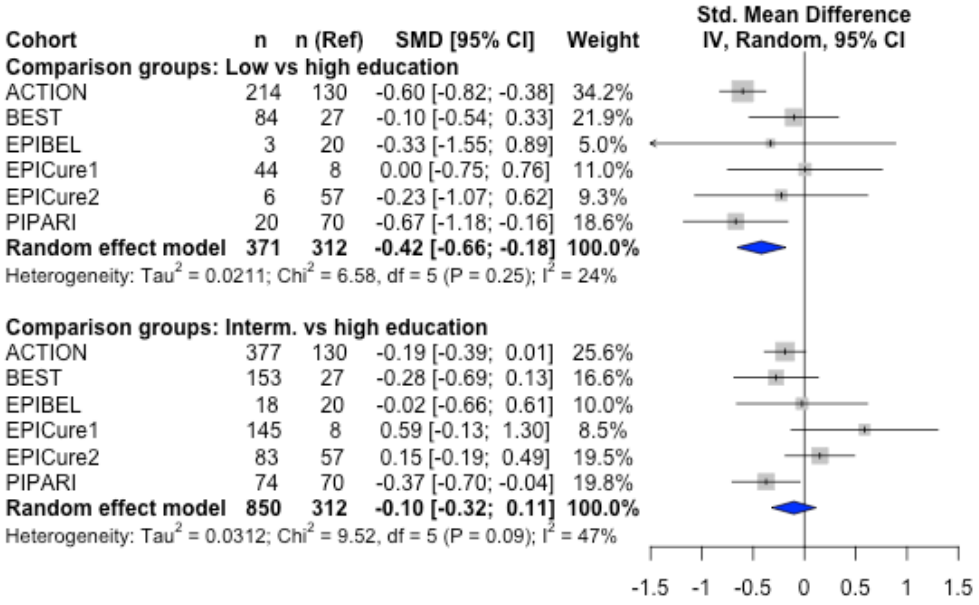
a- Infancy (2-3 years old)



b- Early childhood (4-7 years old)

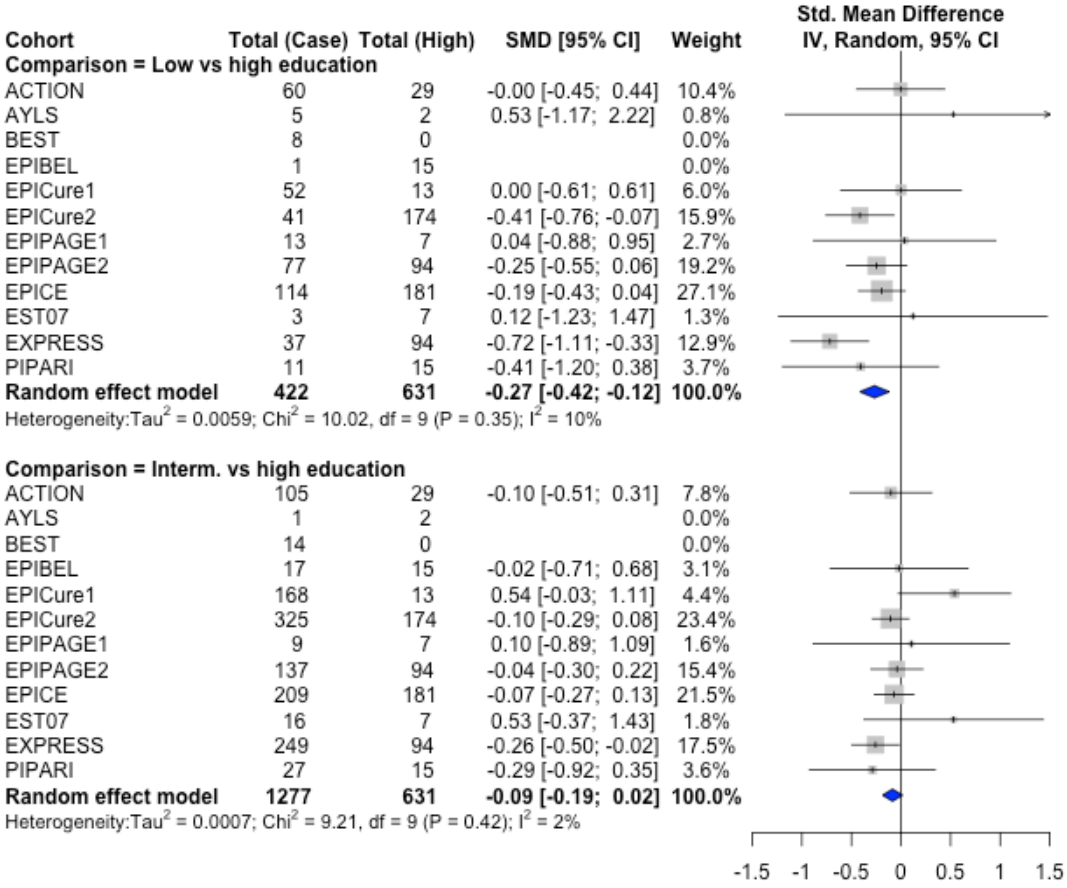


c- Later childhood (8-15 years old)

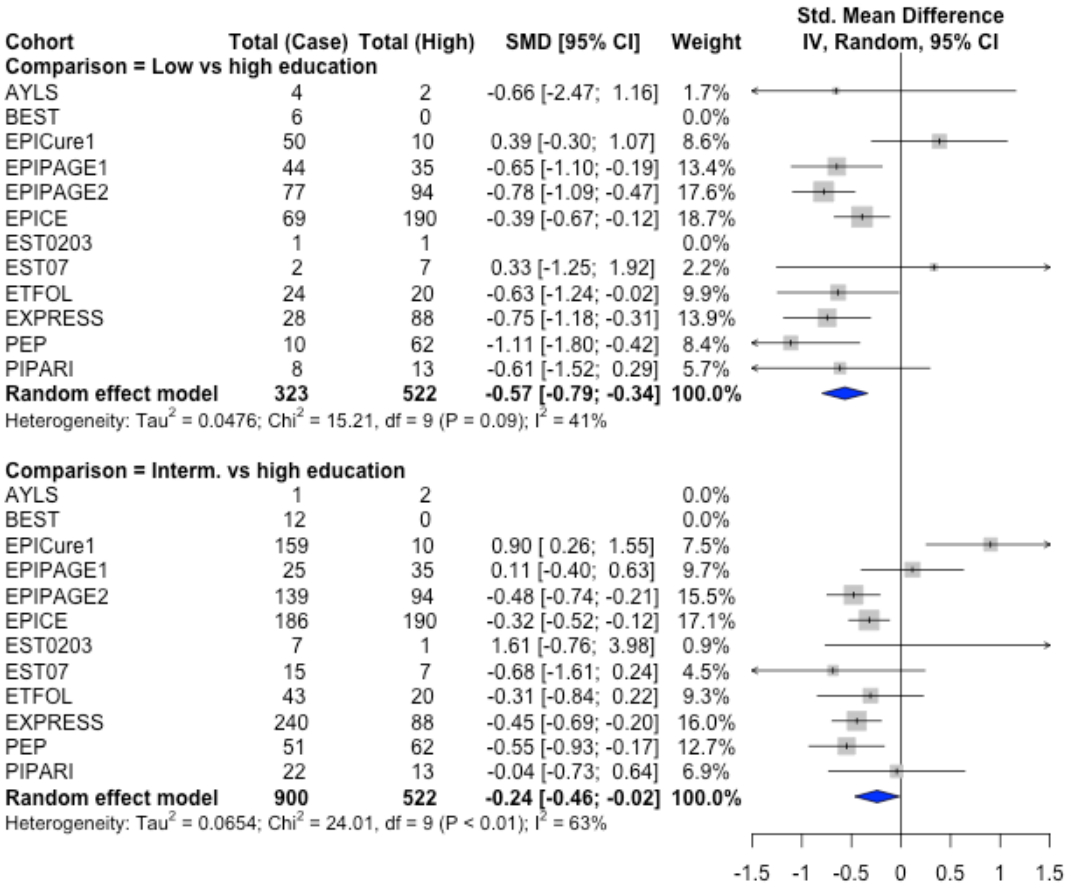


Supplementary Figure S4 – Forest plot of standardized mean differences of adjusted mean IQ scores (SMD and 95% CI) in children born <27 weeks of gestation

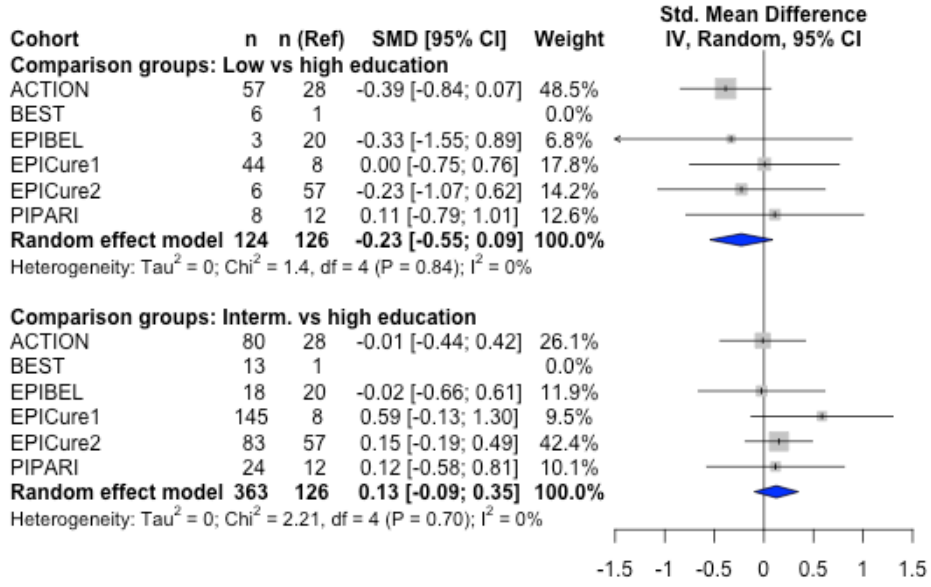
a- Infancy (2-3 years old)



b- Early childhood (4-7 years old)

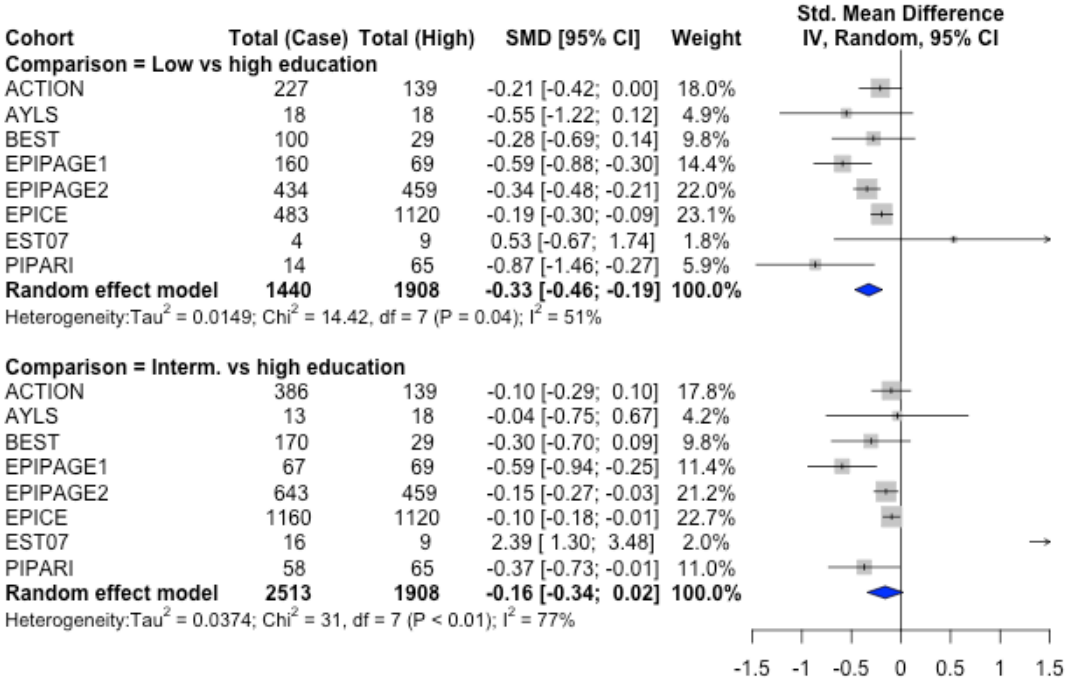


c- Later childhood (8-15 years old)

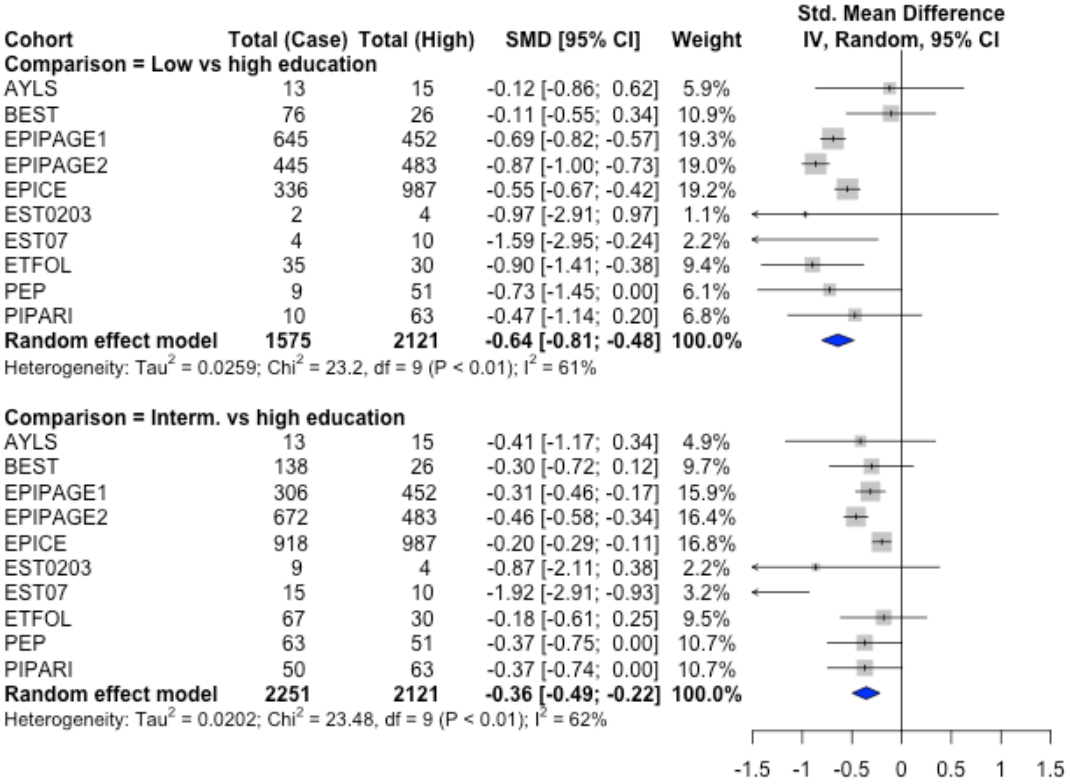


Supplementary Figure S5 – Forest plot of standardized mean differences of adjusted mean IQ scores (SMD and 95% CI) in children born ≥ 27 weeks of gestation

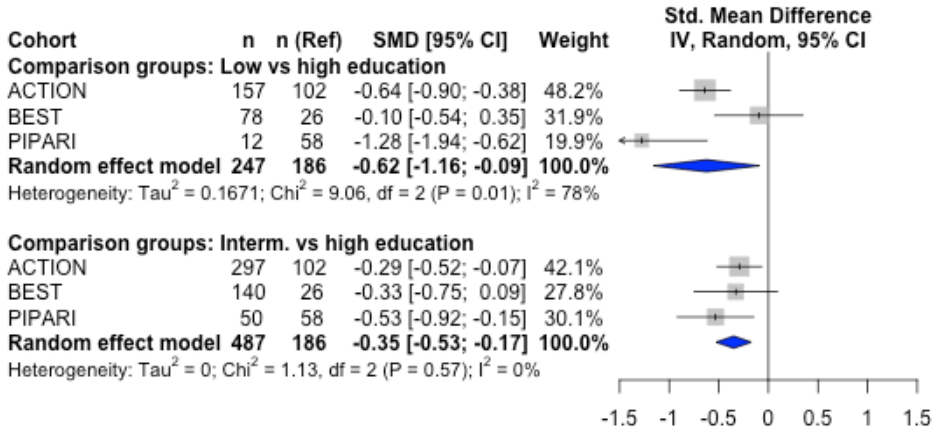
a- Infancy (2-3 years old)



b- Early childhood (4-7 years old)



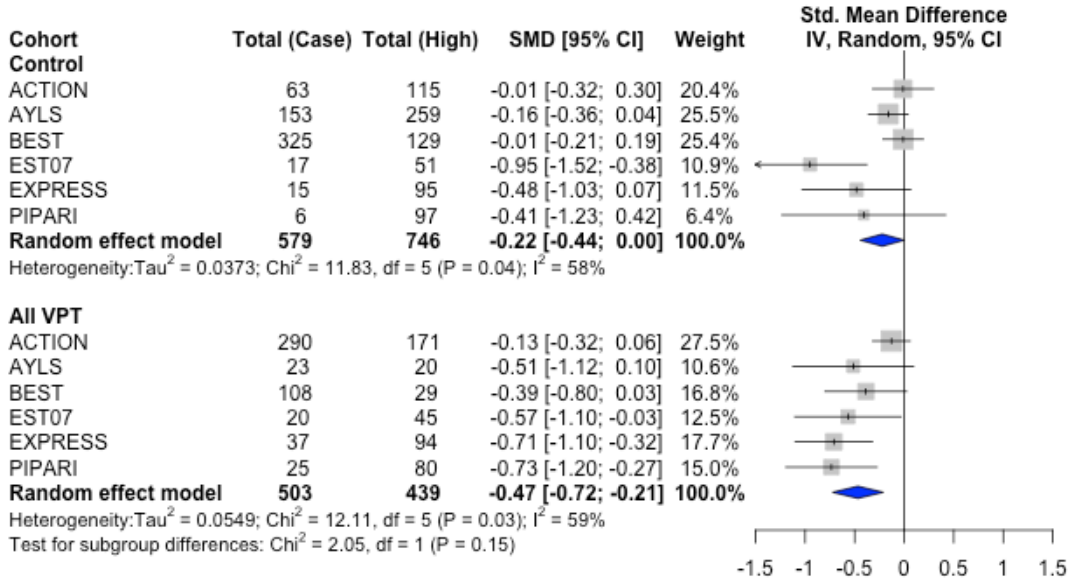
c- Later childhood (8-15 years old)



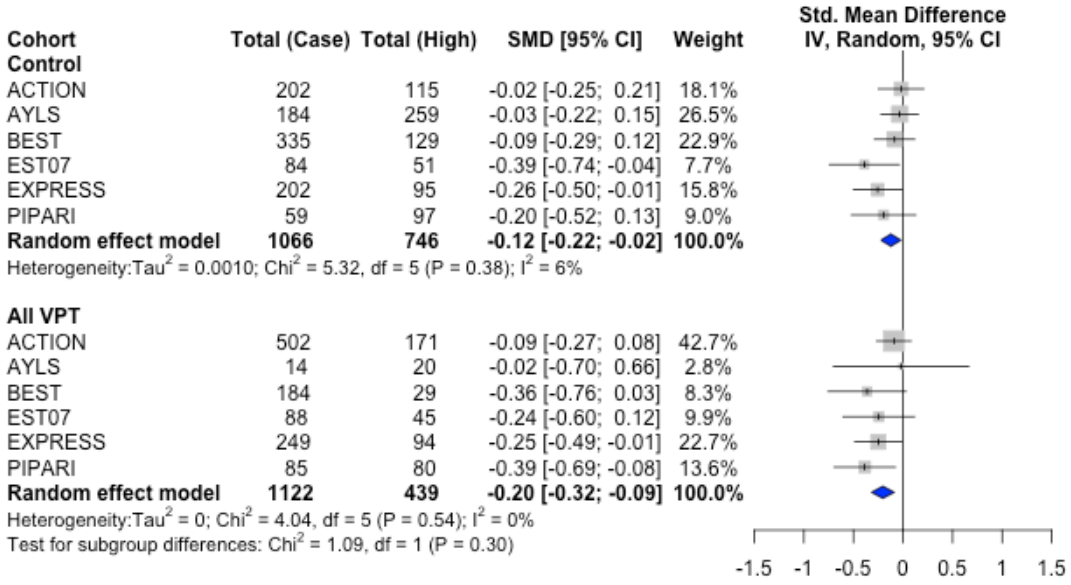
Supplementary Figure S6 – Forest plot of standardized mean differences of unadjusted mean IQ scores (SMD and 95% CI) : VPT vs term controls

a- Infancy (2-3 years old)

i. Low education level vs high education level

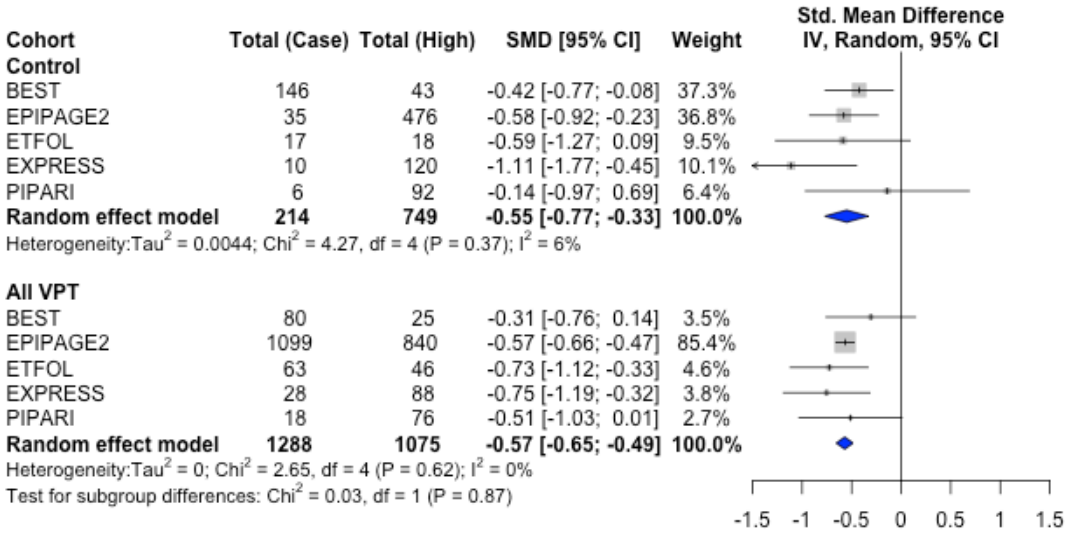


ii. Medium education level vs high education level

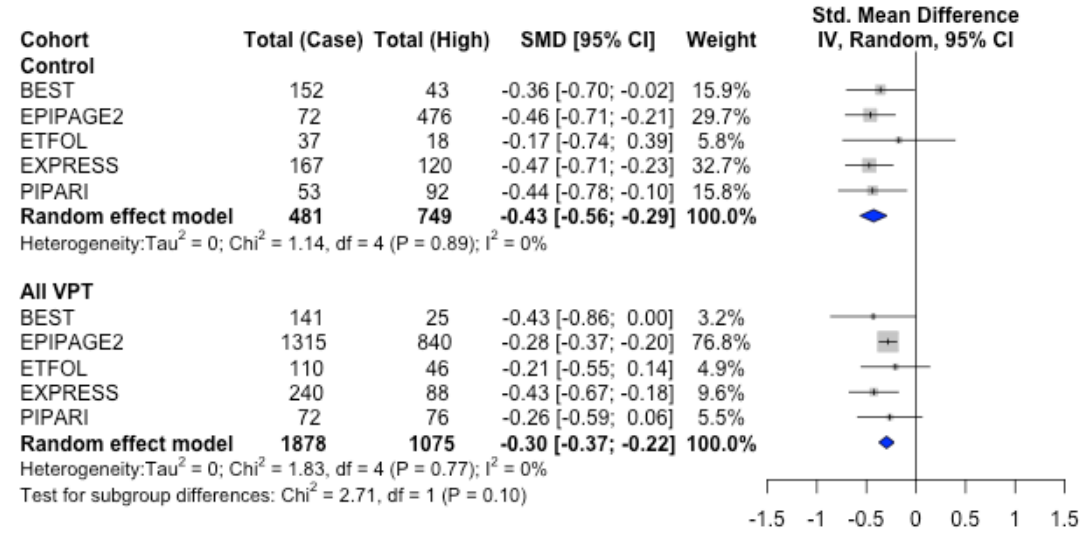


b- Early childhood (4-7 years old)

i. Low education level vs high education level

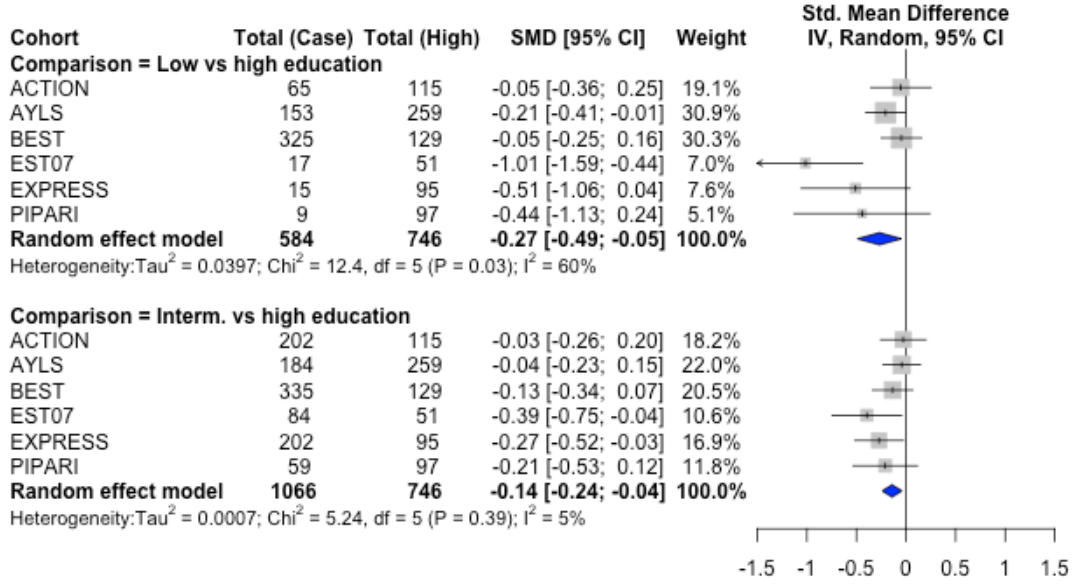


ii. Medium education level vs high education level

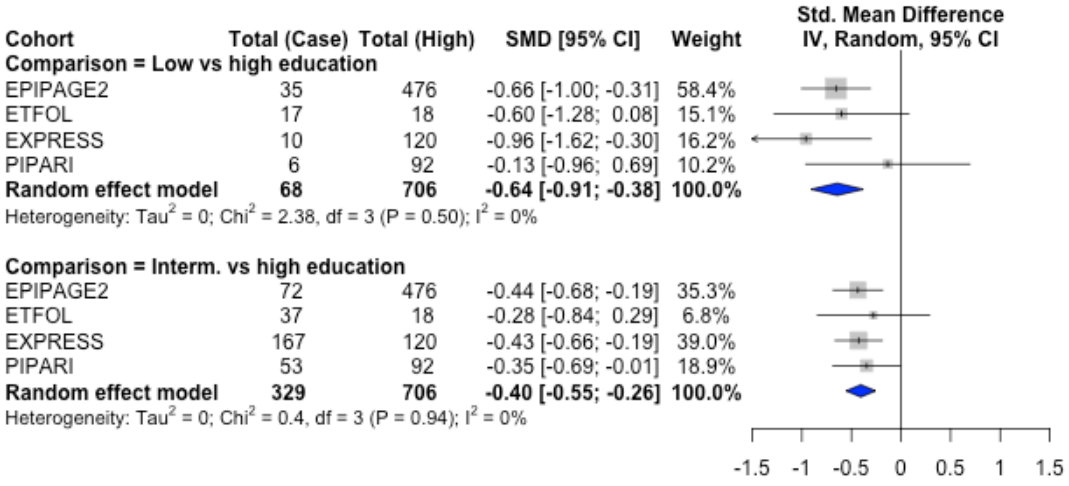


Supplementary Figure S7 – Forest plot of standardized mean differences of adjusted mean IQ scores (SMD and 95% CI) in term controls

a- Infancy (2-3 years old)



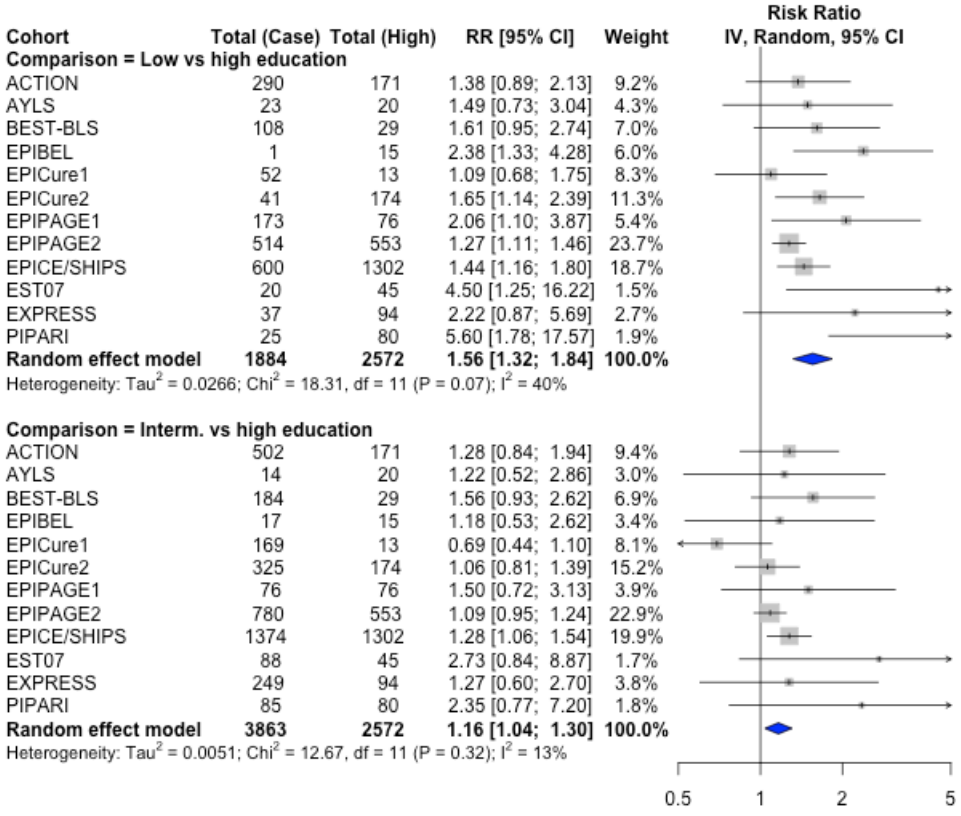
b- Early childhood (4-7 years old)



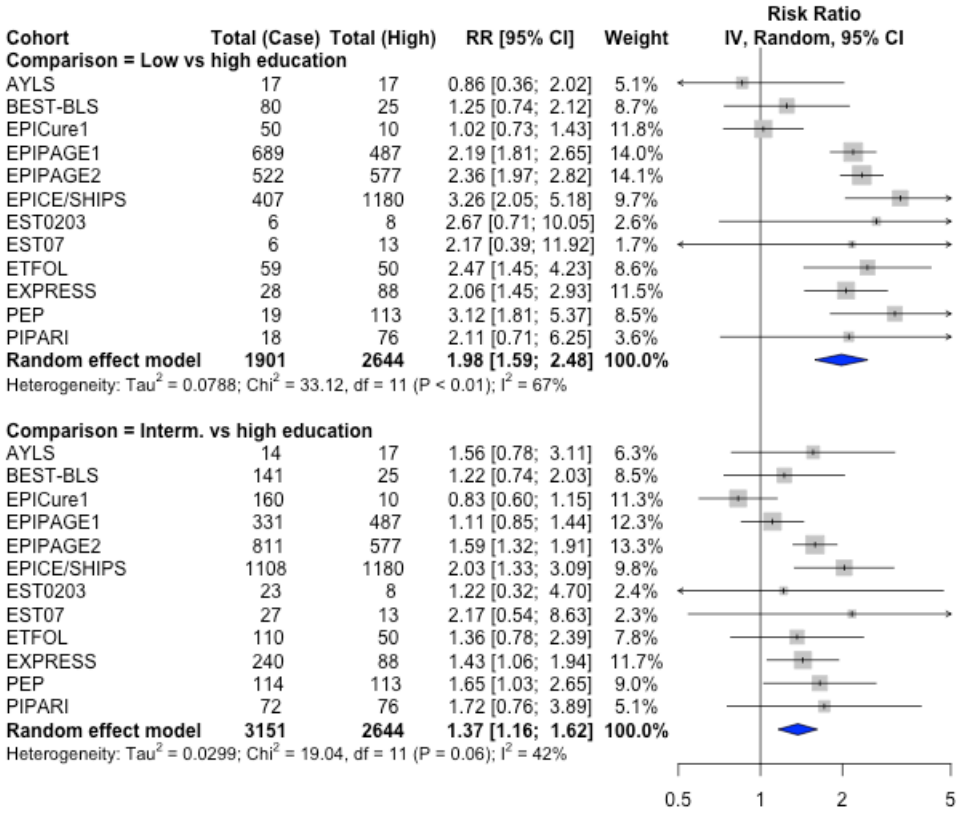
Note: estimates were unadjusted in EPIPAGE2

Supplementary Figure 8 – Forest plot of Relative Risk for cognitive deficit by maternal educational group (and 95% CI) in all VPT children

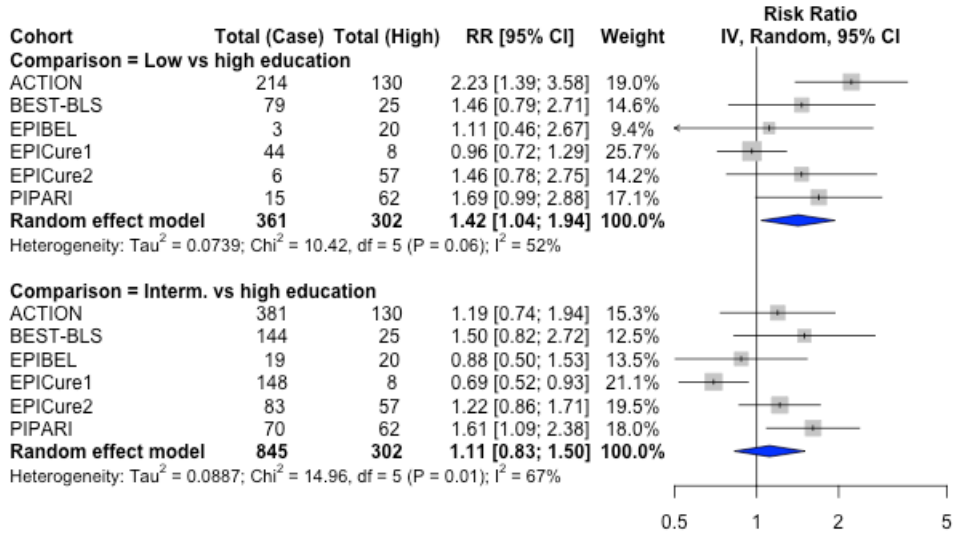
a- Infancy (2-3 years old)



b- Early childhood (4-7 years old)

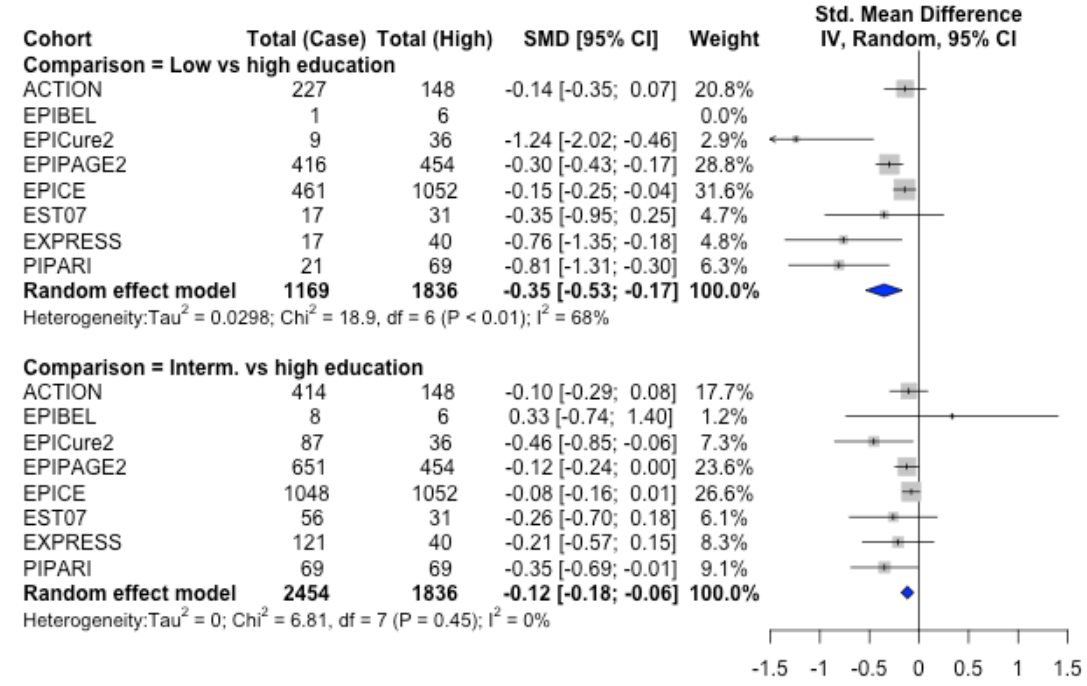


c- Later childhood (8-15 years old)

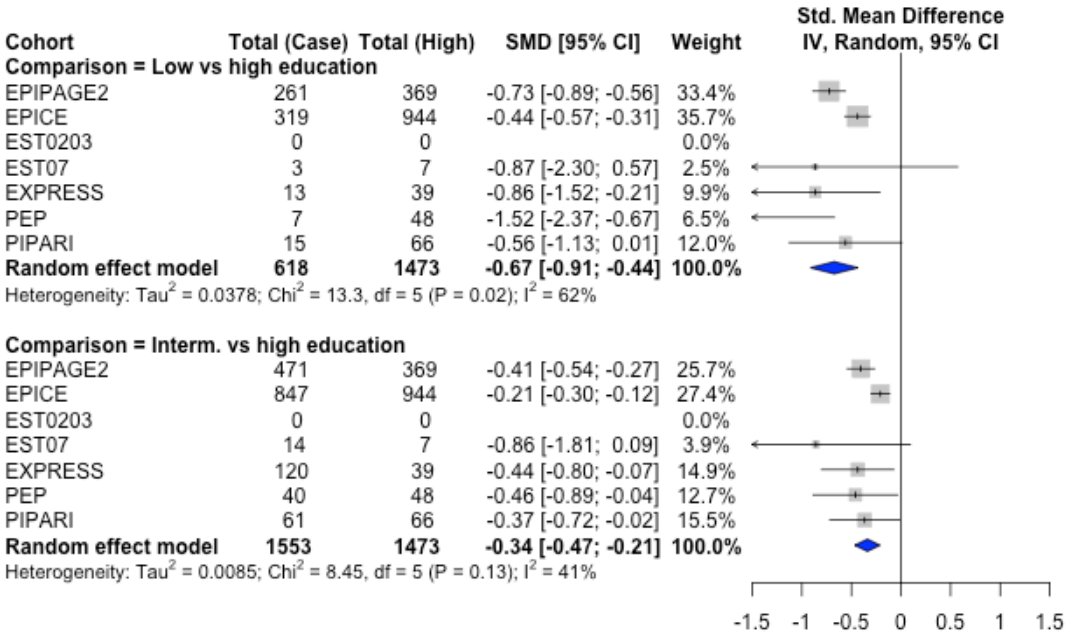


Supplementary Figure S9 – Forest plot of standardized mean differences of unadjusted mean IQ scores (SMD and 95% CI) in children without neonatal morbidities

a- Infancy (2-3 years old)

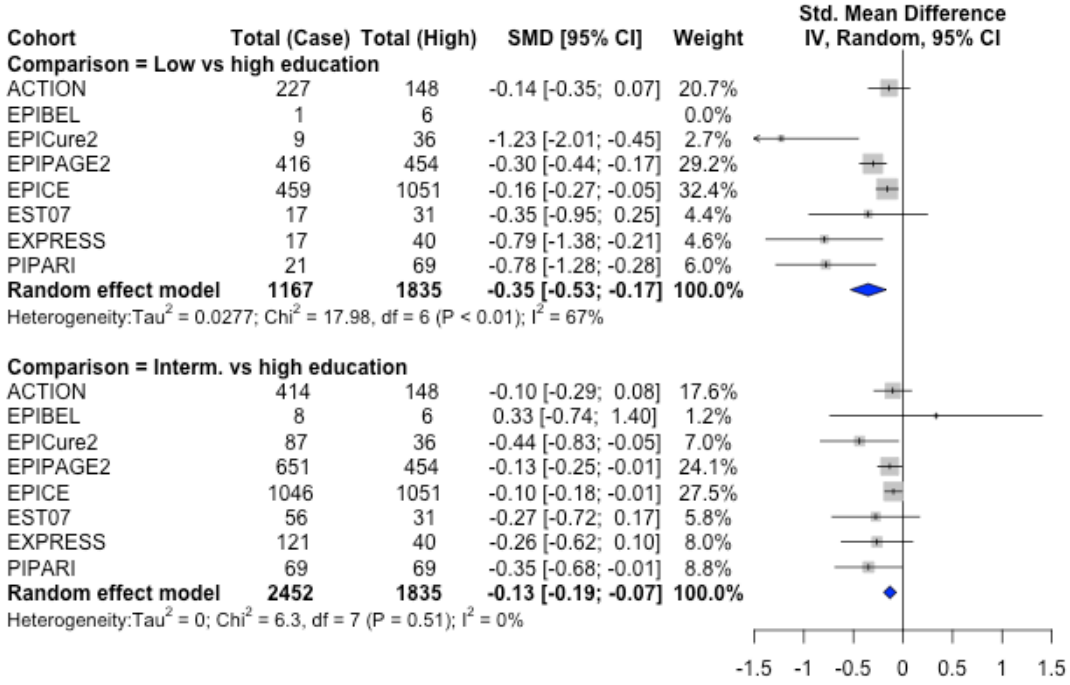


b- Early childhood (4-7 years old)

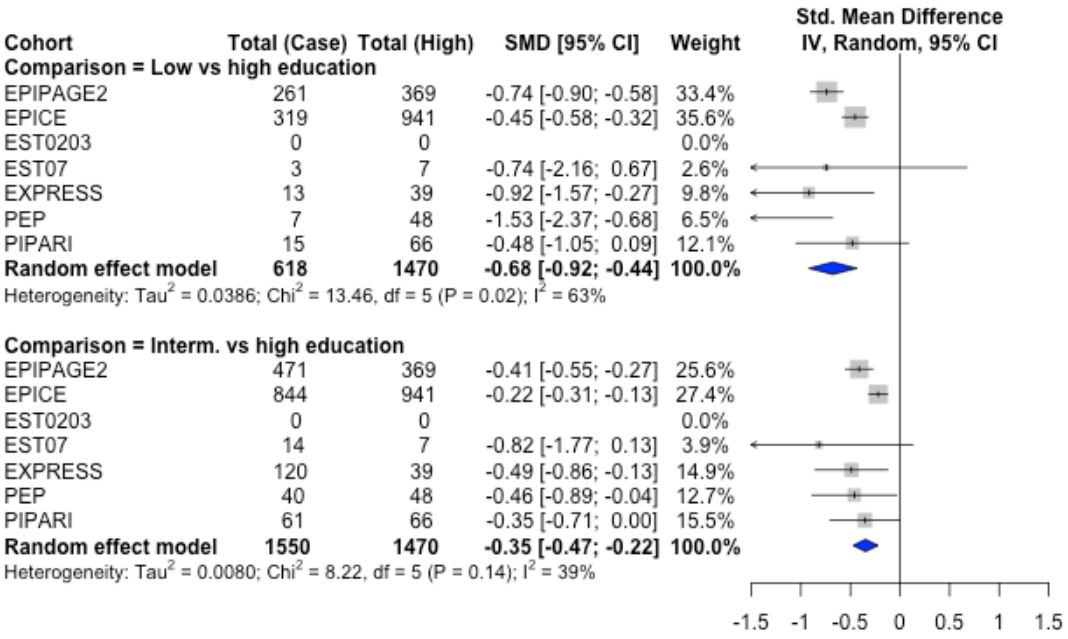


Supplementary Figure S10 – Forest plot of standardized mean differences of adjusted mean IQ scores (SMD and 95% CI) in children without neonatal morbidities

a- Infancy (2-3 years old)

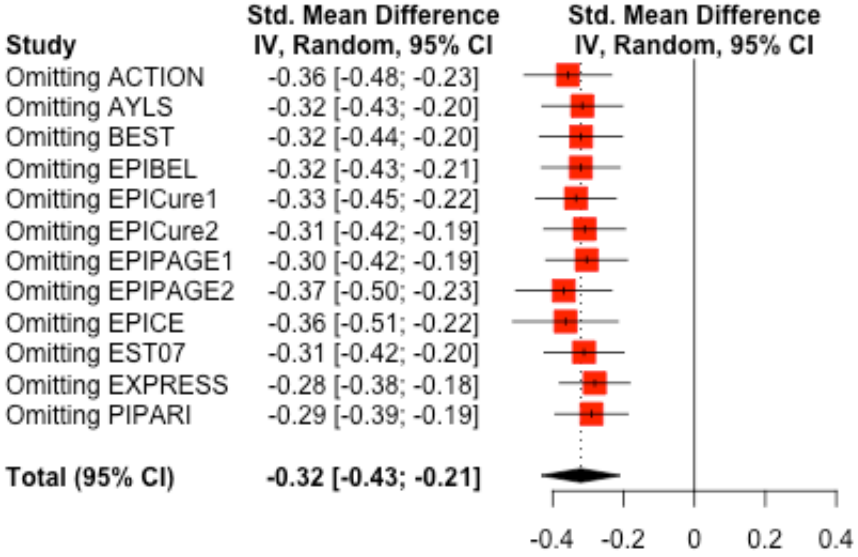


b- Early childhood (4-7 years old)



Supplementary Figure S11 – Forest plots of the results of the leave-one-out sensitivity analysis (standardized mean differences of unadjusted mean IQ scores) applied when meta-analyses with high heterogeneity (I^2>50%)

a- Unadjusted SMDs in all VPT children in infancy (2-3 years old) ; comparison groups : low education vs high education



b- Unadjusted SMDs in all VPT children in early childhood (4-7 years old); comparison groups : medium education vs high education