Social Functioning in Adults Born Very Preterm: Individual Participant Meta-Analysis

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Short title: Social functioning in adults born very preterm

Conflict of Interest Disclosures (includes financial disclosures): Dr 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 to disclose.

Funding: This study was funded by the European Union's Horizon 2020 Research and Innovation Program (grant 733280).

Role of Funder: The funder did not participate in the work.

Abbreviations

APIC, Adults born Preterm International Collaboration

ASEBA, Achenbach System of Empirically Based Assessment

ASR, Adult Self-Report

BPD, bronchopulmonary dysplasia

HPA, hypothalamus-pituitary-adrenal axis

IPD, individual participant data

ISCED, the International Standard Classification of Education

IVH, intraventricular haemorrhage

NSI, neurosensory impairment

RECAP, Research on European Children and Adults born Preterm

REML, restricted maximum likelihood

SES, socioeconomic status

VLBW, very low birth weight

VP, very preterm

Table of Contents Summary

VP/VLBW adults self-reported similar family/partner relationships, work and educational experiences, but scored their relationship with friends lower, compared with term-born controls.

Word count: 4068

Contributors’ Statement

All authors contributed to the data acquisition and the data interpretation, critically reviewed the manuscript for important intellectual content, approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Dr Ni had full access to anonymised individual participant data from all participating cohorts, conceptualised and carried out the data harmonisation and the data analysis, drafted the initial manuscript, and revised the manuscript.

Dr Mendonça contributed to the design of the study, bringing cohort data together and the data harmonisation.

Ms Baumann and Mr Eves contributed to the data harmonisation and the data analysis.

Professor Wolke conceptualised and designed the study, obtained funding, had full access to anonymised individual participant data from all participating cohorts, and revised the manuscript.

Abstract

Context: There is a lack of research on individual perceptions of social experiences and social relationships among very preterm adults in comparison to term-born peers.

Objective: To investigate self-perceived social functioning in adults born very preterm (VP; <32 weeks' gestation)/very low birth weight (VLBW; <1500g) compared with term-born controls (≥37 weeks' gestation) using an individual participant data (IPD) meta-analysis.

Data Sources: Two international consortia: Research on European Children and Adults born Preterm and Adults Born Preterm International Collaboration.

Study Selection: Cohorts that assessed self-perceived social functioning using the Adult Self-Report Adaptive Functioning scales (Friends, Spouse/Partner, Family, Job, Education) in both groups.

Data Extraction: IPD from five eligible cohorts were collected and harmonised. The raw sum scores for each scale were standardised as z-scores using mean and standard deviation of controls for each cohort. Pooled effect size was measured by difference (Δ) in means between groups.

Results: One-stage analyses (385 VP/VLBW adults; 900 controls) showed significantly lower scores for relationships with friends in VP/VLBW adults compared with controls (Δ -0.37, 95% CI -0.61, -0.13). Differences were similar after adjusting for sex, age and socioeconomic status (Δ -0.39, -0.63, -0.15) and after excluding participants with neurosensory impairment (Δ -0.34, -0.61, -0.07). No significant differences were found in other domains.

Limitations: Generalisability of research findings to VP survivors born in recent decades.

Conclusions: VP/VLBW adults scored their relationship with friends lower but perceived their family and partner relationships, as well as work and educational experiences, as comparable to those of controls.

Word: 248/250

Keywords: VP/VLBW adults; IPD meta-analysis; perceptions of social functioning; Achenbach System of Empirically Based Assessment (ASEBA); Adult Self-Report (ASR); Adaptive Functioning scale; friendship

Very preterm birth (VP; <32 weeks of gestation) is associated with increased risk of long-term respiratory, neurological, cognitive, and psychosocial problems.[1-4] Furthermore, adverse impacts on social functioning in adulthood have been reported.[5] Social functioning reflects an individual's interactions with human environments and the ability to fulfil their role within environments such as education, work, and social relationships with friends, partners and family.[6] Two recent systematic reviews[5,7] indicate that VP adults have lower educational attainment, higher rates of unemployment, and decreased likelihood of having a partner compared with term-born adults.

Most studies of VP adults assessed social functioning based on factual information, such as educational attainment, income level, being employed (yes or no), receiving social benefits (yes or no), or being in a romantic relationship (yes or no).[5,7] In contrast, there is a lack of research on VP adults' individual perceptions, that is how they perceive their experiences and relationships with others. Social functioning in preterm adults compared with term-born peers may differ depending on whether it is measured using factual information or individual perceptions. For instance, while VP adults may be less likely to have romantic relationships, previous studies suggest that once they are in a relationship, the quality of the relationship (e.g., satisfaction, intimacy, or closeness) is perceived as similar compared with term-born peers.[5] Little is known about VP adults' perceptions of work and educational experiences (e.g., satisfaction, stress, getting along with colleagues/fellow students) when they are in employment or education.

Adults born VP or very low birth weight (VLBW; birth weight <1500g) report similar relations with family members compared with controls,[8-13] but reported having fewer friends.[8,9,14] There is less exploration of other aspects of friendship, such as getting along with friends and contact/visiting frequency.

Demographic, perinatal, and childhood factors may be associated with social functioning within VP/VLBW adults. Using factual information, compared with VP/VLBW males, more VP/VLBW females are reported to have reached higher education but fewer are in employment.[15,16] No differences exist in social outcomes (e.g., cohabiting with a romantic partner) between singleton and multiple-birth VLBW adults.[17] It is unclear whether sex and multiple birth relate to self-perceived social functioning. Associations are also unclear for socioeconomic status (SES) or neonatal complications such as bronchopulmonary dysplasia (BPD) or intraventricular haemorrhage (IVH), themselves associated with adverse cognitive or motor outcomes.[18] Furthermore, neurosensory disabilities diagnosed in childhood are associated with fewer friends and poorer peer relationships,[14] while being born small for gestational age is not associated with poorer family/friend relations.[8] It is unknown whether these factors relate to other aspects of self-perceived social functioning.

Meta-analysis of individual participant data (IPD) is the gold standard to identify, appraise, and synthesise the evidence on the same research question from multiple studies by obtaining individual-level data on each participant from each eligible study.[19,20] IPD meta-analysis has several advantages over traditional meta-analysis of aggregate data.[21] It permits the use of consistent inclusion and exclusion criteria across studies and the incorporation of unpublished studies to avoid publication bias.[19] Other advantages include using unified criteria to define participants and to harmonise data, standardising the analysis across studies, ensuring sufficient power to examine the role of potential exposure variables, and the application of sophisticated modelling techniques.[22]

We undertook an IPD meta-analysis combining individual-level data from prospective cohorts of VP or VLBW adults and term-born peers within two international consortia: Research on European Children and Adults born Preterm (RECAP Preterm; https://recap-preterm.eu/) and Adults born Preterm International Collaboration (APIC; https://www.apic-preterm.org/). Our objectives were first, to investigate differences in self-perceived social functioning in VP/VLBW adults compared with term-born peers and secondly, to examine whether childhood neurosensory impairment (NSI), demographic and perinatal factors were associated with self-perceived social functioning among VP/VLBW adults.

Methods

This IPD meta-analysis followed the Preferred Reporting Items for a Systematic Review and Meta-Analysis of Individual Participant Data (PRISMA-IPD) reporting guideline[23] and was registered with PROSPERO International prospective register of systematic reviews (CRD42020195610).

Study selection. Cohorts were identified from the APIC and RECAP Preterm consortia for which relevant data on self-perceived social functioning in adulthood were available. APIC and RECAP Preterm comprise cohorts from Europe, Australia, New Zealand, USA and Canada. APIC is a research network aimed at studying health and well-being of adults born preterm through individual participant and aggregate data meta-analyses across multiple cohorts. RECAP Preterm brings together data from European cohorts and other cohorts of APIC members, making it possible to increase the power and generalisability of research, as data reflect broad geographic, cultural and health system diversity. Seven adult cohorts within RECAP and four of the six contacted APIC members who agreed to collaborate were asked to provide data on adult outcome measures, childhood NSI, demographic and perinatal factors. Inclusion criteria were: (1) included individuals born VP (<32 weeks of gestation) or VLBW (<1500 g); (2) included a control group; (3) assessed in adulthood (mean age ≥18 years); (4) measured self-perceived social functioning using the Achenbach System of Empirically Based Assessment (ASEBA) Adult Self-Report (ASR) Adaptive Functioning scales.

To search for possible additional cohorts around the world, we additionally performed a systematic search for articles published in PubMed, PsycINFO, Web of Science, Scopus and Embase on August 4th, 2020. The following keywords were used: (preterm* OR "low birth weight" OR "low birthweight") AND (adult*) AND (ASEBA OR ASR OR YSR OR "Achenbach System of Empirically Based Assessment" OR "Adult Self-Report" OR "Youth Self-Report" OR Achenbach* OR Adaptive Function*). Each potentially eligible study was assessed by two researchers independently, with disagreements resolved by discussion.

Data extraction. Anonymised datasets from eligible cohorts were transferred to the University of Warwick under signed grant agreements or data transfer agreements. Data included cohort level information (e.g., total number of participants, drop-out rates), and individual level information: demographic and perinatal characteristics, childhood NSI, and self-perceived social functioning. Data sharing complied with the ethics approvals of local ethics committees of the separate studies. All assessed participants gave their informed consent.

IPD integrity and risk of bias assessment. Data were checked for internal consistency and missing items and were cross-checked with published reports. Investigators were contacted if there was inconsistent or incomplete information. Item-level data were requested if scale-level data were not available. Each cohort was assessed based on sample size, year of recruitment, assessment of outcome and follow-up rates. Risk of bias of each cohort was assessed by two researchers independently using the Newcastle-Ottawa Scale,[24] with disagreements resolved by discussion. Scores on the scale range from 0-9, with higher scores indicating higher quality.

Measures. We used unified criteria to form preterm or control groups: participants born VP (<32 weeks of gestation) and/or VLBW (<1500g) were included in the VP/VLBW group and term-born (≥37 weeks of gestation) participants in the control group.

Demographic and perinatal variables included age at assessment, sex, SES, birthweight z-score, multiple birth, BPD, IVH. Birthweight z-scores were calculated using the Fenton growth chart.[25] BPD definitions varied but studies either used the criteria of oxygen dependency at 36 weeks postmenstrual age or for more than 28 days after birth.[26] IVH was classified according to Papile et al,[27] but some cohorts provided either grades 3 and 4 or grades 2 and 3 combined. Thus, IVH was harmonised into 'no IVH' versus 'any IVH', and a sub-analysis compared 'No IVH or IVH grades 1-2' versus 'IVH grades 3-4' in cohorts where this was possible. SES was measured using maternal education collected at birth or in childhood and was classified using the International Standard Classification of Education (ISCED)[28]: (1) low: equivalent to ISCED 0-2; (2) Medium: ISCED 3-5; (3) High: ISCED 6-8. Childhood NSI was defined as one or more of the following: visual impairment (blind in one or both eyes), hearing impairment (not corrected by hearing aids), non-ambulatory cerebral palsy, or cognitive impairment (childhood IQ<70 or other information indicating cognitive impairment).

Self-perceived social functioning was measured using the ASR Adaptive Functioning scales which include five domains (Family, Friends, Spouse/Partner, Job, and Education) and a total of 34 items.[29] For each scale, higher scores indicate higher functioning. The Family scale contains nine items that respondents rate about how well they get along with various family members on a Likert scale (0=worse than average, 1=variable or average, 2=better than average). The Friends scale yields a total score based on four items (number of close friends, frequency of contacts with close friends, getting along with close friends, and visits by friends/family), each scored 0-3, with a maximum of 12 points. The Spouse/Partner scale comprises eight items rated 0, 1, or 2 dealing with how well respondents get along with their partner, share responsibilities, enjoy similar activities, are satisfied with their partner, and like their partner's friends and family. The Job scale comprises eight items (rated 0, 1, or 2) dealing with how well respondents get along with co-workers and bosses, do their work, find their work satisfying or stressful, worry about work, or do things that may cause them to lose their job. The Education scale comprises five items (rated 0, 1, or 2) dealing with how well respondents get along with fellow students, achieve in their studies, finish their work, feel satisfied with their educational situation, and do things that may cause them to fail. Respondents who were not living with a spouse/partner, did not have a job, or were not in education during the preceding six months omitted these sections. Achenbach and Rescorla reported alphas of 0.51-0.78 for the Adaptive Functioning scales and these alphas are reasonable for scales that have relatively few items.[30] Raw sum scores were calculated for the five scales within each cohort. Multi-country norms[31] were not available for each country of the cohorts in this study. Raw sum scores were converted to z-scores using mean and standard deviation of controls for each scale within each cohort.

Data Analysis. IPD were harmonised to directly comparable variables. IPD meta-analyses were performed in Stata 16.0. Along with a two-stage approach[32] specified in the published proposal, one-stage approach was also used,[33] as there remain debates regarding which approach is optimal.[34]

Using the two-stage approach mean differences and 95% confidence intervals (CI) for outcomes between the VP/VLBW and control groups were derived using linear regression in each study separately. Pooled effect estimates were then derived from different studies using the random-effects inverse variance method with the restricted maximum likelihood (REML) estimator.[35] Pooled effect size was measured by unstandardised mean difference (Δ) in z-scores, as outcomes were reported on a meaningful scale and all studies used the same scale.[36] Heterogeneity was quantified by I^2 and τ^2.[37] Low heterogeneity was defined as an I^2 value below 40% and considerable heterogeneity defined as a value above 75%.

The one-stage approach analysed the IPD from all studies simultaneously using linear mixed effects models with the REML estimator, which assumed a random group effect (VP/VLBW versus controls). This approach also accounted for the clustering effect of participants in studies.[33,34] The above procedure was repeated to estimate effect sizes after adjusting for covariates (sex, age at assessment, and SES) which were added as fixed effects. Between-study heterogeneity between the two-stage and one-stage approaches were compared using τ^2.[34] As there is evidence indicating that differences in some domains of social functioning (e.g., friends) between VP/VLBW adults and controls were only found for females,[10] sex and group interactions were also tested.

All analyses were repeated by excluding participants with childhood NSI. Analyses were then restricted to VP/VLBW participants only to investigate the effects of NSI, demographic and perinatal variables using linear mixed effects models. Corrections for multiple comparisons were applied using the Benjamini-Hochberg procedure.[38]

Results

Study selection and IPD obtained. Five of the eleven participating RECAP/APIC adult cohorts were eligible for inclusion: the EPICure study (the UK and Ireland),[39] the Preterm Birth and Early Life Programming of Adult Health and Disease Study (ESTER, Finland),[40,41] the Helsinki Study of Very Low Birth Weight Adults (HESVA, Finland),[42,43] the NTNU Low Birth Weight in a Lifetime Perspective study (NTNU LBW Life, Norway),[8,9] and the Arvo Ylppö Longitudinal Study (AYLS, Finland).[44] Literature search of published studies yielded only two cohort studies (NTNU and the Cleveland study in the US[10]). NTNU published data on the Friends and Family scales at ages 20 and 23 years;[8,9] in this analysis, we used data from the most recent follow-up at age 26 years. **Figure 1** illustrates the screening process of the eligible cohort studies. IPD were sought and obtained for the five eligible cohorts. Data for the Cleveland study were not available at the time of final analyses.

Study/participant characteristics. All cohorts were followed from birth to adulthood with drop-out rates ranging from 29.2%-62.1% (**table 1**). They scored 7-8 on the Newcastle-Ottawa Scale (**table A1**). The EPICure study was national, comprising births in 1995, compared to other regional cohorts with births in the 1970s/80s. The VP/VLBW and control groups within each cohort were born during the same period. We used unified criteria for VP/VLBW and control groups, which may differ from the original inclusion criteria for the index children in each cohort (**table 1**).

Although 468 VP/VLBW and 1056 term-born adults met the eligibility criteria for the analysis, outcome data were only available for 385 VP/VLBW and 900 term-born adults. Among those assessed, there were no significant differences between VP/VLBW adults and controls in the proportions of participants with data on all scales, except for the job scale in EPICure and ESTER (**table A2**). Missing data could have resulted from participant failure to complete the questionnaire, participant failure to provide individual responses required to calculate the corresponding scale, or non-applicability of the scales if respondents were not living with a partner, did not have a job, or were not in education during the preceding six months. Due to variations in ages at assessment, younger participants were less likely to live with a partner or be employed while older participants were less likely to be in education. For instance, in EPICure (age 19 years), only 1.6% (2/129) of assessed VP/VLBW participants lived with a partner and 6.2% (4/65) of controls; only 43.4% of VP/VLBW participants were employed and 66.2% of controls (**table A2**). In contrast to EPICure, in NTNU (age 26 years), 24.2% of VP/VLBW participants were in education and 37.8% of controls.

Social functioning. Table 2 provides a summary of adult outcomes, NSI, demographic and perinatal data for VP/VLBW and term-born adults in each cohort. Results were similar between one-stage and two-stage approaches (**figure 2**; **table 3/A3**). We only report the one-stage results in the main text. VP/VLBW participants reported significantly lower ratings on the Friends scale compared with controls (Δ -0.37, 95% CI -0.61, -0.13). This difference remained significant after adjusting for sex, age at assessment and SES (Δ -0.39, 95% CI -0.63, -0.15). The sex and group interaction was insignificant (*p*=0.782). Effect size was slightly reduced after excluding participants with childhood NSI (Δ -0.34, 95% CI -0.61, -0.07). There were no significant differences in the other scales (**figure 2**).

Within VP/VLBW participants, BPD diagnosis was significantly associated with lower ratings on the Friends scale; IVH and low SES associated with lower ratings on the Spouse/Partner scale; and singleton birth and IVH grades 3-4 associated with lower ratings on the Family scale (**table 3**). After correcting for multiple comparisons, only the relationship between BPD and the Friends scale remained significant. We further analysed the difference on the Friends scale between VP/VLBW and control groups after excluding participants with BPD. It remained significant but with a smaller effect size (Δ -0.25, 95% CI -0.39, -0.10).

Discussion

This IPD meta-analysis investigated VP/VLBW adults' perceptions of five different aspects of social functioning. We found that VP/VLBW adults perceived their relations with partner and family, and their experiences of work and education (e.g., satisfaction, ability to finish tasks, relationship with classmates/colleagues) as similar to controls. However, VP/VLBW adults reported significantly lower ratings for their relationships with friends with the lowest reported by those with BPD.

The findings of similar relations with partners, work and educational experiences between VP/VLBW adults and controls appear at odds with studies using factual information which showed a decreased likelihood of having a partner, lower educational attainment, and higher rates of unemployment in preterm adults.[5] Our study focuses on individuals' perceptions of relationships and experiences and provides complementary information on adult social lives in different roles. Our results reassuringly correspond to previous research on the quality of romantic relationship[5] and further extend to other areas of self-perceived social functioning (e.g., work, education) in adulthood. Among VP/VLBW adults who had a partner or a job or were in education, the quality of the relationship and the perception of work and educational experiences were comparable to those of controls. Dissimilarity in findings between factual data and individual perceptions might arise as, opposed to objective circumstances, people tend to perceive their abilities and attributes more favourably compared to an average peer in one's school or workplace – a phenomenon termed as 'the better than average effect' in the field of social comparison.[45,46]

Consistent with existing studies,[7-13] we found similar family relationships between the two groups. In contrast, VP/VLBW adults scored their relationship with friends significantly lower (scores based on the number of close friends, frequency of contacts/visits, and getting along with close friends). The difference remained significant after excluding participants with childhood NSI or those with BPD. Furthermore, we did not find a difference on the Friends scale between VP/VLBW females and term-born females as previously suggested.[10] Previous studies have reported VLBW participants having fewer friends in adulthood.[14] Our finding provides valuable insights into the understanding of friendship and peer relationships in VP/VLBW adults. It indicates that friendship characteristics (e.g., fewer friends, less satisfaction, less time spent with friends) and peer social difficulties (e.g., measured by the Strengths and Difficulties Questionnaire) reported in childhood[47-51] may persist into adulthood. We speculate that less interaction with friends might be explained by mental health problems, personality or autistic traits, behavioural characteristics, or motor difficulties among VP/VLBW adults. VP/VLBW adults have been found to be less socially engaged, more easily worried/anxious, less confident in social relationships, having poorer motor skills, experiencing more challenges in social interaction and communication (autistic features), and exhibiting less frequent risk-taking behaviours.[52-56] All these characteristics might be interrelated and share common causes in early life.

The mechanisms underlying the link between VP birth and adulthood friendship are likely to be complex. One is linked to biological risk: VP birth leads to biological changes affecting long-term social functioning. Research has demonstrated that changes in the brain development in premature infants, such as alterations in amygdala functional connectivity and regional cerebral development, persist into adulthood.[57-62] The amygdala, together with a broad array of other brain regions, plays a central role in the social life of both VP and full-term individuals.[63] Amygdala volume and functional connectivity with cortical regions correlate with measures of social functioning,[57,64,65] including social network size. Furthermore, early alterations in regional cerebral development in VP infants are related to social development by school-age.[60]

The association between VP birth and friendship may also be explained by poorer motor and cognitive abilities following VP birth. Evidence supports the associations of higher motor and cognitive abilities with having more friends and spending more time with them in childhood and as adults.[48,66] Indeed, childhood NSI partly explained the difference in scores on the Friends scale; we found a reduced effect size after excluding VP/VLBW participants with NSI. On average, VP/VLBW individuals have more motor problems which often persist into adulthood[53-55,67] and may thus participate less in physical activity,[68] further relating to more peer problems.[69,70] Furthermore, cognitive ability might be more influential on social competence than is physical ability.[47] Harrison suggested that VLBW children have cognitive and behavioural deficits that isolate them from both their peers and their peers' risk-taking behaviour in the absence of NSI.[71] Cognitive ability is important for the development of social skills, such as emotion regulation, ability to read cues, and interact through gestures and body language.[72] Relatedly, people may be more accepting of social interactions with peers with physical disabilities than cognitive disabilities.[47]

Additionally, the lower scores on the Friends scale in VP/VLBW adults could be due to alternations in hypothalamus-pituitary-adrenal axis (HPA) stress regulating system. There is some evidence suggesting a poorer response to acute (psychosocial) stress in both VP children and adults.[73] Other studies have further linked blunted HPA-axis responses to stress and lower cortisol levels with some personality traits (e.g., less openness),[74] which might subsequently affect how VP/VLBW adults deal with social relationships with friends.

The other mechanism relates to environmental influences: social experiences play an important role in forming and maintaining friendships, such as early parent-infant relationship, parenting, and childhood peer relationships or bullying experiences. There is evidence that higher gestational age predicted better quality of early parent-infant relationships,[50] which subsequently predicted higher friendship scores[50] and better peer relationships in childhood.[66] Research also shows that mothers of VP/VLBW children may be more controlling.[75] This may in turn lead to social isolation, with fewer opportunities for risk-taking behaviours as adults.[15,76] Moreover, VP/VLBW children are more likely to be excluded and bullied at school[47,77-79] which may adversely affect adult peer relationships in both preterm and general population samples.[78,80] Finally, the biological and environmental pathways may individually affect or interact with each other with additive or reinforced effects in influencing adult outcomes. Recent evidence also suggests environmental factors (e.g., bullying) as mediators between VP birth and adult mental health outcomes.[81]

Our study also identifies that VP/VLBW adults with BPD were at greatest risk of having lower scores on the Friends scale, suggesting persisting non-respiratory effects of BPD into adulthood. To our knowledge, this finding has not been previously reported. The BPD-friendship association may be mediated through the associated reduced lung function, poorer motor function and cognitive development through childhood and into adulthood [82-84]. Due to these limitations, VP/VLBW adults with BPD may have more problems with usual activities, such as hobbies, sports, doing things with friends,[4] eventually leading to fewer friends or poorer relations. We also showed that IVH and low SES were significantly associated with lower scores on the Spouse/Partner scale, and that singleton birth and IVH grades 3-4 were related to lower scores on the Family scale, but these became statistically non-significant after correcting for multiple comparisons.

The strengths of this study include the large sample size combining IPD from five European cohorts, the availability of comprehensive perinatal and childhood data allowing us to control for confounders and explore their roles in relation to social functioning, the harmonisation of IPD using unified criteria to control for between-study heterogeneity, and the exploration of social functioning based on the personal view of life experiences measured using the same self-report scale. Several limitations should be acknowledged. The first one is differences in eligibility criteria among cohorts, such as EPICure's stricter inclusion criterion of <26 weeks of gestation. Secondly, potential bias could be attributed to drop-out (due to disability or social disadvantage, etc.) and missing data resulting in overrepresentation of healthier participants. Our differences in friendship between VP/VLBW and control groups may therefore underestimate the true differences. However, this is likely to be minimal as NSI and SES were unrelated to friendship in our study. Thirdly, the finding of the positive association between BPD and friendship needs replication due to variations in the definition of BPD. Fourthly, although self-report questionnaires offer participants the opportunity to describe their own experiences, they are susceptible to report bias associated with social desirability, applicable to both groups. Lastly, survival for infants born at extremely low gestational ages (22-25 weeks) is continuously increasing. It is likely that only a small proportion of infants in this analysis were born at these gestational ages as all recruited participants were born before 1996. Therefore, caution should be taken when generalising our research findings to surviving VP infants born in recent decades.

In conclusion, this analysis highlights the value of including individual perceptions of social functioning and provides a comprehensive picture of adult social life. VP/VLBW adults rated their friendships, in terms of number, contact/visiting frequency and satisfaction, lower than did term-born adults. In contrast, despite being exposed to considerable stress in early life, VP/VLBW adults perceived the quality of their family and partner relationships, as well as work and educational experiences, as comparable to those of controls. Considering the well described wide-ranging negative consequences following VP/VLBW birth, this finding is particularly reassuring. Early interventions in clinical, family and school settings to enhance social skills and social inclusion in childhood may improve peer relationships of VP/VLBW individuals in adulthood.[47,85]

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Figure 1 The PRISMA IPD flow diagram detailing the screen process of the eligible cohort studies for the pooled analysis

Figure 2 A comparison of self-reported social functioning in adulthood between VP/VLBW participants and term-born controls

Table 1 Summary of the five adult cohorts included in the IPD meta-analysis

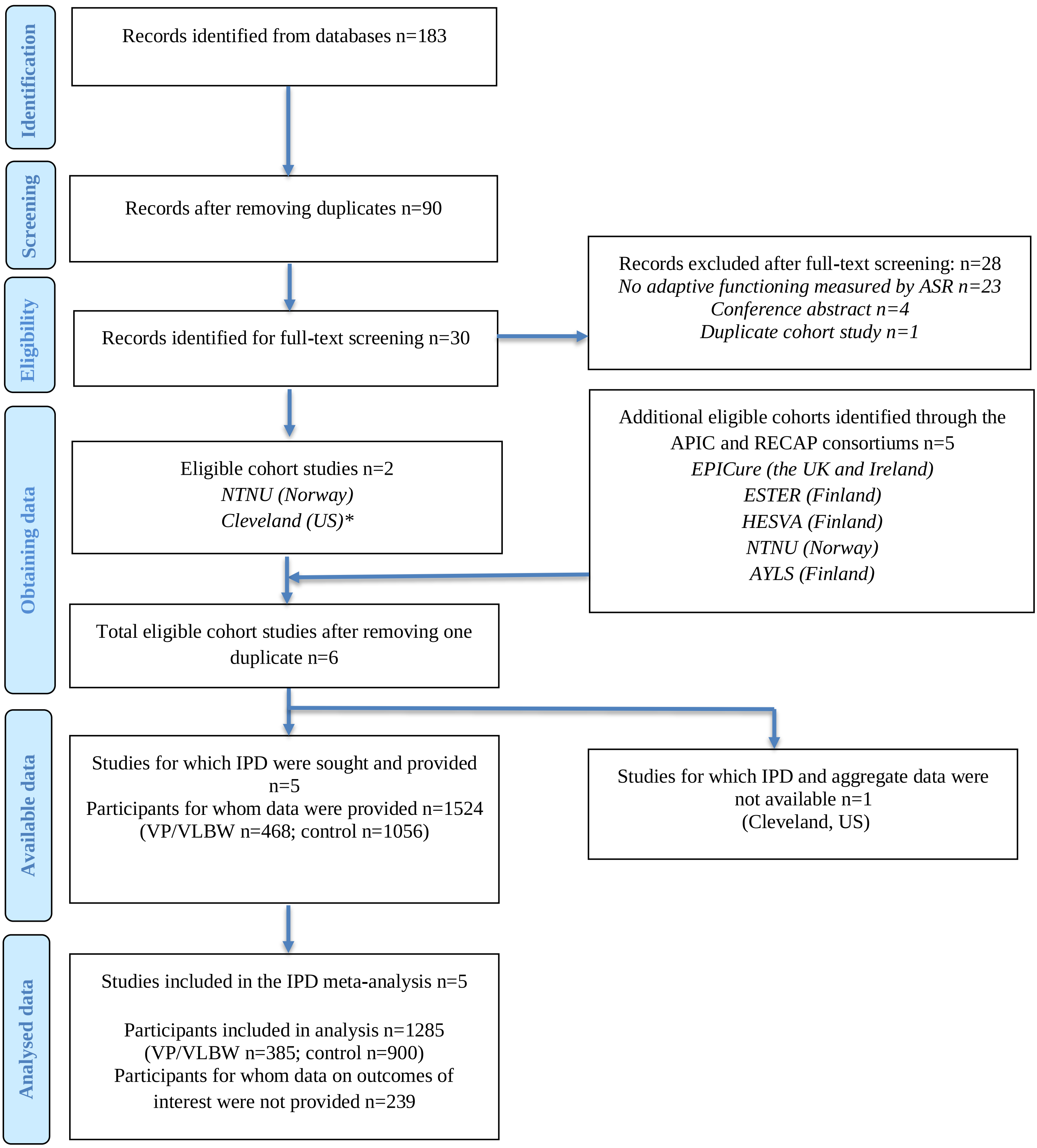
Cohort	Country	Scale	Birth Year	Mean age of Assessment (years)	Original Index Eligibility Criteria	Initial Sample - VP/VLBW Survivors to Discharge	Eligible Sample in Adulthood	Assessed Sample in Adulthood	Sample with data on ASR Adaptive Functioning Scale[¶]	VP/VLBW dropout and missing data%	VP/VLBW with NSI dropout and missing data%	Term-born controls with data on ASR Adaptive Functioning Scale[¶]	Comments
EPICure [39]	The UK and Ireland	National	1995	19	<26 weeks of gestation	315	306	129	116	62.1	71.1	62 (Recruited at ages 6 or 11)	Birth weight and gestational age not available for controls. Drop-out associated with disability and social disadvantage
ESTER [40,41]	Finland	Regional	1985-89	23	<37 weeks of gestation	NA	NA	77	69	60.2[Π]	NA	330 (Recruited at infancy)	SES measured by parent education collected retrospectively; data on IVH and BPD not available at the time of data analysis. Drop-out associated with male sex and physical disabilities
HESVA [42,43]	Finland	Regional	1978-85	25	Birth weight <=1500g	334	254	165	112	55.9	59.1	104 (Recruited in adulthood, no SGA term-born controls)	Maternal education measured retrospectively. Overrepresentation of healthier participants
NTNU [8,9]	Norway	Regional	1986-88	26	Birth weight <=1500g	86	82	62	58	29.2	45.5	88 (Recruited at infancy but no SGA term-born controls)	Maternal education measured at the 14-year assessment. Drop-out associated with male sex
AYLS [44]	Finland	Regional	1985-86	26	Admission for neonatal care within 10 days after birth[Ꞁ]	108	68	35	30	55.9	66.7	316 (Recruited at infancy)	Drop-out associated with lower parental education, male sex and lower cognitive function

Abbreviations: VP/VLBW, very preterm (<32 weeks of gestation)/very low birth weight (birth weight <1500g); NSI, neurosensory Impairment; IVH, intraventricular haemorrhage; BPD, bronchopulmonary dysplasia; SGA, small for gestational age; SES, socio-economic Status.[¶] Participants with data on any of the five Adaptive Functioning scales (education, job, spouse/partner, friends and family). [Π] Extracted from the published paper as an estimate of drop-out of VP/VLBW participants [34]. Gestational age and birthweight only available for participants assessed in adulthood, so it was impossible to calculate numbers of VP/VLBW survivors to discharge and the eligible sample in adulthood, as well as drop-out rates. [Ꞁ]AYLS included infants who had been admitted to the neonatal ward or had been transferred to the neonatal intensive care unit within 10 days after birth, so the original index group ranged from critically ill preterm children to term-born children with minimal complications and inpatient observation times.

Table 2 Characteristics of VP/VLBW adults and term-born controls

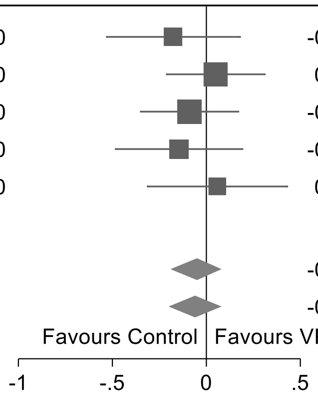
	EPICure			ESTER			HESVA			NTNU			AYLS		
	VP/VLBW adults N=116	Controls N=62	*p*	VP/VLBW adults N=69	Controls N=330	*p*	VP/VLBW adults N=112	Controls N=104	*p*	VP/VLBW adults N=58	Controls N=88	*p*	VP/VLBW adults N=30	Controls N=316	*p*
Adult outcomes[∏]															
Family z-score	-0.18 (1.22) [n=115]	-0.00 (1.00) [n=62]	0.330	0.04 (0.98) [n=69]	-0.01 (1.00) [n=328]	0.711	-0.09 (0.94) [n=112]	0.00 (1.00) [n=104]	0.494	-0.15 (1.02) [n=57]	-0.00 (1.00) [n=88]	0.394	0.06 (0.86) [n=30]	0.00 (1.00) [n=311]	0.760
Friends z-score	**-0.79 (1.23) [n=116]**	**-0.00 (1.00) [n=62]**	**<0.001**	-0.20 (1.05) [n=68]	0.03 (0.99) [n=330]	0.087	**-0.40 (1.03) [n=108]**	**0.00 (1.00) [n=101]**	**0.005**	**-0.39 (1.30) [n=58]**	**0.00 (1.00) [n=88]**	**0.042**	0.00 (1.09) [n=30]	0.00 (1.00) [n=315]	0.972
Spouse/Partner z-score	0.86 (0.00) [n=2]	0.00 (1.00) [n=4]	0.315	0.20 (0.78) [n=42]	-0.01 (0.97) [n=227]	0.186	0.04 (1.26) [n=60]	-0.00 (1.00) [n=63]	0.837	0.12 (0.80) [n=34]	0.00 (1.00) [n=48]	0.577	-0.32 (1.01) [n=21]	0.00 (1.00) [n=229]	0.169
Job z-score	-0.10 (0.83) [n=56]	-0.00 (1.00) [n=43]	0.594	0.08 (0.95) [n=45]	0.01 (0.94) [n=250]	0.641	-0.05 (0.87) [n=91]	0.00 (1.00) [n=93]	0.701	**-0.54 (1.36) [n=48]**	**0.00 (1.00) [n=79]**	**0.012**	0.11 (0.63) [n=30]	0.00 (1.00) [n=299]	0.524
Education z-score	0.16 (0.89) [n=89]	0.00 (1.00) [n=51]	0.345	-0.12 (0.99) [n=42]	0.02 (0.97) [n=196]	0.378	-0.01 (1.15) [n=57]	-0.00 (1.00) [n=64]	0.954	-0.38 (1.03) [n=15]	0.00 (1.00) [n=34]	0.230	0.04 (0.88) [n=26]	-0.00 (1.00) [n=297]	0.778
Demographic data															
Age at assessment in adulthood (years)	19.3 (0.6) [n=116]	19.2 (0.5) [n=62]	0.323	**23.1 (1.4) [n=69]**	**23.5 (1.2) [n=330]**	**0.003**	24.6 (2.1) [n=112]	24.6 (2.2) [n=104]	0.841	26.3 (0.7) [n= 58]	26.5 (0.5) [n= 88]	0.093	**25.8 (0.6) [n= 30]**	**25.5 (0.6) [n=316]**	**0.009**
Males	45.7% (53/116)	37.1% (23/62)	0.269	42.0% (29/69)	46.5% (153/329)	0.497	43.8% (49/112)	43.3% (45/104)	0.943	53.4% (31/58)	43.2% (38/88)	0.224	56.7% (17/30)	57.3% (181/316)	0.141
SES															
Low	**20.0% (22/110)**	**4.8% (3/62)**	**<0.001**	5.8% (4/69)	6.1% (20/327)	0.963	15.5% (17/110)	14.4% (15/104)	0.498	6.4% (3/47)	6.8% (5/74)	0.943	26.7% (8/30)	18.5% (58/314)	0.550
Medium	**76.4% (84/110)**	**75.8% (47/62)**		62.3% (43/69)	60.6% (198/327)		61.8% (68/110)	55.8% (58/104)		53.2% (25/47)	50.0% (37/74)		30.0% (9/30)	32.5% (102/314)	
High	**3.6% (4/110)**	**19.4% (12/62)**		31.9% (22/69)	33.3% (109/327)		22.7% (25/110)	29.8% (31/104)		40.4% (19/47)	43.2% (32/74)		43.3% (13/30)	49.0% (154/314)	
Childhood NSI[˥]	**20.0% (22/110)**	**0.0% (0/51)**	**0.001**	**10.1% (7/69)**	**0.3% (1/330)**	**<0.001**	**8.3% (9/109)**	**1.0% (1/103)**	**0.012**	**16.2% (6/37)**	**0.0% (0/63)**	**0.001**	**21.4% (6/28)**	**1.1% (3/264)**	**<0.001**
Perinatal data															
Gestational age (weeks)	24.5 (0.7) [n=116]	-	-	**30.6 (2.0) [n= 69]**	**40.1 (1.2) [n=330]**	**<0.001**	**29.3 (2.4) [n=112]**	**40.1 (1.1) [n=104]**	**<0.001**	**28.8 (2.6) [n= 58]**	**39.8 (1.2) [n= 88]**	**<0.001**	**29.2 (2.4) [n= 30]**	**39.7 (1.2) [n=316]**	**<0.001**
Birth weight (grams)	745 (122) [n=116]	-	-	**1478(406) [n= 69]**	**3572(491) [n=329]**	**<0.001**	**1128 (220) [n=112]**	**3611 (492) [n=104]**	**<0.001**	**1193 (247) [n= 58]**	**3702 (451) [n= 88]**	**<0.001**	**1317 (316) [n= 30]**	**3622 (470) [n=316]**	**<0.001**
Birthweight z-score	0.23 (0.81) [n=116]	-	-	0.07 (1.18) [n=69]	0.09 (0.94) [n=329]	0.935	**-0.43 (1.01) [n=112]**	**0.15 (1.00) [n=104]**	**<0.001**	**-0.13 (1.04) [n= 58]**	**0.30 (0.81) [n=88]**	**0.006**	0.03 (1.02) [n=30]	0.17 (0.86) [n=316]	0.396
Multiple birth	33.9% (39/115)	-	-	**30.4% (21/69)**	**1.2% (4/330)**	**<0.001**	**15.2% (17/112)**	**0.0% (0/104)**	**<0.001**	**15.5% (9/58)**	**0.0% (0/88)**	**<0.001**	**13.3% (4/30)**	**1.3% (4/316)**	**<0.001**
IVH Grades 3-4	12.2% (14/115)	-	-	-	-	-	4.8% (4/83)	-	-	2.1% (1/47)	-	-	**6.7% (2/30)**	**0.0% (0/316)**	**<0.001**
IVH	67.0% (77/115)	-	-	-	-	-	16.9% (14/83)	-	-	12.8% (6/47)	-	-	**20.0% (6/30)**	**0.0% (0/316)**	**<0.001**
BPD	72.4% (84/116)	-	-	-	-	-	24.1% (26/108)	-	-	**23.2% (13/56)**	**0.0% (0/88)**	**<0.001**	**3.3% (1/30)**	**0.0% (0/316)**	**0.001**

Abbreviations: VP/VLBW, very preterm/very low birth weight; NSI, neurosensory Impairment; IVH, intraventricular haemorrhage; BPD, bronchopulmonary dysplasia; SES, socio-economic Status. [¶]Mean (SD) for continuous variables and %(n/N) for categorical variables. [∏] Raw sum score was converted to z-score using mean and SD of controls for each scale within each cohort. [˥] NSI was defined as one or more of the following: visual impairment (blind in one or both eyes), hearing impairment (not corrected by hearing aids), cerebral palsy (non-ambulatory; i.e. use of wheel chair or bed ridden), or cognitive impairment in childhood.

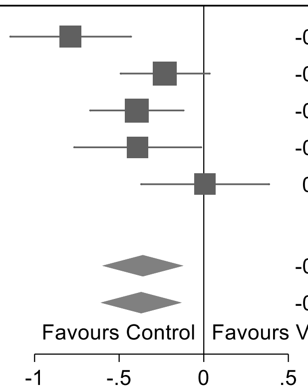


* Data for the Cleveland study were unfortunately not available at the time of final analyses.

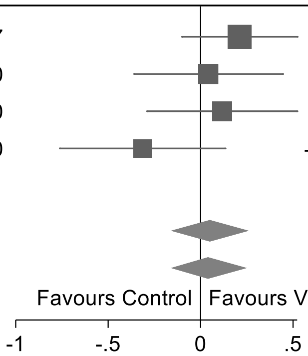
Family	VP/VLBW N	VP/VLBW Mean	VP/VLBW SD	Control N	Control Mean	Control SD	Mean Diff. with 95% CI	Weight
EPICure	115	-0.18	1.22	62	-0.00	1.00	-0.18 (-0.53, 0.18)	14.8%
ESTER	69	0.04	0.98	328	-0.01	1.00	0.05 (-0.21, 0.31)	27.5%
HESVA	112	-0.09	0.94	104	0.00	1.00	-0.09 (-0.35, 0.17)	27.7%
NTNU	57	-0.15	1.02	88	-0.00	1.00	-0.15 (-0.48, 0.19)	16.4%
AYLS	30	0.06	0.86	311	0.00	1.00	0.06 (-0.31, 0.43)	13.5%
Two-stage Overall (I^2=0.0%; τ^2=0.000)							-0.05 (-0.19, 0.08)	
One-stage Overall (τ^2=0.000)							-0.06 (-0.20, 0.08)	



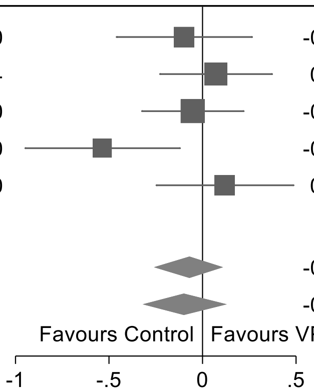
Friends	VP/VLBW N	VP/VLBW Mean	VP/VLBW SD	Control N	Control Mean	Control SD	Mean Diff. with 95% CI	Weight
EPICure	116	-0.79	1.23	62	-0.00	1.00	-0.79 (-1.14, -0.43)	18.7%
ESTER	68	-0.20	1.05	330	0.03	0.99	-0.23 (-0.49, 0.03)	23.1%
HESVA	108	-0.40	1.03	101	0.00	1.00	-0.40 (-0.67, -0.12)	22.5%
NTNU	58	-0.39	1.30	88	0.00	1.00	-0.39 (-0.77, -0.02)	17.9%
AYLS	30	0.01	1.09	315	0.00	1.00	0.01 (-0.37, 0.38)	17.8%
Two-stage Overall (I^2=62.8%; τ^2=0.045)							-0.36 (-0.60, -0.12)	
One-stage Overall (τ^2=0.049)							-0.37 (-0.61, -0.13)	



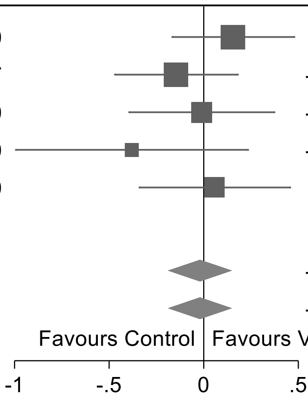
Spouse/Partner	VP/VLBW N	VP/VLBW Mean	VP/VLBW SD	Control N	Control Mean	Control SD	Mean Diff. with 95% CI	Weight
ESTER	42	0.20	0.78	227	-0.01	0.97	0.21 (-0.10, 0.52)	35.1%
HESVA	60	0.04	1.26	63	-0.00	1.00	0.04 (-0.36, 0.44)	23.1%
NTNU	34	0.12	0.80	48	0.00	1.00	0.12 (-0.29, 0.52)	22.7%
AYLS	21	-0.31	1.00	229	0.00	1.00	-0.31 (-0.76, 0.13)	19.1%
Two-stage Overall (I^2=15.0%; τ^2=0.007)							0.05 (-0.16, 0.26)	
One-stage Overall (τ^2=0.004)							0.04 (-0.16, 0.25)	



Job	VP/VLBW N	VP/VLBW Mean	VP/VLBW SD	Control N	Control Mean	Control SD	Mean Diff. with 95% CI	Weight
EPICure	56	-0.10	0.83	43	-0.00	1.00	-0.10 (-0.46, 0.26)	18.2%
ESTER	45	0.08	0.95	250	0.01	0.94	0.07 (-0.23, 0.37)	23.1%
HESVA	91	-0.05	0.87	93	0.00	1.00	-0.05 (-0.32, 0.22)	25.8%
NTNU	48	-0.54	1.36	79	0.00	1.00	-0.54 (-0.95, -0.12)	15.0%
AYLS	30	0.12	0.62	299	0.00	1.00	0.12 (-0.25, 0.48)	17.9%
Two-stage Overall (I^2=35.5%; τ^2=0.016)							-0.07 (-0.26, 0.11)	
One-stage Overall (τ^2=0.034)							-0.10 (-0.32, 0.13)	



Education	VP/VLBW N	VP/VLBW Mean	VP/VLBW SD	Control N	Control Mean	Control SD	Mean Diff. with 95% CI	Weight
EPICure	89	0.16	0.89	51	0.00	1.00	0.16 (-0.17, 0.48)	27.6%
ESTER	42	-0.12	0.99	196	0.02	0.97	-0.15 (-0.47, 0.18)	27.2%
HESVA	57	-0.01	1.15	64	-0.00	1.00	-0.01 (-0.39, 0.37)	19.5%
NTNU	15	-0.38	1.03	34	0.00	1.00	-0.38 (-0.99, 0.23)	7.6%
AYLS	26	0.06	0.88	297	-0.00	1.00	0.06 (-0.34, 0.45)	18.1%
Two-stage Overall (I^2=0.0%; τ^2=0.000)							-0.02 (-0.19, 0.15)	
One-stage Overall (τ^2=0.000)							-0.02 (-0.19, 0.15)	



Notes: EPICure was not included for the Spouse/Partner scale due to small numbers. Effect size is measured by mean difference and 95% confidence intervals for each scale. In the two-stage approach, the size of the squares and the diamonds are proportional to the weight assigned to the relative effect sizes; heterogeneity was quantified by I^2 and τ^2. One-stage and two-stage overall effects are represented by diamonds. Between-study heterogeneity between the two-stage and one-stage approaches were compared using τ^2.

Appendices

Table A1 Quality Assessment using the Newcastle Ottawa Scale

Table A2 Compare numbers of participants with data on the five Adaptive Functioning scales between VP/VLBW adults and term-born controls

Table A3 Univariate analysis of factors associated with social functioning within VP/VLBW participants: comparison of one-stage and two-stage analyses

Table A1 Quality Assessment using the Newcastle Ottawa Scale

Cohort	Selection				Comparability	Outcome			Overall Score
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts (above or below 50%)	
EPICure	☆		☆	☆	☆☆	☆	☆		7
ESTER	☆	☆	☆	☆	☆☆	☆	☆		8
HESVA	☆	☆	☆	☆	☆☆	☆	☆		8
NTNU	☆		☆	☆	☆☆	☆	☆	☆	8
AYLS	☆	☆	☆	☆	☆☆	☆	☆		8

Table A2 Compare numbers of participants with data on the five Adaptive Functioning scales between VP/VLBW adults and term-born controls

Number of participants with outcome data[1]	EPICure			ESTER			HESVA			NTNU			AYLS		
	VP/VLBW adults	**Term-born controls**		**VP/VLBW adults**	**Term-born controls**		**VP/VLBW adults**	**Term-born controls**		**VP/VLBW adults**	**Term-born controls**		**VP/VLBW adults**	**Term-born controls**	
	N=129	N=65	*p*	N=77	N=356	*p*	N=165	N=172	*p*	N=62	N=90	*p*	N=35	N=373	*p*
Family	89.1% (115/129)	95.4% (62/65)	0.147	89.6% (69/77)	92.1% (328/356)	0.467	67.9% (112/165)	60.5% (104/172)	0.156	91.9% (57/62)	97.8% (88/90)	0.091	85.7% (30/35)	83.4% (311/373)	0.721
Friends	89.9% (116/129)	95.4% (62/65)	0.192	88.3% (68/77)	92.7% (330/356)	0.201	65.5% (108/165)	58.7% (101/172)	0.203	93.5% (58/62)	97.8% (88/90)	0.188	85.7% (30/35)	84.5% (315/373)	0.843
Spouse/Partner	1.6% (2/129)	6.2% (4/65)	0.080	54.5% (42/77)	63.8% (227/356)	0.131	36.4% (60/165)	36.6% (63/172)	0.960	54.8% (34/62)	53.3% (48/90)	0.855	60.0% (21/35)	61.4% (229/373)	0.871
Job	43.4% (56/129)	66.2% (43/65)	0.003	58.4% (45/77)	70.2% (250/356)	0.044	55.2% (91/165)	54.1% (93/172)	0.842	77.4% (48/62)	87.8% (79/90)	0.090	85.7% (30/35)	80.2% (299/373)	0.427
Education	69.0% (89/129)	78.5% (51/65)	0.165	54.5% (42/77)	55.1% (196/356)	0.935	34.5% (57/165)	37.2% (64/172)	0.610	24.2% (15/62)	37.8% (34/90)	0.078	74.3% (26/35)	79.6% (297/373)	0.457

Abbreviations: VP/VLBW, very preterm/very low birth weight. [1] Where data on the five scales are not available, this could be due to the non-completion of the questionnaire, missing values in any of the items required to calculate the corresponding scale, or the fact that respondents were not living with a spouse/partner, did not have a job, or were not enrolled in an education program during the preceding 6 months.

Table A3 Univariate analysis of factors associated with social functioning within VP/VLBW participants: comparison of one-stage and two-stage analyses[∏]

	Family		Friends		Spouse/Partner[¶]		Job		Education	
	Two-stage Effect (95% CI)	**One-stage Effect (95% CI)**	**Two-stage Effect (95% CI)**	**One-stage Effect (95% CI)**	**Two-stage Effect (95% CI)**	**One-stage Effect (95% CI)**	**Two-stage Effect (95% CI)**	**One-stage Effect (95% CI)**	**Two-stage Effect (95% CI)**	**One-stage Effect (95% CI)**
Age at assessment	0.00 (-0.07, 0.08)	0.00 (-0.08, 0.08)	0.02 (-0.06, 0.10)	0.01 (-0.07, 0.10)	0.06 (-0.05, 0.17)	0.06 (-0.05, 0.17)	-0.06 (-0.20, 0.07)	-0.06 (-0.17, 0.05)	-0.03 (-0.25, 0.20)	-0.01 (-0.21, 0.19)
Sex (ref.=male)	-0.04 (-0.27, 0.19)	-0.05 (-0.28, 0.17)	-0.09 (-0.31, 0.14)	-0.06 (-0.29, 0.18)	-0.14 (-0.66, 0.38)	-0.14 (-0.65, 0.36)	0.06 (-0.38, 0.50)	0.09 (-0.36, 0.54)	-0.10 (-0.35, 0.16)	-0.12 (-0.38, 0.14)
SES Medium vs Low	0.30 (-0.01, 0.62)	0.27 (-0.05, 0.59)	0.24 (-0.11, 0.59)	0.27 (-0.08, 0.62)	0.28 (-0.29, 0.84)	0.42 (-0.12, 0.97)	-0.05 (-0.57, 0.48)	0.09 (-0.27, 0.45)	0.03 (-0.56, 0.62)	0.16 (-0.28, 0.60)
High vs Low	0.22 (-0.31, 0.74)	0.22 (-0.15, 0.60)	0.37 (-0.07, 0.81)	0.29 (-0.13, 0.70)	**0.64 (0.04, 1.24)**	**0.69 (0.09, 1.28)**	-0.09 (-0.53, 0.36)	-0.01 (-0.41, 0.39)	-0.07 (-0.74, 0.61)	0.11 (-0.47, 0.69)
NSI in childhood (ref.=no)	-0.22 (-0.83, 0.40)	-0.24 (-0.80, 0.31)	-0.50 (-1.05, 0.04)	-0.48 (-1.02, 0.06)	-0.23 (-0.96, 0.49)	-0.40 (-1.01, 0.22)	-0.16 (-0.50, 0.19)	-0.14 (-0.53, 0.24)	**-0.37 (-0.73, -0.02)**	-0.37 (-0.74, 0.00)
Gestational age (weeks)	0.04 (-0.04, 0.12)	0.04 (-0.03, 0.11)	0.06 (-0.02, 0.13)	0.06 (-0.02, 0.13)	-0.01 (-0.09, 0.06)	-0.03 (-0.10, 0.05)	-0.04 (-0.11, 0.03)	-0.03 (-0.11, 0.06)	-0.03 (-0.10, 0.05)	-0.03 (-0.10, 0.04)
Birthweight z-score	-0.03 (-0.14, 0.07)	-0.04 (-0.15, 0.06)	0.03 (-0.11, 0.16)	0.01 (-0.14, 0.16)	0.08 (-0.05, 0.21)	0.08 (-0.07, 0.23)	0.07 (-0.08, 0.22)	0.03 (-0.10, 0.16)	0.05 (-0.09, 0.18)	0.05 (-0.09, 0.19)
Multiple birth (ref.= singleton)	0.25 (-0.06, 0.56)	**0.29 (0.00, 0.58)**	0.07 (-0.31, 0.46)	0.05 (-0.33, 0.43)	0.24 (-0.37, 0.85)	0.31 (-0.31, 0.92)	0.04 (-0.22, 0.31)	0.08 (-0.21, 0.38)	0.07 (-0.26, 0.41)	0.15 (-0.29, 0.59)
IVH Grade 3-4 (ref.= no IVH or IVH grade 1-2) [˥]	**-0.71 (-1.20, -0.21)**	**-0.70 (-1.19, -0.21)**	-0.45 (-0.98, 0.08)	-0.39 (-0.93, 0.14)	-1.27 (-3.87, 1.33)	-1.27 (-3.50, 0.96)	0.19 (-0.34, 0.71)	0.19 (-0.41, 0.78)	0.19 (-0.31, 0.69)	0.20 (-0.34, 0.74)
IVH (ref.= no) [˥]	-0.11 (-0.42, 0.19)	-0.12 (-0.43, 0.19)	0.21 (-0.13, 0.55)	0.24 (-0.11, 0.59)	-0.76 (-1.54, 0.02)	**-0.78 (-1.52, -0.03)**	-0.04 (-0.43, 0.36)	0.07 (-0.42, 0.56)	0.07 (-0.46, 0.61)	0.14 (-0.44, 0.72)
BPD (ref.= no) [˥]	-0.19 (-0.75, 0.37)	-0.18 (-0.75, 0.40)	**-0.45 (-0.76, -0.14)**	**-0.46 (-0.77, -0.15)** [+]	0.26 (-0.26, 0.78)	0.15 (-0.40, 0.71)	-0.21 (-0.50, 0.07)	-0.16 (-0.47, 0.14)	-0.20 (-0.55, 0.14)	-0.23 (-0.58, 0.11)

Abbreviations: VP/VLBW, very preterm/very low birth weight; NSI, neurosensory Impairment; IVH, intraventricular haemorrhage; BPD, bronchopulmonary dysplasia; SES, socio-economic Status. [∏]For categorical variables, effect refers to mean difference; for continuous variables (age at assessment, birth weight, gestational age), this refers to the average change in the outcome per unit increase in the variable. [¶] EPICure was not included for the Spouse/Partner scale due to small numbers (n=2). [˥] No data in ESTER. [+]Remains significant after correcting for multiple comparisons using the Benjamini-Hochberg procedure with a false discovery rate of 0.05.