

Manuscript version: Author's Accepted Manuscript

The version presented in WRAP is the author's accepted manuscript and may differ from the published version or Version of Record.

Persistent WRAP URL:

<http://wrap.warwick.ac.uk/134242>

How to cite:

Please refer to published version for the most recent bibliographic citation information. If a published version is known of, the repository item page linked to above, will contain details on accessing it.

Copyright and reuse:

The Warwick Research Archive Portal (WRAP) makes this work by researchers of the University of Warwick available open access under the following conditions.

Copyright © and all moral rights to the version of the paper presented here belong to the individual author(s) and/or other copyright owners. To the extent reasonable and practicable the material made available in WRAP has been checked for eligibility before being made available.

Copies of full items can be used for personal research or study, educational, or not-for-profit purposes without prior permission or charge. Provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way.

Publisher's statement:

Please refer to the repository item page, publisher's statement section, for further information.

For more information, please contact the WRAP Team at: wrap@warwick.ac.uk.

Behavioural and educational outcomes following extremely preterm birth:

Current controversies and future directions

For Hot Topics and Controversies in Neonatology;

Part 4 Long Term Effects Following Extreme Prematurity

by

Jayne Trickett¹, Samantha Johnson¹, Dieter Wolke²

¹Department of Health Sciences, University of Leicester, Leicester, UK.

²School of Psychology, University of Warwick, Coventry, UK.

Word count: 4771 (4621 without abstract)

Number of figures: 4

Number of references: 110

Permission to reprint required for Figure 2: The paper from which Figure 2 is taken is published under a creative commons CC BY license. We believe this means that permission does not need to be sourced from the publisher to reproduce the figure, as long as the source is acknowledged. As required we have provided the full reference to the paper in the figure caption.

Address for correspondence: Samantha Johnson, Professor of Child Development, Department of Health Sciences, University of Leicester, George Davies Centre, University Road, Leicester, LE1 7RH; Tel: +44 (0)116 252 5798; Email: sjj19@le.ac.uk.

Abstract

As a consequence of improved survival rates for extremely preterm (EP; <28 weeks of gestation) births, there is a growing body of evidence detailing the impact of extreme prematurity on outcomes throughout childhood and adolescence. Historically, attention first focused on documenting rates of sensory impairments and severe neurodevelopmental disabilities. However, over recent years, there has been growing interest in the impact of EP birth on long term mental health and educational outcomes. In this chapter we review literature relating to the impact of EP birth on attention, social and emotional problems, psychiatric disorders and educational outcomes. We also outline current controversies in the field. In particular, we present emergent research exploring developmental trajectories to determine whether the sequelae associated with EP birth represent a developmental delay or persistent deficit, and we consider what approaches to intervention may be most fruitful in improving behavioural and educational outcomes in this population.

Introduction

Extremely preterm (EP) births, before 28 weeks of gestation, continue to pose one of the greatest challenges to neonatal medicine, not just in terms of reducing mortality and short term morbidity, but in minimising the impact of immaturity at birth on lifelong health and development. Since the advent of contemporary neonatal care in the 1980s, and the continued improvement in survival rates, the long term consequences of EP birth have garnered increasing public, parent and professional concern. This has resulted in a growing body of research in which outcomes throughout childhood and adolescence have been well documented, particularly relating to the risk for neurodevelopmental impairments (see Chapter 20). As rates of severe sensory disabilities have fallen, and follow up has become increasingly interdisciplinary, greater attention has been paid to the impact of EP birth on behavioural and educational outcomes and quality of life. Here we present an overview of what is known about behavioural and educational outcomes following EP birth and outline current controversies in the field.

Where possible, we present data from EP birth cohort studies that have utilised gestational age defined inclusion criteria. However, given the continuity in outcomes across the full spectrum of preterm gestations, evidence from extremely low birthweight (ELBW; <1000g) cohorts, very preterm/very low birthweight (VP/VLBW; <32 weeks/<1500g) cohorts or whole population studies are included where these illustrate pertinent findings or where data from EP cohorts are lacking.

Attention, social and emotional problems

Herein we adopt a broad definition of behavioural outcomes, encompassing research relating to behaviour, attention, social and emotional problems and mental disorders. The majority of extant data stem from VP/VLBW cohort studies, and from the use of parent, teacher or self completed rating scales given their utility on a large scale. The results of such studies are largely convergent, and have identified a greater risk for internalising than externalising problems among children born

EP. For example, a recent meta-analysis of parent reported outcomes in EP/ELBW children compared with term born controls identified a moderate effect size for internalising problems (Standardised Mean Difference (SMD) 0.42; 95% CI 0.26, 0.58; 11 studies) and a small effect size for externalising problems (SMD 0.15; 95% CI 0.02, 0.28; 5 studies) (Figure 1a).(1)

FIGURE 1

Results on such summary scales can mask differences in outcomes across functional domains. When the same authors analysed data for specific disorders, they found a large effect size for symptoms of combined Attention-Deficit/Hyperactivity Disorder (ADHD) and moderate effect sizes for inattention, hyperactivity, social problems and autistic symptoms. In contrast, there was a small effect size for conduct problems and no significant difference in oppositional defiant disorder (ODD) problems between EP/ELBW children and controls (Figure 1a).(1) Although there are fewer studies in adolescence, their meta-analyses revealed similar findings. As shown in Figure 1b, there were no significant differences between EP/ELBW adolescents and controls in parent reported externalising, conduct disorder or ODD problems, a small effect size for hyperactivity, but moderate effect sizes for social problems, combined ADHD symptoms, inattention and internalising problems (Figure 1b).(1) Indeed EP children identify poor peer relationships and mental wellbeing as salient characteristics.(2)

These findings are reflective of the broader literature, including studies of VP/VLBW cohorts, which have led to the putative 'preterm behavioural phenotype'. This is a universal pattern of outcomes characterised by an excess of problems and disorders associated with inattention, emotional symptoms, and social problems(3); these are typically paralleled by a smaller or, in some, no increased risk for conduct disorder or ODD problems.(3, 4) This phenotype was evidenced in early reports by a strikingly similar pattern of outcomes in five European and North American ELBW/EP cohorts born in the 1970s-1990s.(5, 6) In each cohort, parents rated ELBW/EP children with a significant excess of attention, social and thought problems on the Child Behavior Checklist (CBCL)

compared with term born controls; this was alongside no increased risk for aggressive or delinquent behaviour problems. These studies highlighted the cross-cultural and temporal consistency in outcomes despite improved neonatal care and the consequent increase in survival of EP babies over this period.

Whilst the majority of research has focused on middle childhood, problems are already evident in the early years.(7-9) Among children born at <29 weeks of gestation in the French EPIPAGE Study, 24% had clinically significant problems compared with 9% of full term controls at three years of age.(10) At five years of age, 38% of Norwegian children born <28 weeks of gestation had clinically significant problems compared with 11% of controls (OR 5.1; 95% CI 3.7, 7.1).(11) An increased risk for regulatory problems, poor socio-emotional competence and withdrawn behaviour has also been observed in EP born infants (12-15) which has been associated with an increased risk for later psychiatric disorders.(16, 17)

A number of studies have also identified an increased risk of conduct problems among children born EP (8, 10, 11, 18), which may be inconsistent with the behavioural phenotype described above. However, externalising problems in early childhood may manifest as inattention, autistic traits or psychiatric disorders later in life.(16, 17) In addition, the phenotype was observed from the co-occurrence of problems at a population level. Although there is greater comorbidity of psychological problems in EP children than controls (19), the extent to which ADHD, ASD and emotional disorders cluster within individuals is less well defined, particularly as not all EP survivors will go on to have long term morbidity. Using latent profile analysis, it was recently reported that 20% of EP survivors exhibit an outcome profile consistent with the preterm behavioural phenotype, with the remaining having only minimal difficulties (55%) or having elevated scores in multiple behavioural domains (25%).(20)

Psychiatric disorders

In a meta-analysis of five cohort studies of children born preterm (<37 weeks of gestation) or with low birthweight (LBW; <2500g), prevalence estimates for psychiatric disorders ranged from 21% to 28%, with a pooled Odds Ratio (OR) of 3.66 (95% CI 2.57, 5.21) relative to term born controls.(21) The authors also identified an increased risk for emotional disorders (anxiety or depression) in preterm/LBW survivors (OR 2.86; 95% CI 1.73, 4.73; 5 studies).(21) Another recent meta-analysis reported a pooled OR of 4.05 (95% CI 2.38, 6.87; 4 studies) for ADHD in EP/ELBW children.(22)

There is growing concern regarding the high risk for ASD in children born preterm, fuelled by reports that 13%-41% of EP children screen positive for autism in the first two years of life.(23-26) However, screening for ASD in EP populations is confounded by the high risk for other neurodevelopmental sequelae.(25, 27) Thus, the predictive validity of early screens is poor, with sensitivity and positive predictive values estimated to be 52% and 20%, respectively, for later ASD diagnoses.(28) A recent meta-analysis identified an ASD prevalence of 7% among children born VP(29), which is markedly increased relative to 62/10,000 reported in the general population.(30)

Behavioural outcomes: current controversies and research directions

One of the key current questions relates to the extent to which behavioural problems observed in childhood persist into adulthood; in particular, whether early sequelae represent a developmental delay, or whether EP birth limits developmental plasticity thus conferring deficits that persist across the lifespan. Data for EP adults remain sparse, but as the VP/VLBW/ELBW cohorts from the 1970s and 1980s transition to adulthood these questions are beginning to be answered.

In a recent narrative review of six studies, the authors reported that ELBW adults are at increased risk for internalising behaviours, anxiety problems, shyness, poor mental health and reduced social functioning. However, they found no excess of ADHD and externalising behaviour problems, and a decreased risk for substance use disorders.(1) This is similar to the results of a recent meta-analysis, which identified that VP/VLBW adults are more likely to have internalising problems and avoidant personality than term born adults, but are less likely to have externalising problems and anti-social

behaviour.(31) These studies are also consistent with other reports in which VP/VLBW adults have been found to be more agreeable, socially withdrawn and introverted, and less likely to engage in substance use and risk taking behaviours.(32, 33)

The most recent data available for EP survivors are from the UK and Irish EPICure Study in which trajectories of parent reported behaviour, attention, social and emotional problems have been explored (Figure 2). Using the Strengths and Difficulties Questionnaire (SDQ) at 6, 11, 16 and 19 years of age, mean scores for ADHD and emotional problems were persistently higher in EP than term born individuals, but the risk for clinically significant problems declined from childhood to adulthood, with the group difference at 19 years no longer being significant. In contrast, the risk for clinically significant peer relationship problems was increased at all ages in EP survivors, peaking in adolescence. Notably, the risk for conduct problems was only increased at 6 years of age and progressively declined with age relative to controls.(34)

FIGURE 2

However, these results were based on parent report. Most recently, the results of self-completed evaluations among this cohort at 19 years of age revealed higher scores for symptoms of anxiety, depression, withdrawn behaviour and avoidant personality. However, there was no increased risk for clinically significant problems in these areas, or for mood and anxiety disorders at 19 years of age(35), similar to reports of mood and anxiety disorders in VP/VLBW samples.(36) This is reassuring and suggests that, whilst sub-clinical problems may persist to adulthood, mental health outcomes for EP survivors may be better than once anticipated. The decreasing risk may be a result of reduced statistical power due to participant attrition, therefore these findings require confirmation in larger studies.

Another focus of current interest is the need to identify interventions to improve outcomes in this population, with a key question being whether these need to be population-specific, reflecting different mechanisms for psychiatric sequelae in preterm populations, or whether existing therapies

are likely to be effective. Forging an understanding of the underlying risk pathways for mental health disorders is therefore a focus of current research, and is particularly evident in relation to ADHD.

In a recent meta-analysis of VP/VLBW cohort studies, the risk for symptoms of inattention (SMD 1.31; 95% CI 0.66, 1.96) was larger than for hyperactivity (SMD 0.74; 95% CI 0.35, 1.13), a finding that has been observed in other population based cohorts.(37-40) These findings are indicative of a different clinical presentation and, potentially, a different aetiology for ADHD in preterm born children. Recent studies have thus focused on elucidating the cognitive processes underlying ADHD in preterm populations and have suggested that, whilst some cognitive impairments are overlapping between VP children and term born children with ADHD, VP children show additional impairments reflecting more wide-ranging cognitive deficits.(41-43) Interruption to fetal brain development in the third trimester may result in trauma to the brain networks associated with ADHD(44), in addition to networks associated with other impairments, resulting not just in ADHD symptoms but in increased comorbidity in neurodevelopmental disorders observed in this population.(41) Similarly, there is growing evidence for an association between deficits in general cognitive functions, such as in executive function and/or working memory, and attention and social problems in children born preterm.(45-49) Improving these cognitive abilities may therefore be a potential target for intervention, the efficacy of which is discussed in the following sections.

Academic attainment and special educational needs

It is well documented that children born EP are at increased risk for intellectual impairments (see Chapter 20). Deficits in a range of general cognitive abilities are frequently reported, including poorer executive function, processing speed, working memory and visuospatial skills relative to term born controls.(50-52) It is therefore unsurprising that preterm birth has a marked impact on children's academic attainment and the need for special educational provision.

Deficits in the acquisition of early learning skills between EP children and their term born peers are already evident before the start of schooling. For example, significant deficits in school readiness

have been observed in children born ELBW/VP(53-55), and these have been shown to predict later achievement in reading, spelling and mathematics.(56) Already at age five, VP children in the UK have poorer attainment at the end of the reception year, with 66% failing to have a good level of achievement compared with 51% of children born at term (RR 1.19; 95% CI 1.00, 1.42).(57) By age seven, in the same cohort, 43% of VP children failed to have a good level of achievement in reading, writing and mathematics, compared with 18% of children born at full term (RR 1.78, 95% CI 1.24, 2.54).(58)

Outcomes for EP children are likely to be even poorer given the gestational age related gradient in outcomes. Indeed poorer mathematical and reading skills have been observed among EP/ELBW children compared with controls at age five in a representative sample of children in the US.(59) In middle childhood, by eight years of age, EP/ELBW children continue to have significantly poorer attainment in reading, spelling and arithmetic compared to children born at term(60), and by 10-11 years of age, substantial deficits in mathematics and reading and poorer performance in national tests have been observed among EP/ELBW children.(61, 62) By the end of primary school, half of all EP children in the EPICure Study of births before 26 weeks of gestation had attainment below the national average compared with just 5% of their term born peers (OR 18.2, 95% CI 8.0, 41.4).(63)

Underachievement compared to term born peers continues to be evidenced at the end of formal schooling. At age 16, poorer scores on school leaving qualifications in mathematics, literacy and foreign language learning have been observed among adolescents born at <29 weeks of gestation, and poorer reading, spelling and mathematics skills have been reported at age 18 years in EP/ELBW young adults.(64, 65) Children born EP are also less likely to complete basic school than their term born peers, a risk that increases with decreasing gestational age at birth, particularly below 31 weeks of gestation.(66)

Poor academic attainment has broader economic consequences, which are evidenced in the increased receipt of special educational needs (SEN) support among children born EP. School census

data from Scotland show a clear gestational age related gradient in SEN, with the proportion of children requiring support increasing exponentially with decreasing gestational age at birth (Figure 3). Among those born EP in this study, 29% had SEN compared with just 4% of children born at 40 weeks of gestation (adjusted OR 6.92, 95% CI 5.58, 8.58).(67) The proportion with SEN is even greater amongst the most immaturely born children, with 62% of children born below 26 weeks of gestation in the EPICure Study having SEN or attending special school compared with just 11% of term born controls (OR 13.1, 95% CI 7.4, 23.3).(62)

FIGURE 3

Ultimately, poorer educational outcomes result in poorer occupational status and wealth in adulthood.(68) A recent meta-analysis of 23 studies identified that VP/VLBW adults are less likely to complete education beyond high school and be employed, and are more likely to be in receipt of benefits than adults born at term; however there was no significant difference in the proportion living independently (Figure 4).(69)

FIGURE 4

Developmental delay or developmental deficit?

Just as is the case for behavioural outcomes, a key controversy relates to whether poorer educational outcomes in childhood represent developmental deficits that persist across the lifespan, or whether, as EP children mature, they catch up with their peers. Similar to studies tracking IQ in EP/VP/VLBW cohorts(70, 71), recent longitudinal studies have failed to provide robust evidence of catch-up in academic outcomes. In a study of VP children and term born controls assessed through Grades 1-6 in the Netherlands, there was no significant difference in the trajectories of VP children and controls in either arithmetic, reading comprehension or spelling. This indicates that between-group differences remained stable over time and that VP children did not catch up with their peers by the end of primary school.(72) Most recently, an investigation of trajectories in results on national

school attainment tests at ages 7, 11, 14 and 16 years in the UK found that children born preterm displayed some catch-up between 7 and 11 years, after which they had similar trajectories to their term born peers. As such, term born adolescents continued to out-perform their preterm counterparts at the end of compulsory schooling.(73) It may be that EP birth places even greater limits on developmental plasticity and that trajectories may be more immutable in this population. To investigate this, the authors examined trajectories for those born VP and, whilst the overall trajectory was similar to the total preterm group, some of the catch-up observed between age 7 and 11 years was lost again at secondary school.(73) The trajectory of attainment in EP children remains to be determined.

Current evidence is consistent with a developmental deficit rather than delay. However, the authors of the above studies argue that, despite the persistent deficits in academic attainment, the similarity in trajectories between preterm and term born children suggests that preterm children have intact learning abilities, thus affording opportunities for intervention.(72, 73) It is therefore important to elucidate the cognitive mechanisms underlying poor academic attainment in preterm populations in order to inform the development of intervention strategies, as discussed in the following sections.

Supporting the learning of children born preterm

Supporting the learning and academic attainment of EP children has never been more crucial since recent reports suggest that motor, cognitive and academic outcomes may be deteriorating despite ongoing advances in neonatal care.(74-76) Interest initially focused on preventive interventions delivered during the neonatal period or during the first few years of life. Whilst there was initial enthusiasm following reports that these might improve outcomes in the short term, meta-analyses have shown that the long term benefit of such programmes is limited; beneficial effects are rarely sustained beyond the period of intervention delivery and any impact on cognitive function is washed

out by school age.(77, 78) Thus, if the aim is to improve academic outcomes, then intervention at school age may be most effective.

The aetiology of academic underachievement following EP birth is a focus of current research, especially in mathematics as EP children have greatest difficulties in this subject.(62, 79, 80) Such studies indicate that EP children's poor achievement in mathematics is not related to a specific deficit in numerical magnitude processing, but rather to deficits in general cognitive abilities such as working memory, executive function, visuospatial skills and processing speed.(48, 52, 81-83) Thus, converging evidence suggests that poor general cognitive abilities may underlie both behavioural and educational problems in EP children and that improving these abilities may improve a range of outcomes. The notion that a single intervention may improve outcomes across multiple developmental domains is certainly enticing; however attempts so far have met with little success. For example, attention has focused on the use of computerised adaptive working memory training for improving cognitive and academic outcomes. Whilst some studies have reported short term positive effects in VP/VLBW samples, these have lacked an active control or have been underpowered.(84, 85) There remains no robust evidence of long term benefits of working memory training, particularly for enhancing academic attainment.(86-88) Given the evidence to date, it is perhaps time to focus efforts on identifying other strategies for improving outcomes in this population.

One approach gaining ground lies in improving educational support in the classroom. Knowledge and preparation about health conditions is crucial for the provision of appropriate educational management(89, 90), yet research has shown that teachers lack training about preterm birth and have poor knowledge of the impact it may have on children's learning.(91) As education professionals have a key role to play in supporting preterm children in the long term this represents a significant public health concern. This was recognised in the recent European Standards of Care for Newborn Health in which it was recommended that education professionals receive training about

preterm birth.(92) Improved communication of clinical research to teachers and better information sharing between healthcare and education services may serve to improve educational support for children born preterm. An evidence-based e-learning resource that has been shown to significantly improve teachers' knowledge of the consequences of preterm birth and their confidence in supporting children in the classroom(93) was released in 2019 (see: www.pretermbirth.info). The impact of this on improving outcomes for children born preterm remains to be seen.

Delayed school entry

Perhaps one of the most controversial potential approaches to supporting the development of children born preterm is that of delayed school entry. The implicit underlying theoretical model for delayed school entry is that, given time, EP children will continue to develop and will reach the same level of cognitive and social maturity as term born children who enter compulsory education at the appropriate age. This is in stark contrast to the studies presented above, which consistently show that deficits in cognitive, attention and emotional function persist into adulthood.(34, 70, 71)

The evidence for or against delayed school entry has been recently reviewed and existing studies are inconclusive.(94, 95) Using a natural experiment we recently investigated the effects of delayed versus age-appropriate school entry on academic attainment and attention using data from the Bavarian Longitudinal Study. The results indicated that delayed school entry had no beneficial effect on teacher ratings of academic performance at the end of the first year of schooling, but was associated with poorer performance in standardised tests of reading, writing, mathematics and attention at 8 years of age.(95, 96) Thus keeping children back for a whole year did not have a noticeable "maturation effect", but deprived these children from learning opportunities so that they did worse in achievement tests at the same age as those who had entered school at the compulsory entry age. Considering the adverse effects that low socio-economic status (SES) or poor parenting

can have on the development of EP children, delaying school entry for EP infants from disadvantaged families may increase social disadvantage further.

Nonetheless, parents of preterm children often believe that delayed school entry may be helpful. Indeed, preterm children should not be disadvantaged compared to term born children due to their preterm birth. For example, in the UK, children enter school in the September after their 4th birthday. However, EP born children who would have had their expected date of delivery in October may be born in July but are expected to enter school, considering post-conceptual age, younger than their term born peers. In these circumstances, delayed entry may be indicated to allow an EP child to enter school at the same time as children of the same post-conceptual age. However, delaying entry for all EP children due to the increased risk for developmental problems may not be beneficial according to the evidence to date.

To test whether delayed school entry may be a simple intervention that works, a randomised controlled trial is needed. Our recent feasibility study indicated that such a trial would not be feasible as parents expressed that the decision about whether or not to delay entry for their child was too important to be determined by randomisation.(94) Despite the controversial evidence, a report published in the UK in 2018 highlighted that the number of parents of summer born children that requested delayed entry doubled in 2016-2017 after legislation allowing this came into force.(97) The report also provided no evidence that delayed school entry improved children's scores in a phonics screening test in Year 1. Thus, evidence will have to rely on future observational studies tracking the impact of delayed school entry on academic achievement controlling carefully for social selection factors.

The need for theory driven research

Moving forwards, the elucidation of effective interventions requires a greater focus on theory driven research. Most EP cohort studies have used a simple main factor model investigating perinatal differences at birth, such as in gestational age or neonatal complications, and documenting whether

these are associated with adverse developmental outcomes. This approach ignores that many other influences may operate between birth and outcomes in childhood and adulthood. One simple environmental factor to assess is the socioeconomic status (SES) of the family. For example, studies have shown that being born into a high versus low SES family has as much of an effect on long term outcomes as being born VP versus at term.(98) Similarly, having a mother whose highest educational attainment was at primary or secondary school compared to one who has received postgraduate education has the same adverse effect on the IQ of EP children as having suffered severe IVH or chronic lung disease.(99) It is thus no surprise that SES has been reported as one of the major influences on cognitive outcomes in VP children.(100, 101) It is, however, disconcerting that, by 2018, only 15 of 70 studies included in a meta-analysis of VP birth and IQ considered some marker of SES.(102)

We recognise that measurement of SES is challenging since it can reflect a multitude of factors including social, family and parenting factors.(103) However, if we wish to unlock the black box of how these factors influence development, we need to measure them in as much detail as we have perinatal complications(103) which will require greater collaboration across disciplines in the design of follow-up studies. Let us consider two examples of such an approach. As described above, EP children are at higher risk for emotional problems in adolescence. Similarly, it is well documented that children who are exposed to trauma, such as being bullied by peers, are at higher risk of emotional problems.(104, 105) In a recent investigation, we noted that a major part of the effect of EP birth on emotional problems was explained by EP children being more than twice as likely to be bullied than their term born peers, which in turn explained the excess of emotional problems in adolescence. Thus bullying was a mediator of the effects of EP birth on emotional problems.(106) Furthermore, it has been shown that the academic achievement of healthy term born children is only minimally influenced by good or poor parenting. In contrast, VP children are strongly and adversely affected by low sensitive parenting while, on the other hand, very sensitive parenting has been found to lead to academic achievement on a par with children born at term.(107, 108)

These examples indicate that parenting and peer behaviour are important mediators or moderators of outcomes in the EP population. There is also increasing evidence that EP birth makes children more sensitive to adverse environmental risk factors.(109) This increased vulnerability leads to even worse outcomes if children are exposed to an average or poor environment, but EP survivors may attain outcomes similar to term born children when exposed to optimal environments. The effects are therefore best described using a diathesis-stress model.(110) Research that considers environmental influences from SES and parenting to peers and friendships and how these protect against, mediate or moderate the impact of EP birth on developmental outcomes is urgently needed. Understanding such developmental mechanisms will be a major step change in current research as it may point to factors that are modifiable and thus are prime targets for intervention.

Summary

EP birth places infants at high risk for attention, social and emotional problems and disorders and for academic deficits later in life. Studies of VP/VLBW cohorts have shown that these deficits persist into adult life but a greater understanding of trajectories of educational and behavioural outcomes for EP survivors are needed. These will naturally ensue as the earliest EP cohorts born in the 1990s transition through adulthood. Attempts to improve long term outcomes for EP children have typically focused on the efficacy of early parenting interventions or of training children's cognitive abilities, but these have met with little success to date. Ongoing efforts to identify effective interventions to improve outcomes for EP children need to be intensified, for which a greater focus on theory driven research may hold the answer.

References

1. Mathewson KJ, Chow CH, Dobson KG, Pope EI, Schmidt LA, Van Lieshout RJ. Mental health of extremely low birth weight survivors: A systematic review and meta-analysis. *Psychol Bull.* 2017;143(4):347-83.
2. Gire C, Resseguier N, Brevaut-Malaty V, Marret S, Cambonie G, Souksi-Medioni I, et al. Quality of life of extremely preterm school-age children without major handicap: a cross-sectional observational study. *Arch Dis Child.* 2019;104(4):333-9.
3. Johnson S, Marlow N. Preterm Birth and Childhood Psychiatric Disorders. *Pediatr Res.* 2011;69(5):11r-8r.
4. Johnson S, Wolke D. Behavioural outcomes and psychopathology during adolescence. *Early Hum Dev.* 2013; 89(4): 199-207.
5. Hille ETM, den Ouden AL, Saigal S, Wolke D, Lambert M, Whitaker A, et al. Behavioural problems in children who weigh 1000g or less at birth in four countries. *The Lancet.* 2001;357:1641-3.
6. Farooqi A, Hagglof B, Sedin G, Gothefors L, Serenius F. Mental health and social competencies of 10- to 12-year-old children born at 23 to 25 weeks of gestation in the 1990s: a Swedish national prospective follow-up study. *Pediatrics.* 2007;120(1):118-33.
7. Scott MN, Taylor HG, Fristad MA, Klein N, Espy KA, Minich N, et al. Behavior disorders in extremely preterm/extremely low birth weight children in kindergarten. *J Dev Behav Pediatr.* 2012;33(3):202-13.
8. Woodward LJ, Moor S, Hood KM, Champion PR, Foster-Cohen S, Inder TE, et al. Very preterm children show impairments across multiple neurodevelopmental domains by age 4 years. *Arch Dis Child Fetal Neonatal Ed.* 2009;94(5):F339-44.
9. Delobel-Ayoub M, Arnaud C, White-Koning M, Casper C, Pierrat V, Garel M, et al. Behavioral Problems and Cognitive Performance at 5 Years of Age After Very Preterm Birth: The EPIPAGE Study. *Pediatrics.* 2009;123(6):1485-92.

10. Delobel-Ayoub M, Kaminski M, Marret S, Burguet A, Marchand L, N'Guyen S, et al. Behavioural outcome at 3 years of age in very preterm infants: The EPIPAGE Study. *Pediatrics*. 2006;117(6):1996-2005.
11. Elgen SK, Leversen KT, Grundt JH, Hurum J, Sundby AB, Elgen IB, et al. Mental health at 5 years among children born extremely preterm: a national population-based study. *Eur Child Adolesc Psychiatry*. 2012;21(10):583-9.
12. Boyd LA, Msall ME, O'Shea TM, Allred EN, Hounshell G, Leviton A. Social-emotional delays at 2 years in extremely low gestational age survivors: correlates of impaired orientation/engagement and emotional regulation. *Early Hum Dev*. 2013;89(12):925-30.
13. Spittle AJ, Treyvaud K, Doyle LW, Roberts G, Lee KJ, Inder TE, et al. Early emergence of behavior and social-emotional problems in very preterm infants. *J Am Acad Child Adolesc Psychiatry*. 2009;48(9):909-18.
14. Ritchie K, Bora S, Woodward LJ. Social development of children born very preterm: A systematic review. *Dev Med Child Neurol*. 2015; 57(10):899-918.
15. Clark CAC, Woodward LJ, Horwood LJ, Moor S. Development of emotional and behavioral regulation in children born extremely preterm and very preterm: Biological and social influences. *Child Dev*. 2008;79(5):1444-62.
16. Treyvaud K, Ure A, Doyle LW, Lee KJ, Rogers CE, Kidokoro H, et al. Psychiatric outcomes at age seven for very preterm children: rates and predictors. *J Child Psychol Psychiatry*. 2013;54(7):772-9.
17. Johnson S, Hollis C, Kochhar P, Hennessy E, Wolke D, Marlow N. Psychiatric Disorders in Extremely Preterm Children: Longitudinal Finding at Age 11 Years in the EPICure Study. *J Am Acad Child Adolesc Psychiatry*. 2010;49(5):453-63.e1.
18. Samara M, Marlow N, Wolke D, for the ESG. Pervasive Behavior Problems at 6 Years of Age in a Total-Population Sample of Children Born at ≤ 25 Weeks of Gestation. *Pediatrics*. 2008;122(3):562-73.

19. Johnson S, Marlow N. Growing up after extremely preterm birth: lifespan mental health outcomes. *Semin Fetal Neonatal Med.* 2014;19(2):97-104.
20. Burnett AC, Youssef G, Anderson PJ, Duff J, Doyle LW, Cheong JLY, et al. Exploring the "Preterm Behavioral Phenotype" in Children Born Extremely Preterm. *J Dev Behav Pediatr.* 2019;40(3):200-7.
21. Burnett AC, Anderson PJ, Cheong J, Doyle LW, Davey CG, Wood SJ. Prevalence of psychiatric diagnoses in preterm and full-term children, adolescents and young adults: A meta-analysis. *Psychol Med.* 2011;41(12):2463-74.
22. Franz AP, Bolat GU, Bolat H, Matijasevich A, Santos IS, Silveira RC, et al. Attention-Deficit/Hyperactivity Disorder and Very Preterm/Very Low Birth Weight: A Meta-analysis. *Pediatrics.* 2018;141(1).
23. Limperopoulos C, Bassan H, Sullivan NR, Soul JS, Robertson RL, Moore M, et al. Positive screening for autism in ex-preterm infants: Prevalence and risk factors. *Pediatrics.* 2008;121:758-65.
24. Kuban KCK, O'Shea TM, Allred EN, Tager-Flusberg H, Goldstein DJ, Leviton A. Positive Screening on the Modified Checklist for Autism in Toddlers (M-CHAT) in Extremely Low Gestational Age Newborns. *J Pediatr.* 2009;154(4):535-40.
25. Moore T, Johnson S, Hennessy E, Marlow N. Screening for autism in extremely preterm infants: problems in interpretation. *Dev Med Child Neurol.* 2012;54(6):514-20.
26. Gray PH, Edwards DM, O'Callaghan MJ, Gibbons K. Screening for autism spectrum disorder in very preterm infants during early childhood. *Early Hum Dev.* 2015;91(4):271-6.
27. Luyster RJ, Kuban KCK, O'Shea TM, Paneth N, Allred EN, Leviton A, et al. The Modified Checklist for Autism in Toddlers in extremely low gestational age newborns: individual items associated with motor, cognitive, vision and hearing limitations. *Paediatr Perinat Epidemiol.* 2011;25(4):366-76.

28. Kim SH, Joseph RM, Frazier JA, O'Shea TM, Chawarska K, Allred EN, et al. Predictive Validity of the Modified Checklist for Autism in Toddlers (M-CHAT) Born Very Preterm. *J Pediatr*. 2016;178:101-7 e2.
29. Agrawal S, Rao SC, Bulsara MK, Patole SK. Prevalence of Autism Spectrum Disorder in Preterm Infants: A Meta-analysis. *Pediatrics*. 2018;142(3): e20180134
30. Elsabbagh M, Divan G, Koh YJ, Kim YS, Kauchali S, Marcin C, et al. Global prevalence of autism and other pervasive developmental disorders. *Autism Res*. 2012;5(3):160-79.
31. Pyhala R, Wolford E, Kautiainen H, Andersson S, Bartmann P, Baumann N, et al. Self-Reported Mental Health Problems Among Adults Born Preterm: A Meta-Analysis. *Pediatrics*. 2017;139(4): e20162690.
32. Eryigit-Madzwamuse S, Strauss V, Baumann N, Bartmann P, Wolke D. Personality of adults who were born very preterm. *Arch Dis Child Fetal Neonatal Ed*. 2015;100(6):F524-9.
33. Hack M, Flannery D, Schluchter M, Cartar L, Borawski E, Klein N. Outcomes in young adulthood for very-low-birth-weight infants. *N Engl J Med*. 2002;346(3):149-57.
34. Linsell L, Johnson S, Wolke D, Morris J, Kurinczuk JJ, Marlow N. Trajectories of behavior, attention, social and emotional problems from childhood to early adulthood following extremely preterm birth: a prospective cohort study. *Eur Child Adolesc Psychiatry*. 2019;28(4):531-42.
35. Johnson S, O'Reilly H, Ni Y, Wolke D, Marlow N. Psychiatric Symptoms and Disorders in Extremely Preterm Young Adults at 19 Years of Age and Longitudinal Findings From Middle Childhood. *J Am Acad Child Adolesc Psychiatry*. 2019; S0890-8567(19): 30260-6.
36. Jaekel J, Baumann N, Bartmann P, Wolke D. Mood and anxiety disorders in very preterm/very low-birth weight individuals from 6 to 26 years. *J Child Psychol Psychiatry*. 2018;59(1):88-95.
37. Ask H, Gustavson K, Ystrom E, Havdahl KA, Tesli M, Askeland RB, et al. Association of Gestational Age at Birth With Symptoms of Attention-Deficit/Hyperactivity Disorder in Children. *JAMA pediatr*. 2018;172(8):749-56.

38. Johnson S, Kochhar P, Hennessy E, Marlow N, Wolke D, Hollis C. Antecedents of Attention-Deficit/Hyperactivity Disorder Symptoms in Children Born Extremely Preterm. *J Dev Behav Pediatr* . 2016;37(4):285-97.
39. Jaekel J, Wolke D, Bartmann P. Poor attention rather than hyperactivity/impulsivity predicts academic achievement in very preterm and full-term adolescents. *Psychol Med*. 2013;43(1):183-196
40. Shum D, Neulinger K, O'Callaghan M, Mohay H. Attentional problems in children born with very preterm or with extremely low birth weight at 7-9 years. *Arch Clin Neuropsychol*. 2008;23:103-12.
41. Rommel AS, James SN, McLoughlin G, Brandeis D, Banaschewski T, Asherson P, et al. Association of Preterm Birth With Attention-Deficit/Hyperactivity Disorder-Like and Wider-Ranging Neurophysiological Impairments of Attention and Inhibition. *J Am Acad Child Adolesc Psychiatry*. 2017;56(1):40-50.
42. James SN, Rommel AS, Cheung C, McLoughlin G, Brandeis D, Banaschewski T, et al. Association of preterm birth with ADHD-like cognitive impairments and additional subtle impairments in attention and arousal malleability. *Psychol Med*. 2018;48(9):1484-93.
43. Retzler J, Johnson S, Groom M, Hollis C, Budge H, Cragg L. Cognitive predictors of parent-rated inattention in very preterm children: The role of working memory and processing speed. *Child Neuropsychol*. 2019;25(5):617-635.
44. Finke K, Neitzel J, Bauml JG, Redel P, Muller HJ, Meng C, et al. Visual attention in preterm born adults: specifically impaired attentional sub-mechanisms that link with altered intrinsic brain networks in a compensation-like mode. *Neuroimage*. 2015;107:95-106.
45. Alduncin N, Huffman LC, Feldman HM, Loe IM. Executive function is associated with social competence in preschool-aged children born preterm or full term. *Early Hum Dev*. 2014;90(6):299-306.

46. Kroll J, Karolis V, Brittain PJ, Tseng CJ, Froudish-Walsh S, Murray RM, et al. Real-Life Impact of Executive Function Impairments in Adults Who Were Born Very Preterm. *J Int Neuropsychol Soc* . 2017;23(5):381-9.
47. Mulder H, Pitchford NJ, Marlow N. Inattentive behaviour is associated with poor working memory and slow processing speed in very pre-term children in middle childhood. *Br J Educ Psychol*. 2011;81(Pt 1):147-60.
48. Aarnoudse-Moens CS, Weisglas-Kuperus N, Duivenvoorden HJ, van Goudoever JB, Oosterlaan J. Executive function and IQ predict mathematical and attention problems in very preterm children. *PLoS One*. 2013;8(2):e55994.
49. Loe IM, Feldman HM, Huffman LC. Executive function mediates effects of gestational age on functional outcomes and behavior in preschoolers. *J Dev Behav Pediatr*. 2014;35(5):323-33.
50. 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(5):452-68.
51. Aarnoudse-Moens CS, Weisglas-Kuperus N, van Goudoever JB, Oosterlaan J. Meta-analysis of neurobehavioral outcomes in very preterm and/or very low birth weight children. *Pediatrics*. 2009;124(2):717-28.
52. Simms V, Gilmore C, Cragg L, Clayton S, Marlow N, Johnson S. Nature and origins of mathematics difficulties in very preterm children: a different etiology than developmental dyscalculia. *Pediatr Res*. 2015;77(2):389-95.
53. Reid LD, Strobino DM. A Population-Based Study of School Readiness Determinants in a Large Urban Public School District. *Matern Child Health J*. 2019;23(3):325-34.
54. Pritchard VE, Bora S, Austin NC, Levin KJ, Woodward LJ. Identifying Very Preterm Children at Educational Risk Using a School Readiness Framework. *Pediatrics*. 2014; 134(3): e825-32.
55. Roberts G, Lim J, Doyle LW, Anderson PJ. High rates of school readiness difficulties at 5 years of age in very preterm infants compared with term controls. *J Dev Behav Pediatr*. 2011;32(2):117-24.

56. Taylor R, Pascoe L, Scratch S, Doyle LW, Anderson P, Roberts G. A simple screen performed at school entry can predict academic under-achievement at age seven in children born very preterm. *J Paediatr Child Health*. 2016;52(7):759-64.
57. Quigley MA, Poulsen G, Boyle E, Wolke D, Field D, Alfirevic Z, et al. Early term and late preterm birth are associated with poorer school performance at age 5 years: a cohort study. *Arch Dis Child Fetal Neonatal Ed*. 2012;97(3):F167-73.
58. Chan E, Quigley MA. School performance at age 7 years in late preterm and early term birth: a cohort study. *Arch Dis Child Fetal Neonatal Ed*. 2014;99(6):F451-7.
59. Lee M, Pascoe JM, McNicholas CI. Reading, Mathematics and Fine Motor Skills at 5 Years of Age in US Children who were Extremely Premature at Birth. *Matern Child Health J*. 2017;21(1):199-207.
60. Hutchinson EA, De Luca CR, Doyle LW, Roberts G, Anderson PJ, Group VICS. School-age outcomes of extremely preterm or extremely low birth weight children. *Pediatrics*. 2013;131(4):e1053-e61.
61. Joseph RM, O'Shea TM, Allred EN, Heeren T, Hirtz D, Jara H, et al. Neurocognitive and Academic Outcomes at Age 10 Years of Extremely Preterm Newborns. *Pediatrics*. 2016; 137(4): :e20154343
62. Johnson S, Hennessy E, Smith R, Trikic R, Wolke D, Marlow N. Academic attainment and special educational needs in extremely preterm children at 11 years. The EPICure Study. *Arch Dis Child Fetal Neonatal Ed*. 2009;94:F283-F9.
63. Johnson S, Wolke D, Hennessy E, Marlow N. Educational outcomes in extremely preterm children: neuropsychological correlates and predictors of attainment. *Dev Neuropsychol*. 2011;36(1):74-95.
64. Doyle LW, Cheong JL, Burnett A, Roberts G, Lee KJ, Anderson PJ. Biological and Social Influences on Outcomes of Extreme-Preterm/Low-Birth Weight Adolescents. *Pediatrics*. 2015;136(6):e1513-20.

65. Hallin A-L, Hellström-Westas L, Stjernqvist K. Follow-up of adolescents born extremely preterm: cognitive function and health at 18 years of age. *Acta Paediatr.* 2010;99(9):1401-6.
66. Mathiasen R, Hansen BM, Andersen AM, Forman JL, Greisen G. Gestational age and basic school achievements: a national follow-up study in Denmark. *Pediatrics.* 2010;126(6):e1553-61.
67. MacKay DF, Smith GC, Dobbie R, Pell JP. Gestational age at delivery and special educational need: retrospective cohort study of 407,503 schoolchildren. *PLoS Med.* 2010;7(6):e1000289.
68. Basten M, Jaekel J, Johnson S, Gilmore C, Wolke D. Preterm Birth and Adult Wealth: Mathematics Skills Count. *Psychol Sci.* 2015;26(10):1608-19.
69. Bilgin A, Mendonca M, Wolke D. Preterm Birth/Low Birth Weight and Markers Reflective of Wealth in Adulthood: A Meta-analysis. *Pediatrics.* 2018;142(1).
70. Linsell L, Johnson S, Wolke D, O'Reilly H, Morris JK, Kurinczuk JJ, et al. Cognitive trajectories from infancy to early adulthood following birth before 26 weeks of gestation: a prospective, population-based cohort study. *Arch Dis Child.* 2018;103(4):363-70.
71. Breeman LD, Jaekel J, Baumann N, Bartmann P, Wolke D. Preterm Cognitive Function Into Adulthood. *Pediatrics.* 2015;136(3):415-23.
72. Twilhaar ES, de Kieviet JF, van Elburg RM, Oosterlaan J. Academic trajectories of very preterm born children at school age. *Arch Dis Child Fetal Neonatal Ed.* 2018; 104(4): F419-F423.
73. Odd D, Evans D, Emond AM. Prediction of school outcome after preterm birth: a cohort study. *Arch Dis Child.* 2019;104(4):348-53.
74. Spittle AJ, Cameron K, Doyle LW, Cheong JL, Victorian Infant Collaborative Study G. Motor Impairment Trends in Extremely Preterm Children: 1991-2005. *Pediatrics.* 2018;141(4): e20173410
75. Cheong JLY, Anderson PJ, Burnett AC, Roberts G, Davis N, Hickey L, et al. Changing Neurodevelopment at 8 Years in Children Born Extremely Preterm Since the 1990s. *Pediatrics.* 2017;139(6): e20164086.
76. Burnett AC, Anderson PJ, Lee KJ, Roberts G, Doyle LW, Cheong JLY, et al. Trends in Executive Functioning in Extremely Preterm Children Across 3 Birth Eras. *Pediatrics.* 2018;141(1): e20171958.

77. Spittle A, Orton J, Anderson PJ, Boyd R, Doyle LW. Early developmental intervention programmes provided post hospital discharge to prevent motor and cognitive impairment in preterm infants. *Cochrane Database Syst Rev.* 2015;11:CD005495.
78. Symington A, Pinelli J. Developmental care for promoting development and preventing morbidity in preterm infants. *The Cochrane database of systematic reviews.* 2006(2):CD001814.
79. Akshoomoff N, Joseph RM, Taylor HG, Allred EN, Heeren T, O'Shea TM, et al. Academic Achievement Deficits and Their Neuropsychological Correlates in Children Born Extremely Preterm. *J Dev Behav Pediatr.* 2017;38(8):627-37.
80. Simms V, Cragg L, Gilmore C, Marlow N, Johnson S. Mathematics difficulties in children born very preterm: current research and future directions. *Arch Dis Child Fetal Neonatal Ed.*2013;98(5):F457-63.
81. Jaekel J, Wolke D. Preterm birth and dyscalculia. *J Pediatr.* 2014;164(6):1327-32.
82. Tatsuoka C, McGowan B, Yamada T, Espy KA, Minich N, Taylor HG. Effects of Extreme Prematurity on Numerical Skills and Executive Function in Kindergarten Children: An Application of Partially Ordered Classification Modeling. *Learn Individ Differ.* 2016;49:332-40.
83. Mulder H, Pitchford NJ, Marlow N. Processing speed and working memory underlie academic attainment in very preterm children. *Arch Dis Child Fetal Neonatal Ed.*2010;95(4):F267-72.
84. Grunewaldt KH, Lohaugen GC, Austeng D, Brubakk AM, Skranes J. Working memory training improves cognitive function in VLBW preschoolers. *Pediatrics.* 2013;131(3):e747-54.
85. Aarnoudse-Moens CSH, Twilhaar ES, Oosterlaan J, van Veen HG, Prins PJM, van Kaam A, et al. Executive Function Computerized Training in Very Preterm-Born Children: A Pilot Study. *Games Health J.* 2018;7(3):175-81.
86. Anderson PJ, Lee KJ, Roberts G, Spencer-Smith MM, Thompson DK, Seal ML, et al. Long-Term Academic Functioning Following Cogmed Working Memory Training for Children Born Extremely Preterm: A Randomized Controlled Trial. *J Pediatr.* 2018;202:92-7 e4.

87. Roberts G, Quach J, Spencer-Smith M, Anderson PJ, Gathercole S, Gold L, et al. Academic Outcomes 2 Years After Working Memory Training for Children With Low Working Memory: A Randomized Clinical Trial. *JAMA pediatr.* 2016;170(5): e154568.
88. Melby-Lervag M, Hulme C. Is working memory training effective? A meta-analytic review. *Dev Psychol.* 2013;49(2):270-91.
89. Johnson MP, Lubker BB, Fowler MG. Teacher Needs Assessment for the Educational Management of Children with Chronic Illnesses. *J Sch Health.*1988;58(6):232-5.
90. Brook U, Galili A. Knowledge and attitudes of high school teachers towards pupils suffering from chronic diseases. *Patient Educ Couns.* 2001;43(1):37-42.
91. Johnson S, Gilmore C, Gallimore I, Jaekel J, Wolke D. The long-term consequences of preterm birth: what do teachers know? *Dev Med Child Neurol.* 2015;57(6):571-7.
92. Infants EFftCoN. European Standards of Care for Newborn Health. Munich, Germany: 2018.
93. Johnson S, Bamber D, Bountziouka V, Clayton S, Cragg L, Gilmore C, et al. Improving developmental and educational support for children born preterm: evaluation of an e-learning resource for education professionals. *BMJ Open.* 2019;9(6):e029720.
94. Wolke D, Dosanjh S, Johnson S, Jaekel J, S. Dantchev. Delayed school entry for preterm children Assessing the feasibility of a randomized controlled trial. 2018.
[https://www.nuffieldfoundation.org/sites/default/files/files/Wolke%2040442%20-%20Nuffield%20report_delayed%20school%20entry%20\(Oct17\).pdf](https://www.nuffieldfoundation.org/sites/default/files/files/Wolke%2040442%20-%20Nuffield%20report_delayed%20school%20entry%20(Oct17).pdf). Accessed 20 June 2019.
95. Jaekel J, Strauss VY, Johnson S, Gilmore C, Wolke D. Delayed school entry and academic performance: a natural experiment. *Dev Med Child Neurol.* 2015;57:652-59.
96. Fastenau PS. Are the data on delayed school entry compelling enough to change policy ... or even pediatrician recommendations? *Dev Med Child Neurol.* 2015;57(7):596-7.
97. Cirin R, Lubwama J. Delayed School admissions for summer born pupils: Reserach report. Department of Education, her Majesty's Government, 2018.

98. Eryigit Madzwamuse S, Baumann N, Jaekel J, Bartmann P, Wolke D. Neuro-cognitive performance of very preterm or very low birth weight adults at 26 years. *J Child Psychol Psychiatry*. 2015;56(8):857-64.
99. Benavente-Fernandez I, Synnes A, Grunau RE, Chau V, Ramraj C, Galss T, et al. Association of socioeconomic status and brain injury with neurodevelopmental outcomes of very preterm children. *JAMA Netw Open*. 2019;2(5):e192914.
100. 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(12):1162-72.
101. Breeman LD, Jaekel J, Baumann N, Bartmann P, Wolke D. Neonatal predictors of cognitive ability in adults born very preterm: a prospective cohort study. *Dev Med Child Neurol*. 2017;59(5):477-83.
102. 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(4):361-67.
103. Wolke D. Editorial: Is social inequality in cognitive outcomes increased by preterm birth-related complications? *JAMA Netw Open*. 2019;2(5):e192902.
104. Zwierzynska K, Wolke D, Lereya TS. Peer Victimization in Childhood and Internalizing Problems in Adolescence: A Prospective Longitudinal Study. *J Abnorm Child Psychol*. 2013;41(2):309-23.
105. Wolke D, Lereya ST. Long-term effects of bullying. *Arch Dis Child*. 2015;100(9):879-85.
106. Wolke D, Baumann N, Strauss V, Johnson S, Marlow N. Bullying of Preterm Children and Emotional Problems at School Age: Cross-Culturally Invariant Effects. *J Pediatr*. 2015; 166(6):1417-22.

107. 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(5):642-7.
108. 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(5):642-7.
109. Van Lieshout RJ, Boyle MH, Favotto L, Krzeczkowski JE, Savoy C, Saigal S, et al. Impact of extremely low-birth-weight status on risk and resilience for depression and anxiety in adulthood. *Child Psychol Psychiatry*. 2018;59(5):596-603.
110. Jaekel J, Pluess M, Belsky J, Wolke D. Effects of maternal sensitivity on low birth weight children's academic achievement: a test of differential susceptibility versus diathesis stress. *Child Psychol Psychiatry*. 2015;56(6):693-701.

FIGURE 1a

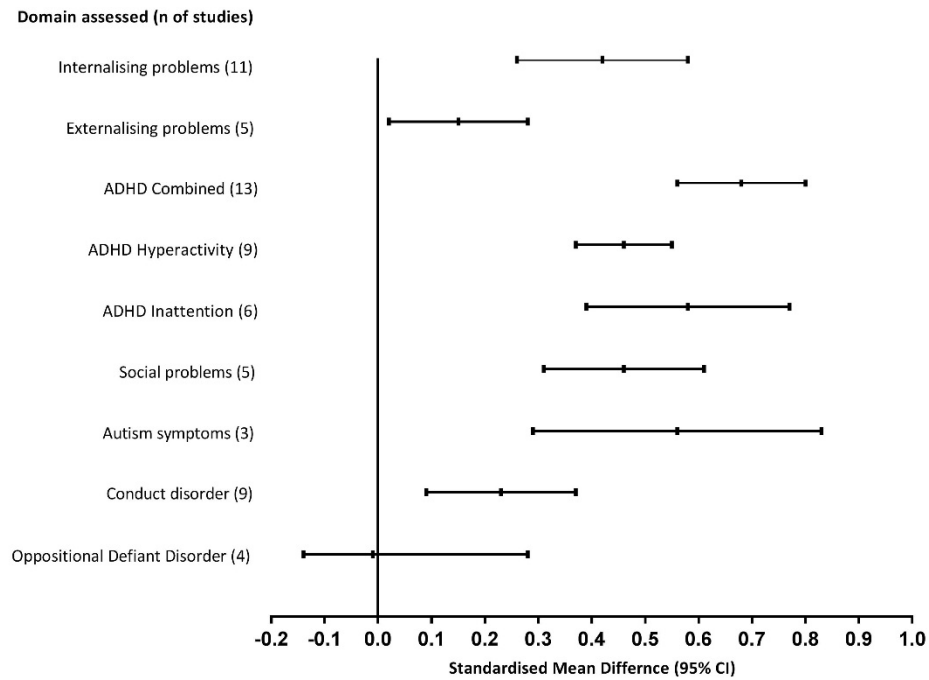


FIGURE 1b

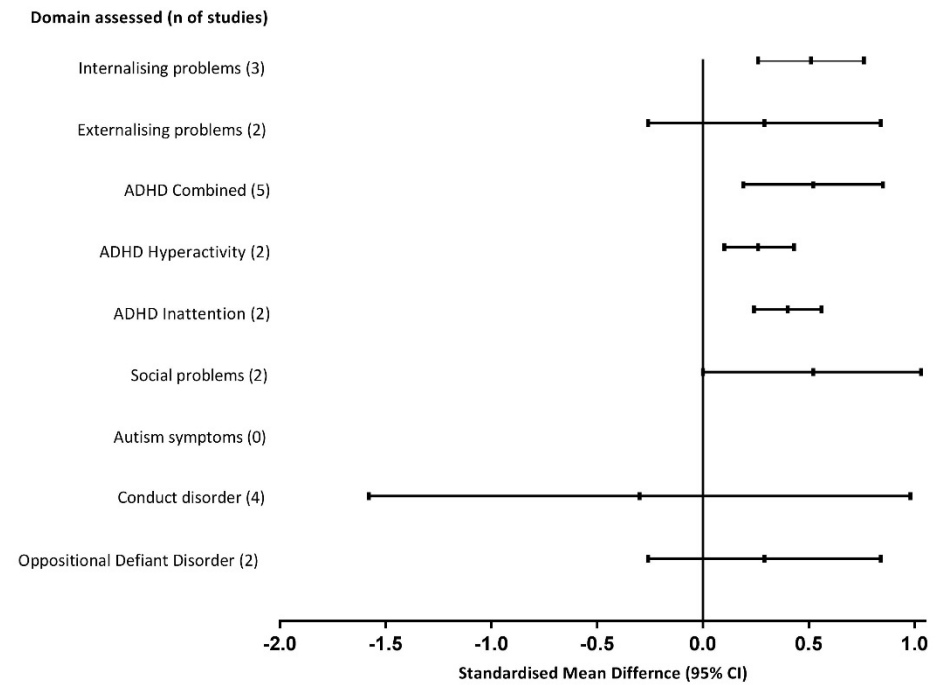


Figure 1. Results of meta-analyses of parent reports of mental health outcomes for extremely low birth weight (<1000g) survivors compared with term born (≥ 37 weeks' gestation) controls. Results are shown as standardised mean differences (SMD) and 95% Confidence Intervals (95% CI) for children aged 5 to 13 years (Figure 1a) and adolescents aged 14 to 18 years (Figure 1b). Figures created using data published by Mathewson KJ, Chow CHT, Dobson KG, Pope EI, Schmidt LA & van Lieshout RJ. Mental Health of Extremely Low Birth Weight Survivors: A systematic Review and Meta-Analysis. *Psychological Bulletin* 2017;143(4):347-383.

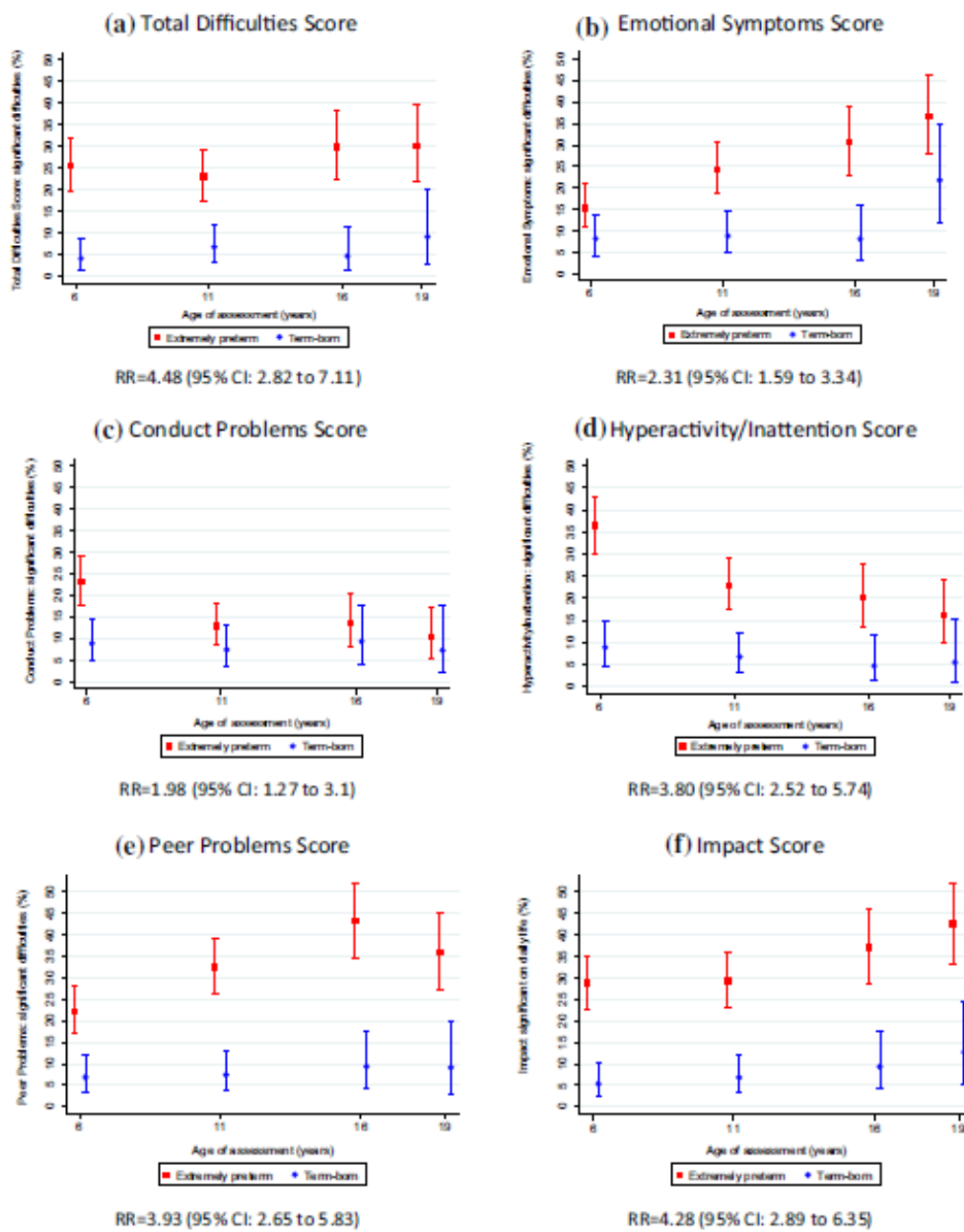


Figure 2. Percentage in the abnormal range and 95% confidence intervals for Strengths and Difficulties Total difficulties and sub-scale scores in the extremely preterm participants and term born controls at age 6, 11, 16 and 19. Figure reprinted from Linsell L, Johnson S, Wolke D, Morris J, Kurinczuk J, Marlow N. Trajectories of behaviour, attention, social and emotional problems from childhood to early adulthood following extremely preterm birth: a prospective cohort study. *Eur Child Adolesc Psychiatry* 2019;28(4):531-42.

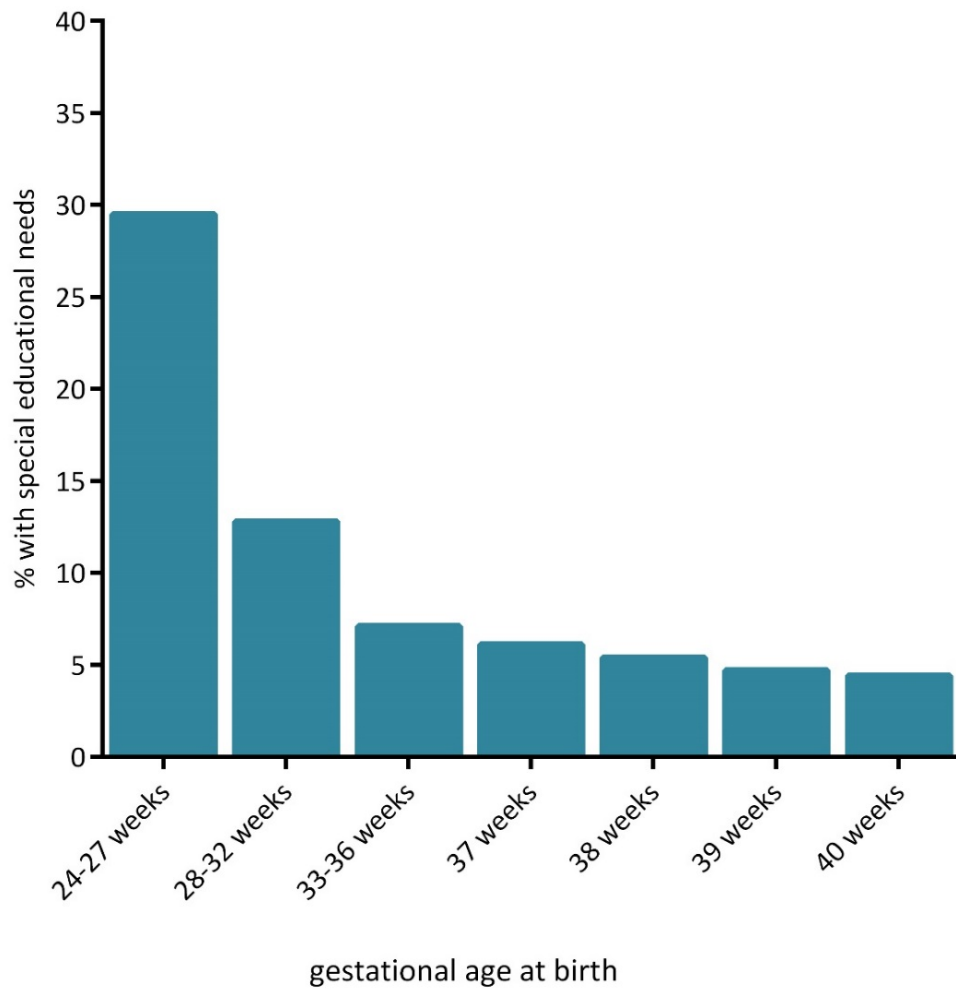


Figure 3. Prevalence of special educational needs in relation to gestational age at birth in a geographic population based cohort in Scotland. Figure created using data published by Mackay D, Smith GCS, Dobbie R, Pell JP. Gestational age at delivery and special educational need: Retrospective cohort study of 407,503 school children. PLOS Medicine 2010;7(6):e10000289.

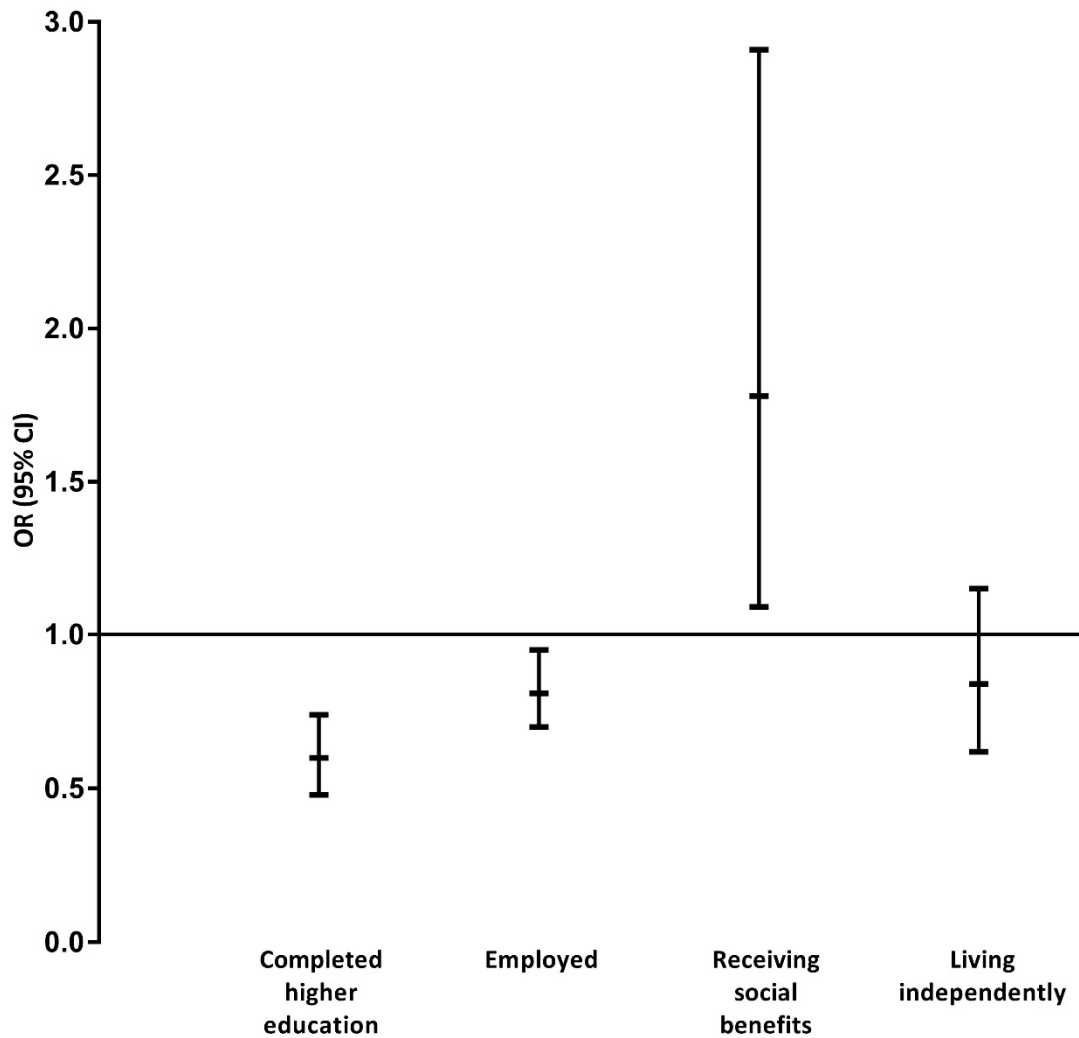


Figure 4. Meta-analysis of 23 studies of the impact of very preterm birth/very low birthweight on educational, occupational and functional outcomes in adulthood. Data shown are Odds Ratios with 95% Confidence Intervals. Figure created using data published by Bilgin A, Mendonca M, Wolke D. Preterm birth/low birth weight and markers reflective of wealth in adulthood: A meta-analysis. *Pediatrics* 2018;142(1):e20173625.