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Academic performance of children born preterm: a meta-analysis and meta-regression

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ABSTRACT

Background Advances in neonatal healthcare have resulted in decreased mortality after preterm birth but have not led to parallel decreases in morbidity. Academic performance provides insight in the outcomes and specific difficulties and needs of preterm children.

Objective To study academic performance in preterm children born in the antenatal steroids and surfactant era and possible moderating effects of perinatal and demographic factors.

Design PubMed, Web of Science and PsycINFO were searched for peer-reviewed articles. Cohort studies with a full-term control group reporting standardised academic performance scores of preterm children (<37 weeks of gestation) at age 5 years or older and born in the antenatal steroids and surfactant era were included. Academic test scores and special educational needs of preterm and full-term children were analysed using random effects meta-analysis. Random effects meta-regressions were performed to explore the predictive role of perinatal and demographic factors for between-study variance in effect sizes.

Results The 17 eligible studies included 2390 preterm children and 1549 controls. Preterm children scored 0.71 SD below full-term peers on arithmetic (p<0.001), 0.44 and 0.52 SD lower on reading and spelling (p<0.001) and were 2.85 times more likely to receive special educational assistance (95% CI 2.12 to 3.84, p<0.001). Bronchopulmonarydysplasia explained 44% of the variance in academic performance (p=0.006).

Conclusion Preterm children born in the antenatal steroids and surfactant era show considerable academic difficulties. Preterm children with bronchopulmonarydysplasia are at particular risk for poor academic outcome.

What is already known on this topic?

- ► The introduction of antenatal steroids and surfactant therapy have resulted in a considerable decline in mortality but not in morbidity rates after preterm birth.
- ► Very preterm children born before the introduction of antenatal steroids and surfactant show moderate to severe academic difficulties.
- ► Several perinatal and demographic factors are associated with poor neurodevelopmental outcomes, but the effects on academic performance have not been aggregated across the available studies.

What this study adds?

- ► This meta-analysis provides insight in academic performance of the current population of preterm children and moderating effects of perinatal and demographic risk factors.
- ► Preterm children have substantial difficulties in reading, spelling and arithmetic and are almost three times more likely to receive special educational assistance compared with controls.
- ► Bronchopulmonary dysplasia was found to be the most important risk factor for poor academic outcomes.

Since 1990, worldwide preterm birth rates have increased to 11.1% in 2010.[1] Since the introduction of antenatal steroids and surfactant in the early 90s, mortality rates of preterm infants (<37 weeks of gestation) have declined considerably.[2] However, the decline in mortality is not accompanied by a similar decline in morbidity.[3 4] Consequently, absolute numbers of preterm children with neurodevelopmental disabilities have increased and likely continue to increase.[2] Providing care, interventions and education fitting the specific needs of these children will therefore place a growing burden on societies.

Academic performance provides an important measure of outcome of preterm children, because it has substantial, causal effects on health, mortality and life chances.[5 6] Preterm birth is associated with lower incomes and increased reliance on social security in adulthood, which was predicted by decreased academic abilities.[7] More insight into academic difficulties of preterm children may help prevent academic failure and thereby reduce long-term individual burden and societal costs. In a meta-analysis on reading abilities in preterm children at school-age, Kovachy and colleagues[8] found worse decoding and reading comprehension abilities in preterm children compared with controls. Furthermore, a meta-analysis by Aarnoudse-Moens and colleagues[9] showed moderate to severe difficulties in reading, spelling and arithmetic in very preterm children (<32 weeks of gestation). However, the vast majority of studies included in that meta-analysis comprised cohorts of children born before the introduction of antenatal steroids and surfactant. The present meta-analysis aims to provide insight into academic outcomes of preterm children born in the antenatal steroids and surfactant era.

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Outcome data of the current population of preterm children is necessary to help guide medical decision making and parental counselling. In addition, data on perinatal and demographic factors may help to identify those children most at risk for adverse outcomes. This will benefit decision making in the neonatal period and may indicate where interventions should focus on to decrease these risks. For example, preterm children suffering from bronchopulmonary dysplasia (BPD) have increased risks for academic difficulties.[10] Other factors predictive of adverse neurodevelopmental outcomes are periventricular leukomalacia (PVL), intraventricular haemorrhage (IVH) and neonatal infectious diseases.[11–13] However, the effects on academic performance remain unclear. The current meta-analysis studies arithmetic, reading and spelling performance of preterm children. In addition, potential moderating effects of perinatal and demographic factors on academic performance are explored.

METHODS

Study selection

This meta-analysis was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[14] Inclusion criteria for study selection were (1) the study concerned preterm children (<37 weeks GA); (2) children were born in the antenatal steroids and surfactant era (ie, 1990 or later or earlier studies explicitly reporting antenatal steroids and surfactant use or use confirmed by authors); (3) age at assessment was 5 years or older; (4) academic performance was evaluated using standardised tests; (5) a full-term control group was included; (6) and publication in a peer-reviewed journal.

PubMed, Web of Science, ERIC and PsycINFO were searched using combinations of the following terms: premature*, preterm, low birth weight, academic, school, learning, reading, spelling, math*, arithmetic (last search: January 2017). Reference lists of relevant articles were scanned to identify additional relevant studies. The selection process is depicted in figure 1. Retrieved records were screened based on title and abstract to further establish relevance. Subsequently, 173 articles were assessed full-text for eligibility. Seventeen studies met all inclusion criteria. For overlapping cohorts, the study with the longest follow-up interval, most complete data and largest sample was selected.

Outcomes and moderators

Details of the included studies are presented in table 1. Arithmetic, reading and spelling performance data for preterm children and controls were extracted from the studies. If necessary, authors were contacted for additional data. The academic tests used in the studies are listed in table 1. All tests are widely used, validated, norm-referenced tests and have age-standardised scores with a mean of 100 and a SD of 15. For special educational needs (SEN), percentages of preterm and full-term children receiving any form of special educational assistance were compared. Definitions of SEN per study are provided as

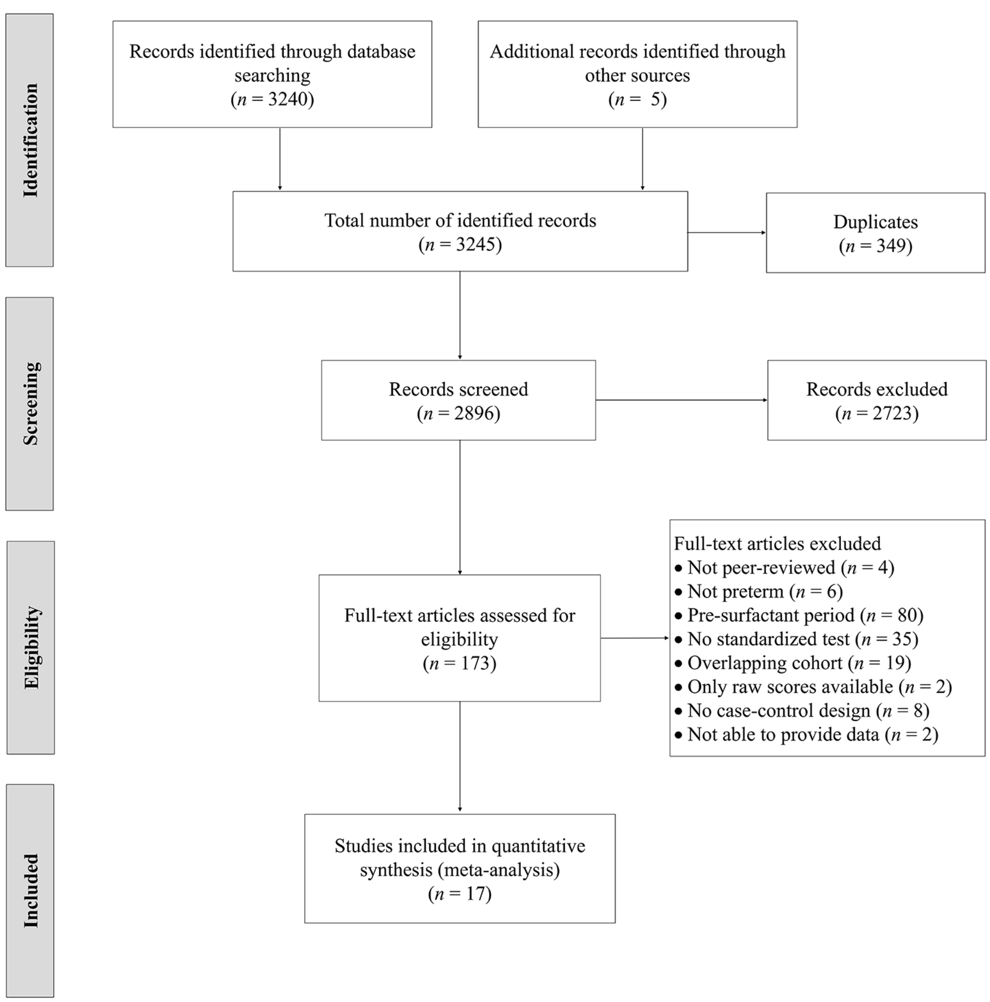

Figure 1 PRISMA flow chart of the study selection procedure.

Table 1 Sample characteristics, tests used to assessment academic achievement, results per academic domain and percentage of children with special educational needs (SEN)

Year	Author	Sample	GA, weeks M (SD)	BW, grams M (SD)	Age, years M (SD)	IQ M (SD)	Test	Study quality	Academic performance test scores M (SD) Reading	Spelling	Arithmetic	SEN, %
2003	Assel *et al*[22]	160 PT	29.7 (2.5)	1111 (264)	8.2 (0.4)	NA	WJTA	5	NA	NA	93.7 (22.3)	NA
		90 FT	39.9 (0.2)	3212 (735)	NA						101.0 (15.4)	
2013	Cheong *et al*[31]	147 EP	25.8 (1.1)	897 (177)	18.0 (NA)	95.7 (15.9)	WRAT	7	95.5 (13.5)	97.1 (15.2)	85.2 (14.0)	23.7
		131 FT	39.3 (1.3)	3441 (457)	NA	107.6 (12.8)			101.1 (13.6)	105.1 (14.0)	95.6 (14.3)	9.4
2015	Clark and Woodward[32]	102 VP/VLBW	27.9 (2.3)	1071 (313)	9.0 (NA)	95.5 (14.6)	WJTA	4	96.8 (15.6)	93.5 (16.0)	89.0 (16.0)	39.0
		108 FT	39.5 (1.2)	3575 (410)	NA	106.9 (11.7)			106.2 (13.4)	101.8 (13.9)	99.4 (15.5)	20.0
2009	Frye *et al*[20]	156 PT	29.6 (2.1)*	1109 (205)	12.7 (0.5)	NA	WJTA	4	103.4 (19.8)*	NA	NA	NA
		97 FT	NA	3242 (630)	NA				93.5 (17.29)			
2013	Hutchinson *et al*[33]	189 EP/ELBW	26.5 (2.0)	833 (164)	8.5 (0.4)	93.1 (16.1)	WRAT	6	98.0 (16.1)	96.8 (15.2)	90.0 (16.9)	NA
		173 FT/NBW	39.3 (1.1)	3506 (1455)	8.5 (0.4)	105.6 (12.4)			105.5 (13.8)	104.2 (14.4)	99.1 (14.5	
2011	Johnson *et al*[24]	219 EP	24.5 (0.7)	745 (130)†	10.9 (0.4)	83.7 (18.0)	WIAT	5	80.2 (20.3)	NA	71.2 (20.9)	61.4
		153 FT	NA	NA	10.9 (0.6)	104.1 (11.1)			98.5 (11.6)		98.5 (15.0)	11.2
2012	Litt *et al*[34]	181 ELBW	26.4 (2.0)	815 (124)	14.7 (0.7)	87.1 (18.9)	WJTA	3	88.6 (21.9)	NA	81.3 (20.7)	48.6
		115 NBW	NA	3260 (524)	14.8 (0.8)	96.4 (13.4)			95.5 (14.1)		93.2 (17.2)	9.6
2012	Loe *et al*[23]	72 PT	28.8 (2.7)	1226 (466)	12.2 (1.8)	102.0 (15.8)	WJTA	4	105 (13.6)	NA	NA	NA
		42 FT	39.7 (1.2)	3474 (492)	12.6 (2.0)	114.0 (13.1)			111 (10.9)			
2009	Luu *et al*[16]	375 VLBW	28.0 (2.0)	961 (174)	12.2 (0.4)	87.9 (18.3)	TOWRE	3	91.2 (20.3)‡	NA	NA	46.6
		111 FT	NA	NA	12.7 (0.8)	103.8 (15.7)	GRST		101.9 (16.7)‡			16.2
2014	McNicholas *et al*[35]	55 VLBW	29.9 (2.8)	1172 (219)	11.6 (1.0)	89.7 (12.5)	WIAT	5	95.3 (15.0)	NA	89.5 (16.1)	33.0
		45 NBW	NA	NA	NA	101.3 (11.7)			101.5 (NA)		94.0 (NA)	9.4
2012	Northam *et al*[36]	50 VP	27.0 (2.0)	1081 (385)	16.2 (1.4)	92.0 (11.8)	WORD	5	96.0 (14.0)	96.0 (14.0)	NA	NA
		30 FT	NA	NA	15.8 (1.2)	108.8 (17.2)			105.0 (12.0)	104.0 (13.0)		
2011	Rose *et al*[17]	44 PT	29.7 (2.8)	1165 (268)	11.2 (0.4)	85.7 (14.3)	WJTA	4	96.9 (14.7)	NA	95.3 (14.0)‡	NA
		87 FT	NA	NA	11.1 (0.4)	95.4 (11.6)			101.0 (11.4)		100.0 (12.3)‡	
2015	Sayeur *et al*[37]	10 PT	28.7 (1.8)	1222 (238)	7.6 (0.5)	111.6 (10.5)	WIAT	2	106.0 (23.1)	NA	NA	NA
		10 FT	38.7 (1.3)	3357 (801)	7.6 (0.5)	112.4 (8.9)			105.1 (18.2)			
2003	Short *et al*[18]	173 VLBW	28.3 (2.0)*	1085 (223)	8.8 (0.6)	86.7 (18.4)	WJTA	5	96.1 (21.3)*‡	NA	92.8 (21.4)*‡	43.4
		99 NBW	NA	NA	NA	101.9 (15.0)			105.1 (18.0)‡		109.3 (17.1)‡	25.3
2015	Simms *et al*[38]	115 VP	28.6 (2.0)	1213 (365)	9.7 (0.7)	97.8 (19.4)	WIAT	5	NA	NA	91.3 (18.8)	NA
		77 FT	NA	NA	9.5 (0.7)	104.9 (20.8)					103.6 (20.7)	
2011	Taylor *et al*[39]	148 EP/ELBW	25.9 (1.6)	818 (174)	6.0 (0.4)	86.3 (21.1)	WJTA	5	106.1 (13.5)	92.1 (15.7)	98.8 (13.5)	58.7
		111 NBW	NA	3382 (446)	6.0 (0.3)	105.5 (16.6)			110.1 (13.5)	100.6 (15.7)	105.8 (13.4)	29.0
2016	Taylor *et al*[40]	194 VP	27.5 (1.9)	962 (223)	7.5 (0.3)	96.0 (15.1)	WRAT	6	98.2 (19.6)	97.9 (19.2)	88.8 (18.4)	41.0
		70 FT	39.1 (1.3)	3323 (508)	7.6 (0.3)	107.0 (12.8)			107.9 (16.9)	106.2 (16.5)	99.7 (14.1)	9.0

*Weighted mean and pooled SD of two subsamples.
†Estimated from median and IQR.
‡Weighted mean and pooled SD of subtests scores.
BW, birth weight; ELBW, extremely low birth weight (<1000 g); EP, extremely preterm (<28 weeks GA); FT, full-term (≥37 weeks GA); GA, gestational age; GRST, Grey Silent Reading Tests; M, mean; NA, not available; NBW, normal birth weight (≥2500 g); PT, preterm (<37 weeks GA); SEN, special educational needs; TOWRE, Test of Word Reading Efficiency; VLBW, very low birth weight (<1500 g); VP, very preterm (<32 weeks GA); WIAT, Wechsler Individual Achievement Test; WJTA, Woodcock Johnson Tests of Achievement; WORD, Wechsler Objective Reading Dimensions; WRAT, Wide Range Achievement Test.

online supplementary material. Information on GA, birth weight (BW), age at assessment, IQ, sex, ethnicity, maternal education, small for gestational age (SGA) status, IVH grade I/II, IVH grade III/IV, PVL, BPD, postnatal corticosteroids use and infectious diseases (necrotising enterocolitis (NEC), meningitis and sepsis) was extracted from the studies to create moderator variables. An overview of these details for each study is provided in table 2.

Study quality

Study quality was assessed using a modified version of the Newcastle-Ottawa Scale for cohort studies.[15] Two authors (EST and JFdK) independently rated studies on a 7-point scale with higher scores indicating better quality.

Statistical analyses

This meta-analysis was performed using Comprehensive Meta-Analysis V.3.0. The standardised mean difference (*SMD*) in test scores between preterm and full-term children was used as effect size for arithmetic, reading and spelling. The mean difference of each study was weighted by the inverse of its variance. Composite scores were computed for three studies[16–18] with more than one subtest per academic domain. Using the reported correlation coefficients between subtest scores, interrelation among outcomes was taken into account.[19] Furthermore, combined effects across subgroups were computed for two studies[18 20] that reported data for independent subgroups of preterm children. For SEN, the risk ratio (RR) was used as effect size.

Random effects meta-analyses were performed to calculate combined effect sizes for arithmetic, reading, spelling and SEN. Dispersion across study effect sizes within each domain was tested using Cochran's Q. I^2 was used to quantify this dispersion. The value of I^2 shows the percentage of variation across studies that is due to heterogeneity rather than chance. I^2 was interpreted as follows: 30%–60%: moderate; 50%–90%: substantial; and 75%–100%: considerable heterogeneity.[21] Publication bias was assessed by visual inspection of funnel plots and Egger's test. Random effects meta-regressions were performed to explore the predictive role of demographic and perinatal factors for between-study variance in effect sizes. As a rule of thumb, meta-regression is thought only to be meaningful with more than 10 studies included in the analysis.[21] Due to the small number of studies with available demographic or perinatal details, meta-regressions were performed irrespective of academic domain to increase the number of available studies. For studies reporting results for more than one academic domain, a composite score was calculated. Composite scores were computed using the correlation between subtests to account for interrelation.[19] Sensitivity analyses were performed to compare results of analyses with all studies included and analyses excluding those studies in which also moderately/late preterm children were included.

RESULTS

The 17 selected studies included 2390 preterm children and 1549 controls. Arithmetic, reading and spelling performance was evaluated in 12, 15 and 6 studies, respectively. Across studies, GA varied from extremely to late preterm (23–36 weeks), with mean GA ranging from 24.5 to 29.9 weeks. Participants' ages ranged from 6 to 18 years.

Arithmetic, reading, spelling and SEN

Meta-analytic results revealed significant differences between preterm and full-term children for all academic domains (see table 3). Arithmetic scores of preterm children were 0.71 SD below scores of full-term peers ($z=-7.67$, $p<0.001$), indicating a medium effect. Preterm children scored 0.44 and 0.52 SD lower on reading and spelling, respectively, compared with controls ($z=-4.38$, $p<0.001$ and $z=-9.53$, $p<0.001$), indicating small-sized and medium-sized effects. Results for arithmetic and reading were highly heterogeneous across studies ($Q=60.81$, $p<0.001$, $I^2=81.91$ and $Q=101.97$, $p<0.001$, $I^2=86.27$), indicating that the pooled effects should be cautiously interpreted. No significant heterogeneity was observed for spelling. Nine studies reported details about SEN for both preterm and full-term children. Based on these studies, preterm children were 2.85 times more likely to receive special educational assistance compared with controls (RR=2.85, 95% CI 2.12 to 3.84, $p<0.001$). Significant heterogeneity of results was observed ($Q=26.19$, $p=0.001$, $I^2=69.46$), indicating cautious interpretation of the pooled estimate. Forest plots are provided as online supplementary material.

Sensitivity analyses excluding four studies[17 20 22 23] in which also moderately/late preterm children were included showed a combined effect of −0.77 for arithmetic ($z=-7.79$, $p<0.001$) and −0.55 for reading ($z=-7.46$, $p<0.001$). Results for spelling and SEN remained unchanged.

Meta-regression

Random effects meta-regression analyses were performed to explain heterogeneity in results across studies. GA explained a significant proportion of variance ($R^2=0.39$, $Q(1)=7.49$, $p=0.006$). Regression plots are shown in figure 2. One study,[24] with a considerably lower mean GA (24.5 weeks) compared with the other studies, played a key role in this effect (see figure 2). Additional analysis without this study showed non-significant results. The same study reported a much higher incidence of PVL (16%) compared with other studies. Meta-regression showed a significant result for PVL ($R^2=0.46$, $Q(1)=7.33$, $p=0.007$), but additional analysis without this study again was non-significant. BPD explained 44% of the variance in academic performance ($Q(1)=7.64$, $p=0.006$) (see figure 2). The difference in intelligence between preterm and controls explained 46% of the variance across studies ($Q(1)=8.31$, $p=0.004$). BW, SGA status, IVH grade I/II, IVH grade III/IV, sex, age at assessment, ethnicity, measure of academic performance and study quality were not found to significantly explain heterogeneity. Less than 10 studies reported the incidence of sepsis, meningitis, NEC, postnatal corticosteroids use and maternal education level. The role of these factors could therefore not be assessed.

Sensitivity analyses without those studies[17 20 22 23] also including moderately/late preterm children revealed results highly similar to those obtained in the full sample of studies. Again, intelligence explained a significant proportion of variance across studies ($R^2=0.42$, $Q(1)=6.64$, $p=0.01$). The proportion of variance explained by BPD increased from 44% in the full sample of studies to 78% in this subsample of studies ($Q(1)=16.44$, $p<0.001$).

Publication bias

Inspection of funnel plots did not suggest publication bias, which was confirmed by non-significant Egger's test (online supplementary material).

DISCUSSION

This meta-analysis shows that preterm children born in the antenatal steroids and surfactant era have considerable difficulties

Table 2 Demographic and perinatal sample characteristics of the studies included in the meta-analysis

Year	Author	GA, weeks M (SD)	BW, grams M (SD)	Age, years M (SD)	% SGA	% IVH I/II	% IVH III/IV	% PVL	% BPD	% NEC	% Meningitis	% Sepsis	% PCS use	% Mothers <12 years education	% Male	% Non-Caucasian
2003	Assel *et al*[22]	29.7 (2.5)	1111 (264)	8.0 (NA)	NA	NA	NA	NA	NA	NA	0.0	NA	NA	NA	54.0	79.0
2013	Cheong *et al*[31]	25.8 (1.1)	897 (177)	18.0 (NA)	2.7	NA	6.8	4.1	38.5	NA	NA	NA	37.2	51.8	47.3	NA
2015	Clark and Woodward[32]	27.9 (2.3)	1071 (313)	9.0 (NA)	10.8	11.8	5.9	4.9	34.0	NA	NA	29.7	5.9	40.2	51.5	88.9
2009	Frye *et al*[20]	29.6 (2.1)	1109 (205)	12.7 (0.5)	NA	15.4	0.0	2.8	31.5	NA	0.0	NA	NA	NA	43.9	79.9
2013	Hutchinson *et al*[33]	26.5 (2.0)	833 (164)	8.5 (0.4)	18.0	NA	3.7	3.2	38.1	5.0	NA	NA	37.0	50.3	52.9	NA
2011	Johnson *et al*[24]	24.5 (0.7)	745 (130)*	10.9 (0.4)	0.5	49.0	10.0	16.0	73.0	3.0	NA	NA	NA	76.0	46.0	18.0
2012	Litt *et al*[34]	26.4 (2.0)	815 (124)	14.7 (0.7)	33.2	34.3	13.3	6.6	41.0	5.5	8.8	49.2	NA	39.0	38.7	60.0
2012	Loe *et al*[23]	28.8 (2.7)	1226 (466)	12.2 (1.8)	5.6	12.5	5.6	9.7	9.7	NA	NA	NA	NA	35.0	47.0	28.0
2009	Luu *et al*[16]	28.0 (2.0)	961 (174)	12.2 (0.4)	25.0	10.8	NA	NA	46.0	NA	NA	NA	NA	11.1	54.4	29.1
2014	McNicholas *et al*[35]	29.9 (2.8)	1172 (219)	11.6 (1.0)	NA	20.0	NA	8.9	NA	NA	NA	NA	NA	NA	51.1	NA
2012	Northam *et al*[36]	27.0 (2.0)	1081 (385)	16.2 (1.4)	14.3	34.0	22.0	4.1	NA	NA	NA	NA	NA	NA	38.0	NA
2011	Rose *et al*[17]	29.7 (2.8)	1165 (268)	11.2 (0.4)	27.3	43.2	0.0	NA	NA	NA	NA	NA	NA	NA	56.8	88.6
2015	Sayeur *et al*[37]	28.7 (1.8)	1222 (238)	7.6 (0.5)	NA	0.0	0.0	0.0	20.0	20.0	0.0	0.0	NA	NA	50.0	NA
2003	Short *et al*[18]	28.3 (2.0)	1085 (223)	8.8 (0.6)	NA	22.5	10.4	NA	57.0	NA	NA	NA	16.2	NA	49.1	47.0
2015	Simms *et al*[38]	28.6 (2.0)	1213 (365)	9.7 (0.7)	NA	NA	NA	NA	NA	NA	NA	NA	NA	62.6	54.8	NA
2011	Taylor *et al*[39]	25.9 (1.6)	818 (174)	6.0 (0.4)	25.0	NA	10.1	NA	52.0	10.1	8.0	41.9	NA	13.5	45.9	61.5
2016	Taylor *et al*[40]	27.5 (1.9)	962 (223)	7.5 (0.3)	8.6	NA	3.6	4.6	35.0	10.6	NA	44.4	NA	NA	52.5	NA

The highest and lowest value for each factor is underlined.
*Estimated from median and IQR.
BPD, bronchopulmonary dysplasia; BW, birth weight; GA, gestational age; IVH I/II, III/IV, intraventricular haemorrhage grade I/II, III/IV; M, mean; NA, not available; NEC, necrotising enterocolitis; PCS, postnatal corticosteroids; PVL, periventricular leukomalacia; SGA, small for gestational age.

Table 3 Individual study and combined effect sizes (SMD) for arithmetic, reading, spelling and SEN (RR)

	Arithmetic				Reading				Spelling				SEN			
Study	SMD	SE	z	I^2	SMD	SE	z	I^2	SMD	SE	Z	I^2	RR	95% CI	z	I^2
Assel *et al*[22]	−0.36	0.13	−2.74**													
Cheong *et al*[31]	−0.74	0.12	−5.92***		−0.41	0.12	−3.40**		−0.55	0.12	−4.46***		2.52	1.45 to 4.40	3.26**	
Clark and Woodward[32]	−0.66	0.14	−4.65**		−0.65	0.14	−4.60***		−0.56	0.14	−3.96***		1.95	1.25 to 3.05	2.92*	
Frye *et al*[20]					0.55	0.13	−4.16***									
Hutchinson *et al*[33]	−0.58	0.11	−5.36***		−0.50	0.11	−4.67***		−0.50	0.11	−4.67***					
Johnson *et al*[24]	−1.46	0.12	−12.31***		−1.06	0.11	−9.40***						5.55	3.49 to 8.81	7.25***	
Litt *et al*[34]	−0.61	0.12	−5.03***		−0.36	0.12	−2.98**						5.06	2.83 to 9.05	5.48***	
Loe *et al*[23]					−0.47	0.20	−2.41*									
Luu *et al*[16]					−0.78	0.11	−6.91***						2.88	1.86 to 4.45	4.74***	
McNicholas *et al*[35]	−0.91	0.21	-4.32***		−0.43	0.20	−2.12*						2.75	1.15 to 6.61	2.26*	
Northam *et al*[36]					−0.59	0.24	−2.49*		−0.59	0.24	−2.49**					
Rose *et al*[17]	−0.42	0.19	−2.26*		−0.36	0.19	−1.94									
Sayeur *et al*[37]					0.04	0.45	0.10									
Short *et al*[18]	−1.02	0.13	−7.66***		−0.54	0.13	−4.20***						1.72	1.17 to 2.51	2.79**	
Simms *et al*[38]	−0.63	0.15	−4.16***													
Taylor *et al*[39]	−0.51	0.13	−3.95***		−0.30	0.13	−2.32*		−0.54	0.13	−4.19***		2.02	1.47 to 2.79	4.31***	
Taylor *et al*[40]	−0.63	0.14	−4.42***		−0.51	0.14	−3.63***		−0.45	0.14	−3.18**		4.56	2.12 to 9.78	3.89***	
Summary effect	−0.71	0.09	−7.67***	81.91	−0.44	0.10	−4.38***	86.27	−0.52	0.06	−9.53***	0.00	2.85	2.12 to 3.84	6.90***	69.46

*p<.05; **p<0.01; ***p<0.001.
RR, risk ratio; SEN, special educational needs; SMD, standardised mean difference.

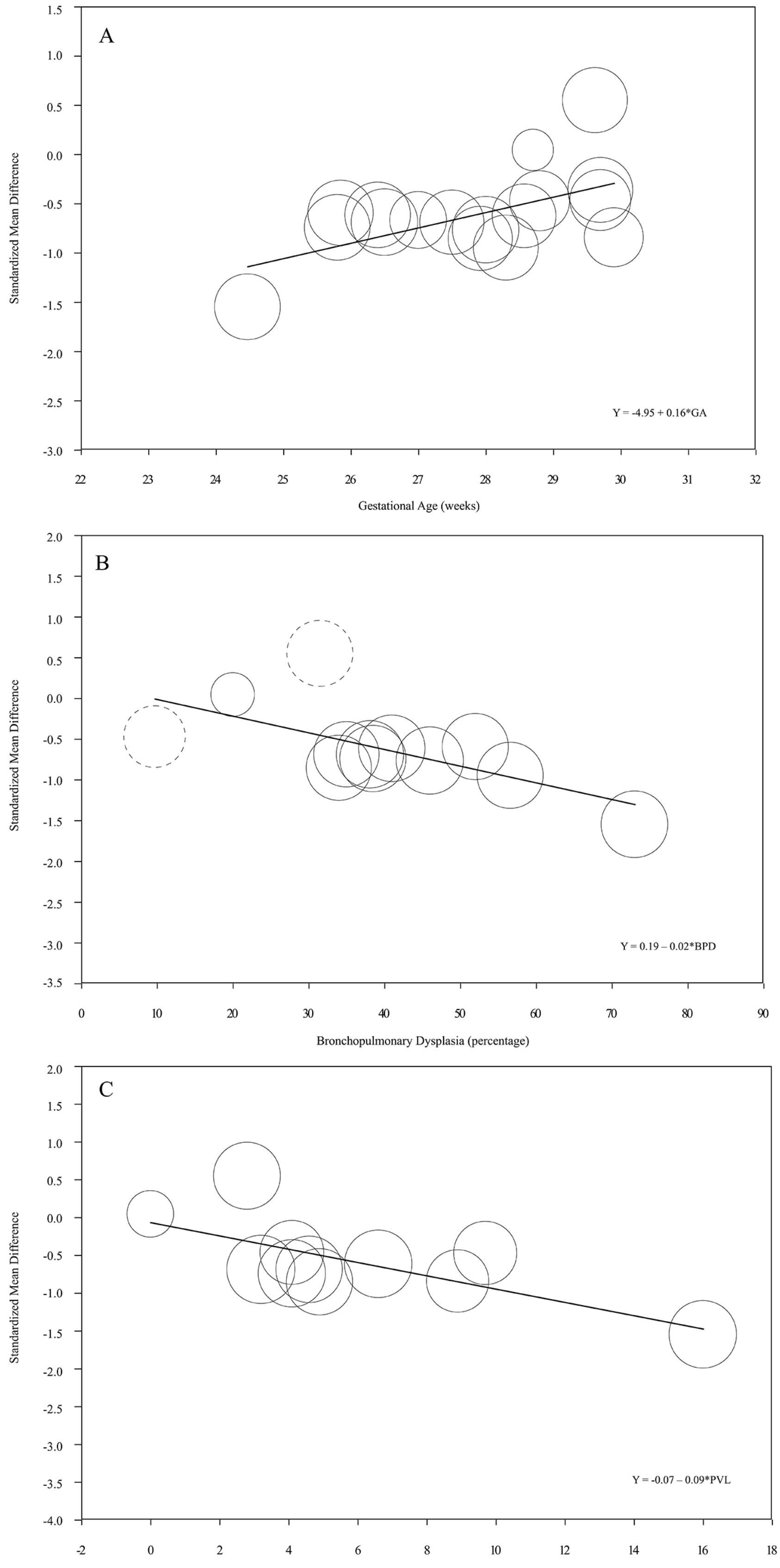

Figure 2 Meta-regression of gestational age (A), bronchopulmonary dysplasia (B) and periventricular leukomalacia (C) on the standardised mean difference in academic performance between preterm and full-term children. The dashed circles in figure B indicate studies also including moderately/ late preterm children.

in arithmetic, reading and spelling. Furthermore, based on the studies included in our meta-analysis, preterm children are almost three times more likely to have SEN. BPD explained 44% of the variance in academic performance across studies. This percentage increased to 78% when focusing solely on studies pertaining to preterm children born at <32 weeks of gestation. Interestingly, this increase is mainly driven by the high incidence of BPD in extremely preterm children and its negative effects on long-term academic outcome. Intelligence explained 46% of the variance, indicating the strong relation between academic performance and intelligence.

Our results show that preterm birth has considerable consequences for academic performance later in life. Given that heterogeneity in results across studies could not be explained by age at assessment, these difficulties seem to remain stable during development from early childhood to adolescence. These findings are in line with the meta-analysis by Kovachy and colleagues[8] focused on reading abilities. Different from that meta-analysis, which showed increased reading difficulties with decreasing GA, our results demonstrate comparable academic performance among children born at 26–30 weeks GA. There was only one study included in this meta-analysis with a sample exclusively consisting of children born before 26 weeks of gestation.[24] In this study, differences in academic performance between preterm and control children were substantially larger compared with the other studies, which can possibly be explained by the higher incidence of other complications such as PVL. The incidence of PVL was considerably higher in this cohort of extremely immature children compared with other included cohorts. Whereas our results show no differences in academic performance between cohorts with 0%–10% PVL incidence, increased academic difficulties are present in this extremely preterm sample with a relatively high PVL incidence (16%).

The current meta-analysis shows that preterm children with BPD are at particular risk for academic difficulties. The detrimental effect of BPD for later neurocognitive outcomes has been shown in previous studies.[10] The exact mechanisms underlying the detrimental effects of BPD on brain development have not been elucidated yet. One explanation is that those children who develop BPD are already more vulnerable and therefore prone to develop BPD. Indeed, the incidence of BPD is increased among neonates with extremely low BW and GA.[18] Furthermore, BPD is associated with infection and inflammation,[25] which affects lung maturation and interferes with cerebral development.[26] Episodic and chronic hypoxia may also contribute to adverse neurocognitive outcomes in BPD.[27] Co-occurrence of risk factors makes it difficult to differentiate the adverse effects of BPD from other risk factors that may also affect brain development and thereby academic outcome. Furthermore, it should be realised that BPD may be a marker for adverse academic outcomes, rather than a cause. However, our analyses of other neonatal risk factors suggest that BPD contributes to differences in magnitude of academic difficulties across studies as a single main risk factor, and thus places preterm children at even greater risk to encounter academic difficulties.

This meta-analysis included only cohorts born in the antenatal steroids and surfactant era. In the meta-analysis of Aarnoudse-Moens *et al*[9] the vast majority of studies included children born before the introduction of these treatments. The two meta-analyses have only one study[18] in common but showed similar results. This suggests that, in spite of increased survival rates, the negative effects of prematurity on academic outcomes remained unchanged. This is in line with other studies showing stable morbidity rates over the last decades.[3 4] Since the studies in both meta-analyses are comparable in terms of GA, the similarity in results cannot simply be explained by an increased survival of the most immature children in the more recent studies in the current meta-analysis.

One limitation of our meta-analysis is that due to the relatively small number of studies reporting details on risk factors, our meta-regression analyses allowed investigation of one single risk factor at a time. Consequently, the inter-relationship between risk factors could not be taken into account. Preterm birth often carries multiple, inter-related risk factors. It is likely that the risk for academic difficulties is not carried by one single risk factor but rather by a combination of risk factors. Future studies should focus on cumulative or interacting effects of risk factors. Another limitation is the restricted availability of data for certain factors, such as sociodemographic and treatment factors like postnatal corticosteroids use, hindering the opportunity to assess their possibly important role for academic outcomes of preterm children.

This is the first meta-analysis examining academic performance in preterm children born in the antenatal steroids and surfactant era. Results are therefore applicable to the current population of preterm children. It should be noted that the included studies mostly comprised cohorts of extremely and very preterm children. These results may be less applicable to moderately/late preterm children.[28] Academic performance is a pre-eminent measure of outcome, given its strong relation with important life outcomes.[5 6] Despite influential advances in neonatal healthcare, preterm children show considerable academic difficulties. Given the increasing number of preterm children and the substantial individual, social and economic consequences of academic difficulties in these children,[7 29] there is a need to develop strategies that will improve outcomes after preterm birth. These interventions may target perinatal factors associated with adverse outcomes. For example, non-invasive methods such as nasal intermittent positive-pressure ventilation techniques have shown promising results in terms of decreased BPD.[30] The results of our meta-analysis emphasise the importance of such developments and innovations.

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