Supplementary Material

Trajectories of behavioural problems from childhood to early adulthood following extremely preterm birth: a prospective cohort study

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Figure S1: Flow of study participants in the EPICure cohort study

Extremely preterm participants   **Term-born controls**

Delivery
- 812 infants <26 completed weeks' gestation born between 1st March to 31st December 1995

Discharge
- 315 alive at hospital discharge
  - → 6 died

2.5 years
- 283/309 (92%) assessed

6 years
- 241/309 (78%) assessed — 160 matched controls
  - → 2 died

11 years
- 219/307 (71%) assessed — 153 matched controls / 110 previously assessed / 43 new controls

16 years
- 138/307 (45%) responded to postal questionnaire — 88 matched controls
  - → 1 died

19 years
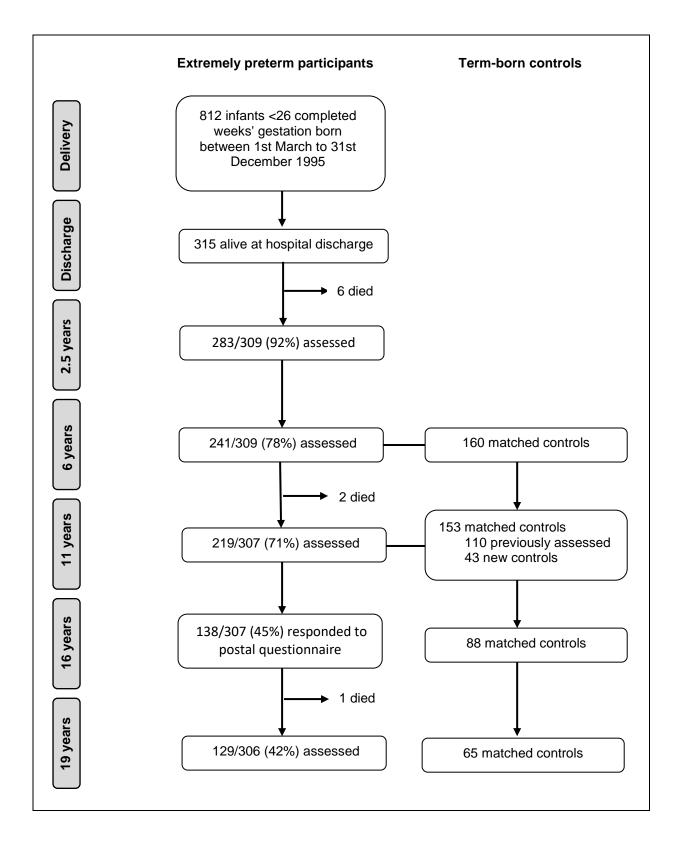- 129/306 (42%) assessed — 65 matched controls

Table S1: Perinatal and neurodevelopmental characteristics of extremely preterm participants according to completeness of behavioural screening assessments

	Completers: 4 assessments (n=82)	Non-completers <4 assessments (n=233)	P value[a]
Maternal/paternal factors			
Maternal age (years), mean [SD]:	29.4 [5.6] (n=81)	28.1 [6.0] (n=232)	0.10
Mother of non-white ethnicity, % (n):	12.4% (10/81)	27.0% (63/233)	0.01
Primigravida, % (n):	37.8% (31/82)	27.6% (64/232)	0.09
Mother smoked during pregnancy, % (n):	24.7% (20/81)	36.5% (73/200)	0.07
Antenatal steroids given, % (n):	81.7% (67/82)	77.9% (180/231)	0.53
Mother's highest educational qualification A 'level or above, % (n):[b]	47.5% (38/80)	31.4% (61/194)	0.01
Father's occupation non-manual, % (n):[b]	54.2% (39/72)	29.1% (46/158)	<0.001
Infant perinatal factors			
Multiple birth, % (n):	32.9% (27/82)	22.4% (52/232)	0.08
Congenital anomaly present, % (n):	2.4% (2/82)	2.6% (6/232)	1.00
Gestational age 24 weeks or less, % (n):	46.3% (38/82)	39.1% (91/233)	0.30
Birthweight (grams), mean [SD]:	733 [120] (n=82)	752 [112] (n=233)	0.19
Male sex, % (n):	41.5% (34/82)	51.9% (121/233)	0.12
Moderate/Severe brain injury during neonatal period, % (n):[c]	17.1% (14/82)	24.6% (57/232)	0.22
Laser or cryotherapy for retinopathy of prematurity, % (n):	13.4% (11/82)	14.9% (34/228)	0.86
Laparotomy for necrotising enterocolitis, % (n):	2.5% (2/79)	3.1% (7/229)	1.00
Supplemental oxygen at 36 weeks, % (n):	76.8% (63/82)	73.0% (170/233)	0.56
Infant developmental outcomes at 2.5 years			
BSID-II Mental Developmental Index, mean [SD]:	84.5 [12.7] (n=82)	76.5 [17.3] (n=201)	<0.001
BSID-II Psychomotor Developmental Index, , mean [SD]:	86.3 [15.1] (n=80)	78.7 [19.0] (n=182)	0.002
BSID-II Behaviour Rating Percentile, , mean [SD]:	39.2 [26.1] (n=79)	34.6 [24.9] (n=180)	0.18
CBCL Total Problem T-score, mean [SD]:	54.5 [9.2] (n=82)	56.2 [9.9] (n=188)	0.17
Neurodevelopmental impairment at last assessment[b]			
Cerebral palsy, % (n):	7.3% (6/82)	22.2% (50/225)	0.002
Moderate/severe cerebral palsy, % (n):	4.9% (4/82)	14.0% (31/222)	0.03
Moderate/severe cognitive impairment, % (n):	45.1% (37/82)	49.1% (103/210)	0.60
Moderate/severe visual impairment, % (n):	7.3% (6/82)	12.1% (27/224)	0.30
Moderate/severe hearing impairment, % (n):	1.2% (1/82)	2.2% (5/225)	1.00
Moderate/severe functional impairment, % (n):[d]	46.3% (38/82)	53.3% (112/210)	0.30
Severe functional impairment, % (n):[d]	18.3% (15/82)	27.1% (57/210)	0.13

BSID-II Bayley Scales of Infant Development (second edition); CBCL Child Behaviour Checklist; EPT Extremely preterm.

[a] Two-sided p-values were calculated using Fisher's Exact Test for binomial variables and the t-test for continuous variables.

[b] Not collected at discharge; first collected at one or two year assessment.

[c] Parenchymal pathology and/or ventriculomegaly on worst cranial ultrasound scan before discharge home.

[d] Functional impairment includes cerebral palsy, cognitive, visual or hearing impairment at clinical assessment.

Table S2: Characteristics of term-born controls according to completeness of behavioural screening assessments

	Completers: 4 assessments (n=37)	Non-completers <4 assessments (n=169)	P value[a]
Mother's highest educational qualification A 'level or above, % (n):	50.0% (18/36)	38.5% (57/148)	0.26
Male sex, % (n):	40.5% (15/37)	43.2% (73/169)	0.86
Any cognitive impairment at last assessment, % (n)	8.1% (3/37)	20.5% (34/166)	0.10
Moderate/severe cognitive impairment at last assessment, % (n):	0.0% (0/37)	3.0% (5/166)	0.59
Any visual impairment at last assessment, % (n):	32.4% (12/37)	18.2% (30/165)	0.07
Any hearing impairment at last assessment, % (n):	2.7% (1/37)	0.0% (0/165)	0.18
Any functional impairment at last assessment, % (n):[b]	40.5% (15/37)	34.6% (57/165)	0.57

[a] Two-sided p-values were calculated using Fisher's Exact Test.
[b] Functional impairment includes cerebral palsy, cognitive, visual or hearing impairment at clinical assessment.

Table S3: Complete case: mixed model analysis of the SDQ Total Difficulties Score and subscales in extremely preterm participants and term-born controls
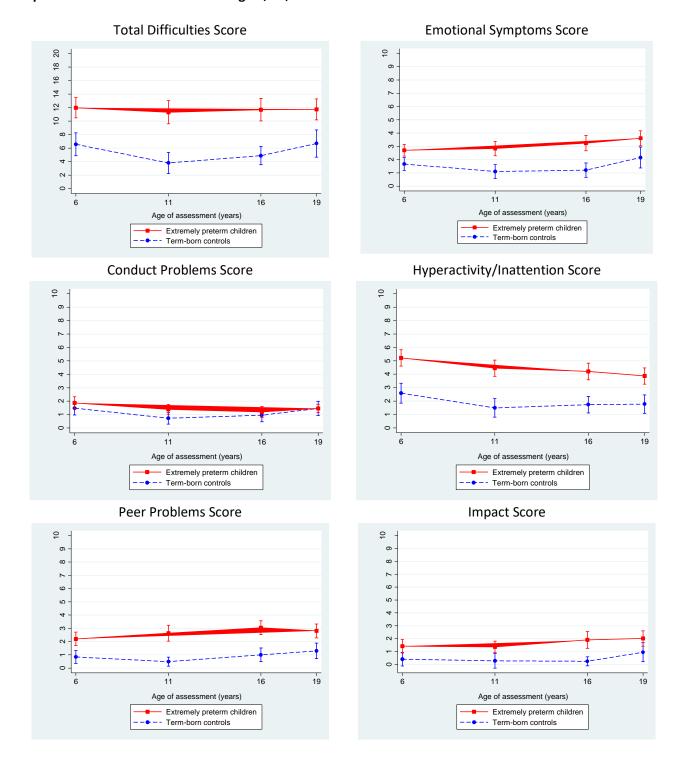
Extremely preterm participants compared to term-born controls

Parameter	SDQ Total Difficulties Score (n=119)		Emotional Symptoms Score (n=119)		Conduct Problems Score (n=119)		Hyperactivity/Inattention Score (n=119)		Peer Problems Score (n=119)	
	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
Constant	6.11	(4.69 to 7.53)	1.49	(0.97 to 2.02)	1.58	(1.10 to 2.06)	2.64	(1.92 to 3.36)	0.57	(0.20 to 0.94)
EPT	6.21	(4.32 to 8.10)	1.39	(0.77 to 2.00)	0.30	(-0.21 to 0.80)	2.54	(1.74 to 3.35)	1.75	(1.18 to 2.32)
Age	-0.45	(-0.69 to -0.20)	-0.10	(-0.21 to 0.003)	-0.19	(-0.26 to -0.11)	-0.21	(-0.32 to -0.11)	0.05	(0.02 to 0.08)
Age^2	0.03	(0.02 to 0.05)	0.01	(0.004 to 0.02)	0.01	(0.007 to 0.017)	0.01	(0.003 to 0.02)	-	-

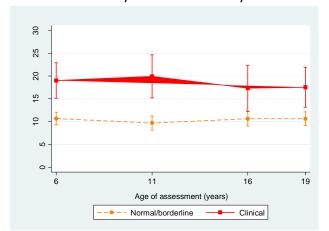**Extremely preterm participants only**

SDQ Total Difficulties Score adjusted for CBCL at 2.5 years (n=82)			SDQ Total Difficulties Score in adjusted for moderate/severe cognitive impairment at last clinical assessment (n=82)		
Parameter	Estimate	95% CI	Parameter	Estimate	95% CI
Constant	10.40	(9.90 to 11.77)	Constant	10.22	(8.31 to 12.12)
Age	-0.007	(-0.10 to 0.09)	Age	-0.007	(-0.10 to 0.09)
CBCL clinically significant at 2.5 years	8.53	(5.17 to 11.89)	Moderate/severe cognitive impairment at last assessment	3.39	(0.69 to 6.10)

CBCL Child Behaviour checklist; EPT Extremely preterm; SDQ Strengths and Difficulties Questionnaire.

Figure S2: Complete case: mean plus 95% confidence intervals for SDQ Total Difficulties and subscale scores in EPT participants and term-born controls at age 6, 11, 16 and 19

Total Difficulties Score

Emotional Symptoms Score

Conduct Problems Score

Hyperactivity/Inattention Score

Peer Problems Score

Impact Score

g) Total Difficulties Score in EPT participants stratified by CBCL score at 2.5 years

h) Total Difficulties Score in EPT participants stratified by moderate/severe cognitive impairment