Movement Difficulties at Age Five Among Extremely Preterm Infants

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abstract

BACKGROUND AND OBJECTIVES: Children born extremely preterm (EPT), <28 weeks' gestational age, face higher risks of movement difficulties than their term-born peers. Studies report varying prevalence estimates and prognostic factors identifying children who could benefit from early intervention are inconsistent. This study investigated the prevalence of movement difficulties in children born EPT and associated risk factors.

METHODS: Data come from a population-based EPT birth cohort in 2011 and 2012 in 11 European countries. Children without cerebral palsy were assessed at 5 years of age ($N = 772$) with the Movement Assessment Battery for Children–Second Edition, which classifies movement difficulties as none (>15th percentile), at risk (6th–15th percentile) and significant (≤5th percentile). Associations with sociodemographic, perinatal, and neonatal characteristics collected from obstetric and neonatal medical records and parental questionnaires were estimated using multinomial logistic regression.

RESULTS: We found 23.2% ($n = 179$) of children were at risk for movement difficulties and 31.7% ($n = 244$) had significant movement difficulties. Lower gestational age, severe brain lesions, and receipt of postnatal corticosteroids were associated with significant movement difficulties, whereas male sex and bronchopulmonary dysplasia were associated with being at risk and having significant movement difficulties. Children with younger, primiparous, less educated, and non-European-born mothers were more likely to have significant movement difficulties. Differences in prevalence between countries remained after population case-mix adjustments.

CONCLUSIONS: This study confirms a high prevalence of movement difficulties among EPT children without cerebral palsy, which are associated with perinatal and neonatal risk factors as well as sociodemographic characteristics and country.

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Mr Aubert and Drs Costa and Zeitlin conceptualized and designed the study, conducted the different analyses, drafted the initial manuscript, and reviewed and revised the manuscript; Drs Ådén and Johnson supervised the different analyses, and critically reviewed and revised the manuscript for important intellectual content; Drs Cuttini, Männamaa, Pierrat, Sarrechia, van Heijst, and Zemlin contributed to the study design, participated in data collection and curation, and critically reviewed and revised the manuscript for important intellectual content; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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WHAT'S KNOWN ON THIS SUBJECT: Movement difficulties are common among children born extremely preterm, but prevalence varies widely between studies. Male sex and gestational age seem to be the only 2 factors consistently associated with movement difficulties following extremely preterm birth.

WHAT THIS STUDY ADDS: In a large European cohort of children born extremely preterm, this study confirms a very high prevalence of movement difficulties and identifies multiple perinatal, neonatal, and sociodemographic risk factors for poor motor function at 5 years of age.

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With advances in obstetric and neonatal care, the survival of children born extremely preterm (EPT), <28 weeks' gestational age (GA), has increased in recent decades.[1–3] These children face higher risks of long-term developmental problems than children born at term, including cerebral palsy (CP) and a wide range of motor, sensory, cognitive, and behavioral impairments.[4–6] In contrast with declining mortality and CP among EPT children, the prevalence of other neurodevelopmental impairments appears to have remained stable over time and has potentially increased.[7,8] The lack of progress in developmental outcomes, accompanied by increasing numbers of survivors, makes research on the consequences of EPT birth a priority to enable early identification of developmental difficulties and timely referral for intervention at the individual and population levels.[9]

Movement difficulties are a common consequence of EPT birth.[7,10–13] Movement difficulties can reduce the child's opportunities to develop in other areas and have been associated with impaired cognitive development, school performance, social integration, and functioning in adulthood.[4,5,10,14–18] Despite this growing evidence base on the consequences of movement difficulties, our understanding of its prevalence and risk factors remains limited,[12,19] particularly among children without CP.[7,13,20] For instance, the prevalence of movement difficulties varies greatly between studies from 8%[21] to >40%,[13,18,20,22] likely because of population inclusion criteria, such as GA and birth weight thresholds and methodological differences. Recent reviews found inconsistent results in relation to early life risk factors with consistent associations with motor impairment among children free of major disability only for male sex and preterm birth.[6,12]

Reviews on motor function among children born very preterm have pointed to the lack of studies reporting the development of these children at school age, the lack of standardization of the measurement tools, the small and heterogeneous samples, as well as the failure to consider different clinical and sociodemographic characteristics that can strongly influence the results.[4,12,23] Using data from a population-based European cohort of EPT children assessed using the Movement Assessment Battery for Children–Second Edition (Movement ABC-2),[24] this study aimed to estimate the prevalence of movement difficulties among 5-year-old children born EPT without CP in 19 regions from 11 European countries and to identify sociodemographic, perinatal, and neonatal risk factors associated with movement difficulties.

METHODS

Study Design and Participants

We used data from the Screening to Improve Health in Very Preterm Infants in Europe (SHIPS) study[25] that followed-up the Effective Perinatal Intensive Care in Europe population-based, prospective cohort of children born before 32 weeks' GA, between 2011 and 2012, in 19 regions in 11 European countries. Data were collected from obstetrical and neonatal records during the neonatal hospitalization using a standardized, pretested instrument by study investigators or medical personnel. When the child was 2 and 5 years of age, questionnaires on health, general development, and socioeconomic circumstances were sent to parents. Clinical assessments evaluating neurocognitive functioning and motor skills (using the Movement ABC-2) were also conducted at 5 years of age for children born EPT.

Our study population was limited to children born EPT who were eligible for the Movement ABC-2 assessment. Out of 1671 EPT infants alive at discharge (Fig 1), 1654 were alive at 5 years, and 1021 were followed-up. As in most studies using the Movement ABC-2, we excluded children with a CP diagnosis ($n = 98$),[26–28] as this is a well-defined neurodevelopmental disorder,[29] as well as children with a severe neurodevelopmental impairment defined as an intelligence quotient (IQ) ≤54 (<−3 standard deviation [SD]) or severe hearing or visual impairment ($n = 32$) because the Movement ABC-2 was not designed to assess movement abilities in these children.[24] Lastly, we excluded children with missing Movement ABC-2 data ($n = 119$): 88 children were assessed by parental questionnaire only, whereas in 31 the test was incomplete or missing and imputation was not possible. The final sample was comprised of 772 children.

Movement Difficulties

The Movement ABC-2,[24] is a validated test to evaluate movement difficulties by age category,[10,30] even in high-risk populations of EPT children.[27] It assesses performance on 8 motor tasks in 3 motor components: manual dexterity, aiming and catching, and balance. Scores from all tests were summed and converted to an age adjusted percentile score based on United Kingdom norms that classify movement difficulties into 3 categories: none (>15th percentile), at risk (6th–15th percentile), and significant (≤5th percentile), within each component and globally.[24] As national norms exist only in Belgium, France, Italy, the Netherlands, and the United Kingdom,[24,31–33] we uniformly applied the United Kingdom norms that are the most commonly used in the literature.[24,34] The Movement

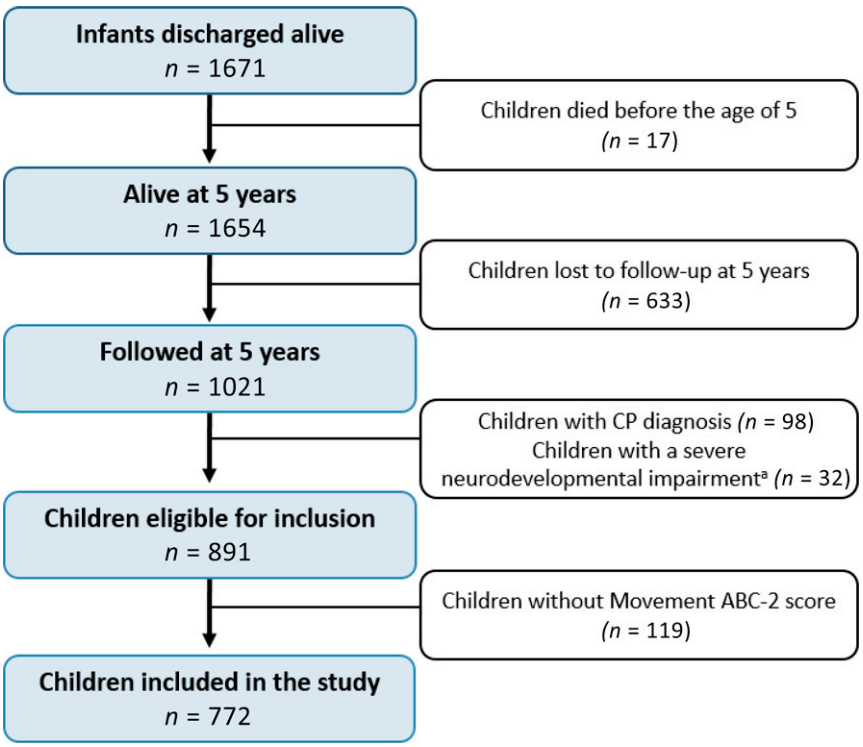

FIGURE 1

Flowchart of the sample selection from the SHIPS cohort (children born <28 gestational weeks). CP, cerebral palsy; Movement ABC-2, Movement Assessment Battery for Children–Second Edition [a]Defined as an IQ ≤54 (<−3SD) or severe hearing or visual impairment.

ABC-2 was administered by trained psychologists or physiotherapists. Assessments were conducted by staff in local routine follow-up programs where available (Belgium, the Netherlands, and Sweden) or by the SHIPS research team (Denmark, Estonia, France, Germany, Italy, Poland, Portugal, and the United Kingdom). Although it was not possible to carry out interrater reliability across countries, common data collection guidelines and a core data collection form were developed to standardize procedures and to ensure consistent reporting of the assessment results. Training sessions were held locally, and an online discussion forum was set up to discuss possible problems emerging during the data collection.

Children who had missing Movement ABC-2 data were reviewed on a case-by-case basis by neurodevelopmental specialists and an epidemiologist (R.C., U.A., S.J., and J.Z.). If a child was unable to complete a test-item or component because of severe motor impairment, the lowest score was assigned for that test-item and/or component ($n = 7$). If data were missing for a test-item or component score in the absence of other developmental problems, the average of the other test-items within the component was used for imputation ($n = 11$). For 11 Belgian children, percentile scores from the Movement ABC (First Edition) were used.[35] In all other cases, scores were left as missing.

Risk Factors

Variables selected for this analysis were those hypothesized to affect risks of movement difficulties based on biological plausibility and the scientific literature.

Sociodemographic factors included maternal age at childbirth, parity, maternal country of birth (from neonatal records), parental cohabiting status, maternal educational level,[36] and household unemployment status (from parental questionnaires). Perinatal and neonatal factors were GA, small for gestational age (SGA),[37] sex, multiple birth, premature rupture of membranes >12 hours, any antenatal corticosteroids, congenital anomaly,[38] severe brain lesions (intraventricular hemorrhage [IVH] grade III or IV or cystic periventricular leukomalacia [cPVL]), retinopathy of prematurity stage III or more, necrotizing enterocolitis (requiring surgery or peritoneal drainage), bronchopulmonary dysplasia ([BPD], defined as supplemental oxygen at 36 weeks' postmenstrual age), postnatal corticosteroids,[39] and breastfeeding at discharge.

Statistical Analyses

We first described the characteristics of children included in the sample and those excluded because of missing Movement ABC-2 scores. We then described the Movement ABC-2 classifications overall and by component. We produced 3 models to measure the association of sociodemographic, perinatal, and neonatal variables with the probability of being at risk or having significant movement difficulties using multinomial logistic regression taking into consideration clustering within multiple pairs: (1) with no adjustment except country modeled as a fixed effect (termed "unadjusted"), (2) adjusted on sociodemographic and perinatal factors, and (3) with additional adjustments on neonatal factors.

To take into account loss to follow-up, we used inverse probability weighting (IPW).[40,41] As described previously for this cohort,[42–44] we

compared the characteristics of responders and nonresponders at the 5-year follow-up (Supplemental Table 5). Variables potentially affecting loss to follow-up were used to estimate the probability of response using multivariate logistic regression and to define a weight inversely proportional to this probability (Supplemental Table 6). Multiple imputation by chained equations was used ($m = 20$) to impute missing data for covariates used to create the weights.[45,46] We also imputed data for covariates in the final models ($m = 20$). Three had a percentage of missing >3.0%: household unemployment status (6.7%), parental cohabiting status (5.8%), and maternal education (4.0%). Data were assumed to be missing at random after taking into consideration observed covariates. We did not impute data for children with missing Movement ABC-2 scores as the missing at random assumptions likely did not hold. However, we compared the characteristics of children with and without Movement ABC-2 scores. Final models used IPW and multiple imputation.[47]

We conducted sensitivity analyses by rerunning models (1) using the unweighted and complete case samples and (2) using national norms in the countries where these were available, as these may affect movement difficulties classification.[34]

All analyses used the statistical software Stata version 15.0 (StataCorp, College Station, TX, USA).

RESULTS

Children in the study sample were assessed at 5.7 (0.4) years (mean SD) (Table 1). There were 28.6% born <26 weeks' GA, 49.8% were males, and 71.9% were singletons. Their mothers were aged 35 years or older for 26.1%, 58.5% were primiparous, 37.0% had at least a bachelor's degree, and 18.6% were born outside of Europe. Compared with children in the sample, those without Movement ABC-2 scores were less likely to have young (<25 years) or old (≥35 years) mothers and were more likely to have lower GA and to not be breastfed at discharge from the neonatal unit. For children followed at 2 years of age, missing Movement ABC-2 scores were more common among those with impairment. Loss to follow-up was mainly related to social disadvantage and GA (Supplemental Table 5).

Movement Difficulties Among EPT Children

Children classified at risk and with significant movement difficulties comprised 23.2% and 31.7% of the sample, respectively (Table 2). The prevalence of significant movement difficulties was higher for the manual dexterity component (37.4%) than the aiming and catching and balance components (19.2% and 19.7%, respectively).

Risk Factors Associated With Movement Difficulties

The prevalence of movement difficulties by risk factor group as well as unadjusted relative risk ratios (RRR) and their 95% confidence intervals (95% CI) are presented in Table 3. Some factors had strong associations with both being at risk for movement difficulties and having significant movement difficulties (ie, household unemployment status, SGA, male sex, retinopathy of prematurity, and BPD), whereas some others were associated with significant movement difficulties only (ie, congenital anomalies, severe brain lesions, and postnatal corticosteroids). Prevalence of significant movement difficulties ranged from 12.4% (the Netherlands) to 72.3% (Poland), whereas the at-risk group ranged from 11.3% (Sweden) to 39.0% (Belgium).

Adjustment on sociodemographic and perinatal factors (model I) slightly attenuated these associations (Table 4). Adjusting for neonatal factors (model II) further reduced the magnitude of associations of low GA, SGA, male sex, and congenital anomalies with significant movement difficulties. Severe brain lesions and postnatal corticosteroids were risk factors for significant movement difficulties, whereas BPD were risk factors for both at risk and significant movement difficulty groups. The other morbidities were no longer significant. These adjustments did not strongly impact the estimated associations with sociodemographic factors. The large differences between countries persisted in adjusted models.

Sensitivity analyses without IPW did not show differences in sample characteristics or prevalence of movement difficulties (Supplemental Tables 7 and 8), and final models using the unweighted and complete case samples yielded similar conclusions (Supplemental Table 9). Redoing models using Movement ABC-2 national norms (Supplemental Table 10) gave broadly similar results and did not affect study conclusions about the key risk factors or the wide variation between countries, although country rankings changed.

DISCUSSION

Among 772 European children born EPT without CP or severe neurodevelopmental impairment, 23.2% and 31.7% were classified as being at risk and having significant movement difficulties, respectively. Children with lower GA, severe brain lesions, and who received postnatal corticosteroids were more

TABLE 1 Characteristics of Children Included in the Study and Comparison With Children Who Had Missing Movement ABC-2 Scores (With IPW)

	Children Included in the Study[a]		Children Eligible for Inclusion but Without Movement ABC-2[a]		
	N = 772	%	*N* = 119	%	*P*[b]
Sociodemographic characteristics					
Maternal age at childbirth, y					.001
<25	123	16.0	16	13.0	
25–34	446	57.9	87	73.5	
≥35	201	26.1	16	13.5	
Missing	2	0.3	0	0.1	
Parental cohabiting status					.89
Married, couple, or cohabiting	617	84.9	101	87.0	
Single or other	110	15.1	15	13.0	
Missing	45	5.8	3	2.5	
Maternal educational level					.88
≤Lower secondary	141	19.0	22	19.5	
Upper secondary or short tertiary	326	44.0	56	48.9	
≥Bachelor	274	37.0	36	31.6	
Missing	31	4.0	5	4.2	
Household unemployment status					
Employed or other situation[c]	623	86.5	93	81.9	
At least 1 parent unemployed	97	13.5	21	18.1	
Missing	52	6.7	5	4.2	
Parity					.75
First child	446	58.5	73	62.1	
Second child	180	23.6	27	22.8	
Third child or more	137	17.9	18	15.1	
Missing	9	1.2	1	0.8	
Maternal country of birth					.94
Native-born	570	74.1	87	72.9	
Other European country	57	7.4	7	6.0	
Non-European country	143	18.6	25	21.1	
Missing	3	0.4	0	0.0	
Perinatal and neonatal characteristics					
GA, wk					.03
≤24	93	12.0	19	16.1	
25	128	16.6	29	24.3	
26	231	29.9	30	24.8	
27	320	41.4	41	34.8	
Missing	0	0.0	0	0.1	
SGA					.24
<3rd percentile	114	14.8	15	12.9	
3rd–9th percentile	64	8.3	6	5.0	
≥10th percentile	594	77.0	98	82.1	
Missing	0	0.0	0	0.0	
Child sex					.19
Female	387	50.2	52	43.6	
Male	385	49.8	67	56.4	
Missing	0	0.0	0	0.0	
Multiple birth					.69
Singleton	555	71.9	84	70.8	
Multiple	217	28.1	35	29.2	
Missing	0	0.0	0	0.0	
Congenital anomaly					.96
No	719	93.2	109	91.6	
Yes	53	6.8	10	8.4	
Missing	0	0.0	0	0.0	
Severe neonatal morbidity[d]					.16
No	604	79.7	88	75.2	
Yes	153	20.3	29	24.8	
Missing	15	1.9	2	1.7	

TABLE 1 Continued

	Children Included in the Study[a]		Children Eligible for Inclusion but Without Movement ABC-2[a]		
	N = 772	%	*N* = 119	%	*P*[b]
BPD					.30
No	500	66.5	82	70.0	
Yes	252	33.5	35	30.0	
Missing	20	2.6	2	1.7	
Breastfeeding at discharge					
No	343	45.1	70	60.8	
Yes	417	54.9	45	39.2	
Missing	12	1.6	4	3.4	
Characteristics of participants					
Age at assessment in years, mean (SD)	5.7	(0.4)	5.6	(0.4)	.90
Neurodevelopmental impairment[e]					.92
None	434	56.3	71	59.9	
Mild	255	33.1	36	30.0	
Moderate	82	10.7	12	10.0	
Missing	0	0.0	0	0.0	
Child development at 2 y of age[f]					
Global motor impairment[g]					.49
No	619	96.3	92	95.5	
Yes	24	3.7	4	4.5	
Missing	129	16.7	23	19.3	
Learning disability[h]					<.001
No	537	85.4	65	69.4	
Yes	92	14.6	29	30.6	
Missing	143	18.5	26	21.8	
Country (region)					
Belgium (Flanders)	50	6.5	9	7.7	
Denmark (eastern region)	46	6.0	10	8.1	
Estonia (entire country)	21	2.7	2	1.6	
France (Burgundy, Ile-de-France, northern region)	122	15.7	16	13.5	
Germany (Hesse, Saarland)	75	9.7	20	16.4	
Italy (Emilia-Romagna, Lazio, Marche)	98	12.6	24	19.8	
the Netherlands (central eastern)	50	6.5	2	1.9	
Poland (Wielkopolska)	24	3.1	9	7.8	
Portugal (Lisbon, northern region)	76	9.9	13	10.9	
United Kingdom (east midlands, northern, Yorkshire, and the Humber)	186	24.1	5	3.8	
Sweden (Greater Stockholm)	24	3.1	10	8.4	

[a] Values are *N* rounded to a whole number, % (excluding missing values) rounded to 1 decimal, and mean (SD) for continuous variables, all with the use of inverse probability weighting (IPW) to correct loss to follow-up.
[b] *P* values from Wald test of logistic regressions adjusted on country.
[c] Other situations included student, parental leave, home parent, and other.
[d] Included IVH grade III or IV, cPVL, retinopathy of prematurity stage III or more, and necrotizing enterocolitis.
[e] Combined cognitive, hearing, and visual impairment.
[f] Data from the parental questionnaire filled at 2 y corrected age: 647 over 772 (83.8%) and 96 over 119 (80.7%) children have been followed at this stage.
[g] Global motor impairment at 2 y of age estimated from 3 parental-reported questions on abilities on walking, sitting, and head holding.
[h] Learning disability at 2 y of age estimated from the Parent Report of Children's Abilities-Revised (or the Ages and Stages Questionnaires for France only).

likely to have significant movement difficulties, whereas SGA (ie, <3rd percentile), male sex, and BPD were associated with both being at risk and having significant movement difficulties. Sociodemographic factors, including having younger, primiparous, less educated, and non-European born mothers, were associated with movement difficulties risks. Wide variations in prevalence existed by country and these persisted after adjustment for individual characteristics.

Prevalence of Movement Difficulties

Although children born EPT are more likely to have movement difficulties compared with their term-born peers,[6,10,20,48] prevalence estimates reported in the literature vary by a factor of 5.[13,18,20–22] Some of this variability results from the use of different motor function measures, including parental report,[49] Movement ABC or other tests,[6,10,12] ages of assessment, and

TABLE 2 Rates of Movement Difficulties, in Total and by Component (Based on Movement ABC-2)

	Movement Difficulties[a]					
	None (>15th Percentile)		At Risk (6th–15th Percentile)[b]		Significant (≤5th Percentile)	
	N	%	*N*	%	*N*	%
Total[c]	349	45.2	179	23.2	244	31.7
Manual dexterity[d]	313	41.2	162	21.3	284	37.4
Aiming and catching[d]	542	71.5	71	9.4	145	19.2
Balance[d]	478	63.0	131	17.3	149	19.7

[a] Values are *N* rounded to a whole number and % (excluding missing values) rounded to 1 decimal; both with the use of inverse probability weighting (IPW) to correct loss to follow-up.
[b] As explained in the Movement ABC-2 manual,24 the 16th percentile is used instead of the 15th percentile to delineate the "at risk of movement difficulties" category.
[c] Total: Movement ABC-2 total score composed of the 3 components (manual dexterity, aiming and catching, and balance).
[d] For the 3 component scores, the total of the *n* is not necessarily equal to 772 because mainly total scores were imputed when a test-item or a component was missing.

population inclusion criteria.[20] When comparisons are restricted to studies with samples and methods similar to ours, prevalence is higher with lower variability. For instance, 37.1% of children had Movement ABC-2 scores ≤5th percentile in a Swedish sample born <27 weeks' GA, after exclusion of children with CP or severe neurodevelopmental impairment.[13] In an Australian sample of 165 children born <30 weeks' GA or <1250 g birth weight without CP or IQ <80 points, 47.9% had a Movement ABC (First Edition) score ≤16th percentile.[18] Nonetheless, contextual variations in prevalence persist even between these more standardized samples, as we observed within our European cohort by the differences between countries. Variation is also seen in proportions classified as being at risk or with significant movement difficulties, with some studies finding more children in the most severe category,[50] as we did. This heavily skewed distribution of scores reflects the high levels of impairment in this population. Finally, when movement difficulties were classified by component, we noted a lower prevalence of impairment for aiming and catching and balance (19% to 20% with significant movement difficulties), compared with manual dexterity (37%). Two previous reviews also noted differences by domain, with lower performance in manual dexterity in some, but not all studies.[10,50]

Risk Factors

Some perinatal and neonatal characteristics associated with movement difficulties were reported previously,[6,12,50] including lower GA, SGA, male sex, severe brain lesions, BPD, and postnatal corticosteroids.[27,51] In a recent review, Van Hoorn et al,[6] reported on several studies showing associations between neonatal brain lesions and motor development. In addition, use of postnatal corticosteroids was associated with motor impairment in 2 out of 3 studies. The risk of developmental coordination disorder (measured by Movement ABC in 22 of 36 studies), was generally inversely related to the GA group, an association found in our sample. Contrary to some reports, premature rupture of membranes, necrotizing enterocolitis, and retinopathy of prematurity were not associated with movement difficulties.[51–53] However, these associations have been inconsistent in the literature[6,12] and may be influenced by population differences (eg, inclusion of children with other major disabilities),[52] or methods for measuring comorbidities.[51] Finally, we found that children who did not receive antenatal corticosteroids were less likely to be at risk for movement difficulties, an association not previously reported[6]; however, as few children were in this group, this may be a spurious finding. Being able to identify children at risk using perinatal and neonatal risk profiles has the potential to improve long-term motor outcomes as studies find beneficial effects of early intervention.[54,55] Further, the identification of risk factors can generate etiological hypotheses; our finding that risk profiles differed for children classified as at risk versus with significant movement difficulties, requiring confirmation in future work, may suggest varying causal pathways.

Several sociodemographic characteristics increased risks of movement difficulties: low maternal age, lower educational level, parental unemployment, primiparity, and non-European maternal country of birth. Previous studies have reported associations with some sociodemographic characteristics, but often only 1 or 2 characteristics and among younger children below 5 years of age.[12,56–59] Null or contradictory findings may result from sociodemographic factors not being consistently or fully explored.[6,12,50] Understanding how social factors interact with medical and biological risk is an important area for study since it makes it possible to target at-risk groups and understand risk and resilience mechanisms.

After adjustment on sociodemographic and clinical factors, differences in movement difficulties persisted by country of birth. We also found that prevalence estimates at the country-level were sensitive to the choice of norm, as previously shown.[34] Taken together,

TABLE 3 Sociodemographic, Perinatal, and Neonatal Characteristics Over Movement Difficulties Classification (Based on Movement ABC-2)

		Movement Difficulties[a]						
		None	At risk			Significant		
	N =	%	%	Unadjusted RRR	(95% CI)	%	Unadjusted RRR	(95% CI)
	772	45.2	23.2			31.7		
Sociodemographic characteristics								
Maternal age at childbirth, y								
<25	123	29.2	24.8	1.80	(0.91–3.57)	45.9	2.71	(1.39–5.29)
25–34	446	46.2	24.6		REF	29.2		REF
≥35	201	53.4	17.6	0.65	(0.41–1.01)	29.0	0.91	(0.59–1.40)
Parental cohabiting status								
Married, couple, or cohabiting	617	46.6	22.2		REF	31.2		REF
Single or other	110	45.7	28.0	1.38	(0.75–2.53)	26.3	1.03	(0.54–1.96)
Maternal educational level								
≤Lower secondary	141	38.9	22.0	1.40	(0.76–2.56)	39.1	2.69	(1.47–4.90)
Upper secondary or short tertiary	326	45.4	22.2	0.99	(0.63–1.57)	32.4	1.21	(0.76–1.93)
≥Bachelor	274	49.2	24.5		REF	26.3		REF
Household unemployment status								
Employed or other situation[b]	623	49.3	21.7		REF	29.0		REF
At least 1 parent unemployed	97	29.9	31.4	2.61	(1.35–5.07)	38.7	2.20	(1.04–4.68)
Parity								
Primiparous	446	41.9	25.2	1.47	(0.97–2.24)	32.9	1.48	(0.97–2.25)
Multiparous	317	49.4	20.1		REF	30.5		REF
Maternal country of birth								
Native-born	570	44.3	25.1		REF	30.5		REF
Other European country	57	40.2	24.7	1.16	(0.53–2.52)	35.1	1.34	(0.64–2.83)
Non-European country	143	50.2	14.2	0.58	(0.31–1.11)	35.6	1.51	(0.83–2.77)
Perinatal characteristics								
GA, wk								
≤24	93	26.8	22.1	1.88	(0.95–3.70)	51.1	4.09	(2.16–7.75)
25	128	38.5	19.4	1.18	(0.66–2.10)	42.1	2.65	(1.52–4.61)
26	231	47.7	24.7	1.17	(0.73–1.86)	27.6	1.31	(0.79–2.18)
27	320	51.3	23.9		REF	24.8		REF
SGA								
<3rd percentile	114	34.3	28.8	2.04	(1.21–3.45)	36.9	2.00	(1.19–3.38)
3rd–9th percentile	64	45.5	18.7	0.86	(0.43–1.74)	35.8	1.17	(0.61–2.28)
≥10th percentile	594	47.2	22.6		REF	30.2		REF
Child sex								
Female	387	53.5	21.3		REF	25.2		REF
Male	385	36.8	25.0	1.77	(1.19–2.63)	38.2	2.46	(1.61–3.74)
Multiple birth								
Singleton	555	41.6	24.1		REF	34.3		REF
Multiple	217	54.3	20.8	0.63	(0.41–0.97)	24.9	0.59	(0.37–0.95)
Premature rupture of membranes								
No	562	45.0	22.5		REF	32.5		REF
Yes	201	45.3	24.8	1.19	(0.76–1.85)	30.0	1.00	(0.63–1.61)
Antenatal corticosteroids								
No	81	54.7	13.5	0.42	(0.19–0.90)	31.9	0.83	(0.39–1.77)
Yes	686	44.2	24.1		REF	31.7		REF
Congenital anomaly								
No	719	45.6	23.8		REF	30.7		REF
Yes	53	39.3	15.2	0.92	(0.39–2.19)	45.5	2.37	(1.02–5.53)
Neonatal characteristics								
Severe brain lesions (IVH or cPVL)[c]								
No	697	46.9	23.5		REF	29.5		REF
Yes	70	28.7	19.1	1.34	(0.66–2.72)	52.2	3.11	(1.69–5.73)
Retinopathy of prematurity								
No	678	48.1	23.1		REF	28.8		REF
Yes	83	22.0	23.1	2.18	(1.08–4.39)	54.9	3.59	(1.88–6.86)
Necrotizing enterocolitis								
No	740	45.8	22.8		REF	31.4		REF
Yes	32	30.5	32.0	1.75	(0.57–5.33)	37.5	1.37	(0.41–4.63)

TABLE 3 Continued

		Movement Difficulties[a]					
		None	At risk			Significant	
	N =	%	%	Unadjusted RRR		%	Unadjusted RRR
	772	45.2	23.2	(95% CI)		31.7	(95% CI)
BPD							
No	500	53.9	22.0	REF		24.1	REF
Yes	252	27.4	25.7	2.25	(1.41–3.59)	46.9	3.65 (2.32–5.73)
Postnatal corticosteroids							
No	541	50.2	23.6	REF		26.1	REF
Yes	220	33.2	21.2	1.56	(0.98–2.46)	45.7	3.55 (2.23–5.65)
Breastfeeding at discharge							
No	343	39.4	23.5	1.38	(0.91–2.11)	37.1	1.69 (1.11–2.59)
Yes	417	50.0	23.1	REF		26.9	REF
Country (region)							
Belgium (Flanders)	50	36.5	39.0	REF		24.5	REF
Denmark (eastern region)	46	52.4	28.1	0.49	(0.19–1.31)	19.6	0.39 (0.14–1.12)
Estonia (entire country)	21	57.6	12.1	0.19	(0.05–0.69)	30.3	0.56 (0.21–1.46)
France (Burgundy, Ile–de–France, northern region)	122	69.9	17.2	0.23	(0.10–0.50)	12.8	0.32 (0.15–0.67)
Germany (Hesse, Saarland)	75	51.1	16.6	0.29	(0.11–0.78)	32.3	0.89 (0.38–2.08)
Italy (Emilia–Romagna, Lazio, Marche)	98	40.0	23.8	0.57	(0.26–1.25)	36.2	1.10 (0.53–2.28)
the Netherlands (central eastern)	50	53.9	33.8	0.58	(0.25–1.33)	12.4	0.28 (0.11–0.68)
Poland (Wielkopolska)	24	15.6	12.1	0.60	(0.14–2.65)	72.3	4.22 (1.36–13.15)
Portugal (Lisbon, northern region)	76	41.2	29.3	0.64	(0.28–1.45)	29.6	0.83 (0.37–1.85)
United Kingdom (east midlands, northern, Yorkshire, and the Humber)	186	30.2	22.7	0.70	(0.30–1.60)	47.1	1.92 (0.89–4.14)
Sweden (Greater Stockholm)	24	56.8	11.3	0.18	(0.04–0.75)	31.9	0.56 (0.20–1.58)

REF, reference category.

[a] Values are *N* rounded to a whole number, % (excluding missing values) rounded to 1 decimal, and RRR and their 95% CI using multinomial logistic regression taking into consideration clustering within multiple pairs, with country modeled as a fixed effect; all with the use of IPW to correct loss to follow–up.

[b] Other situations included student, parental leave, home parent, and other.

[c] Severe brain lesions, defined as having an IVH grade III or IV, and/or a cPVL.

these results raise the possibility that cultural, or policy factors could affect motor outcomes for children born EPT. For instance, preschool, school, or public health programs which differ between European countries[60–62] may influence general motor development and subsequently affect performance on Movement ABC tests, even for children born EPT.[63–65] Further research to confirm and investigate cross-country differences in movement difficulties could inform prevention efforts.

Strengths and Limitations

The main strengths of this study are its large, population-based sample of >750 EPT children, standardized collection of sociodemographic, perinatal, and neonatal data and the measurement of movement difficulties using a validated and widely used clinical assessment.[10,12] Few studies have been conducted on prognostic factors for motor impairment in EPT children without CP and most studies of Movement ABC-2 have much smaller samples.[12] To harmonize results between countries, we applied the Movement ABC-2 United Kingdom norms[24] and were able to conduct sensitivity analyses to confirm that risk factor results were robust to use of national norms. An additional strength is that we analyzed children at risk for movement difficulties as well as those with significant movement difficulties. Minor difficulties are less often examined, but they may substantially impact quality of life and have been identified as an important priority for future investigation.[9]

Limits include possible attrition bias because of loss to follow-up (61.7% follow-up at 5 years) or bias because of children with a missing Movement ABC-2 score. Because we have full data on the cohort at inclusion, these biases could be described and we were able to use IPW to adjust for loss to follow-up, principally related to social factors, as found in other cohorts.[42–44] In contrast, we did not use statistical methods to adjust for bias because of missing Movement ABC-2 scores. These children were a higher risk subgroup and their Movement ABC-2 assessments were likely not missing at random. This may lead to underestimation of movement difficulties in this population. Further, we found large differences in movement difficulties prevalence between countries but could not explore them in more detail because of

TABLE 4 Association Between Movement Difficulties and Sociodemographic and Perinatal (Model I), and Neonatal (Model II) Characteristics Among 5-Year-Old Children Born Extremely Preterm ($N = 772$)

	At Risk for Movement Difficulties[a]				Significant Movement Difficulties[a]			
	Model I		Model II		Model I		Model II	
	RRR (95% CI)		RRR (95% CI)		RRR (95% CI)		RRR (95% CI)	
Sociodemographic characteristics								
Maternal age at childbirth, y								
<25	1.52	(0.72–3.24)	1.74	(0.79–3.84)	2.22	(1.09–4.50)	2.47	(1.15–5.30)
25–34		REF		REF		REF		REF
≥35	0.70	(0.42–1.17)	0.71	(0.43–1.17)	1.11	(0.68–1.81)	1.10	(0.67–1.80)
Parental cohabiting status								
Married, couple, or cohabiting		REF		REF		REF		REF
Single or other	1.41	(0.74–2.69)	1.42	(0.74–2.75)	0.89	(0.41–1.95)	0.91	(0.42–1.95)
Maternal educational level								
≤Lower secondary	1.22	(0.59–2.51)	1.21	(0.58–2.54)	2.14	(0.99–4.65)	2.26	(1.01–5.04)
Upper secondary or short tertiary	0.89	(0.54–1.47)	0.87	(0.53–1.45)	1.04	(0.60–1.78)	1.02	(0.59–1.80)
≥Bachelor		REF		REF		REF		REF
Household unemployment status								
Employed or other situation[b]		REF		REF		REF		REF
At least 1 parent unemployed	3.14	(1.56–6.33)	3.16	(1.58–6.31)	2.00	(0.88–4.55)	1.96	(0.87–4.43)
Parity								
Primiparous	1.43	(0.90–2.27)	1.50	(0.94–2.42)	1.77	(1.10–2.85)	1.76	(1.07-2.91)
Multiparous		REF		REF		REF		REF
Maternal country of birth								
Native-born		REF		REF		REF		REF
Other European country	0.97	(0.43–2.18)	1.04	(0.44–2.43)	1.34	(0.59–3.05)	1.50	(0.62–3.61)
Non-European country	0.53	(0.27–1.04)	0.54	(0.27–1.08)	1.74	(0.95–3.18)	1.90	(1.04–3.46)
Perinatal characteristics								
GA, wk								
≤24	1.84	(0.85–3.99)	1.45	(0.62–3.44)	4.86	(2.38–9.92)	2.30	(1.03–5.13)
25	1.26	(0.69–2.28)	1.10	(0.59–2.07)	3.51	(1.94–6.32)	2.42	(1.31–4.48)
26	1.25	(0.76–2.05)	1.17	(0.71–1.93)	1.60	(0.92–2.79)	1.34	(0.76–2.36)
27		REF		REF		REF		REF
SGA								
<3rd percentile	2.19	(1.25–3.84)	1.82	(1.00–3.30)	2.34	(1.27–4.29)	1.59	(0.83–3.04)
3rd–9th percentile	1.09	(0.51–2.30)	1.02	(0.47–2.18)	1.78	(0.83–3.79)	1.58	(0.73–3.40)
≥10th percentile		REF		REF		REF		REF
Child sex								
Female		REF		REF		REF		REF
Male	1.88	(1.24–2.86)	1.81	(1.18–2.76)	2.62	(1.68–4.08)	2.23	(1.42–3.51)
Multiple birth								
Singleton		REF		REF		REF		REF
Multiple	0.67	(0.44–1.03)	0.65	(0.42–1.01)	0.79	(0.48–1.31)	0.78	(0.46–1.33)
Premature rupture of membranes								
No		REF		REF		REF		REF
Yes	1.12	(0.69–1.84)	1.14	(0.69–1.88)	1.02	(0.61–1.69)	1.04	(0.62–1.72)
Antenatal corticosteroids								
No	0.36	(0.16–0.84)	0.35	(0.15–0.81)	0.86	(0.37–2.02)	0.80	(0.33–1.96)
Yes		REF		REF		REF		REF
Congenital anomaly								
No		REF		REF		REF		REF
Yes	0.69	(0.27–1.75)	0.69	(0.27–1.76)	2.28	(0.92–5.64)	2.33	(0.95–5.72)
Neonatal characteristics								
Severe brain lesions (IVH or cPVL)[c]								
No				REF				REF
Yes			1.31	(0.63–2.73)			2.17	(1.14–4.12)
Retinopathy of prematurity								
No				REF				REF
Yes			1.21	(0.53–2.75)			1.34	(0.66–2.76)
Necrotizing enterocolitis								
No				REF				REF
Yes			1.54	(0.57–4.19)			1.10	(0.41–2.96)

TABLE 4 Continued

	At Risk for Movement Difficulties[a]				Significant Movement Difficulties[a]			
	Model I		Model II		Model I		Model II	
	RRR (95% CI)		RRR (95% CI)		RRR (95% CI)		RRR (95% CI)	
BPD								
No			REF				REF	
Yes			1.94	(1.13–3.33)			2.54	(1.47–4.40)
Postnatal corticosteroids								
No			REF				REF	
Yes			1.05	(0.61–1.82)			1.94	(1.09–3.44)
Breastfeeding at discharge								
No			1.01	(0.62–1.64)			0.98	(0.59–1.62)
Yes			REF				REF	
Country (region)								
Belgium (Flanders)		REF		REF		REF		REF
Denmark (eastern region)	0.40	(0.14–1.13)	0.42	(0.15–1.19)	0.63	(0.18–2.18)	0.66	(0.20–2.21)
Estonia (entire country)	0.15	(0.04–0.55)	0.16	(0.04–0.59)	0.85	(0.28–2.60)	0.85	(0.26–2.82)
France (Burgundy, Ile–de–France, Northern Region)	0.18	(0.08–0.43)	0.19	(0.08–0.47)	0.21	(0.07–0.56)	0.20	(0.07–0.54)
Germany (Hesse, Saarland)	0.21	(0.07–0.61)	0.24	(0.08–0.72)	0.57	(0.19–1.72)	0.64	(0.21–1.97)
Italy (Emilia-Romagna, Lazio, Marche)	0.53	(0.23–1.25)	0.56	(0.23–1.35)	1.85	(0.72–4.78)	1.80	(0.70–4.64)
the Netherlands (central eastern)	0.55	(0.22–1.33)	0.52	(0.21–1.29)	0.31	(0.10–0.98)	0.26	(0.08–0.88)
Poland (Wielkopolska)	0.70	(0.13–3.65)	0.81	(0.15–4.35)	8.75	(1.98–38.59)	9.61	(2.09–44.17)
Portugal (Lisbon, northern region)	0.52	(0.22–1.26)	0.55	(0.22–1.37)	1.10	(0.41–2.98)	1.15	(0.42–3.17)
United Kingdom (east midlands, northern, Yorkshire, and the Humber)	0.63	(0.27–1.48)	0.53	(0.22–1.32)	3.03	(1.16–7.91)	2.46	(0.87–6.92)
Sweden (Greater Stockholm)	0.15	(0.03–0.68)	0.14	(0.03–0.67)	0.56	(0.15–2.06)	0.61	(0.15–2.44)

REF, reference category.

[a] Values are RRR and their 95% CI from multinomial logistic regression models: adjusted on sociodemographic and perinatal factors (Model I) and adjusted additionally on neonatal factors (Model II); both taking into consideration clustering within multiple pairs, with country modeled as a fixed effect, and with the use of IPW and multiple imputed dataset.

[b] Other situations included student, parental leave, home parent, and other.

[c] Severe brain lesions, defined as having an IVH grade III or IV, and/or a cPVL.

limited sample sizes per country. We did not have a control population of children born at term, however studies with controls report good calibration of Movement ABC-2 norms in their control samples.[50] Although test and examiner reliabilities across sites were not assessed, recommendations by the European Academy of Childhood Disability on developmental coordination disorder concluded that the Movement ABC-2 has good to excellent interrater reliability and test-retest reliability.[17] A final limitation is the study's observational design and the measurement of some sociodemographic characteristics at the same time as our study outcome. However, our objective was to identify risk-factor associations, not determine causality.[66]

CONCLUSIONS

In this large population-based sample of 5-year-old children born EPT in Europe without CP, we found that over half were at risk for movement difficulties or had significant movement difficulties. We identified multiple clinical risk factors that could be used to prioritize at-risk children for follow-up and early intervention services. We also showed associations with social factors illustrating the importance of integrating social circumstances into public health programs for children born EPT. Finally, our study found unexplained variability in the prevalence of at risk for or significant movement difficulties by country that raise questions about the role of the broader social or health context in mitigating risks in this population.

Ethical Approval

All study regions obtained ethical approval according to national legislations. The study was also approved by the French Advisory Committee on Use of Health Data in Medical Research and the French National Commission for Data Protection and Liberties. Parents gave their written informed consent to participating in the study before any data collection.

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ABBREVIATIONS

BPD: bronchopulmonary dysplasia
CI: confidence interval
CP: cerebral palsy
cPVL: cystic periventricular leukomalacia
EPT: extremely preterm
GA: gestational age
IPW: inverse probability weighting
IQ: intelligence quotient
IVH: intraventricular hemorrhage
Movement ABC-2: Movement Assessment Battery for Children–Second Edition
RRR: relative risk ratio
SD: standard deviation
SGA: small for gestational age
SHIPS: Screening to Improve Health in Very Preterm Infants in Europe

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