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ORIGINAL ARTICLE

Developmental motor problems and health-related quality of life in 5-year-old children born extremely preterm: A European cohort study

Adrien M. Aubert[1] | **Raquel Costa**[2,3] | **Samantha Johnson**[4] | **Ulrika Ådén**[5,6] | **Véronique Pierrat**[1,7] | **Marina Cuttini**[8] | **Mairi Männamaa**[9] | **Iemke Sarrechia**[10] | **Jo Lebeer**[11] | **Arno F. Van Heijst**[11] | **Rolf F. Maier**[12] | **Mariane Sentenac**[1] | **Jennifer Zeitlin**[1] | **The SHIPS research group**

[1]Université Paris Cité, Inserm, INRAE, Centre for Research in Epidemiology and Statistics (CRESS), Obstetrical Perinatal and Pediatric Epidemiology Research Team, EPOPé, Paris, France

[2]EPIUnit, Instituto de Saúde Pública, Universidade do Porto, Porto, Portugal

[3]Laboratório para a Investigação Integrativa e Translacional em Saúde Populacional, Porto, Portugal

[4]Department of Health Sciences, University of Leicester, Leicester, UK

[5]Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden

[6]Department of Bioclinical Sciences, Linköping University, Linköping, Sweden

[7]Department of Neonatology, Centre Hospitalier Intercommunal Créteil, Créteil, France

[8]Clinical Care and Management Innovation Research Area, Bambino Gesù Children's Hospital, Istituto di Ricovero e Cura a Carattere Scientifico, Rome, Italy

[9]Department of Paediatrics, Institute of Clinical Medicine, University of Tartu, Tartu, Estonia

[10]Department of Medicine & Population Health, Faculty of Medicine & Health Sciences, University of Antwerp, Antwerp, Belgium

[11]Department of Neonatology, Sophia Children's Hospital and Erasmus University Medical Center, Rotterdam, the Netherlands

[12]Children's Hospital, University Hospital, Philipps University Marburg, Marburg, Germany

Correspondence
Jennifer Zeitlin, Maternité de Port-Royal, 53 Avenue de l'Observation, 75014, Paris, France.
Email: jennifer.zeitlin@inserm.fr

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Abstract

Aim: To measure the association between cerebral palsy (CP) and non-CP-related movement difficulties and health-related quality of life (HRQoL) among 5-year-old children born extremely preterm (<28 weeks gestational age).

Method: We included 5-year-old children from a multi-country, population-based cohort of children born extremely preterm in 2011 to 2012 in 11 European countries ($n = 1021$). Children without CP were classified using the Movement Assessment Battery for Children, Second Edition as having significant movement difficulties (≤5th centile of standardized norms) or being at risk of movement difficulties (6th–15th centile). Parents reported on a clinical CP diagnosis and HRQoL using the Pediatric Quality of Life Inventory. Associations were assessed using linear and quantile regressions.

Results: Compared to children without movement difficulties, children at risk of movement difficulties, with significant movement difficulties, and CP had lower adjusted HRQoL total scores (β [95% confidence interval] = −5.0 [−7.7 to −2.3], −9.1 [−12.0

Abbreviations: DCD, developmental coordination disorder; HRQoL, health-related quality of life; IPW, inverse probability weighting; MABC-2, Movement Assessment Battery for Children, Second Edition; NDI, neurodevelopmental impairment; PedsQL, Pediatric Quality of Life Inventory; SHIPS, Screening to Improve Health in Very Preterm Infants in Europe.

to −6.1], and −26.1 [−31.0 to −21.2]). Quantile regression analyses showed similar decreases in HRQoL for all children with CP, whereas for children with non-CP-related movement difficulties, reductions in HRQoL were more pronounced at lower centiles. **Interpretation:** CP and non-CP-related movement difficulties were associated with lower HRQoL, even for children with less severe difficulties. Heterogeneous associations for non-CP-related movement difficulties raise questions for research about mitigating and protective factors.

With advances in obstetric and neonatal care, survival after being born extremely preterm (<28 weeks gestational age) has increased in recent decades,[1] but children born extremely preterm continue to face substantially higher risks of developmental problems and disorders than their peers born at term.[1,2] Developmental motor problems, which include cerebral palsy (CP), developmental coordination disorder (DCD), and other movement difficulties, are common consequences of being born extremely preterm. The prevalence of CP is around 10% among children born extremely preterm[3] and movement difficulties are present in up to 50% of children without CP.[4–7] While CP is clearly defined as a motor disorder with established guidelines for health care provision,[8–10] there is less agreement about whether all children with movement difficulties should be classified as having a disorder. The low use of motor function-related health care services by children born extremely preterm with movement difficulties raises questions about whether this reflects the absence of a health disorder or an unmet need.[11]

Impaired motor function can limit daily activities, schooling, and social relationships, but the consequences of CP and non-CP-related movement difficulties on children's lives and well-being are not well described.[12] One approach to quantifying this impact is to measure health-related quality of life (HRQoL). HRQoL evaluates the level of interference of health limitations in day-to-day functioning by considering the physical, emotional, and social dimensions of health and well-being.[13–15] In a systematic review, Zwicker and Harris[15] concluded that preschool children born preterm or with a very low birthweight (<1500 g) tend to have lower parent-reported HRQoL, whereas evidence in older children is scarce. However, these studies did not explore the extent to which lower HRQoL is associated with specific preterm birth-related developmental comorbidities, including developmental motor problems. Among children with CP or DCD in the general population, studies generally reported worse physical, psychosocial, and social functioning compared with typically developing peers.[12,16]

The existing literature suggests that children's HRQoL is likely to be impacted by movement difficulties associated with being born extremely preterm, but these effects have not been studied and may be heterogeneous. Our principal aim was to measure the associations of CP and non-CP-related movement difficulties with HRQoL among children born extremely preterm. We further sought to assess whether these associations existed in the absence of other neurodevelopmental impairments (NDIs) and among children not receiving motor function-related health care services.

What this paper adds

- Children born extremely preterm with motor function problems had lower health-related quality of life (HRQoL).
- Clinically significant lower HRQoL was observed in children with less severe difficulties.
- Lower HRQoL was also found in children without motor function-related health care use.
- Reductions in HRQoL were less marked in children with higher reported HRQoL.

METHOD

Study design and participants

This study used data from the Screening to Improve Health in Very Preterm Infants in Europe (SHIPS) population-based, prospective cohort of children born very preterm (<32 weeks gestational age) in 2011 to 2012 in 19 regions in 11 European countries. As described in more detail in the cohort profile,[17] inclusions took place over a 12-month period (except for regions in France where they occurred over a 6-month period only), with all births (including stillbirths and terminations of pregnancy) between 22 weeks + 0 days and 31 weeks + 6 days occurring in all maternity units from the selected regions included in the study. Data were collected from obstetric and neonatal records during neonatal hospitalization as well as parental questionnaires at 2 and 5 years of age. At 5 years of age, clinical assessments of neurocognitive and motor functioning were also carried out for the subgroup of children born extremely preterm. Our study population was limited to this subgroup born extremely preterm, including 1021 children born extremely preterm (out of 1654 eligible children) followed at 5 years of age.

Ethics statement

All study regions obtained ethical approval according to national legislation. The study was also approved by the French Advisory Committee on the Use of Health Data in Medical Research and the French National Commission for Data

Protection and Liberties. Parents gave their written informed consent to participate in the study before any data collection.

Developmental motor difficulties

Movement difficulties were assessed and classified using the Movement Assessment Battery for Children, Second Edition (MABC-2),[18] a validated test previously used in high-risk populations such as children born extremely preterm.[5] It considers performance on eight motor tasks in three domains: manual dexterity; aiming and catching; and balance. All tasks are summed and converted to an age-adjusted centile score and classified into: no movement difficulties (>15th centile); at risk of movement difficulties (6th–15th centile); and significant movement difficulties (≤5th centile). Because national norms do not exist in all countries, we applied UK norms, which were originally developed for the test and are most commonly used to derive centile scores for all children.[18,19] The MABC-2 was administered by trained psychologists or physiotherapists in local routine follow-up programmes where available (Belgium, the Netherlands, Sweden), or in the SHIPS research teams (other countries). Common data collection guidelines and a core data collection form were developed to standardize procedures and reporting.

Information on CP diagnosis was reported by parents in the 5-year questionnaire, except in France where CP diagnosis was ascertained during a medical visit.

We classified developmental motor problems into four groups. Children with CP were considered a distinct group because CP is a well-defined neurodevelopmental disorder with a specific aetiology;[8] children without CP were classified according to their MABC-2 centiles. The MABC-2 is not designed to assess movement abilities in children with severe NDIs who have difficulty accomplishing the tasks because of their sensory or cognitive deficits.[18] We therefore excluded children with an IQ < 55 (<−3SD) or severe hearing or visual impairment (Figure S1).

Health-related quality of life

The child's HRQoL was measured using the parent-reported Pediatric Quality of Life Inventory (PedsQL) generic core scales[20] for the ages 5 to 7 years. This instrument has demonstrated reliability and validity in typically developing school populations and in pediatric populations with acute or chronic health conditions.[21,22] It consists of 23 items on a 5-point Likert scale in four domains: physical (eight items); emotional (five items); social (five items); and school functioning (five items). Items were reverse-scored and linearly transformed to a 0 to 100 scale, with higher scores indicating a better HRQoL.[20] Three summary scores were computed: the physical health summary score (eight items on physical functioning); the psychosocial health summary score (15 items on emotional, social, and school functioning); and the total score (23 items).

Covariates

The following covariates were considered as potential confounders: child age and sex, and family sociodemographic characteristics, including maternal age and parity at the child's birth, maternal country of birth, parental cohabiting status, maternal educational level, and household unemployment status. For subgroup analyses, we used information on other NDIs, including low full-scale IQ and parent-reported hearing or visual impairments.

Analytical approach

We first described the characteristics of children included in the study sample and those excluded because of missing MABC-2 or PedsQL scores using means and SDs, as well as frequencies and proportions for continuous and categorical variables respectively. We compared the characteristics of children according to motor category (no movement difficulties, at risk of movement difficulties, significant movement difficulties, and CP). Linear regression analyses were used to measure associations between motor categories and HRQoL, adjusting for child age, sex, and family sociodemographic characteristics.

We carried out subgroup analyses first by excluding children with moderate NDIs (i.e. IQ between 55 and 69 [−2SD to −3SD], implants or hearing aids, or difficulty seeing even with glasses). Because multiple developmental impairments are frequent after extremely preterm birth and the association between these impairments is not clear, we aimed to measure whether developmental motor problems have an impact on HRQoL in the absence of these other difficulties. For the group with CP, children with severe NDIs were also excluded from these analyses that compared them with children without CP, where severe NDI is an exclusion criterion. In a second analysis, we additionally excluded children who were not receiving motor function-related health care services, defined as having at least one visit during the past year with: (1) a physiotherapist, motor development or psychomotor therapist, or kinesiologist; (2) an occupational therapist; or (3) an early intervention specialist.[11]

A final analysis explored possible differential effects over the HRQoL distribution using quantile regression models.[23,24] While linear regression analysis measures the general relationship, on average, between developmental motor problems and HRQoL, quantile regression seeks to determine whether this relationship differs at multiple points of the outcome's distribution,[24] that is, whether this might be stronger or weaker for children experiencing different levels of HRQoL. This analysis was carried out on the population of children without moderate NDIs. Lastly, to facilitate the interpretation of differences in scores, given that HRQoL measurements have no intrinsic clinical thresholds, we calculated Cohen's δ as a measure of effect size, and used thresholds to interpret small (0.2), medium (0.5), and large (0.8) effect sizes.[25]

Loss to follow-up and missing data

We used inverse probability weighting (IPW) to take into account loss to follow-up.[26] As described previously,[7] the characteristics of responders and non-responders were compared (Table S1) and used to estimate the probability of response and create the weight (IPW) (Table S2). Missing data for covariates were imputed using multiple imputation by chained equations for the weights (20 imputed data sets) and the final models (20 imputed data sets).[27] Missing data were less than 2% for covariates in the final models.

We did not impute data for children with missing MABC-2 or PedsQL scores because the 'missing at random' assumptions probably did not hold. However, for eligible children with missing MABC-2 data, neurodevelopmental specialists and an epidemiologist (RC, UA, SJ, and JZ) reviewed each case. If a child was unable to complete a task or component because of severe motor impairment, the lowest score on that particular scale was assigned. If data were missing for a task in the absence of other developmental problems, the average of the other tasks was assigned. In Belgium, some children had centile scores from the Movement Assessment Battery for Children, First Edition that were used.[28] In all other cases, scores were left as missing.

Sensitivity analyses

Linear regression models were used for our main analysis, in line with the HRQoL literature.[29,30] However, these scores are not normally distributed because of right censoring due to bounded data at the maximum (Figure S2). Ignoring this ceiling effect might result in biased and inconsistent estimates.[31,32] In addition, there is no clear criterion for how large the sample size has to be before the central limit theorem applies.[31] Censored regression models make it possible to produce consistent estimates in this situation. Therefore, we verified whether the use of alternative models (the Tobit and censored least absolute deviation models) affected the estimates.[31–33] Because these censored regression models gave very similar results to the linear regression models, and the latter are commonly used in the literature, facilitating the comparison with other studies, we decided to present the results from the linear regression models in the main analysis and the results from the censored regression models as the sensitivity analysis. Lastly, we reran the final models using unweighted and complete case samples, and after excluding children with severe NDIs in the CP group ($n = 15$), as this was an exclusion criterion for children without CP.

All analyses were carried out with Stata version 15.0 (StataCorp, College Station, TX, USA).

RESULTS

Of 1671 infants born extremely preterm and alive at discharge, 1654 survived to 5 years and 1021 (61.7%) were followed (Figure S1). One hundred children had a CP diagnosis (unweighted prevalence = 9.8%, weighted prevalence = 11.1%). Among children without CP, 29 with severe NDIs were excluded. After excluding missing MABC-2 and PedsQL measures, the final sample consisted of 810 children.

Children were assessed at mean 5 years 7 months (SD 5 months) (Table 1); 42.0% were born at 27 weeks gestational age, 51.6% were males, and 72.5% were singleton births. Their mothers were aged 35 years or older for 26.7%, 58.9% were primiparous, 37.3% had at least a bachelor's degree, and 18.6% were born outside Europe. Because loss to follow-up was mainly related to social disadvantage (Table S1), IPW affected the distribution of most sociodemographic characteristics.

Younger maternal age and not breastfeeding were associated with missing MABC-2 ($n = 116$) and PedsQL scores ($n = 63$) (Tables S3 and S4). Missing PedsQL was also more frequent among multiparous and non-European mothers.

The proportion of males increased with the severity of movement difficulties and was highest among children with CP (Table 2). Children without movement difficulties and those at risk of movement difficulties had mothers with similarly distributed educational levels, while those with significant movement difficulties or CP were more likely to have mothers with a lower education. A larger proportion of household unemployment was observed for all children with movement difficulties or CP than children without movement difficulties. Among children with CP, 25.3% and 16.2% had severe and moderate NDIs respectively. For analyses of movement difficulties, severe NDIs were excluded, but moderate NDIs increased with the severity of movement difficulties. In the analyses without IPW, the results were similar, although the proportion of children with significant movement difficulties or CP was reduced while there was a higher proportion of children without movement difficulties or at risk of movement difficulties (Table S5).

Compared to children without movement difficulties, those at risk of movement difficulties, and with significant movement difficulties and CP had lower PedsQL total scores (β and 95% confidence intervals: −5.5 [−8.2 to −2.7], −9.8 [−12.8 to −6.8], and − 26.7 [−31.6 to −21.8] respectively [Table 3]). Decreases were greater for physical than psychosocial scores. Models adjusted on sociodemographic characteristics provided similar results. After exclusion of children with moderate NDIs ($n = 123$), associations with the PedsQL total score were slightly attenuated, particularly for the group with CP. Finally, among children without moderate NDIs, those not receiving motor function-related health care services had higher PedsQL scores than those receiving services. However, they still had lower PedsQL scores than children without movement difficulties. Children with CP were not included in this analysis because almost all received motor function-related health care services. When these estimates were converted to Cohen's δ (Table S6), they were in the ranges of 0.31 to 0.41, 0.38 to 0.60, and 1.16 to 1.61

TABLE 1 Characteristics of children included in the study with and without IPW ($n = 810$).

	Without IPW		With IPW	
	$n = 810$	%	$n = 810$	%
Child characteristics				
Age at assessment, mean (SD)	5 years 7 months (4 months)	–	5 years 7 months (4 months)	–
Male sex	409	50.5	418	51.6
Sociodemographic characteristics				
Maternal age at child's birth, years				
<25	88	10.9	127	15.8
25–34	473	58.7	464	57.5
≥35	245	30.4	215	26.7
Parental cohabiting status (single/other)	118	14.6	124	15.3
Maternal educational level				
Low education ISCED 0–2	137	17.1	147	18.4
Intermediate education ISCED 3–5	346	43.3	354	44.3
High education ISCED 6–8	316	39.5	298	37.3
Household unemployment status (at least one parent unemployed)	101	12.6	116	14.4
Primiparous (at child's birth)	487	61.0	471	58.9
Maternal country of birth				
Native-born	639	79.2	599	74.3
Other European country	51	6.3	58	7.1
Non-European country	117	14.5	150	18.6
Perinatal and neonatal characteristics				
Gestational age, completed weeks				
≤24	85	10.5	96	11.8
25	152	18.8	143	17.7
26	239	29.5	231	28.5
27	334	41.2	340	42.0
Small for gestational age				
<3rd centile	123	15.2	112	13.8
3rd–9th centile	70	8.6	67	8.3
≥10th centile	617	76.2	631	77.9
Multiple birth	234	28.9	223	27.5
Congenital anomaly	66	8.1	63	7.7
Severe neonatal morbidity[a]	194	24.4	212	26.6
Bronchopulmonary dysplasia[b]	274	34.4	291	36.6
Breastfeeding at discharge	464	58.4	428	53.8
Country (region)				
Belgium (Flanders)	51	6.3	59	7.3
Denmark (Eastern Region)	42	5.2	48	6.0
Estonia (entire country)	34	4.2	22	2.7
France (Burgundy, Île-de-France, Northern Region)	156	19.3	135	16.6
Germany (Hesse, Saarland)	59	7.3	87	10.7
Italy (Emilia-Romagna, Lazio, Marche)	136	16.8	110	13.6
Netherlands (Central Eastern)	63	7.8	46	5.6
Poland (Wielkopolska)	39	4.8	31	3.8
Portugal (Lisbon, Northern Region)	96	11.9	83	10.2
UK (East Midlands, Northern England, Yorkshire and the Humber)	102	12.6	161	19.8
Sweden (Greater Stockholm)	32	4.0	30	3.7

Values are frequencies (rounded to a whole number), percentages (excluding missing values and rounded to one decimal point), and mean (SD) for continuous variables, all with and without the use of IPW to correct for loss to follow-up.

Abbreviations: IPW, inverse probability weighting; ISCED, International Standard Classification of Education.[59]

[a]Included intraventricular haemorrhage grade III and IV, cystic periventricular leukomalacia, retinopathy of prematurity stage III or higher, and surgical necrotizing enterocolitis. [b]Defined as supplemental oxygen or ventilatory support (or both) (continuous positive airway pressure or mechanical ventilation) at 36 weeks postmenstrual age.

[b] Defined as supplemental oxygen or ventilatory support (or both) (continuous positive airway pressure or mechanical ventilation) at 36 weeks postmenstrual age.

for children at risk of movement difficulties, children with significant movement difficulties, and children with CP respectively.

In quantile analyses, the estimated decline in PedsQL scores for children at risk or with significant movement difficulties in comparison to children without movement difficulties widened with decreasing quantiles, with non-significant decreases at the 90th centile but up to 15.4 points for the 10th

TABLE 2 Sample characteristics according to motor category ($n = 810$).[a]

	Non-CP-related movement difficulties						CP	
	No movement difficulties		At risk of movement difficulties		Significant movement difficulties		CP	
	$n = 330$[a]	%	$n = 165$[a]	%	$n = 216$[a]	%	$n = 99$[a]	%
Child characteristics								
Age at assessment, mean (SD)	5 years 8 months (4 months)	–	5 years 8 months (5 months)	–	5 years 7 months (4 months)	_	5 years 7 months (5 months)	–
Child sex								
Male	136	41.1	87	52.7	131	60.5	65	65.5
Female	195	58.9	78	47.3	86	39.5	34	34.5
Neurodevelopmental impairment[b]								
None	247	74.9	89	54.1	68	31.2	24	24.2
Mild	75	22.6	69	41.9	88	40.7	34	34.4
Moderate	8	2.5	7	4.0	61	28.2	16	16.2
Severe	–	–	–	–	–	–	25	25.3
Family sociodemographic characteristics								
Maternal age at childbirth, years								
<25	29	8.8	26	16.3	45	20.5	27	28.4
25–34	197	59.5	103	63.9	117	53.7	47	48.5
≥35	105	31.6	32	19.8	56	25.8	22	23.0
Parental cohabiting status								
Married/couple/cohabiting	281	85.0	135	81.7	186	86.6	84	84.4
Single/other	50	15.0	30	18.3	29	13.4	15	15.6
Maternal educational level								
Low education ISCED 0–2	51	15.7	27	16.8	49	22.3	20	21.8
Intermediate education ISCED 3–5	141	43.4	69	42.4	99	45.5	44	48.2
High education ISCED 6–8	134	40.9	67	40.9	70	32.1	28	30.0
Household unemployment status								
Employed or other situation[c]	300	91.3	133	81.5	176	82.7	76	79.0
At least one parent unemployed	29	8.7	30	18.5	37	17.3	20	21.0
Parity								
Primiparous	179	55.0	110	67.7	139	64.7	43	44.4
Multiparous	146	45.0	52	32.3	76	35.3	54	55.6
Maternal country of birth								
Native-born	243	73.9	131	80.0	156	71.8	71	71.4
European born	21	6.4	14	8.5	19	8.7	4	4.0
Non-European born	65	19.7	19	11.5	42	19.5	24	24.7

[a]Values are weighted frequencies (rounded to a whole number), percentages (excluding missing values and rounded to one decimal point), and mean (SD) for continuous variables, all using inverse probability weighting to correct for loss to follow-up. Unweighted results are presented in Table S5.

[b]Integrated cognitive, hearing, and visual impairment. Mild impairment was defined as an IQ between 84 and 70 (–1SD to –2SD), difficulties hearing but not requiring hearing aids or implants, or needing glasses but seeing well when wearing them. Moderate impairment was defined as an IQ between 69 and 55 (–2SD to –3SD), using hearing aids or implants but hearing well when wearing them, or having difficulties seeing even when wearing glasses. Severe impairment was defined as an IQ < 55 (<–3SD), deafness or difficulties hearing even when using hearing aids or implants, or blindness or seeing light only.

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

Abbreviations: CP, cerebral palsy; ISCED, International Standard Classification of Education.[59]

centile (Figure 1). In contrast, children with CP had lower scores for all quantiles. Similar patterns were observed for physical and psychosocial scores (Figures S3 and S4).

Analysis using censored regression models (i.e. Tobit and censored least absolute deviation models) did not show appreciable differences with linear models (Table S7). For

TABLE 3 Unadjusted and adjusted association of PedsQL scores with motor category ($n = 810$).

			PedsQL physical health summary score		PedsQL psychosocial health summary score		PedsQL total score	
		n[a]	β	(95% CI)[b]	β	(95% CI)	β	(95% CI)
Adjusted on child age and sex	No MD	330	REF	REF	REF	REF	REF	REF
	At risk of MD	165	−5.6	(−9.3 to −1.9)	−5.5	(−8.2 to −2.7)	−5.5	(−8.2 to −2.7)
	Significant MD	216	−12.5	(−16.7 to −8.3)	−8.2	(−11.1 to −5.2)	−9.8	(−12.8 to −6.8)
	CP	99	−35.9	(−43.6 to −28.1)	−21.2	(−25.8 to −16.7)	−26.7	(−31.6 to −21.8)
Adjusted on family sociodemographic characteristics[c]	No MD	330	REF	REF	REF	REF	REF	REF
	At risk of MD	165	−5.4	(−9.1 to −1.6)	−4.9	(−7.6 to −2.1)	−5.0	(−7.7 to −2.3)
	Significant MD	216	−11.9	(−16.1 to −7.8)	−7.4	(−10.3 to −4.5)	−9.1	(−12.0 to −6.1)
	CP	99	−35.3	(−42.7 to −27.9)	−20.6	(−25.2 to −16.0)	−26.1	(−31.0 to −21.2)
Subgroup analysis after exclusion of children with moderate NDI ($n = 687$)[d]								
Adjusted on child age and sex and family sociodemographic characteristics	No MD	325	REF	REF	REF	REF	REF	REF
	At risk of MD	161	−6.0	(−9.8 to −2.2)	−5.6	(−8.4 to −2.9)	−5.7	(−8.5 to −3.0)
	Significant MD	156	−11.5	(−16.1 to −7.0)	−6.0	(−9.1 to −2.8)	−8.1	(−11.3 to −4.8)
	CP	44	−20.5	(−28.6 to −12.3)	−13.9	(−19.1 to −8.7)	−16.2	(−21.6 to −10.8)
Subgroup analysis after exclusion of children with moderate NDI and stratified on receipt of motor-function related health care services ($n = 638$)[e]								
No ($n = 507$)	No MD	282	REF	REF	REF	REF	REF	REF
	At risk of MD	123	−5.1	(−9.4 to −0.8)	−4.3	(−7.5 to −1.2)	−4.6	(−7.7 to −1.4)
	Significant MD	102	−8.9	(−14.0 to −3.9)	−3.1	(−6.6 to 0.4)	−5.2	(−8.8 to −1.7)
Yes ($n = 131$)	No MD	40	REF	REF	REF	REF	REF	REF
	At risk of MD	39	−10.1	(−18.0 to −2.1)	−6.1	(−12.7 to 0.6)	−7.4	(−13.7 to −1.0)
	Significant MD	53	−17.4	(−26.2 to −8.6)	−7.7	(−15.1 to −0.2)	−11.4	(−18.6 to −4.3)

[a]Weighted frequencies (rounded to a whole number).

[b]PedsQL score reductions are expressed as β and 95% CI using inverse probability weighting to correct for loss to follow-up.

[c]Maternal age and parity at child's birth, maternal country of birth, parental cohabiting status, maternal educational level, and household unemployment status.

[d]Integrated cognitive, hearing, and visual impairment. Moderate NDI was defined as an IQ between 69 and 55 (−2SD to −3SD), using hearing aids or implants but hearing well when wearing them, or difficulties seeing even when wearing glasses. For the group with CP, children with severe NDI were excluded from these analyses to be comparable to children without CP, where severe NDI is an exclusion criterion (i.e. IQ < 55 [<−3SD], deafness or difficulties hearing even when using hearing aids or implants, or blindness or seeing light only).

[e]Receiving motor function-related health care services was defined as having at least one visit during the last 12 months to any of the following: (1) a physiotherapist, motor development or psychomotor therapist, or kinesiologist; (2) an occupational therapist; or (3) an early intervention specialist.[11]

Abbreviations: CI, confidence interval; CP, cerebral palsy; MD, movement difficulty; NDI, neurodevelopmental impairment; PedsQL, Pediatric Quality of Life Inventory; REF, reference category.

instance, total score reductions for significant movement difficulties were −9.1 (−12.0 to −6.1), −8.1 (−10.8 to −5.4), and −9.2 (−13.6 to −6.2) for the linear, Tobit, and censored least absolute deviation models respectively. One difference, however, was a smaller reduction in physical score for the at-risk category in the censored least absolute deviation model compared to the linear and Tobit models. Linear regressions using the unweighted and complete case samples, and excluding children with a severe NDI ($n = 15$) in the group with CP, yielded similar conclusions, although in the latter analysis, scores were slightly higher for children with CP.

DISCUSSION

Summary of findings

Developmental motor problems were associated with poorer HRQoL among children born extremely preterm aged 5 years, with the lowest level for children with CP, followed by those with significant movement difficulties and at risk of movement difficulties compared with children without movement difficulties. Decreases were greater for physical than psychosocial scores. Decreases were also more pronounced at lower HRQoL centiles for children at risk of movement difficulties or with significant movement difficulties, whereas decreases were observed at all centiles for children with CP. Differences persisted after exclusion of children with moderate NDIs and those not receiving any motor function-related health care services over the past year.

Comparison with the published literature

The results from this European multi-regional cohort, the largest with information on HRQoL and developmental motor problems in children born extremely

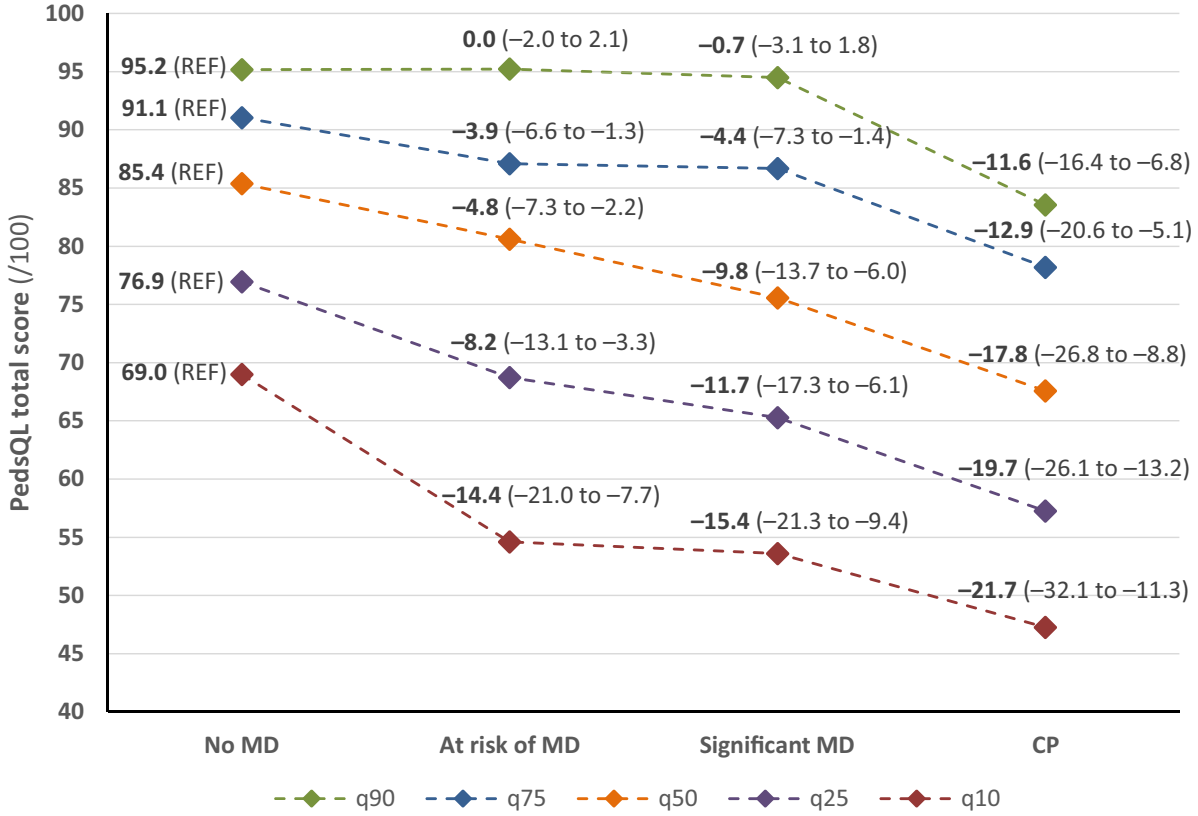

FIGURE 1 Adjusted associations of Pediatric Quality of Life Inventory (PedsQL) quantiles (total score) with motor category for children without moderate neurodevelopmental impairment (NDI). PedsQL total score (REF) and reductions are expressed as β values and their 95% confidence intervals (CIs) rounded to one decimal point, all using inverse probability weighting to correct for loss to follow-up and adjusted for child age and sex and family sociodemographic characteristics, including maternal age and parity at child's birth, maternal country of birth, parental cohabiting status, maternal educational level, and household unemployment status. Children with moderate NDI defined as having an IQ between 69 and 55 (–2SD to –3SD), using hearing aids or implants but hearing well when wearing them, or having difficulties seeing even wearing glasses were excluded. For the group with cerebral palsy (CP), children with severe NDI were excluded from these analyses to be comparable with children without CP, where severe NDI is an exclusion criterion (i.e. IQ < 55 [<–3SD], deafness or difficulties hearing even when wearing hearing aids or implants, or blindness or seeing light only). As an illustrative example, for the quantile 50 (q50), the reference value (category: no movement difficulties [MD]) was 85.4; we observed reductions in the PedsQL total score expressed as β (95% CI) of –4.8 (–7.3 to –2.2), –9.8 (–13.7 to –6.0), and – 17.8 (–26.8 to –8.8) for the categories 'at risk of movement difficulties', 'significant movement difficulties', and 'CP' respectively, compared to the REF category.

preterm,[12,15,34] are consistent with the literature on DCDs where most studies reported worse physical, psychological, and social functioning in children with DCDs than their peers.[12,35] Specifically among children born very preterm, 11-year-old children with DCDs (defined as an MABC-2 score ≤ 5th centile) self-reported lower HRQoL than children born very preterm without motor impairments;[36] children aged 6 to 10 years with global developmental disability and CP had reduced parent-reported HRQoL.[37] Studies that used the 15th or lower centile of the MABC-2 as a cut-off score to indicate DCD suggested that children in the 'borderline' range for motor function experience significant reductions in HRQoL, in line with our findings for the at-risk group.[12] Among children with CP, Makris et al.[16] reported worse physical functioning compared with typically developing peers, but the results were less clear concerning psychosocial functioning, with variations depending on the HRQoL instrument used, whereas we observed decreases in all domains.

Interpretation

There were marked differences in HRQoL scores between children with CP and those with non-CP-related movement difficulties, although they were less striking once children with moderate NDIs were excluded. We did not have information on the type and severity of CP, which are needed to further understand the results in the group with CP.[38] The fact that HRQoL scores followed a gradient reflecting the severity of reduced motor function provides support for a direct association; however, interpreting the scores is complex. In particular, a key question concerns the threshold indicating a clinically meaningful decrease.[39–41] Other studies on HRQoL regarded differences of 5 to 10 points on a 100-point scale as clinically significant.[42] Hilliard et al.[39] established that the amount of change that children and young people with diabetes and their parents perceive as meaningful in everyday functioning or activities was between 4.5 and 6.5 points of the PedsQL score.[39] This result is of the same order of magnitude

as the difference between children with and without health problems found in the initial PedsQL validation study and corresponds to the effect found for children at risk of movement difficulties and without NDIs in our study.[20] Our effect sizes were also consistent with this interpretation using Cohen's δ.

Another question relates to the validity of parent-reported HRQoL with differences existing between self-reported and parent-reported HRQoL.[15,43] Compared to other quality of life measures, the PedsQL instrument focuses on the child's functional status,[44] with better agreement between parents and children on observable items than measures focusing on feelings and lived experiences.[34,43] Given the young age of the children and the high prevalence of NDIs in this study, self-report was not appropriate[34] but future research should assess whether parents' characteristics or beliefs contribute to the variation in HRQoL and confirm these findings using self-reported HRQoL.

Implications for clinical practice, policy, and research

Whereas early interventions to prevent CP and non-CP-related movement difficulties currently have unproved effectiveness,[45,46] interventions to improve motor function in children with developmental motor problems are effective.[47–49] These results showing the consequences of developmental motor problems on the HRQoL of children born extremely preterm at 5 years of age therefore highlight the importance of early screening and support. These findings also reinforce calls for continued follow-up of children born extremely preterm beyond 2 years and for better diagnosis and health service provision for children at risk of movement difficulties or with significant movement difficulties,[50] in particular for children without other developmental problems who may be less likely to receive motor function-related health care services.[11]

Analyses using quantile regression illustrated a heterogeneous association of movement difficulties with HRQoL and suggested that there may be mitigating or protective factors that preserve HRQoL for some children.[23,24] Future studies should focus on identifying protective individual, familial, or broader environmental factors because these may lead to more effective interventions and better identification of children requiring more support.[51] Using integrated measures of day-to-day functioning, such as the PedsQL, for research alongside more traditional neurodevelopmental measures opens up new opportunities for discovery and responds to families' concerns about the well-being of their child born extremely preterm.[52]

Strengths and limitations

The main strengths of this study are its large population-based sample of more than 800 children born extremely preterm with standardized collection of data on motor function and HRQoL using validated instruments. Although test and examiner reliabilities were not assessed across sites, the MABC-2 has good-to-excellent interrater reliability and test–retest reliability.[53] CP was based on a parental report of a clinical diagnosis, which may lead to some misclassification, although almost all children with CP will have received a diagnosis by the age of 5 years in cohorts with high health service use[54,55] such as ours.[56] This is supported by a CP prevalence of 11%, which is in the range of recent cohort studies (9–12%).[3,57,58] However, analysis of the effect of type and severity of CP on HRQoL was not possible. We carried out subgroup analyses excluding children with moderate NDIs to assess the association between motor problems and HRQoL in the absence of these impairments. However, children born extremely preterm experience a range of developmental comorbidities that may affect their HRQoL. How other health and developmental conditions interact with CP and non-CP-related movement difficulties to affect HRQoL is an important area for future research. Finally, there may have been bias from loss to follow-up, although information was available on factors affecting attrition, which were primarily related to social disadvantage and IPW corrected for those characteristics that were under-represented in the follow-up sample.

Conclusion

In children born extremely preterm, developmental motor problems were associated with lower HRQoL at 5 years of age, even among children with less severe difficulties. These results illustrate the importance of follow-up and health service provision for children born extremely preterm across the full spectrum of motor problems to reduce their impact on HRQoL.

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SHIPS research group: Belgium (J Lebeer, I Sarrechia, P Van Reempts, E Bruneel, E Cloet, A Oostra, E Ortibus); Denmark (K Boerch, P Pedersen); Estonia (L Toome, H Varendi, M Männamaa); France (PY Ancel, A Burguet, PH Jarreau, V Pierrat, A Nuytten); Germany (RF Maier, M Zemlin, B Misselwitz, L Wohlers); Italy (M Cuttini, I Croci, V Carnielli, G Ancora, G Faldella, F Ferrari); the Netherlands (A van Heijst, C Koopman-Esseboom); Poland (J Gadzinowski, J Mazela, A Montgomery, T Pikuła); Portugal (H Barros, R Costa, C Rodrigues); Sweden (U Aden); UK (ES Draper, A Fenton, SJ Johnson); European Foundation for the Care of Newborn Infants (S Mader, N Thiele, JM Pfeil); Health Economics Team (S Petrou, SW Kim, L Andronis); Inserm Coordination (J Zeitlin, AM Aubert, C Bonnet, R El Rafei, AV Seppänen).

DATA AVAILABILITY STATEMENT

The dataset analysed during the current study are not publicly available due to health data protection but are available from the corresponding author on reasonable request.

ORCID

Adrien M. Aubert https://orcid.org/0000-0002-5738-1997
Raquel Costa https://orcid.org/0000-0003-1614-540X
Samantha Johnson https://orcid.org/0000-0001-8963-7881
Véronique Pierrat https://orcid.org/0000-0001-7435-5144
Marina Cuttini https://orcid.org/0000-0002-3284-6874
Mairi Männamaa https://orcid.org/0000-0001-5234-6474
Iemke Sarrechia https://orcid.org/0000-0002-4525-5811
Jo Lebeer https://orcid.org/0000-0001-5929-7783
Arno F. Van Heijst https://orcid.org/0000-0003-2276-0177
Mariane Sentenac https://orcid.org/0000-0002-2156-154X
Jennifer Zeitlin https://orcid.org/0000-0002-9568-2969

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SUPPORTING INFORMATION

The following additional material may be found online:

Figure S1. Flow chart of the sample selection from the EPICE-SHIPS cohort (children born at <28 weeks gestational age).

Figure S2. Distribution of PedsQL scores.

Figure S3. Adjusted associations of PedsQL quantiles (physical score) with motor category for children without moderate NDI.

Figure S4. Adjusted associations of PedsQL quantiles (psychosocial score) with motor category for children without moderate NDI.

Table S1. Characteristics of children followed and lost to follow-up at 5 years of age (without IPW).

Table S2. List of the variables used to estimate the probability of response and create the weights (IPW).

Table S3. Characteristics of children without CP included in the study with and without a MABC-2 score (without IPW)

Table S4. Characteristics of children included in the study and comparison with children without a PedsQL score (without IPW).
Table S5. Sample characteristics by motor category (unweighted results).
Table S6. Unadjusted associations of PedsQL scores with motor category for children without moderate NDI expressed as Cohen's δ effect size (standardized mean difference).
Table S7. Adjusted association of PedsQL scores with motor category.

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