Cerebral Palsy in Extremely Preterm Infants

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BACKGROUND AND OBJECTIVES: The risk of cerebral palsy (CP) is high in preterm infants and is often accompanied by additional neurodevelopmental comorbidities. The present study describes lifetime prevalence of CP in a population-based prospective cohort of children born extremely preterm, including the type and severity of CP and other comorbidities (ie, developmental delay and/or cognitive impairment, neurobehavioral morbidity, epilepsy, vision and hearing impairments), and overall severity of disability. In this study, we also evaluate whether age at assessment, overall severity of disability, and available sources of information influence outcome results.

METHODS: All Swedish children born before 27 weeks’ gestation from 2004 to 2007 were included (the Extremely Preterm Infants in Sweden Study). The combination of neonatal information, information from clinical examinations and neuropsychological assessments at 2.5 and 6.5 years of age, original medical chart reviews, and extended chart reviews was used.

RESULTS: The outcome was identified in 467 (94.5%) of eligible children alive at 1 year of age. Forty-nine (10.5%) children had a lifetime diagnosis of CP, and 37 (76%) were ambulatory. Fourteen (29%) had CP diagnosed after 2.5 years of age, 37 (76%) had at least 1 additional comorbidity, and 27 (55%) had severe disability. The probability for an incomplete evaluation was higher in children with CP compared with children without CP.

CONCLUSIONS: Children born extremely preterm with CP have various comorbidities and often overall severe disability. The importance of long-term follow-up and obtaining comprehensive outcome information from several sources in children with disabilities is shown.

WHAT’S KNOWN ON THIS SUBJECT: The risk of cerebral palsy (CP) is high in children born extremely preterm; prevalence rates vary between 7% and 20%. CP is often accompanied by other neurodevelopmental comorbidities.

WHAT THIS STUDY ADDS: Lifetime prevalence of CP in children born extremely preterm is 10.5%. Despite the majority being ambulatory, various comorbidities and often severe disability is shown. The importance of long-term follow-up and obtaining comprehensive outcome information in children with disabilities is demonstrated.
The risk of cerebral palsy (CP) is higher in infants born preterm than in infants born at term; this risk increases with decreasing gestational age (GA).\textsuperscript{1–5} The authors of outcome studies of infants born extremely preterm (EP) have reported prevalence rates ranging from 7% to 20%.\textsuperscript{6–10}

CP describes a group of disorders of movement and posture, causing activity limitations attributed to nonprogressive disturbances in the developing fetal or infant brain. The motor disorders of CP are often accompanied by disturbances of sensation, cognition, communication, perception, and behavior and/or by seizure disorders.\textsuperscript{1–14}

Few studies of children with CP born EP have included the combination of population-based prevalence with categorization of severity, type of CP, and comorbidities.\textsuperscript{15–18} Comorbidities are unequally distributed in children with CP and might be associated with specific neurologic subtypes and motor function status.\textsuperscript{16,19–21} A correlation between decreasing GA and more severe motor impairment and a higher percentage of comorbidities has been described in children with CP.\textsuperscript{19} In a systematic review, including 30 population registry studies on all GA groups of CP, 49% of children had intellectual disability (in 28%, it was severe), 31% could not walk (Gross Motor Function Classification System\textsuperscript{19} [GMFCS] level IV or V), 26% had behavioral disorders, 35% had epilepsy at some point (in 24%, it was active), 11% were functionally blind, and 4% had severe hearing impairment or were deaf.\textsuperscript{22}

The national Extremely Preterm Infants in Sweden Study (EXPRESS), comprising all infants born before 27 weeks in Sweden during a 3-year period, revealed neurodevelopmental outcomes at 2.5\textsuperscript{8} and 6.5 years of age.\textsuperscript{23} The point prevalence of CP was 7.0% and 9.5%, respectively. Comorbidities associated with CP were not described. The primary aim of this study is to describe the lifetime prevalence of CP up to the age of 6.5 years in the EXPRESS cohort of children, including the type and severity of CP and additional comorbidities, such as global developmental delay and/or cognitive impairment, neurobehavioral morbidity, epilepsy, and vision and hearing impairments, as well as the overall severity of disability. A secondary aim is to evaluate if the age at assessment, severity of disability, and sources of information influence outcome results in children with CP.

**METHODS**

In the EXPRESS study, all infants born in Sweden before 27 gestational weeks and between April 1, 2004, and March 31, 2007, were included. There were 1011 infants born EP, of whom 707 were live born and 494 survived to 1 year of age (Fig 1). Perinatal and neonatal data were collected prospectively, and the results have been published.\textsuperscript{24,25} Survivors were clinically assessed at a corrected age of 2.5 years (n = 415) and at 6.5 years (n = 382). At 2.5 years, the Bayley Scales of Infant and Toddler Development III (Bayley-III)\textsuperscript{26} was used to assess cognitive, language, and motor development (n = 398). At 6.5 years, intellectual ability was measured with the Wechsler Intelligence Scale for Children IV (WISC-IV)\textsuperscript{27} (n = 359). These results were compared with the mean and SD of a group of matched control children born at term (Supplemental Table 6). At 6.5 years, motor function was assessed with a clinical examination, the Movement Assessment Battery for Children II\textsuperscript{28} (n = 344), and a modified Touwen examination (n = 369).\textsuperscript{29} In children with CP, the GMFCS and the Bimanual Fine Motor Function (BFMF) classification\textsuperscript{30} were used to assess functional level at 6.5 years. In 40 children at 2.5 years and in 60 children at 6.5 years, who were not clinically examined, medical charts were reviewed by the pediatrician in charge (original chart review). Details and results from these investigations have previously been published.\textsuperscript{8,23}

In the current study, all available information was initially scrutinized for (1) an established CP diagnosis at the 2.5- or 6.5-year examinations; (2) signs of possible CP, such as spasticity (at least 2 of hyperreflexia, increased passive tone, and/or altered body position\textsuperscript{31}) and/or affected motor function (motor developmental scores at the 2.5-year Bayley-III examination <–2 SD of controls, Movement Assessment Battery for Children II centiles <5, noted at any of the examinations or in the original chart review); and (3) potential risk factors for CP defined as intraventricular hemorrhage grade ≥II and/or periventricular leukomalacia.\textsuperscript{12,32} In children who fulfilled any of these 3 criteria, except for those with a well-documented absent combination of spasticity and motor problems, additional information from medical and rehabilitation charts was collected up to the age of 6.5 years (extended chart review). The combined information from the EXPRESS study data and the extended chart reviews was thereafter independently evaluated by 2 experienced pediatric neurologists (M.H., B.S.). A lifetime prevalence of CP was defined as children with an established CP diagnosis and/or children with a combination of spasticity and motor problems diagnosed at any time up to the age of 6.5 years. A search for additional information on neurodevelopmental comorbidities such as global developmental delay and/or cognitive impairment, neurobehavioral morbidity, epilepsy, and vision\textsuperscript{33} and hearing
impairments was also included in this evaluation. The GMFCS and BFMF classifications were applied at the 6.5-year examination. If this was missing, the classification was accomplished retrospectively by using available information.

WISC-IV results were not available, the lowest score from the cognitive and language scale of the Bayley-III examination at 2.5 years was used. The child’s test results at 6.5 and 2.5 years, respectively, were thereafter categorized relative to the mean and SD interval of the term controls into 4 cognitive level categories ranging from normal to severe deficit (Supplemental Table 6). If this information was missing, the development level and/or cognitive function estimated from the extended chart review was used.

In children fulfilling the CP definition, the classification of overall severity of disability was assessed in accordance with the criteria shown in Table 1.

Possible associations between GA (linear continuous variable) and CP (yes/no) and between GMFCS subtypes (linear continuous variable) and developmental and/or cognitive deficit (< −2 SD) (yes/no) were assessed by using linear logistic regression analysis. Fisher’s exact test was used to evaluate binary outcomes for those born at 22 to 24 vs 25 to 26 weeks, GMFCS I to II versus III to V, and normal or mild development impairment versus moderate-severe developmental impairment, respectively. Spearman ρ was used to investigate the correlation between Bayley-III cognitive scale categories 1 to 4 at 2.5 years with WISC-IV cognitive categories 1 to 4 at 6.5 years; the corresponding 95% confidence interval (CI) was obtained by using bootstrapping (2000 bootstrap samples). Statistical analyses were performed by using SPSS version 23 (IBM SPSS Statistics, IBM Corporation, Armonk, NY) and Gauss version 10 (Aptech Systems Inc, Maple Valley, WA). P < .05 was regarded as statistically significant.

The Regional Ethics Review Board, Lund, Sweden, approved the study, and parents provided written consent.
RESULTS

In the EXPRESS study, 494 of 707 live-born (70%) children born EP were alive at 1 year of age. Neonatal information from 490 infants, including cranial ultrasound results in 486, was found. Neurodevelopmental outcome data at 2.5 and 6.5 years of age for 455 and 442 children, respectively, have previously been published.8,23 By combining these data, outcome information was collected for 680 of 707 (96.1%) live-born infants and for 467 of 494 children (94.5%) alive at 1 year of age (Fig 1). Seventy-five of the 467 children met the criteria for an extended chart review, and for 64 of these information was included; 2 had died, 5 had declined participation at 6.5 years, and 4 had no extended chart information available.

CP Prevalence, Type, and FunctionalOutcome

Forty-nine children were identified as having a lifetime diagnosis of CP up to the age of 6.5 years, which corresponds to 10.5% (49/467) of those alive at 1 year of age with a known outcome. The figures were similar across the GA groups, and no linear association between GA and CP was indicated (P = .63). None of the 5 children born at 22 weeks and alive at 1 year had CP. Seventy-six percent (37/49) were ambulant without aid (GMFCS levels I–II). The BF MF classification showed levels corresponding to those of GMFCS. Spastic CP was found in 45 (91%); 35 of them had a bilateral spastic type (Table 2). All children with unilateral CP were ambulant without aid, compared with 71% of the children with bilateral spastic CP. Two children had a probable postnatal explanation for their CP; 1 had paraparesis caused by a spinal injury after neonatal surgery and the other had sequelae after inflicted violence.

NeurodevelopmentalComorbidities and OverallSeverity of Disability

A complete WISC-IV assessment was available for 26 children with CP (and for these children, the Bayley-III results from 2.5-year examination were also available). For 17 children, only the results from the Bayley-III cognitive and languages scores at 2.5 years were available, and for still another 6 children, only data from extended chart reviews were used for approximate developmental- and/or cognitive-level categorization. Among the 26 children with lifetime CP who attended both assessments, there was a positive correlation between the Bayley-III development categories at 2.5 years and the corresponding cognitive categories based on the WISC-IV full-scale results (Spearman ρ: 0.67, 95% CI: 0.37–0.86; P < .001). Fifty-four percent had scores in a lower category on the WISC-IV assessment compared with the scores on Bayley-III.

Thirty of 49 (61%) children had a developmental and/or cognitive level < −2 SD, including all children with GMFCS levels IV and V (Table 3). A linear association between the GMFCS level and the occurrence of a developmental and/or cognitive level < −2 SD was indicated, but this was not statistically significant (odds ratio for 1 GMFCS unit increment: 1.65, 95% CI: 0.92–2.97; P = .10).

Of children born at 22 to 24 weeks, 87% had a developmental and/or cognitive level < −2 SD, compared with 50% among those born at 25 to 26 weeks (P = .03) (Table 2). Eight children with CP were diagnosed with autism spectrum disorder (ASD) and 2 had attention-deficit/hyperactivity disorder (ADHD). An additional 6 children had highly suspicious neurobehavioral symptoms (ie, inattention, hyperactivity, or autistic features). Six children were present on treatment for

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TABLE 1 Classification of the Overall Disability Severity in Children With CP

<table>
<thead>
<tr>
<th>GMFCS level</th>
<th>Developmental level†</th>
<th>Neurobehavioral diagnosis or symptoms</th>
<th>Visually impairment</th>
<th>Hearing impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal or mild impairment (−2 SD)</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>II or III</td>
<td>Moderate impairment (−2 SD to −3 SD)</td>
<td>ADHD, signs of inattention and/or hyperactivity, or autistic features</td>
<td>Visual acuity &lt;20/400 in the better eye</td>
<td>Hearing loss corrected with hearing aid</td>
</tr>
<tr>
<td>IV or V</td>
<td>Severe impairment (−3 SD)</td>
<td>ASD</td>
<td>Blindness, visual acuity &lt;20/400 in the better eye</td>
<td>Deafness, hearing loss not correctable with hearing aid</td>
</tr>
</tbody>
</table>

† All criteria have to be fulfilled.
‡ Any of the criteria have to be fulfilled.
§ Developmental level and/or cognitive function is evaluated in relation to the mean and SD of term controls (Supplemental Table 6), primarily by the total WISC-IV score at 6.5 y of age, thereafter by the lowest score of the Bayley-III cognitive and language scale at 2.5 y, and finally by the information from the extended chart review.
□ Active epilepsy: The child is presently on treatment of epilepsy.
* Epilepsy is not included as a criterion for severe disability.
† Visual acuity was examined by ophthalmologists and classified according to modified World Health Organization criteria.53

87% had a developmental and/or cognitive level < −2 SD, including all children with GMFCS levels IV and V (Table 3). A linear association between the GMFCS level and the occurrence of a developmental and/or cognitive level < −2 SD was indicated, but this was not statistically significant (odds ratio for 1 GMFCS unit increment: 1.65, 95% CI: 0.92–2.97; P = .10).

Of children born at 22 to 24 weeks, 87% had a developmental and/or cognitive level < −2 SD, compared with 50% among those born at 25 to 26 weeks (P = .03) (Table 2). Eight children with CP were diagnosed with autism spectrum disorder (ASD) and 2 had attention-deficit/hyperactivity disorder (ADHD). An additional 6 children had highly suspicious neurobehavioral symptoms (ie, inattention, hyperactivity, or autistic features). Six children were present on treatment for
### Table 2: The Description of EXPRESS Cohort of Children Born EP and Outcome in Children With Lifetime CP According to GA at Birth

<table>
<thead>
<tr>
<th>All Children</th>
<th>GA, wk</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXPRESS cohort</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total born</td>
<td>1011 (100)</td>
<td>142</td>
</tr>
<tr>
<td>Stillborn</td>
<td>304 (30)</td>
<td>91</td>
</tr>
<tr>
<td>Alive at 1 y</td>
<td>494 (49)</td>
<td>5</td>
</tr>
<tr>
<td>Outcome information available (percent of alive at 1 y)</td>
<td>467 (95)</td>
<td>5</td>
</tr>
<tr>
<td>Lifetime CP (percent of those with available outcome information)</td>
<td>49 (10.5)</td>
<td>0</td>
</tr>
<tr>
<td>EXPRESS children with lifetime CP</td>
<td>49 (100)</td>
<td>0</td>
</tr>
<tr>
<td>CP type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral spastic</td>
<td>10 (20)</td>
<td>1</td>
</tr>
<tr>
<td>Bilateral spastic</td>
<td>35 (71)</td>
<td>4</td>
</tr>
<tr>
<td>Dyskinetic</td>
<td>2 (4)</td>
<td>0</td>
</tr>
<tr>
<td>Ataxic</td>
<td>2 (4)</td>
<td>0</td>
</tr>
<tr>
<td>GMFCS level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I–II</td>
<td>37 (76)</td>
<td>4</td>
</tr>
<tr>
<td>III–V</td>
<td>12 (24)</td>
<td>1</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Developmental level (&lt;−2 SD)</td>
<td>30 (61)</td>
<td>5</td>
</tr>
<tr>
<td>ADHD, ASD, or highly suspicious neurobehavioral symptoms</td>
<td>16 (33)</td>
<td>0</td>
</tr>
<tr>
<td>Epilepsy (active and previous)</td>
<td>9 (18)</td>
<td>1</td>
</tr>
<tr>
<td>Visual impairment</td>
<td>11 (22)</td>
<td>4</td>
</tr>
<tr>
<td>Hearing impairment</td>
<td>5 (10)</td>
<td>0</td>
</tr>
<tr>
<td>CP without any other comorbidity</td>
<td>12 (24)</td>
<td>0</td>
</tr>
<tr>
<td>Overall disability</td>
<td>10 (20)</td>
<td>0</td>
</tr>
<tr>
<td>Mild</td>
<td>12 (24)</td>
<td>0</td>
</tr>
<tr>
<td>Moderate</td>
<td>27 (55)</td>
<td>5</td>
</tr>
</tbody>
</table>

Data are presented as n (%). —, not applicable.
* P < .05; *** P < .001.

### Table 3: Comorbidities According to Motor Function (GMFCS Level) in 49 Children With CP

<table>
<thead>
<tr>
<th>All Children With CP</th>
<th>GMFCS Level</th>
<th>P GMFCS I–II versus GMFCS III–V</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I II III IV V</td>
<td>I–II III IV V</td>
</tr>
<tr>
<td>n</td>
<td>49 (100) 31 6 4 7 1 37 12</td>
<td></td>
</tr>
<tr>
<td>Developmental level (&lt;−2 SD)</td>
<td>30 (61) 17 4 1 7 1 21 (57) 9 (75)</td>
<td>.44</td>
</tr>
<tr>
<td>ADHD, ASD, or highly suspicious neurobehavioral symptoms</td>
<td>16 (33) 12 2 0 2 0 14 (58) 2 (17)</td>
<td>.32</td>
</tr>
<tr>
<td>Diagnosed with ASD</td>
<td>8 5 2 1</td>
<td></td>
</tr>
<tr>
<td>Epilepsy (active and previous)</td>
<td>9 (18) 6 1 0 1 1 7 (19) 2 (17)</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Visual impairment</td>
<td>11 (22) 3 4 0 3 1 7 (19) 4 (33)</td>
<td>.51</td>
</tr>
<tr>
<td>Hearing impairment</td>
<td>5 (10) 4 0 0 0 1 4 (10) 1 (8)</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>CP without any other comorbidity</td>
<td>12 (24) 8 (26) 1 (17) 3 (75) 0 (0) 0 (0) 9 (24) 3 (25)</td>
<td>&gt;.99</td>
</tr>
</tbody>
</table>

Data are presented as n (%). * P < .05; *** P < .001.

a Developmental level and/or cognitive function evaluated in relation to the mean and SD of term controls (Supplemental Table 6) primarily by the total WISC-IV score at 6.5 y of age, thereafter by the lowest score of the Bayley-III cognitive and language scale at 2.5 y, and finally by the information from the extended chart review.

b Active epilepsy: the child is presently on treatment of epilepsy.

c Visual impairment: either blind (visual acuity <20/400) or visual acuity <20/63 but ≥20/400 in the better eye.

d Hearing impairment: either hearing loss not correctable with a hearing aid (deaf) or corrected with hearing aid.

* P < .05; *** P < .001.
epilepsy and 3 had been previously treated. Four children with CP were blind, and 7 had a moderate visual impairment. One child had a severe hearing impairment, and 4 children had moderate hearing problems. Seventy-six percent (37/49) of the children had at least 1 additional neurodevelopmental comorbidity. Comorbidities in relation to motor function and developmental level are shown in Tables 3 and 4. Nine of 11 children with visual impairment had a developmental and/or cognitive level < −2 SD (P = .04). No additional associations were found, in relation neither to motor function nor to developmental level and/or cognitive function.

Ten of 49 children (20%) with CP had an overall mild disability, and 27 of 49 (55%) had a severe disability (Table 5). All children with CP born at 22 to 24 weeks (n = 15) had moderate-severe disability, compared with 71% (24/34) of those born at 25 to 26 weeks (P = .02) (Table 2).

**Influence of Sources of Information, Age at Assessment, and Severity of Disability on Outcome Results**

The combined information from all sources in this cohort identified a CP diagnosis in 49 children up to the age of 6.5 years. At the 2.5-year assessment, 32 were identified.9 The extended chart review at 6.5 years revealed another 3 children who already had a CP diagnosis at 2.5 years, which was not registered then. At the 6.5-year assessment, 42 were identified,23 8 of them by the original chart review. In addition, 1 child with a CP diagnosis at 2.5 years who died before 6.5 years, 3 who had a CP diagnosis at the 2.5-year assessment and declined participation in the 6.5-year assessment, and 3 children with significant clinical findings of spasticity and motor developmental problems not previously considered to have CP (1 solely by the extended chart review information) were identified and included in the lifetime prevalence rate. The extended chart reviews also identified...

**TABLE 4 Comorbidities According to the Developmental Level and/or Cognitive Function in 49 Children With CP**

<table>
<thead>
<tr>
<th>Developmental Levela</th>
<th>All Normal Mild Impairment</th>
<th>Moderate Impairment</th>
<th>Severe Impairment</th>
<th>Normal-Mild</th>
<th>Moderate- Severe</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>49 (100)</td>
<td>8</td>
<td>11</td>
<td>8</td>
<td>22</td>
<td>19</td>
</tr>
<tr>
<td>ADHD, ASD, or highly suspicious neurobehavioral symptoms</td>
<td>16 (33)</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>9</td>
<td>5 (26)</td>
</tr>
<tr>
<td>Diagnosed with ASD</td>
<td>8</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Epilepsy (activeb and previous)</td>
<td>9 (18)</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>3 (16)</td>
</tr>
<tr>
<td>Visual impairmentc</td>
<td>11 (22)</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>9</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Hearing impairmentd</td>
<td>5 (10)</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>1 (5)</td>
</tr>
<tr>
<td>CP without any comorbidity except developmental delay</td>
<td>24 (49)</td>
<td>6 (75)</td>
<td>6 (54)</td>
<td>6 (75)</td>
<td>6 (27)</td>
<td>12 (63)</td>
</tr>
</tbody>
</table>

Data are presented as n (%).

a Developmental level and/or cognitive function evaluated in relation to the mean and SD of term controls (Supplemental Table 6), primarily by the total WISC-IV score at 6.5 y of age, thereafter by the lowest score of the Bayley-III cognitive and language scale at 2.5 y, and finally by the information from the extended chart review.

b Active epilepsy: The child is presently on treatment of epilepsy.

c Visual impairment: either blind (visual acuity <20/400) or visual acuity <20/63 but ≥20/400 in the better eye.

d Hearing impairment: either hearing loss not correctable with a hearing aid (deaf) or corrected with hearing aid.

* P < .05.

**TABLE 5 Sources of Information at the 6.5-Year Assessment of the EXPRESS Cohort According to the Occurrence of Lifetime CP (the Information From the Extended Chart Review is Included) and Disability**

<table>
<thead>
<tr>
<th>Lifetime CP</th>
<th>No CPa</th>
</tr>
</thead>
<tbody>
<tr>
<td>All With CP</td>
<td>Severity of Disabilityb</td>
</tr>
<tr>
<td>Mild</td>
<td>Moderate</td>
</tr>
<tr>
<td>n</td>
<td>49</td>
</tr>
<tr>
<td>Alive at 6.5 y of Age</td>
<td>48</td>
</tr>
<tr>
<td>Clinical examination and cognitive assessment with WISC-IV</td>
<td>26 (54)</td>
</tr>
<tr>
<td>Clinical examination without cognitive assessment with WISC-IV</td>
<td>10 (21)</td>
</tr>
<tr>
<td>Evaluation based on original medical chart reviews</td>
<td>9 (19)</td>
</tr>
<tr>
<td>No outcome data at the 6.5-y assessmentc</td>
<td>3 (6)</td>
</tr>
</tbody>
</table>

Data are presented as n (%). Percentages calculated for children alive at 6.5 y.

a Possible disability in children without CP was not classified in the current study.

b Criteria for the overall severity of disability classes are presented in Table 1.

c These results are based on data from the 2.5-y assessment.

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additional details concerning other comorbidities. Twenty-nine percent (14/49) were diagnosed with CP after 2.5 years, and all were ambulant without aid (GMFCS levels I or II).

At the 6.5-year assessment, the probability for not having a complete clinical and formal cognitive assessment was higher in children with CP (22/48; 46%) compared with children without CP (80/413; 19%) \((P = .0001)\). This was true for 62% (16/26) of children with CP and severe disability, compared with 27% (6/22) of those with CP and mild or moderate disability \((P = .02)\) (Table 5). Among 10 children with CP and ASD, blindness, and/or deafness, only 1 had a complete evaluation at 6.5 years.

Only 1 of the 11 children with GMFCS III-V was cognitively assessed by WISC-IV at 6.5 years. In the 16 surviving children with CP and a severe developmental deficit on the Bayley-III test \((-3 SD)\) at 2.5 years, only 5 children were assessed with WISC-IV at 6.5 years.

**DISCUSSION**

In this population-based cohort of children born before 27 weeks’ gestation and surviving beyond 1 year of age, the lifetime prevalence of CP up to the age of 6.5 years was 10.5%. The majority (76%) had ambulatory gross motor function. These results are favorable compared with those of other studies.\(^4,10,22,34\)

No difference in CP prevalence was seen with regard to GA in this population.\(^31\) Seventy-six percent had at least 1 neurodevelopmental comorbidity in addition to CP; global developmental delay and/or cognitive impairment was the most frequent (61%). Severe disability was seen in 55% and was more common in children born at 22 to 24 weeks than in children born at 25 to 26 weeks; none of the 15 children with CP born before 25 weeks were ambulant and without additional comorbidities. These results correspond to those of studies on CP in children in general populations\(^15,16\) and in outcome studies on children born EP.\(^9,35\) This underlines the importance of describing outcomes as comprehensively as possible.\(^22,36\)

The importance of not ruling out CP too early in life is revealed by the difference in point prevalence in the EXPRESS cohort. At 2.5 years,\(^9\) the reported CP prevalence was 32 in 456 (7.0%), and at 6.5 years,\(^21\) the prevalence was 42 in 441 (9.5%). All children diagnosed with CP after the 2.5-year assessment were ambulant. This is in accordance with the authors of studies on CP registers, who recommend inclusion only of children older than 4 years of age to minimize false diagnoses and to include those with milder symptomatology.\(^11,14\)

CP is a clinical descriptive term and its exact diagnostic criteria are under debate.\(^11\) The distinction from other motor impairments, such as developmental coordination disorder and global developmental delay, can be challenging.\(^14,37\) Because available extended information up to the age of 6.5 years was scrutinized by 2 experienced pediatric neurologists in accordance with predefined criteria for CP, a more standardized evaluation was achieved, and 3 previously undiagnosed children were identified. In addition, 3 children with CP who declined participation at 6.5 years and 1 who died before the 6.5-year assessment were included. The total number of children with CP in this cohort of children born EP increased from a point estimate of 42 at 6.5 years\(^23\) to a lifetime (up to the age of 6.5 years) number of 49. This includes 2 children with probable postnatal causes of CP. Although their etiologies were not directly related to extreme prematurity, infants born EP might be more prone to this type of injury. If only children who were clinically assessed at 6.5 years had been included, the number of children with CP would have been 34, because 8 were assessed solely by chart reviews. This study revealed that the probability of not having a full clinical and cognitive assessment is increased in children born EP with CP (46%), compared with those without CP (19%), with the highest probability in children with the most severe disability (62%). The importance of combining data sources to gain more accurate estimates of prevalence rates of CP has been shown and discussed,\(^4,16,18,38\) and with our results, we underline the difficulties and importance in obtaining sufficient outcome information in children with disabilities.\(^7,11,35\)

With our design combining several sources of information, including clinical assessments and chart reviews; a low drop-out frequency; and follow-up to 6.5 years, we created unique possibilities for assessing lifetime prevalence of CP, functional level (GMFCS), and additional comorbidities in children born EP. Because a majority of studies on CP prevalence are based on registers, the differences in completeness of data might explain some of the variation reported.\(^16,38\)

**Strengths of the Study**

This is a population-based study including all infants born EP in Sweden before 27 weeks’ gestation during a 3-year period. Neonatal data were prospectively collected, and all results from assessments up to the age of 6.5 years were available. In children with CP and suspected CP, additional detailed medical information was collected and scrutinized. With this combination of information, we were able to provide reliable outcome data regarding CP in 96% of live-born infants and information on additional comorbidities in those with CP.
Limitations of the Study

Complete information was not available from either the clinical data at the 2 assessments or the extended chart scrutiny. The fact that only 54% of the children with CP had a cognitive assessment with WISC-IV at 6.5 years and that 54% of those with both WISC-IV and Bayley-III assessments scored at a lower developmental and/or cognitive level on the WISC-IV increases the uncertainty regarding their intellectual ability at 6.5 years.21 The proportion of children with cognitive impairment might thus be higher than reported. Twenty-four percent of the children with CP did not have a clinical GMFCS and BFMF classification at 6.5 years of age, and this might have influenced the accuracy of the functional level. The numbers of children with ASD and ADHD is probably underestimated because the evaluations at 2.5 and 6.5 years were not primarily designed to detect neurobehavioral symptoms. Moreover, milder forms of neurobehavioral disorders are difficult to diagnose early in childhood, and children with severe disability are difficult to assess.5,37

CONCLUSIONS

In this population-based follow-up study of children born EP, 10.5% had a lifetime diagnosis of CP up to the age of 6.5 years. The majority (76%) of the children with CP were ambulatory, 76% had at least 1 additional comorbidity, and 55% had an overall severe disability. With the extended study design of lifetime CP, we identified 49 children with CP, compared with the point-estimate findings at 2.5 and 6.5 years of 32 and 42 children, respectively. This underlines the importance of long-term follow-up and of obtaining outcome information that is as comprehensive as possible from several sources.

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ABBREVIATIONS

ADHD: attention-deficit/hyperactivity disorder
ASD: autism spectrum disorder
Bayley-III: Bayley Scales of Infant and Toddler Development III
BFMF: Bimanual Fine Motor Function
CI: confidence interval
CP: cerebral palsy
EP: extremely preterm
EXPRESS: Extremely Preterm Infants in Sweden Study
GA: gestational age
GMFCS: Gross Motor Function Classification System
WISC-IV: Wechsler Intelligence Scale for Children IV

data; Ms Rehn participated in acquisition, analysis, and interpretation of the psychological data; Drs Drake, Farooqi, and Thorngren-Jerneck participated in the acquisition, analysis, and interpretation of data; Dr Ådén participated in acquisition, analysis, and interpretation of data and took part in the funding of the study; and all authors drafted, reviewed, revised, and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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