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ORIGINAL ARTICLE

Neurodevelopmental disorders and somatic diagnoses in a national cohort of children born before 24 weeks of gestation

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Abstract

Aim: This study investigated childhood diagnoses in children born extremely preterm before 24 weeks of gestation.

Methods: Diagnoses of neurodevelopmental disorders and selected somatic diagnoses were retrospectively retrieved from national Swedish registries for children born before 24 weeks from 2007 to 2018. Their individual medical files were also examined.

Results: We studied 383 children born at a median of 23.3 (range 21.9–23.9) weeks, with a median birthweight of 565 (range 340–874) grams. Three-quarters (75%) had neurodevelopmental disorders, including speech disorders (52%), intellectual disabilities (40%), attention deficit hyperactivity disorder (30%), autism spectrum disorders (24%), visual impairment (22%), cerebral palsy (17%), epilepsy (10%) and hearing impairment (5%). More boys than girls born at 23 weeks had intellectual disabilities (45% vs. 27%, $p < 0.01$) and visual impairment (25% vs. 14%, $p < 0.01$). Just over half of the cohort (55%) received habilitation care. The majority (88%) had somatic diagnoses, including asthma (63%) and failure to thrive/short stature (39%).

Abbreviations: ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorders; EPT, extremely preterm; EXPRESS, Extremely Preterm in Sweden Study; ICD-10, International Classification of Diseases, Tenth Revision; IQ, intelligence quotient; NDI, neurodevelopmental impairment; SD, standard deviation; SWEDROP, Swedish National Register for Retinopathy of Prematurity.

Conclusion: Most children born before 24 weeks had neurodevelopmental disorders and/or additional somatic diagnoses in childhood and were referred to habilitation services. Clinicians should be aware of the multiple health and developmental problems affecting these children. Resources are needed to identify their long-term support needs at an early stage.

KEYWORDS
extremely preterm birth, habilitation care, long-term support, neurodevelopmental disorders, somatic disorders

1 | INTRODUCTION

During the last two decades, the survival of extremely preterm (EPT) infants, born before 28 completed weeks of gestation, has increased. This has partly been due to the more proactive care of infants born before they have completed 24 weeks.[1] Initiating intensive care for the most immature infants is a matter of debate, due to their high mortality, the heavy burden of neonatal morbidities and later sequelae. In Sweden, the one-year survival rates for infants born alive 2014–2016 with gestational age 22 and 23 weeks were 30% and 61%, respectively.[1] Neurodevelopmental disorders following EPT birth have been investigated by a number of studies with large cohorts. These disorders have included intellectual disabilities, cerebral palsy and visual and hearing impairment.[2] In addition, speech disorders,[3] attention deficit hyperactivity disorders (ADHD),[4–6] autism spectrum disorders (ASD),[7,8] psychological problems,[9] epilepsy[10] and sleep disturbances[11] have been reported after preterm birth but have not been included in the large cohort studies on neurodevelopmental outcome after EPT birth. The long-term sequelae of EPT birth also include dysfunction of other organ systems that manifest as respiratory dysfunction,[12] poor growth[13] and kidney dysfunction.[14] Outcome data for children born before 24 weeks are scarce. This is mainly due to the limited number of survivors and the fact that studies have not covered the broad range of follow-up diagnoses that these infants receive.

The wide range of neurodevelopmental disorders that have been reported in EPT infants indicates the need for long-term support. Sweden has habilitation centres, where multi-professional teams of neurologists, physiotherapists and psychologists look after patients that have neurodevelopmental disorders with functional impairments. The number of children born EPT that are referred to habilitation centres may reflect the need for special support in this group. Habilitation centres offer treatment, training and medical aids for the children and support for the parents. Low vision clinics offer corresponding services to habilitate visually impaired children.

The primary aim of this large, retrospective, national study was to report clinical diagnoses registered after children born before 24 weeks were discharged from neonatal care. We selected and documented the diagnoses that were likely to have a significant impact on the children's lives. In addition, we wanted to investigate the need that this patient group would have for medical care and habilitation services during childhood.

Key Notes

- This large registry-based study showed that 75% of Swedish children born before 24 weeks of gestation had neurodevelopmental disorders, including intellectual disabilities (40%), autism (24%) and 55% required habilitation services.
- Somatic disorders were diagnosed in 88% of the cohort: 63% had asthma and 39% failed to thrive and/or had a short stature.
- Boys were more likely to have intellectual disabilities and visual impairment than girls if they were born at 23 weeks.

2 | PATIENTS AND METHODS

2.1 | Study population

The study comprised a Swedish national cohort of 399 children born before 24 weeks of gestation from January 2007 to December 2018. They had all survived until 40 weeks of postmenstrual age, and their details were registered in the Swedish National Register for Retinopathy of Prematurity (SWEDROP). In Sweden, all infants born before 30 weeks are included in an ROP screening schedule and the results are reported to SWEDROP, which has been estimated to cover 98% of cases.[15]

The children's diagnoses were retrieved from the National Board of Health and Welfare's National Patient Register and from the National Register of Patients with Cerebral Palsy. In addition, the individual medical charts of the children were examined to validate and complete the diagnoses received from the registries. The Swedish Ethics Review Authority approved the study (D. nr 2019-05265).

2.2 | Birth characteristics

Birth characteristics were recorded, including gestational age, which was determined by routine ultrasound assessments at 17–18 weeks,

birth weight and sex. The birth weight standard deviation (SD) was calculated.[16]

2.3 | Childhood diagnoses

Diagnoses related to prematurity were divided into neurodevelopmental disorders and other somatic diagnoses.

2.4 | Neurodevelopmental disorders

Cerebral palsy (any) was recorded as a neurodevelopmental disorder in children with a Gross Motor Function Classification System level ≥1 and an International Classification of Diseases, Tenth Revision (ICD-10) code of G80.0-G80.9. The diagnoses were double-checked with the National Board of Health and Welfare's Patient Register and the register for patients with cerebral palsy. A diagnosis of intellectual disability was based on developmental tests and estimated adaptive skills and classified using the intelligence quotient (IQ) scores and the ICD-10 codes in brackets. Mild (IQ 50–69), moderate/severe (IQ < 50) and any intellectual disability (F70.0-72.9) as well as epilepsy (G40.1-40.9) were recorded. Hearing impairment was defined as dependence on hearing aids or worse. Visual impairment was defined as being referred to a low vision clinic at any age or having a best-corrected visual acuity of <0.33 (20/60) in the best eye or with both eyes together at 3.5 years or older. In addition, we recorded the neurobehavioral disorders ASD (F84.0) and ADHD (F90.0-90.9) and impressive and/or expressive speech disorders (F80.1-80.9).

2.5 | Other somatic diagnoses

Other somatic diagnoses included diagnoses related to growth, nutrition and gastrointestinal functions, such as failure to thrive (R62.8), short stature due to endocrine disorder (E34.3), obstipation (K59.0), surgically treated inguinal hernia and gastrostomy (K40.9A-B, JDB 10 and Z931). The kidney diseases nephrocalcinosis and nephritis (N20.0, N10.9 and N12.9) were also recorded, as were the respiratory diagnoses of asthma and childhood bronchopulmonary dysplasia (J45.0-J45.9, P27.1), persistent pulmonary hypertension (I27.2) and vocal cord paresis (J38.0). Severe respiratory impairment was defined as a need for oxygen supplementation up to at least 2 years of age or more and/or tracheostomy and/or a home ventilator during childhood. Referrals to habilitation centres were also recorded.

2.6 | Statistical analysis

The statistical analysis was performed using IBM SPSS Statistics for Windows, Version 25.0. (IBM Corp).

Numbers and percentages are provided for categorical variables, with medians and ranges for continuous variables. We used Pearson's chi-square test and Fisher's exact test for dichotomous variables. Logistic regression was used to evaluate the relationships between age and diagnosis. The level of significance was set as a p value of <0.05.

3 | RESULTS

We found that 16 of the 399 infants identified through the SWEDROP died before they could be followed up, and this meant that 383 infants were included in the study. The children's ages at the time of the last visit ranged from 2 to 13 years.

3.1 | Birth characteristics

The 383 infants were born at a median of 23.3 (range 21.9–23.9) weeks of gestation. The median birth weight was 565 (range 340–874) grams, and the median birth weight SD was −0.40 (range minus 3.63–3.17). Two infants, a boy and a girl, were born at 21 weeks, 91 infants were born at 22 weeks (54% boys), and 290 infants were born at 23 weeks (51% boys). The two infants born at 21 weeks were added to the 22-week group.

3.2 | Neurodevelopmental disorders

Table 1 summarises the diagnoses of neurodevelopmental disorders after discharge. This showed that 75% of the children had any neurodevelopmental disorder. These comprised speech disorders (52%), intellectual disabilities (40%), ADHD (30%), ASD (24%), visual impairment (22%), cerebral palsy (17%), epilepsy (10%) and hearing impairment (5%). A larger proportion of children born at 21 and 22 weeks compared to those born at 23 weeks had intellectual disabilities (49% vs. 36%, $p < 0.05$), and a larger proportion were referred for habilitation care (64% vs. 52%, $p < 0.05$ (Figure 1A). More boys than girls were diagnosed with intellectual disabilities (46% vs. 36%, $p < 0.01$), and this difference was more pronounced in those born at 23 weeks (45% vs. 27%, $p < 0.01$) (Figure 1B). When we looked at the 23-week group, more boys than girls were visually impaired (25% vs. 14%, $p < 0.01$) and/or referred for habilitation (60% vs. 43%, $p < 0.01$) (Figure 1B).

3.3 | Somatic diagnoses

Table 2 summarises the somatic diagnoses after discharge. Failure to thrive/short stature was diagnosed in 39% of the children, and it was more frequent in those born at 21 and 22 weeks than those born at 23 weeks (49% vs. 36%, $p < 0.05$). Severe constipation was found in 29% of the total cohort, and 18% had a gastrostomy.

TABLE 1 Diagnoses of neurodevelopmental disorders in children born before 24 weeks of gestation in Sweden 2007–2018

	22 weeks GA ($n = 93$)[a]	23 weeks GA ($n = 290$)	Total ($n = 383$)	Missing value (n)
Cerebral palsy	18/87 (21%)	43/265 (16%)	61/352 (17%)	31/383 (8%)
Epilepsy	8/89 (9%)	30/282 (11%)	38/371 (10%)	12/383 (3%)
Intellectual disability	42/85 (49%)*	93/257 (36%)*	135/342 (40%)	41/383 (11%)
Autism spectrum disorder	22/80 (28%)	59/254 (23%)	81/334 (24%)	49/383 (13%)
ADHD after 6 years of age	8/32 (25%)	43/136 (32%)	51/168 (30%)	54/222 (24%)
Hearing impairment	5/90 (6%)	13/280 (5%)	18/370 (5%)	13/383 (3%)
Visual impairment	25/85 (29%)	48/248 (19%)	73/333 (22%)	50/383 (13%)
Speech disorders	46/82 (56%)	134/261 (51%)	180/343 (52%)	40/383 (10%)
Referred to habilitation services	56/87 (64%)*	138/266 (52%)*	194/353 (55%)	30/383 (8%)
Any neurodevelopmental disorder at follow-up	73/93 (78%)	214/288 (74%)	287/381 (75%)	2/383 (0.5%)

Note: Data expressed as *n* and (%). Any neurodevelopmental disorder diagnosis is defined as one or more of the above-defined diagnoses and disorders.

Abbreviations: ADHD, Attention deficit hyperactivity disorder; GA, gestational age.

[a]The two infants born at 21 weeks GA are included.

*$p < 0.05$ difference between children born at GA 22 and 23 weeks.

Asthma and childhood bronchopulmonary dysplasia, pulmonary hypertension and vocal cord paresis were diagnosed in 63%, 12%, 13%, respectively, and 12% had severe respiratory impairment. There were no significant differences between boys and girls (data not shown).

3.4 | Summary

The majority (96%) of the children had one or more of the diagnoses selected for this study. There were 15 children without any diagnoses, 10 girls and 5 boys, and they included one boy and one girl born at 22 weeks. The medical records clearly stated that 5 of the 15 children were healthy. The data were sporadic for 2 of the children, as they did not attend the planned follow-up visits after the neonatal period. There were medical file indications of disorders in the remaining 8 children, such as lung problems, allergies and neurobehavioral problems, but no ICD diagnoses had been recorded.

Figure 2 reports all the diagnoses stratified by the children's ages at the follow-up visits: 2–5, 6–9 and 10–13 years. There was a significant trend for neurodevelopmental disorders to become more frequent with age, with an odds risk of 1.090 per year and a 95% confidence interval of 1.015–1.169 ($p < 0.05$). However, there were no age-dependent differences for the other diagnoses.

We found that 193 (50%) of the children had further episodes of inpatient care after they were discharged from the neonatal intensive care unit and the median number was 2 (range 0–18). The median number of days in inpatient care was 8 (range 0–276 days), as shown in Figure S1A,B. No inpatient care was needed for the other 190 children. There were no significant differences in the number of episodes or length of care, when gestational age was taken into account.

4 | DISCUSSION

This was a retrospective national file review registry-based study of children born before 24 weeks of gestation, who were followed up until 2 to 13 years of age. We found that 75% had neurodevelopmental disorders at 2–13 years of age and more than half of the children (55%) required assistance from habilitation services. Boys were more likely to be affected by intellectual and visual impairment than girls. The vast majority of the cohort (96%) had a combination of neurodevelopmental disorders and other somatic diagnoses.

In general, Sweden has a proactive approach to neonatal care. The current Swedish guidelines, which were introduced in 2016, state that resuscitation should be considered for infants born at 22 weeks and is recommended for those born at 23 weeks.[17] Survival to discharge increased over time, and further unpublished data from our cohort show that this was particularly pronounced for infants born alive at 22 weeks. Their survival rates rose from 20% in 2013–2015 to 38% in 2016–2018.

The increased survival of EPT infants during the last decades has been accompanied by increasing data on neurodevelopmental impairment (NDI), in terms of cognition, motor function, hearing and vision. Most large cohort studies have not addressed neurobehavioral issues.[18–22] Previous studies have also been limited by the low number of infants born before 24 weeks. Most studies have focussed on children below 3 years of age, and it may have been difficult to diagnose neuropsychiatric problems at this early age. In addition, varying definitions of impairment have complicated comparisons. For example, many studies have used definitions of cognitive deficits that differ from the definitions in ICD-10. Many studies have used an IQ of 70–85 to indicate mild cognitive deficits, but ICD-10 refers to mild intellectual disability as an IQ of 50–69.

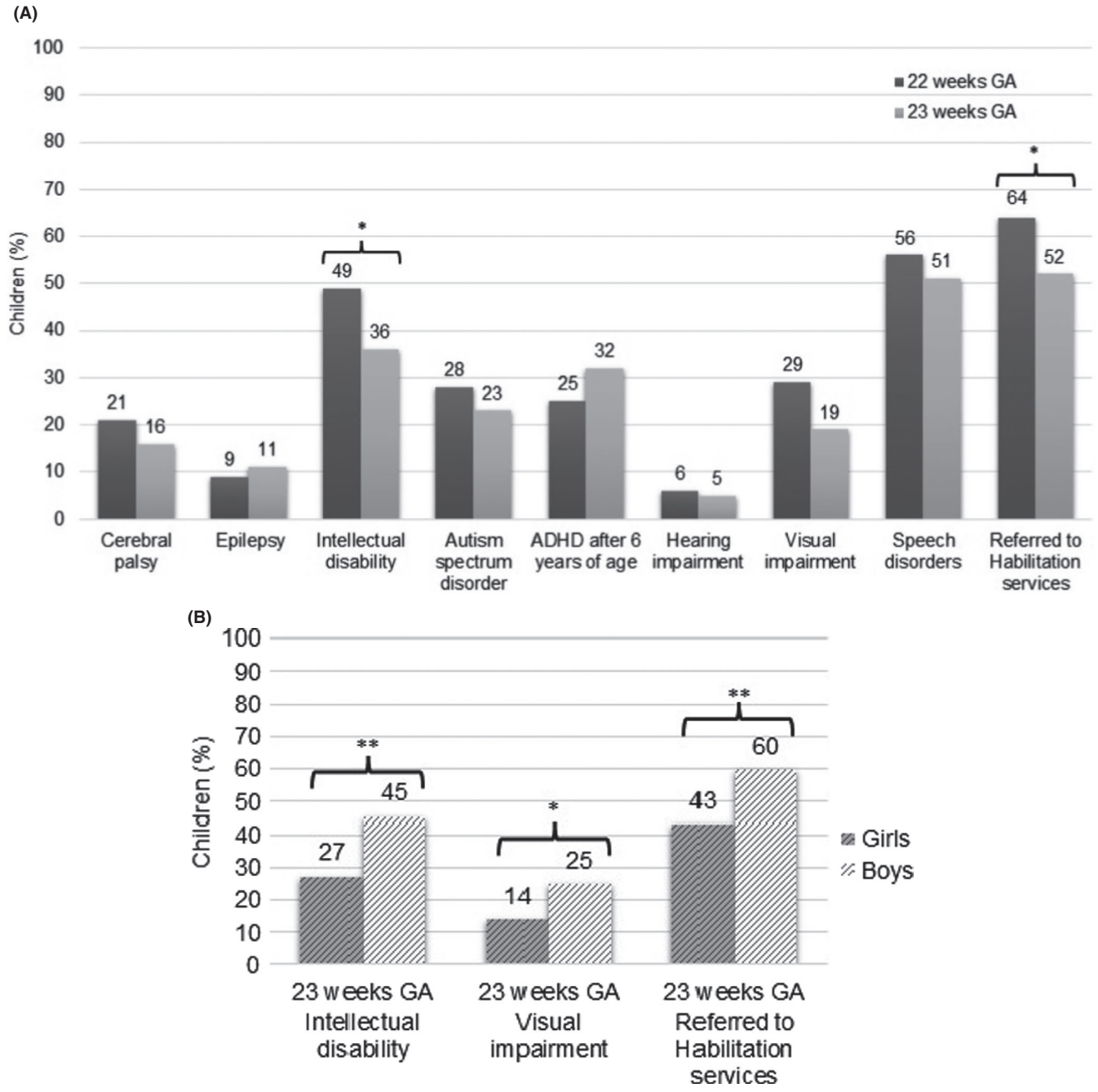

FIGURE 1 (A) Percentage of children diagnosed with neurodevelopmental disorders by gestational age. Significant differences are presented as $^{*}p < 0.05$. (B) Percentage of children diagnosed with neurodevelopmental disorders and significant associations with sex. Significant differences are presented as $^{*}p < 0.05$ and $^{**}p < 0.01$

This study found that diagnoses such as ASD and intellectual disability were more frequent in the older age groups. It is likely that the younger children may have cognitive or neuropsychiatric disorders that will be discovered later. In addition, studies have reported increases in neurodevelopmental dysfunction between 2.5 and 6.5 years of age.[20,23] Another study found that health-related quality of life declined from 11 to 19 years of age, according to reports from adolescents born extremely preterm and their parents.[24] The population-based EPICure study from the UK found that the prevalence of intellectual impairment increased significantly from 11 to 19 years of age and that there was impairment in multiple neuropsychological domains.[25] This may have an impact on social skills later in life.[26] In general, studies of childhood ASD and ADHD have found that these diagnoses had a profound impact on later life, with adults showing decreased independence and need for support.[27,28]

The national Extremely Preterm in Sweden Study (EXPRESS), of infants born from 2004 to 2007, stated that the number of children born at 22 weeks was too small to analyse outcomes at 6.5 years of age.[20] However, the mean (SD) Full-Scale Intelligence

TABLE 2 Other somatic diagnoses in children born before 24 weeks of gestation in Sweden 2007–2018

	22 weeks GA ($n = 93$)[a]	23 weeks GA ($n = 290$)	Total ($n = 383$)	Missing value (n)
Failure to thrive/short-stature	41/84 (49%)*	98/272 (36%)*	139/356 (39%)	27/383 (7%)
Obstipation	28/89 (32%)	78/278 (28%)	106/367 (29%)	16/383 (4%)
Gastrostomy	15/90 (17%)	53/282 (19%)	68/372 (18%)	11/383 (3%)
Kidney disorder	8/89 (9%)	18/281 (6%)	26/370 (7%)	13/383 (3%)
Inguinal hernia (boys)	15/48 (31%)	53/147 (36%)	68/195 (35%)	4/199 (2%)
Asthma	52/90 (58%)	182/281 (65%)	234/371 (63%)	12/383 (3%)
Pulmonary hypertension	12/89 (14%)	31/281 (11%)	43/370 (12%)	13/383 (3%)
Uni- or bilateral vocal cord paresis	13/90 (14%)	35/281 (12%)	48/371 (13%)	12/383 (3%)
Severe respiratory impairment	12/92 (13%)	33/288 (12%)	45/380 (12%)	3/383 (1%)
Any of the other somatic diagnoses at follow-up	81/93 (87%)	256/289 (89%)	337/382 (88%)	1/383 (0.3%)

Note: Data expressed as *n* and (%). Severe respiratory impairment is defined as requiring a home-ventilator and/or tracheostomy and/or having a need for oxygen supplementation up to at least two years of age or more. Any other somatic diagnosis is defined as one or more of the above-defined diagnoses and disorders.

Abbreviation: GA, gestational age.

[a]The two infants born at 21 weeks GA are included.

*$p < 0.05$ difference between children born at GA 22 and 23 weeks.

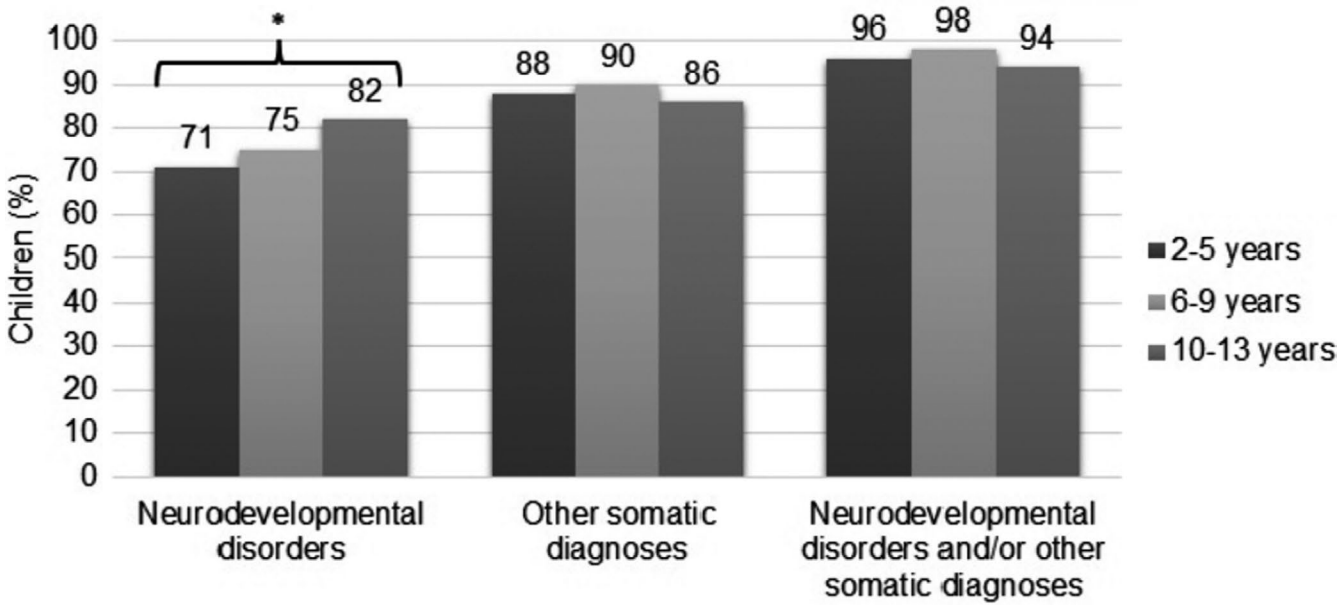

FIGURE 2 Percentage of children with neurodevelopmental disorders, somatic diagnoses and/or a combination of the 2, as defined in Tables 1 and 2, in different age groups. Significant differences over time are presented as *$p < 0.05$

Quotient scores on the Wechsler Intelligence Scale for Children, Fourth Edition, were 76 (5.4) for four children born at 22 weeks and 75 (13.8) for 37 children born at 23 weeks. When children born at 23 weeks were assessed at 6.5 years of age, 22% had severe functional impairment and 35% had moderate impairment. The other 44% had no or mild impairment.[20] Our study found that 17% of children born before 24 weeks had cerebral palsy. In comparison, the Extremely Preterm in Sweden Study reported cerebral palsy in 10% of infants born before 27 weeks and none infant born at term.[20] Our study found that the rates for hearing and visual impairments were 5% and 22%, respectively. These were compared to 2% and 5%, respectively, in children born before 27 weeks in the EXPRESS study and 0.5% and 0.6%, respectively, in term-born children.[20]

EPICure 2 found that it was uncommon for children born at 22 weeks to survive to 3 years of age and that two of three surviving children (67%) had moderate or severe NDI. Of those born at 23 weeks, 31/63 (49%) had moderate-to-severe NDI at that age.[19] These outcomes were similar to the findings of a US National Institute of Child Health and Human Development Neonatal Research Network study, which studied neurodevelopmental impairment at 18–22 months of age. This affected 18/27 (67%) of infants

born at 22 weeks and 155/303 (51%) born at 23 weeks. There was no change in outcomes among the infants born at 22 weeks between 2002–2003 and 2008–2011 and survival without NDI increased with time in those born at 23 weeks.[21]

It has been suggested that more active treatment and increased survival may lead to fewer children affected by morbidities and/or less severe diseases[29] but this has been questioned by others.[30] Changes in survival rates over the years, and differences between hospitals and countries, can be explained by a number of factors. These include rates of initiating active life-supporting care and the quality of neonatal care for very immature infants.[31–33] The trend analyses carried out by our study found that the rates for cerebral palsy did not alter over time (data not shown), which means that initiating active care at younger gestational ages did not result in a lower incidence of cerebral palsy in this Swedish cohort. Trend analyses for other diagnoses were complicated, because they were age-dependent. Analyses between sites were not performed in our study, as the wide age ranges at follow-up, and variations in local routines, could have influenced the results. Our findings agree with the EPICure 2 study, which reported no changes in neurodevelopmental impairment at 11 years of age in children born between 1995 and 2006.[34]

A Japanese multicentre study with comparatively high survival rates found that 12/23 (52%) children born at 22 weeks had NDIs and 30% had profound NDIs at 36–42 months of age. The respective figures for those born at 23 weeks were 65/114 (57%) and 45/114 (40%).[18] A centre in the United States, with an active perinatal approach to births at 22 and 23 weeks in 2006–2015, reported the prevalence of moderate-to-severe NDIs at 18–22 months. These affected 5/11 (45%) children born at 22 weeks and 11/34 (32%) born at 23 weeks.[22] A Swedish centre that adopted a uniform active approach to the most immature infants retrospectively reported that 50% of children born at 22 weeks and 62% born at 23 weeks did not have NDIs at 2.5 years.[35] These results differ from our findings and may be partly explained by the young age at follow-up examinations and the limited number of diagnoses reported in those studies. In comparison, a German study of children born from 1999 to 2003, who received proactive care, reported that 1/6 (17%) born at 22 weeks and 8/35 (23%) born at 23 weeks were considered unimpaired at 7–10 years of age.[36]

The risk for the neuropsychiatric disorders ASD and ADHD is dramatically increased after extremely preterm birth and has been reported to be inversely related to GA at birth.[4,7] In one study, 15% of children born at 23–24 weeks were diagnosed with ASD,[4] compared to 24% of the children in our study. Since autism can be underrecognised at an early age, it cannot be ruled out that additional children might be affected. The proportion of children affected by ASD in our study was significantly higher than in previous reports, and this warrants further investigation in a controlled setting. In addition, almost a third (30%) of the children over 6 years of age in our study were diagnosed with ADHD. Because this was a retrospective study, we did not have access to the children's ADHD phenotype. However, other studies have reported that EPT born children with ADHD are most likely to be affected by the inattentive subtype and associated intellectual disabilities.[5,6,37]

More than half of all children (52%) in our study had been diagnosed with speech disorders, including impaired articulation and language development, and 13% had vocal cord paresis, which may impact both their voice and their respiration.[38]

It is challenging to achieve optimal growth in those born EPT during the neonatal period and childhood. One study reported that children who were born EPT demonstrated catch-up growth in weight and length during childhood, but not head circumference.[13] Poor growth and gastrointestinal problems were common in our study, and 29% had severe constipation.

We found that 7% of the cohort were diagnosed with nephrocalcinosis or nephritis. Nephrocalcinosis is common after EPT birth, but usually resolves during childhood.[39] However, children born EPT are three times as likely to have chronic kidney disease as those born at term.[40]

The majority (63%) of the children in our study had been diagnosed with asthma and/or childhood bronchopulmonary dysplasia, but these diagnoses are often difficult to distinguish from each other and are not consistently applied in different regions. In comparison, another study reported asthma-like disease in 40% of children born EPT and in 15% of controls born at term.[41] Functional difficulties, such as asthma and cerebral palsy, have been linked to anxiety and depression, which are commonly found in children born EPT.[9]

Genetic factors, including sex, influence the development of EPT.[42] It is well known that boys are more vulnerable to oxidative stress-related complications of prematurity than girls.[43] We found no differences in the diagnosis rates between boys and girls, with one exception. Boys born at 23 weeks were more frequently diagnosed with an intellectual disability than girls born at the same age, and they also had higher risks of visual impairment and habilitation referrals.

Perinatal management is challenging when infants are born EPT.[44] There are debates about whether it is right to initiate intensive care for the most immature infants and whether clinicians should withdraw or withhold life-saving actions in certain cases, especially if infants have a severe brain injury.[45]

4.1 | Strengths and weaknesses

One strength of this study is that we were able to use SWEDROP, which has 98% national coverage, to identify infants born before 24 weeks.[15] In addition, this study comprised validated data from 2007-2020 including 2-13 years of follow-up for a large number of infants in a rare patient group. The diagnoses were initially retrieved from national registries, but we also examined the individual medical charts of all the children to validate and complete diagnoses. Furthermore, the Swedish personal identification numbers issued to all citizens enabled us to track the infants and children who were transferred to other hospitals or moved to other addresses.

This retrospective file review of national Sweden data did have some limitations. A major drawback was the large age range at the

latest follow-up visit, which ranged from 2 to 13 years, as some diagnoses only become apparent later in childhood.[23] A further weakness was the variations in regional policies regarding follow-up assessments, as this might have affected referrals and the age at diagnosis.

5 | CONCLUSION

Our study showed that 75% of infants born EPT, before 24 weeks of gestation, were affected by neurodevelopmental disorders during childhood and 88% had somatic disorders. The most common issues included asthma and childhood bronchopulmonary dysplasia, speech disorders, intellectual disabilities, failure to thrive, ADHD and ASD. Boys were more likely to have intellectual disabilities than girls. Further studies are needed to understand functional domains and social skills as these children grow up, so that relevant support can be provided. In addition, neonatal clinical practice needs to adopt a long-term perspective and clinicians treating children and adults should be aware of the complicated health problems of children born before 24 weeks.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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