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Title:
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Date:
2024

Citation:
Doyle, L. W. (2024). Neurodevelopmental outcomes in early childhood for infants born very preterm in countries outside the UK. Archives of Disease in Childhood: Fetal and Neonatal Edition, 109 (2), pp.117-119. https://doi.org/10.1136/archdischild-2023-326400.

Persistent Link:
https://hdl.handle.net/11343/345065

Neurodevelopmental outcomes in early childhood for infants born very preterm in countries outside the UK.

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Short title: Neurodevelopment in preterm infants

Word count: 1287

Conflicts of Interest: The author has no conflicts of interest relevant to this article to disclose.

Financial Disclosure: The author has no financial disclosures to declare.

Funding support: Supported by grants from the National Health and Medical research Council of Australia (Centre of Clinical Research Excellence #546519; Centre of Research Excellence #1060733 & #1153176), and the Victorian Government's Operational Infrastructure Support Program. The funding sources had no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

Knowledge of outcomes beyond the primary hospitalisation for infants born very preterm is vital to understanding the impact of interventions in the perinatal and newborn periods, particularly as more infants born <24 weeks' gestation are being offered active care. In the current issue, van Blankenstein et al(1) report the outcomes at 2 years of age of children born <30 weeks in England and Wales between 2008 and 2018. In their study 0.4% were blind, 1% had a substantial hearing impairment, and delays in language (13%) development (9%) and motor performance (8%) were frequent, based on responses from parent-completed questionnaires. The study raises the question of how their long-term outcome data compare with what is known for recent whole populations of births <30 weeks' gestation outside of England and Wales.

Many countries outside the UK collect data on developmental outcomes into early childhood (2-3 years of age) that might be compared with the study of van Blankenstein et al. The gestational age or birthweight selection criteria vary between countries, as do the years of reporting of the data, and the sample sizes of the cohorts (Table 1). The attempted coverage of all survivors of the defined gestational age or birthweight within the region is 100% or close to it for some cohorts, whereas other databases encompass only approximately 2/3 or fewer of births within the geographic region. Of the eligible survivors, the follow-up rates into early childhood vary from 47% to 93%. Most, but not all, have used corrected age when the children have been assessed. The follow-up assessments predominantly involve direct assessments of neurosensory outcomes and of psychological development by health professionals. Other studies have relied on questionnaires completed by parents or health professionals, rather than direct assessments.

Australia and New Zealand

The Australian and New Zealand Neonatal Network (ANZNN) collects data on developmental outcomes in early childhood for survivors <28 weeks' gestation or <1000 g birthweight from all 30 level-III neonatal intensive care units (NICUs) in Australia and New Zealand.(2) Of the 3728 children born from 2015 to 2018 who were assessed between 18-42 months' corrected age, 3091 (83%) had a formal developmental assessment, 99% with a version of the Bayley Scales of Infant and Toddler Development, and >90% of those were assessed with the Bayley-III. .

Belgium

Since 2014 all infants born in Belgium at <32 weeks' gestation or weighing <1500 g are eligible for systematic, long-term follow-up. Of 1942 eligible infants born in 2014-2016, 1783 (92%) survived to discharge, and 1089 (61% of survivors) were assessed by health professionals at 2 years' corrected age.(3)

Canada

A majority of NICUs in Canada participate in the Canadian Neonatal Follow-Up Network (CNFUN). The CNFUN most recently reported on outcomes for infants born <29 weeks' gestation from April 1, 2009 to December 31, 2019 and cared for in centres participating in the Canadian Neonatal Network.(4) Of 14487 known long-term survivors, 8394 (58%) were assessed in early childhood. Overall, follow-up rates were higher in earlier years than in more recent years. As in the UK and ANZNN studies, follow-up rates were higher for less mature infants than for more mature infants.

France

EPIPAGE 2, a collaboration of French regions covering 98% of the population, aimed to assess outcomes to 2 years' corrected age of 4199 survivors born in 2011 at 22-34 completed weeks' gestation, parents of 244 survivors having refused follow-up.(5) Data on cerebral palsy, blindness and deafness were obtained from referring clinicians for 81% of the cohort, and parents completed the Ages and Stage Questionnaire, which ultimately provided data on developmental outcomes for 59% of the cohort.

Japan

The Neonatal Research Network in Japan (NRNJ) registers births either <32 weeks' gestation or <1500 g birthweight admitted to participating NICUs.(6, 7) As of January 2021, there were 131 participating NICUs contributing data to the NRNJ, covering approximately 65% of births in Japan. Data on long-term outcomes have been reported for births <28 weeks' gestation between 2003 and 2011.(8)

Spain

The Spanish Neonatal Database SEN1500 started in 2002, and now registers 68% of all infants born <1501 g in Spain.(9) In a report of eligible births born 2002-2007, 50% were assessed by health professionals at 2 years of age.(10)

Sweden

The Swedish Neonatal Quality Register collects data for 98-99% of infants born 24-34 weeks' gestation in Sweden. Although it does not seem to report data on long-term outcomes in its Annual Reports, outcomes to 2.5 years of age for 456 survivors born <27 weeks' gestation in 2004-2007 Sweden have been reported.(11) Children were mostly assessed by trained health professionals, but in 9% data were obtained from chart review.

Switzerland

The Swiss Neonatal Network and Follow-up Group (SwissNeoNet) is a collaboration of NICUs in Switzerland; in a recent report it had a population coverage of 97% of livebirths <28 weeks during 2007-2013.(12) In a study of 1256 survivors born <28 weeks' gestation in Switzerland during 2006-2013, 1062 (85%) were assessed at 2 years of age.(13)

The Netherlands

The outcomes for 554 of 651 (85%) survivors born 24-26 weeks' gestation in The Netherlands who were 2 years' corrected age in 2018-2020, and who would have been born mainly in 2016-2018, has been recently reported.(14) Children were assessed by health professionals attached to the NICU that cared for the child.

Summary of neurodevelopmental outcomes from non-UK cohorts

Despite the considerable variation in the gestational age or birthweight selection criteria, the rates of blindness and deafness are low across all non-UK cohorts, and are similar to van Blankenstein et al (Table 1). Rates of cognitive, language or motor delay in the non-UK studies are similar to van Blankenstein et al, but only if lower cut-off scores (<70, or <-2 SD) are used, rather than those that include milder delay (<85; <-1 SD). Cerebral palsy rates, which were not reported by van Blankenstein et al, are typically <10% in the studies from outside the UK.

Challenges for the future.

It will be important to know how problems identified by parental questionnaires or by direct assessments by health professionals in early childhood relate to intellectual, academic, motor, or behavioural problems at school-age, all important consequences of birth before 30 weeks' gestation. The study of van Blankenstein et al has the opportunity to determine if responses to parental questionnaires are better than direct assessments by health professionals in early childhood at predicting later outcomes at school-age because they have many children assessed with both methods.

Obtaining funding for ongoing surveillance programs for high-risk infants is a challenge. Having health professionals directly assess children is expensive and may not be considered to comprise routine clinical care, and hence be unfunded. Even if health professionals are avoided and data are obtained solely from parents, there are still costs involved in collecting, cleaning, analysing, and interpreting the data obtained.

With increasing instances of hacking of data involving corporations and government agencies, there are large amounts of personal data being exposed. This, in turn, leads to increasing reluctance of families to agree to their data being included in health registries, or to participate in any form of research or surveillance that involves collection of data. Those who maintain registries need to increase their vigilance to protect the invaluable data they collect and store.

Opportunities

Large, population-based registries facilitate determination of the causes and effects of the outcomes of preterm birth, with the ultimate goal being to improve long-term outcomes for our most vulnerable infants. A step in the right direction has been the creation of the International Network for Evaluating Outcomes in Neonates (iNeo) a collaboration of population-based national neonatal networks, including the UK and many of the countries mentioned in this review.(15) Data accumulate more quickly when multiple data sources are pooled, allowing speedier answers to the questions being posed.

Table 1. Demographic and developmental outcome data in early childhood for geographical cohort studies outside the UK compared with the study from England and Wales.

	Birth years	Inclusion Criteria	Survivors - n	Coverage of survivors	Corrected age assessed - years	Follow-up rate	Assessment methods	CP	Blind	Deaf	Delay		
Country											Cognitive	Language	Motor
England and Wales(1)	2008-18	<30 weeks	41162	100%	2	58%	Parental questionnaire (PARCA-R)		0.4%	1%	9%	13%	8%
Outside the UK													
Australia and New Zealand(2)	2015-18	<28 weeks or <1000 g	4782	100%	2 to 3	79%	Direct assessment	6.9%	0.6%	1.1%	19% (<85) 7% (<70)	32% (<85) 13% (<70)	22% (<85) 7% (<70)
Belgium(3)	2014-16	<31 weeks or <1500 g	1782	100%	2	61%	Direct assessment	4.3%	0%	0.2%	19% (<85) 4% (<70)	42% (<85) 10% (<70)	19% (<85) 6% (<70)
Canada(4)	2009-19	<29 weeks	14487	90%	1½ to 2	58%	Direct assessment	6.1%	1%	1.8%	16% (<85) 6% (<70)	38% (<85) 14% (<70)	22% (<85) 8% (<70)
France(5)	2011	24-34 weeks	4443	98%	2	81%	Physician questionnaire	4.6%	0.4%	0.5%			
						83%	Parental questionnaire (ASQ)				12%^{f}	25%^{g}	11%^{h}

Japan(8)	2003-11	<28 weeks	10464	65%	3[a]	47%	Direct assessment	9.2%	1.4%	1.3%	30% (<70)[b]		
Spain(10)	2002-07	<1501 g	9934	68%	2	50%	Direct assessment	4.6%	0.5%[c]	0.2%	12%[d]		7%
Sweden(11)	2004-07	<27 weeks	491	100%	2½	93%	Direct assessment	7.0%	0.9%	0.9%	35% (<-1 SD[i]) 11% (<-2 SD[i])	39% (<-1 SD[i]) 16% (<-2 SD[i])	43% (<-1 SD[i]) 15% (<-2 SD[i])
Switzerland(13)	2006-13	<28 weeks	1256	86%	2	85%	Direct assessment	6.5%	0.2%	1.0%			
The Netherlands(14)	2016-18[e]	24-26 weeks	651	100%	2	85%	Direct assessment	4.3%	3.0%	0.9%	19% (<85) 3% (<70)		25% (<85) 4% (<70)

CP=cerebral palsy; PARCA-R=Parent Report of Children's Abilities-Revised; ASQ=Ages and Stages Questionnaire

[a]not corrected for prematurity; [b]on Kyoto Scale; [c]one or both eyes; [d]developmental testing not uniform; some physician judgement included; [e]Inclusion criteria refers to children who were 2-years corrected age in 2018-2020 – two years have been taken off to assume the years of birth; [f]Problem Solving on ASQ; [g]Communication on ASQ; [h]derived from 10.6% Gross Motor and 11.2% Fine Motor on ASQ; [i]relative to controls.

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